ORIGINAL ARTICLE

The Worried Well? Characteristics of Cognitively Normal Patients Presenting to a Rural and Remote Memory Clinic

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ABSTRACT: ***Introduction:*** In an effort to better understand why cognitively normal patients were referred to a memory clinic, we sought to identify features of "worried well" patients to better identify those more likely to be cognitively normal. ***Methods:*** In total, 375 consecutive patients referred by primary care practitioners to a Rural and Remote Memory Clinic were categorized into two groups based on their neurologic diagnosis, "worried well" (cognitively normal, N = 81) or "other" (patients with any neurologic diagnosis, N = 294). Data collected included: age, sex, years of formal education, Mini-Mental Status Examination score from initial visit, Center for Epidemiologic Studies Depression Scale score, Self-Rating of Memory Scale, alcohol consumption, marital status, hours per week of work, past medical history, sleep concerns, and family history of memory concerns. The two groups were compared using *t*-tests and χ^2 tests. The same comparison was done between the same set of "worried well" patients (cognitively normal, N = 81) and the subgroup of patients with a diagnosis of Alzheimer's disease (N = 146) from the "other" group. ***Results:*** Significant differences included younger age, more formal education, more frequently having previous psychiatric diagnosis and more self-reported alcohol consumption in the "worried well" group. The "worried well" and "Alzheimer's disease" comparison had the same significant differences as the "worried well" and "other" comparison. ***Conclusion:*** We observed a pattern of differences unfold between the "worried well" patients and those with cognitive disease. No one variable was pathognomonic of a "worried well" patient. However, taking all the above into account when evaluating a patient may help clinically.

RÉSUMÉ: Que faire des patients «inquiets asymptomatiques» ? Caractéristiques des patients normaux sur le plan cognitif s'étant présentés à une clinique de troubles de la mémoire en région éloignée. ***Introduction:*** Dans un effort visant à mieux comprendre les raisons pour lesquelles des patients normaux sur le plan cognitif ont été orientés vers une clinique de troubles de la mémoire, nous avons cherché à dégager les caractéristiques de patients dits « inquiets asymptomatiques » (*worried well*) afin de mieux identifier les patients les plus susceptibles d'être normaux sur le plan cognitif. ***Méthodes:*** Au total, 375 patients consécutifs, qui avaient été orientés par des fournisseurs de soins primaires vers une clinique de troubles de la mémoire située en région éloignée, ont été répartis en deux groupes selon le diagnostic neurologique alors établi : les patients dits « inquiets asymptomatiques » (autrement dit normaux sur le plan cognitif, N = 81) et les « autres » patients chez qui l'on avait établi, quel qu'il soit, un diagnostic neurologique (N = 294). Les données colletées ont tenu compte des aspects suivants : l'âge, le sexe, le nombre d'années d'instruction, les scores obtenus à partir de la première visite à l'examen mental de Folstein, les scores obtenus pour le *Center for Epidemiologic Studies Depression Scale*, les scores du Questionnaire d'auto-évaluation de la mémoire, les habitudes de consommation d'alcool, l'état civil, les heures de travail par semaine, les antécédents médicaux, des difficultés relatives au sommeil et l'histoire familiale des patients en matière de troubles de la mémoire. Les deux groupes ont été ensuite comparés entre eux au moyen des tests de Student et du χ^2. Le même type de comparaison a ensuite été effectué entre le groupe de patients dits « inquiets asymptomatiques » (normaux sur le plan cognitif, N = 81) et un sous-groupe de patients, inclus dans « l'autre groupe », chez qui l'on avait diagnostiqué la maladie d'Alzheimer (N = 146). ***Résultats:*** On a pu observer des différences notables au sein du groupe de patients dits « inquiets asymptomatiques » : un âge inférieur, davantage d'années d'instruction, une plus grande fréquence de diagnostics psychiatriques et des habitudes (auto-déclarées) de consommation d'alcool plus importantes. Des comparaisons effectuées entre le groupe de patients dits « inquiets asymptomatiques » et les patients atteints de la maladie d'Alzheimer ont révélé les mêmes différences. ***Conclusion:*** Nous avons ainsi pu observer une tendance différenciatrice entre les patients dits « inquiets asymptomatiques » et ceux atteints d'une maladie de nature cognitive. Aucune variable caractéristique d'un patient dit « inquiet asymptomatique » ne s'est avérée pathognomonique. Toutefois, le fait de tenir compte de tous les aspects énumérés ci-dessus pourrait constituer, au moment de l'évaluation d'un patient, un apport sur le plan clinique.

