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ABSTRACT

Prepregnancy Obesity and Birth Outcomes

We investigate the association between prepregnancy obesity and birth outcomes using fixed effect models comparing siblings from the same mother. A total of 7,496 births to 3,990 mothers from the National Longitudinal Survey of Youth 1979 survey are examined. Outcomes include macrosomia, gestational length, incidence of low birthweight, preterm birth, large and small for gestational age (LGA, SGA), c-section, infant doctor visits, mother's and infant's days in hospital post-partum, whether the mother breastfed, and duration of breastfeeding. Association of income outcomes with maternal pre-pregnancy obesity was examined using Ordinary Least Squares (OLS) regression to compare across mothers and fixed effects to compare within families. In fixed effect models we find no statistically significant association between most outcomes and prepregnancy obesity with the exception of LGA, SGA, low birth weight and preterm birth. We find that prepregnancy obesity is associated with a with lower risk of low birthweight, SGA, and preterm birth but controlling for prepregnancy obesity, increases in GWG lead to increased risk of LGA. Contrary to previous studies, which have found that maternal obesity increases the risk of c-section, macrosomia and LGA, while decreasing the probability of breastfeeding, our sibling comparison models reveal no such association. In fact, our results suggest a protective effect of obesity in that women who are obese prepregnancy have longer gestation lengths, and are less likely to give birth to a preterm or low birthweight infant.

JEL Classification: I12, J13

Keywords: infant health, birth outcomes, BMI, maternal obesity, gestational weight gain

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Introduction

One in three adults in the U.S. are obese (1) so it is not surprising that obesity is becoming the most common complication of pregnancy (2-3) and the predominant risk factor for maternal mortality in developed countries (4). Women who are obese prior to pregnancy may suffer poor health before, during, and after pregnancy, which may affect their birth outcomes as well as their willingness or ability to breastfeed. An increasing awareness of the potential adverse consequences of maternal obesity during pregnancy has led to repeated updating of the Institute of Medicine (IOM) pregnancy weight gain recommendations (5).

One explanation for the link between birth weight outcomes and maternal prepregnancy obesity is the fetal origins hypothesis, which posits that prepregnancy obesity and excess gestational weight gain (GWG) deliver greater concentrations of glucose and fatty acids to the developing fetus. The resulting increase in fetal insulin accelerates fetal growth and leads to high birth weights, which may be associated with complications at birth (6-8).

Consistent with this hypothesis, obese mothers have been shown to give birth to macrosomic babies (9-11), which places both mother and baby at risk for birth trauma (3). They are also more likely to give birth by c-section (12-16). Obese women are at greater risk for medically induced preterm birth (2,17) and women who are obese prepregnancy are less likely to initiate breastfeeding and breastfeed for shorter durations (18). However, these findings should be viewed cautiously because they are often based on cross-sectional comparisons across births. Thus, they may be biased by hard-to-measure factors such as shared genetics between a

mother and her baby or other factors that may affect both infant health and prepregnancy obesity.

In this research we examine how prepregnancy obesity and GWG affect birth outcomes, infant health, and breastfeeding initiation and duration. Using data from the National Longitudinal Study of Youth 1979 survey (NLSY79), we compare siblings by estimating mother fixed-effect (FE) models, which allow us to control for unobservable maternal specific factors that may be associated both with prepregnancy obesity and birth outcomes.

Methods

Data and Key Variables

We use the NLSY79 cohort for our analysis. The NLSY79 is a nationally representative survey of 12,686 individuals between the ages of 14 and 21 in 1979. Interviews were conducted annually until 1994 and subsequent interviews were conducted every other year up to 2010 when respondents were aged 45-53. Data and data dictionary are available online. Respondents reported data on their labor market experience, births, and marriages every survey round. The NLSY79 also collected information on the height and weight of respondents. Height was collected in 1985 and 2006, while weight was collected almost every round. We observe complete fertility histories for nearly all women in the sample with 99.97% of births observed by 2000. These data do not provide a nationally representative sample of children or young adults, although they are representative of the population of children born to U.S. women aged 14–22 in 1979 (19-20).

