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REVIEW ARTICLE

Romantic and sexual relationships of young adults born very preterm: An individual participant data meta-analysis

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Abstract

Aim: To compare romantic and sexual relationships between adults born very preterm (VP; <32 weeks of gestation) or with very low birth weight (VLBW; <1500 g) and at term, and to evaluate potential biological and environmental explanatory factors among VP/VLBW participants.

Methods: This individual participant data (IPD) meta-analysis included longitudinal studies assessing romantic and sexual relationships in adults (mean sample age ≥ 18 years) born VP/VLBW compared with term-born controls. Following PRISMA-IPD guidelines, 11 of the 13 identified cohorts provided IPD from 1606 VP/VLBW adults and 1659 term-born controls. IPD meta-analyses were performed using one-stage approach.

Results: Individuals born VP/VLBW were less likely to be in a romantic relationship (OR 0.49; 95% CI 0.31–0.76), to be married/cohabiting (OR 0.70, 95% CI 0.53–0.92), or to have had sexual intercourse (OR 0.21, 95% CI 0.09–0.36) than term-born adults. If sexually active, VP/VLBW participants were more likely to experience their first sexual intercourse after the age of 18 years (OR 1.93, 95% CI 1.24–3.01) than term-born adults. Among VP/VLBW adults, males, and those with neurosensory impairment were least likely to experience romantic relationships.

Conclusions: These findings reflect less optimal social functioning and may have implications for socioeconomic and health outcomes of adults born VP/VLBW.

Abbreviations: AD, aggregate data; BPD, bronchopulmonary dysplasia; CI, confidence interval; IPD, individual participant data; ISCED, International Standard Classification of Education; IVH, intraventricular haemorrhage; NSI, neurosensory impairment; OR, odds ratio; PEL, parental education level; VP, very preterm; VLBW, very low birth weight.

For affiliations refer to page 2523.

1 | INTRODUCTION

Being in an intimate partner relationship has been linked with beneficial health and well-being outcomes.[1–4] For example, married individuals tend to experience better physical and mental health, more wealth, and increased longevity than unmarried individuals.[3–5] Moreover, sexual activity has been shown to positively influence life satisfaction,[1,6] and to decrease the risk of coronary events.[7]

A recent meta-analysis reported that, compared with those born at term (i.e., ≥37 weeks of gestation), adults born very preterm (VP;<32 weeks of gestation), or with very low birth weight (VLBW; <1500 g) have fewer social relationships,[8] including not having a romantic partner or experienced sexual intercourse. However, this study used aggregated data and was unable to examine the influence of early biological and environmental risk factors on the outcomes studied.

VP/VLBW birth affects 1%–2% of all livebirths worldwide[9] and is associated with a range of neonatal complications, such as bronchopulmonary dysplasia[10] (BPD), or intraventricular haemorrhage[11] (IVH). These early complications have been linked to brain injury[12] and subsequent neurosensory impairments (NSI) in childhood, such as cerebral palsy, deafness, blindness, or cognitive impairments,[13,14] that may restrict social participation. Furthermore, brain alterations associated with VP/VLBW birth may encompass the "social brain" which include areas involved in understanding others.[15] Indeed, VP/VLBW birth is associated with a phenotype[16] that includes autistic and shyness traits,[17,18] and children born VP/VLBW have been reported to have poorer social competence and more peer relationship difficulties.[19,20]

Environmental factors, such as parental educational level, have been linked to some outcomes following VP/VLBW birth,[21] but it is unknown if they influence intimate partner relationships. Evolutionary perspectives of human mating suggest females mainly choose sexual and long-term partners due to their greater parental investment, and males in frail condition are less likely than females in similar condition to develop intimate partner relationships.[22,23] Preterm birth is thus associated with greater biological and psychosocial vulnerabilities.[24] On these grounds, we hypothesised that VP/VLBW adults would less frequently form romantic and sexual relationships compared with term-born individuals and differences would be greater in males and those with NSI.

In this study, we aimed to use individual participant data (IPD) meta-analysis to compare reported romantic and sexual relationship outcomes among adults born VP/VLBW and term-born peers, and to examine the contribution of early biological and environmental factors to later relationships outcomes among VP/VLBW adults.

Key Notes

- Adults born very preterm (VP) or with low birth weight (VLBW) have been reported to experience difficulties in establishing social relationship, but what factors contribute to it are unknown.
- Fewer adults born VP/VLBW report being in intimate partner relationships than their term-born peers, particularly those with a neurosensory impairment.
- Lack of intimate relationships may affect quality of life, socioeconomic, and health outcomes of adults born VP/VLBW, including starting a family.

2 | METHODS

2.1 | Protocol and registration

This IPD meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for individual participant data (PRISMA-IPD) guidelines[25] (Table S1) and was registered with PROSPERO (CRD42020168855).

2.2 | Eligibility criteria and search strategy

In this systematic review and IPD meta-analysis, cohorts were eligible for inclusion if they prospectively followed VP/VLBW and term-born participants from birth into adulthood (mean sample age ≥ 18 years), and if they measured at least one of the following outcomes in adulthood: romantic relationships (i.e., of any type: from dating to marriage); partnership status (married, cohabiting with partner, single, and separated/divorced), experience of sexual intercourse (ever/none), age of first sexual intercourse, or number of sexual partners. In total, 13 cohorts were eligible from the RECAP-preterm (Research on European Children and Adults Born Preterm, https://recap-preterm.eu/) and APIC (Adults Born Preterm Collaboration, https://www.apic-preterm.org) consortia, two research collaborations across Europe, North America, and Australasia. To investigate whether additional VP/VLBW birth cohort studies had assessed romantic and sexual outcomes, we included the 21 studies reviewed in the previous meta-analysis on social outcomes,[6] and the first author updated the search for articles published in PubMed, PsycINFO, and Web of Science from August, 2018 to April 28, 2023 (see Figure 1). The following keywords were used: (preterm* OR "low birth weight"), AND (adult*), and AND (romant* OR partner* OR marri* OR cohabit* OR sexual* OR intercourse). The search was limited to English language publications. Eligibility of studies for inclusion was assessed by two researchers (MM and RE), and disagreements were resolved by discussion.

