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A prospective evaluation of the depression–nutrient intake reverse causality hypothesis in a cohort of community-dwelling older Canadians

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Abstract

Studies have investigated the potential protective effects that diet may have on late-life depression incidence. This disorder can, however, affect the person's food intake, widely known as the reverse causality hypothesis of depression. To test this hypothesis, we compared mean nutrient intakes from three 24-h recalls during the year depression was detected (Geriatric Depression Scale ≥11 or antidepressant medication) with intakes from 1 year earlier among community-dwelling older adults (67–83 years) followed up annually in the 4-year Québec Longitudinal Study on Nutrition and Aging, who were free of depression and cognitive impairment at baseline. Participants (*n* 158, 64·4 % female) who became depressed and had data available for all follow-up years were matched by age group and sex with non-depressed participants. General linear mixed models were adjusted for percentage changes in physical activity, functional autonomy and stressful life events reported at the time of positive screening. A significant group effect for the dietary intake of all three B-vitamins was observed, as depression cases had consistently lower dietary intakes than controls ($P < 0{\cdot}01$). Over time, intakes of dietary vitamin B_{12} declined within depressed participants in bivariate analysis, but there was no time × group effect for any nutrient tested in the multivariate analyses. Intakes of energy, protein, saturated fat and total dietary fibre did not change in cases *v.* controls. Among community-dwelling older adults, declines in dietary vitamins B_6, B_{12} and folate may precede depression incidence. To help preventative efforts by programmes and practitioners, longitudinal cohorts of longer duration should investigate the extent of the decline in dietary intakes relative to the time of depression.

Key words: Reverse causality: Diets: Depression: Older adults: Community-dwelling older adults: Longitudinal studies

Depression in late-life is a predisposing factor for chronic diseases and low functional status, consequently affecting older people's quality of life and perceptions of healthy ageing[1–3]. Diet is a modifiable factor that can potentially affect mood and mental health, including depressive symptoms[4–6]. One of the symptoms of depression, however, is altered appetite and increased seclusion and avoidance behaviour, which, in turn, can affect depressed people's food intake[7]. This effect is often referred to as the reverse causality hypothesis of depression and diet, whereby having a poor diet may be one of the consequences of depression and not the cause[8–14]. Research objectively exploring the direction of this association is widely lacking in the scientific literature. To account for the reverse causality hypothesis in population-based cohort studies, researchers often conduct ancillary or sensitivity analyses through the exclusion or control of baseline depression, or they rely on the intrinsic longitudinal design of the study[9,10,13–17]. Findings are often contradictory, as well as age-specific or sex-specific.

In a large cohort of women aged 20–34 years (*n* 2732) in the Southampton Women's Survey, Kendrick *et al.*[18] observed that

Abbreviations: 3MS, Modified Mini-Mental State; EAR, estimated average requirements; GDS, Geriatric Depression Scale; GLM, general linear model; NuAge, Quebec Longitudinal Study on Nutrition and Aging; PASE, Physical Activity Scale for the Elderly; SMAF, Functional Autonomy Measuring System.

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low blood folate levels were associated with prevalent depression at baseline but not with incident depression over the 2 years of follow-up. According to the authors, lower blood folate levels may be a consequence, rather than a cause, of depressive symptoms in women at child-bearing age[18]. Among older adults, however, findings from a similar study in a cohort of 521 community-dwelling Korean older adults aged ≥64 years and followed for 2 years suggest the opposite direction: incident depression was predicted by lower serum folate levels and vitamin B_{12} levels at baseline and was associated with greater declines in serum vitamin B_{12} levels over follow-up after the incident depression[12].

Macronutrients have also been of interest. Using 24-h recall and food frequency data from 1947 men and 2909 women aged 25–74 years followed by an average of 10·6 years in the National Health and Nutrition Examination Follow-Up Study, Wolfe *et al.*[19] noted that the relative risk for developing severe depression (score ≥22 on the Center for Epidemiologic Studies Depression Scale or taking antidepression medication) decreased with increasing tertiles of protein intake among men, but increased among women. The authors hypothesise that potential biochemical differences between men and women linked to brain function and mood (e.g. 5-hydroxytryptophan metabolism, protein and carbohydrate catabolism, and homocysteine levels) may help explain the findings, but they also suggested that the relationship was confounded by differences in saturated fat consumption and the source of protein – as legume consumption was protective among men, but deleterious among women[19].

In testing the hypotheses of types of food and their potential association with depression and the direction of the association, Jacka *et al.*[20] observed that reported current depression was linked with lower scores on a healthy dietary pattern ("prudent") in the Personality and Total Health Through Life, a longitudinal community survey following three age cohorts (in their 20s, 40s and 60s) in the Australian Capital Territory. Furthermore, the 909 participants who received treatment, out of the 1571 reporting depression history – of whom 17·4 % (*n* 273) were also classified as likely current depression cases – scored higher on the "prudent" dietary pattern compared with participants without previous depression[20]. The authors discuss whether the reverse causality hypothesis helps to explain this finding, as a history of depression may have prompted healthier dietary behaviours in the long term. Whereas the study by Jacka *et al.* included relatively young individuals, previous research conducted by our team with participants in the Québec Longitudinal Study on Nutrition and Aging (NuAge) included those aged 75 years on average and did not find a protective effect for those scoring high on a healthy ("varied") dietary pattern[21], suggesting that differences in depression risk may exist between young and old populations. On the other hand, high relative intakes of vitamins B_6 and B_{12} were associated with decreased 3-year incidence of depression among women and men, respectively[21].

