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RESEARCH ARTICLE

Sex differences in the prevalence of fatigue across age groups and associated factors

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ABSTRACT

Background: Although fatigue is frequently reported in the clinical setting, factors influencing the odds of an individual reporting fatigue are not well understood, nor if they are similar between males and females across different age groups.
Objective: To determine age and sex differences in factors previously speculated to influence the odds of self-reported fatigue.
Methods: A retrospective analysis using data from the second wave of the Midlife in the United States (MIDUS 2) national survey.
Results: Fatigue was reported by 58% of the 1805 individuals ages 30–86 years old. The prevalence was greater in females than males (65% vs. 49%, respectively, $p < 0.001$), particularly in those who reported fatigue more frequently across all age groups. Psychological distress was associated with the prevalence of fatigue in both sexes but with greater odds in females, whereas muscle weakness was associated with the prevalence of fatigue in both sexes but with greater odds in males. Joint pain was associated with prevalence of fatigue for males and females.
Conclusions: The prevalence of fatigue was greater in females than males across age groups. The odds of factors associated with reported fatigue can differ between males and females, and they were not influenced by aging. These findings suggest the need for sex-specific intervention strategies to reduce the prevalence of fatigue across age groups.

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1. Introduction

Fatigue is a common complaint prompting individuals to seek medical attention [1, 2], and it is often reported in epidemiological studies regardless of the presence of associated disease [3]. The construct of fatigue can be defined as a disabling symptom in which physical and cognitive function are limited by interactions between performance

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fatigability and perceived fatigability [4, 5]. Performance fatigability typically involves an objective measurement of motor performance such as decline in force, whereas perceived fatigability is often measured via self-reported questionnaire items used to quantify its magnitude as well as presence [5, 6]. Several social and physical factors have been speculated to influence the construct of fatigue such as the presence of pain, education level, lack of sleep and the presence of stress [3, 4, 7]. However, evidence is limited, as there are few reports investigating associations between any of these factors and fatigue [3, 8, 9], particularly accounting for the sex of the individuals across the adult lifespan, or presence of other factors such as obesity [3].

It is important to identify factors related to the reported fatigue for each sex across age groups. Females typically have greater longevity than males [10, 11], however, any sex differences in the prevalence of fatigue across age groups is poorly understood despite the widely documented sex related alterations in physiological function with aging [12]. Additionally, the impact of vulnerabilities, such as psychological stress and the presence of pain, on the prevalence of fatigue in males and females across age groups is not fully understood. Physiological responses to stressors and associated mechanisms can differ with aging and between males and females [13, 14], which could potentially alter the fatigue response between groups. Understanding factors associated with the reported fatigue across age groups for males and females, such as psychological stress and other risk factors, is essential for adequate prevention of age-related functional loss and disability in males and female individuals.

In this study, we used data from a national survey to determine the prevalence of fatigue in males and females across age groups. We also investigated the potential role of psychological distress, joint pain and other demographics previously suggested to be associated with fatigue (e.g. Body mass index), and if the odds ratio of these factors differed between males and females across age groups. We hypothesized the correlates of fatigue would differ between males and females across the age groups, which would be consistent with physiological sex and age-related differences.

2. Methods

We used data from the Daily Diary Project 2, which is an in-depth study conducted with a random subsample from the second wave of the longitudinal National Study of Midlife in the United States (MIDUS 2) [15] matched to participant demographic and health variables reported in the MIDUS 2 Survey Study [16, 17]. The purpose of the Daily Diary Project 2 was to examine how sociodemographic factors, health status and personality characteristics can impact the reactivity of day-to-day life stressors. The MIDUS 2 originated with a stratified probability sampling design of 5,555 English-speaking individuals, ages 35–86 years old, from the contiguous United States. The Daily Diary Project 2 had a 78% response rate and consisted of interviews as well as a self-administered questionnaire assessing a range of sociodemographic, psychosocial, and health topics. A phone interview lasting about 30 min in length was conducted with each participant and repeated for eight consecutive nights. Compensation was given to each individual for participating in the Daily Diary Project. Institutional review board (IRB) and participant informed consent were obtained for all study components [17]. The full dataset can be accessed through the Inter-University Consortium for Political and Science Research [17].

