

Social determinants of health in multiple sclerosis

Ruth Dobson^{1,2}✉, Dylan R. Rice³, Marie D'hooghe^{4,5}, Rachel Horne¹, Yvonne Learmonth^{6,7,8,9}, Farrah J. Mateen³, Claudia H. Marck¹⁰, Saúl Reyes^{11,12,13}, Mitzi Joi Williams¹⁴, Gavin Giovannoni^{1,2,13} & Helen L. Ford^{15,16}

Abstract

Social determinants of health are the conditions in which people are born, grow, live, work and age. These circumstances are the non-medical factors that influence health outcomes. Evidence indicates that health behaviours, comorbidities and disease-modifying therapies all contribute to multiple sclerosis (MS) outcomes; however, our knowledge of the effects of social determinants – that is, the ‘risks of risks’ – on health has not yet changed our approach to MS. Assessing and addressing social determinants of health could fundamentally improve health and health care in MS; this approach has already been successful in improving outcomes in other chronic diseases. In this narrative Review, we identify and discuss the body of evidence supporting an effect of many social determinants of health, including racial background, employment and social support, on MS outcomes. It must be noted that many of the published studies were subject to bias, and screening tools and/or practical interventions that address these social determinants are, for the most part, lacking. The existing work does not fully explore the potential bidirectional and complex relationships between social determinants of health and MS, and the interpretation of findings is complicated by the interactions and intersections among many of the identified determinants. On the basis of the reviewed literature, we consider that, if effective interventions targeting social determinants of health were available, they could have substantial effects on MS outcomes. Therefore, funding for and focused design of studies to evaluate and address social determinants of health are urgently needed.

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A full list of affiliations appears at the end of the paper. ✉ e-mail: ruth.dobson@qmul.ac.uk

Key points

- Addressing an individual's social determinants of health — that is, the conditions under which they are born, grow, live, work and age — could provide opportunities to reduce the burden of living with multiple sclerosis (MS).
- Individual factors that may influence MS-related outcomes include sex, gender and sexuality, race and ethnicity, education and employment, socioeconomic status, and domestic abuse.
- Societal infrastructures, including access to food, health care and social support, can also affect MS-related outcomes.
- Awareness of the specific circumstances of a patient with MS might help neurologists deliver better care.
- Social determinants of health are not static and can change according to wider sociopolitical contexts, as highlighted by the COVID-19 pandemic.
- Rigorous studies of interventions to ameliorate the effects of poor social determinants on people with MS are urgently needed.

Introduction

As defined by the WHO, **social determinants of health** are the conditions under which people are born, grow, live, work, and age (Fig. 1). These conditions are shaped by the distribution of economy, governance and resources at the global, national and local levels. They are also responsible for health inequities and avoidable differences in health status. Social determinants can be more important than health care or lifestyle choices in influencing health, and it has been suggested that social determinants of health account for 30–55% of health outcomes.

Multiple sclerosis (MS) affects over 2.8 million people worldwide and is widely acknowledged to be highly heterogeneous¹. The disease is thought to develop as a result of environmental exposures in genetically susceptible people². Over the past 20 years, the number of disease-modifying therapies available for the treatment of MS has rapidly increased and the emphasis on multidisciplinary health-care management has grown; however, a cure remains elusive. Disease-modifying therapies have had a considerable effect on long-term disease outcomes, with the natural history of MS changing substantially over the past 20 years³. Most neurologists use physical signs and symptoms, and (visible) MRI brain lesions to estimate a person's risk of ongoing disease activity, to direct treatment (including disease-modifying therapies) and to measure outcomes. However, addressing an individual's social determinants of health has the potential to provide additional opportunities to reduce the burden of living with MS.

Despite the growing recognition of the importance of social determinants of health, little progress has been made towards addressing these determinants in people living with MS. Emerging data suggest that the cumulative effects of exposure to social and environmental stressors can manifest in later adulthood and have a negative effect on general and brain health⁴. A holistic approach that includes consideration of social determinants of health, which can be considered the 'risks of risks', offers the potential for opportunities to fundamentally improve health and health care in MS and other neurological diseases.

Although some social determinants of health, such as employment status, have already been investigated in the context of MS, the MS-specific evidence regarding other social determinants of health is of variable quality and quantity, limiting the interpretation of some findings. Nevertheless, we can learn a lot from looking at the wider public health environment — strategies that have been shown to improve general health status by modifying social determinants of health can also be applied to the management of MS. In this Review, we aim to provide an overview of the current literature about the effect of social determinants of health on MS outcomes to increase awareness and encourage high quality research on this topic. We also highlight potential bidirectional relationships between MS outcomes and social determinants of health. We conclude by providing recommendations on how neurologists and the wider clinical team might assess and address social determinants of health in practice, as the first step in managing the influence of these factors on MS care.

Social determinants of health

Social determinants of health can be classified in several ways but for the purposes of this Review we divide them into two categories: individual factors and structural determinants. Individual factors include characteristics such as gender, race and ethnicity that have an effect on health via an interaction with structural or societal inequalities. Structural determinants are societal infrastructures that influence health; for example, health-care access and social support. Importantly, these two categories are not always clearly divided and bidirectional influences exist between individual factors and structural determinants. For example, a person's individual circumstances (such as racial background) can influence their place in society and potentially their access to services such as health care. Furthermore, a person's access to services and infrastructure such as health care or social support can influence how much adverse personal circumstances such as employment status might affect their health.

For the purposes of this Review, we focus on individual-level MS-related outcomes, including clinical (relapses, disability, cognition), radiological (MRI) and patient-reported (quality of life and effect of disease) outcomes. To maintain a clear focus on the person with MS, we do not discuss societal outcomes, such as health economic findings. We review the literature on a range of social determinants of health including gender, race, education, employment, domestic abuse, socioeconomic status, health-care access, food disparities, neighbourhood environment and pollution, social support, and COVID-19 in relation to MS diagnosis, disease progression and disability.