We were unable to find in the literature research that explicitly investigated the reverse causality hypothesis among older adults (aged ≥65 years) living in the community. Most of the evidence on the relationship of diet and depression comes from studies on middle-aged adults. Therefore, the effect of depression on older adults' intakes is largely unknown. A better understanding of the effect of depression on diet – and vice-versa – can help inform possible interventions to either prevent or reduce the impact of this mental health condition on an individual's nutrient intake with the ultimate goal of maintaining an optimal nutritional status. Here, we aim to explore the reverse causality hypothesis in a group of initially healthy, community-dwelling older adults who became depressed at some point over a 4-year follow-up by testing whether depression incidence is associated with declines in intakes of some nutrients (energy, protein, fibre, saturated fat, vitamins B_6, B_{12} and folate) from food.

Methods

Study population

NuAge is a 4-year observational study of 1793 men and women in good general health at recruitment, described in detail elsewhere[22]. In summary, the sample was randomly drawn from the Québec Medicare database for the regions of Montreal, Laval and Sherbrooke and stratified by age and sex. Community-dwelling men and women were included if they spoke French or English, were free of disabilities in activities of daily living, were without cognitive impairment (scores in the Modified Mini-Mental State (3MS) Examination >79), able to walk one block or to climb one flight of stairs without rest and willing to commit to a 5-year study period. Those who had heart failure ≥ class II, chronic obstructive pulmonary disease requiring O_2 therapy or oral steroids, inflammatory digestive diseases or cancer treated either by radiation therapy, chemotherapy or surgery in the past 5 years were excluded. Participants were recruited between December 2003 and March 2005 and examined annually using a series of nutritional, functional, medical, biological and social measurements. Data were collected by trained research dietitians and nurses using computer-assisted personal interview methodology (Multispectra©, 1997–2004 data capture software; William™) following rigorous standardised procedures. The number of participants recruited into each age group was as follows: 68–72 years: 337 females, 329 males; 73–77 years: 305 females, 289 males; ≥78 years: 298 females, 235 males. All participants signed an informed consent approved by the Ethics committees of both of the Geriatric University Institutes of Montréal (*Institut Universitaire de Gériatrie de Montréal*) and Sherbrooke (*Institut Universitaire de Gériatrie de Sherbrooke*). This secondary study was approved by McGill's Faculty of Agricultural and Environmental Sciences Research Ethics Board.

To answer our research question on the reverse causality of depression and diet, we excluded participants deemed depressed at baseline, that is, scores on the thirty-item Geriatric Depression Scale (GDS) ≥11 (*n* 183) or on antidepressant medication (*n* 78), those with invalid or missing GDS scores at baseline (*n* 14), with no GDS scores for all 3 years of follow-up (*n* 141), and with invalid or missing dietary information at baseline (*n* 9). Among the remaining 1368 individuals, 170 developed depression at some time during follow-up. As twelve participants did not have dietary data at the appropriate time points, they were excluded. A final sample size of 158 depression cases (sixty-one males and ninety-seven females) were matched by sex and age group from cohort baseline data to a randomly chosen non-depressed

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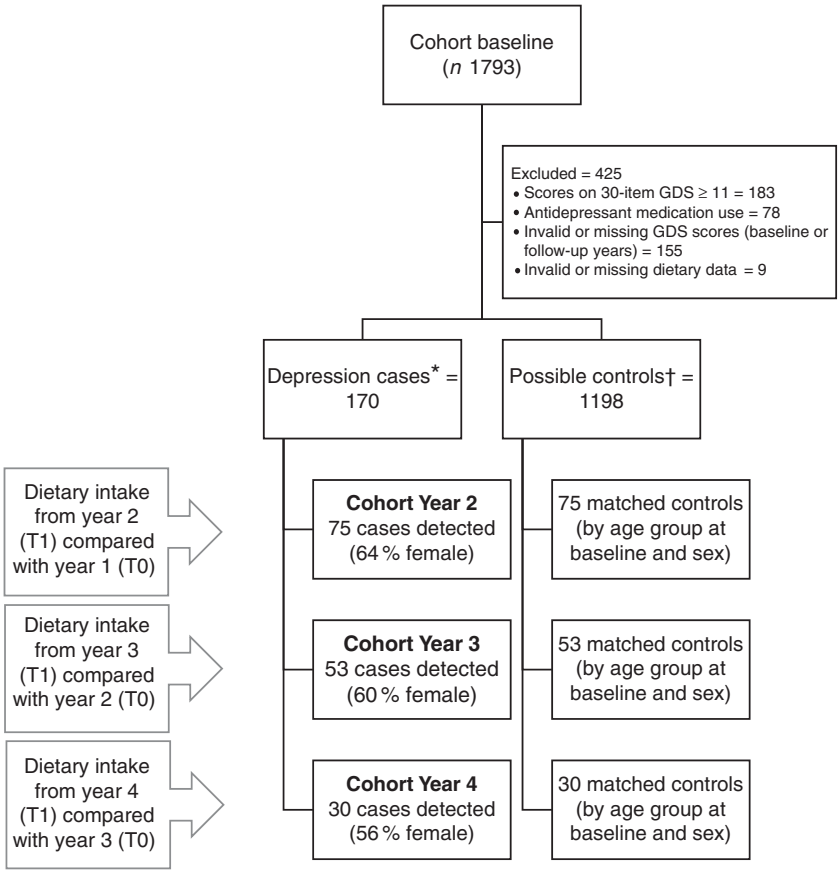