Keywords: Dementia, Worried well, Subjective cognitive impairment

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Introduction

Dementia encompasses multiple sub-types and is a cause of significant disability that includes loss of independence, lower quality of life and significant caregiver burden.[1-3]

As the prevalence of dementia continues to increase, so does the number of people presenting to their primary care physicians with memory complaints.[4,5] This seems to represent an overall improvement in society's awareness of dementia, but with it comes an increased burden on primary care and consequently on the specialists who see these patients.[6] The diagnosis of dementia remains clinical, as no single imaging or laboratory test is necessarily diagnostic of the condition. Therefore, many cases of subjective memory concerns (SMC) are referred on to specialists for assessment. Dementia is a common worry among the aging population.[6,7] With people increasingly aware of dementia, a new trend has been developing in memory clinics: the "worried well".[6,7] This refers to patients who are worried they have dementia, but are in fact neurologically normal, and have a neuropsychological profile within normal limits for age and other demographic factors.[6,7] It has been suggested that these patients often have friends, family or other associates with dementia.[8]

Memory concerns from patients are subjective, and may be influenced by psychological and environmental factors, such as exposure to someone with dementia.[8] There have been conflicting data on the validity of subjective memory complaints from patients and the correlation with the patient's true cognitive function.[7,9] Subjective cognitive impairment (SCI) is common, and it has been suggested that it may be a prognostic indicator.[10] Some have considered SCI the beginning of the Alzheimer's disease spectrum, and others question its validity due to inconsistent evaluation and definition.[10] However, SCI has been identified as a risk factor for mild cognitive impairment (MCI).[10] Many memory clinic patients present with SCI and these patients need to be properly evaluated and followed so as to provide support and close monitoring of changes in memory function.[10] The Self-Rating of Memory Score is a well-validated tool used to evaluate patients' perceived memory concerns, and may therefore provide insight into SCI.[11] Another screening tool used to evaluate cognitive function is the Mini-Mental Status Examination (MMSE), which has long been used and studied as a cognitive screen.[12] Repeat MMSE scores can be an important part of evaluating trends in cognitive ability over time, and has been validated using Telehealth and in person.[12,13] In contrast to screening, neuropsychological testing is an in-depth, standardized assessment of a multitude of cognitive domains with appropriate normative comparisons to facilitate interpretation. Ideally, dementia diagnoses (referred to as major and mild neurocognitive disorders in the new Diagnostic and Statistical Manual of Mental Disorders-V) includes neuropsychological assessment of simple and complex attention, speed of mental processing, language, visuospatial functioning, social cognition, executive function (behavior regulation, planning/organization, sequencing, and inhibition), and memory (encoding, consolidation, and retrieval).[14] Longitudinal neuropsychological testing allows for comparison of a person's performance not only with the average obtained from normative data, but also change within an individual. Aside from SCI, other risk factors for dementia may include age, lower education levels, sleep concerns, and psychiatric illness.[15-18] A study by Kosteniuk et al.[5] in 2015 found that the incidence of dementia increased from 2.8 to 5.1 and the prevalence rate increased from 2.6 to 4.6 every 10 years after the age of 45. The different types of dementia present at different ages, with frontotemporal dementia encompassing 10.2% of dementias in patients less than 65, whereas only accounting for 2.7% of dementias in patients over 65.[1-3] Higher formal education levels have been identified as potentially protective against dementia, although the mechanism has only been theorized to this point.[15] Sleep concerns are common in older adults, regardless of cognitive status.[16] Some of the psychological causes of sleep disturbance, like depression and worry are frequently implicated in the "worried well" patients. However, sleep concerns have also been noted in dementia patients.[6,17] Depression has also been implicated as a risk factor for memory concerns. Patients with MCI who also have depression are twice as likely to develop Alzheimer's disease.[18] The Center for Epidemiologic Studies Depression Scale (CES-D) is a screening tool used to evaluate depression.[19]

The objective of the present study is to identify features of "worried well" patients to better identify those more likely to be cognitively normal. There has been an increasing number of referrals to specialists for memory concerns.[6,7] However, the diagnosed dementia rates are not increasing proportional to the referral rates, leading to what has been described as a "diagnosis gap".[6,7] The rate of referral for memory concerns is growing more quickly than the rate of dementia, further highlighting the need for better indicators of dementia risk.[6,7] It has been shown that a large proportion of patients with SMC will not convert to having objective memory concerns.[20] This paper concluded that further investigation needs to be done to better define risk features of these patients so that they are not over-investigated and triaged appropriately.[20] By identifying those at lower risk of having dementia, specialist resources can be better used.[6,7,21] Limited specialist access is a challenge in rural areas.[21]