2.3 | Study selection

Data dictionaries were obtained from each cohort within RECAP preterm and APIC consortia. All cohorts measured adult outcomes of interest and seven of the eight RECAP preterm adult cohorts (Table 1) were included in an IPD meta-analysis. The POPS study did not have a term-born control group but was included in VP/VLBW analyses assessing the influence of biological and environmental factors on romantic and sexual outcomes. Of the five potential APIC cohorts, the McMaster[26] and the Cleveland studies[27] were not able to

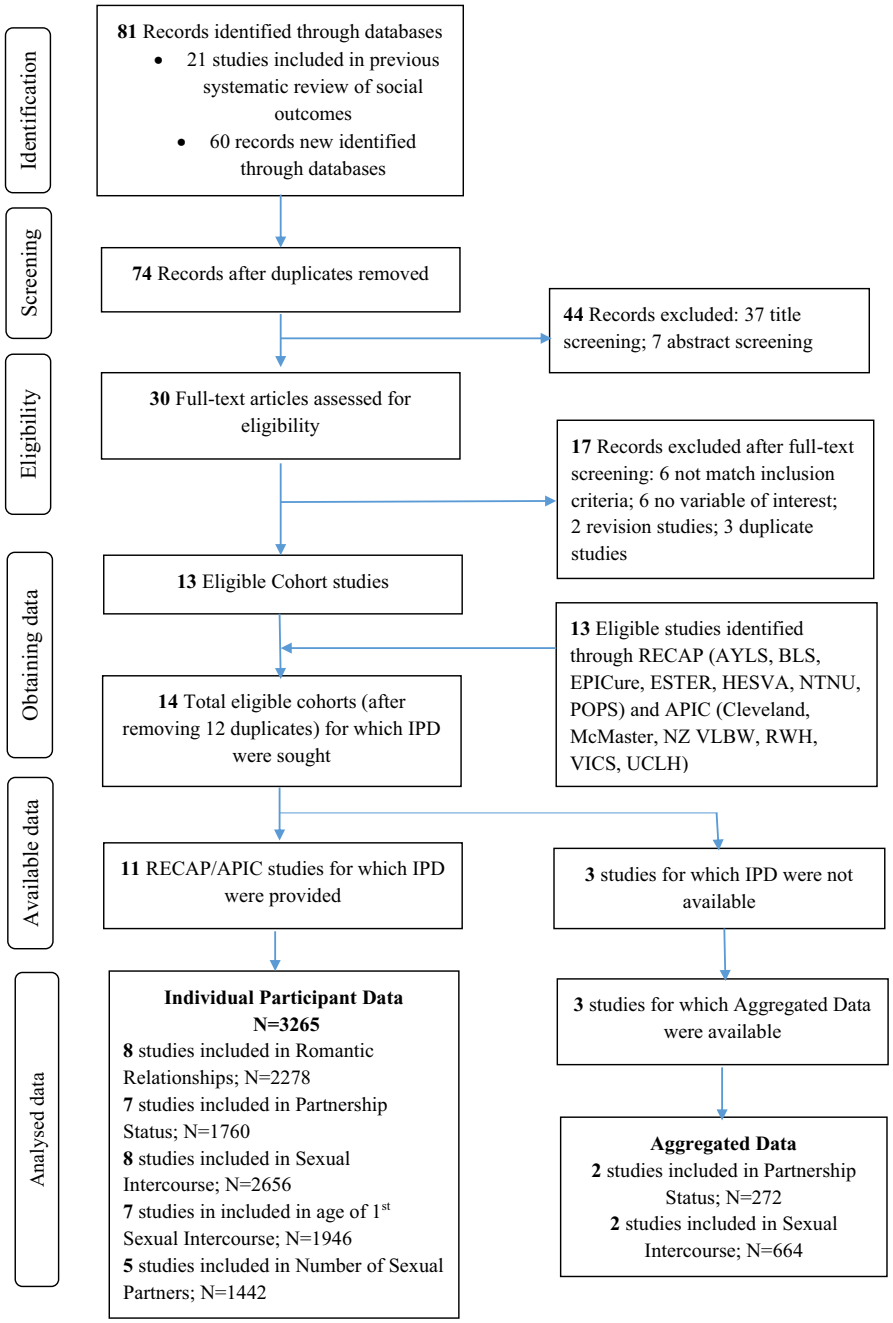


FIGURE 1 Flow diagram of studies included in the individual participant data (IPD) and aggregate meta-analyses. APIC, Adult Born Preterm International Collaboration; RECAP, Research of European Children and Adults Born Preterm; AYLS, Arvo Ylppö Longitudinal Study; BLS, Bavarian Longitudinal Study; ESTER, The Preterm Birth and Early Life Programming of Adult Health and Disease Study; EPICure, EPICure study; HESVA, Helsinki Study of Very Low Birth Weight Adults; NTNU, NTNU Low Birth Weight in a Lifetime Perspective study; NZ VLBW, New Zealand Very Low Birth Weight Study; POPS, Project on Preterm and Small for Gestational Age Infants; RWH, Royal Women's Hospital Study; UCLH, University College London Hospital Cohort Study; VICS, Victorian Infant Collaborative Study.

provide IPD. An additional Norwegian study was identified through the literature search, and summary data were extracted from these three studies (see Figure 1). When studies assessed outcomes of interest in more than one follow-up wave in adulthood, we used data from the oldest age at assessment to provide the most up-to-date assessment of the outcome.

2.4 | Data collection

IPD were transferred through individual data transfer agreements to the University of Warwick. All studies that shared data had received country-specific ethical review, with individual participants having provided written informed consent.

2.5 | IPD Integrity and risk of bias

The quality of studies was assessed independently by two researchers (MM and RE), using the Newcastle-Ottawa Scale[28] (Table S2) with disagreements resolved by discussion. Scores ranged from 0 to 9, with higher scores indicating higher quality. Because we had access to IPD from participating cohorts, selective outcome reporting was not an issue.

TABLE 1 Summary of cohorts included in the IPD analysis.