Fig. 1. Flow chart showing the detection of cases by year of study and time point used for analysis of dietary intake changes. *Cases: score on the thirty-item Geriatric Depression Scale (GDS) ≥11 or antidepressant medication use; †Controls: did not meet the criteria for depression at any time of follow-up (both cases and controls were screened for available dietary data at both time points needed; hence, the number of cases is smaller than the total incidence.).

participant pool whose dietary data were available for the same time points as their depressed counterparts (*n* 158). Fig. 1 shows a flow chart illustrating this process.

Study design

We conducted a case–control study nested within the NuAge cohort. Dietary intake data from the year of depression incidence (henceforth, T1) among selected cases and controls were compared with intakes at the year before detection (henceforth, T0). In T0, cases did not reach the threshold for depression (≥11 depressive symptoms in the screening tool or new use of antidepressant medication, as detailed later). To illustrate, depression cases detected at Year 2 of the NuAge cohort study (this is their corresponding "T1") were matched with a pool of control participants who did not reach the threshold for depression at any point in NuAge. This matching was done at each year of the cohort (Fig. 1). The cases' dietary data were then compared with the controls' intake at the incident year (T1) and the year before (T0) through statistical modelling.

Dietary assessment

Nutrient intake data were obtained from three non-consecutive 24-h dietary recalls at each time point, including 1 weekend day, and averaged across the 3 d. Whereas the 24-h recall method (single or multiple) cannot accurately estimate an individual's usual intakes[23], it is an acceptable tool for assessing the mean usual intake of groups, provided all days of the week are equally represented[24,25]. Dubois & Boivin[26] conducted telephone recalls in a similar older adult population and reported the tool was a valid measure of actual observed intake. In addition, 3 d appear sufficient to describe the usual intake of most nutrients except vitamin A, cholesterol and fatty acids in an older population[27].

The dietary data were recorded by research dietitians, coded for entry by the trained dietitian or assistant, and analysed using the CANDAT software (version 10; Godin©; Godin London Inc.) and the 2007b Canadian Nutrient File[28].

To minimise type I error, we were parsimonious in the choice of outcome nutrients and limited the analysis to certain nutrients generally accepted as markers of diet quality and/or hypothesised to be associated with depression[29,30]: energy ((kJ (kcal)), protein (g/kg body weight), saturated fat (percentage of total energy), and total dietary fibre (g). We were also interested in the dietary intakes of vitamins B_6, B_{12} and folate, as they play an important role in the neurotransmitter synthesis and in the remethylation of homocysteine, which is in turn one of the hypothesised mechanisms of depression[31,32]. Furthermore, some of the dietary B-vitamins have been previously shown to be associated with incident depression risk in this cohort[21].

Intakes from food (i.e. dietary intakes) were the focus of this present study because preliminary analysis showed that the proportion of participants reporting regular use of multivitamin/mineral supplement did not differ significantly between cases and controls (approximately 49% among cases and 51% among controls; *n* 316; Fisher's exact test, two-sided $P=0{\cdot}821$). Moreover, our previous study on B-vitamins showed no association between total intake (food + supplements) and depression risk[21]. Nonetheless, we conducted ancillary analyses on total vitamins B_6, B_{12} and folate intakes from the three 24-h recall data.

Depression cases

Probable depression cases were identified on the basis of the thirty-item GDS scores ≥11 or new use of antidepressant medication at any point of follow-up. The GDS[33] is an inventory with a yes/no answer format in which each response indicating depression contributes one point to a total of thirty points. It is considered a reliable and valid measurement and screening tool, indicating the presence of depressive symptoms in an older adult population[33–35]. At a cut-off score of ≥11, the tool has 84% sensitivity and 95% specificity for case-level depression according to the Research Diagnostic Criteria[34]. Subjects with scores ≤10 are considered not depressed and with ≥21, severely depressed. Medications with the therapeutic classification name, according to the American Hospital Formulary System, as "antidepressants," "miscellaneous antidepressants," "selective-serotonin reuptake inhibitors" and "serotonin modulators" were also used to define cases of depression – benzodiazepine was not included because this class of medication is not an antidepressant and is often mis-prescribed and/or overprescribed by physicians, particularly in older populations[36–38].

Potential confounders

Preliminary linear regression models of changes in intakes controlling for baseline nutrient intake level explored several potential health, social and lifestyle confounders including years of schooling, marital status, smoking status, self-reported hypertension, BMI and measures of social activities. Three variables repeatedly showed significant associations ($P<0{\cdot}05$) with the dependent variables tested: physical activity, functional autonomy and stressful life event measured at the year of depression incidence. These were considered as potential confounders, and, hence, were used in the final analysis.

