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Early Literacy and Childbearing Over the Reproductive Lifecourse

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Early Literacy and Childbearing Over the Reproductive Lifecourse

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ABSTRACT

INTRODUCTION: Literacy is linked to a range of health outcomes, but its association with reproductive health in high-income countries is not well understood. We assessed the relationship between early-life literacy and childbearing across the reproductive lifecourse in the US.

STUDY DESIGN: A prospective cohort design was employed to assess early-life literacy and subsequent childbearing, using data from the National Longitudinal Survey of Youth 1979. US youth aged 14-22 in 1979, including 6,283 women, were surveyed annually through 1994 and biannually thereafter. Literacy was assessed in 1980 using the Armed Services Vocational Aptitude Battery Reading Grade Level (RGL). Cumulative childbearing and grand multiparity (≥ 5 births) was assessed in 2010. Summary statistics, chi-square, and logistic regression were used.

RESULTS: Of 6,283 women enrolled, 4,025 (64%) had complete data and were included in the analyses. In 1980, these women were on average 18 years old and in 2010 were 45. Average cumulative parity decreased for each RGL and ranged from 2.7 ($<5^{\text{th}}$ grade) to 1.8 ($>12^{\text{th}}$ grade) ($p=0.001$). Adjusting for race/ethnicity, poverty status, and age in 1980, odds of grand multiparity were 2.5 (95% CI: 1.4 – 4.5) and 2.0 (95% CI: 1.1 – 3.6) greater among women with $<5^{\text{th}}$ or $5^{\text{th}}-6^{\text{th}}$ grade literacy compared with those $\geq 12^{\text{th}}$ literacy.

DISCUSSION: In the US, early-life literacy is associated with total parity over a woman's lifecourse. Literacy is a powerful social determinant of reproductive health in this high income nation just as it has been shown to be in low income nations.

ARTICLE SUMMARY

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This is a longitudinal study of more than 4,000 women from across race/ethnic and socio-economic groups and through their full reproductive span, which allows a lifecourse perspective to be applied to the question of how literacy relates to health.
- This study extends the evidence that literacy is a powerful social determinant of health, independent of race/ethnicity and poverty status, of a key reproductive health outcome in high income countries.
- Literacy was assessed, unlike in many other studies of the linkage of literacy and health in high-income countries, using a true diagnostic measure rather than a simple and limited screening tool.
- While study non-respondents were somewhat different from those included in the analyses, it is unlikely that this difference affects results; non-respondents were less than a third of the full sample and were more likely to have higher literacy, making our estimates conservative.
- Additional research is needed to assess whether this relationship extends to other reproductive health outcomes.

INTRODUCTION

Literacy, the ability to use written text and numeracy, is primarily formed as a result of early-life educational inputs and is associated with poor health behaviors and outcomes at different life stages from adolescence to old age.[1-4] Despite these two important findings, little research has explored the impact of limited literacy prospectively on trajectories of health through the lifecourse; instead, nearly all research examining literacy and health has assessed the associations between the two at a single point in time or in a very narrow temporal window, which reduces the ability to assess a causal relationship between these variables.[1-4] A number of studies have examined the impact of literacy on health, however, these studies have focused on older adults whose past experiences, exposures, and health behaviors may confound the associations.[1, 4] Lifecourse epidemiology has made evident the importance of taking a longitudinal approach to understanding the magnitude of impact that social factors have on health and to inform both downstream and upstream interventions to deflect poor health trajectories, including on the critical areas of maternal, child, and reproductive health.[5-8]

There has been an increasing interest in literacy as an important and modifiable social determinant of health in high-income nations.[9, 10] Social determinants of health, particularly if modifiable, are increasingly of interest to primary and community health policy because of their association with disparities in health outcomes between vulnerable and majority race/ethnic and economic populations [11, 12]. Because literacy is a quantifiable and modifiable skill it opens the potential for novel intervention strategies.[13, 14] Despite this, nearly all research in the relationship between health and literacy assess short-term risks and consequences, such as misreading medical directions and taking too much medication. However, these studies often fall short of addressing the larger cumulative risk to health that arises from chronic exposures to

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3 disadvantage secondary to low literacy through life and the greater role that literacy could play
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5 as a social determinant of health. In addition, nearly all research on this topic within high-income
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7 nations has used instruments with severely limited capacity to measure literacy and so reducing
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9 the ability to attribute health outcomes to specific levels of literacy [3, 8]. There is a great need to
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11 carry out longitudinal studies which assess the magnitude of effect of literacy on health outcomes
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13 independent of other established social determinants of health and within a lifecourse
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15 framework.
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21 Childbearing is the most common reason for hospitalization, one of the leading causes of
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23 morbidity and mortality in the first half of life, and as many as half of all pregnancies are
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25 unintended; despite these findings the role of literacy in determining these health outcomes has
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27 received little attention.[15] Girls in a high income nation with below average reading skill at
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29 age eleven have greater risk of subsequent teenage childbearing after adjusting for a range of
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31 social factors.[16] Studies in the developing world have also found associations between low
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33 literacy and increased birth rates at the district, state, and individual level.[17-19] Despite this
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35 work, there has been little research in high-income nations looking at the influence of literacy
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37 early in life on subsequent reproductive health outcomes, including unintended pregnancy and
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39 higher parity. This is a critical area of investigation since the lack of recognition of the influence
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41 of literacy on reproductive health has resulted in few interventions addressing this issue.
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47 Unintended pregnancy represents a very high percentage of births in high income nations,
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49 particularly in vulnerable populations at risk for poor birth outcomes.[9, 10] Increased parity, or
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51 number of total births, increases the cumulative risk of poor health outcomes for women; grand
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53 multiparity (delivering 5 or more children) is associated with poor health outcomes for women
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55 and their children, including obstetric complications, neonatal morbidity and perinatal
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3 mortality.[20] In 2011, 190,000 U.S. women delivered a fifth, or higher order child, making up
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5 4.8% of all U.S. births that year.[21, 22] While higher parity is associated with low-
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7 socioeconomic status and low educational attainment; the relationship between early-life low
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9 literacy and grand multiparity has not been explored.[23] In this study we sought to assess the
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11 association between early-life literacy and parity through women's full reproductive lifecourse.
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14 15 **METHODS**