2.1. Variables description

Fatigue: Participants were asked, 'Did you experience fatigue today?' (i.e. answering yes or no) every evening across eight consecutive days. An overall fatigue score was then calculated as the sum of days that each participant reported yes during eight days. Thus, fatigue was a scale variable from 0 to 8, indicating the prevalence of fatigue during the 8-day period of data collection. We further classified the prevalence of fatigue as none (0 days), low frequency (1 response out of 8 days), medium frequency (2-3 days) and high frequency (4 or more days).

Psychological distress: The Negative Affect Scale [18, 19] assessed how often participants felt a range of 14 moods in the past 30 days. Moods assessed were restless or fidgety, nervous, worthless, so sad nothing will cheer you up, everything was an effort, hopeless, lonely, afraid, jittery, irritable, ashamed, upset, angry, and frustrated. Responses were reverse coded, so higher sum scores indicated greater psychological distress.

Presence of joint pain & presence of muscle weakness: For these two distinct variables, participants were asked (yes/no) if they experienced joint pain or muscle weakness at each day of the study (one or both could be present and were recorded as distinct variables). Each of these variables were transformed into a binary variable and indicated in the results if present at least once during the eight days of interviews.

Duration of sleep, time spent on leisure, work and dedicated physical activity: Each one is a distinct variable. During each interview, participants were asked how many hours and minutes they spent performing each of these activities. Data was recorded together with calendar information to distinguish between workdays and weekends. In the current study, these measurements were converted to minutes and averaged across the 8-day period.

Demographics: Age brackets were categorized into 35–45, 46–55, 56–65, 66–75 and 76–86 years old. The MIDUS 2 dataset reports if the individual was male or female, thus this terminology is used throughout the text. Body mass index (BMI) was calculated and classified as underweight (BMI: less than 18.5), normal (BMI: 18.5–24.9), overweight (BMI: 25–29.9) or obese (BMI: 30 or greater) [20]. Each participant ranked the highest level of education on a scale. To facilitate comparisons with other reports [3], they were combined into the following brackets (i.e. transformed in a categorical variable): some high school or less; completed high school; some college; BSc (graduate from college); advanced degree. Education brackets were recorded from the MIDUS 2 survey study dataset.

2.2. Statistical analysis

The Spearman's rho was used to determine the association between presence of fatigue and other scale variables such as psychological distress (Negative Affects), average sleep time (minutes), average leisure time (minutes), average time spent at work (minutes), and average minutes performing a physical activity. The chi-square test was used to determine the associations between the variables sex, age group, education, BMI, the presence of joint pain, and muscle weakness.

Given the multiple frequencies of fatigue as well as the presence of continuous and binary outcomes, multinomial logistic regressions were used to identify factors associated with fatigue prevalence. The Benjamini-Hochberg correction was applied for multiple comparisons. No multicollinearity was observed between the independent variables (Variance Inflation Factor < 10) [21]. Individuals with missing data were excluded from the analysis. First, a general model was computed with the dependent variable *fatigue* measured across four distinct categories (no fatigue, low frequency of fatigue, medium frequency of fatigue, and high frequency of fatigue), and the 'no fatigue' category served as the reference. The independent variables in the model were sex, age, BMI, joint pain, muscle weakness, and psychological distress. Odds Ratios (OR) along with their Confidence Intervals (CI) were reported. In this multinomial regression model, the objective was to determine how different independent variables influence the probability of belonging to a specific category compared to the reference category. The term 'odds ratio' (OR) plays a crucial role in this context, providing an understanding of changes in the odds of belonging to a category compared to the reference category for a one-unit increase in the independent variables. The OR is calculated as the ratio of odds between two categories. Suppose we are analyzing an independent variable X in relation to two categories (A and B), where A is the reference category. The OR for category B compared to category A is calculated as:

$$OR_{BvsA} = \frac{odds_B}{odds_A}$$

where the 'odds' are calculated as the ratio between the probability of an event occurring and the probability of it not occurring. Mathematically, for a variable X:

$$odds_B = \frac{P(Y = B|X)}{P(Y \neq B|X)} \text{ and } odds_A = \frac{P(Y = A|X)}{P(Y \neq A|X)}$$

The interpretation of the OR is: If OR_{BvxA} is equal to 1, it suggests no difference in the odds between categories A and B. If OR_{BvxA} is greater than 1, then the odds of belonging to category B are higher compared to category A, and if OR_{BvxA} is less than 1, the odds are lower for category B compared to category A [22].