Physical activity was measured by the Physical Activity Scale for the Elderly (PASE)[39,40], a ten-item instrument specifically designed and validated to assess physical activity levels in large samples of older adults over a 1-week time period. A total PASE score is calculated by multiplying the average number of h/d spent in these activities and a PASE weight for that item and summing these products. Higher PASE scores indicate higher activity levels.

Functional autonomy status was assessed by the Functional Autonomy Measuring System (*Système de Mesure de l'Autonomie Fonctionnelle* (SMAF))[41,42], a twenty-nine-item rating scale to record functional disabilities and the available material and social resources that could compensate for the disabilities. It assesses present and actual performance – rather than potential – in activities of daily living (seven items), mobility (six items), communication (three items), mental function (five items) and instrumental activities of daily living (eight items). Scores range from 0 to 87, with higher scores indicating greater dependence.

Finally, stressful life events were measured through the question, "Have you recently suffered a stressful life event (e.g. personal illness/death of a loved one)?" from the Elderly Nutrition Screening tool (ENS©)[43].

Treatment of missing data

We analysed patterns of missing data for the independent variables that were potentially associated with the dependent variables (nutrient intake) and were used to describe the study groups at both time points (i.e. at the time depression was detected and the year before): stressful life event, cognitive status (3MS), functional status (SMAF), BMI and physical activity (PASE). Overall, a total of sixty-six unique values (2·1%) were missing, and thirty-nine subjects (12·3%) out of the 316 had at least one missing value for at least one of those variables. At the year of the incident depression (T1), the following data were missing: PASE (5·4%), BMI (4·1%), stressful life event (2·8%), 3MS (1·9%) and SMAF (1·6%). Data missing from the year before (T0) were BMI (2·2%), PASE (1·6%), stressful life event (0·6%), and SMAF and 3MS (each with 0·3% of data missing). Although these are fairly small proportions, one missing value would lead to the exclusion of the person, which would void the age–sex pairing of the groups, introduce bias, and decrease precision and power[44]. Therefore, to treat these missing values, we used the automatic multiple imputation method in SPSS (version 17.0; SPSS Inc.): fully conditional specification method with ten iterations and five imputations using linear regression. The use of multiple imputation was also judged adequate because preliminary sensitivity analysis demonstrated that data were missing at random, an assumption necessary for the reliability of the procedure[45].

Statistical analyses

Bivariate analyses. At recruitment, we used Fisher's exact test (categorical variables) and independent *t* tests (continuous variables) to test for differences in demographic characteristics between depressed (cases) and non-depressed (controls), including marital status (married/other), smoker (yes/no), hypertension (yes/no), age (years) and formal schooling (years). Differences in cognitive function (scores in the 3MS), functional autonomy scores (SMAF), BMI (kg/m^2), and physical activity scores (PASE) were examined using independent *t* tests for between-group differences (depressed *v.* non-depressed) and paired *t* tests for within-group group differences. Continuous variables are presented as pooled mean values and standard deviations, unless otherwise stated. We tested differences in the "stressful life event" variable (yes/no) using McNemar's χ^2 test for proportions within each subject group (non-parametric test for repeated measures with continuity correction) and Fisher's exact test for proportions between groups.

Normality assumption. Normality assumption was tested for all dependent variables using skewness, kurtosis and visual analysis of histograms with a normal curve. Mean absolute intake of vitamins B_6, B_{12} and folate were not normally distributed. Natural logarithmic (ln) transformations showed an approximately normal distribution and were used in the final analyses. Covariates had approximate normal distributions.

Multivariate analyses. A $2 \times 2 \times 2$ (time × group × stress), full factorial, mixed-model ANCOVA was used for hypothesis testing through the general linear model (GLM) repeated measures function in SPSS statistical package for Windows (version 17.0), using the Bonferroni adjustment for multiple tests. The covariates PASE and SMAF scores were entered as percentage change between the year of depression incidence (T1) and the year before (T0) to permit consideration of the magnitude of the change from each participant's initial scores. Separate models were run for each nutrient of interest. Because energy intake did not differ significantly between and within groups in bivariate analysis or in exploratory multivariate analysis with energy as a covariate, intakes of fibre and B-vitamins were not energy adjusted. Saturated fat was analysed as a percentage of total energy. Group (non-depressed *v.* depressed) and stressful life events (no *v.* yes) at the year of depression incidence (T1) were entered as between-subject effects and time (year of incidence (T1) *v.* the year before (T0)) as within-subject effect. The dichotomous variable "stressful life events" was included in the factorial model, but results report time and group as they relate to the research question. Because of the choice of five imputations to treat missing data, GLM mixed models yielded results for six models: original data plus one model for each imputation. We further conducted ancillary GLM analyses with natural log transformations of total intakes of vitamins B_6, B_{12}, and folate (dietary folate equivalent (DFE)) (food + supplement) as dependent variables. Because of significant differences in GDS scores between cases and controls at T0, ancillary analyses with GDS scores as a covariate were also conducted.

Significance level. Two-sided $P < 0{\cdot}05$ were considered as statistically significant (α 0·05). Pooled results from multiple imputations were the preferred choice for reporting when possible.

Results

Subjects' characteristics

Of the 158 depressed cases (61·4 % women, 33 or 21 % on the basis of antidepressant medication alone), 47·5 % were detected at 1st year follow-up (cohort Year 2), 33·5 % at the 2nd year (cohort Year 3), and 19 % at the 3rd year (cohort Year 4) (Fig. 1).