Individual factors

Sex, gender and sexuality. MS is more common in women than in men and the sex ratio seems to be widening⁵. The characteristics of the disease also seem to differ between men and women⁶; however, a detailed description of these epidemiological observations and their potential biological underpinnings is outside the scope of this Review.

The effect of MS on quality of life seems to vary between men and women. Among people with MS, evidence suggests that women report worse fatigue and anxiety than men, whereas men report greater limitations in walking, dexterity and emotional roles than women^{7,8}. In one study, the relationship between Expanded Disability Status Scale (EDSS) scores and the patient-reported Multiple Sclerosis Quality of Life-54 (MSQOL-54) instrument differed between men and women, suggesting that the relationship between the physical aspects of MS and quality of life is weaker in women than in men⁸. That societal influences have a

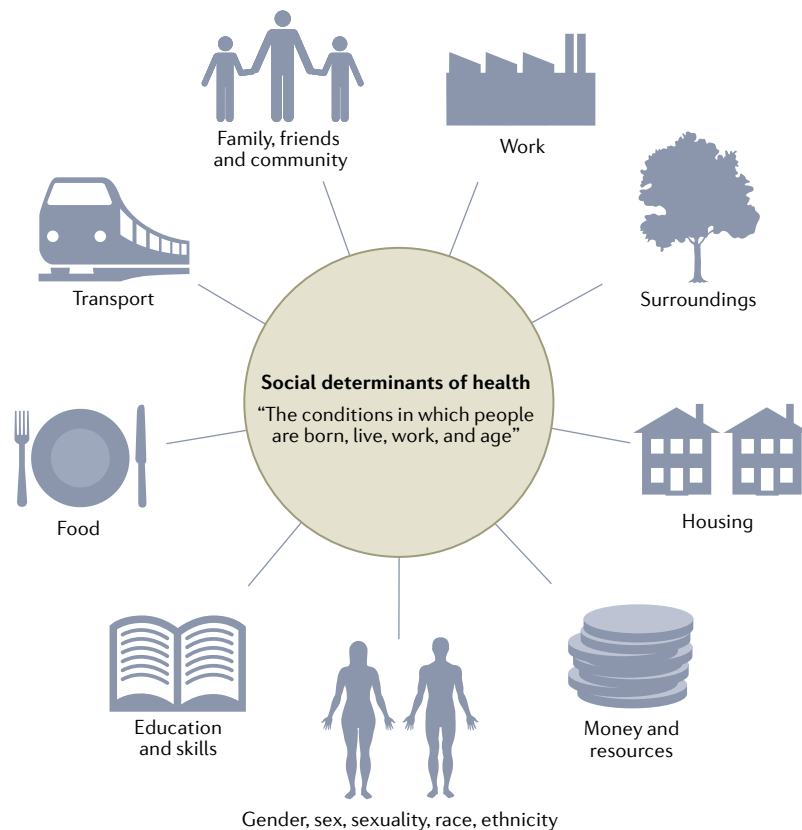


Fig. 1 | WHO social determinants of health. Social determinants of health are the conditions in which people are born, grow, live, work and age. They are non-medical factors that influence health outcomes through a wide-reaching influence on all aspects of life. Social determinants of health can be divided into

two categories: individual factors and structural determinants. Individual factors (for example, gender, race and ethnicity) have an effect via societal inequalities and structural determinants (such as health-care access and social support), which in turn affect health through their influence on the individual.

role in this gender difference seems highly likely; however, unpicking such relationships is complex and studies have not yet fully addressed this question. It should be noted that the social construct of gender is more complex than a binary biological variable. In the studies described above, researchers focused on cisgender men and women, and a wider scope of study is required to represent all people living with MS.

Sexual and gender minority (SGM) people face unique obstacles in accessing quality health care, which subsequently affects disease-related outcomes⁹. The effect of intersectionality between chronic neurological disease and sexual and/or gender minoritization has been poorly studied. One relatively small study performed in San Francisco, which examined people who were at risk of sexual and/or gender minoritization, found that the majority of SGM people living with MS reported that their gender identity or sexual orientation did not affect their health care⁹. Although most of the participants felt comfortable discussing their sexuality or gender identity with their physician, a few reported homophobia or gender discrimination from health-care professionals, limiting their engagement with care and hence their potential access to disease-modifying therapy. Very few participants reported taking part in either SGM or MS support groups⁹. In a second small study, compared with cisgender participants, transgender participants reported that they were less comfortable discussing sexual health with their doctor, which could affect their quality

of life¹⁰. From the studies performed to date, there do seem to be differences between gender groups in terms of how MS affects people and how it might influence their interactions with health-care providers. Further work is required to ensure that the effect of gender on MS is better understood, and that services are able to provide equitable and effective care for all people living with MS.

Race and ethnicity. Interest in the relationship between racial and ethnic background and MS outcomes is increasing, particularly in the USA. Several studies have identified worse clinical outcomes in Black, Hispanic and Latinx people with MS than in white people with MS; these observed differences are unlikely to be solely genetic in origin and are far more likely to result from systemic racism across health and other services¹¹. The magnitude of racial and ethnic influences on social determinants of health are likely to differ across countries and regions; these geographic discrepancies must be considered when attempting to draw population-level conclusions¹².

Although MS was historically thought to be most common in white people, evidence now indicates that it occurs at higher frequency in minoritized racial or ethnic populations than previously thought¹³. In the USA, strong correlations exist between race, health-care access and socioeconomic status. Also in the USA, systemic differences in health-care access, socioeconomic inequalities, cognitive biases and

racism within health care have been shown to have a role in poorer disease-related outcomes in people from minoritized racial and ethnic groups across multiple diseases¹⁴. A multicentre, retrospective study published in 2004, was one of the first to extensively characterize MS in Black Americans¹⁵. Compared with white Americans, Black Americans in this study had a slightly older age at onset and a higher prevalence of opticospinal disease, with more rapid disease progression and shorter time to an EDSS score of 6.0. In support of these clinical observations, a longitudinal study in people with MS identified more rapid brain and retinal atrophy in Americans from African ancestral backgrounds than Americans from European ancestral backgrounds¹⁶.