16 17 **DATA**

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19 Data from the National Longitudinal Survey of Youth 1979 (NLSY-79),[24] a
20
21 representative probability sample of US men and women born between 1957 and 1964, were
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23 used to assess the relationship between early-life literacy and risk of grand multiparity across a
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25 woman's reproductive lifecourse. These data has been used to assess a range of social influences
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27 on birth and birth outcomes.[25, 26] In 1979, the first survey year, 6,283 women were enrolled.
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29 Participants were surveyed annually through 1994 and biannually thereafter. Survey data was
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31 available through 2010. Retention in the survey through 2010 exceeded 80%.
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35 The survey followed women from 1979 when they were 14-22 years old to 2010 when
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37 they were 45-53 years old. These data provided the novel opportunity to examine the full female
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39 reproductive lifecourse, commonly accepted as age 15 to 45.[27] Women missing data on early-
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41 life literacy or total parity and those dropped from the NLSY were excluded from the analysis.
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45 This study was approved by the University of Pennsylvania's Institutional Review Board.
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48 49 **OUTCOME MEASURES**

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51 Parity was measured in each survey year. Total cumulative parity for each woman in
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53 2010 was used to create the variable grand multiparity defined as five or more births. To
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55 decrease the effect of non-response bias, for those women missing parity data in 2010, total
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3 parity in 2008 or 2006 was used; less than 1% of women with parity data in 2010 had a child
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5 between 2006 and 2010.
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8 EXPOSURE MEASURES 9

10 Department of Defense Reading Grade Level (RGL) in 1980 was used as the measure of
11 early-life literacy. RGL categories were created from the Armed Services Vocational Aptitude
12 Battery (ASVAB) using a previously validated conversion method.[28] The ASVAB is a text-
13 based measure of a range of cognitive skills with rigorously assessed psychometric properties.
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15 Components of this well validated instrument have been used in a range of health studies.[29,
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17 30] This measure of early-life literacy was used to construct an ordinal variable for literacy
18 based on commonly accepted RGL cut-points (<5th grade, 5th to 6th grade, 7th to 8th grade, 9th to
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20 11th grade, and $\geq 12^{\text{th}}$ grade).
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29 COVARIATES 30

31 Using an adaptation of the behavioral model described by Andersen, we identified
32 maternal predisposing and enabling factors to predict grand multiparity.[31] Predisposing
33 factors included early-life literacy, as well as age at reading assessment, and race/ethnicity.
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35 Income was included as an enabling factor.
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39 Participants self-reported their age in 1980 when the ASVAB was administered.
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41 Race/ethnicity was assigned in 1979 by NLSY interviewers and reported as Hispanic; Black; or
42 non-Black, non-Hispanic. Poverty status was assessed for every participant in each of the survey
43 years. Participants' family income was compared with the years' Poverty Income Guidelines
44 created by the U.S. Department of Health and Human Services. The respondent's family size,
45 whether or not they lived on a farm, and their state of residence were used in assessing poverty
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status. In following with a lifecourse approach, poverty status in 1979 was used in this study.

Poverty status was dichotomized as: in poverty or not in poverty.

STATISTICAL ANALYSES

Summary statistics, including frequencies, percentages, means, and standard deviations were used to describe the study population. To examine the relationship between presence or absence of grand multiparity (yes/no) and predisposing and enabling factors, the chi-square test was used. To determine the independent association of RGL to grand multiparity, a forced entry logistic regression model was performed, adjusting *a priori* for race/ethnicity and poverty status in 1979. Despite past evidence that without intervention adult literacy is for the most part, fixed,[32] bivariate analysis revealed variation in RGL by age at reading assessment. For this reason, age at time of reading assessment in 1980 was also included in all models. All analyses were performed using Stata statistical software.[33]

RESULTS

Women in the military and poor white supplements who had been dropped from the NLSY (n=1,331), those who were missing ASVAB scores (n=268), and those without parity data in 2006, 2008, and 2010 (n=695) were excluded, resulting in an analytic sample of 4,025 women (64% of women enrolled in NLSY). Those with parity data varied from those missing parity data on several variables of interest (Table 1). Non-respondents were more likely to have higher RGL and lower parity than respondents.

Table 1. Differences between those missing parity data and those with parity data

	Not Missing Parity (4,025)		Missing Parity (659)		p-value
	Frequency	Percent	Frequency	Percent	
Reading Grade Level (RGL)					0.017

<5th grade	572	14.2	64	9.7	
5th-6th grade	562	14.0	86	13.1	
7th-8th grade	653	16.2	107	16.2	
9th-11th grade	1,338	33.2	234	35.5	
12th+ grade	900	22.4	168	25.5	
<i>Race/ethnicity</i>					0.008
Hispanic	774	19.2	132	20.0	
Black	1,258	31.3	167	25.3	
Non-Black, non-Hispanic	1,993	49.5	360	54.6	
<i>HS degree in 1985</i>					<0.0001
No	689	17.1	85	12.9	
Yes	3,251	80.8	482	73.1	
<i>Age in 1980 (years)</i>					0.157
15	345	8.6	54	8.2	
16	531	13.2	104	15.8	
17	573	14.2	82	12.4	
18	543	13.5	98	14.9	
19	544	13.5	72	10.9	
20	497	12.4	81	12.3	
21	416	10.3	83	12.6	
22	442	11.0	69	10.5	
23	78	1.9	7	1.1	
<i>Average (mean age)</i>		18.0	16.7		
<i>Poverty status at age 14</i>					<0.0001
In poverty	1,021	25.4	129	19.6	
Not in poverty	4,025	69.4	473	71.8	

* p-values reported for Pearson's chi-squared test
 Note: percentages do not add to 100% in all cases

Among eligible participants, 49.5% were non-Black, non-Hispanic, 31.3% were Black, and 19.2% were Hispanic (Table 2). The majority of participants (69.4%) were not in poverty from 1978 to 1979. The average age at reading assessment in 1980 was 19.2 years of age, while the average RGL in that year was 9.7; 14.21% had a RGL of less than 5th, 14.0% 5th to 6th grade, 16.2% 7th to 8th grade, 33.2% 9th to 11th grade, and 22.4% 12th grade or greater. By 1985, 80.8% of participants had a high school degree or GED. In 2010, the average woman had 2.1 children; 15.8% of women had no children, 16.5% one, 34.2% two, 20.8% three, 8.3% four, 2.7% five, 1.1% six, 0.4% seven, and 15 (.4%) women had 8 or more children. One hundred and seventy-three women (4.3%) were grand multiparous.

