Title:

The association between deprivation and the access to disease modifying therapies for multiple sclerosis: An England wide community-based study in the UK MS Register.

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Abstract:

Background: Deprivation can impact the access to health interventions in publicly funded health systems where cost is not the dominant barrier. In this study we examined whether deprivation affected the access to disease modifying therapies (DMTs) for multiple sclerosis (MS).

Methods: All English adults on the UK MS register with relapsing remitting MS who were diagnosed between 2010 and 2017, and after the age of 29 years were included. Deprivation was measured using postcode based 2015 English index of multiple deprivation (IMD), which was divided into quintiles.

Results: A total of 1449 participants were eligible and 531/1449 (36.6%) received DMTs. Participants who lived in more deprived areas, based on their IMD scores, were significantly less likely to receive DMTs (odds ratio = 0.69, 95% Confidence interval = 0.49 to 0.98); barriers to housing and services contributed to this disparity. The Nagelkerke R^2 value of these models showed that 2% of variation in accessing DMTs were dependent on deprivation.

Conclusions: Deprivation, as measured by IMD, negatively influences the access to DMTs in England. Our findings also suggest that the lack of access to local MS DMT clinics in deprived areas may contribute to this disparity.

Keywords:

1. Multiple sclerosis,
2. Deprivation,
3. Socioeconomic status,
4. Index of multiple deprivation,
5. Disease modifying therapy,

Highlights:

1. Deprivation negatively affects the access to DMTs for MS.
2. Living in more deprived areas reduced the likelihood of receiving DMTs for MS.
3. Barriers to housing and services contributed to this disparity in accessing DMTs.
4. Overall, effects of deprivation were small in a publicly funded healthcare system.

Introduction:

Disease modifying therapies (DMTs) to treat people with multiple sclerosis (MS) are expensive and as a result access in not equitable. This is clearly evident in privately funded healthcare systems (Iezzoni et al., 2008; Li et al., 2020; Romley J, Goldman D, Eber M, Dastani H, Kim E, 2012; Simacek et al., 2018; Wang et al., 2016; Zaprutko et al., 2017), but inequalities in access have also been found in publicly funded health care systems (Calocer et al., 2018; Owens et al., 2013; Reyes et al., 2020). In small geographically confined areas, deprivation has been found to have some influence on DMT access, but its impact in a large nationwide population is unknown (Calocer et al., 2018; Owens et al., 2013). It is also unknown whether other forms of deprivations besides financial burden associated with costs of DMTs influence the access in publicly funded healthcare systems.

The UK MS register (UKMSR), launched in 2011 aiming to capture real world data about living with MS in the UK, provides a rich source of clinical and socioeconomic data from a geographically diverse population (Ford et al., 2012). In the UK, the office for national statistics measures relative deprivation by using the index of multiple deprivation (IMD). The measure is different in each nation within the UK. The IMD in England combines 7 domains of deprivation including,1) income, 2) employment, 3) education, skills and training, 4) health deprivation and disability, 5) crime, 6) barriers to housing and services, and 7) living environment. The IMD is calculated based on 37 separate indicators that are organized across these 7 domains of deprivation for a lower layer super output area (LSOA). Each LSOA is designed to contain ~1,500 residents or 650 households. These areas are then

ranked from 1 (most deprived area) to 32,844 (least deprived area) for each of these domains of deprivation and also IMD ("English indices of deprivation 2015 - GOV.UK," n.d.). In this study, the impact of overall deprivation on the access to DMTs was assessed in an England-wide population who were part of the UKMSR and we also examined various forms of deprivation unrelated to the affordability of drugs that could influence the access to DMTs in a publicly funded health care system.

Patients and methods:

Study population

The UKMSR population (REC: South West Central Bristol NRES 16/SW/0194) has been previously described (Ford et al., 2012). The inclusion criteria included: 1) a diagnosis of relapsing remitting MS; 2) diagnosed between 2010 and 2017 to minimize recall bias; 3) as education contributes 13.5% of scores that rank IMD, only those who were diagnosed with MS at the age ≥ 30 years expecting to complete their higher educations, were included to avoid reverse causality. In this study deprivation was measured using the postcode-based 2015 English IMD. Any participants who did not provide their age, duration of disease or postcode were excluded from this study.