Cohort	Country	Consortia	Birth year	Mean age assessed	Initial eligibility criteria	Initial N VP/ VLBW surviving to discharge
AYLS (Heinonen et al., 2008)[37]	Finland	RECAP/ APIC	1985–86	26	Preterm <37 weeks (reduced to VP/VLBW for this analysis)	108
BLS (Jaekel et al., 2018)[39]	Germany	RECAP/APIC	1985–86	26	VP/VLBW	510
ESTER (Mannisto et al., 2015)[42]	Finland	RECAP/ APIC	1985–89	23	Preterm <37 weeks (reduced to VP/VLBW for this analysis)	448
EPICure (Marlow et al., 2005)[14]	UK and Ireland	RECAP/APIC	1995	19	EP (<26 weeks)	315
HESVA (Kajantie et al., 2008)[40]	Finland	RECAP/APIC	1978–85	25	VLBW	334
NTNU Evensen et al., 2022)[43]	Norway	RECAP/APIC	1986–88	26	VLBW	86
NZ VLBW (Darlow et al., 2015)[36]	New Zealand	APIC	1986	28	VLBW	338
POPS (Hille et al., 2008)[38]	The Netherlands	RECAP/APIC	1983	28	VP/VLBW	1338
RWH	Australia	APIC	1977–82	26	VLBW	212
UCLH (Kroll et al., 2017)[41]	UK	APIC	1979–84	30	VP (<33 weeks, reduced to VP/VLBW for this analysis)	302
VICS (Roberts et al., 2013)[60]	Australia	APIC	1991–92	18	EP/ELBW (<28 weeks/<1000 g)	299
Total N						4239

Abbreviations: AYLS, Arvo Ylppö Longitudinal Study; BPD, bronchopulmonary dysplasia; BLS, Bavarian Longitudinal Study; EP/ELBW, extremely preterm/extremely low birthweight; ESTER, The Preterm Birth and Early Life Programming of Adult Health and Disease Study; EPICure, EPICure study; HESVA, Helsinki Study of Very Low Birth Weight Adults; NSI, neurosensory impairment; NTNU Low Birth Weight in a Lifetime Perspective study; NZ VLBW, New Zealand Very Low Birth Weight Study; POPS, Project on Preterm and Small for Gestational Age Infants; RWH, Royal Women's Hospital Study; UCLH, University College London Hospital Cohort Study; VICS, Victorian Infant Collaborative Study; VP/VLBW, very preterm/very low birthweight.

2.6 | Variables and data harmonisation

2.6.1 | Romantic and sexual outcomes

Romantic and sexual outcomes were self-reported in adulthood by participants, and the following measures were harmonised across cohorts: *Romantic Relationships* (i.e., currently in any form of romantic relationship vs no relationship); *Partnership Status* (i.e., currently married or cohabiting with romantic partner vs no partner); *Sexual Intercourse* (i.e., ever had sexual intercourse vs never had); *Age of First Sexual Intercourse* (dichotomized as >18 vs. ≤18 years); and *Number of Sexual Partners* (dichotomized as ≥5 vs. <5 sexual partners in their lifetime). The two latter variables were harmonised as binary variables as they were recorded differently across cohorts.

2.6.2 | Neonatal exposure variables

Birth status (i.e., VP/VLBW vs term-born controls) was the main predictor of interest obtained from birth records. The VP/VLBW group

Assessed sample in adulthood	Sample with data on romantic/sexual outcomes[a]	Control group (N) + information	Outcome analysed	Harmonisation issues
35	32	356-recruited infancy	Romantic relationship; Sexual intercourse; age of 1st sexual intercourse; number of sexual partners	None
260	260	229-recruited infancy	Romantic relationship; partnership status; sexual intercourse; age of 1st sexual intercourse	None
77	73	344	Romantic relationship; partnership status; sexual intercourse; age of 1st Sexual intercourse	IVH not available and IVH grade 3–4 only available for 10 participants
129	122	64-recruited at ages 6 or 11	Romantic relationship; sexual intercourse; age of 1st sexual intercourse	None
185	185	190-recruited in adulthood	Romantic relationship; partnership status; sexual intercourse; age of 1st sexual intercourse; number of sexual partners	IVH not available. Maternal education measured in adulthood. NSI did not include cognitive impairment.
62	62	87-recruited infancy	Romantic relationship; partnership status; sexual intercourse; age of 1st sexual intercourse	Maternal education measured at 14 years
250	250	100- recruited in adulthood	Partnership status; sexual intercourse; age of 1st sexual intercourse; number of sexual partners	None
317	314	No controls	Romantic relationship; partnership status; sexual intercourse; age of 1st sexual intercourse	None
97	73	22- Recruited Infancy	Romantic relationship	None
102	102	89- recruited in adulthood	Romantic relationship; partnership status	BPD not available and fully imputed. Maternal education reported by the participant in adulthood. NSI solely based on IQ <70 at 8 years
220	189	166- recruited infancy	Sexual intercourse; number of sexual partners	None
1.660	1606	1.659		

was defined as gestational age < 32 completed weeks and/or birth weight < 1500 g. Term-born participants were specified by each cohort and had a gestational age ≥ 37 weeks.

2.6.3 | Covariates for the whole population

Covariates available for the whole population comprised participant's sex determined at birth, age at follow-up assessment, and parental educational level (of either parent recorded at birth if available or at later follow-up) which was classified according to the International Standard Classification of Education (ISCED 2011)[29] into three levels: (1) low: ISCED 0–2; (2) medium: ISCED 3–5; and (3) high: ISCED 6–8.

2.6.4 | Covariates specific to the VP/VLBW populations

Covariates specific to the VP/VLBW population included: gestational age (completed weeks), birthweight (Z-scores) using the

Fenton growth reference[30], multiple birth, BPD (defined as supplemental oxygen at 28 days after birth or at 36 weeks' postmenstrual age), and IVH grade 3–4 according to Papile,[31] compared with lesser or no grade of IVH.

NSI in childhood comprised one or more of the following: visual impairment (blind in both eyes), hearing impairment (requiring hearing aids or worse), nonambulatory cerebral palsy, or childhood cognitive impairment (childhood IQ <70). This was combined into a binary NSI variable (impairment vs. no impairment).

