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Effectiveness of BNT162b2 Vaccination During Pregnancy in Preventing Hospitalization for SARS-CoV-2 in Infants

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Running title: Effect of Maternal BNT162b2's on SARS-CoV-2 Infant Hospitalization

# Contributed equally.

List of Abbreviations:

SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2

PCR - polymerase chain reaction -

mRNA - messenger ribonucleic acid

CI – confidence interval

IQR – interquartile range

OR – odds ratio

Abstract

Objective: to Assessthe clinical effectiveness of the BNT162b2 vaccine during pregnancy in preventing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) hospitalizations of infants.

Study design: A retrospective, multicenter, 1:3 case-control (test-negative) study. Symptomatic hospitalized infants <6 months, with positive SARS-CoV-2 polymerase chain reaction (PCR) test between 1/3/2021-31/11/2021 were matched by age and time to negative controls, hospitalized with symptoms compatible with SARS-CoV-2 infection. Mothers were defined as fully vaccinated; received 2 doses of BNT162b2 with the second given 2 weeks to 6 months before delivery, or partially vaccinated; received only one dose or 2 doses with the second given >6 months or <2 weeks before delivery. Severe SARS-CoV-2 was defined as need for assisted ventilation.

Results: 116 SARS-CoV-2 positive infants were matched to 348 negative controls with symptoms compatible with SARS-CoV-2 infection. The effectiveness of fully vaccinated mothers was 61.6% (CI: 31.9-78.4) and the effectiveness of partially vaccinated mothers was not significant. Effectiveness was higher in infants 0-2 vs. 3-6 months of age. The effectiveness (57.1%, CI: 22.8-76.4) was similar when excluding mothers who were infected with SARS-CoV-2 during pregnancy. OR of severe infection in infants born to unvaccinated versus fully vaccinated mothers was 5.8.

Conclusions: At least 2 doses of BNT162b2 vaccine administered during the second or third trimester of pregnancy had an effectiveness of 61.6% in reduction of hospitalization for SARS-CoV-2 infection in infants <6 months.

Introduction

Pregnant women are at high risk for severe SARS-CoV-2 infection mainly during the third trimester [1]. Infants <3 months old usually have a benign clinical course and although age <1 year has been associated with increased rates of hospitalization, it may not reflect severity of illness[2].

Vaccination of very young infants by direct immunization might be limited by poor immunogenicity and interference from maternal antibodies[3]. One approach for protecting young infants against vaccine preventable infections is to vaccinate their mothers during pregnancy, as is currently recommended for pertussis, tetanus and influenza virus vaccines.

A national SARS-CoV-2 immunization program started in Israel on December 20, 2020, and by February, 2021 50% of the population >30 years old had received two doses of the vaccine[4]. Data from vaccinated pregnant women have not shown safety concerns and vaccine-induced immune responses in pregnant females were equivalent to non-pregnant females[5-7]. SARS-CoV-2 specific antibodies (immunoglobulin G) cross the placenta from the mother to the fetus, particularly during the final weeks of pregnancy[8]. Additionally, SARS-CoV-2 antibodies (immunoglobulin G+A) were found in breast milk of mothers as early as 2 weeks after vaccination[5, 9]. Nevertheless, the potential role of maternal immunization in protecting young infants against SARS-CoV-2 hospitalizations is less clear[10-12].

According to the Israeli ministry of health pregnant women are eligible for BNT162b2 vaccination during all trimesters of pregnancy based on growing evidence of safety of messenger ribonucleic acid (mRNA) SARS-CoV-2 vaccine in pregnancy and decreased risk of SARS-CoV-2 infection in vaccinated pregnant women. Of note,

no SARS-CoV-2 vaccine other than BNT162b2 was commercially available in Israel during the study period.

The aim of this study was to assess the clinical effectiveness of the BNT162b2 SARS-CoV-2 vaccination during pregnancy in preventing SARS-CoV-2 hospitalizations of infants under 6 months of age.