Mother's Prepregnancy BMI

Mother's self-reports of weight and height are used to calculate prepregnancy Body Mass Index (BMI), given by weight (kg) divided by height-squared (meters). Though there is potential for these self-reported measures to be systematically misreported, Goodman et al. (21) show that own reports of weight and height are highly correlated with height and weight measured by a trained enumerator. We then assign respondents to one of four categories using the World Health Organization Cutoffs. Underweight corresponds to a BMI of less than or equal to 18.5, BMI in the recommended range is between 18.5 and 24.9 inclusive, overweight women are those with a BMI ranging from 25 to 29.9 inclusive, and obese women have a BMI greater than or equal to 30. GWG is given by mother's report of weight change during pregnancy.

At-birth Outcomes

We examine several measures of birth weight: macrosomia (birth weight in excess of 9.92 pounds) (22-23); large for gestational age (LGA); small for gestational age (SGA); and whether the baby was low birth weight (5.5 lbs at birth or less). We calculate LGA and SGA using mother's self reports of child birth weight and gestational age combined with US national reference data, using separate cutoffs for boys and girls (24). We also examine how many days the infant spent in the hospital post-birth, whether the infant was born prematurely (before 37 weeks), and how many times the infant was taken to the doctor for an illness during the first year of life. As a post-natal investment, we examine whether or not the mother breastfed and, conditional on breastfeeding, how many weeks she breastfed. Finally, we

examine c-section birth as obese women are thought to be at higher risk for a c-section birth, which may result in adverse health consequences for both mother and infant (25).

Sample

We observe 9,563 births to women in the NLSY79 between 1979 and 2010. In the first survey after each pregnancy, women report their weight before and at delivery, birth weight of the child, mode of delivery, and weeks of gestation. We exclude 1,952 women with missing information on height or weight or implausible Body Mass Index (BMI) values (less than 15 or greater than 60). We drop observations with reported birth weight in excess of 13 lbs (4 dropped), or less than 32 ounces (22 dropped) and those with a gestational age greater than 44 weeks (75 dropped) as is common in this literature (12). We exclude women who gave birth after the age of 40 (none of these 14 women was obese) and an additional three women who did not report marital status or education.^a Our final sample consists of 7,496 singleton births occurring between 1979 and 2004. Of these 7,496 births, 1,604 mothers have one birth in the sample, 1,549 have two births in the sample, 612 have three, 172 have four, 32 have five, 12 have six, and three have seven births.^b

Data Analysis

Using the sample of mothers with singleton births over the period 1979-2004, we test whether prepregnancy BMI and GWG are correlated with adverse birth outcomes by estimating Ordinary Least Squares (OLS) regression models. The primary explanatory variables of interest are prepregnancy BMI category and GWG. We control for potential confounding factors including mother's education, race, age

at first birth, marital status, age at the current birth, parity, smoking status, use of alcohol and prenatal vitamins, and month of first prenatal visit. The models also include a control for child gender and a linear time trend to capture changes in birth technology or medical care over time common to all mothers. In the specifications for c-section we control for whether the mother had a previous c-section. When infant days in hospital is the outcome, weeks of gestation is included as a control since preterm infants often require extra care.

Despite this rich set of covariates, it is likely that the prepregnancy BMI and GWG coefficients are biased due to genetics and other hard-to-measure maternal characteristics. Thus, as noted earlier, we also estimate maternal fixed-effect (FE) models that compare biological siblings.

Results

Descriptive Results

Table 1 presents unweighted sample means/proportions for our outcome variables and prepregnancy weight measures for the full sample of mothers and then by prepregnancy BMI. Overall, 22 percent of the births were via c-section, 9 percent were LGA, 17 percent were SGA, 2 percent were macrosomic, 9 percent were low birth weight, and 12 percent were premature, defined as before 37 weeks of gestation.^c

Infants whose mothers were obese before pregnancy were more likely to be born via c-section and to be macrosomic or LGA, and less likely to be SGA, low birth weight, or premature as compared to mothers whose prepregnancy BMI was in the

recommended range. Mothers who were obese pre-pregnancy weigh more at the delivery of their child but do not gain as much weight as women in other pre-pregnancy BMI categories. Infants born to overweight and obese mothers experience more doctor visits for illness in the first year of life and, conditional on breastfeeding, they are breastfed for a shorter duration.

Table 2 presents the unweighted means/proportions of our control variables. Older women and those with more children tend to have higher pre-pregnancy BMI. Hispanic women represent the smallest share of obese mothers (16%). Women who are obese are more likely to have a previous c-section.