Table 2. Participant Characteristics

	Frequency	Percent
<i>Race/ethnicity</i>		
Hispanic	774	19.2
Black	1,258	31.3
Non-Black, non-Hispanic	1,993	49.5
<i>Poverty status at 14</i>		
In poverty	1,021	25.4
Not in poverty	2,795	69.4
<i>Average age in 1980</i>		
In 1980		18.24
In 2010		45.05
<i>Reading Grade Level (RGL)</i>		
<5th grade	572	14.2
5th-6th grade	562	14.0
7th-8th grade	653	16.2
9th-11th grade	1,338	33.2
12th+ grade	900	22.4
<i>HS degree in 1985</i>		
No	689	17.1

	Yes	3,251	80.8
<i>Parity</i>			
	0	634	15.8
	1	658	16.4
	2	1,376	34.2
	3	839	20.8
	4	335	8.3
	5	108	2.7
	6	44	1.1
	7	16	0.4
	8	7	0.2
	9	4	0.1
	10	2	0.1
	11	2	0.1
<i>Grand multiparous (≥5 births)</i>			
	Yes	173	4.3
	No	3,852	95.7

Note: Percentages do not add to 100% in all cases.

Bivariate analyses demonstrated differences between women in varying RGL categories (Table 3). Among participants, compared with those in highest RGL category, women with a RGL lower than fifth grade were more likely to be Black or Hispanic (57.6% and 29.2% versus 9.2% and 10.2% respectively), in poverty in 1979 (55.8% versus 7.6%), have a higher average number of siblings (5.4 versus 2.9) and a higher average parity (2.7 versus 1.8). Furthermore, women in the lowest RGL category were also more likely to be grand multiparous than those in the highest RGL category (9.6% versus 2.4%).

Table 3. Cohort by Reading Grade Level

Reading Grade Level	<5 th N (%)	5 – 6 th N (%)	7 – 8 th N (%)	9 – 11 th N (%)	≥12 th N (%)	P-value*
Race/Ethnicity						<0.0001
Hispanic	161 (28.2%)	159 (28.3%)	151 (23.1%)	211 (15.8%)	211 (10.2%)	
Black	329 (57.6%)	287 (51.1%)	279 (42.7%)	280 (20.9%)	83 (9.2%)	
Non-Black/Hispanic	82 (14.3%)	116 (20.6%)	223 (34.2%)	847 (63.3%)	725 (80.6%)	
In Poverty 1979	319 (55.8%)	233 (41.5%)	186 (28.5%)	215 (16.1%)	68 (7.6%)	<0.0001
Siblings (average)	5.4	4.7	4.3	3.5	2.9	0.001
Parity (average)	2.7	2.3	2.0	1.9	1.8	0.001
Grand Multiparous	55 (9.6%)	41 (7.3%)	24 (3.7%)	31 (2.3%)	22 (2.4%)	<0.0001

* p-values reported for Pearson's chi-squared test and Kruskal-Wallis one-way analysis of variance test

Note: Percentages do not add to 100% in all cases

After adjustment for age at reading assessment, race/ethnicity, and poverty status, the odds of grand multiparity was 2.5 times (95% CI: 1.4 – 4.5) and 2.0 times higher (95% CI: 1.1 – 3.6) in the lowest two RGL categories respectively compared to the highest RGL category ($\geq 12^{\text{th}}$ grade, Table 4). Additionally, the adjusted odds of grand multiparity was 2.0 times higher (95% CI: 1.26 – 3.12) for women of Hispanic ethnicity compared to the odds of grand multiparity in non-Hispanic/non Black women.

Table 4. Reading Grade Level (RGL) and Risk of Grand Multiparity, Adjusted for Covariates

	Odds Ratio	(95% CI)	p-value
RGL (reference: $\geq 12^{\text{th}}$)			
<5th	2.50	(1.39 – 4.51)	0.002
5th – 6th	2.01	(1.11 – 3.62)	0.021
7th – 8th	1.07	(0.57 – 2.01)	0.835
9th – 11th	0.82	(0.47 – 1.44)	0.488
Race/ethnicity (reference : non-Black, non-Hispanic)			
Hispanic	1.99	(1.26 – 3.13)	0.003
Black	1.50	(0.96 – 2.35)	0.078
Poverty status (reference: not in poverty)			
	1.35	(0.95 – 1.92)	0.097
Age in 1980			
	1.00	(0.96 – 1.05)	0.868

DISCUSSION

This study of more than 4,000 women followed over three decades demonstrated that early-life literacy is associated with parity in a stepwise manner. Low literacy is a predictor of grand multiparity among US women, even after controlling for identified confounders. Those with the lowest early-life literacy are at the highest risk for grand multiparity; those with less

