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CLINICAL ARTICLE

Obstetrics

Factors associated with COVID-19 vaccination likelihood during pregnancy

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Abstract

Objective: To identify maternal background, medical and gynecological characteristics associated with COVID-19 vaccination likelihood, in the context where COVID-19 vaccination rates among pregnant women are significantly lower than the general population.

Methods: In a retrospective cohort study, including all women who delivered between January and September 2021, background and medical history, including current and previous pregnancies diagnoses, were compared between vaccinated and unvaccinated women. Multivariable logistic models were used to identify factors associated with vaccination for the entire population, and for the two distinctive populations included in the study (Bedouin Arabs and Jewish women).

Results: The study population included 7017 women, of whom 1925 (27.4%) were vaccinated during pregnancy. According to the multivariable analysis, unvaccinated mothers were younger with lower socioeconomic score. They were more likely to be Bedouin Arabs, have a poor obstetrical history or recurrent pregnancy loss, and insufficient prenatal care. Additional risk factors were inconsistent between the two ethnicities included in the study.

Conclusions: Ethnicity, insufficient prenatal care, and having a poor obstetric history were consistently associated with lower vaccination among pregnant women. These factors should be considered in future plans aimed at increasing vaccination among pregnant women.

KEYWORDS
COVID-19, COVID-19 vaccination, prenatal care, prenatal vaccination, retrospective cohort, vaccination hesitancy

1 | INTRODUCTION

The COVID-19 mRNA vaccine has been approved and used since December 2020, a year after the pandemic outbreak. Since its approval, ongoing research has shown the vaccine to be safe and highly effective in prevention of severe disease and death.[1] Even with recently approved medications to treat COVID-19, vaccination is the only solution to end the pandemic. It is important that all people, especially populations at risk for infection and its complications, get vaccinated.[2] Although pregnancy is not a risk factor for COVID-19 infection, pregnant women are considered a vulnerable population and are at risk of severe COVID-19 and complications.[3] The immunological

and physiological changes that occur over the course of pregnancy are necessary to support a healthy pregnancy, but may also increase maternal vulnerability to infectious diseases and the risk of severe complications.[4] Indeed, there is evidence that pregnancy is associated with increased severity of influenza, hepatitis E, herpes simplex virus (HSV) infection, malaria, measles, smallpox, and varicella.[5] Some maternal infections, including rubella and varicella, can be transmitted prenatally to the fetus and are associated with complex congenital anomalies.[6]

Maternal COVID-19 infection may affect the mother, the pregnancy, and the fetus. The infected mother may be at greater risk of severe COVID-19 complications compared with non-pregnant women. Infected mothers are more likely than non-pregnant women to require hospitalization, be admitted to the intensive care unit (ICU), and receive invasive ventilation and extracorporeal membrane oxygenation (ECMO),[3,7,8] and the risk of death is up to 70% higher.[9] Pregnancies of infected mothers are at risk of pregnancy complications, including preterm birth and low birthweight,[8,10] as well as newborn complications, including longer hospital stay, neonatal intensive care unit admission, and neonatal death before discharge from hospital.[10]

Several studies have found the COVID-19 vaccine to be safe for pregnant women and to be as effective in disease prevention among pregnant women.[11] The antibodies mothers develop in response to these vaccines protect them and, in addition, the mRNA COVID-19 vaccine-induced maternal antibodies are transferred across the placenta to the fetus and could provide passive immune protection to the newborns during their early life.[12]

Several long-established vaccines are considered safe during pregnancy, including those for tetanus, diphtheria, acellular pertussis (Tdap), and influenza.[13] Still, there is hesitancy surrounding vaccination during pregnancy[12,14] in general, and even more so regarding the newly introduced COVID-19 vaccine.

The aim of the present study was to identify maternal background, and health and gynecological characteristics associated with COVID-19 vaccination during pregnancy.

2 | MATERIALS AND METHODS

A retrospective cohort study was conducted, including all women who delivered between January and September 2021 at the Soroka University Medical Center (SUMC) and who were insured by Clalit, the largest Israeli HMO, covering >60% of the Israeli population. A comparison between women who were covered by Clalit HMO and those who were not covered is presented in the Appendix S1. Based on this comparison, women covered by Clalit represent 75% of the population, and most clinical characteristics were similar between the two groups. The study protocol has been approved by the SUMC IRB committee (number SOR 0085–21), and informed consent was waived.