Methods

In total, 375 consecutive patients seen at a rural and remote memory clinic (RRMC) between March 2004 and October 2015 were included in this analysis. The University of Saskatchewan's Rural and Remote Memory Clinic provides a one-stop interdisciplinary assessment for patients with memory concerns from across Saskatchewan. At the initial visit, patients are seen by a neurologist, a physiotherapist, a dietitian, a nurse and undergo neuropsychological testing.[21] Each patient receives a standard work-up for reversible/vascular causes of memory concerns which includes: a complete blood count (CBC), electrolytes including calcium, thyroid stimulating hormone (TSH), vitamin B_{12}, a non-contrast CT scan of their head and other investigations when indicated. More detailed information about the clinic can be found in previous publications.[21-31] Data collected at the initial visit include: age, sex, years of formal education, MMSE score from the initial RRMC visit, CES-D depression scores, Self-Rating of Memory Scale, alcohol consumption, marital status, hours per week of work, past medical history, sleep concerns, possession of a driver's licence, and information on a family history of memory concerns. By the end of the day, patients are given a diagnosis as agreed upon by the assessment team. A patient received a diagnosis of "worried well" if all the following criteria were met: they had no clinical evidence of a neurologic disease, they had normal neuro-imaging, and if they had normal age, sex and education adjusted performance on neuropsychological testing. The neuropsychological battery includes measures of attention, speeded mental processing, language, visuospatial abilities, executive function, memory for stories, a word list, and a complex figure. The repeatable battery for the assessment of neuropsychological status (RBANS) is a brief assessment tool designed to

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Table 1: Characteristics of normal and all other patients*

	All other (n = 294)	"Worried well" (n = 81)	
Variables	**Mean ± SD**	**Mean ± SD**	**P value**
Age at clinic day (years)	73.5 ± 9.7	60.8 ± 13.0	<0.0001
Years of formal education	10.6 ± 2.6	12.4 ± 3.2	<0.0001
Total years smoked	30.7 ± 17.4	24.0 ± 13.0	0.008
Number of times engage in physical activity or exercise per week	3.3 ± 3.5	3.4 ± 3.7	0.765
Cups of caffeinated tea/coffee per day	2.9 ± 2.9	3.2 ± 2.7	0.593
Drinks of alcohol per week	1.3 ± 3.1	3.5 ± 5.9	0.003
CES-D (depression score)	13.1 ± 9.2	18.8 ± 10.9	<0.0001
MEM (self-rating of memory scale)	− 11.4 ± 7.7	− 12.1 ± 9.4	0.495
3MS, total score/100	74.2 ± 15.4	92.8 ± 8.6	<0.0001
MMSE, total score/30	23.4 ± 4.4	28.2 ± 2.3	<0.0001
	n (%)	n (%)	P value
Sex			
Male	120 (40.8)	40 (49.4)	0.168
Female	174 (59.2)	41 (50.6)	
Education level			
<High school	156 (54.2)	23 (28.8)	<0.0001
≥High school	132 (45.8)	57 (71.2)	
Marital status			
Married/common law	193 (67.0)	67 (84.8)	0.002
Other (single, divorced, separated, widowed)	95 (33.0)	12 (15.2)	
Hours currently working			
0-19 hours	248 (92.2)	43 (62.3)	<0.0001
≥20 hours	21 (7.8)	26 (37.7)	
Valid driver's license			
No	77 (26.9)	5 (6.2)	<0.0001
Yes	209 (73.1)	76 (93.8)	
Experiencing sleep difficulties			
Not at all	96 (36.6)	10 (14.5)	<0.0001**
A little	71 (27.1)	10 (14.5)	
Moderately	50 (19.1)	18 (26.1)	
Quite a bit	38 (14.5)	20 (29.0)	
Extreme	7 (2.7)	11 (15.9)	
Diagnosed with memory problems/confusion			
No	13 (5.1)	5 (7.7)	0.382**
Yes	240 (94.9)	60 (92.3)	
Family history of memory problems and/or dementia or senility			
No	121 (47.1)	33 (51.6)	0.521
Yes	136 (52.9)	31 (48.4)	
Family history of dementia			
No	127 (44.1)	40 (50.0)	0.348
Yes	161 (55.9)	40 (50.0)	
Diagnosed with stroke			
No	193 (84.3)	58 (93.5)	0.060
Yes	36 (15.7)	4 (6.5)	
Diagnosed with head injury			
No	191 (78.0)	47 (69.1)	0.131
Yes	54 (22.0)	21 (30.9)	
Diagnosed with psychiatric/ psychological problem and depression			
No	176 (76.2)	39 (61.9)	0.023
Yes	55 (23.8)	24 (38.1)	

CES-D = Center for Epidemiologic Studies Depression Scale; MEM = memory; MMSE = Mini-Mental Status Examination; 3MS = Modified Mini-Mental State.

*All variables have missing values except age.

