

Dietary patterns and their associations with symptom levels among people with Multiple Sclerosis: A real-world digital study

Supplementary materials

Lasse Skovgaard¹, Philipp Trénel², Katrine Westergaard¹ og Astrid Karnøe Knudsen¹.

¹ The Danish MS Society, Valby, Denmark.

² Danish Technological Institute, Aarhus, Denmark.

Fig. S1: Directed acyclic graph (DAG) of hypothesized causal relationships among background variables, exposure (Diet) and outcome (Symptoms) that passed the Shipley test on the current data (Fisher’s C test pvalue = 0.14). In order to obtain lack of DAG rejection, a covariance on Education and MS-type needed to be enforced. The putative relationships were according to the following reasoning: Diet was hypothesized to be affected by Region, with healthier diets in urban areas, by Education, with healthier diets among higher educated persons, by Gender, with men stereotypically expected to eat more meat products, by Age, with younger persons expected to be more open to new diets, but also intaking more snack food and soft drinks. The two time-associated variables Age and Diagnosis time may function as proxies of unmeasured causally relevant factors and interconnect the diet-related sub-DAG and the MS-related sub-DAG. MS-symptoms are expected to be heavily affected by MS type, disease progression state and associated disease severity as indicated by Diagnosis time, Aid, Sequelae, Work status, and Disease modifying treatment (DTM). Besides MS severity, Work status is affected by Education and Age. Smoking is a known risk factor for MS symptoms, but the probability of smoking is expected to be reduced by increasingly higher Education and by increased contact with health professionals as indicated by DTM. Marital status was not included in the putative DAG.