The SUMC, which serves a population of more than one million citizens, is located in southern Israel and includes the largest birth center in the country, with more than 17 000 births in 2020. Excluded from the study were women previously diagnosed with COVID-19 (to avoid interest in receiving vaccination based on severity of the disease) or with unknown vaccination status or background and pregnancy follow-up information. In Israel the COVID-19 vaccine is provided to all citizens, free of charge, by all HMOs, and so are hospitalizations and pregnancy follow-up. The vaccines were given in all HMO clinics, community centers, medical centers and many facilities throughout Israel, so that it was accessible to all citizens.

Maternal background characteristics, including health, and current and historic pregnancies, were compared between women who were vaccinated (at least once) during pregnancy and those who were not.

Pregnancy follow-up and vaccination information was available from the "Clalit" computerized database.

2.1 | Variables definitions

Socioeconomic position was a 1–10 score assigned by the Israeli Central Bureau of Statistics, based on residency. A higher score indicates a better socioeconomic position. Each woman was scored based, among others, on the following characteristics of the population in the region: median age of the residents; percent of families with four or more children; mean years of education among adults; rate of residents with academic education; rate of employed residents; mean income; and mean number of vehicle owned by adults.

In our population, ethnicity is a strong indicator of socioeconomic level. The study population includes two distinct ethnic groups: Jewish and Bedouin Arab women. These populations differ in religion, education level, mean household income, occupation, housing, familial and traditional beliefs, access to and utilization of healthcare services and, in most cases, residency. While all Jewish and Bedouin Arab women are Israeli citizens and therefore covered by a universal national health insurance, and entitled to free perinatal health services, utilization of prenatal care services is lower among Bedouin Arab than among Jewish women for a variety of social, cultural, and access issues.[15]

Socioeconomic position and ethnicity are not based on self-report; instead these variables are drawn at admission from the Ministry of Interior database which is linked to the admission-discharge transfer (ADT) computerized database in all hospitals in Israel.

Obesity was defined as maternal body mass index (calculated as weight in kilograms divided by the square of height in meters) > 30. Fertility treatments included ovulation induction or in vitro fertilization. Insufficient prenatal care was defined as four or fewer visits throughout pregnancy or initiation of prenatal follow-up during the third trimester. Recurrent pregnancy loss was defined as the loss of two or more pregnancies before 24 weeks of gestation. Psychiatric morbidities included anxiety, depression, schizophrenia, or bipolar diagnoses, and poor obstetric history was defined as having a history of late fetal death (500–999 g; 20–27 weeks) or stillbirth.

2.2 | Statistical analysis

The comparison between vaccinated and unvaccinated women was performed using *t*-tests and χ^2 tests. The same comparisons were

performed separately among the two ethnic groups included in the study: Jewish and Bedouin Arab (Muslim) women. The *r* (Spearman) correlation was used to evaluate collinearity between the independent variables, prior to their inclusion in the multivariable analysis. An $r_{(Spearman)}$ of 0.55 ($P < 0.001$) was found between parity and maternal age, and an $r_{(spearman)}$ of 0.79 ($P < 0.001$) was found between ethnic group and socioeconomic grade; therefore only maternal age and ethnic group were included in the multivariable analyses. Variables that were associated with vaccination ($P < 0.05$) were included in the multivariable logistic models, which addressed the association between maternal and pregnancy characteristics and vaccination likelihood. The multivariable analysis was also performed for the entire study population, as well as separately by ethnic group.

3 | RESULTS

The study population included 7017 women, of whom 1925 (27.4%) were vaccinated during pregnancy. Characteristics of the study groups are presented in Table 1. The strongest risk factor for no vaccination was being a Bedouin Arab (versus Jewish). Mothers who were unvaccinated were younger, with lower socioeconomic score, and were less likely to adhere to the recommended prenatal care. They were also more likely to have a poor obstetric history. Vaccinated women were more likely to smoke, be obese, have comorbidities, and to conceive following infertility treatments.