Because of the strong sex differences observed in the general model, sex-stratified models were constructed, one for males and another for females, aiming to investigate the weight of specific factors associated with fatigue by each sex.

For all analysis, the statistical significance was set as 5% ($p < 0.05$), and analyses were conducted in R using the packages *nnet, lmtest, DescTools* and *car*.

3. Results

Merging the demographic data from the MIDUS 2 and the Daily Diary Project 2 resulted in 1805 participants (55.8% female vs. 44.2% male, Table 1). From these individuals, approximately 57.7% (i.e. 1,041 participants) reported some fatigue. Females had greater prevalence of fatigue across the 8 days compared with males (pooled data from low, medium and high fatigue: 64.7% vs 49.2%, respectively, $p < 0.001$). Table 1 shows that fatigue prevalence is similar between males and females for the low frequency of fatigue category. However, for the high frequency of fatigue category, the proportion of individuals reporting fatigue was lower for males than females (11% vs. 20.7%,

Table 1. Physical characteristics of the participants according to the prevalence of fatigue.

Variables		Fatigue									
		No		Low Frequency		Medium Frequency		High Frequency		Total	% Total
		n	%	n	%	n	%	n	%		
Sex											
Male		405	50.8%	175	22.0%	129	16.2%	88	11.0%	797	44.2%
Female		359	35.6%	216	21.4%	224	22.2%	209	20.7%	1008	55.8%
Age											
35–45	All	109	37.3%	66	22.6%	64	21.9%	53	18.2%	292	16.2%
	Male	56	49.6%	25	22.1%	20	17.7%	12	10.6%	113	14.2%
	Female	53	29.6%	41	22.9%	44	24.6%	41	22.9%	179	17.8%
46–55	All	196	42.3%	99	21.4%	95	20.5%	73	15.8%	463	25.7%
	Male	106	48.4%	50	22.8%	36	16.4%	27	12.3%	219	27.5%
	Female	90	36.9%	49	20.1%	59	24.2%	46	18.9%	244	24.2%
56–65	All	215	42.5%	116	22.9%	91	18.0%	84	16.6%	506	28.0%
	Male	118	52.0%	47	20.7%	38	16.7%	24	10.6%	227	28.5%
	Female	97	34.8%	69	24.7%	53	19.0%	60	21.5%	279	27.7%
66–75	All	151	42.4%	78	21.9%	71	19.9%	56	15.7%	356	19.7%
	Male	78	52.3%	36	24.2%	20	13.4%	15	10.1%	149	18.7%
	Female	73	35.3%	42	20.3%	51	24.6%	41	19.8%	207	20.5%
76–86	All	93	49.7%	32	17.1%	32	17.1%	30	16.0%	187	10.4%
	Male	47	52.8%	17	19.1%	15	16.9%	10	11.2%	89	11.2%
	Female	46	46.9%	15	15.3%	17	17.3%	20	20.4%	98	9.7%
Education											
Some High School or Less	All	36	39.6%	22	24.2%	17	18.7%	16	17.6%	91	5.0%
	Male	19	50.0%	6	15.8%	6	15.8%	7	18.4%	38	4.8%
	Female	17	32.1%	16	30.2%	11	20.8%	9	17.0%	53	5.3%
Completed High School	All	191	43.4%	92	20.9%	89	20.2%	68	15.5%	440	24.4%
	Male	86	50.6%	44	25.9%	19	11.2%	21	12.4%	170	21.3%
	Female	108	39.6%	48	17.6%	70	25.6%	47	17.2%	273	27.1%
Some College	All	215	39.7%	120	22.2%	109	20.1%	97	17.9%	541	30.0%
	Male	101	46.3%	52	23.9%	42	19.3%	23	10.6%	218	27.4%
	Female	114	35.3%	68	21.1%	67	20.7%	74	22.9%	323	32.0%
BSc (Graduate from College)	All	196	44.0%	95	21.3%	89	20.0%	65	14.6%	445	24.7%
	Male	124	53.2%	44	18.9%	42	18.0%	23	9.9%	233	29.2%
	Female	72	34.0%	51	24.1%	47	22.2%	42	19.8%	212	21.0%
Advanced Degree	All	124	43.5%	62	21.8%	49	17.2%	50	17.5%	285	15.8%
	Male	78	55.3%	29	20.6%	20	14.2%	14	9.9%	141	17.7%
	Female	46	31.9%	33	22.9%	29	20.1%	36	25.0%	144	14.3%
BMI											
Underweight	All	4	22.2%	8	44.4%	4	22.2%	2	11.1%	18	1.0%
	Male	0	–	2	66.7%	1	33.3%	0	–	3	0.4%
	Female	4	26.7%	6	40.0%	3	20.0%	2	13.3%	15	1.5%
Normal	All	224	42.9%	117	22.4%	103	19.7%	78	14.9%	522	28.9%
	Male	95	53.4%	42	23.6%	25	14.0%	16	9.0%	178	22.3%
	Female	129	37.5%	75	21.8%	78	22.7%	62	18.0%	344	34.1%
Overweight	All	318	47.0%	135	19.9%	123	18.2%	101	14.9%	677	37.5%
	Male	188	54.2%	72	20.7%	48	13.8%	39	11.2%	347	43.5%
	Female	130	39.4%	63	19.1%	75	22.7%	62	18.8%	330	32.7%
Obese	All	175	36.5%	103	21.5%	100	20.9%	101	21.1%	479	26.5%
	Male	95	44.8%	49	23.1%	42	19.8%	26	12.3%	212	26.6%
	Female	80	30.0%	54	20.2%	58	21.7%	75	28.1%	267	26.5%
Joint Pain											
No	All	466	52.2%	197	22.1%	148	16.6%	82	9.2%	893	49.5%
	Male	249	61.5%	79	19.5%	49	12.1%	28	6.9%	405	50.8%
	Female	217	44.5%	118	24.2%	99	20.3%	54	11.1%	488	48.4%
Yes	All	298	32.7%	194	21.3%	205	22.5%	215	23.6%	912	50.5%
	Male	156	39.8%	96	24.5%	80	20.4%	60	15.3%	392	49.2%
	Female	142	27.3%	98	18.8%	125	24.0%	155	29.8%	520	51.6%
Muscle weakness											
No	All	691	48.6%	322	22.6%	263	18.5%	147	10.3%	1423	78.8%