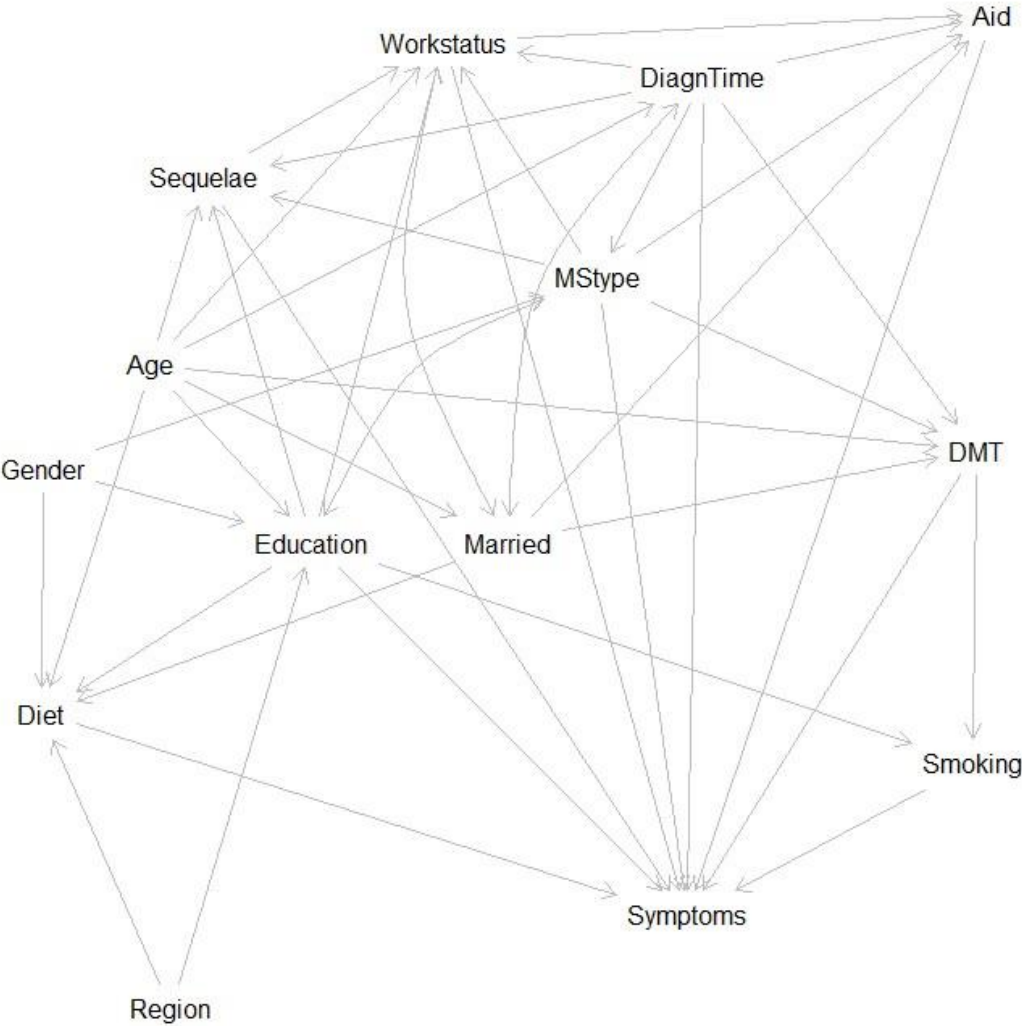


Table S1: All logged foods were coded in three levels; food categories, food groups, and food items. In this article, results from analysis of food groups are presented.

Food Category	Food group	Food item
whole_grain_cereals	Cereals_wholegrain	oat_muesli
		bread_rye
		bread_coarse
		bread_crisp
		corn
		bulgur
		quinoa
		wholegrain_rice
		seeds
		grain_flour
		wholegrain_pasta
		breakfast_cereals
	Cereals_wholegrain_glutenfree	oat_muesli_gf
		bread_rye_gf
		bread_coarse_gf
		bread_crisp_gf
refined_grain_cereals	cereals_refined	bread_white
		rice
		pasta
		corn
		couscous
		porridge
	cereals_refined_gf	bread_white_gf
		pasta_gf
potatoes	Potatoes	potato_boiled
		potato_baked

		potato_fried
vegetables		potato_mashed
		potato_stewed
		potato_processed
	Leafyvegetables	salad
		Spinach
		chard
	fruitingvegetables	tomato
		avocado
		peas_beans
		bell_pepper
		chili
		pumpkin
		squash_cucumber
		eggplant
	otherrootvegetables	carrot
		beet
		sweetpotato
		parsnip_jeru
		radish
		ginger
	cabbages_all	cauliflower
		brusselssprout
		broccoli
		kale
		cabbages

		redcabbages
	mushrooms	mushroom
		fungal_other
	onions_garlic	onion

		garlic
	stalkvegetables_sprouts	leek
		broccoli
		sprout
		artichoke
		corn
		aspargus
		fennel_celery
	legumes	beans
		chickpeas
		legumes_processed
		green_beans_peas
	Soy_product	soy_beans
		soy_sauce
		soy_processed
	vegetables_misc	Misc
fruit	Citrus_fruits	Orange
		lemon_lime
		Grapefruit
	Other_fruits	Apple
		Strawberry
		Pineapple
		Banana

		Melon
		Grape
		Berries
		peach_apricot
		Other_fruits
	Nuts	Peanut
juice		Peanutbutter
		other_nuts
		other_nutbutters
		nuts_processed
	Dried_fruit	raisins
		figs
		prune
		other_driedfruit
	Fruitjuices	juice_orange
		juice_apple
		juice_otherfruit
	Vegetablejuices	Juice_tomato
		Ginger_juice
		Other_vegjuice
	Plant_milk	Coconut_milk
		nut_milk
		rice_milk
		oat_milk
red_meat	redmeat_pork	pork
		roastpork
		kassler

		friedpork
		porkfillet
		porkchop
		skikeschnitzel
		pork_withsth
	redmeat_beef	roastbeef
		beefsteak
		beef_roast
		beef_withsth
		redmeat_veal
		veal_withsth
		veal_steak
		redmeat_misc
		veal_pork_mince
		redmeat_lamb
		lambchop
		lamb_withsth
		redmeat_game
		deer
		elk
		rabbit
		game_other
processed_meat	processed_meat_redmeat	Bacon
		cold_cut_pork
		cold_cut_beef
		sausage
		kebab
		salami
		liver_pate
		ready_meal
		hamburger

	processed_meat_poultry	Chicken_burger
		Chicken_coldcut
		chicken_salad_mayo
		chicken_readymeal
		chicken_spread
		ready_salad_chicken
poultry	Poultry	chicken_whole_roasted
		chicken_stew
		chicken_mince
		chicken_chopped
fish		goose
		turkey
		pheasant
		duck
		vagtel_pigeon
	fish_lean_fresh	cod
		tuna
		flatfish
		roe
		lean_fish_fresh
	fish_lean_processed	fried_battered_fish
		canned_tuna
		fish_salad_mayo
		fishballs
		cod_roe
		smoked_lean_fish
		lean_fish_proc