A comparison between vaccinated and unvaccinated mothers was performed among Jewish and Bedouin Arab women separately. This analysis identified factors associated with vaccination among Bedouin Arabs only, including obesity, smoking, multiple gestation, and diabetes mellitus diagnosis, and factors that were common in both ethnic groups, including insufficient prenatal care, infertility treatments, poor obstetric history, age, and socioeconomic score.

In a multivariable model (Table 2) the following variables were significantly associated with higher likelihood for vaccination: maternal age (adjusted odds ratio [OR] 1.02, 95% confidence interval [CI] 1.00–1.04); infertility treatments (adjusted OR 1.47, 95% CI 1.18–1.83), and the following variables were associated with lower likelihood for vaccination: Bedouin Arab versus Jewish ethnicity (adjusted OR 0.20, 95% CI 0.18–0.23), insufficient prenatal care (adjusted OR 0.36, 95% CI 0.30–0.42), and a poor obstetric history (adjusted OR 0.65, 95% CI 0.49–0.87).

Separate multivariable models were created for each of the two ethnic groups. Some factors were associated with vaccination in both ethnicities, including insufficient prenatal care (associated with lower vaccination rates). The findings regarding poor obstetric history, although showing a similar effect on vaccination likelihood (adjusted OR 0.72, 95% CI 0.45–1.13, and adjusted OR 0.71, 95% CI 0.45–1.10 for Jewish and Bedouin Arab women, respectively) were no longer statistically significant. The power to test these associations were 50% and 46.8% for Jewish and Bedouin Arab women, respectively. Obesity was associated with vaccination only among Bedouin Arabs (positive association), and infertility treatments were associated with vaccination only among Jewish women (positive association). Among Bedouin Arabs, vaccination was associated with lower socioeconomic score, and among Jewish women it was associated with higher socioeconomic score.

4 | DISCUSSION

In this retrospective cohort study, which included detailed information on background characteristics, health, and gynecological history, lower COVID-19 vaccination rates during pregnancy were found among Bedouin Arab women, as well as women with insufficient prenatal care, poor obstetric history, and younger maternal age. Additional risk factors were inconsistent between the two ethnic groups in the study, including socioeconomic score and obesity.

Among Jewish women, the differences between vaccinated and unvaccinated women were smaller, and fewer characteristics, including social and health variables, were associated with vaccination and included in the multivariable analysis.

While it was expected that vaccination rates would be higher with higher socioeconomic score, as found in the general and Jewish population, among Bedouin Arabs the association was reversed. It is possible that Bedouin Arab women with the lowest socioeconomic score, who reside in distant settlements, isolated from rumors, trends and the internet, were not aware of a trend against vaccination and were more likely to adhere to the recommendations.

Although the findings regarding the association between age, ethnicity, and comorbidities were expected based on studies of non-pregnant population,[16] additional risk factors have been identified in this study, including poor obstetric history and insufficient prenatal care.

Unlike live attenuated vaccines, inactivated vaccines are considered to be safe during pregnancy, and are recommended based on weighing the risks and benefits of maternal-fetal exposure to the vaccine versus the exposure to infection and risks of morbidity and mortality.[17] There is no evidence on risk to the fetus from vaccinating pregnant women with inactivated vaccine. None of the currently approved vaccines contain a live SARS-CoV-2 virus and hence it is extremely improbable that a vaccine pathogen could replicate, cross the placenta and infect the fetus.[18]

In the current study, mothers undergoing infertility treatments were more likely to be vaccinated. This could be due to requirements of clinics that patients be vaccinated prior to treatment initiation, or due to intense follow-up and appointments at the fertility clinic, and therefore ongoing patient education regarding the importance of vaccination. This could also explain the lower vaccination rates among women with insufficient prenatal care.[19] Women with a poor obstetric history of late fetal death (500–999 g; 20–27 weeks) or stillbirth were also less likely to get vaccinated. This may be due to greater maternal fear and anxiety regarding the pregnancy as compared with women without such a history, accompanied by lack of knowledge about the vaccine

TABLE 1 Characteristics of the study groups, and comparison between vaccinated and unvaccinated women, for the entire population and separately by ethnic group.