(*Continued*)

Table 1. Continued.

Variables		Fatigue									
		No		Low Frequency		Medium Frequency		High Frequency		Total	% Total
		n	%	n	%	n	%	n	%		
	Male	366	57.5%	140	22.0%	93	14.6%	38	6.0%	637	79.9%
	Female	325	41.3%	182	23.2%	170	21.6%	109	13.9%	786	78.0%
Yes	All	73	19.1%	69	18.1%	90	23.6%	150	39.3%	382	21.2%
	Male	39	24.4%	35	21.9%	36	22.5%	50	31.3%	160	20.1%
	Female	34	15.3%	34	15.3%	54	24.3%	100	45.0%	222	22.0%

respectively; $p < 0.001$). The fatigue frequencies (low, medium and high) were similarly distributed across and within age brackets without interaction between them (all $p > 0.05$).

There was no difference in education across age groups or sex ($p = 0.95$). Another factor addressed in this study was BMI. In this sample 68.2% of the participants were overweight or obese and there was a very low proportion of underweight individuals (1.1%). It is noteworthy that females had greater proportion of simultaneously reporting fatigue and being obese compared with males (70% vs. 55%, respectively; $p < 0.01$). Similar observation was found for the overweight group (61% vs. 46%, respectively) and normal weight (63% vs. 47%, respectively) (all with sex effect: $p < 0.01$).

Approximately 50.5% of participants (i.e. 912 individuals) that answered the fatigue question also reported joint pain. When scrutinizing joint pain, as the frequency of fatigue escalated from 'Low' to 'High,' there was a slight concurrent increase in the percentage of females reporting joint pain, reaching 29.8% in the 'High Fatigue' category, whereas males had a slight reduction in the prevalence of fatigue (from 24.5% to 15.3%) ($p < 0.001$) (Table 1).