**Due to small expected values exact test p value was reported.

identify mild to severe forms of dementia in older adults.[32] We then categorized patients into one of two groups based on their neurologic diagnosis, "worried well" (cognitively normal, N = 81) or "other" (includes all neurologic diagnosis, N = 294). The "other" group included patients given a diagnosis of MCI. A diagnosis of MCI required: memory complaints corroborated by a collateral history, objective signs of memory impairment, relatively preserved functional abilities and that the patient's presentation does not meet criteria for dementia.[33] To directly compare cognitively normal patients and dementia patients we did further analysis. This second analysis used the same set of "worried well" patients (N = 81) and the subgroup of patients diagnosed with Alzheimer's disease as per NINCDS-ADRDA criteria (N = 146) from the "other" group.[34] The same patient information was isolated, and then re-analyzed comparing these two groups. Statistical analyses were conducted using SPSS version 24.[35] Descriptive analyses were completed using frequencies, measures of central tendency, variability and χ^2 test of associations. The two groups (worried well vs. other/worried well vs. Alzheimer's disease group) were compared using independent sample *t*-tests for continuous variables and χ^2 tests for categorical variables. When the cell sizes were small, χ^2 exact p values were reported. Effect size was then calculated using Cohen's *d*. Ethics approval was obtained from the University of Saskatchewan Biomedical Research Ethics Board.

Results

In total, 375 patients who underwent an initial clinical assessment were included in this analysis. When comparing the "worried well" group (N = 81) and the "other" group (N = 294), the "worried well" group was significantly younger (Table 1). Other significant differences included more formal education, more self-reported alcohol consumption, and higher MMSE scores in the "worried well" group (Table 1). Self-reported memory concerns showed no difference between the "worried well" group and the "other" group. There was no statistically significant difference in self-reported family history of memory concerns or dementia between these two groups. There was

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Table 2: Characteristics of Alzheimer's disease (AD) and normal patients*

	AD (n = 146)	"Worried well" (n = 81)	
Variables	**Mean ± SD**	**Mean ± SD**	**P value**
Age at clinic day (years)	76.3 ± 7.4	60.8 ± 12.9	<0.0001
Years of formal education	10.3 ± 2.9	12.4 ± 3.2	<0.0001
Total years smoked	28.8 ± 18.4	24.0 ± 13.0	0.113
Number of times engage in physical activity or exercise per week	3.5 ± 3.5	3.5 ± 3.7	0.974
Cups of caffeinated tea/coffee per day	3.4 ± 3.5	3.2 ± 2.7	0.648
Drinks of alcohol per week	1.2 ± 2.6	3.5 ± 5.9	0.002
CES-D (depression score)	12.3 ± 9.7	18.8 ± 10.9	<0.0001
MEM (self-rating of memory scale)	−11.8 ± 7.5	−12.1 ± 9.4	0.822
3MS, total score/100	67.5 ± 13.7	92.8 ± 8.6	<0.0001
MMSE, total score/30	21.6 ± 4.0	28.2 ± 2.3	<0.0001
	n (%)	n (%)	P value
Sex			
Male	49 (33.6)	40 (49.4)	0.019
Female	97 (66.4)	41 (50.6)	
Education level			
<High school	81 (57.4)	23 (28.8)	<0.0001
≥High school	60 (42.6)	57 (71.3)	
Marital status			
Married/common law	87 (60.8)	67 (84.8)	<0.0001
Other (single, divorced, separated, widowed)	56 (39.2)	12 (15.2)	
Hours currently working			
0-19 hours	129 (96.3)	43 (62.3)	<0.0001
≥20 hours	5 (3.7)	26 (37.3)	
Valid driver's license			
No	45 (31.5)	5 (6.2)	<0.0001
Yes	98 (68.5)	76 (93.8)	
Experiencing sleep difficulties			
Not at all	55 (41.0)	10 (14.5)	<0.0001
A little	37 (27.6)	10 (14.5)	
Moderately	29 (21.7)	18 (26.1)	
Quite a bit	12 (9.0)	20 (29.0)	
Extreme	1 (0.7)	11 (15.9)	
Diagnosed with memory problems/confusion			
No	5 (3.8)	5 (7.7)	0.306**
Yes	125 (96.2)	60 (92.3)	
Family history of memory problems and/or dementia or senility			
No	63 (47.7)	33 (51.6)	0.614
Yes	69 (52.3)	31 (48.4)	
Family history of dementia			
No	53 (36.8)	40 (50.0)	0.055
Yes	91 (63.2)	40 (50.0)	
Diagnosed with stroke			
No	108 (93.1)	58 (93.5)	1.000**
Yes	8 (6.9)	4 (6.5)	
Diagnosed with head injury			
No	102 (81.6)	47 (69.1)	0.048
Yes	23 (18.4)	21 (30.9)	
Diagnosed with psychiatric/ psychological problem and depression			
No	92 (76.7)	39 (61.9)	0.035
Yes	28 (23.3)	24 (38.1)	

CES-D = Center for Epidemiologic Studies Depression Scale; MMSE = Mini-Mental Status Examination.

*All variables have missing values except age.

**Due to small expected values exact test p value was reported.

a significant difference between self-reported previous history of psychiatric or psychologic problems, with the "worried well" group more frequently having a previous diagnosis or problem. The "worried well" group also had a significantly higher CES-D depression screening score, with a moderate effect size (Cohen's $d = 0.57$). The full comparison between the "worried well" and "other" groups is presented in Table 1.