	fish_fatty_fresh	salmon
		sardins_anchovies
		mackerel
		trout
		herring
	fish_fatty_processed	Smoked_salmon
		pickled_herring
		ready_meal_salmon
		mackerel_tomato
		Salad_mayo_fattyfish
	fish_shell_fresh	smoked_mackerel_trout
		clam

		squid
		lobster_crayfish_crab
		shrimp
	fish_shell_processed	mayo_salad_shellfish
		ready_meal_shellfish
egg	Egg	egg
		egg_ready_meal
		egg_salad_mayo
		yolk
		egg_white
low_fat_dairy	dairy_products_lean	Milk_skimmed
		milk_semiskimmed
		butter_milk
		skyr
		yoghurt_Natural_b2

		yoghurt_Fruit_2p5
		lean_cheese
		yoghurt_drink
		Creemefraiche_lean
	dairy_lean_lactosefree	yoghurt_lactosefree
		milk_lactosefree
	high_fat_dairy	dairyproducts_fatty
		whole_milk
		yoghurt_natural_a2
		cream
		cremefraiche_fatty
		coldbowl_fruitfoghurt_3
		cheese_misc
		creamcheese
		Danish_cheese

		soft_cheese_brie_similar
		hard_cheese
		feta_mozarella
		goatcheese
	dairy_fatty_lactosefree	lactosefree_cheese_cream
butter	butter	Butter
		Butter_oil_product
		plant_oil_spread
vegetable_oil	vegetableoils	olive_oil
		sunflower_oil
		coconut_oil
		flaxseed_oil
		sesame_oil

		rape_seed_oil
		vegetable_oil_misc
	mayonnaise_and_dressings	mayo_salad
		mustard
		oil_based_salad_dressing
		mayo_based_salad_dressing
		mayonnaise
		salsa_processed
		Pesto_currypaste
		Remoulade
		Ketchup
		Dressings_misc
		frying_oil
	Sauce_processed	Sauce_powder
		sauce_asian
		sauce_white
		sauce_misc
margarine	margarines	Margarine
		coconut_butter
		vegan_cheese
jam_syrups_sugar	sugar_honey_jam_syrups	syrup
		whitesugar
		honey
		marmelade
		coconut_fruit_sugar
		chocolate_syrup
		cola

soft_drinks	softdrinks	cola_light	
		sparkling_softdrink	
		sparkling_softdrink_light	
		lemonade	
		lemonade_light	
		energy_drink	
	waters	water	
		sparkling_water	
	cocoa	cocoa_powder	
		cocoa	
		milkshake	
		lactosefree_cocoay	
snack_food	potatoes_fatty	Fries	
		chips	
	chocolate_candy_bars	chocolate	
		dark_chocolate	
		candy_bars	
	confectionary_nonchocolate	toffee	
			hard_candy
			hard_candy_licorice
licorice			
jelly			
marzipan_creampuffs			
mints			
mixed_nonchocolate			
Cookie			

	cake	cake
		musli_bar
		danish
		biscuit_waffles_pancake
		dessert_notbaked
	ice cream	sorbet
		cream_milk_icecream
		yoghurt_icecream
		lactose_free_icecream_soy
	sacoury_snacks	corn_snacks
		wheat_crackers
		pork_crackle
		rye_crackers
		savoury_snacks_mixed
coffee	coffees	coffee_reg
		coffee_decaf
		coffee_instant
tea	teas	teas_reg
alcohol	wines	red_wine
		white_wine
		sparkling_wine
		muscat_port
		alcohol_free_wine
	beer	beers
		alcohol_free_beer
		cider

Misc	spirits_brandy	vodka
		alcohol_misc
	soup_processed	fond
		soups_processed_veg
		soups_processed_meat
	spices	salt
		peppers
		vinegar
		spices_misc
	health_nutrition_supplements	psyllium_fibers
		fish_oils
		nut_suppl_misc
	protein_powder_nonclassified	protein_powers
		non_classified

Table S2: Participant flow and attrition in the current study. DMT: disease modifying treatment.