2.7 | Data analysis

Statistical analyses were performed in Stata, version 17.0 (Stata Corp, College Station, TX). First, the association between VP/VLBW birth and each relationship outcome was tested using a one-stage IPD meta-analysis approach, where IPD from all studies were analysed simultaneously. A generalised linear mixed-effects (GLME) model for binary outcomes was used to estimate odds ratios (ORs) with 95% confidence intervals (CI) in VP/VLBW adults relative to term-born adults. Random intercepts were specified to account for the clustering of participants within cohorts. This procedure was repeated to estimate effect sizes after removing VP/VLBW participants with NSI and adjusting for age at assessment, parental educational level (PEL), and sex. A sex-birth status interaction was added to test if any differences between groups were stronger in males or females. If an interaction was found, group differences were reported among males and females separately. Covariates were added as fixed effects. Between-study heterogeneity was assessed using τ^2,[32] with τ^2 values closer to zero indicating lower heterogeneity among studies.

Second, we investigated the effects of neonatal and sociodemographic factors and NSI on outcomes among VP/VLBW participants only. Covariates were added as fixed effects to GLME models. ORs with 95% CIs are reported from both univariable and multivariable analyses to determine their independent and combined associations.

Missing data on predictor variables were handled using multiple imputation by chained equations (MICE).[33] Less than 5% of data on PEL were imputed for analyses involving the whole population. The same procedure was used to impute missing neonatal data for the multivariable analyses among VP/VLBW participants. See Tables 3 and 4 for number of cases imputed. Complete case analyses are presented in Table S7.

2.8 | Sensitivity analyses

Sensitivity analyses were performed to assess whether studied relationships observed in cohorts contributing IPD were representative of all cohorts of VP/VLBW adults. The results of IPD analyses were compared with aggregate data (AD) estimates from the McMaster[26] and Norwegian[34] studies for *Partnership Status*, and the McMaster and Cleveland[30] studies for *Sexual Intercourse*. This was performed by conducting subgroup analysis using two-stage IPD meta-analysis. AD were extracted and meta-analysed, and the log ORs of VP/VLBW adults and term-born controls were used as effect sizes. Two-stage IPD meta-analysis integrating both IPD and AD cohorts were conducted next for each outcome. The effects sizes in each cohort were pooled through random effects meta-analysis using STATA's *ipdmetan* command.[35] Heterogeneity was quantified by I^2, with low heterogeneity defined <40% and high defined as >75%.

3 | RESULTS

3.1 | Study selection and IPD obtained

The systematic search resulted in 14 eligible cohorts from the 74 articles screened (Figure 1). All 13 RECAP-preterm/APIC cohorts were eligible for inclusion in the study, and 12 were identified through the systematic literature search of published studies. Only the Royal Women's Hospital (RWH) cohort was not identified in the search. IPD were sought and obtained for 11 eligible RECAP preterm/APIC cohorts. In total, we obtained IPD for 1606 VP/VLBW and 1659 term-born adults and summary level data for 379 VP/VLBW and 368 term-born adults. See Table 1 for a description of the cohorts providing IPD and Table S4 for studies providing summary data.

3.2 | Study and participant characteristics

The IPD cohorts[36–43] were from seven different countries (Germany, Norway, Finland, UK, Netherlands, New Zealand, and Australia). The years of birth ranged from 1977 to 1995, and the mean ages at assessment ranged from 18 to 30 years. The distribution and descriptive statistics of variables in each cohort are provided in Table S5, S6.

3.3 | IPD integrity and risk of bias within studies

The quality of studies mean on Newcastle-Ottawa Scale[28] was 6.9 (range 5–8), indicating overall good quality (Table S3). However, some studies differed in initial recruitment criteria. Rates of attrition among VP/VLBW participants were above 50% in 7/11 cohorts.

3.4 | Results of syntheses

3.4.1 | IPD meta-analysis of all participants

The results of IPD meta-analysis of all participants show that fewer VP/VLBW young adults reported being in a romantic relationship (unadjOR 0.49, 95% CI 0.31–0.76, Table 2; 52% VP/VLBW vs. 68% Controls; Table S5) and in a partnership (married/cohabiting)

(unadjOR 0.70, 95% CI 0.53–0.92; 43% VP/VLBW vs. 46% Controls) than their term-born peers. Similarly, fewer VP/VLBW reported experience of sexual intercourse (unadjOR 0.21, 95% CI 0.09–0.36; 67% VP/VLBW vs. 89% Controls). Among those with experience of sexual intercourse, young adults born VP/VLBW were more likely to have first experienced sexual intercourse after the age of 18 years (unadjOR 1.93, 95% CI 1.24–3.01; 26% VP/VLBW vs. 16% Controls) than those born at term and fewer reported having five or more sexual partners (unadjOR 0.66, 95% CI 0.32–1.38; 28% VP/VLBW vs. 37% Controls), but the 95% CI of the OR crossed unity. Adjusting for sex, age, and PEL had little effect on conclusions (Table 2). Sex was associated with all outcomes except for number of sexual partners with males less likely to have *Romantic Relationship*, *Partnership Status* and *Sexual Intercourse*, and earlier *Age of First Sexual Intercourse* than females. There was a significant interaction between sex and birth status for *Age of First Sexual Intercourse* (OR 0.54, 95% CI 0.34–0.85). VP/VLBW females more frequently had sexual intercourse for the first time after the age of 18 years than term-born females (OR 2.50, 95% CI 1.75–3.57). VP/VLBW males also reported later sexual initiation, but the 95% CI of the OR crossed unity (OR 1.47; 95% CI 0.80–2.73). Effect sizes reduced slightly after excluding participants with childhood NSI in some outcomes (Table 2).

3.4.2 | Multivariable analysis among VP/VLBW adults

Regarding multivariable analyses among adults born VP/VLBW for romantic outcomes (Table 3), VP/VLBW men and those with NSI were less likely to be in a romantic relationship and in a partnership; additionally, individuals assessed at older ages had higher frequencies of partnerships. Regarding sexual outcomes (Table 4), there was evidence that higher gestational age, birthweight z-score, and age at assessment were associated with having experienced sexual intercourse, whereas having a NSI decreased the likelihood of ever having experienced sexual intercourse. Individuals with NSI and higher PEL more frequently reported first sexual intercourse after 18 years.