Of the 375 total patients, 227 patients were included in the second analysis which compared the same "worried well" group (N = 81) to the patients who received a diagnosis of Alzheimer's disease (N = 146). This comparison had similar differences as in the first analysis. The full comparison between the "worried well" and "Alzheimer's Disease" groups is detailed in Table 2.

This data are mostly self-reported, as it is acquired through a questionnaire completed by patient and family at the patient's initial clinic assessment. As a result, all variables other than age have missing values. The number of values for each variable is included in the previously mentioned Tables 1 and 2. Breakdown of the "other" diagnoses can be found in Table 3.

Table 3: "Other" diagnosis

Diagnosis	Number of patients (%)
Mild cognitive impairment	47
Alzheimer's dementia	146
Vascular dementia	10
Frontotemporal dementia	33
Lewy body dementia	14
Other	44

Other group includes: corticobasal degeneration, hydrocephalus, Parkinson's dementia, medication side effects, Huntington's disease, Fragile X associated dementia, Herpes encephalitis, hypoxic ischemic encephalopathy, multiple systems atrophy, progressive supranuclear palsy.

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Table 4: Comparison of clinic day neuropsychological data: "worried well" versus Alzheimer's disease (AD)

Variables	Group	N	Mean	SD	SEM	*t* value	Degrees of freedom	P value
Clinic day: 3MS	Worried well	66	93.50	5.789	0.713	14.390	193	0.000
	AD	129	67.98	13.787	1.214			
Clinic day: MMSE	Worried well	66	28.26	1.774	0.218	12.424	193	0.000
	AD	129	21.77	4.046	0.356			
Clinic day: WRAT Reading (Index)*	Worried well	64	96.88	11.243	1.405	1.511	182	0.133
	AD	120	94.51	9.474	0.865			
Clinic day: WAIS III similarities (SS)**	Worried well	56	10.86	2.583	0.345	3.881	102	0.000
	AD	48	8.90	2.554	0.369			
Clinic day: WAIS III block design (SS)**	Worried well	56	10.25	2.466	0.330	3.997	97	0.000
	AD	43	8.19	2.648	0.404			
Clinic day: WAIS III LNS (SS)**	Worried well	44	10.25	2.926	0.441	4.991	62	0.000
	AD	20	6.50	2.439	0.545			
Clinic day: WAIS III symbol search (SS)**	Worried well	56	10.43	2.641	0.353	6.277	103	0.000
	AD	49	7.08	2.820	0.403			
Clinic day: RBANS immediate memory (Index)*	Worried well	66	93.61	14.977	1.844	15.440	183	0.000
	AD	119	58.62	14.644	1.342			
Clinic day: RBANS visuospatial/const (Index)*	Worried well	64	96.39	14.559	1.820	6.725	171	0.000
	AD	109	78.29	18.402	1.763			
Clinic day: RBANS language (Index)*	Worried well	65	96.80	11.732	1.455	8.352	183	0.000
	AD	120	77.95	16.007	1.461			
Clinic day: RBANS attention (Index)*	Worried well	64	94.25	15.470	1.934	7.617	170	0.000
	AD	108	74.75	16.659	1.603			
Clinic day: RBANS delayed memory (Index)*	Worried well	64	90.66	14.577	1.822	21.943	178	0.000
	AD	116	49.69	10.301	0.956			
Clinic day: RBANS total scale (Index)*	Worried well	64	92.33	11.680	1.460	17.276	161	0.000
	AD	99	61.95	10.477	1.053			
Clinic day: RBANS list learning (SS)**	Worried well	65	9.03	2.767	0.343	10.483	182	0.000
	AD	119	4.87	2.458	0.225			
Clinic day: RBANS story memory (SS)**	Worried well	65	10.20	2.676	0.332	11.833	185	0.000
	AD	122	5.43	2.594	0.235			
Clinic day: RBANS figure copy (SS)**	Worried well	63	8.87	2.893	0.365	5.184	181	0.000
	AD	120	6.53	2.904	0.265			
Clinic day: RBANS line orientation (SS)**	Worried well	64	10.30	2.580	0.323	5.504	173	0.000
	AD	111	7.67	3.282	0.311			
Clinic day: RBANS picture naming (SS)**	Worried well	64	10.44	1.876	0.235	8.336	182	0.000
	AD	120	7.55	2.407	0.220			
Clinic day: RBANS semantic fluency (SS)**	Worried well	64	10.22	2.925	0.366	7.553	183	0.000
	AD	121	6.83	2.885	0.262			
Clinic day: RBANS digit span (SS)**	Worried well	65	9.18	3.015	0.374	4.419	185	0.000
	AD	122	7.40	2.397	0.217			
Clinic day: RBANS coding (SS)**	Worried well	63	9.70	3.657	0.461	6.783	170	0.000
	AD	109	6.28	2.871	0.275			
Clinic day: RBANS list recall (SS)**	Worried well	65	8.23	3.194	0.396	7.133	184	0.000
	AD	121	5.97	1.040	0.095			
Clinic day: RBANS list recognition (SS)**	Worried well	65	8.51	3.549	0.440	8.830	182	0.000
	AD	119	4.60	2.426	0.222			