At cohort baseline, demographic characteristics such as marital status, smoking status and self-reported hypertension did not differ between those who became cases and their matched controls (Table 1).

Between-group and within-group differences on health status are shown in Table 2. Depression cases scored significantly higher on the GDS tool, including at the year before depression incidence. Cases reported more stressful life events than controls both at the year of depression incidence (T1) and 1 year before (T0), but there was no change in stressful life events over time in either cases or controls. Cases and controls were similar in cognitive functioning, which decreased significantly in both groups from one year to the next. Although dependence level (SMAF scores) increased over time within cases and controls, cases had higher dependence levels when compared with the controls. Cases with incident depression decreased their physical activity level from 1 year earlier and had lower scores compared with the non-depressed matched controls. BMI did not differ between the two groups at any time point.

Table 1. Participants' demographic characteristics at recruitment (Quebec Longitudinal Study on Nutrition and Aging baseline)*
(Numbers and percentages; mean values and standard deviations)

	Controls (non-depressed, *n* 158)		Cases (depressed, *n* 158)		
Variables	*n*	%	*n*	%	*P*†
Female	97	61·4	97	61·4	–
Married	84	53·2	87	55·1	0·821
Smoker	7	4·4	12	7·6	0·344
Hypertension	75	47·8	89	56·3	0·143
Income satisfies needs‡	128	94·8	122	94·5	1·000
Age (years)					0·436
Mean	74·8		75·1		
SD	4·3		4·0		
Formal schooling (years)					0·176
Mean	11·9		11·3		
SD	4·4		4·4		

* Depression detected on the basis of Geriatric Depression Scale scores ≥11 and/or use of antidepressant medication over 3 years of follow-up. Depressed subjects were matched by sex and age group with subjects deemed not depressed and whose dietary data were available for the same time points as the depression cases.
† Fisher's exact test for categorical variables. Independent *t* tests for continuous variables. 95 % significance level ($\alpha = 0{\cdot}05$).
‡ Income: non-depressed controls (*n* 135), depression cases (*n* 129).

Table 2. Measures of health status of depression cases and matched controls at the year of depression incidence (T1) and the year before (T0)‡ (Mean values and standard deviations; numbers and percentages)

	Controls (*n* 158)				Cases (*n* 158)			
	Year before (T0)		Matched year of incidence (T1)		Year before (T0)		Year of incidence (T1)	
Variables	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Depression scores (GDS)	3·3††	2·4	3·3††	2·6	6·8**††	2·5	10·8**††	4·1
Stressful life event								
Original								
n	56††		61††		82††		87††	
%	35·4		39·6		52·6		56·9	
Pooled (*n*)	56		62·2		83		89·2	
Cognitive function (3MS scores)	93·6**	5·3	92·5**	6·5	93·2**	5·4	92·0**	6·5
Functional autonomy (SMAF scores)	4·4**††	4·0	5·3**††	4·8	6·1**††	4·1	8·3**††	5·1
BMI (kg/m^2)	28·0	6·0	27·8	4·2	27·4	4·5	27·4	4·7
Physical activity scores (PASE)	97†	50	95††	50	84**†	43	72**††	42

GDS, Geriatric Depression Scale; 3MS, Modified Mini-Mental State examination (range: 0–100 %); SMAF, Functional Autonomy Measuring System (range: 0–87); PASE, Physical Activity Scores for the Elderly (range: 0–793).

** Difference in within-group means is statistically significant ($P<0·01$) according to dependent *t* tests for continuous variables with five multiple imputations for missing data. Difference in between-group means (non-depressed *v.* depressed at the same time point) is statistically significant (†$P<0·05$, ††$P<0·01$), according to independent *t* tests for continuous variables and Fisher's exact test for categorical variables, with five multiple imputations for missing data.

‡ Depression was detected on the basis of GDS scores ≥11 and/or use of antidepressant medication over 3 years of follow-up. Depressed subjects were matched by sex and age group with subjects deemed not depressed and whose dietary data were available for the same time points as the depression cases (mean values and standard deviation for scores are pooled from five multiple imputations).

Bivariate analyses

Mean energy, protein and fibre did not differ between or within cases and controls, with the exception of saturated fat and B-vitamins (Table 3). A small, yet detectable, increase in saturated fat was noted for depression cases. Dietary intakes of the three B-vitamins were consistently higher among controls, without significant changes over time within each of the groups, except for vitamin B_{12}. Mean group intake of dietary vitamin B_{12} did not differ significantly between cases and controls at the year before depression incidence (T0), but differed at the time of depression (T1). The decline over time in dietary vitamin B_{12} intake was significant within cases (Table 3).

Multivariate analyses

Table 4 details the significant results from the GLM mixed models and the difference between groups based on their estimated marginal means. Intakes of energy, fibre and protein did not change significantly over time in depression cases compared with their matched controls (i.e. interaction terms time × group and time × group × stress had $P>0·05$ in all models – not shown in the table). There was a significant main effect of time on saturated fat intake (as percentage of kJ (kcal)) in the models with the original ($P=0·018$) and the multiple imputed data (P 0·023–0·029), meaning that both groups significantly increased their saturated fat intake over time.