OLS Results

Tables 3 and 4 present the OLS models that include the full set of control variables although the coefficients on controls are not shown. Results in Table 3 reveal strong positive correlations between pre-pregnancy obesity and the outcomes weeks of gestation and LGA ($P < .01$), controlling for GWG. We find a weak association between pre-pregnancy obesity and the probability of macrosomia ($P < .10$), controlling for GWG. We find negative associations between pre-pregnancy obesity and the outcomes low birth weight ($P < .01$), SGA ($P < .01$), and preterm birth ($P < .10$), controlling for GWG. The effect sizes are not trivial. For example, pre-pregnancy obesity is associated with 7.6 percentage point (ppt) higher probability of LGA, corresponding to an 84.4 percent $((7.6/9.0) * 100)$ higher incidence of LGA. In addition, each additional pound gained in pregnancy by mothers who begin their pregnancy obese increases the probability of having an LGA infant by 0.3 ppt ($P < .01$).

Estimates in table 4 indicate that women who are obese prepregnancy are 8.2 ppt more likely to have a c-section ($P<.01$) and, conditional on initiating breastfeeding, they breastfeed for 3.8 fewer weeks than their non-obese counterparts ($P<.01$). Children whose mothers begin pregnancy obese have more doctor visits for illness in the first year of life ($P<.05$).

Mother FE RESULTS

The most stringent test of the hypothesis that maternal weight affects the outcomes of interest occurs when we include maternal FEs, limiting comparisons to within rather than across mothers (Table 5). These models require that the women in the sample have had more than one birth, so the sample size is reduced ($N=5,892$). The effects of prepregnancy obesity are identified off of discordant siblings, i.e., siblings whose mothers changed prepregnancy BMI category across pregnancies ($N=2,166$). Obesity is a persistent weight status; nearly 88 percent of women who are obese in the first pregnancy we observe are also obese in the last pregnancy we observe. No women who start their first observed pregnancy obese transition to underweight by the last pregnancy observed. The reverse is true as well: none of the women who are underweight at the time of the first pregnancy we observe are obese at their last pregnancy.

Once controlling for maternal fixed effects, many of the correlations estimated in Table 3 disappear. For example, the top panel of Table 5 shows no effect of prepregnancy obesity on macrosomia or LGA. The results in Table 5 reveal that starting pregnancy obese may exert a protective effect in that these mothers are significantly less likely to have a low birth weight ($P<.01$) or SGA baby ($P<.01$). They

also have longer gestation lengths ($P < .05$) and are less likely to have a preterm birth ($P < .05$). Comparing Table 4 to the bottom panel of Table 5, there is no longer a significant association between prepregnancy obesity and any of the outcomes.

We also run our OLS regressions using the full set of control variables on the sub-sample of women with more than one birth used to estimate the maternal FE and find results qualitatively similar to results on the full sample. Therefore, we conclude that it is the addition of the mother FEs and not the change in sample composition that is responsible for the differences across the OLS and mother FE models that we observe. This further underscores that controlling for unobservable, maternal specific factors is important.

Discussion

Our results, while largely confirming the findings of prior studies when we use OLS, differ from previous research when we compare siblings, a method which renders some of the associations between prepregnancy obesity and adverse birth outcomes insignificant. Specifically, using maternal FE, we do not find an effect of prepregnancy obesity on the probability of a c-section birth, macrosomia, duration of post-partum hospital stays, or duration of breastfeeding. We do find that maternal prepregnancy obesity is still associated with a lower probability of a preterm birth, low birth weight, and SGA. Similar to Ludwig and Currie (7) and Lawlor et al.,(8) who also make sibling comparisons, we find that controlling for prepregnancy BMI, increased GWG leads to a higher probability of an infant who is LGA in the maternal FE models.

In contrast to others, we find no effect of maternal prepregnancy obesity on preterm birth (17). However, previous work on this topic has focused on preterm births that were medically induced and our data do not identify preterm births that are medically induced thus our results are not directly comparable.

Many of the outcomes we consider, such as breast-feeding, low birthweight, macrosomia, and preterm birth have been linked to children's cognitive ability, future income and/or educational attainment, highlighting the potential long-term consequences of the outcomes we study (26-34). Furthermore, prepregnancy obesity itself has been linked directly to children's cognitive ability (35). Other outcomes, such as the probability of a c-section and preterm birth, are linked to higher medical costs as well as complications for the mother and infant (36).