	Participant flow			In-study group
	Participants that received / accepted invitation	Participants that finalized consent form and baseline registration	Participants that contributed with data	Participants that fulfilled the inclusion criteria
N (% passing)	7,249 / 735 (10.1%)	550 (74.8%)	413 (75.1%)	163 (39.5%)
Active days %, Median (Q1, Q2)	-	-	25.0 (2.0, 65.0)	73.0 (53.0, 69.1)
Gender = Female (%)	-	434 (78.9)	328 (79.4)	132 (81.0)
Married or co-living (%)	-	416 (75.6)	315 (76.3)	124 (76.1)
Workstatus (%)				
Working	-	321 (62.2)	249 (63.7)	96 (58.9)
Student	-	22 (4.3)	19 (4.9)	5 (3.1)

Early ret.	-	141 (27.3)	99 (25.3)	41 (25.2)
Otherwise/not working	-	32 (6.2)	24 (6.1)	21 (12.9)
Missing	-	34 (6.2)	22 (5.3)	0 (0.0)
Region (%)				
Capital region	-	175 (31.8)	134 (32.4)	45 (27.6)
Zealand region	-	88 (16.0)	68 (16.5)	30 (18.4)
Northern and central region	-	171 (31.1)	139 (31.2)	52 (31.9)
Southern Denmark	-	112 (20.4)	80 (19.4.3)	36 (22.1)
Missing	-	4 (0.7)	2 (0.5)	0 (0.0)
Education (%)				
Primary school	-	21 (3.8)	20 (4.8)	5 (3.1)
Highschool	-	48 (8.7)	35 (8.5)	16 (9.8)
Vocational education	-	93 (16.9)	64 (15.5)	22 (13.5)
Short-cycle higher education	-	79 (14.4)	54 (13.1)	18 (11.0)
Medium-cycle higher education	-	205 (37.3)	154 (37.3)	63 (38.7)
Long cycle higher education	-	104 (18.9)	86 (20.8)	39 (23.9)
MStype (%)				
RRMS	-	427 (83.2)	322 (83.9)	132 (81.0)
SPSMS	-	46 (9.0)	35 (9.1)	13 (8.0)
PPMS	-	40 (7.8)	27 (7.0)	7 (4.3)
Don't know	-	37 (6.7)	29 (7.0)	11 (6.7)
Aid = No (%)	-	379 (68.9)	290 (70.2)	114 (69.9)
Sequelae (%)				
0	-	280 (50.9)	213 (51.6)	48 (29.4)
1-2	-	236 (42.9)	173 (41.9)	92 (56.4)
3 or more	-	34 (6.2)	27 (6.5)	23 (14.1)
DMT = Yes (%)	-	412 (74.9)	302 (73.1)	119 (73.0)
Age (%)				
Under 43 years	-	231 (42.5)	178 (43.5)	62 (38.0)
43-51 years	-	154 (28.4)	121 (29.6)	53 (32.5)
Over 51 years	-	158 (29.1)	110 (26.9)	48 (29.4)
Missing	-	7 (1.3)	4 (1.0)	
Diagnosis time (%)				
Year 2013-2017	-	188 (34.2)	142 (34.4)	59 (36.2)
Year 2008-2012	-	157 (28.6)	122 (29.5)	47 (28.8)
Year 2003-2007	-	102 (18.6)	77 (18.6)	28 (17.2)
Year 2002 or before	-	102 (18.6)	72 (17.4)	29 (17.8)
Missing	-	1 (0.2)	0 (0.0)	0 (0.0)

Table S3: Local independence test statistics for the DAG tested against the current data.

	rmsea	97.5% CL	x2	df	p.value
DgnT _ _ Gndr	0.00000000	0.1298718	0.6451123	3	0.88603164
Aid _ _ DMT Age, DgnT, MSty	0.06279935	0.7874392	5.3324955	9	0.80441426
Age _ _ Regn	0.00000000	0.1252439	3.2791226	6	0.77308611

