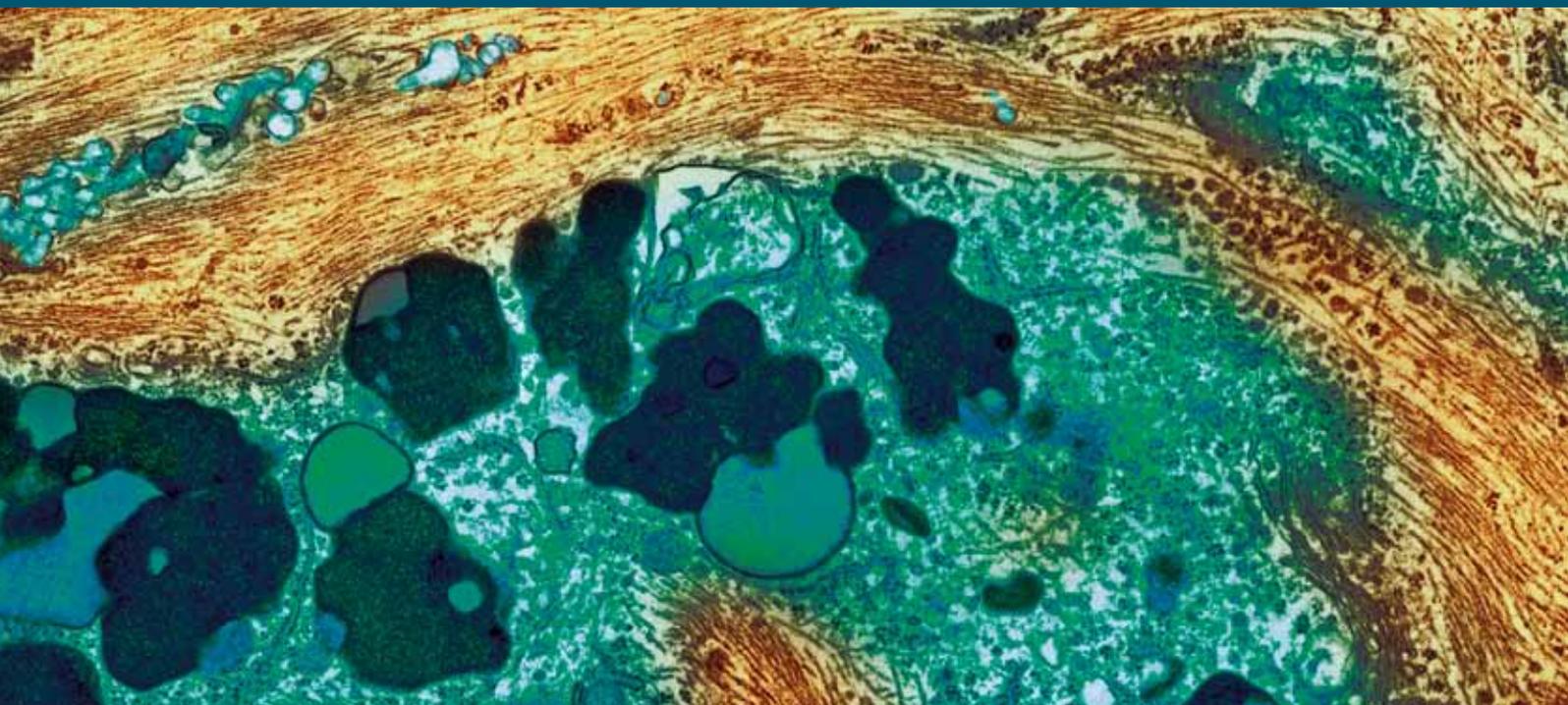


Care for Alzheimer's Disease

Guest Editors: Hiroyuki Umegaki, Hajime Takechi, and Hiroko H. Dodge





Care for Alzheimer's Disease

International Journal of Alzheimer's Disease

Care for Alzheimer's Disease

Guest Editors: Hiroyuki Umegaki, Hajime Takechi,
and Hiroko H. Dodge



Copyright © 2013 Hindawi Publishing Corporation. All rights reserved.

This is a special issue published in “International Journal of Alzheimer’s Disease.” All articles are open access articles distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Editorial Board

D. Allsop, UK
Craig S. Atwood, USA
Brian Austen, UK
Jess Avila, Spain
B. J. Bacsikai, USA
Andrew Budson, USA
Roger A. Bullock, UK
Ashley I. Bush, Australia
Gemma Casadesus, USA
Rudolph J. Castellani, USA
James R. Connor, USA
Suzanne M. de la Monte, USA
Justo G. de Yebenes, Spain
S. M. Debanne, USA
Steven D. Edland, USA
Cheng-Xin Gong, USA
Paula Grammas, USA

George T. Grossberg, USA
Harald J. Hampel, Germany
Kurt A. Jellinger, Austria
Mark Kindy, USA
Amos D. Korczyn, Israel
Jeff Kuret, USA
Andrew J. Larner, UK
Hyoung-Gon Lee, USA
Jerzy Leszek, Poland
Seth Love, UK
Michelangelo Mancuso, Italy
James G. McLarnon, Canada
Patrizia Mecocci, Italy
Kenichi Meguro, Japan
Judith Miklossy, Canada
Paula I. Moreira, Portugal
Ricardo Nitri, Brazil

Michal Novák, Slovakia
Leonardo Pantoni, Italy
Francesco Panza, Italy
Lucilla Parnetti, Italy
George Perry, USA
M. C. Polidori, Germany
Jeffrey R. Powell, USA
John Powell, UK
Marcella Reale, Italy
Vincenzo Solfrizzi, Italy
Akihiko Takashima, Japan
Matti Viitanen, Sweden
B. Winblad, Sweden
David Yew, Hong Kong
Henrik Zetterberg, Sweden

Contents

Care for Alzheimer's Disease, Hiroyuki Umegaki, Hajime Takechi, and Hiroko H. Dodge
Volume 2013, Article ID 516852, 2 pages

Longitudinal Changes in the Government-Certified Index Stage and Requisite Costs for Long-Term Care Insurance System among the Community-Dwelling Demented Elderly in Japan, Shunichiro Shinagawa, Shiori Nakamura, Makoto Iwamoto, Norifumi Tsuno, Masahiro Shigeta, and Kazuhiko Nakayama
Volume 2013, Article ID 164919, 6 pages

The Needs of Older People with Mental Health Problems: A Particular Focus on Dementia Patients and Their Carers, Joaquim Passos, Carlos Sequeira, and Lia Fernandes
Volume 2012, Article ID 638267, 7 pages

A Warning Index Used in Prescreening for Alzheimer's Disease, Based on Self-Reported Cognitive Deficits and Vascular Risk Factors for Dementia in Elderly Patients with Type 2 Diabetes, Toshioki Matsuzawa, Toshihiro Takata, Koichi Yokono, Hiroo Ueda, Kensuke Moriwaki, Isao Kamae, Katsuya Urakami, and Takashi Sakurai
Volume 2012, Article ID 124215, 8 pages

Gender Differences in Dementia Spousal Caregiving, Minna Maria Pöysti, Marja-Liisa Laakkonen, Timo Strandberg, Niina Savikko, Reijo Sakari Tilvis, Ulla Eloniemi-Sulkava, and Kaisu Hannele Pitkälä
Volume 2012, Article ID 162960, 5 pages

Efficacy of Music Therapy in Treatment for the Patients with Alzheimer's Disease, H. Fukui, A. Arai, and K. Toyoshima
Volume 2012, Article ID 531646, 6 pages

Editorial

Care for Alzheimer's Disease

Hiroyuki Umegaki,¹ Hajime Takechi,² and Hiroko H. Dodge^{3,4}

¹ Department of Geriatrics, Nagoya University Graduate School of Medicine, 65 Tsuruma-cho, Showa-ku, Aichi, Nagoya 466-8550, Japan

² Department of Geriatric Medicine, Graduate School of Medicine, Kyoto University, Sakyo-ku, Kyoto 606-8507, Japan

³ Department of Neurology, Oregon Health & Sciences University, Portland, Oregon 97239, USA

⁴ Michigan Alzheimer's Disease Center, Ann Arbor, Michigan, USA

Correspondence should be addressed to Hiroyuki Umegaki; umegaki@med.nagoya-u.ac.jp

Received 28 February 2013; Accepted 28 February 2013

Copyright © 2013 Hiroyuki Umegaki et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Cognitive impairment due to dementia deprives those afflicted with the disease of their autonomy and ability to take care of themselves, making them dependent on care provided by formal and informal resources. Moreover, as the disease progresses, behavioral and psychological symptoms of dementia (BPSD) may occur. BPSD are often troublesome to both caregivers and the patients themselves. The care burden is often heavy and disrupts the lives of family members surrounding the patient.

Early screening and identification of cognitive decline will help those with the disease and family members prepare for better care and may reduce the patients' BPSD. Effective screening for dementia, which can be administered at ambulatory care facilities, is warranted. Vascular risk factors, especially type 2 diabetes mellitus, have been found to increase the risk of developing Alzheimer's disease (AD). The prevalence of type 2 diabetes mellitus is increasing in Japan. In this special issue, T. Matsuzawa et al. describe an index for screening for mild or moderate AD cases among the elderly with type 2 diabetes mellitus. The index includes self-reported answers to a questionnaire regarding subjective memory complaints and daily functioning and information on vascular risk factors obtained from clinical charts. The index had satisfactory discriminatory ability to identify those with AD among patients with diabetes. This may contribute to an effective screening for AD among those with diabetes, that is, known high-risk populations.

Current treatments for AD are limited to alleviating symptoms, but not reversing the pathological progress.

Pharmacological treatments for BPSD, which are critical for the well-being of both patients and caregivers, are also limited in their effectiveness. The study by H. Fukui et al. examines changes in sex hormones associated with the pathogenesis of AD before and after music therapy among patients with AD. They show that music therapy modified the secretion of sex hormones, and the results also suggest that problematic behavior may be reduced this way. The therapy has the potential to become a safe alternative treatment that is as effective as hormone replacement, but with fewer side effects. The underlying biological mechanism of effects shown in this study is convincing and a welcome addition to the field.

The number of those suffering from dementia is increasing worldwide. Effective caregiving strategies and targeted care management programs are urgently needed to enhance the well-being of those with AD and their caregivers. T. Passos et al. examined the met and unmet needs of the elderly with mental health problems and their care in Portugal. The main unmet needs identified were daytime activities, social benefits, company, psychological distress, and incontinence. Some of these unmet needs may be universal across countries worldwide, but others may differ depending on specific health care systems and cultures. A comparison with similar surveys in other countries may help identify common unmet needs for patients and caregivers. M. M. Pöysti et al. compare the characteristics and burdens of male and female spousal caregivers of patients with dementia in Finland. This is an important issue because the proportion of male caregivers is rapidly increasing in many countries. In the study, male

caregivers experienced a lower burden than female caregivers even though female caregivers were responsible for more severe cases. The finding should be confirmed, and the reasons behind it should be explored further, so that factors that may reduce high caregiver burden can be identified.

Finally, the economic and social costs for caring of the demented are of significant importance as the at-risk population grows rapidly around the globe. Japan has one of the fastest growing elderly populations, and in 2000 it launched a new public long-term care insurance system [1]. S. Shinagawa et al. report that the requisite costs in the Japanese long-term care insurance are different between AD and vascular dementia (VD).

In this special issue, we highlight several important themes in the care for dementia. We hope that the results presented contribute to developing and providing better care of the demented and increase awareness of the importance of international studies of dementia caregiver issues.

*Hiroyuki Umegaki
Hajime Takechi
Hiroko H. Dodge*

References

- [1] N. Tamiya, H. Noguchi, A. Nishi et al., "Population ageing and wellbeing: lessons from Japan's long-term care insurance policy," *The Lancet*, vol. 378, pp. 1183–1192, 2011.

Research Article

Longitudinal Changes in the Government-Certified Index Stage and Requisite Costs for Long-Term Care Insurance System among the Community-Dwelling Demented Elderly in Japan

Shunichiro Shinagawa,¹ Shiori Nakamura,¹ Makoto Iwamoto,^{1,2} Norifumi Tsuno,¹ Masahiro Shigeta,³ and Kazuhiko Nakayama¹

¹ Department of Psychiatry, Jikei University School of Medicine, 3-25-8 Nishi-shinbashi, Minato-ku, Tokyo 105-8461, Japan

² Kiyokawa-Enju Hospital, 3414 Kiyokawa, Aiko District, Kanagawa 243-0112, Japan

³ Faculty of Health and Sciences, Tokyo Metropolitan University, 7-2-10 Higashiogu, Arakawa-ku, Tokyo 116-8551, Japan

Correspondence should be addressed to Shunichiro Shinagawa; shinagawa@jikei.ac.jp

Received 21 December 2012; Revised 31 January 2013; Accepted 1 February 2013

Academic Editor: Hiroyuki Umegaki

Copyright © 2013 Shunichiro Shinagawa et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. A new public long-term care (LTC) insurance was launched in 2000 in Japan. However, there have been few studies involving factors that increase LTC costs of demented subjects; no follow-up studies involving the Government-Certified Index (GCI) and requisite costs related to the causes of dementia. **Method.** An epidemiological survey was conducted in a rural area in Japan in 1999, and 271 subjects were diagnosed as dementia patients. Age, sex, mini-mental state examination, clinical dementia rating, activity of daily living, causes of dementia, and coexisting physical disease were confirmed. After the LTC insurance has been launched, we tracked the GCI stages and payment amounts every month for 8 years. **Result.** 209 subjects were certified to be eligible for LTC insurance; however, 13 did not receive any payment. Only 49 out of 209 were alive after the follow-up period. The most common cause of dementia was Alzheimer's disease (AD), followed by vascular dementia (VaD). There was no significant difference between the mortality rates of the two groups. VaD subjects required higher costs than AD subjects in the total certified period and in GCI stage 5. **Conclusion.** Our results indicate that causes of dementia can have an impact on the requisite costs for the LTC insurance.

1. Introduction

A growth of the elderly population consequently increases the number of demented subjects, and dementia is one of the major challenges of health care systems in most countries, especially in aging societies such as Japan. The presence of dementia is strongly related to a decline in the level of daily functioning [1], and the severity of dementia is one of the predictors of higher levels of care [2]. Furthermore, the presence of dementia has an impact on patients' physical condition, increase the burden on caregivers [3], and can even diminish the life expectancy of elderly people [4, 5].

In Japan, the public long-term care (LTC) insurance system was launched in 2000 to deal with an increasing number of impaired elderly and was revised in 2006. The

aims of the LTC insurance system are to allocate limited resources to impaired elderly in a way that adequately reflects need and to reduce the burden on caregivers [6]. Services are allocated based on the Government-Certified Index (GCI), which indicates the amount that can be spent on services for a particular patient with a given GCI stage, basically ranging from 0 (need only support) to 5. Once this procedure has been completed, a care management agency steps are taken to provide the level of services indicated by the GCI stage. Disabled elderly can apply for care services including home help, nurse visits, day services, respite care, and institutional care (nursing homes, etc.). The GCI stage is reevaluated regularly twice a year or if necessary.

However, some researchers have claimed that the LTC insurance system does not adequately take into account

problems associated with dementia, specifically Alzheimer's disease (AD) [7–9]. Patients with AD were supposed to require caring because of not only physical reasons but also other many reasons. Moreover, there have been few follow-up studies involving the GCI stage with requisite costs for the LTC insurance system for the demented elderly. Furthermore, as far as we know, there have been no studies investigating such transition in the GCI stage and requisite costs specifically related to the causes of dementia. The burden on caregivers for demented elderly differs largely depending on the causes of dementia [10]. The different causes of dementia may generate different costs [11].

In order to evaluate the extent of care services required by demented elderly, we need to ascertain the correlation between the GCI stage and requisite costs related to specific causes of dementia. The aim of this study is (1) to understand the present situation of LTC insurance costs among community-dwelling demented elderly through the 8-year followup of the GCI stage and requisite costs and (2) to ascertain whether LTC insurance costs can differ according to the causes of dementia.

2. Methods

Written informed consent was obtained after a complete description of the study had been given to all subjects or their informants. This study was approved by the Ethics Committee of Jikei University.

2.1. Baseline Assessment. An epidemiological survey of dementia was conducted in Itoigawa city, a rural area of Japan, in 1998–1999. In 1998, there were a total of 33,120 inhabitants and 7,847 of them were over 65 years old. Two-phased, semistructured screening tests were conducted, including items on education, occupation, medical history, risk factors such as hypertension, diabetes, and hyperlipidemia, psychiatric and behavioral symptoms, severity of dementia measured by clinical dementia rating (CDR) [12], cognitive functions measured by mini-mental state Examination (MMSE) [13], and activity of daily living (ADL) measured by N-ADL [14]. N-ADL is an assessment tool for elderly ADL developed in Japan; it contains 5 domains including gait, daily milieu, clothing, eating, and excretion. Each domain scores from 0 to 10, with total score from 0 to 50. Zero shows that the subject requires complete assistance in every aspect, 50 means that the subject is independent.

Subjects who met the criteria (scored ≤ 19 on MMSE scored ≥ 20 on MMSE but had any psychiatric symptoms had been diagnosed to have dementia before the survey, etc.) in the first phase were recruited into the second phase. The second phase was conducted with a total of 1114 subjects, using a door-to-door survey by a clinical team including a psychiatrist and a public health nurse. A total of 271 of these subjects were CDR ≥ 1 , 252 of them were CDR = 0.5 and 306 were CDR = 0. The other 285 subjects did not participate in the second phase due to refusal, death, or as a result of moving to other communities. The details of the design and methods of sampling in the baseline survey have been described elsewhere [15, 16].

A total of 271 of these subjects were diagnosed as having dementia. The diagnosis of dementia was established according to the DSM-IV criteria and Consortium to Establish a Registry for Alzheimer's Disease (CERAD) criteria [17, 18]. The demented subjects were classified into subgroups, according to the cause of dementia, on the basis of the DSM-IV criteria.

2.2. Follow-Up Assessment. Among the 271 demented elderly, seven subjects moved to other communities (due mainly to institutionalization) or refused to participate in the follow-up investigation, and 55 subjects (or their family) did not enroll in the LTC insurance system. Two hundred and nine subjects were included in this study. We confirmed the age, sex, MMSE score, CDR score, causes of dementia, and any coexisting physical diseases of each of the 209 demented subjects.

After the LTC insurance system was launched in April 2000, we tracked the GCI stage and payment amounts from the government every month through December 2007, according to the data provided by the Health Improvement Section of the Welfare and Health Division of Itoigawa city. In addition, we compiled information pertaining to mortality (i.e., the date of death and causes of death), according to the data provided by the same agency.

2.3. Statistical Analysis. All data analyses were carried out using the SPSS16.0-PC software package. The significance of the differences between the groups was assessed by *t*-test for age, MMSE score, N-ADL score, and the caring costs; by Chi-square test with Fisher's exact test (extended) for sex, CDR, proportion of subjects, proportion of coexisting physical diseases; and by Mann-Whitney *U* test for caring periods. Median survival times were estimated based on the Kaplan-Meier method and survival curves were generated. Log-rank tests were performed to test the differences between the survival curves. A *P* value < 0.05 (two tailed) was considered statistically significant.

3. Result

3.1. Demographic Background of 209 Subjects. A total of 209 demented elderly were certified to receive care insurance. The mean age in April 2000 was 84.5 ± 7.1 . The sex ratio was 57 : 152 (male/female, female 73%), the CDR ratio was 78 : 72 : 59 (1 : 2 : 3), and the mean MMSE score was 15.7 ± 5.1 . The mean N-ADL score was 31.4 ± 13.2 . The most common cause of dementia was AD ($N = 110$, 52.6%), followed by vascular dementia (VaD) ($N = 48$, 23.0%), dementia with Lewy bodies, frontotemporal dementia, and other causes of dementia.