Methods

SARS-CoV-2 in Israel

Since the first SARS-CoV-2 case occurred in Israel on February 21, 2020, Israel has had five waves of SARS-CoV-2. 9during February-March 2020 and May-November 2020) and over 8,000 deaths waves occurring during November 2020-April 2021 and June 2021-November 2021 were predominantly due to the delta variant. The fifth wave which is predominantly caused by the omicron variant started on January 2022 and is still ongoing[4, 6]. Israel launched its BNT162b2 SARS-CoV-2 vaccination program in December 2020

Study design

We performed a multicenter, observational 1:3 case-control, test-negative study involving three tertiary pediatric hospitals in central and southern Israel (Soroka Medical Center, Schneider Medical Center, and Shamir Medical Center). The patients enrolled were selected from all hospitalized infants 0-6 months of age who underwent SARS-CoV-2 PCR testing between March 1, 2021, and November 31, 2021. Infants whose test was part of a screening protocol (pre-procedure/surgery, pre-transport or post-delivery) were excluded from analysis.

Variables and definitions

Cases were defined as all SARS-CoV-2 RT-PCR positive infants. Three PCR negative controls were selected for each case using frequency-matching with cases based on age (by week), date of test (by week) and ethnicity (Jews vs. non-Jews). Prior data indicated that the probability of exposure among controls and cases were 68% and 84%, respectively[11]. For power calculation we estimated a sample size of 103 cases and 309 matched controls to reject the null hypothesis that odds ratio (OR) equals 1 with power of 80%, assuming that the type I error probability associated with the test of this null hypothesis is 5%[13, 14]. A positive SARS-CoV-2 PCR test was defined according to the Israeli Ministry of Health. Two testing methods were used in the hospitals' virology laboratories during the study period. BGI's Real-Time Fluorescent PCR kit was used for detection of SARS-CoV-2 spike protein (S gene), results were reported as positive- cycle time (Ct) value <36, negative- Ct value >40 or borderline- Ct value 36-40. Seegene SARS-COV-2 PCR kit (AllplexTM2019-nCoV Assay) was used for the detection of E, RdRP and N genes, results were reported as positive- positive for all three genes, any two genes or one gene for E or RdRP genes, negative- negative for all genes, or borderline- positive only for the N gene. Borderline test results were excluded; only positive SARS-COV-2 PCR infants were enrolled as cases.

Severe acute SARS-CoV-2 infection was defined as need for assisted ventilation.

The study was approved by the ethics committee at each institution.

SARS-CoV-2 PCR test results and date of testing were retrieved from the virology laboratory at each institution. Demographic and clinical data of the infants were collected from the patients' computerized medical records and included age, sex, ethnicity, premature birth <37 weeks of gestation, oxygen saturation during hospital

admission, use of supplemental oxygen, non-invasive or invasive ventilation, mortality within 30 days of admission, and lactation prior to or during the time of hospital admission. The maternal BNT162b2 vaccination status by number of doses and dates of vaccination were collected from the computerized medical records and by phone interviews (**Figure 1; available at www.jpeds.com**).

A fully vaccinated mother was defined as a mother who had received at least two doses of BNT162b2 vaccine, with the second dose given two weeks to six months prior to delivery. A partially vaccinated mother was defined as one who had received only one dose of the vaccine or two doses with the second dose given more than 6 months or less than two weeks prior to delivery.

Mothers with a positive SARS-CoV-2 PCR test were considered recovered.

Analysis

All data were described using summary statistics. Comparisons of demographic and clinical characteristics between infants with SARS-CoV-2 positive PCR test and infants with SARS-CoV-2 negative PCR test, and of demographic and clinical characteristics between unvaccinated, fully vaccinated and partially vaccinated mothers were performing using student t-test for quantitative variables and chi-square or Fishers exact tests for categorical variables. Vaccine effectiveness with 95% confidence interval (CI) against infant COVID19 hospitalization was calculated using the equation: Vaccine effectiveness = 100%*(1-OR). Multivariate logistic regression model was performed to evaluate the mother's vaccine status on infant COVID19 hospitalization, adjusted for variables found to be statistically significant relating the mothers' vaccine status (infants' age at PCR date and ethnic group). All

statistical analyses were perform using SPSS 28.0 software. P value <0.05 were considered statistically significant.