Overall, complete cases analyses showed similar findings, with weakened associations between IVH Grade 3–4 and sexual intercourse, and stronger associations between BPD and sexual outcomes (Table S7).

3.4.3 | Sensitivity analysis

Sensitivity analysis comparing IPD and aggregate data showed convergent findings for *Partnership Status*, which contrasted with

TABLE 2 One-stage IPD meta-analysis of the association between VP/VLBW and romantic/sexual outcomes.

Outcomes	Studies included	*N*	OR	95% CI	*p*	τ^2
Romantic relationships						
Unadjusted model	8	2278	0.49	[0.31, 0.76]	0.002	0.31
Adjusted for sex, age, PEL	8	2278	0.48	[0.30, 0.76]	0.002	0.30
Excluding participants withNSI	8	2139	0.53	[0.37, 0.77]	0.01	0.17
Partnership status						
Unadjusted model	6	1761	0.70	[0.53, 0.92]	0.01	0.02
Adjusted for sex, age, PEL	6	1761	0.67	[0.50, 0.91]	0.01	0.00
Excluding participants with NSI	6	1656	0.76	[0.61, 0.95]	0.01	0.00
Sexual intercourse						
Unadjusted model	8	2656	0.21	[0.09, 0.36]	<0.001	0.49
Adjusted for sex, age, PEL	8	2656	0.20	[0.11, 0.39]	<0.001	0.59
Excluding participants with NSI	8	2.274	0.31	[0.17, 0.55]	<0.001	0.41
If ever experienced sexual intercourse, age (>18 years) at first sexual intercourse						
Unadjusted model	7	1946	1.93	[1.24, 3.01]	0.004	0.20
Adjusted for sex, age, PEL	7	1946	2.03	[1.31, 3.11]	<0.001	0.18
Excluding participants with NSI	7	1887	1.91	[1.27, 2.89]	0.002	0.15
If ever experienced sexual intercourse, number (≥5) of sexual partners						
Unadjusted model	5	1442	0.66	[0.32, 1.38]	0.27	0.43
Adjusted for sex, age, PEL	5	1442	0.63	[0.27, 1.46]	0.22	0.00
Excluding participants with NSI	5	1408	0.71	[0.35, 1.47]	0.36	0.40

Abbreviations: NSI, neurosensory impairment; PEL, parental educational level.

TABLE 3 Very preterm/very low birth weight (VP/VLBW) only analysis: One-stage IPD univariable and multivariable effects on romantic outcomes.

	Current romantic relationship (*N* = 1222)				Partnership status (*N* = 1140)			
	Univariable estimates		Multivariable estimates[c]		Univariable estimates		Multivariable estimates[d]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Gestational age (weeks)	1.06*	[1.01, 1.12]	1.06	[0.99, 1.15]	1.08**	[1.02, 1.14]	1.07	[0.99, 1.15]
Birthweight *z*-score	0.99	[0.88,1.09]	1.11	[0.97, 128]	0.95	[0.85, 1.04]	1.07	[0.94, 1.22]
Multiple birth (ref. = singleton)	1.08	[0.80,1.46]	1.08	[0.79, 1.49]	1.03	[0.77, 1.37]	1.03	[0.77, 1.39]
IVH grade 3–4 (ref. = no IVH or IVH grade 1–2)[a]	0.59*	[0.35,0.97]	0.75	[0.44, 1.29]	0.62	[0.44, 0.98]	0.82	[0.54, 1.23]
BPD (ref. = no)[b]	0.63**	[0.46, 0.88]	0.72	[0.50, 1.02]	0.66*	[0.47,0.91]	0.82	[0.58, 1.15]
NSI in childhood (ref. = no)	0.37***	[0.26, 0.56]	0.40***	[0.27,0.60]	0.36***	[0.23, 0.55]	0.39***	[0.25, 0.60]
Age at assessment	1.07	[0.97, 1.19]	1.05	[0.99, 1.23]	1.12*	[1.01. 1.23]	1.15*	[1.02, 1.28]
Sex (ref. = female)	0.61***	[0.48, 0.78]	0.62***	[0.47, 0.79]	0.68**	[0.53, 0.87]	0.68**	[0.53, 0.87]
PEL (ref. = low) medium	0.98	[0.72, 1.36]	0.93	[0.68, 1.29]	0.98	[0.72, 1.33]	1.02	[0.73, 1.48]
High	0.99	[0.56,1.27]	0.86	[0.53, 1.21]	0.99	[0.68, 1.43]	1.05	[0.73, 1.54]

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular haemorrhage; NSI, neurosensory impairment; PEL, parental educational level.

[a]Only 10 participants from the ESTER cohort were included in the univariable estimate for romantic relationship and partnership status, but had their values imputed for the multivariable estimate.

[b]Participants from the UCLH cohort were not included in the univariable estimate, but had their values imputed for the multivariable estimate.

[c]Missing values were imputed in multivariable model: IVH 3–4 = 225; BPD = 138; PEL = 131.

[d]Missing values were imputed in multivariable model: IVH 3–4 = 191; BPD = 103; PEL = 122.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

TABLE 4 Very preterm/very low birth weight (VP/VLBW) only analysis: One-stage IPD univariable and multivariable effects on sexual outcomes.