With respect to dietary B-vitamins, none of the time × group interactions were significant, suggesting that intakes did not decrease more over time when comparing depressed seniors and non-depressed seniors (Table 4). Ancillary analyses with total intakes of vitamins B_6, B_{12} and folate (DFE) as dependent variables while controlling for the same confounders yielded the same results for time × group interactions (Table 5).

As mean GDS scores before depression were higher among cases – albeit not sufficiently high to achieve the cut-off point for major depression – we tested the models with all study nutrients further controlling for GDS scores before depression. No differences in the findings were observed (data not shown).

Although we did not aim to evaluate adequacy of intakes relative to estimated average requirements (EAR)[46], which must account for within-person variability, it is noteworthy that most participants had mean dietary intakes above the EAR for adults aged ≥51 years, regardless of depression: 76 % for vitamin B_6 (EAR at 1·3 mg/d), 86 % for vitamin B_{12} (EAR at 2·0 µg/d) and 68·7 % for folate (EAR at 320 µg DFE/d) (data not shown). Approximately 90 % had a mean protein intake above the EAR of 0·66 g/kg per d for adults >50 years of age[46] and 50 % above other higher recommendations (1·0 g/kg per d) deemed necessary to maintain N balance in the healthy older adult[47].

Discussion

In this case–control study nested within the NuAge cohort, community-dwelling seniors deemed depressed at follow-up did not change significantly the intakes of energy, fibre and protein over 1-year period compared with their non-depressed, age–sex-matched counterparts. Saturated fat showed a significant increase over time in both depression cases and non-depressed matched controls, which cannot, therefore, be attributed to depression. Findings indicate that dietary vitamins B_6, B_{12} and folate intakes differed significantly between cases and controls regardless of time-point, and, albeit not statistically significant, tended to decrease slightly at the time depression was detected. Taken together, the results suggest that no major changes in diet occur shortly after depression manifests. We did detect a small decline in B-vitamin intake from the diet, which may precede depression incidence in this cohort of older Canadian adults living in the community. It should be noted, however, that we did not examine intakes of other vitamins and minerals, so we cannot determine whether the small changes that we observed were

Table 3. Mean dietary intakes of key nutrients for depression cases and matched controls at the year of depression incidence (T1) (or matched year for controls) and the year before (T0)‡
(Mean values and standard deviations; geometric means with their standard errors)

	Matched controls (*n* 158)				Depression cases (*n* 158)			
	Year before (T0)		Matched year of incidence (T1)		Year before (T0)		Year of incidence (T1)	
Variables	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Energy intake (kJ/d)	7786	2113	7640	1962	7376	1946	7401	2008
Energy intake (kcal/d)	1861	505	1826	469	1763	465	1769	480
Protein intake (g/kg body weight)	1·1	0·4	1·0	0·3	1·0	0·3	1·0	0·3
Total dietary fat (% of total energy)	33·0	5·6	34·0	5·6	33·6	6·1	34·2	5·7
Total saturated fat (% of total energy)	11·1	2·6	11·3	2·9	11·1*	2·9	11·5*	2·9
Total dietary fibre (g/d)	19·9	7·2	19·9	7·1	19·4	7·5	20·1	8·1
Dietary vitamin B_6 (mg/d)	2·2††	0·4	2·3††	0·3	1·5††	0·04	1·5††	0·04
Total vitamin B_6 (mg/d)								1·0
Geometric mean	2·9†		2·9†		2·3†*		2·0†*	
SEM	0·9		0·7		1·1		1·0	
Dietary vitamin B_{12} (μg/d)								
Geometric mean	3·8		3·6††		3·4*		3·0††*	
SEM	0·6		0·6		0·5		0·2	
Total vitamin B_{12} (μg/d)								
Geometric mean	6·0		5·4		5·5*		4·5*	
SEM	5·8		9·9		3·6		1·8	
Dietary folate (μg/d)								
Geometric mean	383·3†		374·8†		350·1†		344·4†	
SEM	10·5		9·4		10·1		9·3	
Total folate (DFE μg/d)								
Geometric mean	473·9		451·6		492·6*		445·9*	
SEM	31·2		34·6		152·3		137·1	

DFE, dietary folate equivalent.
* Difference in within-group means (comparing T0 and T1 for each group) is statistically significant ($P<0·05$) according to dependent *t* tests.
Difference in between-group means (non-depressed *v.* depressed at the same time point) is statistically significant (†$P<0·05$, ††$P<0·001$), according to independent *t* tests. Vitamins B_6, B_{12} and folate were transformed to natural log for testing, but geometric means with their standard errors are shown for untransformed data.
‡ Depression was detected on the basis of Geriatric Depression Scale scores ≥11 and/or use of antidepressant medication over 3 years of follow-up. Depression cases were matched by sex and age group with participants deemed not depressed at any time point of the yearly follow-up and whose dietary data were available for the same time points as the depression cases. Mean daily intakes are from three non-consecutive 24-h recalls for food only (do not include supplements).

specific to B-vitamins, or occurred for other nutrients as well. Nevertheless, our overall results do not seem to support the reverse causality hypothesis.