Results

163 SARS-CoV-2 PCR positive infants aged 0-6 months were hospitalized during the study period of which 116 symptomatic SARS-CoV-2 PCR positive infants were included in the study group; 42 asymptomatic infants whose SARS-CoV-2 PCR test was taken for screening were excluded. 1,452 hospitalized infants aged 0-6 months had a negative SARS-CoV-2 PCR test during the same period however only 932 infants had symptoms compatible with SARS-CoV-2 infection (fever, respiratory or gastrointestinal symptoms). Each of the 116 SARS-CoV-2 positive infants was successfully matched to three SARS-CoV-2 negative infants (348 controls) by the matching criteria of week of birth, week of PCR testing and ethnicity (**Figure 2**).

The SARS-CoV-2 positive infants had a median age of 6.2 (interquartile range [IQR] 3.7-9.1) weeks; 59 (50.9%) were males, 74 (63.8%) Jewish, 21 (18.1%) were born prematurely <37 weeks of gestation, and 17 (14.7%) required supplementary oxygen/ assistant ventilation. None of the infants died within 30 days of admission. There were no significant differences in demographic and clinical characteristics between case and control infants **(Table I)**.

Nineteen mothers of SARS-CoV-2 positive infants were fully vaccinated during pregnancy; 2 (10.5%) and 17 (89.5%) in the second and third trimester,

respectively, compared with 105 mothers of SARS-CoV-2 negative infants; 29 (27.6%) and 76 (72.4%) in the second and third trimester, respectively.

The effectiveness of fully vaccinated mothers was 59.6% (CI 29.6-76.8), P-value 0.001 and the effectiveness of partially vaccinated mothers was 42.3% (CI 0.0-68.6), P-value 0.045 **(Table II)**. Six mothers had received 3 doses of the BNT162b2 vaccine prior to delivery (all during the second or third trimester of pregnancy). When excluding those 6 mothers from the fully vaccinated group vaccine effectiveness was 57.1% (CI 22.8%-76.4%), P-value 0.004.

Unvaccinated mothers were more likely to be non-Jewish and their infants were older at time of PCR testing compared with fully vaccinated mothers. When using a multivariable analysis controlling for ethnicity and infant age vaccine effectiveness for fully vaccinated mothers was 61.6% (CI 31.9-78.4). The infants of unvaccinated mothers had higher rates of prematurity compared with those of partially vaccinated mothers, and their mothers were more likely to be non-Jewish. However, when using a multivariable analysis controlling for ethnicity and prematurity vaccine effectiveness for partially vaccinated mothers was not significant **(Figure 3, Table III; available at www.jpeds.com)**. Unvaccinated and vaccinated mothers had similar breastfeeding rates.

The vaccine effectiveness in fully vaccinated mothers was higher in infants 0-2 months of age (63.8%; CI 31.9-80.8), compared with infants 3-6 months of age 46.1% (CI 0.0-83.4) **(Table II)**.

Seventeen (14.7%) infants in the case group and 61 (17.5%) infants in the control group had severe infection, defined as need for assisted ventilation. In the SARS-CoV-2 positive group, 81 unvaccinated mothers had 13 (16.0%) infants with

severe infection compared with 1 (5.3%) infant with severe infection in the 19 fully vaccinated mothers. The OR of severe infection between infants born to unvaccinated versus fully vaccinated mothers was 5.8, (P-value 0.09).

Overall, 130 mothers had SARS-CoV-2 infection documented by PCR; 6 mothers before conception [4 (66.6%) unvaccinated, 2 (33.4%) partially vaccinated, 0 (0.0%) fully vaccinated], 25 mothers during pregnancy (but at least 2 weeks before delivery) [16 (64%) unvaccinated, 6 (24%) partially vaccinated, 3 (12%) fully vaccinated] and 99 mothers post-delivery [61 (61.6%) unvaccinated, 21 (21.2%) partially vaccinated, 17 (17.2%) fully vaccinated]. Mothers who had SARS-CoV-2 infection during pregnancy had similar rates of infants' prematurity as mothers who did not have infection during pregnancy [5/25 (20%) vs. 70/439 (16%), P-value 0.592].