Similarly, when examining the relationship between self-reported muscle weakness and fatigue prevalence, 21.2% of total participants with muscle weakness also reported the presence of some fatigue (low, medium or high frequency). For the low and medium frequencies of fatigue males and females had similar proportion of muscle weakness, however the proportion of males and females reporting muscle weakness increased in the high frequency of fatigue category compared with the low and medium frequencies. Additionally, the increase from medium to high frequency of fatigue was larger for males compared with females (males 24.3–45%; females: 22.5–31.3%, respectively) ($p < 0.001$) (Table 1).

Results of the negative affect scale were positively associated with increased prevalence of fatigue (i.e. from low to high frequency) either combining both males and females or separating the sexes (all $p < 0.001$). Details of association values are available in Supplemental tables.

3.1. Multinomial model including both males and females to identify factors associated with the prevalence of fatigue across age groups

Multinomial logistic regression analysis was used to identify factors associated with the fatigue frequencies: No Fatigue, Low Fatigue, Medium Fatigue, and High Fatigue Frequency. The 'No Fatigue' was used as the reference value. The regression model indicates sex difference for the medium and high frequencies of fatigue, but not for the low frequency of fatigue. Specifically, as prevalence of fatigue increased from medium to high, females exhibited greater odds of experiencing fatigue when compared to males (2.14 for Medium Fatigue, and 3.08 for High Fatigue; $p < 0.001$) (Table 2).

Age brackets analysis indicates the odds ratio is lower in the very old individuals (76–86 years old) particularly for the medium frequency of fatigue category (Odds ratio of 0.43; $p = 0.014$), but high frequency of fatigue did not reach statistical significance (Odds ratio of 0.47; $p = 0.059$) compared with the younger bracket (35–45 years old) (Table 2). The prevalence of fatigue for the low frequency of fatigue category and other age brackets (i.e. 46–55; 56–65, 66–75 years old) were also not statistically different than the reference category (35–45 years old). Being overweight or obese was not associated with any frequency of fatigue (all $p > 0.05$) (Table 2).

The presence of joint pain was positively associated with all fatigue frequencies (all $p <$ 0.05), with the strongest association observed in high frequency of fatigue (OR: 2.71; $p <$ 0.001). Similar positive association was found for muscle weakness, and greater odds at high frequency of fatigue (OR: 7.16; $p < 0.001$) compared with low and medium frequencies of fatigue (OR: 1.74 and 2.85, respectively; both $p < 0.05$) (Table 2).

Psychological distress, quantified with the negative affects scale, exhibited a significant positive association with all fatigue frequencies. Those with higher psychological distress had greater odds of fatigue particularly at high frequency (OR: 2.78; $p < 0.001$) compared with low and medium fatigue frequencies (OR: 1.87 and 1.84, respectively; all $p < 0.001$) (Table 2).

Variables not included in the multinomial regression model were the ones that had a very weak association with prevalence of fatigue [i.e. Sleep time (rho: −0.12; $p < 0.0001$)

Table 2. Results of the multinomial regression model to identify factors associated with the prevalence of fatigue including both males and females.

Variables	Low Frequency of Fatigue			Medium Frequency of Fatigue			High Frequency of Fatigue		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Sex									
Male	–	–	–	–	–	–	–	–	–
Female	1.32	1.01, 1.72	0.080	2.14	1.61, 2.85	<0.001	3.08	2.18, 4.36	<0.001
Age									
35–45	–	–	–	–	–	–	–	–	–
46–55	1.01	0.66, 1.54	0.973	0.94	0.61, 1.44	0.837	0.84	0.50, 1.41	0.655
56–65	1.08	0.71, 1.64	0.812	0.7	0.45, 1.09	0.203	0.9	0.54, 1.51	0.810
66–75	0.98	0.62, 1.56	0.964	0.72	0.45, 1.15	0.273	0.68	0.39, 1.20	0.273
76–86	0.63	0.36, 1.10	0.187	0.43	0.24, 0.77	0.014	0.47	0.24, 0.92	0.059
BMI									
Normal	–	–	–	–	–	–	–	–	–
Overweight	0.82	0.60, 1.12	0.304	0.9	0.65, 1.26	0.685	1.05	0.70, 1.57	0.855
Obese	1.07	0.76, 1.51	0.810	1.18	0.83, 1.69	0.480	1.52	1.00, 2.31	0.093
Joint Pain									
No	–	–	–	–	–	–	–	–	–
Yes	1.41	1.07, 1.84	0.032	1.94	1.45, 2.58	<0.001	2.71	1.90, 3.85	<0.001
Muscle Weakness									
No	–	–	–	–	–	–	–	–	–
Yes	1.74	1.17, 2.58	0.015	2.85	1.95, 4.17	<0.001	7.16	4.84, 10.6	<0.001
Negative Affects	1.87	1.53, 2.29	<0.001	1.84	1.49, 2.26	<0.001	2.78	2.26, 3.42	<0.001