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3 than a seventh or fifth grade reading level at the time of assessment were 2.0 to 2.5 times more
4 likely to be grand multiparous at the end of the reproductive lifecourse respectively compared to
5 those with a 12th grade or greater RGL. These results provide important additions to the
6 understanding of literacy as a distinct social determinant of health across the lifecourse in a high
7 income country and echo findings from low and middle income countries.[17, 18]
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11 We also found that after controlling for early-life literacy status, Hispanic women are at
12 an increased risk of grand multiparity compared with non-white, non-Hispanic women. Despite
13 this finding, we did not find evidence for an interaction between race/ethnicity and literacy in
14 contrast to previous work that found an interaction between these variables in the risk of teenage
15 childbearing in a US sample.[16] Additional research is needed to clarify the relationships
16 between race/ethnicity, reproductive outcomes, and early-life literacy.
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30 Increased appreciation of the influence of social determinants on health outcomes has led
31 to new efforts to incorporate these forces into primary and community health.[11, 12] Their
32 contribution to health across the lifecourse raises the question of what novel interventions can be
33 implemented to alter health trajectories. Literacy, because it is modifiable, has particular
34 potential in this regard and some efficacious interventions have been implemented.[13, 14]
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LIMITATIONS

This study had several limitations. First NLSY-79 participants self-reported total parity in 2010, which could be vulnerable to reporting bias. It is unlikely however that this would result in a systematic bias as reporting of such major life events has been found to be accurate.[34, 35] Second, we made the assumption that early-life literacy measured in 1980 was stable over the

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3 course of the study, which does not account for potential changes in RGL over a woman's life.
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5 This assumption is supported by a large body of educational research indicating that few
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7 individuals experience dramatic changes in literacy over time.[36] We also controlled for
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9 possible effects of changes in literacy for women whose literacy was assessed at an early age by
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11 including age at assessment in the multivariate model. Furthermore, we made use of a true
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13 measure of literacy, the ASVAB, as opposed to limited proxy or brief screening measures most
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15 commonly employed in studies of the connection between literacy and health [3, 4]. Third, we
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17 were unable to control for cultural factors that may be related to childbearing. Such cultural
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19 factors, including religiosity may account for the persistent increased risk of grand multiparity in
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21 Hispanic women as compared with non-Black, non-Hispanic women. The association between
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23 high fertility and low early-life literacy among Hispanic women may be confounded by cultural
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25 factors, including religion. Future work should further investigate the role of cultural factors on
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27 reproductive outcomes. Finally, non-respondents were different from study participants in total
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29 parity. However, we do not believe that their omission would result in a change in our
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31 fundamental findings since non-respondents had higher early-life literacy and fewer children
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33 than respondents, which would result in a larger estimate of the association between early-life
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35 literacy and parity if included.
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43 CONCLUSIONS

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46 Contributing to the growing literature demonstrating a relationship between literacy and
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48 health, we found that early-life literacy is associated with cumulative total births among women
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50 in the US. Grand multiparity, which has associated health risks,[6-8] was elevated among the
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52 lowest literacy groups when compared to those with greater than high school literacy level.
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55 These findings represent strong evidence that literacy is a critical social determinant of health
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3 independent of other established factors known to influence health outcomes. The current study
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5 represents evidence for the influence of literacy on childbirth, the single greatest cause for
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7 hospitalization among adults under age 45.[37] The current work contributes to the field of
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9 research in literacy and health by: 1) focusing on childbearing, 2) providing evidence of
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11 cumulative effects through the lifecourse, and 3) making use of true measures of literacy
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13 providing precise and comparable reading levels. These finding strengthen the call for additional
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15 attention to be paid to literacy in the development of interventions and policy that aims to
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17 influence health outcomes. This work also shows the importance of attending to literacy needs of
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19 reproductive age women.
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27 WHAT IS ALREADY KNOWN ON THIS SUBJECT?

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29 Literacy has been associated with a range of health outcomes, including parity, in cross sectional
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31 and short longitudinal studies. However, there have been nearly no investigations of the role of
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33 early-life literacy in reproductive health outcomes such as childbearing over the lifecourse.
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39 WHAT DOES THIS STUDY ADD?

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41 Literacy measured at the beginning of the reproductive life of women in the US is associated
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43 with cumulative childbearing over their full reproductive life span (age 18-45). The risk of
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45 having five or more children is more than twice as high for women with primary school as
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47 compared to those with greater than high school literacy after controlling for other known
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49 determinants of health. These findings have implications for clinicians and those developing
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51 policy to improve reproductive health.
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COMPETING INTERESTS

The authors report no competing interests.

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No additional data available.

CONTRIBUTORSHIP STATEMENT

JWS conceived of the study, executed analyses, and was the primary manuscript writer. RF and IB advised and contributed to study execution and to the writing. FS advised and contributed to analyses and manuscript writing.

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STROBE Statement—checklist of items that should be included in reports of observational studies

Note from authors – we have used the following checklist to prepare and edit our manuscript.

	Item No	Recommendation	Page number
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	n/a
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	5
		(d) <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	n/a
		(e) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	n/a

Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	n/a
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	n/a
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Table 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

BMJ Open

A Cohort Study of Early Literacy and Childbearing Over the Reproductive Lifecourse

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ABSTRACT

INTRODUCTION: Literacy is linked to a range of health outcomes, but its association with reproductive health in high-income countries is not well understood. We assessed the relationship between early-life literacy and childbearing across the reproductive lifecourse in the US.

STUDY DESIGN: A prospective cohort design was employed to assess early-life literacy and subsequent childbearing, using data from the National Longitudinal Survey of Youth 1979. US youth aged 14-22 in 1979, including 6,283 women, were surveyed annually through 1994 and biannually thereafter. Literacy was assessed in 1980 using the Armed Services Vocational Aptitude Battery Reading Grade Level (RGL). Cumulative childbearing and grand multiparity (≥ 5 births) was assessed in 2010. Summary statistics, chi-square, Kruskal-Wallis, test for trend, and logistic regression were used.

RESULTS: Of 6,283 women enrolled, 4,025 (64%) had complete data and were included in the analyses. In 1980, these women were on average 18 years old and in 2010 were 45. Median cumulative parity decreased for each RGL and ranged from 3.0 ($<5^{\text{th}}$ grade) to 2.0 ($>12^{\text{th}}$ grade) ($p=0.001$). Adjusting for race/ethnicity, poverty status, whether a woman had had a child in 1980, and age in 1980, odds of grand multiparity were 1.9 (95% CI: 1.1 – 3.5) and 1.8 (95% CI: 1.0 – 3.3) greater among women with $<5^{\text{th}}$ or $5^{\text{th}}-6^{\text{th}}$ grade literacy compared with those $\geq 12^{\text{th}}$ literacy.