When excluding the mothers who were infected with SARS-CoV-2 during pregnancy the effectiveness of infant protection of fully vaccinated mothers was 61.4% (CI 32.5-77.9), P-value <0.001 and for partially vaccinated mothers 49.9% (CI 4.9-73.6), P-value 0.032.

Six mothers had SARS-CoV-2 infection documented by PCR while breast-feeding (but at least two weeks prior to their infants' PCR test) of which 4 were unvaccinated and had 1 positive SARS-CoV2 infant.

Discussion

Among hospitalized infants, at least two doses of maternal BNT162b2 vaccine administered during the second or third trimester had an effectiveness of 61.6% in reduction of hospitalization for SARS-CoV-2 infection in infants during the first 6 months of life, with higher effectiveness during the first two months of life.

Multiple studies on immunogenicity of COVID-19 mRNA vaccination during pregnancy have shown neonatal humoral responses during delivery with positive association between maternal and neonatal titers, which are highest after late second and early third trimester vaccination[5, 8]. Earlier vaccination, during the first trimester of pregnancy, has been shown to elicit significantly lower maternal anti-SARS-CoV-2 antibody levels and neutralizing titers at the time of delivery[5, 15], thus we divided vaccinated mothers to "fully vaccinated" mothers who had received two doses of vaccine during the second or third trimester of pregnancy (months 4-9 of pregnancy) but longer than two weeks prior to delivery, allowing a sufficient time for a complete immune response and placental transmission, and "partially vaccinated" mothers, who had received their second dose of vaccine during the first trimester of pregnancy or earlier (pre-conception and first 3 months of pregnancy). we showed significant higher effectiveness in the fully vaccinated group compared with the partially vaccinated group. For mothers who were vaccinated early, a third booster dose could potentially augment antibody levels, however, since the BNT162b2 booster campaign started in Israel only in September 2021, only 6 mothers received the booster prior to delivery.

Several studies have addressed the dynamics of protective maternal antibodies in the infants. Though a majority of infants had persistence of antibodies at 6 months of age, waning of antibody titers was observed as early as 2 months of age and indeed, in our real-life study, effectiveness was higher in infants 0-2 months of age[16].

Completion of a two-dose vaccination series either with Pfizer-BioNTech or Moderna mRNA COVID-19 vaccine reduced the risk of SARS-CoV-2 hospitalizations of infants 0-6 months in 20 US pediatric hospitals during a period of delta and omicron variant circulation by 61%. We showed similar effectiveness of late

vaccination of at least two doses of Pfizer-BioNTech of 61.6%, however, the effectiveness of late vaccination was lower in our cohort than in the studies by Halasa et al[11, 12], (61.6% vs. 80% during the delta predominant period). One possible explanation could be differences in the rate of mothers who were infected with SARS-CoV2 during pregnancy in our cohort compared with the Halasa studies, however, the latter did not include data on maternal past infection status.

Our study has several strengths; first, all vaccine doses and specific dates of administration were verified by interviews and review of maternal computerized medical records. In addition, all mothers were vaccinated with the BNT162b2 vaccine because no other COVID-19 vaccine was available in Israel during the study period. Second, we included data that potentially could affect infants' protection against SARS-CoV-2 like maternal infection status before, during and after pregnancy and lactation. Third, our cohort included only symptomatic infants who were suspected of SARS-CoV-2 infection by a physician, whereas infants who were tested during screening or were asymptomatic were excluded from analysis because SARS-CoV-2 PCR "positivity" rates might be biased by behavioral differences between parents and the parents' threshold for testing.