Our present findings are in agreement with observations from other longitudinal studies investigating the association between B-vitamins and incident depression[8–10,13,14,16,17]. Most of these studies focus, however, on middle-aged adults, limiting appropriate comparisons with our study. It does reinforce a previous related study conducted by our team[21] indicating that higher dietary intakes of vitamin B_6 among women and vitamin B_{12} among men may be protective of late-life depression among these generally healthy seniors living in the community.

In Korean older adults, Kim *et al.*[12] observed greater declines in serum vitamin B_{12} levels among those deemed depressed at 2 years of follow-up. In our study, older adults deemed depressed showed a significant decline in mean vitamin B_{12} intake from food in bivariate analyses. This decline, coupled with the greater proportion of stressful life events among depressed participants, could be an indication of changes in lifestyle factors, such as food choices, physical activity or social engagement. The latter two may not offer, however, the best explanation for this observation, as physical activity was included in our present models, and social engagement was not associated with the outcome in an earlier work[21]. A plausible explanation for the observed decline in vitamin B_{12} may be related to changes in food choices, such as replacing meat products with plant alternatives (e.g. legumes)[48–50], given that (i) protein intake remained stable over time, (ii) it did not differ between cases and controls and (iii) food items of animal origin are the only source of vitamin B_{12}[46]. However, such a change would have to be translated into higher intakes of dietary fibre among depression cases, as plant sources are also rich in fibre, but such an increase was not observed. It is noteworthy that declines in vitamin B_{12} intakes were rather small (from 3·4 μg/d at the year before to 3·0 μg/d at the year of incidence) and unlikely to put seniors at risk of deficiency for the period studied. The high proportion of individuals with mean dietary intakes of all three B-vitamins above the EAR further supports this notion.

The focus on intakes from food and the exclusion of supplements might raise the question as to whether supplementation could decrease the risk of depression in late-life. Randomised, placebo-controlled trials have been conducted and found no clear effect of B-vitamin supplementation on seniors' affective health[51–57]. It then leaves the question of whether B-vitamins from food have different associations with health[58] possibly their synergistic effect with other nutrients – partially the reason for the increasing interest in dietary patterns[59] – or certain lifestyle factors[30,60] or social determinants of health[61].

The significant main effect of group and the lack of significant declines in dietary intakes over time (time × group interactions) among those deemed depressed in this study when compared with non-depressed age–sex-matched controls suggest that

Table 4. Multivariate analysis results for saturated fat and B-vitamins in community-dwelling older Canadians*
(Estimated mean differences with their standard errors)

	Original data†		Imputation 1†	
Mixed-model terms‡	*F*	*P*	*F*	*P*
Saturated fat				
Mean§	0·237		0·100	
SEM	0·285		0·274	
Intercept	5425·8	<0·001	5834·5	<0·001
Group‖	0·696	0·405	0·134	0·715
Time	5·713	0·018	4·834	0·029
Time × Group	0·073	0·787	0·361	0·549
Time × Group × Stress	0·330	0·566	0·158	0·691
Vitamin B_6				
Mean§	−0·349		−0·365	
SEM	0·044		0·040	
Intercept	649·97	<0·001	784·26	<0·001
Group‖	62·807	<0·001	81·653	<0·001
Time	0·518	0·472	0·645	0·422
Time × Group	1·377	0·242	1·475	0·226
Time × Group × Stress	1·456	0·229	1·985	0·160
Vitamin B_{12}				
Mean§	−0·092		−0·115	
SEM	0·062		0·057	
Intercept	1404·23	<0·001	1643·39	<0·001
Group‖	2·231	0·136	4·076	0·044
Time	1·655	0·199	3·366	0·068
Time × Group	0·821	0·366	1·020	0·313
Time × Group × Stress	0·350	0·555	0·179	0·673
Folate				
Mean§	−0·065		−0·086	
SEM	0·032		0·031	
Intercept	119 053	<0·001	131 315	<0·001
Group‖	4·076	0·044	7·904	0·005
Time	0·596	0·441	0·833	0·362
Time × Group	0·005	0·944	0·012	0·913
Time × Group × Stress	0·002	0·966	0·090	0·764

* For simplicity, data shown are restricted to nutrients with significant results from mixed-model ANCOVA. Saturated fat measured as percentage of total energy content (kcal). Vitamins B_6 (mg/d); B_{12} (μg/d) and folate (dietary folate equivalent μg/d) were transformed to natural log for normality.
† Covariates appearing in the model are functional autonomy (% change of Functional Autonomy Measuring System) and physical activity (% change of Physical Activity Scores for the Elderly) and are, respectively, evaluated at the following values: original data, 70·3814 and 7·5252; imputation 1, 73·0718 and 6·9502. df_{error} is 270 for original data and 310 for imputed data.
‡ 2 × 2 × 2 (time × group × stress), full factorial, mixed-model ANCOVA. Only relevant between- and within-factor terms for models using the original data and first set of imputed data are shown (the other four sets of imputed data had similar results and were excluded from the table for simplicity).
§ Mean difference between depression cases minus matched controls based on estimated marginal means from pairwise comparisons with their standard errors. *P* value adjusted for multiple comparisons according to Bonferroni.
‖ Group = depression cases *v.* matched controls.