DISCUSSION: In the US, early-life literacy is associated with total parity over a woman's lifecourse. Literacy is a powerful social determinant of reproductive health in this high income nation just as it has been shown to be in low income nations.

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ARTICLE SUMMARY

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This is a longitudinal study of more than 4,000 women from across race/ethnic and socio-economic groups and through their full reproductive span, which allows a lifecourse perspective to be applied to the question of how literacy relates to health.
- This study extends the evidence that literacy is a powerful social determinant of health, including childbearing, a key reproductive health outcome, and this relationship holds true in a high income country and independent of educational attainment and poverty.
- Unlike most studies assessing the linkage of literacy and health, literacy was assessed here using a robust and precise measure of reading skill rather than a simple and limited screening tool.
- While study non-respondents were somewhat different from those included in the analyses, it is unlikely that this difference affects results; non-respondents were less than a third of the full sample and were more likely to have higher literacy, making our estimates conservative.
- Additional research is needed to assess whether this relationship extends to other reproductive health outcomes.

INTRODUCTION

Literacy, the ability to use written text and numeracy, is primarily formed as a result of early-life educational inputs and is associated with poor health behaviors and outcomes at different life stages from adolescence to old age.[1-4] Despite these two important findings, little research has explored the impact of limited literacy prospectively on trajectories of health through the lifecourse; instead, nearly all research examining literacy and health has assessed the associations between the two at a single point in time or in a very narrow temporal window, which reduces the ability to assess a causal relationship between these variables.[1-4] A number of studies have examined the impact of literacy on health, however, these studies have focused on older adults whose past experiences, exposures, and health behaviors may confound the associations.[1, 4] Lifecourse epidemiology has made evident the importance of taking a longitudinal approach to understanding the magnitude of effect that social factors have on health and to inform interventions both upstream (earlier in the life course) and downstream (later in the life course) to moderate the impact of these social factors have on health trajectories, including on the critical areas of maternal, child, and reproductive health.[5-8]

Although historically much attention has been paid to the effect of educational attainment on health outcomes, there has been an increasing awareness of the independent role of literacy on health. [9, 10] Literacy is an assessment of actual skill and is an independent risk factor for outcomes traditionally related to educational attainment.[1, 11-12] Furthermore, modifiable social determinants of health are of interest to primary and community health policy because of their association with racial and economic disparities in health outcomes.[13, 14] Because literacy is a modifiable skill, it opens the potential for novel interventions.[15, 16] Despite this, most research in the relationship between health and literacy focus on short-term risks and

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3 consequences, such as misreading medical directions. As a result, these studies fall short of
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5 addressing the larger cumulative risk to health that arises from chronic exposures to disadvantage
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7 secondary to low literacy through life and the greater role that literacy could play as a social
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9 determinant of health. In addition, nearly all research on this topic within high-income nations
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11 has used instruments with severely limited capacity to measure literacy, instead using rapid
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13 screening assessments of risk of low literacy, reducing the ability to attribute health outcomes to
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15 specific levels of literacy skills.[3, 8] In order to inform public policy and interventions there is a
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17 great need to carry out longitudinal studies, which assess the magnitude of effect of literacy on
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19 health outcomes independent of other established social determinants of health and within a
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21 lifecourse framework.
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27 Childbearing plays a major role in women's health and is the most common reason for
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29 hospitalization in the US among adults under age 45.[17] While most childbirths do not affect
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31 the health of mothers, severe maternal morbidity affects more than 60,000 U.S. women
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33 annually[18] and the maternal mortality ratio is higher in the US than other high income
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35 nations.[19] Furthermore, unintended pregnancy represents a very high percentage of births in
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37 high income nations, particularly in vulnerable populations at risk for poor birth outcomes.[9, 10]
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39 Girls in the US with below-average reading skill at age eleven have increased risk of subsequent
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41 teenage childbearing compared with girls with average reading skill, even after adjusting for a
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43 range of social factors.[20] In the developing world, associations between low literacy and
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45 increased birth rates have been observed at the district, state, and individual level.[21-23]
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51 Despite these findings, there has been little research in high-income nations examining
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53 the influence of early-life literacy on subsequent reproductive health outcomes such as
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55 childbearing.[24] Increased parity, or number of total births, increases the cumulative risk of
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3 poor health outcomes for women; grand multiparity (delivering 5 or more children) is associated
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5 with poor health outcomes for women and their children, including obstetric complications,
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7 neonatal morbidity and perinatal mortality.[25] In 2011, 190,000 U.S. women delivered a fifth,
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9 or higher order child, making up 4.8% of all U.S. births that year.[26, 27] While higher parity is
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11 associated with low-socioeconomic status and low educational attainment[28] and may be
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13 associated with cultural norms the relationship between early-life low literacy and grand
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15 multiparity has not been explored. In this study we sought to assess the association between
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17 early-life literacy and parity through women's full reproductive lifecourse. We hypothesized that
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19 women with lower early-life literacy levels would be at an increased risk of grand multiparity
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21 compared with those with higher early-life literacy levels.
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26 27 **METHODS**

28 29 **DATA**

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31 Data from the National Longitudinal Survey of Youth 1979 (NLSY-79),[29] a
32
33 representative probability sample of US men and women born between 1957 and 1964, were
34
35 used to assess the relationship between early-life literacy and risk of grand multiparity across a
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37 woman's reproductive lifecourse. These data has been used to assess a range of social influences
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39 on birth and birth outcomes.[30, 31] In 1979, the first survey year, 6,283 women were enrolled.
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41 Participants were surveyed annually through 1994 and biannually thereafter. Survey data through
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43 2010 was used in analyses. Retention in the survey through 2010 exceeded 80%.
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48 The survey followed women from 1979 when they were 14-22 years old to 2010 when
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50 they were 45-53 years old. These data provided the novel opportunity to examine the full female
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52 reproductive lifecourse, commonly accepted as age 15 to 45.[32] Women missing data on early-
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3 life literacy or total parity, including those dropped from the NLSY prior to 2010, were excluded
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5 from the analysis.
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8 This study was approved by the University of Pennsylvania's Institutional Review Board.
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10 OUTCOME MEASURES