	Ever experienced sexual intercourse (*N* = 1463)				Age of first sexual intercourse>18 (*N* = 969)			
	Univariable estimates		Multivariable estimates[a]		Univariable estimates		Multivariable estimates[b]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Gestational age (weeks)	1.15***	[1.07, 1.22]	1.13*	[1.03, 1.22]	0.91*	[0.86, 0.97]	0.91	[0.83, 0.99]
Birthweight *z*-score	0.97	[0.86,1.10]	1.17*	[1.01, 1.37]	1.09	[0.97, 1.22]	0.96	[0.82, 1.12]
Multiple birth (ref. = singleton)	0.93	[0.69,1.26]	0.97	[0.70, 1.33]	1.06	[0.76, 1.49]	0.99	[0.70, 1.41]
IVH Grade 3–4 (ref. = no IVH or IVH grade 1-2)[c]	0.44***	[0.28,0.69]	0.68	[0.42, 1.09]	1.72*	[1.02, 2.88]	1.16	[0.64, 2.14]
BPD (ref. = no)	0.56***	[0.42, 0.76]	0.74	[0.54, 1.02]	1.36	[0.94, 1.97]	1.11	[0.75, 1.64]
NSI in childhood (ref. = no)	0.19***	[0.13, 0.27]	0.20***	[0.14, 0.30]	2.00**	[1.19, 3.35]	1.88*	[1.11, 3.22]
Age at assessment	1.13	[0.99, 1.30]	1.19*	[1.03, 1.38]	0.93	[0.79. 1.10]	0.96	[0.81, 1.14]
Sex (ref. = female)	0.87	[0.66, 1.15]	0.92	[0.70, 1.20]	0.97	[0.73, 1.28]	0.94	[0.70, 1.25]
PEL (ref. low) medium	0.91	[0.65, 1.27]	0.88	[0.65, 1.32]	1.46*	[1.01, 2.10]	1.38	[0.95, 2.00]
High	0.74	[0.48,1.13]	0.72	[0.47, 1.19]	2.24***	[1.45, 3.45]	2.13**	[1.37, 3.24]

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular haemorrhage; NSI, neurosensory impairment; PEL, parental educational level.

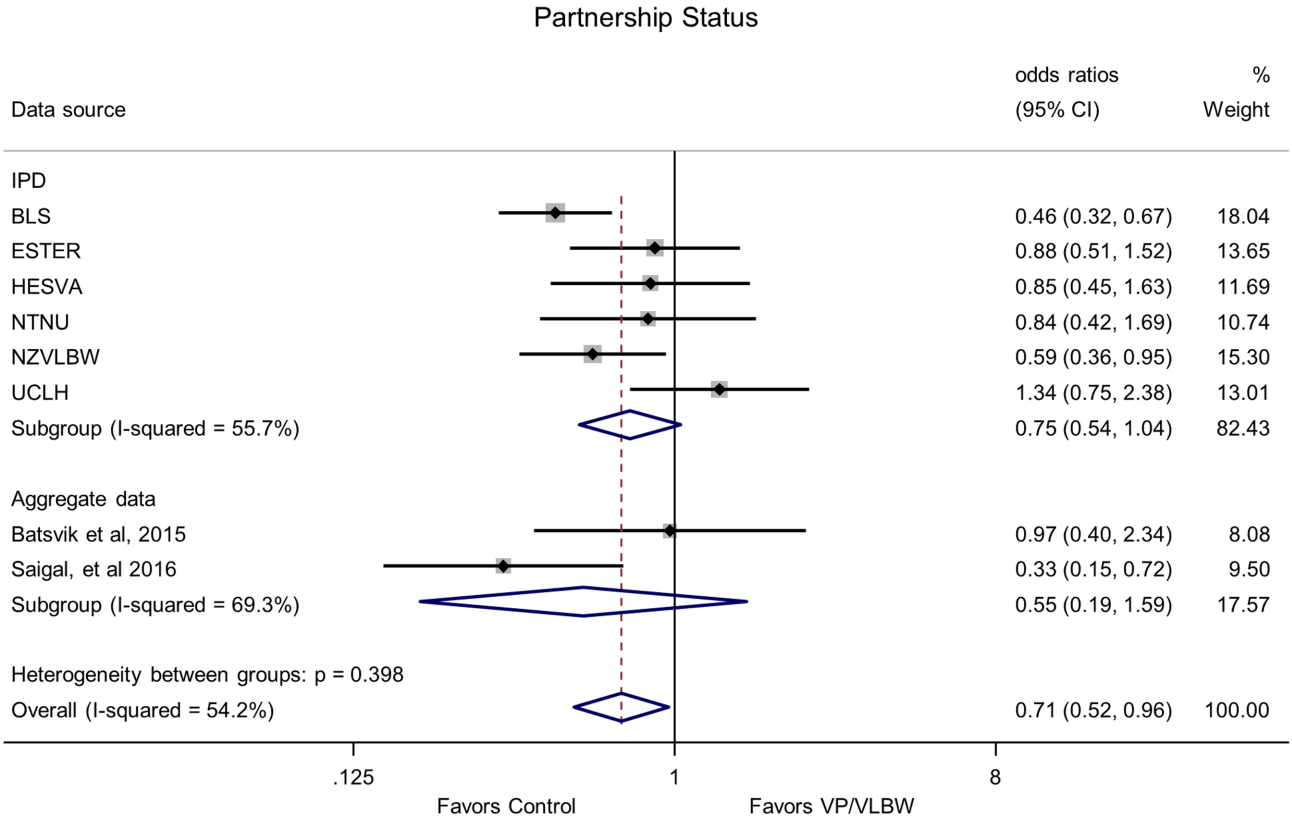
[a]Missing values were imputed in multivariable model: IVH = 223: BPD = 39, PEL = 178.

[b]Missing values were imputed in multivariable model: IVH = 186: BPD = 32; PEL = 81.

