

Child maltreatment, adult partner violence, and young onset dementia: Sequential causal mediation analysis in the UK Biobank



Marie-Céline Schulte, Child Protection Research Group, Brain Health Group Faculty of Epidemiology and Population Health, LSHTM

Nicholas Magill, Department of Medical Statistics, Faculty of Epidemiology and Population Health, LSHTM
Karen Devries, Child Protection Research Group, Faculty of Epidemiology and Population Health, LSHTM



Background

- **Child maltreatment** globally prevalent (1B+ children)
- **Dementia burden:** 57M cases in 2019, projected 153M by 2050
- **YOD underdiagnosed**, prevalence underestimated
- Child maltreatment + other adversities contribute to **neuroinflammation, accelerated brain aging, neurodegeneration**
- **Child maltreatment and partner violence associations overlap with YOD risk factors:** e.g., socioeconomic deprivation, alcohol misuse, high BMI, cardiometabolic, and other neurobiological risks
- **Child maltreatment and partner violence under-researched as upstream YOD determinants;** prior studies focus on late-onset
- Clarifying mediators could enable **earlier detection and intervention**

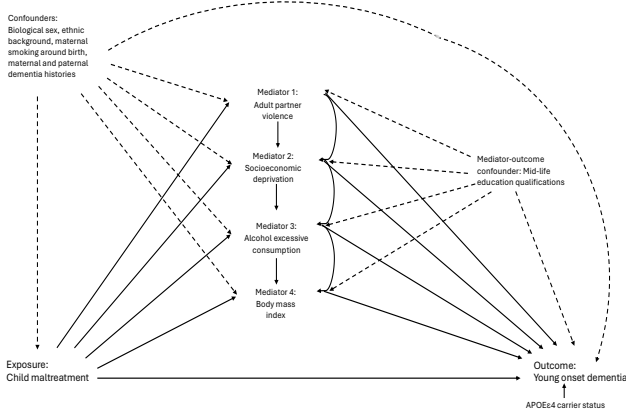
Aims

- **Test** whether child maltreatment and adult partner violence link with **younger age at dementia diagnosis**
- **Evaluate sequential causal mediation pathways:** partner violence → socioeconomic deprivation → alcohol misuse → body mass index

Methods

- **Cohort:** UK Biobank, n = 147,938 with Mental Health Questionnaire + APOEε4 genotype data
- **Cases:** 915 dementia diagnoses → 128 YOD (≤68 years), 787 late onset
- **Exposures:** Self-reported child maltreatment (before 18; none, 1+ types) and partner violence (after 18; none, 1, 2+ types)
- **Mediators:** Adult partner violence and 22 evidenced YOD risk factors
- **Outcomes:** Date at 'all-cause dementia' diagnosis from hospital, physician, self-report, and mortality records. YOD versus late onset
- **Analyses:**
 - **Weibull Accelerated Failure Time (AFT) models, time from age 18 to age at diagnosis**
 - **Causal mediation analysis:** direct vs. indirect child maltreatment → YOD effects
 - **Multiple imputation by chained equations (MICE, 20 datasets)** to handle missing data

Figure 1. Hypothesized direct and indirect sequential causal mediation pathways, child maltreatment → YOD



Results

- **Violence exposures:**
 - **Child maltreatment more common in YOD (38%)** vs. late onset (27%)
 - **Partner violence more common in YOD (34%)** vs. late onset (21%)
- **Age at dementia diagnosis:**
 - **YOD median = 63.5 years** [IQR: 8; Range: 40 to 68]
 - Late onset median = 76.0 years [IQR: 6; Range: 69 to 84]
- **Time from age 18 to age at dementia diagnosis** (Table 1):
 - **Child maltreatment + adult partner violence: Estimated 2+ years younger average age at diagnosis, additively**