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12 Parity was measured in each survey year. Total cumulative parity for each woman in
13 2010 was used to create the variable grand multiparity defined as five or more births. To
14 decrease the effect of non-response bias, for those women missing parity data in 2010, total
15 parity in 2008 or 2006 was used; less than 1% of women with parity data in 2010 had a child
16 between 2006 and 2010.
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24 EXPOSURE MEASURES

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26 Department of Defense Reading Grade Level (RGL) in 1980 was used as the measure of
27 early-life literacy. RGL categories were created from the Armed Services Vocational Aptitude
28 Battery (ASVAB) using a previously validated conversion method.[33] The ASVAB is a text-
29 based measure of a range of cognitive skills with rigorously assessed psychometric properties.
30 Components of this well validated instrument have been used in a range of health studies.[34,
31 35] This measure of early-life literacy was used to construct an ordinal variable for literacy
32 based on commonly accepted RGL cut-points (<5th grade, 5th to 6th grade, 7th to 8th grade, 9th to
33 11th grade, and $\geq 12^{\text{th}}$ grade).
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46 COVARIATES

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48 Using an adaptation of the behavioral model described by Andersen, we identified
49 maternal predisposing and enabling factors to predict grand multiparity.[36] This study focused
50 on early-life factors and covariates that did not change over time (time-invariant), as opposed to
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3 covariates that change with time. Predisposing factors included early-life literacy, as well as age
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5 at reading assessment, and race/ethnicity. Income was included as an enabling factor.
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8 Participants self-reported their age in 1980 when the ASVAB was administered.
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10 Race/ethnicity was assigned in 1979 by NLSY interviewers and reported as Hispanic; Black; or
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12 non-Black, non-Hispanic. Poverty status was assessed for every participant in each of the survey
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14 years. Participants' family income was compared with the years' Poverty Income Guidelines
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16 created by the U.S. Department of Health and Human Services. The respondent's family size,
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18 whether or not they lived on a farm, and their state of residence were used in assessing poverty
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20 status. In following with a lifecourse approach, poverty status in 1979 was used in this study.
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22 Poverty status was dichotomized as: in poverty or not in poverty. Whether or not a woman was
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24 parous prior to 1980 (i.e. before the literacy assessment was administered) was dichotomized as:
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26 parous or nulliparous.
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31 STATISTICAL ANALYSES

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34 Summary statistics, including frequencies, percentages, means, and standard deviations
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36 were used to describe the study population. To examine the relationship between presence or
37
38 absence of grand multiparity (yes/no) and predisposing and enabling factors, the chi-square and
39
40 Kruskal-Wallis tests were used for categorical and continuous variables, respectively. To
41
42 determine the independent association of RGL to grand multiparity, a logistic regression was
43
44 employed, adjusting *a priori* for race/ethnicity and poverty status in 1979. Despite past evidence
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46 that without intervention adult literacy is for the most part, fixed,[37] bivariate analysis revealed
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48 variation in RGL by age at reading assessment. For this reason, age at time of reading assessment
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50 in 1980 was also included in all models. Furthermore, having a child prior to age at reading
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52 assessment may confound the relationship between RGL and grand multiparity and was also
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included in all models. A Cochran-Armitage test for trend was employed to test whether there was a decreasing trend in multiparity with increasing RGL. Analyses were performed using Stata statistical software.[38]

RESULTS

Women in the military and poor white women who had been oversampled and subsequently dropped from the NLSY prior to 2010 (n=1,331), those who were missing ASVAB scores (n=268), and those without parity data in 2006, 2008, and 2010 (n=659) were excluded, resulting in an analytic sample of 4,025 women (64% of women enrolled in NLSY). Those with parity data varied from those missing parity data on several variables of interest (Table 1). Those missing parity data had higher RGL and lower parity than respondents. Similarly, the group missing RGL had higher proportions of Black and Hispanic women, without a high school degree in 1985, and in poverty at age 14 compared with respondents.

Table 1. Differences between those missing parity data and those with parity data

	Not Missing Parity (4,025)		Missing Parity (659)		Missing ASVAB (268)	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
<i>Reading Grade Level (RGL)</i>						
<5th grade	572	14.2	64	9.7	-	-
5th-6th grade	562	14.0	86	13.1	-	-
7th-8th grade	653	16.2	107	16.2	-	-
9th-11th grade	1,338	33.2	234	35.5	-	-
12th+ grade	900	22.4	168	25.5	-	-
<i>Race/ethnicity</i>						
Hispanic	774	19.2	132	20.0	74	27.6
Black	1,258	31.3	167	25.3	52	19.4
Non-Black, non-Hispanic	1,993	49.5	360	54.6	142	53.0
<i>HS degree in 1985</i>						

	No	689	17.1	85	12.9	85	31.7
	Yes	3,251	80.8	482	73.1	60	22.3
<i>Age in 1980 (years)</i>							
	15	345	8.6	54	8.2	5	1.9
	16	531	13.2	104	15.8	15	5.6
	17	573	14.2	82	12.4	17	6.3
	18	543	13.5	98	14.9	18	6.7
	19	544	13.5	72	10.9	20	7.5
	20	497	12.4	81	12.3	19	7.1
	21	416	10.3	83	12.6	19	7.1
	22	442	11.0	69	10.5	22	8.2
	23	78	1.9	7	1.1	10	3.7
<i>Average (mean age)</i>							
		18.0		16.7		19.3	
<i>Poverty status at age 14</i>							
	In poverty	1,021	25.4	129	19.6	76	61.6
	Not in poverty	4,025	69.4	473	71.8	165	28.4
<i>Parous in 1980</i>							
	Parous	756	23.9			34	28.3
	Nulliparous	2,404	76.1			86	71.7