	Total population			Jewish ($n = 2081$)			Bedouin Arab, $n = 4837$		
	Vaccinated ($n = 1925$ [27.4%])	Not vaccinated ($n = 5092$ [72.6%])		Vaccinated ($n = 1212$ [55.6%])	Not vaccinated ($n = 968$ [44.4%])		Vaccinated ($n = 713$ [14.7%])	Not vaccinated ($n = 4124$ [85.3%])	
	n (%)	*n* (%)	*P*-value	*n* (%)	*n* (%)	*P*-value	*n* (%)	*n* (%)	*P*-value
Maternal characteristics									
Maternal age (year) (mean ± SD)	30.3 ± 5.4	27.8 ± 5.8	<0.001	31.8 ± 4.7	30.9 ± 5.0	<0.001	27.8 ± 5.5	27.1 ± 5.7	0.002
<20	59 (3.1)	466 (9.2)		6 (0.5)	13 (1.3)		53 (7.4)	453 (11.0)	0.011
20–35	1402 (72.8)	3897 (76.5)		840 (69.3)	721 (74.5)		562 (78.8)	3176 (77.0)	
≥35	464 (24.1)	729 (14.3)		366 (30.2)	234 (24.2)		98 (13.7)	495 (12.0)	
Socioeconomic score (mean ± SD)	4.3 ± 2.4	2.6 ± 2.0	<0.001	5.5 ± 1.6	5.1 ± 1.5	<0.001	1.5 ± 1.3	1.8 ± 1.4	<0.001
1	608 (31.6)	3166 (62.2)	<0.001	2 (0.2)	8 (0.8)	0.072	606 (85.0)	3158 (76.6)	<0.001
2	89 (4.6)	840 (16.5)		4 (0.3)	4 (0.4)		85 (11.9)	836 (20.3)	
≥3	1228 (63.8)	1086 (21.3)		1206 (99.5)	956 (98.8)		22 (3.1)	130 (3.2)	
	n (%)	*n* (%)	OR; 95% CI	*n* (%)	*n* (%)	OR; 95% CI	*n* (%)	*n* (%)	OR; 95% CI
Ethnicity			7.24; 6.45–8.13						
Jewish	1212 (55.6)	968 (44.4)							
Bedouin Arab	713 (14.7)	4124 (85.3)							
Obese (BMI > 30)	360 (18.7)	795 (15.6)	1.24; 1.08–1.43	209 (17.2)	156 (16.1)	1.08; 0.86–1.36	151 (21.2)	639 (15.5)	1.46; 1.20–1.79
Smoker, current or past	400 (20.8)	384 (7.5)	3.22; 2.76–3.74	371 (30.6)	300 (31.0)	0.98; 0.82–1.18	29 (4.1)	84 (2.0)	2.04; 1.33–3.13
Health characteristics									
Diabetes mellitus[a]	62 (3.2)	106 (2.1)	1.56; 1.14–2.15	34 (2.8)	29 (3.0)	0.93; 0.56–1.54	28 (3.9)	77 (1.9)	2.15; 1.38–3.34
Epilepsy	12 (0.6)	17 (0.3)	1.87; 0.89–3.93	10 (0.8)	3 (0.3)	2.68; 0.73–9.75	14 (0.3)	2 (0.3)	0.83; 0.19–3.64
Psychiatric morbidity	64 (3.3)	108 (2.1)	1.59; 1.16–2.17	47 (3.9)	39 (4.0)	0.96; 0.62–1.48	17 (2.4)	69 (1.7)	1.43; 0.84–2.45
Thyroid abnormality	151 (7.8)	304 (6.0)	1.34; 1.09–1.64	107 (8.8)	81 (8.4)	1.06; 0.78–1.43	44 (6.2)	223 (5.4)	1.15; 0.82–1.61
Pregnancy characteristics									
Gravidity			<0.001			0.069			0.006
1	363 (18.9)	947 (18.6)		196 (16.2)	188 (19.4)		167 (23.5)	759 (18.4)	
2–3	822 (42.7)	1764 (34.6)		603 (49.8)	441 (45.6)		219 (30.8)	1323 (32.1)	
>4	739 (38.4)	2381 (46.8)		413 (34.1)	339 (35.0)		326 (45.8)	2042 (49.5)	
Insufficient prenatal care	183 (9.5)	1634 (34.1)	0.20; 0.17–0.24	61 (5.0)	89 (9.2)	0.52; 0.37–0.73	122 (17.1)	1645 (39.9)	0.31; 0.25–0.38
Infertility treatments	209 (10.9)	217 (4.3)	2.74; 2.24–3.33	170 (14.0)	77 (8.0)	1.89; 1.42–2.51	39 (5.5)	140 (3.4)	1.65; 1.14–2.37