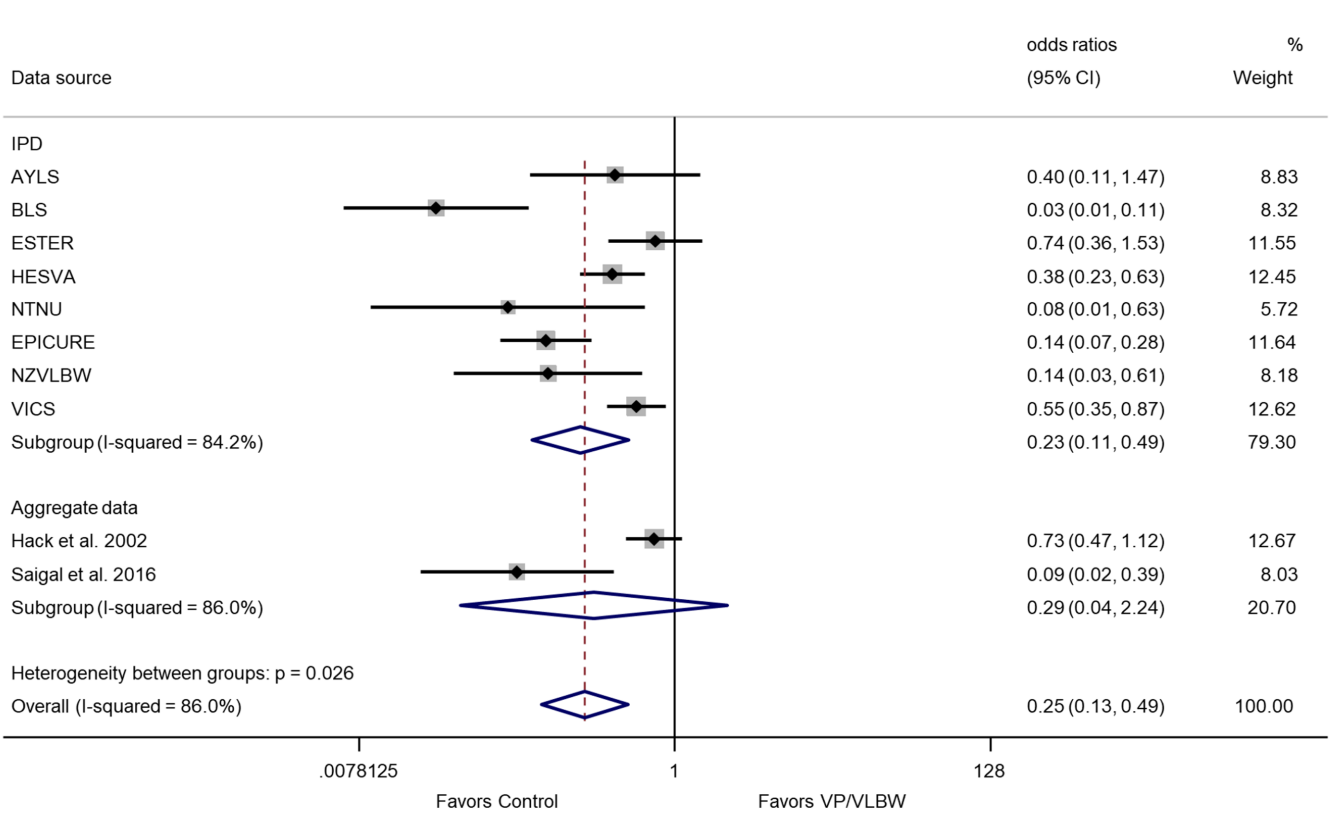
[c]Only 10 participants from the ESTER cohort were included in the univariable estimate, but had their values imputed for the multivariable estimate.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

FIGURE 2 Two-stage independent participant data (IPD) meta-analysis comparing partnership status/sexual intercourse in IPD versus aggregate data of adults born very preterm or/and very low birth weight. Diamonds represent pooled estimates from either the IPD or aggregate data subgroup analysis or from all cohorts. Diamond size indicates the 95% CI for the pooled estimate. Horizontal lines represent the 95% CI of the estimates for each cohort. Box sizes represents the weighting given to the study.



NOTE: Weights are from random-effects model



NOTE: Weights are from random-effects model

the lack of difference in frequency of reported *Sexual Intercourse* (Figure 2). The overall pooled effect sizes for each outcome indicate a significant association between prematurity and both outcomes, with VP/VLBW adults being less likely to report partnerships (OR 0.71; 95% CI 0.52–0.96) or sexual intercourse (OR 0.25; 95% CI 0.13–0.49) than their term-born peers. Heterogeneity analysis indicated high variation in sexual intercourse effects and moderate variation in partnership status between studies.

4 | DISCUSSION

In this IPD meta-analysis, romantic relationships, partnerships, and sexual activity of 18–30-year-old individuals born VP/VLBW were less frequent when compared with term-born controls. If sexually active, VP/VLBW individuals were more frequently older than 18 years at first sexual intercourse but as likely to have had five or more sexual partners. The associations of VP/VLBW birth with intimate partner relationships were robust even after adjusting for covariates, excluding participants with NSI, or integrating AD. Among VP/VLBW adults, the presence of NSI was independently associated with fewer romantic relationships, partnerships and exposure to sexual activity, and men reported fewer romantic relationships and partnerships than women. Overall, our IPD findings are consistent with a previous aggregate-data meta-analysis,[8] and extend our understanding about the association between preterm birth and intimate partner relationships in two ways: First, by examining further experiences (i.e., age of first sexual intercourse and number of sexual partners), and second by providing insight into early biological and environmental factors may affect such relationships among VP/VLBW individuals.

Young adults born VP/VLBW were about half as likely to be in a romantic relationship and even less likely to ever have experienced sexual intercourse than their term-born peers. This suggests that VP/VLBW individuals are less likely to receive the social and economic supports of having an intimate partner relationship, which may be associated with poorer health, wealth, and lower levels of well-being,[1,2,44,45] as well as increased risk of not becoming parents.[8] Previous research has shown that VP/VLBW born children score lower on social competence, have fewer friends, and more peer relationship difficulties.[19,46,47] These social difficulties may persist into adulthood, and limited social contact may contribute to reduced opportunities to develop the social skills to meet and establish romantic relationships in adulthood. VP/VLBW birth is also associated with traits[17,48,49] of introversion, shyness, social withdrawal, and low risk-taking, which may further challenge the development of these relationships. Hence, our findings highlight the need for continued monitoring and tailored support that considers VP/VLBW individuals' specific characteristics and needs throughout the lifespan. New avenues for fostering adults born VP/VLBW romantic relationships should be explored, which may involve the development of programmes supporting interpersonal skills or dating applications.[50]

In multivariable analysis among VP/VLBW individuals, having a NSI was consistently associated with fewer intimate partner relationships. The significant associations with neonatal variables, namely BPD and IVH, on univariable analysis were not confirmed on multivariable testing, but it is likely that these exert influence through the presence of NSI.[21,51] Individuals with disabilities have fewer opportunities to socialise,[52] and marry less often.[53] Furthermore, negative attitudes in young people to dating partners with disability have been described, and intellectual or developmental disability represent a greater barrier to dating than physical disability.[54] Despite young people identifying loyalty, honesty, dedication, humour, or kindness as preferred characteristics for partners, which are unrelated to disability, preferences for actual romantic relationships may be more determined by choosing a mate for best reproductive success.[55]