A more recent study compared MS mortality rates among five groups that the authors defined by ethnicity and race: non-Hispanic white, non-Hispanic Black, non-Hispanic Asian or Pacific Islander, non-Hispanic American Indian or Alaska Native, and Hispanic¹⁷. Among individuals aged under 55 years, non-Hispanic Black Americans had the highest MS mortality rate of all these groups. In another single-centre study, decreased cortical thickness, decreased subcortical volume and decreased cognitive scores were observed in Black Americans with MS compared with white Americans with MS¹⁸. Some of these disparities in outcome might be partially explained by disparities in age at disease onset – later disease onset is a known indicator of poor prognosis. Furthermore, compared with white people, Hispanic people were less likely to present with late-onset MS, but more likely to present with motor symptoms at onset, another poor prognostic indicator¹⁹. Confounding factors including diagnostic delay, selection bias and other socioeconomic factors, which were not fully addressed in the studies discussed above, are likely to contribute to racial disparities in MS outcome¹⁵.

Despite progress in understanding MS in diverse populations, substantial gaps in our knowledge remain. Barriers to filling these gaps include low enrolment of minoritized populations in clinical trials and substantial limitations to many of the current datasets. For example, much of the existing data is retrospective and focuses on measures of physical disability. Research examining other measures such as cognitive dysfunction and brain changes on MRI often have small sample sizes and do not control for socioeconomic status and other social determinants of health, which are inextricably linked to race and might affect outcomes. Furthermore, reference scores and norms used in tests such as detailed cognitive assessments are often based on white control populations. For example, a study examining early cognitive dysfunction in MS used healthy control groups consisting of Black and Hispanic people and found no significant difference in oral Symbol Digit Modalities Test (SDMT) scores between participants with early MS and healthy participants with the same racial background²⁰. Importantly, overall scores were lower in Black and Hispanic people than white people (both healthy controls and participants with MS), possibly a result of the influence of race on other social determinants of health such as educational attainment and socioeconomic status.

In a number of US-based military studies, data on service-connected disability were used to identify people with MS – MS is considered a service-connected disability when it manifests during or within 7 years of military service²¹. However, receiving a service-connected MS diagnosis is likely to be more difficult for Black people owing to delays caused by racism and inequality within the health-care system. This means that within US military cohorts – often the most complete in terms of data, and used to understand the influence of race²² – biases unrelated to MS could influence findings including those related to MS incidence and prevalence, and age and disability

at diagnosis. Existing studies focus on countries without universal health-care systems and with majority white populations. This narrow focus leaves considerable gaps in our knowledge when it comes to non-white-majority countries and those with universal health-care systems, which are still vulnerable to racial biases²³.

Education. Evidence suggests that level of education has an influence on clinical outcomes related to MS, but few MS-specific studies have examined the effect of education on patient-reported or health economic outcomes, as discussed in more detail below. Education precedes and influences occupation, income and often wealth; in some studies it is considered a proxy measure of socioeconomic status. Measures of educational level, commonly completion of high school (12 years of schooling in most countries), have been widely used in MS research, and the results of these studies suggest that higher levels of education are protective against disability progression in people with relapsing MS. For example, in a study of 1,372 Belgian people with relapse-onset MS, participants with <12 years of formal education had a higher risk of reaching an EDSS score of 6.0 than participants with >12 years of formal education in a Cox proportional hazards model adjusted for gender, age, age at onset and disease-modifying therapy, although this relationship was not observed in participants with progressive-onset MS²⁴. Similarly, in another study, a lower level of education in Brazilian people with MS was associated with higher EDSS scores, longer disease duration and a higher T2 lesion load²⁵.

However, all of the studies examining links between education and MS outcomes are limited by their design; as with all case-control studies they are subject to ascertainment bias and involve analysis of selected retrospective data. First, reverse causation might explain some of the observed differences, so prospective longitudinal studies are needed to investigate this possibility. Second, low levels of education are associated with exposure to a range of factors that increase the risk of MS and of worse disease outcomes. Such factors include smoking, low levels of health literacy, lack of employment and low socioeconomic status, and the studies performed so far have not been designed in a way that enables researchers to dissect out the contribution of these different relationships. Third, the studies performed to date focused on years of education, whereas quality of education has not been studied in any meaningful way. Last, it is possible that prodromal MS influences educational achievement²⁶ and thus limits access to higher levels of education, which would place people with earlier MS onset at an educational disadvantage.

Employment. Employment is crucially important when considering population health and health inequalities; however, the relationship between employment status and health or chronic disease is complex and bidirectional. Exclusion from the workplace results in material deprivation, and can adversely affect social status and identity²⁷. As we discuss in this section, few studies have examined the effect of unemployment on health outcomes in MS; however, greater disability, as measured by EDSS, has been consistently associated with lower rates of employment^{28,29}. The strength of this relationship varies between and within countries, and more recent data suggest a narrowing in the difference in employment rates between people with and without MS³⁰. Evidence indicates that higher EDSS scores, fatigue³¹ and cognitive impairment³² are independently associated with a greater likelihood of unemployment in people with MS³³, whereas clinical stability is associated with a reduced risk of leaving employment^{34,35}. Progressive MS is associated with a higher risk of leaving employment than relapsing

MS^{29,36,37}. Unemployed people with MS seem to have a higher number of physical comorbidities than employed people with MS³⁸; however, the results of one study suggest that this difference is substantially reduced after adjustment for MS symptom severity, suggesting that the comorbidities and MS symptoms do not act independently³⁷. Furthermore, most studies performed to date compared sociodemographic, clinical and psychosocial variables between employed and unemployed people with MS, using employment status as the outcome variable, which means they did not examine the true complexity of any relationship.