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Table 4: *Continued*

Variables	Group	N	Mean	SD	SEM	*t* value	Degrees of freedom	P value
Clinic day: RBANS story recall (SS)**	Worried well	65	10.11	2.658	0.330	14.760	184	0.000
	AD	121	5.29	1.772	0.161			
Clinic day: RBANS figure recall (SS)**	Worried well	63	8.03	2.862	0.361	12.790	181	0.000
	AD	120	3.73	1.690	0.154			
Clinic day: mental control (*z*)***	Worried well	63	−0.2111	1.10994	0.13984	6.439	168	0.000
	AD	107	−1.5093	1.35442	0.13094			
Clinic day: digit span forward (*z*)***	Worried well	66	−0.1682	1.00997	0.12432	4.304	187	0.000
	AD	123	−0.8065	0.95116	0.08576			
Clinic day: digit span backward (*z*)***	Worried well	66	−0.2894	1.03643	0.12758	4.664	184	0.000
	AD	120	−0.9725	0.90850	0.08293			
Clinic day: Stroop test color (*z*)***	Worried well	62	0.0177	0.90798	0.11531	4.029	151	0.000
	AD	91	−0.8440	1.50718	0.15800			
Clinic day: Stroop test word-color (*z*)***	Worried well	60	−0.6533	1.45363	0.18766	5.262	124	0.000
	AD	66	−1.9000	1.20307	0.14809			
Clinic day: Trails A (*z*)***	Worried well	63	−0.6825	1.36601	0.17210	5.266	173	0.000
	AD	112	−1.8500	1.43049	0.13517			
Clinic day: Trails B (*z*)***	Worried well	61	−0.7770	1.34826	0.17263	5.530	131	0.000
	AD	72	−2.0319	1.26567	0.14916			

The repeatable battery for the assessment of neuropsychological status (RBANS) is a brief assessment tool designed to identify mild to severe forms of dementia in older adults.[32] LNS = Letter Number Sequencing; WAIS = Wechsler Adult Intelligence Scale; WRAT = Wide Range Achievement Test.
*Index score is a composite score with a mean (*M*) of 100 and a SD of 15.
**Scaled score (SS) is a linear transformation of raw scores with $M = 10$, SD = 3.
***z Score is a linear transformation of raw scores with $M = 0$, SD = 1.

The initial neuropsychological data are outlined in Tables 4 and 5. Comparison of neuropsychological test results between the "worried well" and the "other" group is presented in Table 4. Comparison between the "worried well" and Alzheimer's Disease patients is outlined in Table 5.

Discussion

With the increasing awareness surrounding degenerative neurologic disease, patients with self-expressed memory concerns are often cognitively normal.[4] This has previously been described as a "worried well" patient, often someone who has a family member or friend with a memory concern who then is more aware of common memory lapses that every individual occasionally makes.[7] With no conclusive diagnostic test for AD, evaluating memory concerns is a somewhat subjective task. In order to better address the issues of the "worried well" we sought to identify trends in their characteristics so as to better identify who is at greater risk of a degenerative disease and who might be more likely to benefit from reassurance and education on cognitive aging.

With over 20% of patients at the RRMC being diagnosed as cognitively normal, we have a fair sample size to assess differences. Of the many significant differences between the cognitively normal and other groups, age and MMSE stand out as highly valuable clinical indicators. Alzheimer's disease classically presents later in life, and statistically most of the "worried well" patients were in their early sixties, whereas those with dementia had a mean age of 76.3 years. There was a significant difference in age between the "normal" or "worried well" group and both the "other" group and the "Alzheimer's Disease" group. Although other forms of dementia do indeed occur earlier, these diseases are not as common as Alzheimer's Disease.

We found that the cognitively normal patients tended to have more years of formal education. It may be that those with higher levels of education are more aware of the impact of dementia, and as a result are more likely to be "worried well" or that they are more impacted by normal cognitive changes with aging.[15] The cognitively normal patients were also more likely to be working part-time or more. The demands of work may make small lapses in memory more apparent resulting in more awareness of one's own mistakes leading to this category of the "worried well" patient. Alcohol intake also differed between the two groups, with the "worried well" patients having higher rates of consumption. However, both groups were still within the recommended consumption guidelines. We wondered about the potential cognitive impacts alcohol consumption had on these patients, although causation or association with memory concerns is not clear. The "worried well" patients were more likely to have a driver's licence, and this fits with their lower age and increased prevalence of part-time or more work.