OR: Odds Ratio; CI: Confidence interval. There were few individuals classified as underweight (n = 18), so this category was excluded from the analysis. Nagelkerke pseudo-R^2: 0.2712.

Table 3. Results of the multinomial regression model to identify factors associated with the prevalence of fatigue separated by sex.

Variables		Low Frequency of Fatigue			Medium Frequency of Fatigue			High Frequency of Fatigue		
		OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age										
35–45	–	–	–	–	–	–	–	–	–	–
46–55	Male	1.22	0.65, 2.30	0.741	0.97	0.49, 1.92	0.941	1.21	0.48, 3.03	0.871
	Female	0.86	0.48, 1.54	0.775	0.91	0.52, 1.59	0.828	0.69	0.36, 1.34	0.435
56–65	Male	1.04	0.55, 1.97	0.941	0.72	0.36, 1.45	0.595	1.14	0.45, 2.89	0.871
	Female	1.14	0.65, 2.01	0.775	0.71	0.40, 1.26	0.422	0.85	0.45, 1.61	0.775
66–75	Male	1.07	0.53, 2.17	0.896	0.60	0.27, 1.34	0.414	0.85	0.30, 2.38	0.871
	Female	0.94	0.50, 1.74	0.900	0.80	0.44, 1.46	0.670	0.65	0.33, 1.30	0.406
76–86	Male	0.75	0.33, 1.71	0.741	0.50	0.20, 1.26	0.362	0.46	0.15, 1.48	0.414
	Female	0.52	0.23, 1.15	0.272	0.40	0.18, 0.86	0.067	0.52	0.23, 1.18	0.272
BMI										
Normal	–	–	–	–	–	–	–	–	–	–
Overweight	Male	0.82	0.51, 1.30	0.616	0.90	0.51, 1.57	0.871	1.26	0.61, 2.60	0.741
	Female	0.83	0.54, 1.26	0.565	0.92	0.61, 1.40	0.823	0.96	0.59, 1.57	0.900
Obese	Male	1.10	0.66, 1.84	0.871	1.51	0.84, 2.73	0.403	1.58	0.72, 3.47	0.467
	Female	1.04	0.66, 1.65	0.900	0.98	0.62, 1.56	0.946	1.46	0.88, 2.43	0.296
Joint Pain										
No	–	–	–	–	–	–	–	–	–	–
Yes	Male	1.64	1.11, 2.42	0.038	2.08	1.32, 3.27	0.006	2.13	1.18, 3.85	0.038
Yes	Female	1.24	0.85, 1.82	0.435	1.84	1.26, 2.69	0.007	2.91	1.87, 4.55	<0.001
Muscle Weakness										
No	–	–	–	–	–	–	–	–	–	–
Yes	Male	1.88	1.08, 3.26	0.071	3.10	1.74, 5.50	0.001	10.70	5.76, 20.0	<0.001
Yes	Female	1.51	0.86, 2.66	0.296	2.47	1.48, 4.12	0.003	5.42	3.24, 9.06	<0.001
Negative Affects	Male	1.72	1.31, 2.25	0.001	1.55	1.14, 2.10	0.017	2.32	1.72, 3.13	<0.001
	Female	2.05	1.53, 2.76	<0.001	2.14	1.60, 2.87	<0.001	3.31	2.47, 4.44	<0.001

OR: Odds Ratio; CI: Confidence interval. Nagelkerke pseudo-R^2: 0.225 and 0.2721 for male and female, respectively.

and dedicated time spent with physical activity (rho: −0.08; $p = 0.018$)], as well as variables that were not associated with prevalence of fatigue [i.e. education, time spent on leisure, time spent on work and time spent with dedicated physical activity (all $p > 0.05$)]. Supplemental Tables 1 and 2 detail group averages and associations with fatigue, respectively.