In one study, people with MS who were not working at 10 years after diagnosis had a significant reduction in functioning (in terms of bodily function, as well as activities and participation in activities of daily life), an increased self-reported effect of MS and decreased fine hand function compared with people with MS who were working at this time point³⁹. Another cross-sectional study identified increased perceived stress, reduced self-reported physical and mental health related quality of life, and decreased life satisfaction in unemployed people with MS compared with employed people with MS⁴⁰. The results of another study indicate that employment status is the most important variable for predicting mental health status in people with MS under 45 years of age⁴¹. Similar to education, we note that employment status is associated with a number of risk factors for MS development and subsequent disability such as smoking and low health-care literacy; however, the studies performed to date have not addressed this relationship.

Evidence indicates that other social determinants of health interact with the relationship between employment and MS. For example, younger age and higher education level are consistently associated with a higher employment rate in people living with MS^{29,36}, and in one study a high frequency of social or lifestyle activities at baseline was associated with a greater likelihood of being employed 10 years later³¹. Studies that investigated sex differences in the likelihood of leaving employment as a result of MS reported a range of results, including no difference, greater likelihood in men and greater likelihood in women^{29,34,42}. In a study of people with MS in the USA, non-Hispanic white people had higher employment rates (48%) than Hispanic people (45%) and non-Hispanic Black people (36%)⁴³, highlighting the potential role of other sociodemographic factors in determining employment status.

Socioeconomic status. Socioeconomic status refers to relative position within the social hierarchy and is measured by indicators such as income, occupation and place of residence. Therefore, socioeconomic status draws on multiple social determinants of health, but it also exerts an independent effect. Evidence has shown that socioeconomic status has an effect on health across a wide range of indicators, settings and populations⁴⁴. Although reducing socioeconomic inequalities in health is an international policy priority, large disparities persist in both countries with and countries without universal health-care systems⁴⁵.

To date, studies investigating the relationship between socioeconomic status and MS have mainly focused on the risk of developing MS. Overall, findings are conflicting, with some studies finding an association between high socioeconomic status and risk of MS, some finding an association between low socioeconomic status and risk of MS, and others finding no association^{46,47}. In a meta-analysis published in 2015, all the studies that identified a link between high socioeconomic status and MS risk were from countries that were considered to have more inequality; a potential explanation for this relationship could be differences in the skills that are required to navigate complex health-care systems or differences in insurance status in payer-based systems.

Available data regarding the effect of socioeconomic status on MS disability outcomes indicate a relationship between greater deprivation at disease onset and greater disability even in countries with a universal health-care system, including a higher risk of reaching EDSS scores of 4.0 and 6.0 in Cox proportional hazards models^{46,48}, faster retinal neurodegeneration⁴⁹ and onset of secondary progression⁴⁶. Evidence also indicates that higher socioeconomic status in people with MS is associated with a lower burden of psychiatric symptoms and a higher likelihood of symptom recovery following mental health treatment^{50,51}.

In regions without universal health care, lower socioeconomic status is associated with reduced access to highly effective disease-modifying therapy for MS⁵². People living in poverty are less likely than other people to be able to access insurance systems that cover comprehensive disease-modifying therapy, and large studies have shown a direct effect of this disparity on cancer outcomes⁵³. Therefore, the relationship between socioeconomic status and disability in MS could be mediated by access to disease-modifying therapy. However, this hypothesis is still a matter of debate and the mechanisms underlying the relationship are likely to vary substantially within and between geographical regions. The results of some studies indicate that, in countries with a universal health-care system, people with MS with higher socioeconomic status are more likely to be prescribed disease-modifying therapy and less likely to experience delays in disease-modifying therapy escalation than people with lower socioeconomic status^{54–56}, however, other studies have found no evidence to support this conclusion^{57,58}. These contrasting results are likely to be related to the specific scope and limitations of individual studies, along with differences in local prescribing ‘cultures’. Evidence also suggests that socioeconomic status-related disparities in disease severity, health-care access and literacy can affect prescribing decisions in MS^{54,57,58}; however, research into ways to overcome barriers and/or enact local change is lacking.

Substantial associations exist between socioeconomic status and MS disability risk factors, such as smoking, obesity and comorbid disease, which might influence any observed relationship between socioeconomic status and disability outcomes. Most studies that examine the relationship between socioeconomic status and MS diagnosis or disability outcomes do not control for these risk factors⁵⁹. As mentioned above, comorbidities have been associated with poorer long term outcomes in MS⁶⁰; actively addressing these, especially in more deprived populations, is a potential means through which MS outcomes could be improved. The relationship between socioeconomic status and MS diagnosis and disability is not unidirectional; evidence from the UK MS Register indicates that MS restricts social and economic opportunities, even several years before diagnosis⁶¹ (Fig. 2). Critical study of the timing and mechanism(s) through which socioeconomic factors might exert their influence on MS outcomes, along with means by which neurology teams can intervene to ameliorate these, thus has the potential to markedly change outcomes for many people living with MS.

Domestic abuse. Domestic abuse is defined as “a pattern of behaviour in any relationship that is used to gain or maintain power and control over an intimate partner”, which can be “physical, sexual, emotional, economic or psychological actions or threats of actions that influence another person”⁶². This abuse has a serious effect on the individual, the family and the health-care system; however, no data on domestic abuse and disease-related outcomes in MS have been published to date.