The study also has several limitations; first the sample size was limited. Second, our study was unable to examine the impact of administration of a booster dose during pregnancy on preventing infant SARS-CoV-2 hospitalizations. Third, other factors that potentially affect maternal immunogenicity and hence neonatal antibody titers, such as maternal age (which is negatively correlated to BNT162b2 vaccine immune response)[17] and presence of immunodeficiency were not addressed in our study. Fourth, the study period, March 1st, 2021, throughout November 31st, 2021, was predominated by the delta variant, with the first cases of the omicron variant

reported in Israel only in January 2022. Thus, our findings might not be indicative of vaccine effectiveness against other SARS-CoV-2 variants.

With increasing data on the safety of SARS-CoV-2 mRNA vaccines during pregnancy[18] and the effectiveness against infections of pregnant woman[19-23], our findings may further strengthen the recommendation for routine mRNA SARS-CoV-2 vaccination during pregnancy.

Legend to figures

Figure 1: Telephone questionnaire for mothers

Figure 2: Study enrollment

Figure 3: Outcomes of infants according to maternal vaccination status

References

.1 Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320.

.2 Yarden Bilavski H, Balanson S, Damouni Shalabi R, Dabaja-Younis H, Grisaru-Soen G, Youngster I, et al. Benign course and clinical features of COVID-19 in hospitalised febrile infants up to 60 days old. *Acta Paediatr*. 2021;110:2790-5.

.3 Healy CM, Baker CJ. Prospects for prevention of childhood infections by maternal immunization. *Curr Opin Infect Dis*. 2006;19:271-6.

.4 Health SoIMo. Up-to-date guidelines for validating and releasing test results for the new Corona virus by the Israeli Ministry of Health . https://govextra.gov.il/media/18274/ld-176449420.pdf. Accessed 21 March 2022.

.5 Collier AY, McMahan K, Yu J, Tostanoski LH, Aguayo R, Ansel J, et al. Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women. *JAMA*. 2021;325:2370-80.

.6 Health SoIMo. COVID-19 Data Repository of the Israeli Ministry of Health https://data.gov.il/dataset/covid-19. Accessed 21 March 2022.

.7 Pham A, Aronoff DM, Thompson JL. Maternal COVID-19, vaccination safety in pregnancy, and evidence of protective immunity. *J Allergy Clin Immunol*. 2021;148:728-31.

.8 Beharier O, Plitman Mayo R, Raz T, Nahum Sacks K, Schreiber L, Suissa-Cohen Y, et al. Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine. *J Clin Invest*.131;2021 .

.9 Perl SH, Uzan-Yulzari A, Klainer H, Asiskovich L, Youngster M, Rinott E, et al. SARS-CoV-2-Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women. *JAMA*. 2021;325:2013-4.

.10 Carlsen EO, Magnus MC, Oakley L, Fell DB, Greve-Isdahl M, Kinge JM, et al. Association of COVID-19 Vaccination During Pregnancy With Incidence of SARS-CoV-2 Infection in Infants. *JAMA Intern Med*. 2022;182:825-31.

.11 Halasa NB, Olson SM, Staat MA, Newhams MM, Price AM, Boom JA, et al. Effectiveness of Maternal Vaccination with mRNA COVID-19 Vaccine During Pregnancy Against COVID-19-Associated Hospitalization in Infants Aged <6 Months - 17 States, July 2021-January 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71:264-70.

.12 Halasa NB, Olson SM, Staat MA, Newhams MM, Price AM, Pannaraj PS, et al. Maternal Vaccination and Risk of Hospitalization for Covid-19 among Infants. *N Engl J Med*. 2022;387:109-19.

.13 Dupont WD. Power calculations for matched case-control studies. *Biometrics*. 1988;44:1157-68.

.14 Stevenson M, Nunes T, Heuer C, J. M, Sanchez J, Thornton R, et al. An R package for the analysis of epidemiological data. *epiR*. 2015;Version 0.9-69.

.15 Mithal LB, Otero S, Shanes ED, Goldstein JA, Miller ES. Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy. *Am J Obstet Gynecol*. 2021;225:192-4.