Psychiatric illness or psychological problems play an important role in evaluating patients with memory concerns.[18,36,37] Psychiatric problems can impair memory, and may be implicated as the etiology behind the memory problems.[18,36,37] However, some psychiatric problems co-occur with memory concerns, as depression is common in Alzheimer's disease.[17,33,34] Therefore, it

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Table 5: Comparison of clinic day neuropsychological data: "worried well" versus "other"

Variables	Group	N	Mean	SD	SEM	*t* value	Degrees of freedom	P value
Clinic day: 3MS	Worried well	66	93.50	5.789	0.713	10.033	319	0.000
	Other	255	74.23	15.310	0.959			
Clinic day: MMSE	Worried well	66	28.26	1.774	0.218	8.811	319	0.000
	Other	255	23.49	4.294	0.269			
Clinic day: WRAT Reading (SS)**	Worried well	64	96.88	11.243	1.405	1.340	300	0.181
	Other	238	94.94	9.993	0.648			
Clinic day: WAIS III similarities (SS)**	Worried well	56	10.86	2.583	0.345	4.621	174	0.000
	Other	120	8.90	2.633	0.240			
Clinic day: WAIS III block design (SS)**	Worried well	56	10.25	2.466	0.330	3.699	160	0.000
	Other	106	8.56	2.918	0.283			
Clinic day: WAIS III LNS (SS)**	Worried well	44	10.25	2.926	0.441	4.717	103	0.000
	Other	61	7.61	2.765	0.354			
Clinic day: WAIS III SS (SS)**	Worried well	56	10.43	2.641	0.353	6.245	175	0.000
	Other	121	7.36	3.202	0.291			
Clinic day: immediate memory (Index)*	Worried well	66	93.61	14.977	1.844	12.191	302	0.000
	Other	238	65.27	17.152	1.112			
Clinic day: visuospatial/const (Index)*	Worried well	64	96.39	14.559	1.820	6.969	284	0.000
	Other	222	79.88	17.256	1.158			
Clinic day: language (Index)*	Worried well	65	96.80	11.732	1.455	7.075	300	0.000
	Other	237	81.73	16.028	1.041			
Clinic day: attention (Index)*	Worried well	64	94.25	15.470	1.934	8.207	280	0.000
	Other	218	75.55	16.183	1.096			
Clinic day: delayed memory (Index)*	Worried well	64	90.66	14.577	1.822	13.273	293	0.000
	Other	231	57.85	18.216	1.199			
Clinic day: total scale (Index)*	Worried well	64	92.33	11.680	1.460	13.781	265	0.000
	Other	203	66.95	13.191	0.926			
Clinic day: list learning (SS)**	Worried well	65	9.03	2.767	0.343	9.802	300	0.000
	Other	237	5.40	2.611	0.170			
Clinic day: story memory (SS)**	Worried well	65	10.20	2.676	0.332	9.236	303	0.000
	Other	240	6.42	2.990	0.193			
Clinic day: figure copy (SS)**	Worried well	63	8.87	2.893	0.365	4.700	299	0.000
	Other	238	6.87	3.038	0.197			
Clinic day: line orientation (SS)**	Worried well	64	10.30	2.580	0.323	5.987	289	0.000
	Other	227	7.74	3.128	0.208			
Clinic day: picture naming (SS)**	Worried well	64	10.44	1.876	0.235	6.794	302	0.000
	Other	240	8.18	2.481	0.160			
Clinic day: semantic fluency (SS)**	Worried well	64	10.22	2.925	0.366	6.859	301	0.000
	Other	239	7.21	3.172	0.205			
Clinic day: digit span (SS)**	Worried well	65	9.18	3.015	0.374	4.886	304	0.000
	Other	241	7.49	2.328	0.150			
Clinic day: coding (SS)**	Worried well	63	9.70	3.657	0.461	7.192	279	0.000
	Other	218	6.48	2.964	0.201			
Clinic day: list recall (SS)**	Worried well	65	8.23	3.194	0.396	6.530	302	0.000
	Other	239	6.18	1.909	0.123			
Clinic day: list recognition (SS)**	Worried well	65	8.51	3.549	0.440	7.305	300	0.000
	Other	237	5.38	2.911	0.189			