Note: percentages do not add to 100% in all cases

Among eligible participants, 49.5% were non-Black, non-Hispanic, 31.3% were Black, and 19.2% were Hispanic. The majority of participants (69.4%) were not in poverty from 1978 to 1979. The average age at reading assessment in 1980 was 19.2 years of age, while the average RGL in that year was 9.7; 14.21% had a RGL of less than 5th, 14.0% 5th to 6th grade, 16.2% 7th to 8th grade, 33.2% 9th to 11th grade, and 22.4% 12th grade or greater. By 1985, 80.8% of participants had a high school degree or GED. In 2010, the average woman had 2.1 children; 15.8% of women had no children, 16.5% one, 34.2% two, 20.8% three, 8.3% four, 2.7% five, 1.1% six, 0.4% seven, and 15 (.4%) women had 8 or more children. One hundred and eighty-three women (4.6%) were grand multiparous. Participant characteristics differed between those who were grand multiparous and those that were not (Table 2). Greater proportions of women who were grand multiparous were Hispanic, Black, in poverty 1980, did not have a high school degree in 1985, and were parous in 1980 compared with non-grand multiparous women.

Table 2. Participant Characteristics

	Non-Grand Multiparous (n=3,852)		Grand Multiparous (n=183)	
	Frequency	Percent	Frequency	Percent
<i>Race/ethnicity</i>				
Hispanic	717	18.7	57	31.2
Black	1,182	30.8	76	41.5
Non-Black, non-Hispanic	1,943	50.6	50	27.3
<i>Poverty status at 14</i>				
In poverty	942	24.5	79	43.2
Not in poverty	2,697	70.2	98	53.6
<i>Average age in 1980</i>				
In 1980		18.25		18.15
In 2010		45.03		45.48
<i>Reading Grade Level (RGL)</i>				
<5th grade	513	13.4	59	32.2

5th-6th grade	519	13.5	43	23.5
7th-8th grade	628	16.4	25	13.7
9th-11th grade	1,305	34.0	33	18.0
12th+ grade	877	22.8	23	12.6
<i>HS degree in 1985</i>				
No	606	15.8	83	45.4
Yes	3,155	82.0	96	52.5
<i>Parous in 1980</i>				
Parous	678	18.7	78	45.1
Nulliparous	2,943	81.3	95	54.9

Note: Percentages do not add to 100% in all cases.

Bivariate analyses demonstrated differences between women in varying RGL categories (Table 3). Among participants, women with a RGL lower than fifth grade were likely to be Black or Hispanic (57.6% and 29.2% respectively), in poverty in 1979 (55.8%), have a high average number of siblings (5.4) and a high average parity (3.0). Women in the highest RGL category were unlikely to be Black or Hispanic (9.2% and 10.2%, respectively), in poverty in 1979 (7.6%), have a lower median number of siblings (2.0), and had a lower median parity (2.0). Furthermore, 10.3% of women in the lowest RGL category were grand multiparous and 2.6% of those in highest RGL were grand multiparous. Forty-two percent of those in the lowest RGL were parous before 1980, while only 13.9% of those in the highest RGL were parous in 1980.

Table 3. Cohort by Reading Grade Level

Reading Grade Level	<5 th N (%)	5 – 6 th N (%)	7 – 8 th N (%)	9 – 11 th N (%)	≥12 th N (%)	P-value*
Race/Ethnicity						<0.0001*
Hispanic	161 (28.2)	159 (28.3)	151 (23.1)	211 (15.8)	211 (10.2)	
Black	329 (57.6)	287 (51.1)	279 (42.7)	280 (20.9)	83 (9.2)	
Non-Black/Hispanic	82 (14.3)	116 (20.6)	223 (34.2)	847 (63.3)	725 (80.6)	
In Poverty 1979	319 (55.8)	233 (41.5)	186 (28.5)	215 (16.1)	68 (7.6)	<0.0001

Siblings (median)	5.0	4.0	4.0	3.0	2.0	0.001**
Parity (median)	3.0	2.0	2.0	2.0	2.0	0.001**
Parous in 1980	207 (42.0)	126 (27.4)	132 (25.6)	200 (19.3)	91 (13.9)	<0.0001*
Grand Multiparous	59 (10.3%)	43 (7.7%)	25 (3.8%)	33 (2.5%)	23 (2.6%)	<0.0001**

* p-values reported for Pearson's chi-squared test comparing all RGL

** p-values reported for Kruskal-Wallis test comparing all RGL

Note: Percentages do not add to 100% in all cases

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After adjustment for age at reading assessment, race/ethnicity, poverty status, and parous in 1980, the odds of grand multiparity was 1.94 times (95% CI: 1.1 – 3.5) and 1.84 times higher (95% CI: 1.0 – 3.3) in the lowest two RGL categories respectively compared to the highest RGL category ($\geq 12^{\text{th}}$ grade, Table 4). Additionally, the adjusted odds of grand multiparity was 2.99 times higher (95% CI: 1.3 – 3.2) for women of Hispanic ethnicity compared to the odds of grand multiparity in non-Hispanic/non Black women. Compared to those who were nulliparous in 1980, those who were had 2.86 times (95% CI: 2.0 – 4.0) the odds of grand multiparity. A Cochran-Armitage test for trend showed a significant decreasing trend in grand multiparity as RGL increased ($p < 0.001$). The final bivariate model was also run with only those not missing 2010 parity data and results did not vary from the model presented in Table 4, except that the effect of Hispanic ethnicity was not as great (OR: 2.01, 95% CI: 1.27 -3.17).