.16 Shook LL, Atyeo CG, Yonker LM, Fasano A, Gray KJ, Alter G, et al. Durability of Anti-Spike Antibodies in Infants After Maternal COVID-19 Vaccination or Natural Infection. *JAMA*. 2022;327:1087-9.

.17 Rottenstreich A, Zarbiv G, Oiknine-Djian E, Vorontsov O, Zigron R, Kleinstern G, et al. The effect of gestational age at BNT162b2 mRNA vaccination on maternal and neonatal SARS-CoV-2 antibody levels. *Clin Infect Dis*. 2.022

.18 Goldshtein I, Steinberg DM, Kuint J, Chodick G, Segal Y, Shapiro Ben David S, et al. Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes. *JAMA Pediatr*. 2022.

.19 Blakeway H, Prasad S, Kalafat E, Heath PT, Ladhani SN, Le Doare K, et al. COVID-19 vaccination during pregnancy: coverage and safety. *Am J Obstet Gynecol*. 2022;226:236 e1- e14.

.20 Chavan M, Qureshi H, Karnati S, Kollikonda S. COVID-19 Vaccination in Pregnancy: The Benefits Outweigh the Risks. *J Obstet Gynaecol Can*. 2021;43:814-6.

.21 Goldshtein I, Nevo D, Steinberg DM, Rotem RS, Gorfine M, Chodick G, et al. Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women. *JAMA*. 2021;326:728-35.

.22 Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med*. 2021;384:2273-82.

.23 Wainstock T, Yoles I, Sergienko R, Sheiner E. Prenatal maternal COVID 19-vaccination and pregnancy outcomes. *Vaccine*. 2021;39:6037-40.

Table 1: Demographic and clinical characteristics, comparison between positive and negative SARS-CoV2 PCR hospitalized infants

	SARS-COV-2 PCR positive infants (n=116)	SARS-COV-2 PCR negative infants (n=348)	P value
Age at PCR test week, median [IQR]	6.2 (3.7-9.1)	6.6 (3.9-10.1)	0.814
Males *n* (%)	59 (50.9%)	206 (59.2%)	0.116
Ethnicity, Jews *n* **(%)**	74 (63.8%)	222 (63.8%)	1.00
Prematurity, <37 weeks, *n* **(%)**	21 (18.1%)	54 (15.5%)	0.512
Lactation *n* (%)	43/81 (53.1%)	165/347 (47.6%)	0.369
Saturation <94 *n* (%)	15 (12.9%)	61 (17.5%)	0.247
Supplementary oxygen / assistant ventilation *n* (%)	17 (14.7%)	61 (17.5%)	0.474
Mortality within 30 days *n* (%)	0 (0.0%)	1 (0.3%)	0.563
Mother positive for SARS-COV-2 PCR before pregnancy	0 (0.0%)	6 (1.7%)	0.343
Mother positive for SARS-COV-2 PCR during pregnancy	3 (2.6%)	22 (6.3%)	0.192

Table 2: Effectiveness* of maternal BNT162b2 SARS-CoV-2 vaccination against SARS-CoV2 associated hospitalization in infants <6 months, for fully and partially vaccinated mothers by infant age at admission