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Table 5: *Continued*

Variables	Group	N	Mean	SD	SEM	*t* value	Degrees of freedom	P value
Clinic day: story recall (SS)**	Worried well	65	10.11	2.658	0.330	10.261	301	0.000
	Other	238	6.32	2.629	0.170			
Clinic day: figure recall (SS)**	Worried well	63	8.03	2.862	0.361	8.344	297	0.000
	Other	236	4.75	2.754	0.179			
Clinic day: mental control (*z*)***	Worried well	63	−0.2111	1.10994	0.13984	6.232	280	0.000
	Other	219	−1.3365	1.30354	0.08808			
Clinic day: digit span forward (*z*)***	Worried well	66	−0.1682	1.00997	0.12432	4.352	309	0.000
	Other	245	−0.7469	0.94494	0.06037			
Clinic day: digit span backward (*z*)***	Worried well	66	−0.2894	1.03643	0.12758	5.104	305	0.000
	Other	241	−0.9544	0.90916	0.05856			
Clinic day: Stroop test color (*z*)***	Worried well	62	0.0177	0.90798	0.11531	3.763	248	0.000
	Other	188	−0.7559	1.53118	0.11167			
Clinic day: Stroop test word-color (*z*)***	Worried well	60	−0.6533	1.45363	0.18766	6.077	209	0.000
	Other	151	−1.8172	1.16772	0.09503			
Clinic day: Trails A (*z*)***	Worried well	63	−0.6825	1.36601	0.17210	5.707	285	0.000
	Other	224	−1.7857	1.35265	0.09038			
Clinic day: Trails B (*z*)***	Worried well	61	−0.7770	1.34826	0.17263	5.732	220	0.000
	Other	161	−1.9068	1.29664	0.10219			

The repeatable battery for the assessment of neuropsychological status (RBANS) is a brief assessment tool designed to identify mild to severe forms of dementia in older adults.[32]

*Index score is a composite score with a mean (*M*) of 100 and a SD of 15.

**Scaled score is a linear transformation of raw scores with $M = 10$, $SD = 3$.

***z Score is a linear transformation of raw scores with $M = 0$, $SD = 1$.

is interesting to note the significant difference between CES-D depression screening scores in the "worried well" and both the "other" and "Alzheimer's disease" groups. A recent study was done at this RRMC to look at depression prevalence between no cognitive impairment (NCI) patients and dementia patients.[36] This study found that depression was more common in the NCI patients.[37] However, a study done in 2005 looking at CES-D scores in Alzheimer's disease patients found that higher scores were found in dementia patients.[37] It was concluded that a CES-D score of 21 was a significant statistical predictor of dementia.[37] Another study found that SMC were more strongly associated with depression than with cognitive impairment.[34] Our data shows a mean CES-D score of 12.3 in dementia patients, and a significantly higher mean score of 18.8 in the "worried well" (Cohen's $d = 0.63$). This creates an interesting contrast, as depression may be an early symptom of dementia but can also independently contribute to memory concerns.[36,37] Depression and dementia may also share common behavioral symptoms such as lack of interest in activities or apathy.[36,37] Our data appears to reflect higher CES-D scores in "worried well" patients, and may be attributed to part of their subjective memory complaint. This data supports the supposition that depression may be more likely to cause independent memory concerns, rather than be an early sign of dementia, depending on the patient's other risk factors.[38] Anxiety or worry about getting dementia, coupled with increased awareness surrounding the disease likely leads many patients to become more aware of lapses in memory that are normal rather than a sign of a degenerative disease. The "Alzheimer's disease" group had significantly less concerns with sleep than the "worried well" group. This may be associated with psychologic factors discussed previously that seem to be prevalent in "worried well" patients or poor sleep may have contributed to memory symptoms. The "worried well" group also had greater incidence of previous psychiatric diagnosis. This is an interesting point, as psychiatric illness may be a predictor of SCI. Psychiatric illness may independently cause memory concerns, or psychiatric symptoms might overlap with behaviors that are an early sign of dementia, such as apathy. Therefore, further investigation is warranted. Taken with the fact that the "worried well" patients were generally younger; it may be that depressive symptomatology is a major cause of memory concerns in younger patients. Therefore, it is essential to evaluate mood and mental health when discussing memory concerns with patients.

A number of variables we examined showed no significant difference between groups leading us to question their validity in characterizing a patient as "worried well" or not. Most notable was the lack of significant difference in family history of memory concerns or dementia between the two groups. This could be because dementia is so common. Stroke and head injuries were also not more prevalent in one group or the other.

Study limitations include a lack of biomarkers that have been studied as predictors of dementia, and a cross-sectional study design where follow-up is not reported. Longitudinal follow-up would be an interesting topic of future research papers.

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Conclusions

Overall, we observed a pattern of differences unfold between the "worried well" patients and those with cognitive disease. No one variable is pathognomonic of a "worried well" patient. However, taking age, MMSE score, psychiatric/psychological condition, substance use, sleep concerns and clinical picture into consideration when evaluating a patient may help with clinical decision making. The over-arching theme of increased awareness, exposure to the disease and psychological factors help illustrate a typical "worried well" patient. By better identifying the "worried well" we can make better use of resources, like specialist referrals, and improve patient care by providing appropriate management aimed at the underlying cause of the concern.

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Statement of Authorship

All mentioned authors contributed in the design, analysis, and execution of this project.

Disclosure

Ryan Verity, Andrew Kirk, Megan E. O'Connell, Chandima Karunanayake, and Debra G. Morgan do not have anything to disclose.

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