Table 6 Change in UPDRS part III score from baseline (SAS)

	PLA-DON10				DON5-DON10				DON10-DON10			
Evaluation points	n	Score	Change	P value ^b	n	Score	Change	P value ^b	n	Score	Change	P value ^b
Screening	46	21.4 ± 12.5	-	-	47	20.6 ± 11.9	-	_	49	19.3 ± 12.3	-	-
Week 12	37	20.1 ± 13.2	-1.1 ± 4.7	P = 0.184	32	17.0 ± 11.9	-3.0 ± 7.6	P = 0.032*	44	19.6 ± 13.2	0.3 ± 5.3	P = 0.711
Week 24	36	19.1 ± 12.0	-1.8 ± 4.6	P = 0.023*	29	17.0 ± 11.5	-3.5 ± 8.3	<i>P</i> = 0.029*	43	19.4 ± 14.7	-0.2 ± 8.6	P = 0.873
Week 40	33	19.9 ± 13.8	-2.0 ± 6.9	P = 0.106	25	16.1 ± 12.6	-5.0 ± 9.5	P = 0.014*	42	20.6 ± 15.7	0.6 ± 10.0	P = 0.680
Week 52	34	20.6 ± 16.0	-0.7 ± 9.4	P = 0.677	26	16.1 ± 13.2	-4.8 ± 10.2	P = 0.023*	40	21.1 ± 16.2	0.9 ± 10.0	P = 0.584
Week 52 (LOCF)	42	20.6 ± 14.9	-1.1 ± 8.9 .	P = 0.431	44	19.2 ± 13.9	-1.8 ± 9.6	P = 0.211	48	20.1 ± 15.5	1.0 ± 9.4	P = 0.474

UPDRS, Unified Parkinson's Disease Rating Scale; SAS, safety analysis set; LOCF, last observation carried forward.

Bolds indicate the period when the patients in each group took placebo.

Italics indicate the period when the PLA-DON10 and DON5-DON10 patients took 5 mg study drug (the PLA-DON10 and DON5-DON10 groups took 3 mg from Week 16 to 18 and Week 0 to 2, respectively).

blood pressure was reported by 2.3% (3 of 131) each. Abnormal change in pulse rate was reported by 3.1% (4 of 131), none of which led to any related serious AEs. Weight was decreased by 7% or more in 31.3% (41 of 131) of all the patients; only 4 of them were reported as AEs. None of the changes were reported as serious AEs.

Discussion

The DON5-DON10 and DON10-DON10 groups showed a significant improvement on the MMSE compared with baseline for 52 weeks. The previous long-term study presented a similar treatment effect of 5 mg donepezil over 52 weeks [23]. These results suggest that improvement of

Table 7 Incidence of psychiatric events^a (SAS)

AE ^a	PLA-DON10	DON5-DON10	DON10-DON10	DON-DON10b
	(n =37)	(n = 47)	(n =49)	(n =96)
Subjects with any psychiatric events, n (%)	6 (16.2)	9 (19.1)	9 (18.4)	18 (18.8)
Irritability	1 (2.7)	2 (4.3)	0	2 (2.1)
Cognitive disorder	0	1 (2.1)	0	1 (1.0)
Somnolence	2 (5.4)	0	0	0
Affect lability	1 (2.7)	0	0	0
Aggression	0	0	1 (2.0)	1 (1.0)
Agitation	1 (2.7)	3 (6.4)	0	3 (3.1)
Anxiety	0	1 (2.1)	0	1 (1.0)
Apathy	0	1 (2.1)	0	1 (1.0)
Delirium	0	0	1 (2.0)	1 (1.0)
Depression	0	1 (2.1)	1 (2.0)	2 (2.1)
Disinhibition	0	1 (2.1)	1 (2.0)	2 (2.1)
Disturbance in sexual arousal	0	0	1 (2.0)	1 (1.0)
Eating disorder	0	1 (2.1)	0	1 (1.0)
Hallucination	0	1 (2.1)	2 (4.1)	3 (3.1)
Hallucination, visual	0	3 (6.4)	0	3 (3.1)
Insomnia	0	4 (8.5)	2 (4.1)	6 (6.3)
Paranoia	0	1 (2.1)	1 (2.0)	2 (2.1)
Sleep disorder	1 (2.7)	1 (2.1)	0	1 (1.0)

SAS, safety analysis set; AE, adverse event.

The rest indicates the period when the patients took 10 mg (the DON10-DON10 group took 3 mg from Weeks 0 to 2, and 5 mg from Weeks 2 to 6).

^aA positive value of the UPDRS part III change indicates deterioration in motor function.

^bStudent paired t test.

^{*}P < 0.05.

^a"Psychiatric events" included Preferred Terms (PTs) classified as the SOC "Psychiatric disorders" as well as "irritability," "cognitive disorder," and "somnolence." bDON5-DON10 and DON10-DON10 groups.