The current study has several strengths. First, there are only two papers that we are aware of that use maternal FE to examine associations between prepregnancy obesity and infant outcomes. Ludwig and Currie (7) use a sample containing all births in Michigan and New Jersey from 1989 to 2003 to examine the effect of maternal GWG on infant birth weight. They report that maternal weight gain during pregnancy is associated with increased birth weight. However, they do not have information on the mother's prepregnancy weight, a key control we include. Lawlor et al. (8) explore the effect of GWG on birth weight. Their sibling comparisons, using a sample from Sweden, reveal that women who gained excessive weight in pregnancy have larger babies. However, they lack a good measure of GWG. Instead, they compare pre-delivery weight with the mother's weight at her first antenatal doctor visit.

A second strength of this study is that we examine a wide array of infant health and at birth outcomes using a large sample that spans the entire U.S. and contains a rich array of control variables. One possible drawback of these measures is that they are self-reported and subject to recall error.

Another limitation of our study is that we cannot control for unobservable, time-variant, mother-specific characteristics. For instance, if mothers who changed weight categories from one pregnancy to the next were aware of the dangers associated with excess weight gain or low prepregnancy BMI they may have engaged in compensatory behavior to counteract the potential adverse effects of their prepregnancy weight status. Or, if there was an unobserved random stressor that caused the mother to change prepregnancy BMI category, it potentially could have affected the birth outcome as well, rendering the association between the birth outcome and BMI category spurious. We cannot observe or control for these compensating behaviors and random events, so if they are systematic, they may bias our maternal FE results.

Overall, our findings suggest that the relationship between prepregnancy obesity and adverse birth outcomes is complex and merits further exploration by researchers.

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^a As is common in survey data, a significant number of women do not report their income. Rather than exclude them from our analysis, we measure income categorically including a category for missing. Categories are then adjusted for inflation.

^b Although the NLSY does not ask directly about gestational diabetes, respondents are asked retrospectively if they have ever been diagnosed with diabetes. We match that with information on her child's year of birth and identified 46 women who were diagnosed with diabetes when they would have been pregnant. If we omit these women from our analysis, as Ludwig and Currie⁷ do, our results are virtually identical.

^c Although the rate of c-section observed in the sample is lower than the current national rate of approximately 33 percent, recall that our data are observed from 1979 to 2004. Our annual c-section rates do increase over time similar to those in the U.S. over this period.

Table 1:
Unweighted sample means/proportions for infant outcome variables by mother's prepregnancy BMI category

Variable	All Mothers	BMI<18.5	BMI 18.5-24.9	BMI 25.0-29.9	BMI >30
LGA	0.09	0.04	0.08	0.10	0.14
SGA	0.17	0.24	0.17	0.14	0.12
Macrosomic	0.02	0.01	0.02	0.02	0.03
C-section	0.22	0.15	0.21	0.27	0.34
Low birth weight	0.09	0.14	0.08	0.07	0.07
Born before 37 weeks	0.12	0.18	0.12	0.11	0.11
Weeks of gestation	38.62	38.20	38.65	38.66	38.75
	(2.13)	(2.43)	(2.11)	(2.05)	(1.99)
# dr. visits infant year 1	1.76	1.68	1.71	1.89	1.99
	(3.77)	(3.77)	(3.47)	(4.70)	(3.96)
# days mom hosp	3.45	3.65	3.41	3.44	3.51
	(3.70)	(4.06)	(3.77)	(3.51)	(2.96)
Mom breastfed	0.47	0.42	0.49	0.44	0.43
# wks breastfed	18.84	19.12	19.10	18.41	16.99
	(21.13)	(21.59)	(21.12)	(21.51)	(19.79)
# days infant hosp. postpartum	4.46	5.72	4.37	4.14	4.35
	(8.75)	(17.73)	(7.50)	(5.83)	(6.63)
GWG	31.60	32.61	32.35	30.48	26.65
	(14.30)	(14.55)	(13.71)	(14.78)	(16.51)
Mom's BMI	23.06	17.52	21.46	26.91	34.47
	(4.62)	(0.73)	(1.70)	(1.41)	(4.46)
Observations	7496	697	4937	1261	601

Sample means/proportions. Standard deviations for continuous variables in parentheses.