3.2. Multinomial model to identify factors associated with the odds of fatigue across age for each sex

Further analyses were conducted splitting the regression models between males and females to determine if the odds differed between the sexes. These analyses revealed there is no association of age bracket with low, medium or high frequency of fatigue for males or female participants (all $p > 0.05$) (Table 3).

Males with joint pain showed a significant association with different fatigue frequencies. They had 1.64 times greater odds to experience low frequency of fatigue ($p = 0.038$), 2.08 times greater odds to experience medium frequency of fatigue ($p = 0.006$), and 2.13 times greater odds to experience high frequency of fatigue ($p = 0.038$) compared to those without joint pain. Conversely for females, no association was present between joint pain and low frequency of fatigue compared with the reference group without joint pain (OR = 1.24, $p = 0.435$). However, females reporting joint pain had 1.84 times greater odds of experiencing medium fatigue frequency (OR = 1.84, $p = 0.007$) and 2.91 times greater odds of experiencing high fatigue frequency (OR = 2.91, $p < 0.001$) compared to those without joint pain (Table 3).

The association between muscle weakness and prevalence of fatigue indicated that males had larger odds than females particularly for the individuals with high frequency of fatigue (10.7 vs 5.4, respectively) (Table 3). Specifically, muscle weakness was not associated with low frequency of fatigue for males or females ($p = 0.071$ and $p = 0.296$). However, males had 3.10 times greater odds to report medium frequency of fatigue ($p < 0.001$), and 10.70 times greater odds to report high frequency of fatigue ($p < 0.001$). For females, muscle weakness was associated with medium ($p = 0.003$) and high fatigue frequency ($p < 0.001$), but the odds were lower than males (medium frequency of fatigue OR = 2.47 vs 3.10; high frequency of fatigue OR = 5.42 vs. 10.70 for females and males, respectively) (Table 3).

For the Negative Affect Scale, the odds were higher in females than males at all fatigue frequencies (OR: 2.05, 2.14, 3.31 vs. 1.72, 1.55, 2.32 for low, medium and high frequency of fatigue, respectively; all $p < 0.001$) (Table 3).

Similarly with the multinomial model including both males and females, no significant associations were identified between BMI categories (Normal, Overweight and Obese) and frequencies of fatigue when separating males and females (all $p > 0.05$).

4. Discussion

This study investigated age and sex differences in self-reported fatigue and associated variables. Using data from a national survey the main findings were: (1) the prevalence of fatigue was greater in females compared with males and this sex difference became more pronounced at high frequency of fatigue (fatigue reported in 4 or more days of the survey), (2) although psychological distress was associated with fatigue in both sexes, the odds were higher in females than males, (3) self-reported muscle weakness was associated with the prevalence of fatigue for both sexes, particularly at higher fatigue frequencies, but males had greater odds than females, (4) joint pain was associated with greater prevalence of fatigue in both males and females, (5) BMI was not associated with the prevalence of fatigue for males or females.

Our findings indicate the prevalence of self-reported fatigue is greater in females, and the novelty is showing that associated factors can vary between males and females. For example, females reporting fatigue had greater associated odds with psychological distress than males, and males reporting fatigue had greater associated odds with reported muscle weakness than females. Our findings agree with previous observations of greater prevalence of fatigue in females compared with males [3, 23, 24, 25]. However, associated factors driving the sex differences across age groups were minimally assessed previously. A better understanding of the factors associated with fatigue is important because others have observed that approximately 66% of the individuals reporting fatigue also indicated lost productive time at work [24].

4.1. Psychological distress and fatigue

Psychological distress was previously speculated to impact the overall construct of fatigue [4], but the evidence on this topic is limited. Our results indicate the greater psychological distress, quantified with a widely used scale, was associated (i.e. $p < 0.05$) with prevalence of fatigue for both sexes. Additionally, when contrasting sex differences in the variables we investigated, the association between fatigue frequency and psychological distress has a large odds ratio for females compared with males (Table 3). A previous study in England that quantified both duration and severity of fatigue in individuals 18–45 years old, found that stress factors related to work and family obligations, which frequently fall upon females, were the main variables associated with the metrics of fatigue followed by anxiety and depression [26]. It is important to mention that the previous observation and our data do not indicate that fatigue is caused by psychosocial factors, but that these conditions can overlap, in greater prevalence in females.