According to data from Public Health England, people with disabilities experience disproportionately higher rates of domestic abuse over a longer period of time, with greater severity and frequency, than

non-disabled people⁶³. In addition to practices such as gaslighting and physical abuse, less widely recognized forms of abuse, such as ridiculing or physical neglect, have been reported⁶⁴. Domestic abuse

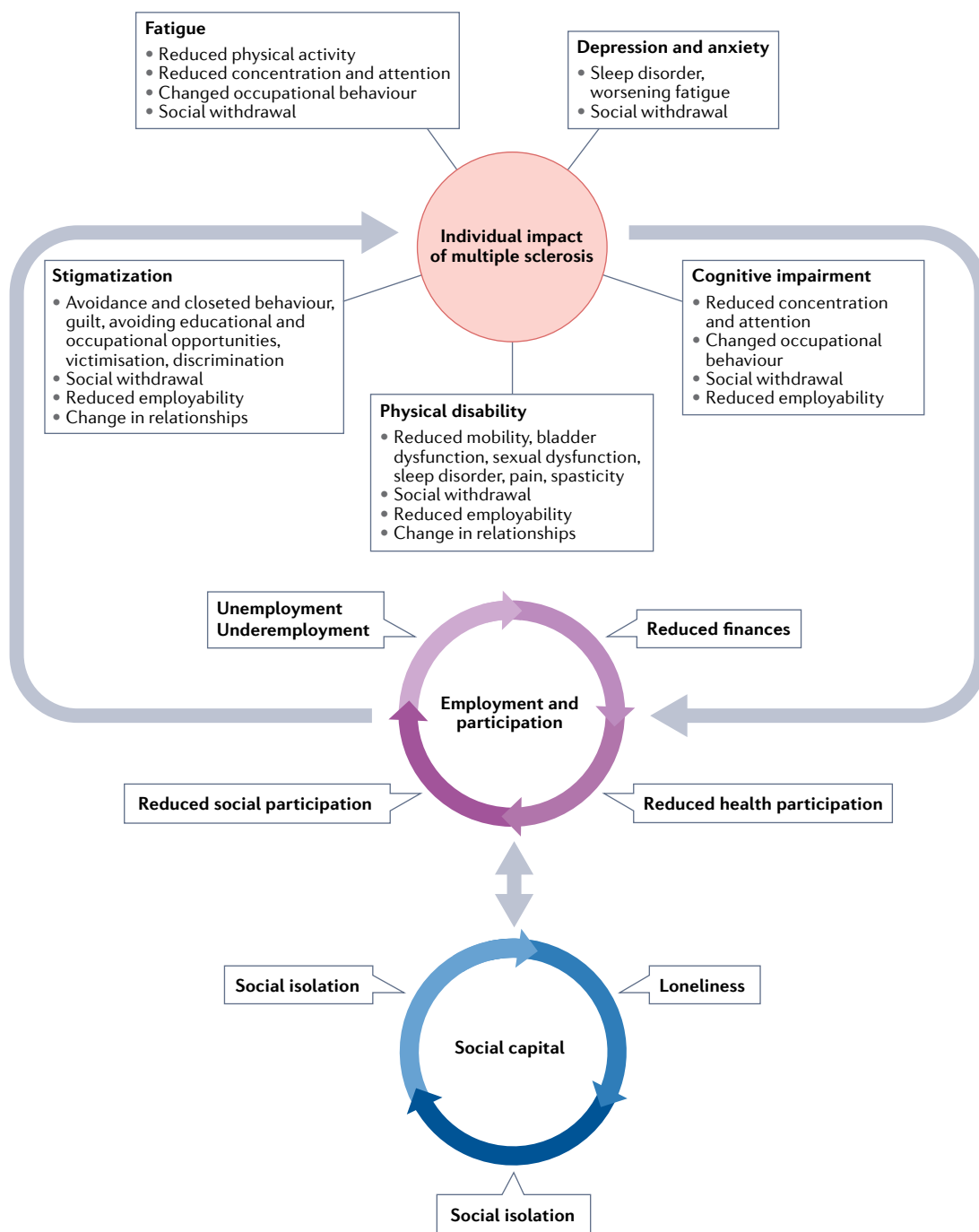


Fig. 2 | Potential interactions between selected social determinants of health and multiple sclerosis outcomes. Many social determinants of health interact and intersect with each other, leading to poorer outcomes, in either an additive or even a multiplicative manner. There are potential further interactions between living with chronic multiple sclerosis symptoms such as cognitive impairment and bladder or bowel impairment, and social determinants of

health. Multiple sclerosis and its symptoms might reduce an individual's social determinants of health, particularly those related to employment and social isolation, which might then amplify the effect of multiple sclerosis. Studying this vicious cycle is complex owing to the multiple and varying influences that exist at both the individual and group level.

can involve a range of people including intimate partners, family members and carers, and disabled women are much more likely to experience abuse than disabled men⁶³. In a survey of US adults with advanced MS, more than half of the respondents reported abuse from their caregivers⁶⁵, and the WHO has identified substantial barriers to disabled people seeking support after abuse⁶⁶. Further research is needed to understand the best and most sensitive means of applying this knowledge across clinical practice in MS; although this is a challenging area, given the potential risk that people living with MS are at, it is clearly important.

Intermediate determinants

Health-care access. Health care for people living with MS includes not only care associated with MS management, but also care of any comorbidities, health screening and preventive care, and access to services for transient acute health issues. Studies of health-care access that consider the progression of MS as an outcome of interest have investigated access and the use of neurologists⁶⁷, investigation and treatment of MS-related bladder symptoms⁶⁸, and the use of disease-modifying therapy^{58,69}. Other studies have investigated access to cancer screening, management of hypertension and osteoporosis in women with severe MS⁷⁰, general health needs⁷¹ and social support⁷²; studies addressing health care are discussed in more detail below.