One hundred fifty-nine of the subjects suffered from other coexisting physical diseases in April 2000, such as hypertension ($N = 77$, 36.8%), brain disease ($N = 41$, 19.6%), heart disease ($N = 36$, 17.2%), digestive organ disease ($N = 33$, 15.8%), diabetes ($N = 22$, 10.5%), urologic disease ($N = 14$, 6.7%), hyperlipidemia ($N = 14$, 6.7%), and other diseases.

At the end of our research period (December 2007), only 49 (23.4%) were alive. The average age at death was

TABLE 1: Comparison between subjects who received payment and those who did not.

	No payment (<i>N</i> = 13)	Payment (<i>N</i> = 196)	<i>P</i> value
Mean age (at 2000)	86.8 ± 8.4	84.4 ± 7.0	0.233 (<i>t</i> test)
Sex (M:F)	8:5	49:147	0.004 (χ^2 test)
CDR grade (1:2:3 at 2000)	1:8:4	77:64:55	0.044 (χ^2 test)
MMSE score (at 2000)	16.7 ± 6.6	15.7 ± 5.0	0.601 (<i>t</i> test)
N-ADL score (at 2000)	25.5 ± 15.1	31.8 ± 13.0	0.141 (<i>t</i> test)

TABLE 2: Demographic variables of AD and VaD patients.

	AD (<i>N</i> = 110)	VaD (<i>N</i> = 48)	<i>P</i> value
Mean age (at 2000)	85.8 ± 7.0	82.2 ± 5.9	0.002 (<i>t</i> test)
Sex (M:F)	15:95	15:33	0.009 (χ^2 test)
CDR grade (1:2:3 at 2000)	35:40:35	23:15:10	0.134 (χ^2 test)
MMSE score (at 2000)	15.7 ± 5.0	14.8 ± 5.5	0.413 (<i>t</i> test)
N-ADL score (at 2000)	32.7 ± 12.3	28.6 ± 14.5	0.124 (<i>t</i> test)
Coexisting physical diseases (any/nothing at 2000) (%)	71:39 64%	44:4 92%	0.000 (χ^2 test)
Survival ratio (alive/dead at 2007)	39:79	9:31	0.210 (χ^2 test)
Total duration of certified until 2007 (month)	50.9 ± 31.6	57.3 ± 30.3	0.260 (Mann-Whitney <i>U</i> test)

AD: Alzheimer's disease; VaD: vascular dementia.

89.0 ± 6.9; the most common cause of death was respiratory disease (*N* = 70), followed by heart disease (*N* = 34), brain infarction (*N* = 27), and other causes of death. The estimated median survival was 4.3 years (95% confidence interval, 3.6 to 5.1 years) from the beginning of the research period and 5.3 years from the diagnosis of dementia.

Average duration of the certified to receive care insurance was 52.3 ± 32.1 months. 26.3% of the subjects required more than 84 months (7 years), and 14.8% of them required less than 12 months (1 year). Average costs (total payment amount from the government) was 7.39 ± 7.49 million Japanese yen (JPY) (0~28.95 million JPY). Thirteen of them (6.2%) did not receive any payment although they were certified to receive care insurance benefit. Five of them suffered from AD, 3 suffered from VaD, and 5 suffered from other causes of dementia. At their initial certification in April 2000, two were GCI = 0 (need only support), two were GCI = 1, one was GCI = 2, two were GCI = 3, one was GCI = 4, and 5 were GCI5. After one year of follow up in April 2001, none of them applied for certification again. A comparison of the 13 subjects who received no payment and the remaining 196 subjects is shown in Table 1. Significant differences were found for sex (*P* = 0.004) and CDR grade (*P* = 0.044).

3.2. Difference between Alzheimer's Disease and Vascular Dementia. We also compared the GCI stage and requisite costs according to the causes of dementia. We excluded AD with cerebrovascular disease, dementia with Lewy bodies, frontotemporal dementia, and other causes of dementia because the number of these patients was too small to perform efficient statistical analysis. Finally, patients with AD and VaD were included in the analysis. For the care-giving costs analysis, we also excluded the above mentioned 13 subjects. This is because they did not receive any payment to

compare and none of them applied for certification again after 1 year of follow up. Demographic variables of the two patient groups are summarized in Table 2. There were significant differences in age, sex, and proportion of coexisting physical diseases between the two groups. However, there were no significant differences in the CDR grade, with MMSE score at 2000. There were also no significant differences in the total N-ADL score and between each of 5 domains in N-ADL subscale between AD and VaD groups. Total duration of certified to receive care insurance until 2007 was 50.9 ± 31.6 month in AD patients, whereas 57.3 ± 30.3 month in VaD patients. There was no significant difference between the two groups (*P* = 0.260 by Mann-Whitney *U* test).

The survival curves of the two patient groups are shown in Figure 1. There was no significant difference (*P* = 0.873) between the mortality rates of the two groups.

GCI stage and payment amounts generally increase as time passes in both patient groups; however, the patterns of change vary widely according to each individual. Therefore, we investigated the total duration of time and the total payment amounts recorded for each GCI stage. Figure 2 shows percentages for each time period (0–3 months/4–6 months/7–9 months/10–12 months/over 13 months) that patients spent at each GCI stage. One AD subject died soon after the beginning of the research period. Therefore, we excluded this subject from Figure 2. Generally, patients in both groups spent a longer duration in each of the subsequent periods as the GCI stage increased. However, there was no significant difference between the two groups in the duration of any of the GCI stages (by Mann-Whitney *U* test).

AD patients required an average of 6.99 ± 6.85 million JPY, and VaD patients required an average of 9.97 ± 8.62 million JPY. Average payments per month for each GCI stage for both AD and VaD groups are summarized in Table 3.

TABLE 3: Average payments for each GCI stage for both AD and VaD groups per month.

	AD (N = 105)	VaD (N = 45)	P value
GCI 1	7.2 ± 27.4	16.7 ± 48.3	0.129
GCI 2	34.3 ± 64.4	43.4 ± 69.6	0.436
GCI 3	67.1 ± 83.6	67.6 ± 91.7	0.969
GCI 4	103.7 ± 105.7	121.2 ± 124.2	0.379
GCI 5	94.7 ± 118.5	140.8 ± 113.6	0.037
Total	113.4 ± 76.8	141.1 ± 97.9	0.047

(thousand JPY/month).

AD: Alzheimer’s disease; VaD: vascular dementia.

Mean duration of both patient groups for each GCI stage was summarized in Figure 2.

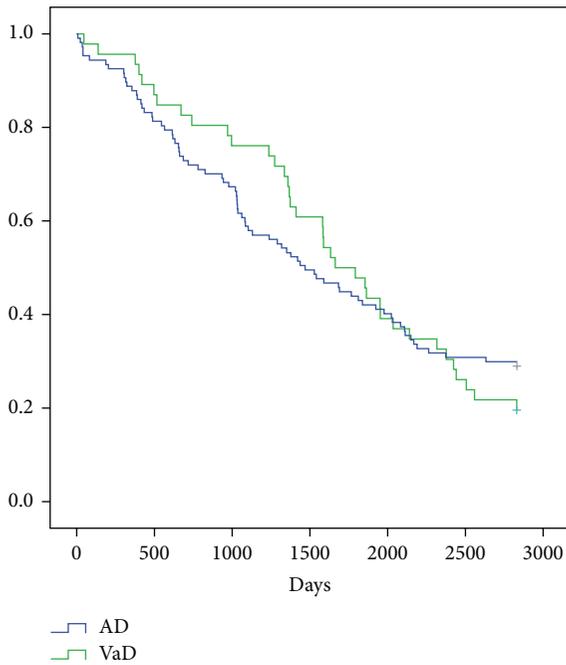


FIGURE 1: Survival curves of the two patient groups. AD: Alzheimer’s disease; VaD: vascular dementia. No significant difference ($P = 0.873$) between the mortality rates of the two groups.

There was a significant difference between the two groups in the total payment amount per total certified period ($P = 0.047$). There was also significant difference between the two groups in GCI 5 ($P = 0.037$); VaD patients required a higher costs than AD groups.

4. Discussion

This study is the first to practice the follow-up study of the GCI stage and requisite costs for the LTC insurance system among community-dwelling demented elderly according to the causes of dementia. During 8 years of followup since the LTC insurance system was launched, 77% of the demented elderly died, and the average age at death was 89.0 years old. The median survival was 5.3 years from the diagnosis of dementia. Previous studies reported the median survival time from the diagnosis of dementia as 5.7 years [19] and 3.3 years [5]; our result does not differ largely from these results.

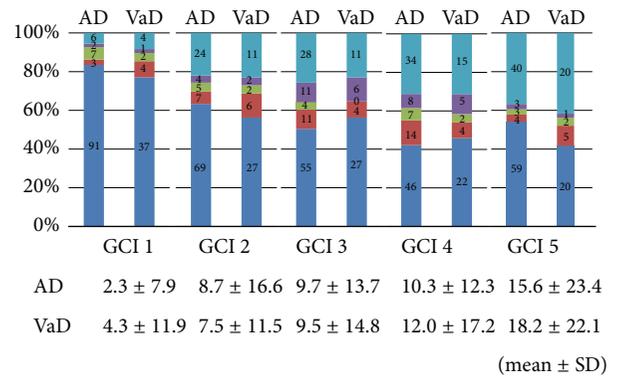


FIGURE 2: Percentages for each time period (0–3 months/4–6 months/7–9 months/10–12 months/over 13 months) that AD and VaD patients spent at each GCI stage. Mean duration for each GCI stage (month). AD: Alzheimer’s disease; VaD: vascular dementia. Number in the figure is the number of the patients in each time period. As the GCI stage increased, patients in both groups spent a longer duration in each of the subsequent periods. However, there was no significant difference between the two groups in the duration of any of the GCI stages.

The average LTC cost (total payment amount from the government) was 7.39 million JPY (0~28.96 million JPY), or 1.72 million JPY per year. This result is based on the LTC cost of single local government (Itoigawa city). There is a possibility that LTC costs differ between each local government according to its financial state. We need further reports based on other local governments in order to generalize our result. However, there are some previous researches considering care costs in other countries. Recent research in Germany mentioned that care costs for dementia patients in community were average 47,747 (Euros) per patient annually, or 4.91 million JPY (1 Euro = 103.3 JPY on September 24, 2011) [20]. Eighty percent of that total costs were for informal care, 9396 (0.97 million JPY) were for formal care. Even though the LTC systems of the two countries (i.e., the way to decide the payment amount and the way to pay for care giving) were different, and the demographic background of two researches (i.e., all kinds of dementia were included in Germany subjects) was different, the results of our study in Japan and the result in Germany do not differ largely when

changes in exchange rates have been taken into consideration. And therefore, we believe that our results are valid enough.

Six percent of the demented elderly patients (primarily males and severely demented subjects) did not receive any payment although they were eligible. Furthermore, none of them applied for certification again after 1 year of followup. The reason why these subjects did not receive benefits is still unclear; this may have been due to their own refusal or some other familial reasons. We should be careful not to make these subjects being left out of the support.

In our research, there was no significant difference between the mortality rates of AD and VaD patients. This result is consistent with previous studies [5, 19] reporting the mortality rates of AD and other demented patients. However, in our research, VaD patients received significant higher total payments than AD patients. Furthermore, VaD patients required significant higher costs per total certified period than AD patients especially in GCI 5 stage. VaD patients required higher caring cost in the high CGI stage, although there was no significant difference in the duration of the GCI subsequent periods.

There are a few possible reasons of this higher cost of VaD patients. First, the incidence of coexisting physical diseases is higher in VaD patients than AD patients (92% versus 64%); although VaD patients were younger, and the total and each of subscales (gait, daily milieu, clothing, eating, and excretion) of N-ADL scores did not differ between the two groups among the background factors in 2000. These coexisting physical diseases include vascular risk factors such as hypertension, diabetes, and hyperlipidemia. VaD patients generally have more risk factors such as diabetes or hypertension [21]. These risk factors may cause other coexisting physical diseases such as brain disease and heart disease. During the 8 years of the follow-up period, numbers and the severity of these coexisting physical diseases may have been exacerbated and ADL levels of VaD patients may have been more exacerbated, and resulting from higher caring cost. Even though demented elderly require caring for many reasons, VaD patients may require higher costs due to their physical conditions. However, we could not follow the rate of coexisting physical diseases and transition of ADL during the follow-up period. There is also significant difference in sex ratio; there are relatively more male subjects in VaD groups. However, there is a research in Germany that females incurred greater LTC costs than males of the same age [22]. Therefore, we believe that there is little possibility that this sex ratio may have an effect on the caring costs. The aims of this study are to understand the present situation; therefore, we dare not adjust these background factors.

Second, there is a possibility that the kind of provided service (home help, nurse visits, day services, respite care, and institutional care) differs between the two groups. There may be more institutionalized VaD subjects in GCI 5 who required higher caring cost. However, we followed only GCI stage and payment amounts in this study and we cannot investigate the kind of provided service. Therefore, we cannot certify this hypothesis.

There are some researches comparing healthcare costs of VaD and other diseases in the United States [22, 23]. They reported that healthcare costs for VaD patients were substantially higher than other groups because of higher hospital costs. They also reported that the pattern of healthcare utilization for VaD was substantially different from other groups; VaD patients had lower utilization for physician office visits and prescription drugs. VaD patients may not receive adequate medical care, placing them at greater risks for more costly inpatient care. Although healthcare costs and LTC insurance costs are different and the systems in Japan and United States are different, their assumption can be applied to our results.

There are a few methodological issues that should be taken into consideration to appreciate our results fully. First, we compared only patients with AD and VaD because the number of other causes of dementia is too small to make an effective analysis in this research. In our cohort, there were few patients with DLB and FTLD. This may be because our basic research was conducted in 1998-1999 when the concept of DLB was not so widely known at that time. However, DLB and FTLD were assumed to require higher costs because of their behavioral symptoms and neurological symptoms. Further research on other causes of dementia is required.

Second, in this research, we focused on the causes of dementia and tracked only the GCI stage and payment amounts as outcome measurements. It is difficult for us to discuss the influences of other factors such as residential state, numbers of family caregivers, new physical disease that could have occurred during the follow-up period, the transition of ADL of subject, and the kind of provided service.

Third, our data is based only on the costs for LTC insurance system; informal care-giving costs, and other medical costs are not included in this research. We cannot discuss the total care-giving costs and caregiver's burden in this study. We need further researches on the total care costs of demented elderly.

In conclusion, our results indicate that the requisite costs of LTC insurance system for demented elderly differ depending on the causes of dementia. In order to reduce costs for LTC insurance of demented elderly, prior control of the risk factors may be important to prevent suffering from VaD. Further research on the detailed effects of cognitive function and behavioral problems for care-giving costs for demented elderly is required.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgments

The present study was supported by the Health Improvement Section of the Welfare and Health Division of Itoigawa city. The authors also wish to thank Itoigawa city's public nurses for their great contribution. This work was supported in part by a grant from Grant-in-Aid for Scientific Research (to S. Nakamura).

References

- [1] E. J. Warren, A. Grek, D. Conn et al., "A correlation between cognitive performance and daily functioning in elderly people," *Journal of Geriatric Psychiatry and Neurology*, vol. 2, no. 2, pp. 96–100, 1989.
- [2] F. Boersma, J. A. Eefsting, W. van Den Brink, and W. van Tilburg, "Care services for dementia patients: predictors for service utilization," *International Journal of Geriatric Psychiatry*, vol. 12, no. 11, pp. 1119–1126, 1997.
- [3] L. Etters, D. Goodall, and B. E. Harrison, "Caregiver burden among dementia patient caregivers: a review of the literature," *Journal of the American Academy of Nurse Practitioners*, vol. 20, no. 8, pp. 423–428, 2008.
- [4] P. T. van Dijk, D. W. Dippel, and J. D. Habbema, "Survival of patients with dementia," *Journal of the American Geriatrics Society*, vol. 39, no. 6, pp. 603–610, 1991.
- [5] C. Wolfson, D. B. Wolfson, M. Asgharian et al., "A reevaluation of the duration of survival after the onset of dementia," *New England Journal of Medicine*, vol. 344, no. 15, pp. 1111–1116, 2001.
- [6] Ministry of Health and Welfare, *White Paper on Welfare (kousei hakusho)*, Gyousei, Tokyo, Japan, 1996.
- [7] J. C. Campbell and N. Ikegami, "Long-term care insurance comes to Japan: a major departure for Japan, this new program aims to be a comprehensive solution to the problem of caring for frail older people," *Health Affairs*, vol. 19, pp. 26–38, 2000.
- [8] S. Nandi, "Quantifying dementia care in Japan: a discussion on the long-term care insurance," *Psychogeriatrics*, vol. 1, pp. 100–107, 2001.
- [9] Y. Arai, S. H. Zarit, K. Kumamoto, and A. Takeda, "Are there inequities in the assessment of dementia under Japan's LTC insurance system?" *International Journal of Geriatric Psychiatry*, vol. 18, no. 4, pp. 346–352, 2003.
- [10] N. Matsumoto, M. Ikeda, R. Fukuhara et al., "Caregiver burden associated with behavioral and psychological symptoms of dementia in elderly people in the local community," *Dementia and Geriatric Cognitive Disorders*, vol. 23, no. 4, pp. 219–224, 2007.
- [11] G. Rojas, L. Bartoloni, C. Dillon, C. M. Serrano, M. Iturry, and R. F. Allegri, "Clinical and economic characteristics associated with direct costs of Alzheimer's, frontotemporal and vascular dementia in Argentina," *International Psychogeriatrics*, vol. 3, pp. 1–8, 2010.
- [12] C. P. Hughes, L. Berg, W. L. Danziger, L. A. Coben, and R. L. Martin, "A new clinical scale for the staging of dementia," *British Journal of Psychiatry*, vol. 140, pp. 566–572, 1982.
- [13] M. F. Folstein, S. E. Folstein, and P. R. McHugh, "Mini mental state. A practical method for grading the cognitive state of patients for the clinician," *Journal of Psychiatric Research*, vol. 12, no. 3, pp. 189–198, 1975.
- [14] T. Kobayashi, S. Hariguchi, and T. Nishimura, "A new clinical scale for rating of mental stage and activities of daily living of the elderly (NM scale and N-ADL)," *Rinsho Seishin Igaku*, vol. 17, pp. 1653–1658, 1988 (Japanese).
- [15] S. Nakamura, M. Shigeta, M. Iwamoto et al., "Prevalence and predominance of Alzheimer type dementia in rural Japan," *Psychogeriatrics*, vol. 3, pp. 97–103, 2003.
- [16] S. Shinagawa, S. Nakamura, M. Iwamoto, N. Tsuno, and M. Shigeta, "Identification of high-risk dementia cohorts in a community sample of Japanese elderly," *Psychiatry and Clinical Neurosciences*, vol. 63, no. 6, pp. 735–740, 2009.
- [17] American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV)*, American Psychiatric Association, Washington, DC, USA, 1995.
- [18] J. C. Morris, R. C. Mohs, H. Rogers, G. Fillenbaum, and A. Heyman, "Consortium To Establish a Registry for Alzheimer's Disease (CERAD) clinical and neuropsychological assessment of Alzheimer's disease," *Psychopharmacology Bulletin*, vol. 24, no. 4, pp. 641–652, 1988.
- [19] S. C. Waring, R. S. Doody, V. N. Pavlik, P. J. Massman, and W. Chan, "Survival among patients with dementia from a large multi-ethnic population," *Alzheimer Disease and Associated Disorders*, vol. 19, no. 4, pp. 178–183, 2005.
- [20] L. Schwarzkopf, P. Menn, S. Kunz et al., "Costs of care for dementia patients in community setting: an analysis for mild and moderate disease stage," *Value in Health*, vol. 14, no. 6, pp. 827–835, 2011.
- [21] K. A. Jellinger, "The pathology of "vascular dementia": a critical update," *Journal of Alzheimer's Disease*, vol. 14, no. 1, pp. 107–123, 2008.
- [22] L. Schwarzkopf, P. Menn, R. Leidl et al., "Excess costs of dementia disorders and the role of age and gender—an analysis of German health and long-term care insurance claims data," *BMC Health Services Research*, vol. 19, article 165, 2012.
- [23] J. Hill, H. Fillit, S. N. Shah, M. C. Del Valle, and R. Futterman, "Patterns of healthcare utilization and costs for vascular dementia in a community-dwelling population," *Journal of Alzheimer's Disease*, vol. 8, no. 1, pp. 43–50, 2005.