In addition to the psychosocial factors mentioned above, sex differences in physiology are well documented and they can potentially impact the association between stressors and fatigue. For example, males and females use distinct physiological mechanisms to regulate cardiovascular response after laboratory-based tests designed to induce stress and anxiety [27, 28, 29]. Sex differences in performance fatigability in presence of stressors were also observed. Specifically, imposing a difficult cognitive challenge that increased biomarkers of stress and anxiety during a sustained contraction increased performance fatigability, showed by shorter time to task failure of the upper extremity muscles in young and older females (>65 years old), but not young males [30, 31, 32]. Given the interaction between perceived and performance fatigability [5], combined these findings suggest this interaction could be distinct for males and females in the presence of stressors. Ultimately, the physiological sex difference in response to stressors can potentially be another factor elucidating the larger odds ratio of women compared with men for the association between fatigue and psychological distress observed in our study.

4.2. Pain and fatigue

Pain is a complex phenomenon and involves an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage [33]. Persistent pain after tissue has healed is also common, and it is thought to be associated with alterations within the peripheral and central nervous system. A theoretical model suggests that pain can have adverse effects on the overall construct of fatigue but experimental evidence is limited [4]. Results from the current study, using data from a national survey, support this theoretical model as we found a significant and strong association between joint pain and fatigue for both males and females, particularly at high frequencies of fatigue (Table 3). Although there was minimal sex differences in the odds of joint pain across fatigue categories (Table 3), the association between pain and fatigue is important, particularly for females, because the prevalence of chronic benign pain is frequently greater in females than males [34].

Stress-related alterations of pain response are often reported in mechanistic physiological studies [35], however in the current study composed of a relatively healthy sample of individuals, joint pain was prevalent and not associated with psychological stress (i.e. negative affect scale). Given the multitude of factors influencing acute and chronic pain responses, and not quantified in the current study, future studies should further investigate their association with fatigue and psychological distress across age groups in males and females.

4.3. BMI and fatigue

BMI was not associated with any frequency of fatigue when combining males or females or splitting the analysis between the sexes. In individuals aged 20–59 years old, it was previously observed that BMI was positively associated with the presence of fatigue [36]. Our results, however, agree with a longitudinal study that tracked older individuals (70–88 years old) showing minimal influence of BMI on the sex differences in self-reported fatigue [25]. Given the separate observations of the association between lost days at work with obesity [37] and fatigue [24], it is relevant to determine factors that can contribute to the potential of interaction between these variables in working individuals. Other risk factors, such as diet and physical activity levels, can potentially modify these associations differently across age groups for males and females and can be of particular relevance in addition to psychosocial factors.

4.4. Limitations

Although results from this study are based on a well-designed survey of non-institutionalized individuals, this is a retrospective study using observational data. Physiological mechanisms are only speculated, and objective metrics of motor performance are not available, nor details of some clinical conditions. Another limitation is that it is unclear if all participants were able to fully differentiate the variables fatigue and weakness during the 8-day interview process. However, given our results showed the greater odds of reported muscle weakness on fatigue in males compared with females suggests the sexes interpreted the variables differently and highlight the factors associated with fatigue can differ between males and females.

5. Conclusions

In summary, the prevalence of fatigue was greater in females compared with males, independent of age groups among midlife and older individuals. Sex differences in the factors associated with fatigue included psychological distress with greater odds in females and self-reported muscle weakness with greater odds in males. Another important associated factor, for both males and females, was the presence of joint pain. Because reported fatigue is often associated with reduced productivity in the workforce as well as increased healthcare cost, strategies to reduce the prevalence of fatigue should be specific for males and females. Future studies should specifically address the physiological mechanisms involved as well as to determine the efficacy of sex specific interventions to reduce the prevalence of fatigue.

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Disclosure statement

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Conflict of interest

No conflict of interest to declare.

Authors contribution

Conceptualization: RLB, CB, JOA and HMP. Formal analysis: RLB and MBS conducted the main analysis. Writing: HMP updated the original draft written by RLB. Review & editing: RLB, MBS, CB, JOA and HMP edited, reviewed and approved the final version of the manuscript.

Compliance with ethical standards

This study was conducted in accordance with the Declaration of Helsinki.

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