

Understanding the Relationship between Education and Clinical Outcomes in Multiple Sclerosis

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Introduction Multiple Sclerosis (MS) is a debilitating chronic inflammatory-demyelinating disease of the central nervous system. Clinical outcomes such as clinical severity are important considerations for treating MS. Clinical severity is highly variable in MS, which is predicted by typical prognostic factors such as age, sex, disease course, and treatment exposure (Klineova and Lublin, 2018). Typical prognostic factors only explain a partial variation of clinical severity in MS. There has been growing interest concerning the effect of sociodemographic factors on MS severity (Dobson et al., 2022). To knowledge, education has not been explored as a novel prognostic factor of clinical severity in MS. At present, educational attainment is linked to health-state and health-altering behaviours. Further, educational attainment has been linked to clinical severity in MS, but the mechanisms for this are unclear.

We investigated whether the effect of educational attainment on clinical severity in MS was mediated by obesity, smoking, and comorbidities, all which are themselves associated with educational attainment, or if educational attainment exerts an independent effect on clinical severity in MS.

Methods We conducted a cross sectional cohort study using observational clinical data from a single tertiary centre at University College London Hospital. *Participants* included adults with relapsing remitting MS (RRMS) aged ≥ 23 years at the time of assessment. The *main exposures* were highest educational attainment stratified as (1. primary school, 2. secondary school / BTEC, NVQ, diploma 3. undergraduate / postgraduate), obesity (BMI>30), smoking status (current smoker/ non-smoker), and comorbidities (0, 1, 2, 3, 4, 5). The *main outcome* was clinical severity measured by The Expanded Disability Status Scale (EDSS).

Statistical Analysis Generalized linear model using ordinal logistic regression investigated the effect of educational attainment on EDSS, BMI, smoking status, and comorbidities, and the effect of BMI, smoking status, and comorbidities on EDSS. Mediation analysis with bootstrapping was conducted for total, direct, and indirect effects of educational attainment on EDSS. Both models controlled for age, gender, and disease duration.

Conclusions Education exerts an independent effect on clinical severity in MS, which is not mediated by obesity. Higher education levels are associated with less disability in MS patients. We present a novel finding, that educational attainment is an independent prognostic factor of clinical severity in MS.

It is thought provoking how educational attainment exerts an independent effect on clinical severity in MS. Perhaps education exerts a direct neuroprotective effect on brain function and structure, by encouraging greater neurological resilience to injury. This theory is known as the brain reserve hypothesis (Sumowski et al., 2010). The presence of an effect of education on disability in MS, which is primarily neurodegenerative, is complementary evidence in support of this hypothesis.

Conscientiousness has been recognised as the strongest trait predictor of educational attainment (Bergold and Steinmayr, 2018). MS patients who had higher trait conscientiousness had slower rates of longitudinal brain atrophy and lower EDSS scores (Fuchs et al., 2020). The findings from our study are supplementary evidence in support of this theory.

Our findings have implications in clinical practice, early predictors of disease severity aid clinicians in making early treatment decisions. Our findings indicate that future MS patients who are less educated, are at risk of worse disability, and may benefit from early initiation of high efficacy treatment.

References

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Results 554 patients were studied (32.1% males, 66.8% females, 1.1% other gender, 38% smokers, 18% obese). The mean age was 42.6 years [SD 10.9], and the mean disease duration was 25 months [SD 39.7]. Education was associated with BMI (beta = -.166, $p < 0.05$) and smoking status (beta = .200, $p < 0.05$), but not with comorbidities. BMI was associated with EDSS (beta = .164, $t = 1.937$, $p < 0.05$), though smoking status was not. Therefore, a mediation analysis only investigated obesity as a mediator. Total effect of education level on EDSS was significant (beta = -.575, 95% CI [-0.875, -0.275], $p < 0.05$). The direct effect of education level on EDSS was significant (beta = -.553, 95% CI [-.853, -.252], $p < 0.05$). There was no significant indirect effect of education level on EDSS, the proportion mediated by obesity was zero.