Research Article

The Needs of Older People with Mental Health Problems: A Particular Focus on Dementia Patients and Their Carers

Joaquim Passos,¹ Carlos Sequeira,² and Lia Fernandes³

¹ Health Sciences, School of Health of Viana do Castelo, 4900-314 Viana do Castelo, Portugal

² Nursing Unit, School of Nursing of Porto, 4200-072 Porto, Portugal

³ Clinical Neuroscience and Mental Health Department, Faculty of Medicine, University of Porto/Psychiatry of S. João Hospital Centre, 4200-319 Porto, Portugal

Correspondence should be addressed to Lia Fernandes, liapnsf@gmail.com

Received 29 July 2012; Revised 20 September 2012; Accepted 28 September 2012

Academic Editor: Hiroyuki Umegaki

Copyright © 2012 Joaquim Passos et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The problems and needs of older people are often associated with mental illness, characterized by a set of clinical manifestations, which constitute important domains for investigation and clinical practice. This paper presents the results of a pilot study whose main purpose was to identify met and unmet needs and to analyze the relationship between those needs, psychopathology and functionality in older people with mental health problems. A sample of 75 patients aged 65 or over, of both sexes, diagnosed with mental illness using ICD-9. The main diagnoses were depression (36%) and dementia (29.3%). Most patients had cognitive impairment (MMSE, 52%; CDT, 66.7%), depression (GDS, 61.3%), anxiety (ZAS, 81.3%), and moderate dependence (BI, 49.3% and LI, 77.3%). The main unmet needs found were daytime activities (40%), social benefits (13.3%), company (10.7%), psychological distress (9.3%), and continence (8%). The majority of these unmet needs occur with dementia patients. The majority of the carers of these patients had global needs (met and unmet) in terms of psychological distress. Findings also reveal that a low level of functionality is associated with dementia diagnoses. The association analyses suggest that dementia is an important determinant of the functional status and needs.

1. Introduction

The ageing of the population worldwide has been followed by an increase in the prevalence of mental illness, making this one of the most important causes of morbidity. In this context, there are numerous psychological and behavioural symptoms associated with dementia that strongly affect the objectives and life expectations of the elderly and increase the difficulties in the process of assessment, diagnosis, and treatment of these people [1].

Dementia occupies a central place as a condition of morbidity in this population, with a significant increase as we advance in age, constituting one of the most common causes of disability in western society [1–7].

The change in the age pyramid, which occurred mainly after the 50s, makes the study of ageing and old age a primary

focus of attention and concern of health professionals and researchers, in order to deepen their knowledge and create evidence that will allow the development of more structured and targeted responses to meet specific needs of older people and to promote active and successful ageing.

As part of this work, elderly needs assessment is the fundamental base for a social/health policy definition and intervention. There is a met need if the person has a (moderate or serious) problem in the area for which they require assistance, which they receive and it is appropriate to met that need. There is an unmet need when individual has a significant problem in the area for which they are not receiving appropriate assistance (wrong kind of help or no assistance) [1, 8–11].

This paper aims to present the results of a pilot study conducted in the context of the Research Project “The needs

of older people with mental health problems” developed under the Doctoral Program in Gerontology and Geriatrics in the Abel Salazar Biomedical Sciences Institute, University of Oporto/Aveiro, Portugal. The aim of the study was to identify the met and unmet needs of the elderly and their carers and to analyze the relationship between those needs, psychopathology and functionality in older people with mental health problems.

2. Materials and Methods

2.1. Participants. An elderly sample (over 65 years) of both sexes diagnosed with mental disorder according to the ICD-9—International Classification of Diseases [12] was recruited consecutively from the National Health Service in the Inpatient and Outpatient Department of Psychiatry and Mental Health (DSMP) at a Health Unit in Northern Portugal.

Also, 52 carers and 71 staff members were interviewed using the Camberwell Assessment of Need for the Elderly (CANE) to identify met and unmet needs.

It was established as inclusion criteria: ≥ 65 years old; mental disease (ICD-9 criteria) [12]; it was admitted as inpatients or outpatients in the Psychiatry and Mental Health Department (DSMP). The exclusion criteria were: blind/deaf and severe impairment in communication.

2.2. Instruments. The following instruments were used: the Camberwell Assessment of Need for the Elderly (CANE) [11]; the Minimal State Examination/MMSE [13]; the Clock Draw Test/CDT [14]; the Geriatric Depression Scale/GDS [15]; the Zung Anxiety Scale/ZAS [16]; the Barthel Index/BI [17]; the Lawton Index/LI [18]; and the Graffar's Social Classification/GSC [19].

In order to fit the assessment protocol to the context of the investigation, previously validated versions of the instruments or versions adapted to the Portuguese population were used. In that sense, the following were used: the Portuguese version of CANE [1]; the Portuguese version of the MMSE [20], with the new normative values adapted to the Portuguese population [21] (cognitive deficit: 0–2 school years ≤ 22 ; 3–6 school years ≤ 24 ; 7 or more school years ≤ 27). Regarding the Clock Draw Test, since a version adapted to the Portuguese population is still being developed, the original version was used [14] with the coding system proposed by Cacho et al. [22] (scores 0–10: >6 normal; ≤ 6 abnormal), which is being used by some institutions in Portugal. As to the Geriatric Depression Scale [23] (15 items version) and Zung Anxiety Scale [24], the Portuguese versions were used. Regarding the functionality, Portuguese versions of the Barthel Index [25] (scores 0–20: total independence 20; moderate dependence 13–19; severe dependence 9–12; total dependence 0–8) and Lawton Index [26] (scores 0–23: total independence 23; some level of dependence < 23) were also used. Finally, concerning the social classification, an adapted version of the Graffar's Social Classification [27] (scores 0–10: 0–2 class I; 3–4 class II; 5–6 class III; 7–8 class IV; 9–10 class V) was used.

2.3. Procedure. The participants were identified by the researcher through a contact with the mental health services. In the context of this study, the individuals were contacted and interviewed when they accessed the outpatient service or were inpatients during the study period. The researcher gave them information about the study and asked them if they wanted to participate. The researcher then tried to identify a suitable member of staff and a primary caregiver to perform the assessment.

After this, 21 inpatients, 46 outpatients, 6 in nursing homes, and 2 at home were assessed consecutively during the period from April to September 2011.

Despite the assessment being planned at the moment the patients had access to the health unit, in some of the cases the researcher had to go to their homes or nursing homes. Also, 52 carers and 71 staff members (psychiatrists, psychologists, social workers, and psychiatric nurses) were interviewed separately by the researcher using the Camberwell Assessment of Need for the Elderly (CANE). The CANE was given as a structured interview to the patients, their informal carer, staff, and evaluator from items 1 to 24, A and B sections. After the data collection, using the instruments and procedures listed above, the data was organized and classified and the statistical analysis was carried out using IBM SPSS, version 19.

In the development of this study, all procedures concerning ethical approval were obtained from the ethics committee and from the board of the institution where the study was held. All the necessary measures to safeguard participants' anonymity and confidentiality of information were also thoroughly followed.

3. Results and Discussion

The data was collected from a convenience sample of 75 patients, with ages ranging from 65 to 93 years (mean = 73.3 years and SD = 6.6). The majority were female (73.3%), married (49.3%), living with a partner (50.7%), and in rural areas (74.7%); a high percentage belonged to a very low social class (94.7%), according to the Graffar classification [19]. Most of them were interviewed as outpatients (73.3%), and the main diagnosis was depressive disorder (36%), followed by dementia (29.3%) and somatic comorbidity (98.7%). In 69.3% of the cases, there was an informal carer, and of these only 56% lived with the carer; most (80%) did not care for anyone else.

The main sociodemographic and clinical characteristics of the participants are presented in detail in Table 1.

Also, 52 carers with ages ranging from 21 to 80 years (mean = 58.9; SD = 15.02) were interviewed. The majority were male (51.9%), married (76.9%), a primary carer (94.2%), and patient's partner (50%).

The main sociodemographic characteristics of the carers are presented in Table 2.

3.1. Global Results of Applied Instruments. According to the global results of the applied instruments (Table 3), the majority of the patients had cognitive deficits in the

TABLE 1: Sociodemographic and clinical characteristics of subjects.

Characteristics	<i>n</i> = 75
Age (years)	73.3 (SD = 6.6; range 65–93)
Gender <i>n</i> (%)	
Male	20 (26.7)
Female	55 (73.3)
Marital status <i>n</i> (%)	
Single	14 (18.7)
Married	37 (49.3)
Common law	1 (1.3)
Widowed	14 (18.7)
Divorced	8 (10.7)
Separated	1 (1.3)
Living situation <i>n</i> (%)	
Alone	12 (16.0)
With partner	38 (50.7)
With other relatives	15 (20.0)
With others	10 (13.3)
Status at interview <i>n</i> (%)	
Inpatient	20 (26.7)
Outpatient	55 (73.3)
Psychiatric diagnosis <i>n</i> (%)	
Depressive disorder	27 (36.0)
Dementia	22 (29.3)
Bipolar disorder	9 (12.0)
Schizophrenia and other psychoses	4 (5.3)
Alcohol dependence	4 (5.3)
Adjustment disorder	4 (5.3)
Anxiety	3 (4.0)
No diagnosis	2 (2.7)
Somatic comorbidity <i>n</i> (%)	
Yes	74 (98.7)
No	1 (1.3)
Socioeconomic classification (Graffar) <i>n</i> (%)	
Class IV—low	4 (5.3)
Class V—very low	71 (94.7)
Geographical area <i>n</i> (%)	
Urban	12 (16.0)
Suburban	7 (9.3)
Rural	56 (74.7)
Has a carer? <i>n</i> (%)	
Yes	52 (69.3)
No	23 (30.7)
Lives with carer? <i>n</i> (%) (<i>n</i> = 52)	
Yes	42 (56.0)
No	10 (13.3)
Is also a carer? <i>n</i> (%)	
Yes	15 (20.0)
No	60 (80.0)

evaluation with the MMSE (52%) and in the Clock Draw Test (66.7%). They also had high levels of depression (GDS, 61.3%) and anxiety (ZAS, 81.3%). As far as the degree of functionality is concerned, most had moderate dependence on basic activities of daily living (BADL) (BI, 49.3%) and

TABLE 2: Sociodemographic characteristics of carers.

Characteristics	<i>n</i> = 52
Age (years)	58.9 (SD =15; range 21–80)
Gender <i>n</i> (%)	
Male	27 (51.9)
Female	25 (48.1)
Marital status <i>n</i> (%)	
Single	9 (17.3)
Married	40 (76.9)
Widowed	2 (3.8)
Divorced	1 (1.9)
Primary carer? <i>n</i> (%)	
Yes	49 (94.2)
No	3 (5.8)
Family carer <i>n</i> (%)	
Children	17 (32.7)
Husband/wife	26 (50.0)
Brother/sister	3 (5.8)
Other	2 (3.8)
Unrelated	4 (7.7)

some level of dependence on instrumental activities of daily living (IADL) (LI, 77.3%).

According to the identified needs of the patients, the results of the CANE on the evaluator's perspective (Table 4) show that the main met needs are related to physical health (93.3%), memory (81.3%), psychological distress (72%), information (70.7%), household skills (65.3%), eyesight/hearing (62.7%), and food (58.7%). The majority of unmet needs were found in the domain of daytime activities (40%), social benefits (13.3%), company (10.7%), psychological distress (9.3%), and continence sphincter (8%). None of the participants had unmet needs for caring for others, abuse/neglect and alcohol abuse. Also regarding the abuse/neglect, no participant registered any needs.

Concerning the carers' needs, on the evaluator's perspective, the results show that 45.3% had met needs and 6.7% unmet needs for psychological distress; another 21.3% had met needs for information.

3.2. Analysis of the Relationship between Psychopathology, Needs, and Functionality. Since the most common diagnoses were depression and dementia (which together represented 65.3% of the sample), some analyses were carried out to identify possible associations between these diagnoses and other sociodemographic and clinical variables. Those analyses were carried using chi-square (χ^2) and point biserial correlation coefficient (r_{pb}).

The results indicated a significant positive correlation between the medical diagnosis of dementia and depression and global needs (met and unmet) identified by CANE, from the perspective of carers, $r_{pb} = .42$, $P < .05$, staff, $r_{pb} = .47$, $P < .01$, and of the evaluator, $r_{pb} = .46$, $P < .01$. These findings reveal that a high level of global needs is associated

TABLE 3: Overall results of the instruments applied.

Instruments	<i>n</i> = 75	Mean (SD)	Median	Range
MMSE: <i>n</i> (%)				
Total score		22.28 (6.45)	25.00	5–30
Without cognitive deficit	36 (48.0)			
With cognitive deficit	39 (52.0)			
Clock Draw Test: <i>n</i> (%)				
Total Score		4.65 (3.40)	4.00	0–10
Normal	23 (30.7)			
Abnormal	50 (66.7)			
No response	2 (2.7)			
GDS: <i>n</i> (%)				
Total score		8.14 (4.32)	9.00	0–15
No depression	28 (37.3)			
Depression	46 (61.3)			
No response	1 (1.3)			
Zung anxiety scale: <i>n</i> (%)				
Total score		48.49 (8.41)	49.00	25–69
No anxiety	13 (17.3)			
Anxiety	61 (81.3)			
No response	1 (1.3)			
Barthel index: <i>n</i> (%)				
Total score		17.52 (3.68)	19.00	3–20
Total independence	32 (42.7)			
Moderate dependence	37 (49.3)			
Severe dependence	3 (4.0)			
Total dependence	3 (4.0)			
Lawton index: <i>n</i> (%)				
Total score		13.41 (8.05)	15.00	1–23
Total independence	17 (22.7)			
Some level of dependence	58 (77.3)			

with dementia diagnoses, while a slightly lower level of those same global needs is associated with depression.

The main unmet needs found, on the evaluator's perspective, were daytime activities, social benefits, company, and psychological distress. In the present study it was found that, in relation to daytime activities and benefits, the number of unmet needs is higher than those found in other studies [11, 28, 29]. In this view, it appears to be related to the fact that in Portugal there is an inadequate social network to address social problems and needs of older people with dementia or other mental health problems. The present Portuguese policies fall well short of the practice in other European countries, particularly in Northern Europe.

Moreover, in this sample, most patients lived in poor rural areas (74.7%), in a peripheral region of Northern Portugal, belonging to a very low socioeconomic class (94.7%), in contrast to the cited studies, where most patients were from urban or suburban areas [1, 8, 11]. In line with this, in the present study, it appears that the majority of

the elderly (96%) had low education and lived alone or with a partner, of similar age and level of education. In most cases, this partner was designated as carer. Taking into account the low level of education, the poor rural areas where they live, and the family's typology (with only one or two elderly members), many of these people reported the lack of company as a significant problem. Also due to the lack of knowledge of rights and social benefits, the results of the CANE from the patients' perspective showed a lower level of unmet needs in daytime activities (12%) when compared to the evaluator's perspective (40%). On the other hand, it remains also a policy difficulty concerning health and social services accessibility.

This highlights what has been reported in the literature regarding the management of care for patients with dementia, since the importance of systematically assessing needs and planning coordinated management of interdisciplinary care has been recognized. The importance is also assumed of ensuring a coverage that not only takes into account physical and environmental, but also psychological and social needs.

Regarding the psychological distress of the patients, the present results are in line with other studies in terms of global needs (met and unmet) [1, 8, 11, 28, 29], and the level of unmet needs is lower than those reported by these studies. This is probably related to the fact that in the present study a significant percentage of patients (26.7%) were psychiatric inpatients and 73.3% were psychiatric outpatients, in contrast to the majority of the referred studies [1, 8, 28, 29], where participants were evaluated mostly in the community or in an outpatient setting. This is also consistent with the Reynolds et al. study [11], where the level of unmet needs was lower than the previous studies.

Analyzing these results in relation to the dementia patients, it was found that the majority of unmet needs in daytime activities, social benefits, company, and psychological distress occurs in these participants, and the same is true for global needs (met and unmet). On the other hand, regarding functionality, the results show a significant negative correlation between the medical diagnosis of dementia and depression and the total scores obtained in Barthel, $r_{pb} = -.37$, $P = .009$, and Lawton Indexes, $r_{pb} = -.49$, $P < .001$, suggesting that low total scores in these two indexes are associated with dementia diagnosis, while slightly higher total scores are associated with depression diagnosis. These findings reveal that these patients present a wide range of needs in physical, psychological, and social areas that require great physical and psychological availability and good preparation by carers. This suggests that carers of patients with dementia are exposed to a greater demand, which can lead to higher levels of psychological distress.

With respect to the two items evaluated on the carers' needs, the majority had met or unmet needs in the domain of psychological distress, while in terms of information needs, this percentage is lower. Although there were no significant correlations between the diagnosis of dementia and the carers' psychological distress ($P = .566$), the high level of 59.1% of carers of the elderly with dementia, with global needs (met and unmet) in terms of psychological distress, is in line with the results obtained in most studies that

TABLE 4: Levels of need, as rated by the evaluator.

Items /domains	Needs identified <i>n</i> (%)			
	No need	Met need	Unmet need	Not known
(1) Accommodation	60 (80.0)	12 (16.0)	3 (4.0)	—
(2) Household skills	21 (28.0)	49 (65.3)	5 (6.7)	—
(3) Food	26 (34.7)	44 (58.7)	5 (6.7)	—
(4) Self-care	39 (52.0)	31 (41.3)	5 (6.7)	—
(5) Caring for other	66 (88.0)	9 (12.0)	—	—
(6) Daytime activities	26 (34.7)	19 (25.3)	30 (40.0)	—
(7) Memory	12 (16.0)	61 (81.3)	2 (2.7)	—
(8) Eyesight/hearing	24 (32.0)	47 (62.7)	4 (5.3)	—
(9) Mobility	45 (60.0)	29 (38.7)	1 (1.3)	—
(10) Continence	45 (60.0)	24 (32.0)	6 (8.0)	—
(11) Physical health	2 (2.7)	70 (93.3)	3 (4.0)	—
(12) Drugs	51 (68.0)	21 (28.0)	3 (4.0)	—
(13) Psychotic symptoms	61 (81.3)	12 (16.0)	2 (2.7)	—
(14) Psychological distress	14 (18.7)	54 (72.0)	7 (9.3)	—
(15) Information	20 (26.7)	53 (70.7)	2 (2.7)	—
(16) Safety (deliberate self-harm)	57 (76.0)	16 (21.3)	2 (2.7)	—
(17) Safety (accidental self-harm)	59 (78.7)	11 (14.7)	5 (6.7)	—
(18) Abuse/neglect	75 (100)	—	—	—
(19) Behaviour	66 (88.0)	6 (8.0)	3 (4.0)	—
(20) Alcohol	71 (94.7)	4 (5.3)	—	—
(21) Company	34 (45.3)	33 (44.0)	8 (10.7)	—
(22) Intimate relationships	64 (85.3)	7 (9.3)	4 (5.3)	—
(23) Money	36 (48.0)	36 (48.0)	3 (4.0)	—
(24) Benefits	56 (74.7)	9 (12.0)	10 (13.3)	—
(A) Carer's need for information	35 (46.7)	16 (21.3)	1 (1.3)	23 (30.7)
(B) Carer's psychological distress	13 (17.3)	34 (45.3)	5 (6.7)	23 (30.7)

suggest the existence of a high level of psychological distress in carers of patients with dementia, when compared to carers of patients with other chronic diseases [30–33]. In relation to the information and training needs of carers of elderly people with dementia, there is only a marginally significant association between the presence of these needs and the diagnosis of dementia, $X^2(2) = 5.82$, $P = .055$, verifying that, in this case, there is a tendency 41% of carers of elderly people with dementia registering global information needs. These data are also coherent with other studies that indicate that a high number of carers of people with dementia have information needs [34]. In this regard, other authors [35] state that in dementia lack of information may be a reason to use the health service, since many families surveyed do not understand executive deficits the meaning of an apraxia or delusional symptomatology.