Table 1. Weibull Accelerated Failure Time: CM-dementia age at diagnosis

Variable	Time ratio	95% CI for time ratio	p-value	Estimated mean change in age at dementia diagnosis
Child maltreatment, ≥ 1 type	0.985	[0.9725, 0.9966]	0.012	-1.15 years
Adult partner violence, ≥ 1 type	0.986	[0.9737, 0.9990]	0.034	-1.02 years
Biological sex (female)	0.998	[0.9878, 1.0085]	0.722	.
APOEε4 carrier	0.999	[0.9904, 1.0068]	0.731	.
Townsend Deprivation Index score	0.998	[0.997, 1.000]	0.082	.
Education qualifications	1.006	[1.000, 1.011]	0.049	+0.42 year
Maternal smoking around birth	0.997	[0.984, 1.009]	0.608	.
Maternal dementia	0.987	[0.974, 1.001]	0.065	.
Paternal dementia	0.990	[0.970, 1.011]	0.339	.

Note: CM = Child maltreatment. Time ratios <1 = earlier dementia diagnosis. Years of change estimated from mean diagnosis age (74.2). Bold = statistically significant (p < 0.05). Estimates pooled across 20 imputed datasets using Rubin's Rules. Sample: n=915.

78% of child maltreatment association with YOD mediated indirectly through adult partner violence, socioeconomic deprivation, alcohol excessive consumption, and high body mass index (Table 2)

Table 2. Sequential causal mediation analysis: direct and indirect effects of child maltreatment on YOD

Models 1-4	CDE OR (95% CI)	NDE OR (95% CI)	NIE OR (95% CI)	TCE OR (95% CI)	Proportion mediated (%)	Additional contribution (%)	E-value: NIE OR
M1: Adult partner violence, ≥ 1 type	1.25 (0.75, 2.11)	1.27 (0.83, 1.98)	1.21 (1.01, 1.47)	1.53 (1.02, 2.29)	44.8%	.	1.71
M2: Partner violence + Socioeconomic deprivation	1.19 (0.68, 2.08)	1.27 (0.81, 2.00)	1.24 (1.01, 1.55)	1.57 (1.06, 2.33)	47.7%	2.9%	1.79
M3: Partner violence + Socioeconomic deprivation + Alcohol misuse	0.81 (0.45, 1.54)	1.14 (0.98, 2.14)	1.27 (1.02, 1.58)	1.41 (0.74, 1.76)	69.6%	21.9%	1.86
M4: Partner violence + Socioeconomic deprivation + Alcohol excessive consumption + Body mass index	0.78 (0.41, 1.50)	1.10 (0.69, 1.73)	1.38 (1.09, 1.75)	1.51 (1.01, 2.29)	78.2%	8.6%	2.10

Note: CDE = Controlled direct effect; NDE = Natural direct effect; NIE = Natural indirect effect; TCE = Total causal effect. Sample = 915 dementia cases (128 YOD, 787 late onset). OR = Odds ratio. 95% CIs pooled from sequential causal mediation models across 20 imputed datasets (Stata18 *gformula*, Monte Carlo simulations + 1000 bootstrap replications for bias correction). Models adjusted for sex, maternal smoking, parental dementia, education, and APOEε4 genotype.

Discussion

- **Child maltreatment x partner violence: 1-2 years younger diagnosis on average**
- **78% child maltreatment → YOD mediated** through partner violence, socioeconomic deprivation, alcohol misuse, and high body mass index
- Supports: **exposome¹, neuroinflammation², and accelerated brain ageing³**
- **Violence prevention and risk factor modification could delay dementia onset**
- Clinicians should consider **violence histories when assessing mid-life YOD risk**
- Policy should **integrate violence prevention and risk reduction and mitigation to delay YOD**

1. Migeot, J, et al. 2025. doi:10.1038/s41467-025-63277-6
2. Soraci, L, et al. 2024. doi:10.14338/AD.2023.1001
3. Chaudhari, PR, et al. 2022. doi:10.3389/fnmol.2022.822917

Connect:

marie-celine.schulte@lshtm.ac.uk

LinkedIn: Marie-Céline Schulte →