In a US-based study, participants with lower levels of MS-related disability were more likely to receive their usual care directly from a neurologist, and those with higher disability were less likely to receive medical care⁶⁷. In another study, women with an EDSS score of ≥ 7 had an uptake of breast, ovarian and colorectal cancer screening tests that was far below the general population average in the USA⁷⁰. Although this study did not include people with mild or moderate MS-related disability, this finding highlights an area of potential concern in comprehensive MS care. An important limitation of studies performed in the USA is that they primarily include participants who receive health care through a private health-care insurance system, meaning that those without health-care insurance are not studied. Studies of health-care needs in countries with a public or universal health-care system have identified health-care needs of people with MS outside MS-related specialists, tests or treatments. One such study found that overall health needs are not met as MS disability increases⁷¹; individuals with greater disability had greater unmet physiotherapy, occupational therapy and social needs.

Food access. Food poverty refers to the inability to acquire or consume an adequate quantity of nutritious food. In 2021, 8% of UK households were food insecure, and of this 4% were living in food poverty⁷³. To date, no publications have described the effect of food poverty on MS disease activity or outcomes. However, the effect of dietary interventions on MS outcomes has been studied, with the overwhelming majority of studies examining food supplements rather than overall diet quality. An observational study identified an association between a healthier diet and higher mental and physical health quality of life scores; a dose–response relationship was observed between diet habits questionnaire score and quality of life score⁷⁴. In a second study, healthier dietary intake on subscales for fibre, fruit and vegetables, and fat was associated with better quality of life scores⁷⁵. However, this study identified no association between diet scores and disability. With all of these studies, participant bias, potential reverse causation and confounding are major concerns, and in 2020, a systematic review concluded that many of the studies investigating dietary interventions for MS had

major problems with design or implementation that substantially limit their interpretation⁷⁶.

Air pollution. Exposure to particulate matter via air pollution has been associated with poor brain health⁷⁷; additionally it might lie on the MS causative pathway and/or trigger relapses due to pro-inflammatory influences⁷⁸. Studies of the relationship between air pollution and MS outcomes have generally focused on ecological-level assessments and have reported modest but statistically significant negative effects. Outcomes that have been studied so far include relapses, EDSS score and new MRI lesions. Specific findings are discussed in more detail below.

Associations between air pollutants and MS outcomes have been identified in France^{79,80}, Iran⁸¹, Israel⁸² and Italy^{83,84}. These studies all studied particulate matter $< 10 \mu\text{m}$ (PM_{10}) and were performed in locations that were generally less polluted with low levels of deprivation. In Lombardy, Italy, admissions to hospital for MS relapse increased by 42% when PM_{10} was in the highest quartile, with a maximal effect observed 0–7 days after exposure⁸³. A study in France of 1,783 MS relapses in 424 participants with MS assessed the effects of PM_{10} , NO_2 , and O_3 (ozone) in a multi-pollutant model, but found a significant association between only MS relapses and O_3 (ref.⁷⁹). Another study in France with a case–crossover design in 536 people with MS found that PM_{10} concentrations were significantly increased in the days prior to clinical relapse onset compared with other time points⁸⁰. In 287 Israeli people with MS, exposure to $\text{PM}_{2.5}$ was independently associated with MS relapses in those who did not smoke; an inverse relationship was found between O_3 exposure and relapses in participants < 40 years old⁸². In Isfahan, Iran, increases in the air quality index – a measure of six air pollutants – were modestly associated with higher EDSS scores among people with MS⁸¹. Only one study examined the effect of pollution at the level of individual participants, finding that higher PM_{10} exposure was associated with gadolinium-enhancing lesions independent of smoking status, disease-modifying therapy and season⁸⁴.

Overall, the relatively small number of studies, inconsistent inclusion of smoking status, different MS disease outcomes, and the older nature of several studies in locations with limited air pollution, make it difficult to draw any definitive conclusions on the effect of neighbourhood air pollution on MS outcomes. The complex association between poor air quality and deprivation⁸⁵ adds to its strength as a social determinant of health; however, this specific relationship has not been studied in MS.

Social support. Social support can be tangible (for example, financial assistance) or intangible (for example, emotional support or companionship) and can come from many potential sources, including health-care providers, government-funded social support schemes, charitable organizations, family, friends, pets, neighbours and coworkers. MS is a disabling and stigmatizing disease that can lead to social isolation and exclusion⁸⁶. People with MS report reduced social participation compared with before their diagnosis, owing to disability, physical barriers and often reduced financial resources^{87,88}. Two studies found that people with MS who have cognitive impairment and reduced mobility have reduced social contacts, higher unemployment rates and lower standards of living than those without disability in these domains^{89,90}. Other evidence indicates that MS symptoms, including bladder dysfunction, poor sleep, pain, spasticity and fatigue, negatively affect social interactions and quality of life^{91,92}. People with MS also report changes in family relationships and friendships; for example, divorce, or needing support from family members to assist with activities of

daily living⁹⁰. One study found that even relatively mild MS-related disability has a negative effect on social activities, as measured by the Environmental Status Scale (ESS)⁹³.

Evidence indicates that the social isolation and exclusion caused by MS can result in poor mental health, worse quality of life, and poor engagement with care⁹⁴. In a study in 140 participants with MS, social isolation was associated with suicidal intent⁹⁵, and in another study, higher social capital, which refers to the many resources derived from the social interaction between individuals and groups, was associated with lower self-reported physical and psychological effects of the disease⁹⁶. The often intangible nature of social support can make it complex to study and develop interventions for; however, there seems to be an opportunity for further work in this area, with the potential to substantially improve quality of life for people with MS.

COVID-19. The effect of the COVID-19 pandemic on every facet of life cannot be underestimated. People with chronic diseases, including MS, experienced the pandemic differently from those without chronic diseases; health inequity between these two groups has been highlighted and exacerbated by the crisis. In the USA, evidence indicates that people with MS with poorer social determinants of health (that is, lower predicted health status) reported more depressive symptoms and worse general mental health in the midst of the pandemic⁹⁷. In a US-based study, 69 people with MS were surveyed in mid-2020 and 20% of participants reported losing their job as a result of the pandemic⁹⁸. Black participants, Hispanic and Latinx participants, and participants with lower levels of education seemed to have a greater risk of job loss than other participants. Studies performed in Spain and Australia found that lockdown and isolation precautions, including inability to go outside, led to reclusion and lack of outdoor walks, resulting in worse mental health among people with MS^{99,100}. In Italy, a web-based survey performed during the pandemic found that people with MS reported significantly less social support, higher perceived stress and more depression than a control group of people without MS¹⁰¹. In one study,

52 of 324 participants with MS reported a positive effect of the COVID-19 pandemic on their quality of life, with strategies such as working from home allowing greater time and flexibility to overcome MS symptoms¹⁰².