4. Conclusions

This study shows a large deficit at the level of daytime activities associated with the progressive worsening of cognitive and functional deterioration in older people, resulting in the loss of levels of autonomy and the capability to satisfy their

own needs. It also reveals a high prevalence of dementia in the elderly associated with a wide range of needs related to memory, personal safety, satisfying basic and instrumental daily living activities, and psychological distress (in both the elderly and the caregivers).

The high overall number of needs of the elderly with dementia and the high level of psychological distress of their carers highlight the importance of taking into account the suffering of carers and the need to provide supportive interventions to maintain their emotional well being and enable them to provide high quality care. Despite the attention paid to the role of families in the care of patients with dementia, carers still express low levels of knowledge about the disease and high levels of psychological distress. In this sense, much more must be done to improve information on the disease, training in appropriate skills for cognitive disorders and behavioural management, and possible psychological support.

The results also suggest the need to structure activities and interventions, maximizing the potential of each person, encouraging abilities, and preventing progressive deterioration of elderly people's skills in order to improve their independence and quality of life.

Acknowledgments

The authors acknowledge the opportunity created by the Alto Minho Local Health Unit (ULSAM, EPE), Northern Portugal, for the realization of this study. Similarly, they recognize the contribution made by professionals in the Department of Psychiatry and Mental Health without whom it would not have been possible to pursue the aims and objectives of the study.

References

- [1] L. Fernandes, M. Gonalves-Pereira, A. Leuschner et al., "Validation study of the Camberwell Assessment of Need for the Elderly (CANE) in Portugal," *International Psychogeriatrics*, vol. 21, no. 1, pp. 94–102, 2009.
- [2] M. S. Mayor, O. Ribeiro, and C. Paúl, "Satisfaction in dementia and stroke caregivers: a comparative study," *Revista Latino-Americana de Enfermagem*, vol. 17, no. 5, pp. 620–624, 2009.
- [3] T. R. B. Benedetti, L. J. Borges, E. L. Petroski, and L. H. T. Gonçalves, "Atividade física e estado de saúde mental de idosos," *Revista Saúde Pública*, vol. 42, no. 2, pp. 302–307, 2008.
- [4] T. A. Marra, L. S. M. Pereira, C. D. C. M. Faria, D. S. Pereira, M. A. A. Martins, and M. G. A. Tirado, "Avaliação das atividades de vida diária de idosos com diferentes níveis de demência," *Revista Brasileira de Fisioterapia*, vol. 11, no. 4, pp. 267–273, 2007.
- [5] C. Paúl, "Old-old people: major recent findings and the European contribution to the state of the art," in *Geropsychology: European Perspectives for an Ageing World*, R. Fernández-Ballesteros, Ed., pp. 128–144, Hogrefe and Huber, Gottingen, Germany, 2007.
- [6] R. M. C. Rodrigues, *Avaliação comunitária de uma população de idosos: da funcionalidade à utilização de serviços [Dissertação de Doutoramento]*, Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto, 2007.
- [7] P. B. Baltes and J. Smith, "Novas fronteiras para o futuro do envelhecimento: a velhice bem-sucedida do idoso jovem aos dilemas da quarta idade," *A Terceira Idade*, vol. 17, no. 36, pp. 7–31, 2006.
- [8] M. Gonçalves-Pereira, L. Fernandes, A. Leuschner et al., "Versão portuguesa do CANE (Camberwell Assessment of Need for the Elderly): desenvolvimento e dados preliminares," *Revista Portuguesa de Saúde Pública*, vol. 25, pp. 7–18, 2007.
- [9] R. Mateos, M. Ybarzábal, M. Garcia, M. Amboage, and I. Fraguera, "Spanish CANE: validation study and utility in epidemiological surveys," in *CANE: Camberwell Assessment of Need for the Elderly*, M. Orrell and G. Hancock, Eds., pp. 21–28, Gaskell, London, UK, 2004.
- [10] M. Orrell and G. Hancock, *CANE: Camberwell Assessment of Need for the Elderly*, Gaskell, London, UK, 2004.
- [11] T. Reynolds, G. Thornicroft, M. Abas et al., "Camberwell assessment of need for the elderly (CANE). Development, validity and reliability," *British Journal of Psychiatry*, vol. 176, pp. 444–452, 2000.
- [12] A. C. Hart, M. S. Stegman, and B. Ford, *ICD-9-CM, 2010 Professional for Hospitals: International Classification of Diseases, 9th Revision, Clinical Modification*, vol. 1–3, Ingenix, Salt Lake City, Utah, USA, 6th edition, 2009.
- [13] M. F. Folstein, S. E. Folstein, and P. R. McHugh, "Mini mental state: a practical method for grading the cognitive state of patients for the clinician," *Journal of Psychiatric Research*, vol. 12, no. 3, pp. 189–198, 1975.
- [14] K. I. Shulman, R. Shedletsky, and I. L. Silver, "The challenge of time: clock-drawing and cognitive function in the elderly," *International Journal of Geriatric Psychiatry*, vol. 1, pp. 135–140, 1986.
- [15] J. A. Yesavage, T. L. Brink, and T. L. Rose, "Development and validation of a geriatric depression screening scale: a preliminary report," *Journal of Psychiatric Research*, vol. 17, no. 1, pp. 37–49, 1983.
- [16] W. W. Zung, "A rating instrument for anxiety disorders," *Psychosomatics*, vol. 12, no. 6, pp. 371–379, 1971.
- [17] F. I. Mahoney and D. W. Barthel, "Functional evaluation: the barthel index," *Maryland State Medical Journal*, vol. 14, pp. 56–61, 1965.
- [18] M. P. Lawton and E. M. Brody, "Assessment of older people: self-maintaining and instrumental activities of daily living," *Gerontologist*, vol. 9, no. 3, pp. 179–186, 1969.
- [19] M. Graffar, "Une méthode de classification sociale d'échantillons de population," *Courrier*, vol. 6, pp. 455–459, 1956.
- [20] M. Guerreiro, *Contributo da neuropsicologia para o estudo das demências [Dissertação de Doutoramento]*, Faculdade de Medicina de Lisboa, 1998.
- [21] J. Morgado, C. S. Rocha, C. Maruta, M. Guerreiro, and I. P. Martins, "New normative values of Mini-Mental State Examination," *Sinapse*, vol. 9, no. 2, pp. 10–16, 2009.
- [22] J. Cacho, R. García-García R, J. Arcaya, J. L. Vicente, and N. Lantada, "Una propuesta de aplicación y puntuación del test del reloj en la enfermedad de Alzheimer," *Revista Neurologia*, vol. 28, no. 7, pp. 648–655, 1999.
- [23] J. Barreto, A. Leuschner, F. Santos, and M. Sobral, *Escala de Depressão Geriátrica: Tradução Portuguesa da Geriatric Depression Scale, de Yesavage, et al.*, Grupo Estudos de Envelhecimento Cerebral e Demências, Lisboa, Portugal, 2003.
- [24] A. V. Serra, E. Ponciano, and J. Relvas, "Aferição da escala de auto-avaliação de ansiedade, de Zung, numa amostra de população portuguesa—II.-Sua avaliação como instrumento de medida," *Psiquiatria Clínica*, vol. 3, no. 4, pp. 203–213, 1982.
- [25] F. Araújo, J. L. P. Ribeiro, A. Oliveira, and C. Pinto, "Validação do Índice de Barthel numa amostra de idosos não institucionalizados," *Revista Portuguesa de Saúde Pública*, vol. 25, no. 2, pp. 59–66, 2007.
- [26] F. Araújo, J. L. P. Ribeiro, A. Oliveira, C. Pinto, and T. Martins, "Validação da escala de Lawton e Brody numa amostra de idosos não institucionalizados," in *Actas do 7 Congresso Nacional de Psicologia da Saúde*, pp. 655–659, Universidade do Porto, 2008.
- [27] L. Fernandes, *Fatores biopsicológicos e dinâmica familiar na doença asmática [Tese de Doutoramento]*, Faculdade de Medicina, Universidade do Porto, 2004.
- [28] W. Houtjes, B. van Meijel, D. J. H. Deeg, and A. T. F. Beekman, "Unmet needs of outpatients with late-life depression; a comparison of patient, staff and carer perceptions," *Journal of Affective Disorders*, vol. 134, no. 1, pp. 242–248, 2011.
- [29] C. Miranda-Castillo, B. Woods, K. Galboda, S. Oomman, C. Olojugba, and M. Orrell, "Unmet needs, quality of life and support networks of people with dementia living at home," *Health and Quality of Life Outcomes*, vol. 8, article 132, 2010.
- [30] J. M. García-Alberca, B. Cruz, J. P. Lara et al., "Disengagement coping partially mediates the relationship between caregiver burden and anxiety and depression in caregivers of people

with Alzheimer's disease. Results from the MÁLAGA-AD study," *Journal of Affective Disorders*, vol. 136, no. 3, pp. 848–856, 2012.

- [31] J. R. Day and R. A. Anderson, "Compassion fatigue: an application of the concept to informal caregivers of family members with dementia," *Nursing Research and Practice*, vol. 2011, Article ID 408024, 10 pages, 2011.
- [32] B. Schoenmakers, F. Buntinx, and J. Delepeleire, "Supporting the dementia family caregiver: the effect of home care intervention on general well-being," *Aging and Mental Health*, vol. 14, no. 1, pp. 44–56, 2010.
- [33] C. Cooper, T. B. S. Balamurali, A. Selwood, and G. Livingston, "A systematic review of intervention studies about anxiety in caregivers of people with dementia," *International Journal of Geriatric Psychiatry*, vol. 22, no. 3, pp. 181–188, 2007.
- [34] E. Rosa, G. Lussignoli, F. Sabbatini et al., "Needs of caregivers of the patients with dementia," *Archives of Gerontology and Geriatrics*, vol. 51, no. 1, pp. 54–58, 2010.
- [35] M. Gonçalves-Pereira and D. Sampaio, "Psicoeducação familiar na demência: da clínica à saúde pública," *Revista Portuguesa de Saúde Pública*, vol. 29, no. 1, pp. 3–10, 2011.

Research Article

A Warning Index Used in Prescreening for Alzheimer's Disease, Based on Self-Reported Cognitive Deficits and Vascular Risk Factors for Dementia in Elderly Patients with Type 2 Diabetes

Toshioki Matsuzawa,¹ Toshihiro Takata,¹ Koichi Yokono,¹ Hiroo Ueda,² Kensuke Moriwaki,³ Isao Kamae,³ Katsuya Urakami,⁴ and Takashi Sakurai^{1,5}

¹ Department of General Medicine, Kobe University Graduate School of Medicine, Kobe 650-0017, Japan

² Department of Metabolism, Kobe Mahoshi Hospital, Kobe 651-1242, Japan

³ Department of Biotatistics, Kobe University Graduate School of Medicine, Kobe 650-0017, Japan

⁴ Department of Biological Regulation, School of Health Sciences, Faculty of Medicine, Tottori University, Yonago 683-8503, Japan

⁵ Center of Comprehensive Care and Research on Memory Disorders, National Center for Geriatrics and Gerontology, Obu 474-8511, Japan

Correspondence should be addressed to Takashi Sakurai, tsakurai@ncgg.go.jp

Received 20 June 2012; Revised 9 September 2012; Accepted 10 September 2012

Academic Editor: Hiroyuki Umegaki

Copyright © 2012 Toshioki Matsuzawa et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background/Aims. Diabetes might increase the risk of Alzheimer's disease (AD). For detecting dementia, it is typical to obtain informants' perceptions of cognitive deficits, but such interviews are usually difficult in routine care. We aimed to develop a model for predicting mild to moderate AD using a self-reported questionnaire and by evaluating vascular risk factors for dementia in elderly subjects with diabetes. *Methods.* We recruited 286 diabetic and 155 nondiabetic elderly subjects. There were 25 patients with AD and 261 cognitively normal individuals versus 30 with AD and 125 normal subjects, respectively. Each participant answered subjective questions on memory deficits and daily functioning. Information on vascular risk factors was obtained from clinical charts, and multivariate logistic regression was used to develop a model for predicting AD. *Results.* The predicted probabilities used in screening for AD in diabetic subjects constituted age, education, lower diastolic blood pressure, subjective complaints of memory dysfunction noticeable by others, and impaired medication, shopping, and travel outside a familiar locality. Receiver operating characteristic analysis revealed a satisfactory discrimination for AD specific for diabetic elderly subjects, with 95.2% sensitivity and 90.6% specificity. *Conclusion.* This is the first useful index that can prescreen for AD in elderly subjects with diabetes.

1. Introduction

The link between vascular risk factors and dementia has recently attracted considerable attention and the impact of diabetes on a significant correlation of such factors with dementia is consistent [1–4]. However, mild cognitive dysfunction remains undetected and untreated in a considerable proportion of patients, resulting in several difficulties when treating diabetic elderly individuals. In screening for dementia-related disorders, handy cognitive tests such as the mini-mental state examination (MMSE) and the Hasegawa dementia scale-revised (HDS-R) are available. We have

proposed screening indices for Alzheimer's disease (AD) using some weighted subscales of the MMSE and HDS-R, which are useful to discriminate early AD in diabetic elderly subjects [5, 6]. However, even such brief neuropsychological tests impose burdens on practitioners in ambulatory care, because the number of patients with diabetes is increasing markedly in Japan [7]. A more simple and succinct prescreening procedure is thus needed to identify individuals with high risks for cognitive decline among diabetic elderly subjects.

In the diagnostic workup for patients with dementia, it is typical to obtain information from an informant about

cognitive deficits and problems in daily functioning. It has been postulated that the informant's perception of cognitive deficits correlates with objective memory testing and can differentiate between groups with and without dementia [8]. A more reliable predictor can be a discrepancy between the demented patient's and an informant's reports on cognitive status [9]. However, to obtain information on cognitive deficits from caregivers is usually difficult in the routine care of patients with diabetes. To overcome this dilemma in screening for AD in diabetic elderly subjects, we aimed to develop a disease-specific model for predicting mild to moderate AD. The first goal of this study was to administer a questionnaire about those patients' perceptions of memory problems and impaired daily functioning that are specifically evident in AD. Second, we aimed to test the association of vascular risk factors, such as hypertension, dyslipidemia, and obesity, with AD. The final goal was to propose a predictive index for AD using a comprehensive assessment of these clinical variables and to verify its propriety in nondiabetic participants.

2. Materials and Methods

2.1. Study Participants. A total of 286 diabetic patients and 155 nondiabetic individuals aged 65 or older were recruited from the outpatient's clinic of the Kobe University Hospital, Japan. The institutional review boards of Kobe University Hospital approved the research protocol, and written informed consent was obtained from each patient and his or her family members. The diabetic group had 25 subjects with mild to moderate AD and the nondiabetic group had 30. AD was diagnosed as "probable AD" from a complete medical, neuropsychological, and neuroimaging evaluation by the multidisciplinary geriatric team at each site, based on the criteria from the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association [10]. In this study, mild to moderate AD was defined as a score of greater than 14 on the MMSE [11]. Patients were evaluated to rule out other causes of cognitive impairment including alcohol or drug abuse, major depression, delirium, systemic cancer, chronic infections, stroke, hypoxia, severe cardiopulmonary disorders, nutritional disorders, intracranial mass lesions, psychoses, brain trauma, or other neurological disorders including Parkinson disease or Huntington disease.

The cognitively normal participants comprised 261 and 125 participants in the diabetic and nondiabetic groups, respectively. For the primary selection of cognitive normal group, geriatric physicians, who were familiar to consultation of the demented disorders, asked the patients and their caregivers about their complaints on cognitive decline and the daily life function. Their cognitive functions were evaluated using the MMSE and a computerized test battery for AD screening [12]. They had no neurological or psychiatric disorders. After this consultation, each physician determined their cognitive status as normal.

2.2. Self-Reported Questionnaire for Subjective Complaints of Memory and Daily Functioning. During the first visit, one

of three trained research assistants in the geriatric division assessed participants using a self-reported questionnaire that measures perception of memory deficits and impairment of activities in daily living (ADLs). The questionnaire contained three questions about each patient's perception of memory problems, which were derived from the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX) interview on memory complaints [13]. The questions were as follows. (1) Do you have any complaints concerning your memory? (2) Do other people find you forgetful? (3) Do you often use notes to avoid forgetting things?

Achievement of basic and instrumental ADLs was also investigated for each individual. Basic ADLs referred to the ability to complete simple functions including walking and showering, whereas instrumental ADLs comprised more complex activities required for independent living, including grocery shopping, managing finances, meal preparation, travel outside a familiar locality, taking medication, and using public transportation [14, 15]. We assigned "1" and "0", to "yes" and "no" answers for each question, respectively.

2.3. Clinical Characteristics of Diabetes and Vascular Risk Factors for Dementia. Information on diabetes and other vascular risk factors for dementia was obtained from clinical charts. Body mass index (BMI), blood pressure, levels of HbA1c, total cholesterol, triglycerides, and high density lipoprotein (HDL)-cholesterol, duration of diabetes, therapeutic use of antihyperglycemic agents and/or insulin (insulin dose and frequency of injection per day), and previous hypoglycemic episodes (number of occasions in the previous year) were investigated. The HbA1c levels are expressed in the National Glycohemoglobin Standardization Program units. The participants were also asked questions on the compliance with diet and exercise therapies (in minutes per week) by the physicians.

2.4. Statistical Analysis. Logistic regression analysis and χ^2 test were used to compare the demographic, subjective cognitive complaints, and vascular risk factors between subjects with AD and cognitively normal individuals in both groups. Any significant items were then entered into a multivariate logistic regression to develop a model for predicting AD, using stepwise selection with an inclusion criteria of $P < 0.15$ and exclusion criteria of $P > 0.2$ [16]. Using a developed model, a receiver operating characteristic (ROC) curve was constructed to test the relationship between sensitivity and specificity using varying cutoff points of the model for predicting AD. The area under the curve was calculated. Statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The level of significance was set at $P < 0.05$ for all statistical analyses.

3. Results

3.1. Demographics and Clinical Profiles. The demographic and clinical features of diabetic and nondiabetic subjects are presented in Table 1. Among the subjects with diabetes, having AD was characterized by being older, being female, having a lower educational level, and having lower diastolic

TABLE 1: Demographic and clinical profile of study participants.