Table 2: Unweighted sample means/proportions of control variables by mother's prepregnancy BMI

Variable	All Mothers	BMI<18.5	BMI 18.5-24.9	BMI 25.0-29.9	BMI >30
Not black/Hispanic	0.54	0.59	0.57	0.46	0.48
Hispanic	0.19	0.17	0.18	0.23	0.16
Black	0.27	0.25	0.25	0.31	0.36
Child is male	0.51	0.52	0.51	0.52	0.49
Mom's age at first birth	21.95 (4.58)	20.53 (3.88)	21.98 (4.59)	22.24 (4.56)	22.72 (4.90)
Mom's age at birth of child	25.08 (4.76)	22.99 (4.48)	24.91 (4.71)	26.00 (4.59)	27.04 (4.71)
Birth order	1.94 (1.07)	1.78 (1.01)	1.89 (1.04)	2.11 (1.17)	2.18 (1.14)
Child birth year	1986.14 (4.70)	1984.31 (4.16)	1985.89 (4.61)	1987.05 (4.77)	1988.37 (4.76)
Mom's yrs of education	12.27 (2.37)	11.61 (2.23)	12.36 (2.38)	12.31 (2.41)	12.24 (2.18)
Mother is married	0.67	0.58	0.67	0.70	0.65
Mother is sep./div./wid.	0.08	0.09	0.08	0.08	0.09
Low Income	0.26	0.36	0.25	0.27	0.26
Middle Income	0.28	0.26	0.27	0.29	0.35
Urban residence	0.74	0.72	0.74	0.74	0.74
Month of first prenatal visit	2.58 (1.63)	2.62 (1.56)	2.57 (1.60)	2.57 (1.71)	2.62 (1.74)
Took prenatal vitamins	0.90	0.88	0.90	0.90	0.91
Used alc. in preg. <1 per month	0.23 (0.42)	0.23 (0.42)	0.25 (0.43)	0.21 (0.40)	0.19 (0.40)
Used alc. monthly during preg.	0.04 (0.20)	0.04 (0.20)	0.04 (0.20)	0.04 (0.20)	0.03 (0.18)
Used alc. weekly during preg.	0.04 (0.20)	0.04 (0.19)	0.05 (0.21)	0.03 (0.17)	0.04 (0.20)
Did not smoke during preg.	0.99	0.99	0.99	0.99	0.99
Had a previous c-section	0.14	0.10	0.13	0.16	0.18
Observations	7496	697	4937	1261	601

Sample means/proportions. Standard deviations for continuous variables in parentheses.

Table 3: OLS Models, all infants

VARIABLES	Macrosomia	Weeks of Gestation	Low Birth Weight	Preterm Birth	LGA	SGA
Mom BMI<18.5	-0.002 (0.005)	-0.524*** (0.102)	0.051*** (0.015)	0.061*** (0.016)	-0.032*** (0.009)	0.065*** (0.019)
Mom 25<BMI<29.9	0.003 (0.004)	0.108 (0.069)	-0.023*** (0.009)	-0.011 (0.011)	0.025** (0.010)	-0.043*** (0.012)
Mom BMI>30	0.014* (0.007)	0.327*** (0.094)	-0.041*** (0.012)	-0.026* (0.015)	0.076*** (0.015)	-0.075*** (0.017)
GWG	0.001*** (0.000)	0.017*** (0.002)	-0.002*** (0.000)	-0.002*** (0.000)	0.003*** (0.000)	-0.003*** (0.000)
Constant	-0.746 (1.557)	134.477*** (24.744)	-6.295* (3.308)	-12.667*** (3.995)	4.490 (3.402)	3.622 (4.387)
Observations	7,496	7,462	7,496	7,487	7,496	7,496
R-squared	0.013	0.035	0.034	0.019	0.035	0.047

Robust standard errors in parentheses. All models include controls for cigarette and alcohol use during pregnancy as well as income, race, mother's age at first birth, mother's age at current birth, birth order, birth year, mother's education and marital status, and prenatal vitamin use and month of first prenatal visit. Low birth weight refers to infant born less than 5.5 pounds. Pre-term birth refers to infants born before 37 weeks. *** p<0.01, ** p<0.05, * p<0.1