Table 5. Ancillary multivariate analysis for total intakes (food + supplements) of vitamins B_6, B_{12} and folate (dietary folate equivalent (DFE)) in community-dwelling older Canadians in the Quebec Longitudinal Study on Nutrition and Aging cohort*
(Estimated mean differences with their standard errors)

	Original data†		Imputation 1†	
Mixed-model terms‡	*F*	*P*	*F*	*P*
Vitamin B_6				
Mean§	−0·273		−0·296	
SEM	0·092		0·089	
Intercept	354·85	<0·001	383·10	<0·001
Group‖	8·859	0·003	11·217	0·001
Time	0·377	0·540	0·392	0·532
Time × Group	1·798	0·181	2·102	0·148
Time × Group × Stress	1·89	0·170	3·116	0·079
Vitamin B_{12}				
Mean§	−0·088		−0·135	
SEM	0·117		0·111	
Intercept	714·113	<0·001	803·591	<0·001
Group‖	0·569	0·451	1·479	0·225
Time	5·002	0·026	8·153	0·005
Time × Group	0·739	0·391	1·427	0·233
Time × Group × Stress	0·054	0·817	0·504	0·478
Folate				
Mean§	−0·013		−0·005	
SEM	0·072		0·069	
Intercept	714·113	<0·001	803·591	<0·001
Group‖	0·569	0·451	1·479	0·225
Time	5·022	0·026	8·153	0·005
Time × Group	0·739	0·391	1·427	0·233
Time × Group × Stress	0·054	0·817	0·504	0·478

* For simplicity, data shown are restricted to nutrients with significant results from mixed-model ANCOVA. Vitamins B_6 (mg/d); B_{12} (μg/d) and folate (DFE μg/d) were transformed to natural log for normality.
† Covariates appearing in the model are functional autonomy (% change of Functional Autonomy Measuring System) and physical activity (% change of Physical Activity Scores for the Elderly) and are respectively evaluated at the following values: original data, 70·3814 and 7·5252; imputation 1, 73·0718 and 6·9502. df_{error} is 270 for original data and 310 for imputed data.
‡ 2 × 2 × 2 (time × group × stress), full factorial, mixed-model ANCOVA. Only relevant between- and within-factor terms for models using the original data and first set of imputed data are shown (the other four sets of imputed data had similar results and were excluded from the table for simplicity).
§ Mean difference between depression cases minus matched controls based on estimated marginal means from pairwise comparisons with their standard errors. *P* adjusted for multiple comparisons according to Bonferroni.
‖ Group = depression cases *v.* matched controls.

vitamin B intakes could be declining for a period longer than 1 year. In fact, compared with controls at the year before depression, cases already had significantly higher GDS scores, but not high enough to reach the GDS threshold for major depression. On the other hand, intakes of some macronutrients did not change significantly in any way. Future research from longitudinal studies of longer duration can shed light as to when the intakes start to decline relative to depression incidence and how quickly when compared with non-depressed seniors.

NuAge's unique, detailed, high-quality dietary data allowed us to shed some light on the reverse causality hypothesis between diet and depression among community-dwelling seniors. Notwithstanding, caution should be used when interpreting the findings. Mean dietary intakes do not necessarily reflect usual intakes, particularly for micronutrients consumed sporadically, such as vitamin B_{12}[23,62]. This shortcoming is more limiting, however, in comparisons with reference intakes, whose reliability require usual intakes. This comparison was done to further describe the sample and was not the aim of our study. Though all the necessary steps were taken to meet required statistical assumptions (e.g. log transformations), some variables showed high variance, which can decrease statistical power. The multiple imputation method to treat missing data had the advantage of maintaining the strength of a paired design, but also lead to multiple tests, which can increase type I error – this was accounted for by choosing key nutrients and using the Bonferroni adjustment in the GLM analyses. Moreover, in addition to having an overall good health, living independently in the community and almost all participants stating sufficient revenue for their needs, these

seniors had only mild levels of depression according to the GDS screening tool, which may not have been enough to change dietary habits in a clinically significant way. In the study by Jacka *et al.*[20], participants who had a history of depression and received treatment fared better in their eating patterns than those not treated or without a history of depression. In our study, while we excluded depression cases at cohort baseline, such a relationship cannot be disregarded.

In conclusion, community-dwelling seniors who became depressed did not change their dietary intake in any substantial way shortly after possible depression was detected. They may have been, however, experiencing declines in dietary intakes of B-vitamins (and potentially of other vitamins and minerals not assessed in our study) over a longer period of time. Practitioners should, nonetheless, investigate for multiple signs of impending depression among seniors beyond just nutrient intake, such as lifestyle and social factors, shown to be associated with incidence of depression in this population, in order to help their clients to either prevent depression or decrease the impact depression may have on their clients' overall health. To ensure successful ageing and minimise the effects of disease and disability, participation of dietitians in community-based programmes for seniors is essential[63].

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L. G. designed and conducted the research, analysed the data, performed statistical analysis and wrote the paper. H. P. was the principal investigator for the NuAge cohort study and provided essential materials. H. P., J. A. M., P. G. and B. S. provided expertise for the research. K. G.-D. had primary responsibility for the final content. K. G.-D, J. A. M., P. G. and B. S. were co-principal investigators for the NuAge cohort study. J. A. M., P. G. and B. S provided feedback on the manuscript. All authors have read and approved the final manuscript.

None of the authors has any conflicts of interest to declare.

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