	Diabetic subjects		Nondiabetic subjects	
	AD	CN	AD	CN
Number	25	261	30	125
Age (years)	78.6 (5.8)*	72.7 (5.6)	77.5 (6.3)	72.6 (4.6)
Female (%)	68.0*	50.2	80.0 [#]	50.4
Education (years)	9.3 (2.0)*	11.9 (3.0)	11.0 (2.5)	12.5 (3.0)
BMI (kg/m ²)	23.2 (4.6)	23.0 (3.4)	21.7 (2.2) [#]	23.6 (4.2)
Systolic blood pressure (mmHg)	127.0 (16.0)	130.0 (13.3)	126.6 (17.3)	128.6 (15.7)
Diastolic blood pressure (mmHg)	60.0 (15.1)*	70.0 (9.4)	58.5 (16.0) [#]	72.0 (9.0)
Total cholesterol (mg/dL)	197.8 (43.7)	206.1 (30.0)	214.4 (34.1)	196.1 (29.8)
Triglyceride (mg/dL)	118.9 (49.3)	157.4 (83.7)	131.0 (61.6)	109.8 (54.0)
HDL-cholesterol (mg/dL)	60.2 (12.5)	53.4 (14.7)	69.5 (18.6)	60.9 (17.9)
HbA1c (%)	7.1 (0.8)	7.2 (1.1)	—	—
Duration of diabetes (years)	16.6 (9.9)	14.6 (10.7)	—	—
Hypoglycemic episodes (times/year)	4.5 (13.0)	11.4 (47.2)	—	—
Insulin use (%)	40.0	30.3	—	—
Insulin dose (U/day)	17.0 (11.6)	22.7 (12.9)	—	—
Insulin injection (times/day)	2.4 (1.0)	2.4 (1.0)	—	—
Oral hypoglycemic agent use (yes = 1, no = 0)	0.8 (0.4)	0.7 (0.5)	—	—
Exercise (minutes/week)	72.3 (12.9)*	221.9 (468.7)	209.3 (161)	225.8 (208.7)
Diet therapy compliance (very poor = 1, poor = 2, normal = 3, good = 4)	3.2 (0.9)	3.3 (0.6)	3.3 (0.7)	3.4 (0.8)
History of heart disease (%)	4.0	19.9	3.7	20.0
History of cerebrovascular disease (%)	12.0	10.0	6.7	8.0
MMSE (score)	20.6 (3.8)*	28.0 (0.0)	20.8 (3.7) [#]	27.4 (2.1)
Computer-based screening test (score)	9.0 (2.9)*	14.3 (0.5)	9.9 (2.9) [#]	14.4 (0.5)

Values are the mean and (SD) and percentages. * $P < 0.05$ and [#] $P < 0.05$ compared with cognitively normal subjects in the diabetic and nondiabetic groups, respectively. AD: Alzheimer's disease; CN: cognitively normal; BMI: body mass index; MMSE: mini-mental state examination.

blood pressure compared with cognitively normal controls. Exercise was less frequently performed by patients with AD. In contrast, HbA1c levels, duration of diabetes, and lipid profiles were not significantly different between subjects with AD and cognitively normal individuals. Although pharmacological treatment of diabetes and previous hypoglycemic episodes have been reported to increase the risk of dementia [1, 17], the incidence of hypoglycemic episodes and the frequency of use of oral antihyperglycemic agents and/or insulin (insulin doses, frequency of injection) did not show any difference between the AD and cognitively normal groups. In nondiabetic participants, being female and having a lower BMI and lower diastolic blood pressure were characteristics of patients with mild to moderate AD.

The overall mean scores and ranges of the MMSE were 20.6 (14–28) and 20.8 (14–27) for AD in the diabetic and nondiabetic elderly subjects, respectively. This suggests that our subjects with AD had mild to moderate forms [11]. Cognitive status was also evaluated by a computerized neuropsychological test battery for screening AD, of which a score of 14 suggests normal cognition and one of ≤ 12 is associated with AD, according to the original study data of the developer [12]. The averaged scores of this cognitive test among the diabetic and nondiabetic elderly subjects were 9.0 and 9.9 for those with AD, and 14.3 and 14.4 for the cognitively normal subjects, respectively.

3.2. Subjective Complaints of Memory and Daily Functioning. Among three distinct questions on subjective memory complaints (Table 2), self-perception of memory dysfunction noticeable by himself/herself was not different between subjects with AD and normal controls in both diabetic and nondiabetic participants, while subjective complaint of memory deficits noticeable by others was significantly increased among the patients with AD. Responses to the question about the use of notes to avoid forgetting things tended to decrease in those with AD.

Although basic ADLs such as walking and showering were similar between the subjects with AD and the cognitively normal controls, the self-reported achievement of instrumental ADLs (grocery shopping, managing finances, meal preparation, travel outside familiar surroundings, correct use of medication, and public transportation) was significantly impaired in patients with AD among those with diabetes (Table 3). In the nondiabetic group, activities for shower, finance management, cooking, traveling, medication compliance, and use of public transport were impaired in AD.

3.3. Prediction of AD Using a Self-Reported Questionnaire and Risk Factors for Dementia. To develop a model for predicting AD using stepwise selection, clinical variables that were shown to be different at $P < 0.05$ (Tables 1–3)

TABLE 2: Subjective complaints of memory deficits.

	Diabetic subjects		Nondiabetic subjects	
	AD	CN	AD	CN
Do you have any complaints concerning your memory? (yes, %)	64.0	70.1	83.3	67.2
Do other people find you forgetful? (yes, %)	60.0*	29.9	60.0 [#]	30.4
Do you often use notes to avoid forgetting things? (yes, %)	72.0*	82.3	73.3	86.4

Values are the percentages of “yes” answer to each question. Comparison of subjective cognitive complaints between subjects with AD and cognitively normal subjects was performed by using the χ^2 test. * $P < 0.05$ and [#] $P < 0.05$ compared with cognitively normal subjects in the diabetic and nondiabetic groups, respectively. AD: Alzheimer's disease; CN: cognitively normal.

TABLE 3: Self-reporting of basic and instrumental activities of daily living (ADLs).

	Diabetic subjects		Nondiabetic subjects	
	AD	CN	AD	CN
Basic ADL				
Walking (able, %)	80.0	90.0	80.0	89.6
Shower (able, %)	92.0	97.8	80.0 [#]	96.8
Instrumental ADL				
Grocery shopping (able, %)	80.0*	96.1	90.0	97.6
Managing finances (able, %)	68.0*	96.2	73.3 [#]	96.8
Meal preparation (able, %)	76.0*	91.2	90.0	96.0
Travel outside familiar surroundings (able, %)	48.0*	95.0	50.0 [#]	95.2
Medication compliance (able, %)	48.0*	96.2	63.3 [#]	95.2
Ability to use public transport (able, %)	76.0*	96.2	83.3 [#]	96.0

Values are the percentages of “able” answer to each life function. Comparison of ADLs between subjects with AD and cognitively normal subjects was performed by using the χ^2 test. * $P < 0.05$ and [#] $P < 0.05$ compared with cognitively normal subjects in the diabetic and nondiabetic groups, respectively. AD: Alzheimer's disease; CN: cognitively normal.

were entered into a multivariate logistic regression. This showed that advanced age ($P < 0.001$), lower education ($P < 0.001$), lower diastolic blood pressure ($P = 0.029$), memory dysfunction noticeable by others ($P = 0.018$), and impaired activity in taking medication ($P = 0.001$) were independently correlated with AD in diabetic elderly subjects. The predicted probabilities from the multivariate logistic regression analysis in screening for AD were as follows: $\text{Log } p/(1-p) = 0.253x_1 - 0.078x_2 - 3.740x_3 - 1.888x_4 + 1.883x_5 - 1.405x_6 - 0.453x_7 - 6.769$; where $x_1 = \text{age (years)}$, $x_2 = \text{diastolic blood pressure (mmHg)}$, $x_3 = \text{medication (yes, 1; no, 0)}$, $x_4 = \text{shopping (yes, 1; no, 0)}$, $x_5 = \text{memory dysfunction noticeable by others (yes, 1; no, 0)}$, $x_6 = \text{travel outside familiar surroundings (yes, 1; no, 0)}$, and $x_7 = \text{education (years)}$.

ROC analysis revealed a satisfactory discrimination for predicting AD in diabetic elderly subjects with a sensitivity of 95.2% and a specificity of 90.6%, when the cutoff point of the model was set at 0.7888 (Figure 1(a)). When predicted probabilities from the regression analysis in diabetic participants were applied for nondiabetic subjects, a prediction of AD was discriminated with 56.7% sensitivity and 89.6% specificity.

Similarly, multivariate logistic regression revealed independent associations of lower diastolic blood pressure ($P = 0.001$) and medication compliance ($P = 0.017$) with AD in the nondiabetic group. The predicted

probabilities for screening of mild to moderate AD in nondiabetic participants were found to be: $\text{Log } p/(1-p) = -0.156x_1 - 1.608x_2 - 2.791x_3 - 0.919x_4 - 1.11x_5 + 12.6$; where $x_1 = \text{diastolic blood pressure (mmHg)}$, $x_2 = \text{sex (male, 1; female, 0)}$, $x_3 = \text{medication (yes, 1; no, 0)}$, $x_4 = \text{finance (yes, 1; no, 0)}$, and $x_5 = \text{travel outside familiar surroundings (yes, 1; no, 0)}$. The ROC curve of the nondiabetic subjects was shown in Figure 1(b).

4. Discussion

This study demonstrates a simple but effective strategy that can be used in screening for mild to moderate AD in diabetic elderly subjects. Although the significance of an informant's perception of a patient's cognitive deficits has been emphasized previously for detecting dementia [8, 9], our results clearly indicate that comprehensive assessment of symptomatic deficits of memory and daily functioning, together with vascular risk factors for dementia, enables the discrimination of a subject developing mild to moderate AD with good sensitivity and specificity. The best prediction was obtained by the multivariate regression model that included older age, lower educational level, lower diastolic blood pressure, memory deficits noticeable by others, and impaired instrumental ADLs (shopping, medication, and travel outside familiar surroundings), which was specific for diabetic elderly subjects. For nondiabetic participants,

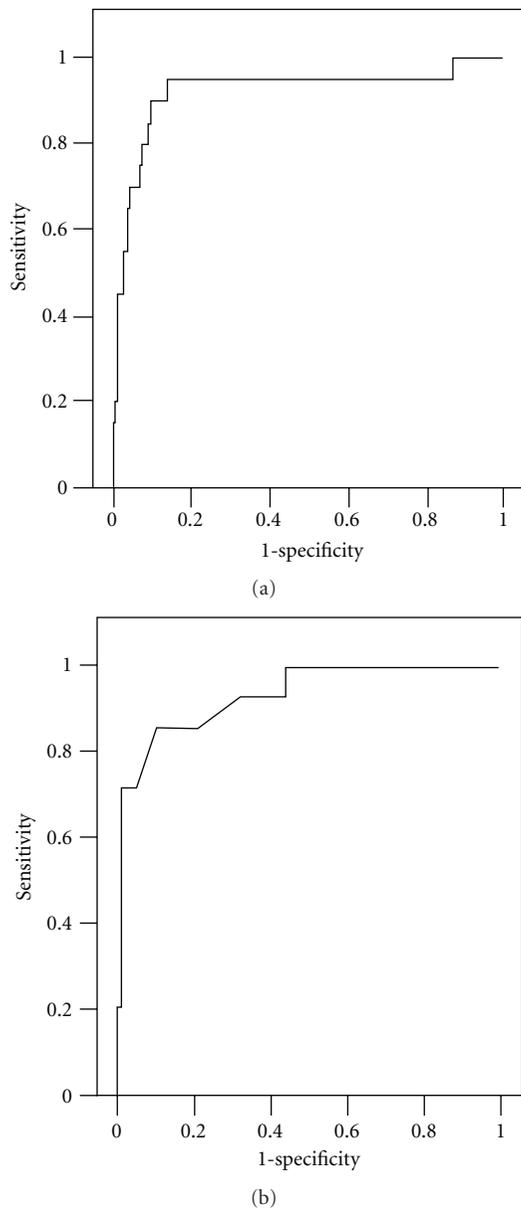


FIGURE 1: Receiver operating characteristic (ROC) curve of the best multivariate logistic regression analysis model for predicting mild to moderate Alzheimer's disease among diabetic elderly subjects (a) and nondiabetic individuals (b). The area under the curve (AUC) was 0.97 (a) and 0.93 (b).

a distinct set of variables including female gender, lower diastolic blood pressure, and impairment in dealing with finances, medication, and travel predicted AD. Our results for the first time provide a handy and succinct tool to serve as an index for predicting mild to moderate AD in elderly Japanese subjects with type 2 diabetes mellitus.

4.1. Subjective Complaints of Memory Deficits. This study indicates that particular questions about subjective memory complaints are predictive for AD in diabetic participants. This finding is somewhat surprising, given the rather

mixed results in the literature on the value of subjective memory complaints [18]. Subjective complaints of memory deficits are often observed among subjects in the early stage of AD, but decrease gradually as the disease progresses [19]. Many studies have reported that subjective memory complaints are more often associated with depressed mood rather than cognitive impairment [8, 20, 21]. However, recent community-based studies with longitudinal designs indicate that memory complaints are predictive of cognitive decline and incident dementia, particularly in nondemented individuals with cognitive impairment, although not all studies show this association among aged persons [22–28]. Self-reported poor memory is indeed a main component of the diagnostic criteria for mild cognitive impairment [29]. In this connection, a clear definition of memory complaints might be important to explain the divergent results on their significance. Thus, this study evaluated the reliability of three different questions on subjective memory complaints originating from the CAMDEX interview [13]. Although two out of three questions on self-perception of memory deficits did not predict AD, the last question asking about memory decline noticeable by others was distinguishable even after adjustment with possible confounders, indicating the significance of particular self-reported questionnaires about subjective memory complaints when screening for AD in diabetic elderly subjects.

4.2. Meaning of Self-Reported Performance of Instrumental ADLs. Loss of functional, but not of basic ADLs, proved to be predictive for having mild to moderate AD. Even mild degrees of cognitive deterioration can have negative impacts on the ability to perform complex ADLs [30–32]. The completion of instrumental ADLs requires competent memory, but also involves executive functions. These entail complex cognitive abilities that enable an individual to perform tasks that include planning, problem solving, anticipation, and inhibition of irrelevant processing [33]. In a recent review by the Committee on Research of the American Neuropsychiatry Association, an expert panel suggested that measures of executive functions correlate strongly with functional capacities [34]. However, clinical assessment of functional abilities in the daily life of subjects with AD is also dependent on accurate information. Most instruments designed to assess instrumental ADLs can be influenced by the patient's personality, mood, and cognitive status [35]. Patients with AD often overestimate their functional abilities. In this respect, it should be mentioned that the capacity for self-observation is considerably preserved in patients with mild to moderate AD, although a decline in patient self-reporting on this issue is less dramatic than that seen in family reports [36, 37].

Our results indicate that among the ADL disability, impaired ability to deal with medication is the most predictive for AD in both diabetic and nondiabetic individuals. Besides impaired activity for travel outside familiar surroundings, shopping activity was specifically involved with AD in the diabetic participants, and financial ability in the nondiabetic subjects. Shopping and managing finances are classified in the identical subdomain of functional ADLs

that correspond to the identical staging of dementia [38]. Errors in shopping tasks are more likely to be associated with decrements in visual searching skills, selective attention, and rapid information processing [39]. Impaired attention and decreased information processing speed have been reported in aged persons with type 2 diabetes [40].

4.3. Vascular Risk Factors for Predicting AD. There is a growing consensus that vascular disease may exacerbate or contribute to the manifestation of symptoms in subjects with dementia [41]. Barnes et al. [42] have reported that a late-life dementia risk index, composed of age, cognitive test performance, body mass index, apolipoprotein E ϵ 4 alleles, cerebral white matter disease, ventricular enlargement, internal carotid artery thickening, history of bypass surgery, slow physical performance, and lack of alcohol consumption, can accurately stratify older adults into those with low, moderate, and high risk of developing dementia. It has been postulated that midlife high blood pressure is a risk for late-life cognitive impairment and dementia, and low diastolic pressure in older adults might be associated with the subsequent development of dementia and AD [43, 44]. Accelerated atherosclerosis and low perfusion of cerebral blood flow in diabetic elderly subjects could be implicated in a mechanism of how abnormal blood pressure affects the onset of dementia. In contrast, no predictive power for other aspects of diabetes, including HbA1c level, lipid abnormalities, obesity, hypoglycemia, or treatment modality was found in the present study [1, 17].

4.4. Limitation and Strength. This study had several limitations. There were several biases in the selection of our participants, who were treated in the outpatient clinic of the Kobe University hospital. They tended to have serious diabetic complications and other morbidities, while they were also motivated for treatment of their illness. Despite this, our data might represent a best-case scenario for practitioners because we approached many physicians treating diabetes in aged persons. In addition, the effects of depressive mood on cognitive status were not evaluated, although patients with major depression were excluded from our participants. Finally, it might be possible that cognitive normal subjects include some individuals with mild cognitive impairment, because detailed cognitive tests were not performed in the cognitive normal group. However, geriatric physicians, who were familiar to consultation of the demented disorders, asked the patients and their caregivers about their complaints on cognitive decline and the daily life function. Their cognitive functions were evaluated using the MMSE and a computerized test battery for AD screening. After this consultation, each physician determined their cognitive status as normal.

On the other hand, the present study had several strengths. The advantage of screening for mild to moderate AD using this discriminating index has been clearly demonstrated in diabetic elderly subjects. Second, the model for predicting AD is so succinct and easily available that nonclinical staff in outpatient clinics could administer it with ease. This would greatly improve the burden of practitioners

who must face several clinical problems in elderly patients with diabetes. When considering a total scheme for detecting AD in diabetic elderly subjects, high-risk individuals can be selected using this warning index for AD. Such persons can then continue to a secondary evaluation using brief cognitive tests such as the MMSE and HDS-R [5, 6] and ultimately consult with specialists for dementia-related disorders.

5. Conclusions

We have proposed the importance of this maneuver in prescreening for AD, using this self-reported questionnaire and including vascular risk factors in the model. This approach is also applicable for nondiabetic elderly subjects. The clinical relevance of this index aimed at prescreening for AD should be validated by further investigations.

References

- [1] A. Ott, R. P. Stolk, F. Van Harskamp, H. A. P. Pols, A. Hofman, and M. M. B. Breteler, "Diabetes mellitus and the risk of dementia: the Rotterdam Study," *Neurology*, vol. 53, no. 9, pp. 1937–1942, 1999.
- [2] M. Yamada, F. Kasagi, H. Sasaki, N. Masunari, Y. Mimori, and G. Suzuki, "Association between dementia and midlife risk factors: the radiation effects research foundation Adult Health Study," *Journal of the American Geriatrics Society*, vol. 51, no. 3, pp. 410–414, 2003.
- [3] G. J. Biessels, S. Staekenborg, E. Brunner, C. Brayne, and P. Scheltens, "Risk of dementia in diabetes mellitus: a systematic review," *Lancet Neurology*, vol. 5, no. 1, pp. 64–74, 2006.
- [4] L. E. Middleton and K. Yaffe, "Promising strategies for the prevention of dementia," *Archives of Neurology*, vol. 66, no. 10, pp. 1210–1215, 2009.
- [5] T. Sakurai, M. Kuranaga, T. Akisaki, T. Takata, H. Endo, and K. Yokono, "Differential mini-mental state examination profiles of older people with diabetes mellitus with early Alzheimer's disease," *Journal of the American Geriatrics Society*, vol. 55, no. 6, pp. 955–956, 2007.
- [6] R. Tsukamoto, T. Akisaki, M. Kuranaga, T. Takata, K. Yokono, and T. Sakurai, "Hasegawa Dementia Scale—revised, for screening of early Alzheimer's disease in the elderly with type 2 diabetes," *Geriatrics and Gerontology International*, vol. 9, no. 2, pp. 213–215, 2009.
- [7] T. Sakurai, H. Taniguchi, S. Nambu et al., "Education of lifestyle risk factors associated with dementia likely to help primary care physicians to improve consultation for elderly people with dementia," *Journal of the American Geriatrics Society*, vol. 57, no. 12, pp. 2358–2361, 2009.
- [8] J. McGlone, S. Gupta, D. Humphrey, S. Oppenheimer, T. Mirsen, and D. R. Evans, "Screening for early dementia using memory complaints from patients and relatives," *Archives of Neurology*, vol. 47, no. 11, pp. 1189–1193, 1990.
- [9] M. C. Tierney, J. P. Szalai, W. G. Snow, and R. H. Fisher, "The prediction of Alzheimer disease: the role of patient and informant perceptions of cognitive deficits," *Archives of Neurology*, vol. 53, no. 5, pp. 423–427, 1996.
- [10] G. McKhann, D. Drachman, and M. Folstein, "Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health