Aid _ _ Regn DgnT, MSty, Wrks	0.16666667	1.1320565	21.4238328	27	0.76604731
DMT _ _ Gndr DgnT, MSty	0.02286930	0.8286605	4.3073264	6	0.63516302
Gndr _ _ Regn	0.00000000	0.1499855	1.7759756	3	0.62017681
Seq1 _ _ Smkn DMT, Edct	0.11762075	0.6218461	25.6638232	28	0.59151744
DMT _ _ Seq1 Age, DgnT, MSty	0.17351971	1.0018522	16.2793719	18	0.57305692
MSty _ _ Regn	0.00000000	0.1280652	7.8373387	9	0.55061818
Aid _ _ DMT DgnT, MSty, Wrks	0.14056203	1.0900732	8.3549550	9	0.49880857
DMT _ _ Edct Age, DgnT, MSty	0.18639744	0.7655741	32.0359840	32	0.46496078
Age _ _ Smkn DMT, Edct	0.12569994	0.6339240	31.6297875	31	0.43482599
DgnT _ _ Smkn DMT, Edct	0.08202334	0.5500205	47.6306561	46	0.40616810
DgnT _ _ Diet Age	0.03997881	0.2514458	18.7948389	18	0.40455820
DMT _ _ Regn	0.00000000	0.1661136	2.9450777	3	0.40017086
Age _ _ Aid DgnT, MSty, Wrks	0.09487755	0.9274533	14.9513580	14	0.38148788
Aid _ _ Smkn DgnT, MSty, Wrks	0.19257715	1.1365244	19.2805928	18	0.37473942
Aid _ _ Edct DgnT, MSty, Wrks	0.29681027	1.3182315	36.9482989	34	0.33429515
Smkn _ _ Wrks DMT, Edct	0.09654250	0.5657461	41.7116875	38	0.31256142
Age _ _ Gndr	0.03646123	0.1914897	2.4307324	2	0.29660138
DgnT _ _ Regn	0.03900122	0.1413957	11.2177565	9	0.26107772
Aid _ _ Diet DgnT, MSty, Wrks	0.29310191	1.3294655	21.0887680	17	0.22234481
DgnT _ _ Edct Age	0.05343214	0.2224310	48.7374880	42	0.22034680
Regn _ _ Smkn DMT, Edct	0.12289047	0.5728836	57.0277175	46	0.12773469
DMT _ _ Diet Age, DgnT, MSty	0.21965726	1.0462300	24.0892711	17	0.11702964
Gndr _ _ Smkn DMT, Edct	0.11919551	0.7039604	23.3453793	16	0.10480902
Aid _ _ Smkn DMT, Edct	0.17263708	0.7336442	23.4581989	16	0.10202399
Aid _ _ Seq1 DgnT, MSty, Wrks	0.36068814	1.3350994	26.0598406	18	0.09839752
Aid _ _ Gndr DgnT, MSty, Wrks	0.40151358	1.3441318	14.9012663	9	0.09368397
Diet _ _ Smkn DMT, Edct	0.13797642	0.6663829	37.2213883	27	0.09100878
DMT _ _ Wrks Age, DgnT, MSty	0.22552471	0.9176952	24.0248520	15	0.06467266
MSty _ _ Smkn DMT, Edct	0.13106530	0.6246666	39.1946602	27	0.06082247
Age _ _ MSty DgnT	0.09004398	0.3379624	34.2616396	22	0.04619536

Table S4: Correlation matrix for log-transformed symptom burden variables. Pearson correlations and significance stars are shown above diagonal and 95% confidence intervals below diagonal. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Walking difficulty	-	0.39***	0.49***	0.64***	0.4***	0.57***	0.56***	0.47***	0.45***
2. Sensory disturbances (0.19, 0.56)	-	0.41***	0.41***	0.43***	0.4***	0.46***	0.32***	0.27**	
3. Fatigue (0.28, 0.65)	(0.2, 0.59)	-	0.54***	0.51***	0.38***	0.52***	0.17*	0.4***	
4. Dizziness (0.47, 0.77)	(0.19, 0.56)	(0.27, 0.64)	-	0.43***	0.51***	0.53***	0.49***	0.39***	
5. Pain (0.2, 0.57)	(0.28, 0.65)	(0.24, 0.62)	(0.2, 0.57)	-	0.45***	0.55***	0.27**	0.38***	
6. Spasticity (0.37, 0.71)	(0.47, 0.77)	(0.2, 0.59)	(0.37, 0.71)	(0.2, 0.59)	-	0.6***	0.44***	0.39***	
7. Muscle weakness	(0.37, 0.71)	(0.2, 0.57)	(0.19, 0.56)	(0.37, 0.71)	(0.19, 0.56)	(0.2, 0.57)	-	0.41***	0.41***
8. Bladder dysfunction	(0.27, 0.64)	(0.37, 0.71)	(0.28, 0.65)	(0.27, 0.64)	(0.28, 0.65)	(0.37, 0.71)	(0.27, 0.64)	-	0.47***
9. Bowel dysfunction	(0.24, 0.62)	(0.37, 0.71)	(0.47, 0.77)	(0.24, 0.62)	(0.47, 0.77)	(0.37, 0.71)	(0.24, 0.62)	(0.2, 0.59)	-