Measuring distance between the participant's residence and treatment centre

An origin-destination matrix for each LSOA in England and the postal code of the treatment centres was created. The population weighted centroids, and postcode

centroids for each pairing of LSOA-Postcode was snapped to the nearest OpenStreetMap road location ("OpenStreetMap," n.d.) and the distance (km) was calculated between the two snapped points using the Open Source Routing Machine for each pair combination in the dataset using Python (Luxen and Vetter, 2011). Neuroscience centres were also classified into tier 1 to 4 based on the Getting it Right First Time (GIRFT) report (Fuller et al., 2019). The nearest distance from any neuroscience centre and tier 1 to 4 neuroscience centres were calculated.

Statistical analysis

Mean ± standard deviation (SD) and median with range were used to summarise demographic and clinical details. Logistic regression was used to estimate odds ratios (OR) and 95% confidence interval (CI) to quantify the association between IMD and receiving DMTs. All statistical models were adjusted for age and duration of disease. The final model was additionally adjusted for their own education attainment, employment status, and occupations. IMD was categorised in quintiles. Age and duration of disease were included to statistical models as continuous variables whereas IMD, education levels, employment status and occupation were included as categorical variables.

Results:

Demographics

A total of 1449 people, who had relapsing remitting MS with mean age of 45.3 (standard deviation (SD), 8.6) years and mean disease duration of 3.3 (SD, 2.4) years, fulfilled the inclusion criteria. 1117 (77.1%) participants were female, and 531

(36.6%) participants received DMTs. 175 (12.1%) participants were from the lowest IMD quintile, the most deprived areas, whereas 362 (25.0%) were from the top quintile, the least deprived areas (Table 1).

Impact of deprivation on access to DMTs

Access to DMTs was affected at both extremes of the IMD scale. Participants from the most deprived areas were *less likely* to receive DMTs than others with an OR ratio of 0.69 (CI, 0.49 to 0.98) (Table 2). On the other hand, participants from the least deprived areas were *more likely* to receive DMTs compared to the rest of the cohort with an OR of 1.41 (CI, 1.11 to 1.81) (Table 2).

High barriers to housing and services subdomain were associated with reduced access to DMTs

The IMD domain, *'barriers to housing and services'* reflects the accessibility to housing and local services, including healthcare. Participants who were most deprived of housing and services due to physical and financial barriers were less likely to receive DMTs compared to others with an OR of 0.71 (CI, 0.53 to 0.95) (Table 2). These findings remain statistically significant even after further adjusting for their own education attainment, employment status and occupations (data not shown).

This IMD domain has two sub-domains: 'geographical barriers', which measures the physical proximity of local services, and 'wider barriers' which measures accessibility

to housing, that includes affordability and homelessness (Table 2). The access to DMTs was not associated with either of these two sub-domains of deprivation in isolation. IMD or barrier to housing and local services only explained 2% of variation in accessing DMTs among UKMSR participants, based on the Nagelkerke R^2 value of these models.

We did not find any correlation between the access to DMTs and other 4 domains of deprivations unrelated to the affordability of drugs including education, skills and training, health deprivation and disability, crime and living environment (data not shown). The access to DMTs also did not depend on the distance from neuroscience centres ($p > 0.05$ for each of these statistical models).

Discussion:

We demonstrated that the access to DMTs was associated with patients' IMD scores in an England-wide community-based population, with those in the highest quintile were more likely and those in the lowest quintile were less likely, to receive DMTs, than the other groups combined. A neighbourhood-based measurement of deprivation, such as IMD, provides a more collective measurement of the resources, and adverse factors to which participants are exposed. We also found that barriers to housing and services negatively affects the access to DMTs, suggesting that homelessness, poor housing and high average distance to the nearest local services could be associated with a reduced likelihood of receiving DMTs. Although there was no association between the 'shortest' distance from neuroscience centres and the likelihood of receiving DMTs, people living in deprived areas may use public

transport to travel and the access to the local neuroscience centres may be challenging because of poor public transport. Poorer access to DMTs in people from deprived areas, may lead to faster progression of disability and further impoverishment resulting in more deprivation and worsening access to healthcare. Similarly, progressive forms of MS may also result in faster accumulation of disability and higher level of deprivation.