- and Human Services Task Force on Alzheimer's disease," *Neurology*, vol. 34, no. 7, pp. 939–944, 1984.
- [11] B. Reisberg, S. G. Sclan, E. Franssen, A. Kluger, and S. Ferris, "Commentary: dementia staging in chronic care populations," *Alzheimer Disease and Associated Disorders*, vol. 8, no. 1, pp. S188–S205, 1994.
 - [12] M. Inoue, D. Jinbo, Y. Nakamura, M. Taniguchi, and K. Urakami, "Development and evaluation of a computerized test battery for Alzheimer's disease screening in community-based settings," *American Journal of Alzheimer's Disease and other Dementias*, vol. 24, no. 2, pp. 129–135, 2009.
 - [13] M. Roth, E. Tym, and C. Q. Mountjoy, "CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia," *British Journal of Psychiatry*, vol. 149, pp. 698–709, 1986.
 - [14] C. P. Hughes, L. Berg, and W. L. Danziger, "A new clinical scale for the staging of dementia," *British Journal of Psychiatry*, vol. 140, no. 6, pp. 566–572, 1982.
 - [15] R. Lindeboom, M. Vermeulen, R. Holman, and R. J. De Haan, "Activities of daily living instruments: optimizing scales for neurologic assessments," *Neurology*, vol. 60, no. 5, pp. 738–742, 2003.
 - [16] S. Menard, *Applied Logistic Regression Analysis*, Sage University Paper Series on Quantitative Applications in the Social Sciences, Series No. 07-1062002, Sage, Thousand Oaks, CA, 2nd edition.
 - [17] R. A. Whitmer, A. J. Karter, K. Yaffe, C. P. Quesenberry Jr., and J. V. Selby, "Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus," *JAMA*, vol. 301, no. 15, pp. 1565–1572, 2009.
 - [18] V. Kirchner, M. D. Elloy, L. E. Silver, and C. A. Kelly, "Are memory complaints predictive for dementia? A review of clinical and population-based studies," *International Journal of Geriatric Psychiatry*, vol. 15, no. 11, pp. 983–991, 2000.
 - [19] B. Reisberg, S. H. Ferris, M. J. De Leon, and T. Crook, "The global deterioration scale for assessment of primary degenerative dementia," *American Journal of Psychiatry*, vol. 139, no. 9, pp. 1136–1139, 1982.
 - [20] D. W. O'Connor, P. A. Pollitt, M. Roth, C. P. B. Brook, and B. B. Reiss, "Memory complaints and impairment in normal, depressed, and demented elderly persons identified in a community survey," *Archives of General Psychiatry*, vol. 47, no. 3, pp. 224–227, 1990.
 - [21] C. Derouesné, L. Lacomblez, S. Thibault, and M. LePoncin, "Memory complaints in young and elderly subjects," *International Journal of Geriatric Psychiatry*, vol. 14, no. 4, pp. 291–301, 1999.
 - [22] R. Tobiansky, R. Blizard, G. Livingston, and A. Mann, "The gospel oak study stage IV: the clinical relevance of subjective memory impairment in older people," *Psychological Medicine*, vol. 25, no. 4, pp. 779–786, 1995.
 - [23] B. Schmand, C. Jonker, C. Hooijer, and J. Lindeboom, "Subjective memory complaints may announce dementia," *Neurology*, vol. 46, no. 1, pp. 121–125, 1996.
 - [24] P. W. Schofield, K. Marder, G. Dooneief, D. M. Jacobs, M. Sano, and Y. Stern, "Association of subjective memory complaints with subsequent cognitive decline in community-dwelling elderly individuals with baseline cognitive impairment," *American Journal of Psychiatry*, vol. 154, no. 5, pp. 609–615, 1997.
 - [25] M. I. Geerlings, C. Jonker, L. M. Bouter, H. J. Adèr, and B. Schmand, "Association between memory complaints and incident Alzheimer's disease in elderly people with normal baseline cognition," *American Journal of Psychiatry*, vol. 156, no. 4, pp. 531–537, 1999.
 - [26] C. Jonker, L. J. Launer, C. Hooijer, and J. Lindeboom, "Memory complaints and memory impairment in older individuals," *Journal of the American Geriatrics Society*, vol. 44, no. 1, pp. 44–49, 1996.
 - [27] L. Bäckman, S. Jones, A. K. Berger, E. J. Laukka, and B. J. Small, "Multiple cognitive deficits during the transition to Alzheimer's disease," *Journal of Internal Medicine*, vol. 256, no. 3, pp. 195–204, 2004.
 - [28] A. F. Jorm, K. H. Masaki, H. Petrovitch, G. W. Ross, and L. R. White, "Cognitive deficits 3 to 6 years before dementia onset in a population sample: the Honolulu-Asia Aging Study," *Journal of the American Geriatrics Society*, vol. 53, no. 3, pp. 452–455, 2005.
 - [29] R. C. Petersen, "Mild cognitive impairment as a diagnostic entity," *Journal of Internal Medicine*, vol. 256, no. 3, pp. 183–194, 2004.
 - [30] D. C. Marson, S. M. Sawrie, S. Snyder et al., "Assessing financial capacity in patients with Alzheimer disease: a conceptual model and prototype instrument," *Archives of Neurology*, vol. 57, no. 6, pp. 877–884, 2000.
 - [31] R. Perneczky, C. Pohl, C. Sorg et al., "Complex activities of daily living in mild cognitive impairment: conceptual and diagnostic issues," *Age and Ageing*, vol. 35, no. 3, pp. 240–245, 2006.
 - [32] S. T. Farias, D. Mungas, B. R. Reed, D. Harvey, D. Cahn-Weiner, and C. DeCarli, "MCI is associated with deficits in everyday functioning," *Alzheimer Disease and Associated Disorders*, vol. 20, no. 4, pp. 217–223, 2006.
 - [33] M. D. Lezak, *Neurobehavioral Variables and Diagnostic Issues: neuropsychological Assessment*, Oxford University Press, New York, NY, USA, 3rd edition, 1995.
 - [34] D. R. Royall, E. C. Lauterbach, D. Kaufer, P. Malloy, K. L. Coburn, and K. J. Black, "The cognitive correlates of functional status: a review from the Committee on Research of the American Neuropsychiatric Association," *Journal of Neuropsychiatry and Clinical Neurosciences*, vol. 19, no. 3, pp. 249–265, 2007.
 - [35] M. Weinberger, G. P. Samsa, K. Schmader, S. M. Greenberg, D. B. Carr, and D. S. Wildman, "Comparing proxy and patients' perceptions of patients' functional status: results from an outpatient geriatric clinic," *Journal of the American Geriatrics Society*, vol. 40, no. 6, pp. 585–588, 1992.
 - [36] H. A. Kiyak, L. Teri, and S. Borson, "Physical and functional health assessment in normal aging and in Alzheimer's disease: self-reports vs family reports," *Gerontologist*, vol. 34, no. 3, pp. 324–330, 1994.
 - [37] K. Pérès, V. Chrysostome, C. Fabrigoule, J. M. Orgogozo, J. F. Dartigues, and P. Barberger-Gateau, "Restriction in complex activities of daily living in MCI: impact on outcome," *Neurology*, vol. 67, no. 3, pp. 461–466, 2006.
 - [38] E. Gleichgerricht, J. Camino, M. Roca, T. Torralva, and F. Manes, "Assessment of functional impairment in dementia with the spanish version of the activities of daily living questionnaire," *Dementia and Geriatric Cognitive Disorders*, vol. 28, no. 4, pp. 380–388, 2009.
 - [39] V. G. Wadley, O. Okonkwo, M. Crowe, and L. A. Ross-Meadows, "Mild cognitive impairment and everyday function:

- evidence of reduced speed in performing instrumental activities of daily living," *American Journal of Geriatric Psychiatry*, vol. 16, no. 5, pp. 416–424, 2008.
- [40] M. W. J. Strachan, I. J. Deary, F. M. E. Ewing, and B. M. Frier, "Is type II diabetes associated with an increased risk of cognitive dysfunction? A critical review of published studies," *Diabetes Care*, vol. 20, no. 3, pp. 438–445, 1997.
- [41] F. Panza, A. D'Introno, A. M. Colacicco et al., "Cognitive frailty: predementia syndrome and vascular risk factors," *Neurobiology of Aging*, vol. 27, no. 7, pp. 933–940, 2006.
- [42] D. E. Barnes, K. E. Covinsky, R. A. Whitmer, L. H. Kuller, O. L. Lopez, and K. Yaffe, "Predicting risk of dementia in older adults: the late-life dementia risk index," *Neurology*, vol. 73, no. 3, pp. 173–179, 2009.
- [43] J. Verghese, R. B. Lipton, C. B. Hall, G. Kuslansky, and M. J. Katz, "Low blood pressure and the risk of dementia in very old individuals," *Neurology*, vol. 61, no. 12, pp. 1667–1672, 2003.
- [44] C. Qiu, B. Winblad, and L. Fratiglioni, "The age-dependent relation of blood pressure to cognitive function and dementia," *The Lancet Neurology*, vol. 4, no. 8, pp. 487–499, 2005.

Research Article

Gender Differences in Dementia Spousal Caregiving

**Minna Maria Pöysti,¹ Marja-Liisa Laakkonen,² Timo Strandberg,³ Niina Savikko,⁴
Reijo Sakari Tilvis,⁵ Ulla Eloniemi-Sulkava,⁶ and Kaisu Hannele Pitkälä⁴**

¹ *The Social Insurance Institution of Finland and Unit of Primary Health Care, Helsinki University Central Hospital, P.O. Box 20, 00014 University of Helsinki, Helsinki, Finland*

² *Unit of Primary Health Care, Helsinki University Central Hospital and City of Helsinki Health Center, P.O. Box 20, 00140 University of Helsinki, Helsinki, Finland*

³ *Geriatric Clinic, Department of General Internal Medicine and Geriatric, Helsinki University Central Hospital and Institute of Health Sciences and Geriatrics, University of Oulu, P.O. Box 5000, 90014 Oulu, Finland*

⁴ *Unit of Primary Health Care, Helsinki University Central Hospital and Department of General Practice, University of Helsinki, P.O. Box 20, 00140 University of Helsinki, Helsinki, Finland*

⁵ *Geriatric Clinic, Department of General Internal Medicine and Geriatric, Helsinki University Central Hospital, P.O. Box 20, 00140 University of Helsinki, Helsinki, Finland*

⁶ *Palmenia Centre for Continuing Education, University of Helsinki, P.O. Box 58, 00014 University of Helsinki, Helsinki, Finland*

Correspondence should be addressed to Minna Maria Pöysti, minna.poysti@geri.fi

Received 6 July 2012; Accepted 24 August 2012

Academic Editor: Hajime Takechi

Copyright © 2012 Minna Maria Pöysti et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The proportion of male caregivers is rapidly increasing. However, there are few large scale studies exploring gender differences in the burden or coping with caregiving. We investigated this among caregivers of patients with dementia. The study cohort consisted of 335 dyads of wife-husband couples from two studies including dementia patients and their spousal caregivers. Baseline mini-mental state examination (MMSE), clinical dementia rating scale (CDR), neuropsychiatric inventory (NPI), cornell depression scale and charlson comorbidity index (CCI) were used to describe patients with dementia, Zarit burden scale and geriatric depression scale were used to measure experienced burden and depression of caregivers. Mean age of caregivers was 78 years. There were no differences in depression, satisfaction with life, or loneliness according to caregivers' gender. Male caregivers had more comorbidities than females (CCI 1.9 versus 1.1, $P < 0.001$), and the wives of male caregivers had a more severe stage of dementia than husbands of female caregivers (CDR, $P = 0.048$; MMSE 14.0 versus 17.7, $P < 0.001$). However, the mean Zarit burden scale was significantly lower among male than female caregivers (31.5 versus 37.5; $P < 0.001$). Lower education of male caregivers tended to be associated with less experienced burden. In conclusion, male caregivers of dementia experienced lower burden than female caregivers despite care recipients' more severe disease.

1. Introduction

Alzheimer's disease and other dementias are the main reasons for need of caregiving at home and for permanent institutional care, and, therefore, they are among the most expensive diseases for our society [1]. Caregivers' high burden has been examined in a number of studies on dementia [2, 3]. Our society is changing—while caregiving has traditionally been considered as women's activity [4], the number of male caregivers is rapidly increasing. In fact,

men over 65 years in the UK soon outnumber women as caregivers [4, 5]. Women and men may approach their caregiving differently. Whereas men seem to consider it more as a task, women may take it more comprehensively [4, 6, 7]. Coping strategies such as active problem-solving skills are beneficial in caregiving irrespective of caregiver gender [8].

A review of 93 articles on gender differences in caregiving studies [4] reports that most studies conclude that women experience more distress and use more services than men. However, in respect to worrying and stress, studies have had

contradictory findings. Furthermore, several studies have reported no gender differences [4, 9]. Ten studies have focused on male caregivers and characteristics that predict their distress or coping [4, 9]. All these studies have been cross-sectional, with limited number of participants, and eight being qualitative. Only two studies used quantitative analysis of a structured interview data on males [9, 10]. Thus, we lack knowledge on gender differences of continuous caregiving affecting distress and wellbeing. Therefore, we compared the characteristics and burden of male and female spousal caregivers of patients with dementia.

2. Materials and Methods

The present study cohort included 335 dyads of wife-husband married couples from two intervention trials (Family Care as Collaboration trial [11] and FINnish Alzheimer EXercise [FINALEX] trial [12]) using the same measures to characterize participants. In the dyads, one of the spouses was suffering from dementia (care recipient) and the other was the caregiver. There were no differences in the caregivers' burden between the intervention and control groups of the two original trials. In the family care as collaboration trial, 125 dyads were randomized into a multicomponent intervention program ($N = 63$) (including case coordinator, geriatric consultations when needed, support groups for caregivers, and tailored services for two years), or in a control group ($N = 62$). In the FINALEX trial 210 dyads were randomized to a group-based exercise ($N = 70$) or tailored home-based exercise of the demented spouse ($N = 70$), while 70 dyads served as controls. The intervention lasted for one year, with final followup until two years. The baseline data of these trials were used to study gender differences of caregivers and care recipients. All demographic data and medical diagnoses of the dyads were confirmed both from medical records, comorbidity was assessed by the Charlson comorbidity index (CCI), a weighted index taking into account the number and severity of comorbid conditions [13]. At baseline, patients with dementia were assessed with the clinical dementia rating scale (CDR) [14] for functioning and the stage of dementia, and with the mini-mental state examination (MMSE) [15] for cognitive status. The neuropsychiatric inventory (NPI) [16] was used to describe neuropsychiatric symptoms and the Cornell depression scale for mood [17]. Among caregivers, the Zarit burden Scale [18] was used to measure experienced burden (high burden >40 points) and the geriatric depression scale (GDS) [19] to measure depression. Also the one-year follow-up Zarit points among males and females are reported. Caregivers' life satisfaction was inquired by question "Are you satisfied with life?" (yes/no). Experience of loneliness was inquired by question "Do you suffer from loneliness?" (never/sometimes/often or always) and those responding "sometimes" or "often or always" were categorized as suffering from loneliness. All data were collected by experienced study nurses. The Ethics Committee of Internal Medicine of the Hospital District of Helsinki and Uusimaa, Finland approved the protocol.

2.1. Statistical Analyses. Males and females were compared with χ^2 -test for categorical variables and Mann-Whitney test for nonnormally distributed continuous variables. Logistic regression analysis was used to determine the independent value of gender on experienced burden in caregiving. Both caregivers' and care recipients' age and CCI, caregivers' education and use of home care services, and care recipients' MMSE points, NPI points and Cornell points were used as covariates in the analyses.

3. Results

Altogether 335 husband-wife dyads were examined. At baseline the mean age of both the caregivers and dementia patients was 78 years. The age of male and female caregivers was similar, but the husbands of female caregivers were slightly older than the wives of male caregivers. Only 13.3% of male and 11.6% of female caregivers used home care services ($P = 0.65$). Male caregivers had significantly more comorbidity than female caregivers (CCI 1.9 versus 1.1, $P < 0.001$). However, the female caregivers experienced a significantly higher burden than males according to the Zarit burden scale (37.5 versus 31.5, $P < 0.001$) and females also had higher points in GDS depression scale than males (8.8 versus 7.0, $P = 0.0025$). There were no significant differences between genders in life satisfaction nor in experience of loneliness (Table 1).

The patients with dementia differed in several ways. The female patients suffered from significantly more severe dementia according to CDR and their mean MMSE points were significantly lower than female caregivers' care recipients' points. There were no differences in respect to care recipients' depressive symptoms according to Cornell scale, neuropsychiatric symptoms according to NPI, or comorbidities according to Charlson (Table 1).

In logistic regression analysis adjusted for caregivers' and care recipients' age and CCI, caregivers' education and use of home care services and care recipients' MMSE, NPI, and Cornell scale points, the male gender was protective against high burden (OR 0.33, 95%CI: 0.18 to 0.62; $P < 0.001$). In this analysis, higher NPI points (OR 1.05, 95%CI: 1.03 to 1.08, $P < 0.001$) and higher Cornell points of the care recipient predicted caregivers' high burden (OR 1.07, 95%CI: 1.00 to 1.14, $P = 0.005$). Caregivers' low education tended to be protective against high burden (OR 0.58, 95%CI: 0.31 to 1.08), $P = 0.08$) (Table 2).

The burden of caregiving decreased during the follow-up year in both genders: at 12 months the mean Zarit points were 27.3 (SD 14.4) and 35.9 (SD 15.0) among male and female caregivers, respectively ($P < 0.001$).

4. Discussion

Male caregivers having higher level of comorbidities cared for their wives with more severe dementia but did not suffer as much as female caregivers from burden or from depressive symptoms. Even adjusting for various covariates, male gender seemed to be protective when caregiving a person with Alzheimer's disease.

TABLE 1: Characteristics of caregivers and care recipients with dementia according to gender.

Characteristic	Male caregivers (N = 128)	Female caregivers (N = 207)	P value ¹
Caregivers			
Mean age, years (SD)	77.0 (6.2)	78.4 (5.6)	0.071
Education <8 years, %	33.6	22.7	0.029
Charlson comorbidity index, mean (SD)	1.9 (1.9)	1.1 (1.4)	<0.001
Zarit burden scale, mean (SD)	31.5 (14.9)	37.5 (14.6)	<0.001
GDS, mean (SD)	7.0 (5.2)	8.8 (5.7)	0.0025
Satisfied with life, %	83.1	78.6	0.33
Suffers from loneliness, %	76.8	66.7	0.051
	Female care recipients (N = 128)	Male care recipients (N = 207)	
Care recipients			
Mean age, years (SD)	76.9 (6.2)	78.4 (5.6)	0.041
MMSE, mean (SD)	14.0 (7.1)	17.7 (6.2)	<0.001
CDR score			
0.5	4.7	2.9	
1	20.3	30.4	
2	50.8	52.5	0.048
3	24.2	14.5	
Charlson comorbidity index, mean (SD)	1.9 (1.6)	2.3 (1.9)	0.17
Cornell, mean (SD)	5.0 (4.3)	6.0 (5.1)	0.099
NPI, mean (SD)	21.9 (13.8)	22.4 (14.7)	0.97
Home care services	13.3	11.6	0.65

Abbreviations: GDS: geriatric depression scale; MMSE: mini-mental state examination; CDR: clinical dementia rating scale; NPI: neuropsychiatric inventory; SD: standard deviation.

¹Males and females were compared with χ^2 -test for categorical variables and Mann-Whitney test for nonnormally distributed continuous variables.

TABLE 2: Logistic regression analysis exploring independent determinants associated with high burden (Zarit >40 points) in dementia spousal caregiving.

Covariates	OR (Odds ratio)	95% Confidence intervals	P value
Caregiver			
Age	1.14	0.73–1.78	0.57
Male gender	0.33	0.18–0.62	<0.001
Education < 8 years	0.58	0.31–1.08	0.09
Cornell depression scale	1.07	1.00–1.14	0.03
Using home care services	1.98	0.93–4.22	0.08
Charlson comorbidity index	1.14	0.96–1.36	0.12
Care recipient			
Age	0.85	0.54–1.32	0.46
MMSE	0.96	0.92–1.00	0.07
NPI	1.05	1.03–1.08	<0.001
Charlson comorbidity index	1.02	0.87–1.19	0.84
Cornell	1.07	1.00–1.14	0.03

Abbreviations: MMSE: mini-mental state examination; NPI: neuropsychiatric inventory.