		SARS-COV-2 PCR negative infants (n=348)	SARS-COV-2 PCR positive infants (n=116)	**Vaccine effectiveness* (CI)**	**P-value**
All infants Unadjusted					
	Unvaccinated mothers	181(69.1%)	81(30.9%)		
	Partially vaccinated mothers	62(79.5%)	16(20.5%)	42.3% (0.0-68.6)	0.045
	Fully vaccinated mothers	105(84.7%)	19(15.3%)	59.6% (29.6-76.8)	0.001
All infants Adjusted					
	Unvaccinated mothers	181(69.1%)	81(30.9%)		
	Partially vaccinated mothers[r]	62(79.5%)	16(20.5%)	41.7% (0.0-68.6)	0.087
	Fully vaccinated mothers[±]	105(84.7%)	19(15.3%)	61.6% (31.9-78.4)	0.001
All infants excluding mothers that received a 3rd dose of the vaccine					
	Unvaccinated mothers	181(69.1%)	81(30.9%)		
	Partially vaccinated mothers	62(79.5%)	16(20.5%)	42.3% (0.0-68.6)	0.045
	Fully vaccinated mothers	105(84.7%)	19(15.3%)	57.1% (22.8-76.4)	0.004
Infants <2 months					
	Unvaccinated mothers	119(67.2%)	58(32.8%)		
	Partially vaccinated mothers	43(78.2%)	12(21.8%)	42.7% (0.0-71.9)	0.122
	Fully vaccinated mothers	85(85.0%)	15(15.0%)	63.8% (31.9-80.8)	0.001
Infants 2-6 months					
	Unvaccinated mothers	62(72.9%)	23(27.1%)		
	Partially vaccinated mothers	19(82.6%)	4(17.4%)	43.3% (0.0-82.6)	0.342
	Fully vaccinated mothers	20(83.3%)	4(16.7%)	46.1% (0.0-83.4)	0.298
Infants with severe infection					
	Unvaccinated mothers	36(73.4%)	13(26.6%)		
	Partially vaccinated mothers	9(75%)	3(25%)	7.7 (0.0-78.0)	1.0
	Fully vaccinated mothers	16(94.1%)	1(5.9%)	82.7 (0.0-97.9)	0.093
All infants excluding infants of SARS-COV-2 infected mothers during pregnancy					
	Unvaccinated mothers	166(67.5%)	80(32.5%)		
	Partially vaccinated mothers	58(80.6%)	14(19.4%)	49.9% (4.9-73.6)	0.032
	Fully vaccinated mothers	102(84.3%)	19(15.7%)	61.4% (32.5-77.9)	<0.001

*Vaccine effectiveness estimates were based on odds of antecedent maternal vaccination during pregnancy in case infants versus control-infants

[r] Adjusted for ethnicity and infant age

± Adjusted for ethnicity and prematurity

Online Table 3: Demographic and clinical characteristics of hospitalized infants by mothers' vaccination status, comparison between unvaccinated, fully vaccinated and partially vaccinated mothers

	Unvaccinated mothers (n=262)	Fully vaccinated mothers (n=124)	Partially vaccinated mothers (n=78)	P value[1, 2]
Age at PCR test <2 months *n* **(%)**	177 (67.6%)	100 (80.6%)	55 (70.5%)	**0.008**[1], 0.623[2]
Males *n* **(%)**	158 (60.3%)	66 (53.2%)	41 (52.6%)	0.188, 0.223
Ethnicity, Jews *n* **(%)**	142 (54.2%)	99 (79.8%)	55 (70.5%)	**<0.001, 0.010**
Prematurity, <37 weeks, *n* **(%)**	51 (19.5%)	17 (13.7%)	7 (9.0%)	0.166, 0.031
Lactation *n* **(%)**	116/241 (48.1%)	61/119 (51.3%)	31/68 (45.6%)	0.577, 0.711

[1] P-value unvaccinated mothers vs. fully vaccinated mothers
[2] P-value unvaccinated mothers vs. partially vaccinated mothers