(Continues)

TABLE 1 (Continued)

	n (%)	n (%)	OR; 95% CI	n (%)	n (%)	OR; 95% CI	n (%)	n (%)	OR; 95% CI
Multiple gestation	82 (4.3)	185 (3.6)	1.18; 0.90–1.54	43 (3.5)	35 (3.6)	0.98; 0.62–1.54	39 (5.5)	150 (3.6)	1.53; 1.07–2.21
Hyperemesis gravidarum	56 (2.9)	110 (2.2)	1.36; 0.98–1.88	41 (3.4)	33 (3.2)	0.99; 0.62–1.58	15 (2.1)	77 (1.9)	1.13; 0.65–1.98
Gynecological history									
Recurrent pregnancy loss	118 (6.1)	383 (7.5)	0.80; 0.65–0.99	74 (61)	62 (6.4)	0.95; 0.67–1.35	44 (6.2)	321 (7.8)	0.78; 0.56–1.08
Previous preterm delivery	188 (9.8)	542 (10.6)	0.91; 0.76–1.08	106 (8.7)	65 (6.7)	1.33; 0.97–1.83	82 (11.5)	477 (11.6)	0.99; 0.77–1.27
Poor obstetric history (history of late fetal death [500–999g; 20–27weeks] or stillbirth)	71 (3.7)	335 (6.6)	0.54; 0.42–0.71	35 (2.9)	45 (4.6)	0.61; 0.39–0.96	36 (5.0)	290 (7.0)	0.70; 0.49–1.00

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CI, confidence interval; OR, odds ratio.

[a]Not including gestational diabetes mellitus.

safety and insufficient experience and data regarding vaccination during pregnancy.

Smoking during pregnancy was more prevalent among Jewish or vaccinated women. As smoking is a known risk factor for COVID-19 complications, as well as obesity and comorbidities, this could explain why women who smoked were more likely to be vaccinated in the general population, although among Jewish women no association was observed between smoking and vaccination.

Differences were found in the risk factors for non-vaccination between the two ethnic groups included in the study. This suggests that specific intervention strategies to improve vaccination acceptance among pregnant women should be tailored for subgroups in the population with low vaccination rates. These interventions must include information about vaccine safety and the importance of vaccination, especially among women with a poor obstetric history who were less likely to be vaccinated, according to our findings.

Despite the elevated risk of severe illness from COVID-19 for pregnant women, and even with mounting evidence about the safety and effectiveness of COVID-19 vaccination during pregnancy, vaccination rates among pregnant women remain low. The latest data from the Centers for Disease Control and Prevention estimated that only 34.3% of pregnant women aged 18–49 years in the United States were fully vaccinated against COVID-19, with only 19.2% obtaining a dose during pregnancy.[20] The vaccination rate for any vaccine is not expected to be 100%, and individuals or groups in the population may choose not to get vaccinated. Still, the COVID-19 vaccination rate in Israel is 62% among eligible citizens,[21] and according to current findings, vaccination rates during pregnancy are significantly lower (27.4%; lower, too, when compared with the worldwide vaccination rates [44.4%]). Low vaccination rates during pregnancy have also been reported by Kharbanda et al.[22] (14.3%), although higher rates (40.2%) have been reported by Rottenstreich et al.[23] in another Israeli study. Differences between the latter and our findings are likely due to differences in ethnic groups of the studies. In the current study, 60% of the population are Bedouin Arabs who reside in southern Israel. This ethnic group is unique in healthcare utilization and the attitude towards vaccination, although antenatal and childhood vaccination rates among Bedouin Arabs are high.[24]