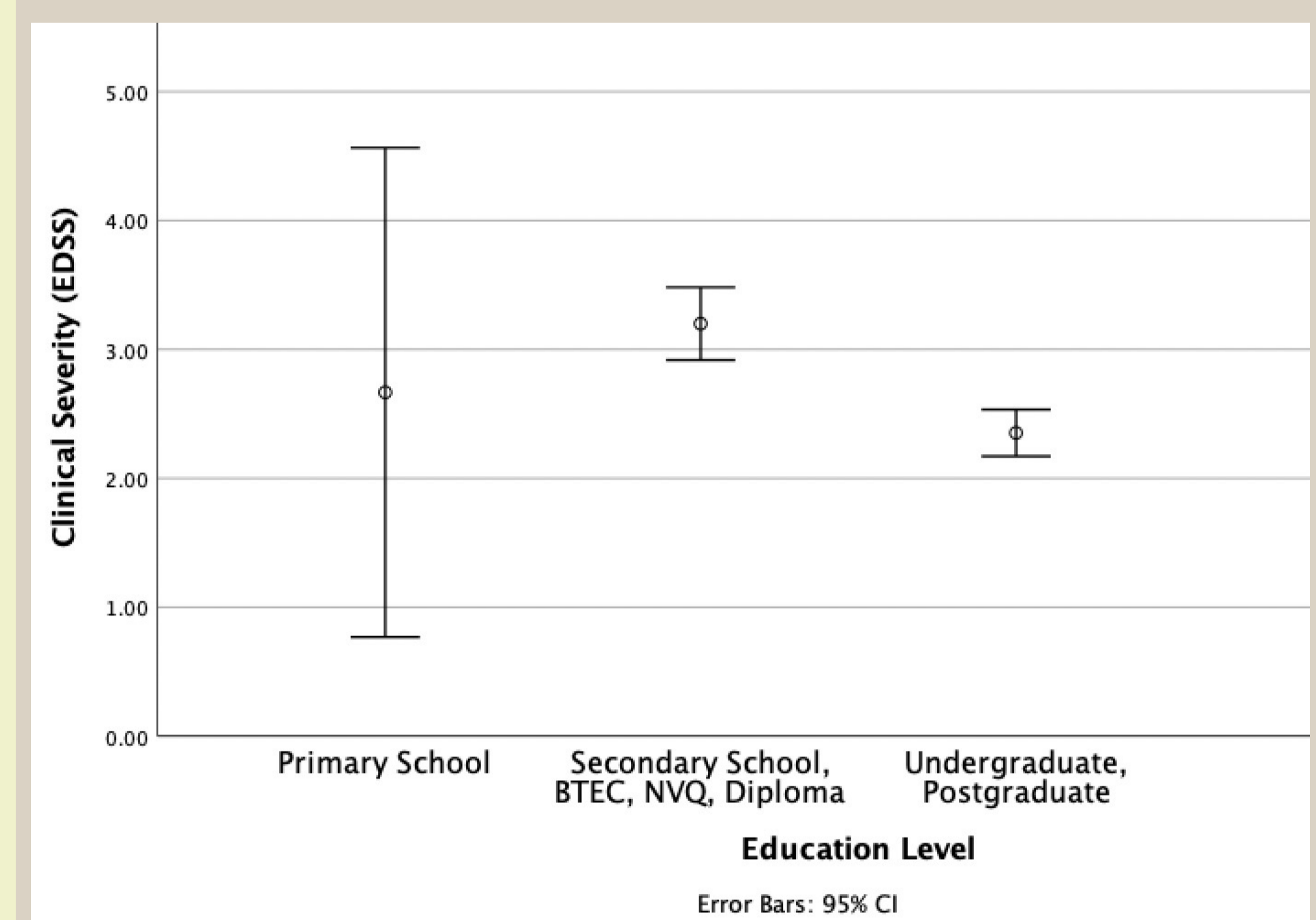


Figure 6. Boxplot demonstrating EDSS scores stratified by educational level

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