Our study population has been examined very carefully and the diagnosis of dementia was always confirmed by careful diagnostic work-up by geriatricians or neurologists, which is a strength of this study. When compared to other studies, this is by far the largest quantitative study about gender differences in dementia spousal caregiving.

Limitation of our study is its cross-sectional nature. Because of the two interventions, where also control group may have some benefit compared to persons not attending any study program, we used only the baseline data in our logistic regression analysis. An intervention effect can be one reason for reduced burden in both genders in one-year

follow-up. It can also be assumed that the most severely demented persons with most neuropsychiatric symptoms were dropped-out from our intervention studies because of deaths or hospitalizations during 12 months.

Our quantitative findings are in line with findings of previous, mostly qualitative studies [4]. There are some contradictory findings [9, 20], but most studies report lower level of stress among male caregivers [4, 10, 21]. An unexpected result of lower education associating with lower burden among male caregivers [10] was given tentative support in this larger quantitative study.

Why do males experience lower burden? Some prior studies have suggested that males do not take caregiver's role similarly to females and their coping strategies are different. Studies concerning caregivers' help-seeking behaviour and gender differences suggest that male caregivers are not as likely as women to be aware of nor to use community services [22]. Males may prefer family independence. In addition, they may perceive that by accepting community services they admit being weak and losing control [23]. In Finland, where most of the women work full-time also outside home, elderly couples often want to handle their own daily life and protect their adult children as far as possible. Quite rare use of home care services is in line with our previous results of 1214 caregivers from year 2005 [24].

A large-scale study of 170 patient-spouse dyads concluded that male caregivers' sense of coherence was higher than female caregivers' [25]. Sense of coherence indicates a person's ability to cope with different life situations. The most recent study investigating coping strategies of nine husband caregivers of their cognitively impaired wives [7] identified six strategies these husbands dealt with caregiving: exerting force, focusing on tasks, blocking emotions, minimizing disruption, distracting attention, and self-medicating. Once having a problem-solving method for coping, Kramer [10] also found that less education, satisfaction with one's social participation, and better health were linked to less burden. Why could lower education be associated with lower burden in caregiving? Lower education might be associated with satisfaction with narrower and more simple daily life without any specific events or new experiences in contrary to academic multitasking lifestyle. If you are content with simple life, you do not need to give up with your previous daily habits, which inevitably happens in caregiving a person with dementia.

Women usually take more responsibility of the well-being of the family from childbearing to care older family members. Considering the usually high emotional responsibility by female nature, it is quite understandable that they have more emotional stress when facing the situation. Cultural aspects also have a great impact on caregiving, possibly women are expected to be more altruistic and more suitable for caregiving than men [2].

Male sex seems to be protective for a family when a caregiver is needed. The coping methods among males, which may lead to this result, are worth of focusing when planning support and services for these families. Coping strategies have been examined in only few studies. They suggest that caregivers reporting high levels of distress appeared

more likely to use an emotion-focused coping strategy, for example, wishful thinking, denial, suppressive feelings, self-blaming and avoidance. Caregivers with low levels of distress, in contrast, used problem-solving strategies such as acceptance and instrumental coping [10, 21]. Given the idea that these differences in coping methods are associated with gender differences in dementia caregiving, we could add this aspect also to continuous support program of these families.

5. Conclusions

Males experience significantly less burden while taking care of their wives with dementia, irrespective of the more severe stage of cognitive decline of their spouse. These findings should be confirmed and the reasons behind should be explored in further studies.

Conflict of Interests

The authors declare they that have no conflict of interests directly relevant to this paper. However, the authors report professional cooperation with various companies. Dr. Pöysti reports having professional cooperation including lecturing fees from pharmaceutical companies (Novartis, Pfizer, Janssen-Cilag, Lundbeck, Leiras, Orion, and Servier) and having participated in clinical trials funded by pharmaceutical companies. Dr. Strandberg reports having professional cooperation including consulting/lecturing fees from pharmaceutical and other health care companies (including AstraZeneca, Boehringer Ingelheim, Leiras, MSD Finland, Novartis, Pfizer, and Servier) and having participated in clinical trials funded by pharmaceutical companies. Dr. Tilvis has received lecturing fees from the following pharmaceutical companies: AstraZeneca, Boehringer Ingelheim, Jansen-Cilag, Lundbeck, MSD Finland, Novartis, Orion Pharma, Pfizer, and Sanofi-Aventis. Dr. Pitkälä reports having professional cooperation including lecturing fees from pharmaceutical and other health care companies (including Janssen-Cilag, Lundbeck, MSD Finland, Novartis, Pfizer, Nestle) and having participated in clinical trials funded by pharmaceutical companies. Dr. Laakkonen and researchers Eloniemä-Sulkava and Savikko have no conflict of interests.

Acknowledgments

This study was supported by the Social Insurance Institution of Finland, the Central Union for the Welfare of the Aged, the Sohlberg Foundation, and the King Gustaf V and Queen Victoria's Foundation, and Finland's Slot Machine Association. The sponsors did not have any role in the study design, analysis or interpretation of data, nor in the writing of the paper or in the decision to submit this paper for publication. The authors were independent researchers not associated with the funders.

References

- [1] A. Gustavsson, M. Svensson, F. Jacobi, CDBE2010 Study Group et al., "Cost of disorders of the brain in Europe 2010," *European Neuropsychopharmacology*, vol. 21, pp. 718–779, 2011.
- [2] C. Collins and R. Jones, "Emotional distress and morbidity in dementia carers: a matched comparison of husbands and wives," *International Journal of Geriatric Psychiatry*, vol. 12, no. 12, pp. 1168–1173, 1997.
- [3] H. Brodaty and M. Donkin, "Family caregivers of people with dementia," *Dialogues in Clinical Neuroscience*, vol. 11, no. 2, pp. 217–228, 2009.
- [4] K. L. Baker and N. Robertson, "Coping with caring for someone with dementia: reviewing the literature about men," *Aging and Mental Health*, vol. 12, no. 4, pp. 413–422, 2008.
- [5] M. Hirst, "Trends in informal care in Great Britain during the 1990's," *Health and Social Care in the Community*, vol. 9, no. 6, pp. 348–357, 2001.
- [6] R. Russell, "In sickness and in health a qualitative study of elderly men who care for wives with dementia," *Journal of Aging Studies*, vol. 15, no. 4, pp. 351–367, 2001.
- [7] T. Calasanti and N. King, "Taking 'women's work' 'like a man': husbands' experiences of care work," *Gerontologist*, vol. 47, no. 4, pp. 516–527, 2007.
- [8] K. Saad, J. Hartman, C. Ballard, M. Kurian, C. Graham, and G. Wilcock, "Coping by the carers of dementia sufferers," *Age and Ageing*, vol. 24, no. 6, pp. 495–498, 1995.
- [9] K. L. Baker, N. Robertson, and D. Connelly, "Men caring for wives or partners with dementia: masculinity, strain and gain," *Aging and Mental Health*, vol. 14, no. 3, pp. 319–327, 2010.
- [10] B. J. Kramer, "Differential predictors of strain and gain among husbands caring for wives with dementia," *Gerontologist*, vol. 37, no. 2, pp. 239–249, 1997.
- [11] U. Eloniemi-Sulkava, M. Saarenheimo, M. L. Laakkonen et al., "Family care as collaboration: effectiveness of a multicomponent support program for elderly couples with dementia. Randomized controlled intervention study," *Journal of the American Geriatrics Society*, vol. 57, no. 12, pp. 2200–2208, 2009.
- [12] K. H. Pitkala, M. M. Raivio, M. L. Laakkonen, R. S. Tilvis, H. Kautiainen, and T. E. Strandberg, "Exercise rehabilitation on home-dwelling patients with Alzheimer's disease—a randomized, controlled trial. Study protocol," *Trials*, vol. 11, article 92, 2010.
- [13] M. E. Charlson, P. Pompei, K. A. Ales, and C. R. MacKenzie, "A new method of classifying prognostic comorbidity in longitudinal studies: development and validation," *Journal of Chronic Diseases*, vol. 40, no. 5, pp. 373–383, 1987.
- [14] C. P. Hughes, L. Berg, and W. L. Danziger, "A new clinical scale for the staging of dementia," *British Journal of Psychiatry*, vol. 140, no. 6, pp. 566–572, 1982.
- [15] M. F. Folstein, S. E. Folstein, and P. R. McHugh, "'Mini mental state'. A practical method for grading the cognitive state of patients for the clinician," *Journal of Psychiatric Research*, vol. 12, no. 3, pp. 189–198, 1975.
- [16] J. L. Cummings, M. Mega, K. Gray, S. Rosenberg-Thompson, D. A. Carusi, and J. Gornbein, "The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia," *Neurology*, vol. 44, no. 12, pp. 2308–2314, 1994.
- [17] G. S. Alexopoulos, R. C. Abrams, R. C. Young, and C. A. Shamoian, "Cornell scale for depression in Dementia," *Biological Psychiatry*, vol. 23, no. 3, pp. 271–284, 1988.
- [18] S. H. Zarit and J. M. Zarit, "The memory and behavior problems Checklist—1987R and burden interview," Tech. Rep., Pennsylvania State University, University Park, Pa, USA, 1987.
- [19] J. A. Yesavage, T. L. Brink, and T. L. Rose, "Development and validation of a geriatric depression screening scale: a preliminary report," *Journal of Psychiatric Research*, vol. 17, no. 1, pp. 37–49, 1982.
- [20] C. Adler, G. Wilz, and T. Gunzelmann, "'I never feel free'—women take care of their husbands, fathers or mothers with dementia," *Gesundheitswesen*, vol. 58, supplement 2, pp. 125–131, 1996.
- [21] S. K. Rose, M. E. Strauss, M. M. Neundorfer, K. A. Smyth, and J. C. Stuckey, "The relationship of self-restraint and distress to coping among spouses caring for persons with Alzheimer's disease," *Journal of Applied Gerontology*, vol. 16, no. 1, pp. 91–103, 1997.
- [22] M. Stommel, C. E. Collins, B. A. Given, and C. W. Given, "Correlates of community service attitudes among family caregivers," *Journal of Applied Gerontology*, vol. 18, no. 2, pp. 145–161, 1999.
- [23] L. W. Kaye and J. S. Applegate, "Family support groups for male caregivers: benefits of participation," *Journal of Gerontological Social Work*, vol. 20, no. 3-4, pp. 167–185, 1993.
- [24] M. Raivio, U. Eloniemi-Sulkava, M. L. Laakkonen et al., "How do officially organized services meet the needs of elderly caregivers and their spouses with Alzheimer's disease?" *American Journal of Alzheimer's Disease and Other Dementias*, vol. 22, no. 5, pp. 360–368, 2007.
- [25] T. H. Välimäki, K. M. Vehviläinen-Julkunen, A. M. K. Pietilä, and T. A. Pirttilä, "Caregiver depression is associated with a low sense of coherence and health-related quality of life," *Aging and Mental Health*, vol. 13, no. 6, pp. 799–807, 2009.

Clinical Study

Efficacy of Music Therapy in Treatment for the Patients with Alzheimer's Disease

H. Fukui,¹ A. Arai,² and K. Toyoshima¹

¹Department of Education, Nara University of Education, Takabatake, Nara 630-8528, Japan

²Ongakunomori Nonprofit Organization, 1-12 Kobocho, Saidaiji, Nara 631-0827, Japan

Correspondence should be addressed to H. Fukui, fukuiah@nara-edu.ac.jp

Received 5 July 2012; Revised 21 August 2012; Accepted 26 August 2012

Academic Editor: Hiroyuki Umegaki

Copyright © 2012 H. Fukui et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

We report that music therapy is effective in the treatment of Alzheimer's disease. We found that the secretion of 17β -estradiol and testosterone, hormones that are supposed to have preventive effects on Alzheimer's disease, is significantly increased by music therapy. During the sessions, patients with Alzheimer's disease were allowed to listen to music and songs with verbal contact from the therapist. It was found that problematic behaviors such as poriomania (fugue) had decreased. Music therapy has the potential as an alternative treatment for adverse hormone replacement therapy.

1. Introduction

In both sexes, sex hormone levels decrease with aging. These reductions have been correlated to various symptoms in the elderly including diminished cognitive function, disturbance of memory, mind and mood, depression, and climacteric disturbance [1].

In an attempt to mitigate these symptoms, hormone replacement therapies are administered, for example, estrogen in females and androgen in males [2–4] and females [5, 6]. Even within the elderly population, sex hormone levels are lower in Alzheimer patients than in healthy counterparts [4, 7].

In Alzheimer's disease, the aging-related reductions in sex hormones, especially estrogen, represent a critical risk factor [8–10]. This is because estrogen protects the nerves and acts to control cell proliferation. Moreover, estrogen decreases the β amyloid peptide content in the neurons which is a typical pathologic finding in Alzheimer's disease [11, 12] and protects the body from neurotoxicity from β peptide [13, 14]. Estrogen has also shown to suppress the increase and deposition of β -amyloid and to prevent nerve cell damage [12, 15, 16]. In addition to these effects on amyloid metabolism, estrogen improves cognitive function and delays the onset of dementia by increasing cholinergic activity in the brain, stimulating axonal budding and dendrite

formation and retarding cerebral arteriosclerosis [9]. Hence, estrogen replacement therapy has been recommended as a prophylaxis of Alzheimer's disease in particular for the elderly female patients with decreased estrogen levels [8, 17].

In actual clinical settings, estrogen is used to treat postmenopausal women with Alzheimer's disease and has shown its effect to improve their verbal memory and attention remarkably [18–20]. It has also shown that the onset of dementia is delayed significantly in elderly women who had been receiving estrogen for long periods than those who had not [21–23]. Another report shows that the incidence of Alzheimer's disease was significantly lower in estrogen recipients than in controls [24]. Estrogen has proved to be effective in the treatment and prevention for Alzheimer's disease [7].

In recent years, the nerve-protecting action of androgens, especially of testosterone, has been noticed attentively. A study of cortical neurons of cultured rats has shown that testosterone increases NGF (nerve growth factor) and p-75 nerve growth factor receptor and decreases β amyloid peptide in mouse model of Alzheimer's disease [25, 26]. Similarly, in the human neurons, it has been reported that androgens, such as testosterone, enanthate, methyl testosterone and epitestosterone, suppress nerve apoptosis and protect the nerves [8, 17]. Since the action of testosterone is especially distinct in the portions of the brain that control cognition

and memory, the relationship between this hormone and cognitive function has also been investigated. According to Yaffe et al. [27], with the increase in testosterone levels, cognitive test score increases in elderly males. Therefore, prescription of testosterone supplements for males has been suggested as possibly reducing the risk of diminishment of cognitive ability, a prodrome of Alzheimer's disease. Hence, the reductions in testosterone levels with aging represent a risk factor of Alzheimer's disease [8, 9]. However, hormone replacement therapy has its drawbacks and is not used today. This topic is discussed later (Section 4).

Recent studies revealed that music is closely associated with hormones which govern the emotion and human behavior, especially with steroid hormones including sex hormones. It has been shown that there is a correlation between spatial ability or music ability and testosterone [28], and listening to music has effects on testosterone and cortisol [29–31]. The correlation between musical ability and spatial cognition has long been known [32–34]. Many studies have investigated the relationship of musical ability to spatial perception and cognition in human being. The assumption that some correlation exists between musical ability and steroid hormones seems to be appropriate. In fact, Hassler discovered that the relationship between T and musical ability (music composition) resembles the one between T and other forms of spatial perception and cognition [33, 35].

Furthermore, the relationship between music and steroid hormones is not limited to musical ability. In the field of behavioral endocrinology and neuroendocrinology, many studies have documented that musical stimulation (listening) affects various biochemical substances [36–38]. In particular, many studies-based findings on C. Experiment had shown that listening to music is effective in alleviating and decreasing stress. In many studies, stress reduction due to music listening has been attributed to reductions in C [39, 40]. It also has been noted that listening to music alters levels of T (increase and decrease) [41, 42]. The research reported that musical activities (listening and playing) adjust steroid secretion in elderly individuals and are likely to alleviate psychological states such as anxiety and tension. Moreover, levels of steroids changing in both directions, increasing in subjects with low hormone levels, and decreasing in subjects with high hormone levels were found [43]. Additionally, there has been a report that listening to the music enhances cognitive recovery of mood after middle cerebral artery stroke, and listening to the music during the early poststroke stage can enhance cognitive recovery and prevent negative mood [44]. Also, music-supported therapy (MST) on patients who had an acute and chronic stroke could bring the neuroplastic changes in the neural circuit underlying audiomotor coupling [44].

2. Materials and Methods

In the present study, we monitored testosterone and 17β -estradiol levels over time in patients with Alzheimer's disease stimulated with music, to determine whether music therapy has the potential as an alternative treatment for hormone

replacement therapy, focusing on the fact that the hormones bearing a causative relation to the onset of Alzheimer's disease are also closely related to music.

Traditionally, studies of the efficacy of music therapy in patients with Alzheimer's disease have focused on changes in symptoms such as dementia most typically and other problematic behaviours: aggressive behaviors, depression, disturbance of mood, and decreased sociality [45–52]. In general, behavioral therapy has shown an alleviation on behavioral deterioration by enhancing the patient's social interactions, more specifically one to one interactions with carers, therapists, and others [49, 53]. In these studies, mitigation of symptoms was achieved but the mechanism of action remained unexplained.

In music therapy, whether the observed therapeutic effects are attributable to the music, the therapist, or their synergism is often obscure and unidentified. The study population comprised of six patients with an established diagnosis of Alzheimer's disease (6 females, ages ranging from 67 to 90 years, mean age 81.8 years) residing in a special nursing home for the elderly. Every subject's family or guardian had received the written informed consent before participating in this study based on the Declaration of Helsinki (1964). The patients were allocated with three conditions (within subjects designs)

- (1) The subjects had only been greeted and been questioned upon their health and mood by the therapist. There was no music involved in this condition.
- (2) 12 songs that had been selected in a preliminary survey were sung by the therapist. It was then used for the subjects to listen to.
- (3) Music therapy that comprises of (1) and (2).

The session was carried out for the duration of a month, and each session took about an hour. Salivary hormone levels were measured before and after each session. The effects and differences on hormone levels were compared between the before and the after. The therapist contacted the subjects verbally whose scenarios were formulated prior to the session. A total of 12 songs were selected on the basis of preference by each subject in a preliminary survey. Then, the therapist sang chosen songs without microphone accompanied by the keyboard sound from an amplified speaker. At the same time, each subject's behavior was evaluated with each condition for three consecutive days: a day before the session, a day of the session, and a day after the session.

Before starting the experiments, a survey was conducted on medical aspects: past history, medication status, and so forth, daily life: lifestyle (possible, but preferably life-style or life style or could use preference of life), daily activity dependence, extent of care, food preference, hobbies, personal relations, communication capability, personality, and other aspects of each subject. Additionally, they were asked of their experiences of performing the music, music-related activities in daily life. Regarding their hearing status, the subjects were examined to have acceptable auditory senses, provided that they retained hearing ability that permits them to have everyday life without difficulty even

though the ability had been diminished naturally with aging. None of the subjects were on hormone replacement therapy and known of used any drug use that significantly influence steroid hormones. All subjects had already received music therapy for at least four consecutive months (4 years and 4 months at maximum, 4 months at minimum).

36 samples, 6 subjects \times before the session and after session \times three conditions were collected. Saliva samples were kept frozen at -20°C until assayed. Salivary 17β -estradiol and testosterone levels were assayed in duplicate by EIA kit (Assay Designs, Inc.). The kit is used for the quantitative measurement of 17β -estradiol (E) and testosterone (T). It occupies a monoclonal antibody to each hormone to bind in a competitive manner, and it targets in a sample or an alkaline phosphatase molecule which has hormones covalently attached to it. The established intra-assay coefficient of E and T variance was 5.7% and 7.8%, respectively, and the interassay coefficient of variations for E and T is 6.2%, and 9.3%, respectively. The measured intraassay coefficient of variations for E and T was 5.3%, 6.2%, respectively, and the interassay coefficient of variations for E and T were 5.6%, and 7.4%, respectively.