Consistent with this evolutionary hypothesis—that selection is based on the "quality" of the mate—VP/VLBW males were less likely to be in romantic relationships or being married than their female counterparts. No interaction was found between sex and birth status for these two outcomes indicating that this is not a VP/VLBW specific phenomenon. Indeed, population reports show that men are less likely to marry than women, and the gender gap has widened over the past decades[56] with women's enhanced economic status. Considering that females mainly choose[18] and prefer males with higher or equivalent resources, the ratio of "marriageable" males has declined.[56] Evidence shows that men tend to benefit more than women from being in a romantic partnership with respect to their health,[4] and the risk of poorer health may be higher for VP/VLBW men due to increased biological vulnerabilities.[57] Contrary to predicted, we found no differences in sexual relationships between VP/VLBW men and women, which may be due to partner quality being less relevant in short-term sexual strategy. An interaction between sex and birth status shows that VP/VLBW females more frequently experience their first sexual intercourse after age 18 than term-born females. Late sexual debut has been linked to less risk-taking behaviours, shyness, and overprotective parents,[58] more often found among preterm individuals,[24] and may be more salient for VP/VLBW females due to stricter female sexuality norms.[59]

In contrast to biological variables, parental educational level was unrelated to our relationship variables, apart from age of first sexual intercourse. However, other environmental factors, such as quality of parent-infant relationship, parenting practices, participation in leisure activities, or peer relationships, may play a role and have often been overlooked in research. Thus, more research on the environmental factors that may alter the impact of VP/VLBW birth is needed to inform early interventions.

The strengths of this study include the large sample size from combining individual participant data from 11 international cohorts. The availability of comprehensive perinatal and childhood data allowed to control for confounders and explore their roles in relation to romantic and sexual relationships. The harmonisation of variables in IPD reduced between-study heterogeneity, which is not possible in aggregated meta-analysis. However, there are

also limitations. Eligibility criteria differed among cohorts, ranging from <26 weeks of gestation to VLBW, which we accounted for in multivariable analysis using gestational age at birth and birthweight as covariates. Studies used different methods to recruit term-born participants. We cannot exclude potential bias due to selective drop-out and overrepresentation of healthier participants which may affect estimates of true differences. Binary variables were used for age of first sexual intercourse and number of sexual partners that were defined by data availability rather than empirical evidence. Lastly, neonatal variables were imputed for some cohorts and different definitions for BPD were used. However, analyses were repeated for complete cases and overall similar results emerged. Finally, there is an 18-year spread of birth dates (1977–1995) across the studies included in this IPD meta-analysis, representing distinct neonatal care practices, ages, and generational beliefs and practices in romantic partnering. The few studies with younger participants limited the ability to explore these differences in a statistically robust manner.

5 | CONCLUSION

In this large IPD meta-analysis, fewer adults born VP/VLBW reported experience of romantic relationships, marriage/cohabitation, or sexual intercourse compared with those born at term. Within the VP/VLBW population, men were less likely to form romantic partnerships than women, and those with NSI reported the lowest rate of romantic and sexual partners. These findings are relevant for clinicians, researchers, and policymakers, as fewer intimate partner relationships suggest lower levels of social support, which may have implications for socioeconomic and health outcomes of adults born VP/VLBW. Furthermore, not being engaged in romantic relationships may be a major reason for fewer VP/VLBW having children.

Recognition of the wide-ranging effects of very preterm birth is important to inform interventions fostering social relationships into adult life.

AUTHOR CONTRIBUTIONS

Marina Mendonça: Conceptualization; investigation; writing – original draft; methodology; validation; visualization; formal analysis; project administration; data curation. **Yanyan Ni:** Methodology; writing – review and editing; formal analysis. **Nicole Baumann:** Writing – review and editing; data curation; validation. **Brian A. Darlow:** Resources; writing – review and editing; data curation; validation. **John Horwood:** Data curation; writing – review and editing; methodology. **Lex W. Doyle:** Writing – review and editing; data curation; resources; validation. **Jeanie L. Y. Cheong:** Writing – review and editing; data curation; resources. **Peter J. Anderson:** Writing – review and editing; data curation; resources. **Peter Bartmann:** Writing – review and editing; data curation; resources. **Neil Marlow:** Data curation; resources; writing – review and editing; validation. **Samantha Johnson:** Funding acquisition; writing – review and editing; data curation; resources. **Eero Kajantie:** Funding acquisition; writing – review and editing; data curation; resources; validation. **Petteri Hovi:** Writing – review and editing; data curation; resources. **Chiara Nosarti:** Writing – review and editing; data curation; resources; validation. **Marit S. Indredavik:** Funding acquisition; writing – review and editing; data curation; resources; validation. **Kari Anne I. Evensen:** Writing – review and editing; data curation; resources; validation. **Katri Räikkönen:** Funding acquisition; writing – review and editing; data curation; resources; validation. **Kati Heinonen:** Writing – review and editing; data curation; resources. **Sylvia van der Pal:** Funding acquisition; writing – review and editing; data curation; resources; validation. **Lianne J. Woodward:** Data curation; resources; writing – review and editing; validation. **Sarah Harris:** Data curation; resources; writing – review and editing. **Robert Eves:** Methodology; writing – review and editing; formal analysis. **Dieter Wolke:** Conceptualization; funding acquisition; writing – review and editing; investigation; resources; data curation; supervision; project administration; validation.

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CONFLICT OF INTEREST STATEMENT

All authors declare no competing interests.

DATA AVAILABILITY STATEMENT

The IPD database is stored at UoW's data node and can be shared subject to the approval of the corresponding authors of the original studies, and the signing of a data sharing agreement. Requests to access this dataset should be directed to the first author (marina.mendonca@warwick.ac.uk).

REGISTRATION

This IPD meta-analysis was registered with PROSPERO: CRD42020168855.

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SUPPORTING INFORMATION

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

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