One UK study between 2002 and 2005 has shown a similar effect of deprivation on prescribing when the current national structure of prescribing centres was set up to deliver DMTs as part of the 'UK MS risk sharing scheme' (Owens et al., 2013). Unlike here they did not adjust for any confounding factors such as age, disease duration or reverse causality and the population was also derived from only two geographic locations. In England DMTs are still prescribed through MS DMT prescribing centres located in tertiary MS clinics or hospital neurology clinics and our findings suggest that nationally deprivation remains a barrier. However, here we were able to pinpoint that 'barrier to housing and services' was driving this effect implying a lack of access to these clinics may be one of the factors which drives this disparity. One approach to improve this access would be to have DMT clinics at their local district general hospitals. The rate of DMT prescription in people with relapsing remitting MS was substantially lower in this England-based population than that is usually seen among similar population in a range of health systems throughout Europe (Whicher et al., 2020). However, similar barriers to housing and services have had an impact in uptake of widely available breast screening services in the UK and Australia (Maheswaran et al., 2006).

This study has a number of limitations. The sub-population of the UKMSR, who contribute to this study, were more frequently from higher socioeconomic backgrounds. People from higher socioeconomic backgrounds are more likely to engage voluntarily with health surveys (Cheung et al., 2017). In this study, participants provided their own data and recall bias, though we tried to adjust for this, is a known limitation in this context.

Conclusions:

In this study, utilising the UKMSR, we demonstrated that deprivation, as measured by IMD, had a negative impact on the access to DMTs in England. Our findings also suggested that the lack of access to local MS DMT clinics in deprived areas probably contributed to this disparity.

Declarations of interest:

None

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Table 1: Demographic characteristics and levels of deprivation

Demographic characteristics		**N**
Age	Mean (SD, year)	45.3 (8.6)
	Median (range, year)	44 (30 - 85)
Duration of disease	Mean (SD, year)	3.3 (2.4)
	Median (range, year)	3 (0 - 8)
Gender	Male (%)	332 (22.9)
	Female (%)	1117 (77.1)
Received DMT	No (%)	918 (63.4)
	Yes (%)	531 (36.6)
IMD		**N (%)**
Q 1 (most deprived)		175 (12.1)
Q 2		275 (19.0)
Q 3		315 (21.7)
Q 4		322 (22.2)
Q 5 (least deprived)		362 (25.0)

DMT = Disease modifying therapies; IMD = Index of multiple deprivation, Q = Quintiles and SD = Standard deviation

Table 2: The impact of deprivation on the access to DMTs for MS.

Quintiles	ß	S.E.	p	OR (95%CI)	Nagelkerke R^2
IMD					
Q1 (most deprived)				1 (reference)	
Q2-5	-0.368	0.176	0.037	0.692 (0.490 - 0.978)	0.021
Q5 (least deprived)				1 (reference)	
Q1-4	0.346	0.126	0.006	1.414 (1.105 - 1.809)	0.024
Barriers to housing and services					
Q1 (most deprived)				1 (reference)	
Q2-5	-0.349	0.150	0.020	0.705 (0.525 - 0.947)	0.022
Q5 (least deprived)				1 (reference)	
Q1-4	-0.070	0.135	0.601	0.932 (0.716 - 1.214)	0.017
Geographical barriers					
Q1 (most deprived)				1 (reference)	
Q2-5	0.004	0.127	0.973	1.004 (0.783 - 1.288)	0.023
Q5 (least deprived)				1 (reference)	
Q1-4	-0.163	0.153	0.288	0.850 (0.630 - 1.147)	0.018
Wider barriers					
Q1 (most deprived)				1 (reference)	
Q2-5	-0.307	0.176	0.082	0.735 (0.520 - 1.039)	0.020
Q5 (least deprived)				1 (reference)	

Q1-4	-0.090	0.130	0.488	0.914 (0.708 - 1.179)	0.017

CI = Confidence interval, IMD = Index of multiple deprivation, OR = Odds ratio, Q = quintiles and S.E. = Standard error