3. Results

Regarding the influence of physical factors involved in the individual conditions, analysis of variance (ANOVA) and t -test were employed to determine whether there are differences in duration, tempo, and sound pressure of music between "listening to the music" and "music therapy." As a result, no such differences were found ($F(1, 22) = 2.284$, $P = 0.1450$; $F(1, 22) = 2.754$, $P = 0.1112$; $t = -1.475$, $P = 0.1462$). Therefore, it can be concluded that there are no differences in physical factors of music conditions between "listening to the music listening" and "music therapy."

The mean 17β -estradiol level for the subjects was 253.539 pg/mL. Two-way ANOVA with more than one observation was conducted with "hormonal changes between before and after stimuli" and "group," "listening to the music," "therapist," and "music therapy"—as variables. As a result, statistically significant differences were found in terms of "main effect of group" ($F(2, 9) = 4.760$, $P = 0.0389$), "main effect of changes in 17β -estradiol level" ($F(1, 9) = 16.987$, $P = 0.0026$), and "interaction with group" ($F(2, 9) = 6.528$, $P = 0.0177$). Although the 17β -estradiol level increased after the "listening to the music," the greatest increase was obtained after the "music therapy" (Figure 1). On the other hand, the 17β -estradiol level decreased after the "therapist" conditioned intervention. A post hoc test (Fisher's PLSD) revealed a significantly increased 17β -estradiol level for the "music therapy" condition as compared to the "therapist" condition ($P = 0.0130$).

The mean testosterone level for the subjects was 450.672 pg/mL. Two-way ANOVA with more than one observation was conducted with "group" under three conditions and "hormonal changes between before and after stimuli" as variables. As a result, statistically significant differences were found in terms of main effect of "group"

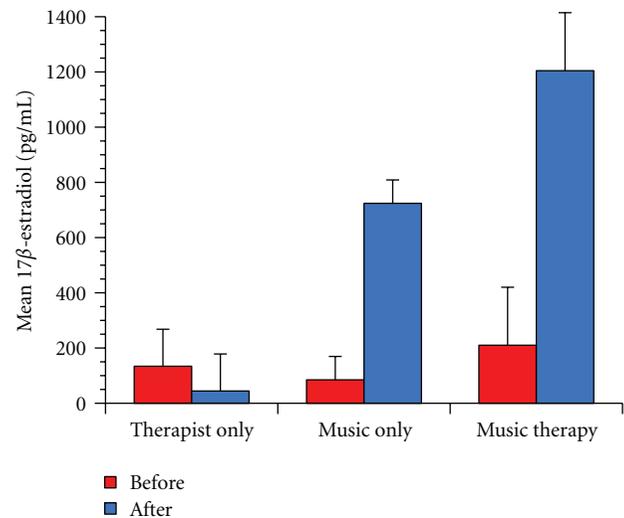


FIGURE 1: Changes in 17β -estradiol concentrations. Changes in 17β -estradiol concentrations in 6 patients with Alzheimer's disease at each experimental condition. Two-way ANOVA revealed that the main effect of group ($P = 0.0389$), main effect of changes in 17β -estradiol level ($P = 0.0026$), and interaction with group ($P = 0.0177$) were significant.

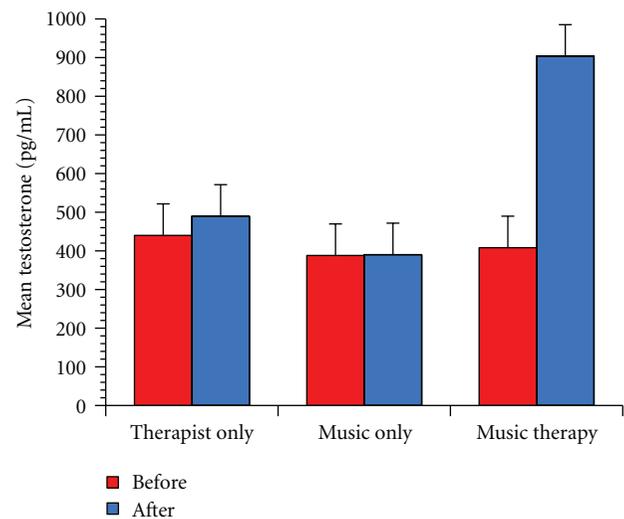


FIGURE 2: Changes in testosterone concentrations. Changes in testosterone concentrations in 6 patients with Alzheimer's disease at each experimental condition. Two-way ANOVA revealed that the main effect of group ($P = 0.05$), main effect of changes in testosterone level ($P = 0.0066$), and interaction with group ($P = 0.0063$) were significant.

($F(2, 5) = 5.72$, $P = 0.05$), main effect of testosterone level changes ($F(1, 5) = 19.9$, $P = 0.0066$), and interaction with "group" ($F(2, 5) = 16.5$, $P = 0.0063$). A post hoc test (Fisher's PLSD) revealed a significantly increased testosterone level for the "music therapy" condition as compared to the "music listening" condition ($P = 0.0213$) (Figure 2). Carers have reported that problematic behavior

was decreased after the “music therapy” condition, and it lasted till a day after the session.

4. Discussion

These achieved results demonstrate that the “music therapy” condition increased the testosterone level significantly after stimuli in comparison to the other conditions. Also, the results suggest that problematic behavior can be reduced by music therapy.

Since behavioral therapy involves human relations, it is inevitable that the therapy is strongly dependent on social interactions [49, 51, 53]. In the present study, the effects of “music” and “therapist” were separately evaluated using endocrine indices. It showed that with patients with Alzheimer's disease at the initial stage, the greatest effect is obtained by “music therapy,” a combination of “therapist” and “listening to the music,” as opposed to the ones being employed alone. The hormones, 17β -estradiol and testosterone that served as indices in this study, have been reported to suppress the degeneration and diminishment of neurofibrils, which a typical character of Alzheimer's disease is supposed to be caused by. As it was seen in this study, the increases in 17β -estradiol and testosterone levels observed in the patients with Alzheimer's with diminishing hormones suggest that music therapy may contribute to decelerate the progression of Alzheimer's disease or even to delay its onset. It is considered that music therapy restores normal hormone levels and suppresses nerve cell damage and protects nerve cells, thus terminating the progression of Alzheimer's disease.

In general, hormone replacement therapy (HRT) is expected to be highly effective in the prevention and the treatment for Alzheimer's disease. However, HRT is not applicable to all Alzheimer's patients as there is risk of causing adverse reactions such as invasive breast cancer, heart disease, and strokes [54]. In fact, there have been a report that adverse reactions were caused in Alzheimer's patients on HRT. The reactions include increased risks of carcinogenicity in females, feminization in males with estrogen replacement therapy, increased risks of prostatic cancer, elevated cholesterol levels, acne, alopecia, and other symptoms in males receiving testosterone replacement therapy [28, 55]. Therefore, there is a strong demand for a development of an appropriate treatment that can avoid causing such aversive and unwanted reactions [21, 56].

Based on this current study, music therapy seems to be an alternative that is more unlikely to cause risks of harmful reactions to the patients than HRT. The possibility of causing such risks is thought to be significantly lower when music therapy is used than when HRT is used. It is vital to note that no aversive reactions were induced by the music, except music epilepsy [57], which has been reported in a very small percentage of cases. For this reason, music therapy has a potential to become as a safe alternative treatment that is as effective as HRT but with lower prevalence of unwanted reactions. Moreover, music therapy can be expected to serve as an effective prophylaxis of Alzheimer's disease for the healthy elderly. Music therapy therefore has a potential to be

an alternative to HRT hormone replacement therapy for the healthy elderly population.

References

- [1] J. M. Daniel, “Estrogens, estrogen receptors, and female cognitive aging: the impact of timing,” *Hormones and Behavior*. In press.
- [2] H. Sternbach, “Age-associated testosterone decline in men: clinical issues for psychiatry,” *American Journal of Psychiatry*, vol. 155, no. 10, pp. 1310–1318, 1998.
- [3] S. W. J. Lamberts, A. W. Van Den Beld, and A. J. Van Der Lely, “The endocrinology of aging,” *Science*, vol. 278, no. 5337, pp. 419–424, 1997.
- [4] J. Holland, S. Bandelow, and E. Hogervorst, “Testosterone levels and cognition in elderly men: a review,” *Maturitas*, vol. 69, no. 4, pp. 322–327, 2011.
- [5] S. Rako, “Testosterone deficiency: a key factor in the increased cardiovascular risk to women following hysterectomy or with natural aging?” *Journal of Women's Health*, vol. 7, no. 7, pp. 825–829, 1998.
- [6] E. Hogervorst, C. De Jager, M. Budge, and A. D. Smith, “Serum levels of estradiol and testosterone and performance in different cognitive domains in healthy elderly men and women,” *Psychoneuroendocrinology*, vol. 29, no. 3, pp. 405–421, 2004.
- [7] R. S. Vest and C. J. Pike, “Gender, sex steroid hormones, and Alzheimer's disease,” *Hormones and Behavior*. In press.
- [8] J. Hammond, Q. Le, C. Goodyer, M. Gelfand, M. Trifiro, and A. LeBlanc, “Testosterone-mediated neuroprotection through the androgen receptor in human primary neurons,” *Journal of Neurochemistry*, vol. 77, no. 5, pp. 1319–1326, 2001.
- [9] J. J. Manly, C. A. Merchant, D. M. Jacobs et al., “Endogenous estrogen levels and Alzheimer's disease among postmenopausal women,” *Neurology*, vol. 54, no. 4, pp. 833–837, 2000.
- [10] A. M. Barron and C. J. Pike, “Sex hormones, aging, and Alzheimer's disease,” *Frontiers in Bioscience (Elite Edition)*, vol. 4, pp. 976–997, 2012.
- [11] H. Xu, G. K. Gouras, J. P. Greenfield et al., “Estrogen reduces neuronal generation of Alzheimer β -amyloid peptides,” *Nature Medicine*, vol. 4, no. 4, pp. 447–451, 1998.
- [12] L. Mateos, T. Persson, S. Katoozi et al., “Estrogen protects against amyloid- β toxicity by estrogenreceptor α -mediated inhibition of Daxx translocation,” *Neuroscience Letters*, vol. 506, no. 2, pp. 245–250, 2012.
- [13] C. Behl, T. Skutella, F. Lezoualc'h et al., “Neuroprotection against oxidative stress by estrogens: Structure- activity relationship,” *Molecular Pharmacology*, vol. 51, no. 4, pp. 535–541, 1997.
- [14] Y. Goodman and M. P. Mattson, “Ceramide protects hippocampal neurons against excitotoxic and oxidative insults, and amyloid β -peptide toxicity,” *Journal of Neurochemistry*, vol. 66, no. 2, pp. 869–872, 1996.
- [15] S. Gandy, O. P. Almeida, J. Fonte et al., “Chemical andropause and amyloid- β peptide,” *Journal of the American Medical Association*, vol. 285, no. 17, pp. 2195–2196, 2001.
- [16] V. Kumar, U. N. B. Durai, and T. Jobe, “Pharmacologic management of Alzheimer's disease,” *Clinics in Geriatric Medicine*, vol. 14, no. 1, pp. 129–146, 1998.
- [17] A. Markou, T. Duka, and G. M. Prelevic, “Estrogens and brain function,” *Hormones (Athens, Greece)*, vol. 4, no. 1, pp. 9–17, 2005.

- [18] S. Asthana, L. D. Baker, S. Craft et al., "High-dose estradiol improves cognition for women with ad results of a randomized study," *Neurology*, vol. 57, no. 4, pp. 605–612, 2001.
- [19] I. Wickelgren, "Estrogen stakes claim to cognition," *Science*, vol. 276, no. 5313, pp. 675–678, 1997.
- [20] D. H. S. Silverman, C. L. Geist, H. A. Kenna et al., "Differences in regional brain metabolism associated with specific formulations of hormone therapy in postmenopausal women at risk for AD," *Psychoneuroendocrinology*, vol. 36, no. 4, pp. 502–513, 2011.
- [21] M. X. Tang, D. Jacobs, Y. Stern et al., "Effect of oestrogen during menopause on risk and age at onset of Alzheimer's disease," *Lancet*, vol. 348, no. 9025, pp. 429–432, 1996.
- [22] A. Paganini-Hill and V. W. Henderson, "Estrogen replacement therapy and risk of Alzheimer disease," *Archives of Internal Medicine*, vol. 156, no. 19, pp. 2213–2217, 1996.
- [23] H. M. Fillit, "The role of hormone replacement therapy in the prevention of Alzheimer disease," *Archives of Internal Medicine*, vol. 162, no. 17, pp. 1934–1942, 2002.
- [24] S. A. Shumaker, B. A. Reboussin, M. A. Espeland et al., "The Women's Health Initiative Memory Study (WHIMS): a trial of the effect of estrogen therapy in preventing and slowing the progression of dementia," *Controlled Clinical Trials*, vol. 19, no. 6, pp. 604–621, 1998.
- [25] G. K. Gouras, H. Xu, R. S. Gross et al., "Testosterone reduces neuronal secretion of Alzheimer's β -amyloid peptides," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 97, no. 3, pp. 1202–1205, 2000.
- [26] E. R. Rosario, J. Carroll, and C. J. Pike, "Testosterone regulation of Alzheimer-like neuropathology in male 3xTg-AD mice involves both estrogen and androgen pathways," *Brain Research*, vol. 1359, pp. 281–290, 2010.
- [27] K. Yaffe, L. Y. Lui, J. Zmuda, and J. Cauley, "Sex hormones and cognitive function in older men," *Journal of the American Geriatrics Society*, vol. 50, no. 4, pp. 707–712, 2002.
- [28] M. Hassler, "Creative musical behavior and sex hormones: musical talent and spatial ability in the two sexes," *Psychoneuroendocrinology*, vol. 17, no. 1, pp. 55–70, 1992.
- [29] H. Fukui, "Music and testosterone: a new hypothesis for the origin and function of music," *Annals of the New York Academy of Sciences*, vol. 930, pp. 448–451, 2001.
- [30] H. Fukui and M. Yamashita, "The effects of music and visual stress on testosterone and cortisol in men and women," *Neuroendocrinology Letters*, vol. 24, no. 3-4, pp. 173–180, 2003.
- [31] H. Fukui and K. Toyoshima, "Music facilitate the neurogenesis, regeneration and repair of neurons," *Medical Hypotheses*, vol. 71, no. 5, pp. 765–769, 2008.
- [32] M. Hassler and N. Birbaumer, "Musical talent and spatial ability," *Archiv fur Psychologie*, vol. 136, no. 3, pp. 235–248, 1984.
- [33] M. Hassler, "Creative musical behavior and sex hormones: musical talent and spatial ability in the two sexes," *Psychoneuroendocrinology*, vol. 17, no. 1, pp. 55–70, 1992.
- [34] G. C. Cupchik, K. Phillips, and D. S. Hill, "Shared processes in spatial rotation and musical permutation," *Brain and Cognition*, vol. 46, no. 3, pp. 373–382, 2001.
- [35] M. Hassler, "Testosterone and artistic talents," *International Journal of Neuroscience*, vol. 56, no. 1–4, pp. 25–38, 1991.
- [36] M. Hassler, D. Gupta, and H. Wollmann, "Testosterone, estradiol, ACTH and musical, spatial and verbal performance," *International Journal of Neuroscience*, vol. 65, no. 1–4, pp. 45–60, 1992.
- [37] S. D. VanderArk and D. Ely, "Cortisol, biochemical, and galvanic skin responses to music stimuli of different preference values by college students in biology and music," *Perceptual and Motor Skills*, vol. 77, no. 1, pp. 227–234, 1993.
- [38] G. Kreutz, S. Bongard, S. Rohrmann, V. Hodapp, and D. Grebe, "Effects of choir singing or listening on secretory immunoglobulin A, cortisol, and emotional state," *Journal of Behavioral Medicine*, vol. 27, no. 6, pp. 623–635, 2004.
- [39] S. Khalfa, S. Dalla Bella, M. Roy, I. Peretz, and S. J. Lupien, "Effects of relaxing music on salivary cortisol level after psychological stress," *Annals of the New York Academy of Sciences*, vol. 999, pp. 374–376, 2003.
- [40] U. M. Nater, E. Abbruzzese, M. Krebs, and U. Ehlert, "Sex differences in emotional and psychophysiological responses to musical stimuli," *International Journal of Psychophysiology*, vol. 62, no. 2, pp. 300–308, 2006.
- [41] H. Fukui, "Music and testosterone: a new hypothesis for the origin and function of music," *Annals of the New York Academy of Sciences*, vol. 930, pp. 448–451, 2001.
- [42] H. Fukui and M. Yamashita, "The effects of music and visual stress on testosterone and cortisol in men and women," *Neuroendocrinology Letters*, vol. 24, no. 3-4, pp. 173–180, 2003.
- [43] H. Fukui, K. Toyoshima, K. Kuda et al., "The effect of music to sex hormones of elderly person," *Neuroscience Research Supplements*, vol. 55, p. S58, 2006.
- [44] T. Särkämö, M. Tervaniemi, S. Laitinen et al., "Music listening enhances cognitive recovery and mood after middle cerebral artery stroke," *Brain*, vol. 131, no. 3, pp. 866–876, 2008.
- [45] L. A. Gerdner, "Effects of individualized versus classical 'relaxation' music on the frequency of agitation in elderly persons with Alzheimer's disease and related disorders," *International Psychogeriatrics*, vol. 12, no. 1, pp. 49–65, 2000.
- [46] S. B. Hanser and L. W. Thompson, "Effects of a music therapy strategy on depressed older adults," *Journals of Gerontology*, vol. 49, no. 6, pp. P265–P269, 1994.
- [47] T. R. Lord and J. E. Garner, "Effects of music on Alzheimer patients," *Perceptual and Motor Skills*, vol. 76, no. 2, pp. 451–455, 1993.
- [48] R. W. Groene, "Effectiveness of music therapy 1:1 intervention with individuals having senile dementia of the Alzheimer's type," *Journal of Music Therapy*, vol. 30, no. 3, pp. 138–157, 1993.
- [49] M. Barinaga, "Alzheimer's treatments that work now," *Science*, vol. 282, no. 5391, pp. 1030–1032, 1998.
- [50] A. M. Kumar, F. Tims, D. G. Cruess et al., "Music therapy increases serum melatonin levels in patients with Alzheimer's disease," *Alternative Therapies in Health and Medicine*, vol. 5, no. 6, pp. 49–57, 1999.
- [51] A. M. Cevasco, "Effects of the therapist's nonverbal behavior on participation and affect of individuals with Alzheimer's disease during group music therapy sessions," *Journal of Music Therapy*, vol. 47, no. 3, pp. 282–299, 2010.
- [52] H. B. Svansdottir and J. Snaedal, "Music therapy in moderate and severe dementia of Alzheimer's type: a case-control study," *International Psychogeriatrics*, vol. 18, no. 4, pp. 613–621, 2006.
- [53] J. Cohen-Mansfield and P. Werner, "Management of verbally disruptive behaviors in nursing home residents," *Journals of Gerontology A*, vol. 52, no. 6, pp. M369–M377, 1997.
- [54] M. Enserink, "The vanishing promises of hormone replacement," *Science*, vol. 297, no. 5580, pp. 325–326, 2002.
- [55] N. Nigro and M. Christ-Crain, "Testosterone treatment in the aging male: myth or reality?" *Swiss Medical Weekly*, p. 142, 2012.

- [56] J. Compton, T. Van Amelsvoort, and D. Murphy, "Mood, cognition and Alzheimer's disease," *Best Practice and Research: Clinical Obstetrics and Gynaecology*, vol. 16, no. 3, pp. 357–370, 2002.
- [57] J. C. M. Brust, "Music and the neurologist: a historical perspective," *Annals of the New York Academy of Sciences*, vol. 930, pp. 143–152, 2001.