Acting on the evidence

Addressing social determinants of health in MS is complex in clinical practice. Not only are there difficulties related to the variable quality of and biases within the literature, variation within different health-care systems and national contexts require careful consideration. Effecting change will require a multidisciplinary effort, including primary care providers and allied health-care professionals. Many of the steps required to assess and improve social determinants of health might seem to be outside the scope of individual neurologists, and this, together with time and service pressures, can mean that many of these determinants remain unidentified in clinical practice, and potentially modifiable risk factors are left unaddressed.

As neurologists, we increasingly understand that non-medical factors related to the individual and societal social context can have an effect on health. For example, findings from the wider public health literature have identified effects of structural and societal changes on population health¹⁰³, and being aware of a patient's specific circumstances might help the neurologist to deliver better care. However, population-level metrics do not directly translate to individual needs – living in a deprived area is not the same as being deprived – so identifying those at greatest need requires clinicians to actively enquire¹⁰⁴. The Core-5 screening tool¹⁰⁵ was developed to identify individuals with poor social determinants of health in health-care settings, and is way to identify those at greatest need of input. The tool was independently tested within both inpatient and outpatient settings; staff survey data indicated high acceptance and usability¹⁰⁶. In Box 1, we suggest a short screening questionnaire, based on the Core-5 screening tool, that can be used to assess social determinants of health in people living with MS. Although not all of the questions are applicable across all health-care and welfare systems, they provide a framework for systematic inquiry to identify individuals with the greatest need of support.

Box 1

Suggested screening questions for social determinants of health

1. Has a lack of transport kept you from work, attending medical appointments, or from getting things you need for your daily life?
2. Do you currently have worries about your access to utilities, such as water, gas, electricity or heating for any reason?
3. Are you homeless or worried about losing your home?
4. Do you or your family worry that you will run out of food and you won't be able to get any more for any reason?
5. Are you worried that someone might hurt you or your family?
6. Can you afford your medical expenses? (in countries with mixed payor and private health-care systems)

These questions were based on the Core-5 screening tool. Adapted with permission from ref.¹⁰⁶, BMJ.

Individual determinants

Sex, gender, sexuality, race, ethnicity. As discussed above, sex, gender, sexuality and race affect all aspects of health care. Addressing the effect of these factors within our individual clinical practices requires reflection and thought. There remains a belief among some clinicians that people from minoritized racial and ethnic populations are at lower risk of MS than those of white European ancestries; however, this is not necessarily the case^{14,107}. We suggest that neurologists ensure that they consider MS in all individuals in whom the clinical history and investigations support the diagnosis, and consider auditing the time to diagnosis among different racial and ethnic groups. Algorithms for the treatment of MS exist in a number of public health-care systems¹⁰⁸, have been recommended within mixed health-care systems¹⁰⁹, and are recognized as an aspiration in private health-care systems⁵². Auditing practice against these algorithms might provide a practical benchmark for neurologists.

People from under-represented ethnic groups and genders might struggle to access and navigate health-care services equitably, and neurologists should ensure that their practice is inclusive and mindful of the difficulties that these individuals might encounter. Patient mistrust related to prior negative health-care experiences should also be recognized and addressed¹¹⁰. MS teams should advocate for, and support, all of their patients to have equal access to diagnostic and monitoring

investigations through tailored support where necessary. We suggest that where neurologists are involved in recruitment to research studies, they should ensure that recruitment patterns from their centre match the demographic characteristics of their local population in terms of age, gender and race.

Risk of abuse. Given that individuals with MS are at higher risk of domestic and carer abuse than the general population, safety should routinely be enquired about, ideally as part of routine reviews. By embedding this inquiry within routine care, with appropriate training and education for those carrying out such reviews, biases leading to people at risk of abuse being either missed or singled out can be reduced. This approach has been successfully deployed in other areas of medical care¹¹¹. Neurologists should be mindful of who accompanies people to their appointments, and ensure that they have the time and ability to ask and address this issue during the appointment. They should also be aware of how to raise safeguarding concerns.

Education. Most people with MS seen in adult services have completed their education at the time of diagnosis; however, some might still be in, or wish to return to, either full or part time education, and MS teams have an important role in supporting patients in this. MS teams also need to ascertain the educational level of individuals with MS to provide appropriate information and support for complex decision-making.

Employment. In contrast to many other social determinants of health, validated scales, such as the Multiple Sclerosis Work Instability Scale (MS-WIS)¹¹² and the Buffalo Vocational Monitoring Survey (BVMS)^{113,114}, can be used to identify individuals living with MS who are at higher risk of job loss. Early use of disease-modifying therapies in order to minimize the risk of cognitive impairment and disability is key in enabling people with MS to remain in employment.

The MS team should discuss with their patients the pros and cons of disclosing a diagnosis of MS to employers. A work instability review might be useful for some people with MS; those at high risk of unemployment should have targeted interventions to support job retention. Such interventions include effective symptom management¹¹⁵, optimal treatment of comorbidities³⁷ and assessment of cognition, mood and self-efficacy^{32,116}. Employment support including vocational services, flexibility in the workplace^{28,36} and balance between working and private life³¹ is important to enable individuals with MS to achieve a sustainable working life over time.