Table 4: OLS Models, all infants

VARIABLES	C-section Birth	# dr. visits Infant's first yr	# days Mom in hosp. Post delivery	Infant was Breastfed	If breastfed, weeks Breastfed	# days Infant in hosp Post delivery
Mom BMI<18.5	-0.019* (0.010)	-0.023 (0.161)	0.092 (0.174)	-0.017 (0.022)	1.626 (1.587)	0.220 (0.581)
Mom 25<BMI<29.9	0.030*** (0.011)	0.250 (0.164)	0.125 (0.123)	-0.045*** (0.017)	-1.580 (1.049)	-0.024 (0.185)
Mom BMI>30	0.082*** (0.018)	0.374** (0.168)	0.295* (0.156)	-0.033 (0.025)	-3.869*** (1.392)	0.539* (0.320)
GWG	0.001*** (0.000)	0.002 (0.004)	0.006 (0.004)	0.000 (0.000)	-0.079*** (0.027)	0.006 (0.006)
Mom had prev. c-sec	0.906*** (0.005)					
Weeks of gestation						-1.171*** (0.174)
Low birthweight						6.830*** (0.616)
Constant	-1.629 (3.502)	41.398 (43.053)	181.399*** (42.272)	-1.131 (6.280)	-237.523 (381.382)	279.524*** (80.652)
Observations	7,425	7,433	7,004	7,285	3,422	7,008
R-squared	0.582	0.014	0.022	0.174	0.065	0.194

Robust standard errors in parentheses. All models include controls for cigarette and alcohol use during pregnancy as well as income, race, mother's age at first birth, mother's age at current birth, birth order, birth year, mother's education and marital status, and prenatal vitamin use and month of first prenatal visit. Low birth weight refers to infant born less than 5.5 pounds. Pre-term birth refers to infants born before 37 weeks. *** p<0.01, ** p<0.05, * p<0.1

Table 5: Maternal Fixed Effects Models, all infants with siblings

Variables	Macrosomia	Weeks of Gestation	Low Birth Weight	Preterm Birth	LGA	SGA
Mom BMI<18.5	0.016 (0.010)	-0.917*** (0.191)	0.057** (0.024)	0.109*** (0.028)	-0.004 (0.014)	-0.069** (0.031)
Mom 25<BMI<29.9	-0.002 (0.008)	0.168 (0.127)	-0.046*** (0.015)	-0.031* (0.019)	0.003 (0.017)	-0.038* (0.020)
Mom BMI>30	0.016 (0.017)	0.493** (0.215)	-0.069*** (0.025)	-0.075** (0.034)	0.037 (0.035)	-0.093*** (0.033)
GWG	0.000 (0.000)	0.023*** (0.004)	-0.002*** (0.000)	-0.003*** (0.000)	0.002*** (0.000)	-0.002*** (0.001)
Observations	7,496	7,462	7,496	7,487	7,496	7,496
R-squared	0.023	0.035	0.023	0.025	0.024	0.016
Number of CASEID	3,987	3,981	3,987	3,984	3,987	3,987
Variables	C-section Birth	# dr. visits Infants first yr	# days Mom in hosp Post delivery	Infant was Breastfed	If breastfed, weeks Breastfed	# days Infant in hosp Post delivery
Mom BMI<18.5	0.008 (0.015)	0.328 (0.296)	0.166 (0.267)	-0.007 (0.026)	1.786 (2.991)	1.100 (1.333)
Mom 25<BMI<29.9	-0.019 (0.013)	-0.396 (0.324)	-0.514** (0.235)	0.025 (0.022)	2.343 (1.839)	-0.793** (0.365)
Mom BMI>30	0.030 (0.021)	-0.537 (0.390)	-0.321 (0.320)	0.014 (0.038)	0.625 (3.060)	-0.299 (0.652)
lbs gained preg.	-0.001** (0.000)	-0.009 (0.006)	-0.003 (0.006)	0.001 (0.001)	-0.044 (0.051)	-0.013 (0.020)
Observations	7,425	7,433	7,004	7,285	3,422	7,008
R-squared	0.445	0.014	0.016	0.013	0.029	0.187
Number of CASEID	3,978	3,974	3,852	3,910	2,084	3,850

Robust standard errors in parentheses. See footnotes for tables 3 and 4. *** p<0.01, ** p<0.05, * p<0.1