Table 4. Reading Grade Level (RGL) and Risk of Grand Multiparity, Adjusted for Covariates

	Odds Ratio	(95% CI)	p-value
RGL (reference: $\geq 12^{\text{th}}$)			
<5th	1.94	(1.07 – 3.53)	0.029
5th – 6th	1.84	(1.02 – 3.32)	0.044
7th – 8th	0.97	(0.51 – 1.82)	0.914
9th – 11th	0.76	(0.43 – 1.34)	0.350
Race/ethnicity (reference : non-Black, non-Hispanic)			
Hispanic	2.99	(1.27 – 3.17)	0.003
Black	1.37	(0.87 – 2.15)	0.178
Poverty status (reference: not in poverty)	1.21	(0.85 -1.73)	0.300
Age in 1980	0.98	(0.95 – 1.02)	0.319
Parous in 1980 (reference: nulliparous)	2.86	(2.03 – 4.01)	<0.0001

DISCUSSION

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This study of more than 4,000 women followed over three decades demonstrated that early-life literacy is associated with parity in a stepwise manner. Low literacy is a predictor of grand multiparity among US women, even after controlling for identified confounders. Those with the lowest early-life literacy are at the highest risk for grand multiparity; those with less than a seventh or fifth grade reading level at the time of assessment were nearly two times more likely to be grand multiparous at the end of the reproductive lifecourse respectively compared to those with a 12th grade or greater RGL. These results provide important additions to the understanding of literacy as a distinct social determinant of health across the lifecourse in a high income country and echo findings from low and middle income countries.[22, 23]

We also found that after controlling for early-life literacy status, Hispanic women are at an increased risk of grand multiparity compared with non-white, non-Hispanic women. In contrast to previous work that found an interaction between these variables in the risk of teenage childbearing in a US sample we did not find evidence for an interaction between race/ethnicity and literacy in this sample of women somewhat later in their lifecourse.[21] Additional research is needed to clarify the relationships between race/ethnicity, culture, reproductive outcomes, and early-life literacy.

Increased appreciation of the influence of social determinants on health outcomes has led to new efforts to incorporate these forces into primary and community health.[13, 14] Their contribution to health across the lifecourse raises the question of what novel interventions can be implemented to alter health trajectories. Literacy, because it is modifiable, has particular potential in this regard and some efficacious interventions have been implemented.[15, 16] Additional work is needed to assess the benefits of these strategies on health outcomes, to determine the causal pathways through which literacy effects health, and to explore additional

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3 opportunities to improve health and reduce health disparities through literacy, including
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5 assessment of timing of births across women's reproductive lifecourse.
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8 LIMITATIONS

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10 This study had several limitations. First NLSY-79 participants self-reported total parity in
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12 2010, which could be vulnerable to reporting error resulting in outcome misclassification. It is
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14 unlikely however that this would result in a systematic bias as reporting of such major life events
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16 has been found to be accurate.[39, 40] Similarly, there is potential for bias due to outcome
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18 misclassification because we used 2008 and 2006 parity for those missing 2010 parity.
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20 However, when final model results were re-run including only those respondents not missing
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22 2010 parity, results were similar. For this reason, we are confident that using 2008 and 2006
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24 parity did not introduce significant bias. Second, we made the assumption that early-life literacy
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26 measured in 1980 was stable over the course of the study, which does not account for potential
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28 changes in RGL over a woman's life. This assumption is supported by a large body of
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30 educational research indicating that few individuals experience dramatic changes in literacy over
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32 time.[41] We also controlled for possible effects of changes in literacy for women whose literacy
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34 was assessed at an early age by including age at assessment in the multivariate model.
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36 Furthermore, we made use of a true measure of literacy, the ASVAB, as opposed to limited
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38 proxy or brief screening measures most commonly employed in studies of the connection
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40 between literacy and health [3, 4]. Third, there may have been unmeasured confounding. We
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42 were unable to control for cultural factors that may be related to childbearing. Such cultural
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44 factors, including religiosity, may account for the persistent increased risk of grand multiparity in
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46 Hispanic women as compared with non-Black, non-Hispanic women. The association between
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48 high fertility and low early-life literacy among Hispanic women may be confounded by cultural
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3 factors that lead to a preference for larger families. Similarly, we focused on time-invariant and
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5 early-life covariates. Potential time-varying confounders, including employment status, marital
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7 status, income, and health status, were not controlled. Future work should further investigate the
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9 role of cultural factors on reproductive outcomes and time-varying covariates. Finally, non-
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11 respondents were different from study participants in total parity. However, we do not believe
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13 that their omission would result in a change in our fundamental findings since non-respondents
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15 had higher early-life literacy, and fewer children than respondents, which would result in a larger
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17 estimate of the association between early-life literacy and parity, if included.
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22 CONCLUSIONS

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24 Contributing to the growing literature demonstrating a relationship between literacy and health,
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26 we found that early-life literacy is associated with cumulative total births among women in the
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28 US. Grand multiparity, which has associated health risks,[6-8] was elevated among the lowest
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30 literacy groups when compared to those with greater than high school literacy level. These
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32 findings represent strong evidence that literacy is a critical social determinant of health
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34 independent of other established factors known to influence health outcomes. The current study
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36 represents evidence for the influence of literacy on childbirth, the single greatest cause for
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38 hospitalization among adults under age 45.[17] The current work contributes to the field of
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40 research in literacy and health by: 1) focusing on childbearing, 2) providing evidence of
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42 cumulative effects through the lifecourse, and 3) making use of true measures of literacy
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44 providing precise and comparable reading levels. These finding strengthen the call for additional
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46 attention to be paid to literacy in the development of interventions and policy that aims to
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48 influence health outcomes. Furthermore, this builds on the literature indicating that literacy
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50 should be considered an additional risk factor when creating policy to reduce maternal risk. This
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work affirms the importance of attending to literacy needs of reproductive age women and developing and testing literacy interventions appropriate to this population.

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COMPETING INTERESTS

The authors report no competing interests.

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DATA SHARING STATEMENT

No additional data available.

CONTRIBUTORSHIP STATEMENT

JWS conceived of the study, executed analyses, and was the primary manuscript writer. RF and IB advised and contributed to study execution and to the writing. FS advised and contributed to analyses and manuscript writing.

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STROBE Statement—checklist of items that should be included in reports of observational studies

Note from authors – we have used the following checklist to prepare and edit our manuscript.

	Item No	Recommendation	Page number
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	n/a
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	5
		(d) <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	n/a
		(e) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	n/a

Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	n/a
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	n/a
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Table 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16