Intermediate determinants

Socioeconomic status. According to a systematic review published in 2021, socioeconomic inequalities in health-care access seem to be more prevalent for specialist visits than for primary care, and in non-universal health-care systems than in universal health-care systems¹¹⁷. Across Europe, people with a higher socioeconomic status are more likely to use health-care specialists; education and occupation are also important contributing factors¹¹⁸. Improving access to health care is a structural task beyond the remit of neurologists; however, neurologists working in private or mixed health-care systems might be able to help by exploring how financial considerations might limit health-care choices, and ensuring that where possible steps are taken to mitigate this limitation. Working with communities and charitable groups that support individuals facing challenges in navigating local health-care services can also help improve health outcomes¹¹⁹.

Neurologists and the wider MS team should be aware of local services that aim to support individuals at risk of food insecurity and food poverty. We suggest that raising awareness of these services within patient groups in a non-judgemental manner could be a practical step to address food poverty. Identifying individuals who might benefit from this type of support is not always straightforward, and simple interventions such as publicity or posters might substantially increase awareness among those in need.

Social prescribing. The aim of social prescribing is to connect patients to non-clinical services and support, and to give individuals the knowledge, skills, motivation and confidence to manage their own health and well-being¹²⁰. Social prescribing has a limited but increasing evidence base. Professional society and patient advocacy resources could be provided to remind people with MS of their rights as employees, citizens and patients. However, as highlighted by some minoritized groups with MS, the response to such resources varies across individuals; people do not always want to be defined by their need for support⁹. Systems that have a broad approach to social prescribing¹²¹ are being studied to identify strategies to address some of these concerns; where available, MS teams are encouraged to take part in such studies.

Conclusions

Social determinants of health are not static, and change according to wider sociopolitical contexts – as highlighted by the COVID-19 pandemic. Some have argued that digital literacy could be an increasingly important social determinant of health¹²². The rapid move to online communication – both for health-care and wider purposes – that was caused by the COVID-19 pandemic has created substantial inequities with direct relevance to people living with chronic neurological conditions.

We do not address income directly as part of this Review. As with other social determinants, the relationship between income and MS is bidirectional that is, diagnosis of MS is associated with lower income¹²³, and lower income is associated with worse health outcomes. This relationship is mediated via social determinants of health. In non-universal health-care systems, where people with MS might need to meet the cost of disease-modifying therapy, the high cost of these medications will adversely affect those on lower incomes. This means that these individuals will accrue the risk of worse disease outcomes owing to lack of treatment access as well as low income and often poor social determinants of health. Intersectionality, that is, the interactions among multiple social determinants of health, has been shown to be important in dictating outcomes in cancer⁵³, and the same is likely to be true for MS. Other previously unidentified social determinants of health undoubtedly exist, but require rigorous research to investigate.

In our view, the existing evidence supports a potentially major effect of social determinants of health on outcomes in people with MS. However, the evidence is limited, and the potential bidirectional and complex relationships, which involve multiple confounding factors have not been adequately addressed. Rigorous studies of interventions to ameliorate the effect of poor social determinants of health are almost completely lacking, and this Review highlights an important and urgent need for these. The importance of minimizing the effect of MS through early effective treatment with disease-modifying therapies, and the subsequent downstream implications of such disability prevention should not be underestimated. In our opinion, it is possible to change poor MS disease outcomes via a holistic approach, targeting either in isolation might mean that opportunities to comprehensively modify disease outcomes are missed.

Although addressing many social determinants of health is outside the role of neurologists, it is increasingly clear that ignoring the societal context of someone living with MS would be to neglect a potentially substantial effect on disease outcomes. Treating inflammatory neurological disease without holistically considering the person means that we are only addressing one factor that affects MS disability, thus unintentionally putting people with MS at risk of poorer outcomes.

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Competing interests

The authors declare no competing interests.

Additional information

Correspondence should be addressed to Ruth Dobson.

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Review criteria To ensure an inclusive overview, we searched PubMed, Scopus, CINAHL through EBSCOhost, MEDLINE through OVID, all other Web of Science (BCI OR SciELO OR WoS OR CABI OR RSCI OR CCC) core collection, PsychINFO and Emcare (OVID) using a search strategy based on the WHO social and immediate determinants of health and a wide range of MS terms on 17 January 2022. We considered any original studies examining social determinants of health and MS outcomes from 2004 onwards, and did not restrict based on language, given the wide-reaching effects of social determinants of health. Out of 2,453 papers screened, a total of 194 papers were considered for inclusion, and the final decision was based on relevance to social determinants of health and MS, along with novelty and current relevance.

Related links

Social determinants of health: https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1

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¹Preventive Neurology Unit, Wolfson Institute of Population Health, Queen Mary University of London, London, UK. ²Department of Neurology, Royal London Hospital, London, UK. ³Department of Neurology, Massachusetts General Hospital, Boston, MA, USA. ⁴Department of Neurology, National MS Center, Melsbroek, Belgium. ⁵Center for Neurosciences, Vrije Universiteit Brussel, Brussels, Belgium. ⁶Discipline of Exercise Science, Murdoch University, Perth, WA, Australia. ⁷Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Perth, WA, Australia. ⁸Centre for Healthy Ageing, Murdoch University, Perth, WA, Australia. ⁹Perron Institute for Neurological and Translational Science, University of Western Australia, Perth, WA, Australia. ¹⁰Disability and Health Unit, Melbourne School of Population and Global Health, University of Melbourne, VIC, Australia. ¹¹Department of Neurology, Fundación Santa Fe de Bogotá, Bogotá, Colombia. ¹²School of Medicine, Universidad de los Andes, Bogotá, Colombia. ¹³Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK. ¹⁴Joi Life Wellness MS Center, Smyrna, GA, USA. ¹⁵Department of Neurology, Centre for Neurosciences, Leeds Teaching Hospitals, Leeds, UK. ¹⁶Faculty of Medicine and Health, University of Leeds, Leeds, UK.