Figure 1 online only: Telephone questionnaire for mothers

Serial number of infant _____

Have you received SARS-CoV-2 vaccine prior to delivery date? Yes / No

If yes, how many doses have you received? _____

Dose 1 date_____

Dose 2 date_____

Dose 3 date_____

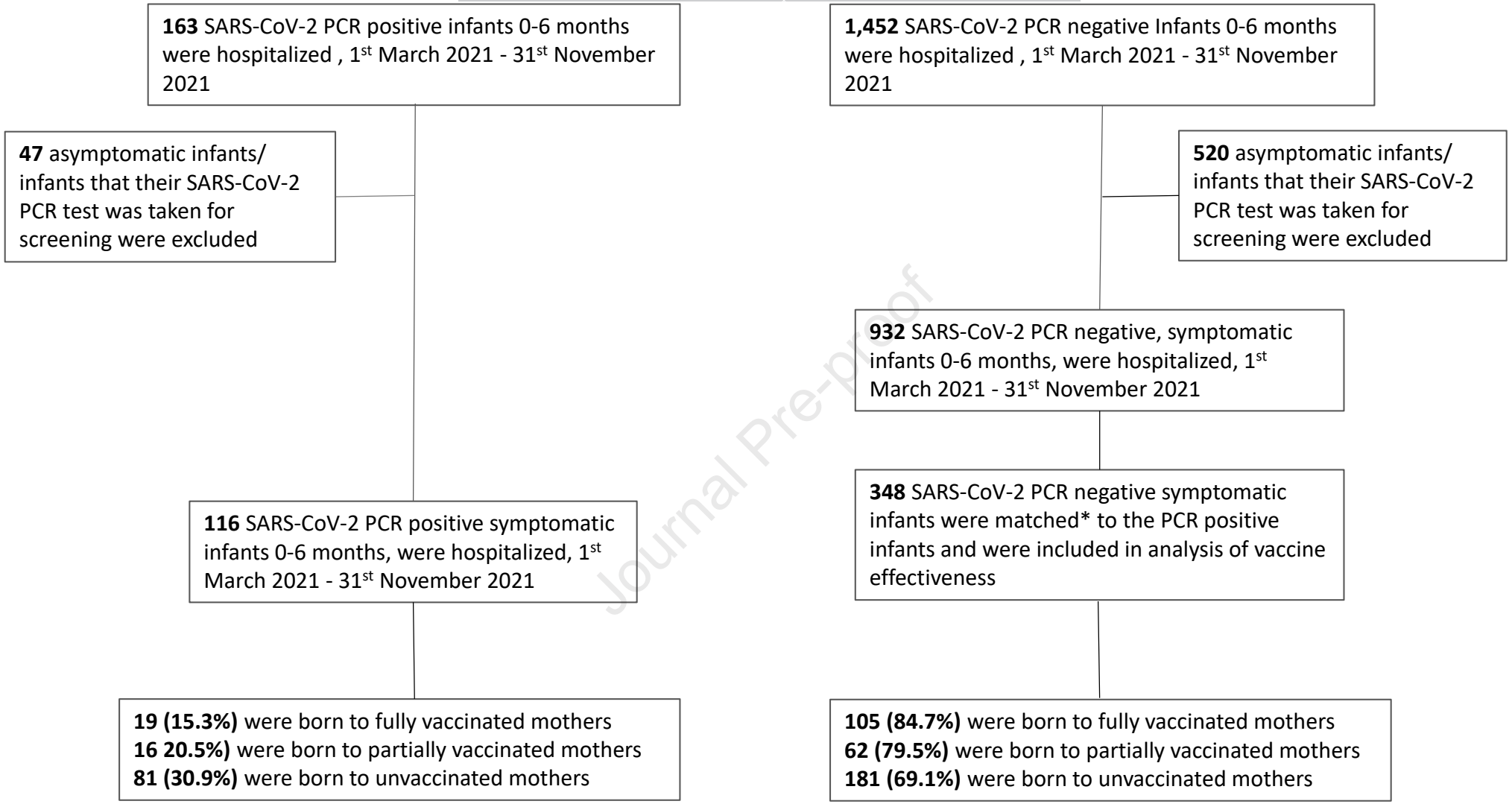
Did you have a positive SARS-CoV-2 PCR test? Yes / No

If yes, date of positive test _____

date of positive test _____

date of positive test _____

Figure 1



* Matched based on age (by week), date of test (by week) and ethnicity (Jews vs. non-Jews)
Fully vaccinated mother- received at least two doses of BNT162b2 vaccine, with the second dose given two weeks to six months prior to delivery.
Partially vaccinated mother- received only one dose of the vaccine or two doses with the second dose given more than 6 months or less than two weeks prior to delivery. Unvaccinated mother- not received any doses of vaccine before pregnancy or during pregnancy

Figure 2