The low vaccination rate during pregnancy, also found in the current study, could be due to the newly introduced vaccine and therefore the hesitancy surrounding this vaccine specifically. During pregnancy, besides the personal concerns regarding the new vaccine, there are concerns regarding its safety and possible effects on the pregnancy and the offspring, both in the immediate period and in the long term. Indeed, factors influencing vaccination acceptance among pregnant women, which have been extensively studied (mainly in relation to the influenza vaccination[25]) include vaccine safety, belief that the vaccine is not needed or effective, no recommendation by a healthcare worker, low knowledge about vaccines, access issues, cost, and conflicting advice. Although some factors are irrelevant in the current study and population, including access issues or costs (as the vaccine is free in Israel and provided nationwide throughout all HMOs covering all

TABLE 2 Multivariable logistic models for characteristics associated with vaccination, for the entire study population and separately by ethnic group[a].

	All women	Jewish	Bedouin Arab
	Adjusted OR; 95% CI	Adjusted OR; 95%CI	Adjusted OR; 95%CI
Bedouin Arab (versus Jewish)	0.20; 0.18–0.23	–	–
Maternal age (year)	1.03; 1.02–1.05	1.02; 0.99–1.04	1.02; 0.99–1.04
Socioeconomic score	–	1.11; 1.03–1.19	0.84; 0.75–0.94
Obesity	1.16; 0.99–1.36	–	1.33; 1.02–1.75
Smoker, current or past	0.98; 0.82–1.16	–	1.24; 0.63–2.42
Diabetes mellitus[b]	1.18; 0.82–1.70	–	1.31; 0.71–2.45
Psychiatric morbidity	1.04; 0.73–1.48	–	–
Thyroid abnormality	0.97; 0.77–1.21	–	–
Insufficient prenatal care	0.36; 0.30–0.42	0.59; 0.40–0.87	0.34; 0.26–0.45
Infertility treatments	1.47; 1.18–1.83	1.67; 1.17–2.38	0.97; 0.53–1.80
Multiple gestation	–	–	1.21; 0.76–1.92
Recurrent pregnancy loss	0.78; 0.61–0.99	–	–
Poor obstetric history	0.65; 0.49–0.87	0.72; 0.45–1.13	0.71; 0.45–1.10

Abbreviation: CI, confidence interval; OR, odds ratio.

[a]Not including gestational diabetes mellitus.

[b]Only characteristics considered as confounding or clinically significant variables were included in each model.

citizens), other factors can be addressed by patient education programs, and by applying a maternal immunization platform among obstetric care providers.[26]

As in all observational studies, this study has several limitations, including the possible effect of unmeasured confounding variables. These variables may change the measured effect of the identified risk factors on vaccination likelihood. Still, some characteristics such as ethnicity were very strongly associated with vaccination likelihood and it is unlikely that this effect would diminish due to a third unmeasured variable. Additional characteristics were unavailable and might be associated with vaccination likelihood, such as vaccination hesitancy in general (not specifically regarding COVID-19), a characteristic that may increase the possibility of identifying pregnant women at risk for refusing vaccination.

Studies show that one of the strongest influences on patient vaccination acceptance is the recommendations by a healthcare provider (obstetrician, general practitioner or midwife) and that vaccination rates are higher when the healthcare provider offers and administers the vaccine during the same visit as the standard clinical care (rather than referring the women elsewhere to receive the vaccine).[26] High vaccination rates are necessary to achieve herd immunity and control the disease outbreak.

5 | CONCLUSIONS

Although the findings regarding the association between age, ethnicity, and comorbidities were expected based on studies on the total (non-pregnant) population, among pregnant women additional risk factors have been identified, including a poor obstetric history and insufficient prenatal care. The findings of the current study could aid in the planning of targeted intervention to increase vaccination among pregnant women, with the aim of fighting the COVID-19 pandemic or future pandemics.

AUTHOR CONTRIBUTIONS

TW took part in study conception, prepared the initial draft of the work, ran the analysis, and approved the final version of the manuscript. RS took part in data acquisition, and revised, reviewed, and approved the final draft. SO took part in the interpretation of the results and preparing the discussion; she revised, reviewed, and approved the final draft. ES took part in the study conception, data acquisition, and revised, reviewed, and approved the final draft. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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