Table 8 Incidence of arrhythmic events (SAS)

AE	PLA-DON10	DON5-DON10	DON10-DON10	DON-DON10 ^a
	(n =37)	(n = 47)	(n =49)	(n =96)
Subjects with any arrhythmic events, n (%)	3 (8.1)	4 (8.5)	5 (10.2)	9 (9.4)
Atrioventricular block	0	0	2 (4.1)	2 (2.1)
Palpitations	0	1 (2.1)	0	1 (1.0)
Sinus bradycardia	0	1 (2.1)	1 (2.0)	2 (2.1)
Supraventricular extrasystoles	0	1 (2.1)	0	1 (1.0)
Ventricular extrasystoles	0	0	1 (2.0)	1 (1.0)
Electrocardiogram QT prolonged	0	1 (2.1)	0	1 (1.0)
Loss of consciousness	2 (5.4)	0	1 (2.0)	1 (1.0)
Syncope	1 (2.7)	0	0	0

SAS, safety analysis set; AE, adverse event. aDON5-DON10 and DON10-DON10 groups.

cognitive impairment by donepezil at 5 mg and 10 mg is sustainable for at least 1 year in patients with DLB. In an open-label long-term study of donepezil in patients with mild to moderate AD, the improvement in MMSE was maintained until 24 weeks after administration start, and gradually waned and deteriorated afterward [32]. Considering this result in the context of a similar or faster progression in cognitive impairment in DLB than in AD [3-6], the duration during which the cognitive improvement induced by donepezil persists in patients with DLB may surpass those with AD. Although learning effects due to repeated tests possibly contributed to the improvement in the extension phase, a 1-year lasting effect of cognitive impairment is of clinical significance.

For behavioral and psychiatric symptoms, donepezil administration at any dose (5 or 10 mg) reduced the NPI-2 and NPI-10 over 52 weeks. However, similar improvement seen in the PLA-DON10 group, even from the RCT phase, makes it difficult to attribute the improvement to the study drug. It is conceivable that caregiver education about the disease and instructions on coping, which were likely given at the beginning of and during the study, affected the behavioral and psychiatric symptoms. However, because it is unlikely to last long, such an effect on the symptom improvement may be replaced or enhanced by donepezil after treatment initiation and may lead to a 1-year lasting improvement, even in the PLA-DON10 group.

With regard to the effect of dose increment in the DON5-DON10 group, although no significant improvement due to the dose increment was detected either in MMSE score or in NPI-2 score as a whole, the subgroup either with an MMSE change of <3 points or with a NPI-2 change of <30% from the baseline at Week 24 showed an improvement after the dose increment. There may be a range of doses at which the maximum improvement can be obtained, and 5 mg can provide a sufficient effect to some patients. The expected further

improvement by increasing to 10 mg may allow recommendation for a dose increase to 10 mg based on the individual safety when 5 mg is insufficient.

After Week 24, 18 patients experienced a dose reduction from 10 mg to 5 mg. Because MMSE scores remained above the baseline at all times, without deterioration of more than 0.7 points, the effects can be maintained even with a reduction to 5 mg. When intolerable at 10 mg, treatment could effectively be continued by dose reduction to 5 mg.

No great difference was observed in the occurrence of AEs due to the length of the administration period. Thus, the possibility of delayed onset of AEs with longterm treatment seems low. Most of the treatment-related AEs were mild or moderate, and only parkinsonism had an incidence of 5% or more. Of the 107 patients who continued the treatment beyond Week 24, dosage was reduced in 21 (19.6%) of patients. The main adverse events leading to dose reduction were gastrointestinal, psychiatric, and parkinsonian symptoms. All of these resolved or were relieved after dose reduction, and did not lead to discontinuation after the reduction. Gastrointestinal events are well-known adverse events of ChEIs. Gastrointestinal events most frequently reported by the patients who received 10 mg of donepezil in the 52-week study in AD patients were diarrhea (12.7%), nausea (12.2%), and vomiting (10.1%) [33]; the equivalent incidences of these in the present study in patients with DLB were lower. A slight increase in the incidence after a dose increase from 5 to 10 mg suggests the need to pay attention to the occurrence of gastrointestinal events on dose increase. However, this comparison, the present result of mostly mild to moderate severity and the absence of an increasing trend in the incidence over time support a low risk for clinically significant gastrointestinal symptoms.

Another AE of specific concern is parkinsonism; donepezil may induce or exacerbate extrapyramidal symptoms, which are threatening for DLB patients in whom parkinsonism occurs frequently. However, none of the reported parkinsonian symptoms was severe or serious. Neither the incidence nor UPDRS part III scores were inclined to increase over time, representing no notable deterioration over time. Psychiatric events were not considered to be notable safety concerns, according to their incidence (including lower rate in 10 mg group in the RCT). Arrhythmic events require particular attention, based on the incidence of 9.0% (12 of 133) of all the included patients and 3 cases of loss of consciousness, one of which was severe. In the RCT phase, the incidence of arrhythmic events did not clearly tend to increase in the active groups (placebo, 5, and 10 mg: 4.3%, 4.3%, and 6.1%, respectively). In the extension phase, the incidence by 12-week intervals did not exceed the incidence in the placebo group during the RCT phase. As loss of consciousness reported by 1 patient in the placebo group during the RCT phase is certainly attributed to the disease itself, those reported in patients who received donepezil might not be necessarily attributed to donepezil.

Another safety event to be noted is abnormal weight loss, which was reported in a substantial proportion of patients. However, it was mostly self-limited and not serious, as it was rarely recognized to be an adverse event.

The findings suggest that no major concerns exist regarding the safety or tolerability profile of long-term administration of donepezil at up to 10 mg. Safe and tolerable treatment can be assured by alerting the patients and their caregivers about the occurrence of parkinsonism and gastrointestinal or arrhythmic symptoms and managing the risks for such events by reducing the dose.

The major limitations include the short duration (12 week) of the RCT phase and the open-label design of the extension phase as well as the small sample size. Because of the progressive nature of this disease and the increasing caregiver stress, it would be difficult to enroll patients with DLB in a long-term placebo-controlled trial. For these reasons, the long-term efficacy and safety of 10 mg of done-pezil over 5 mg or placebo cannot be stated assertively.

Conclusions

The open-label long-term administration of donepezil at 10 mg/day improved impaired cognitive function for up to 52 weeks in patients with DLB without increasing the risk of clinically significant safety events.

Additional file

Additional file 1: List of all institutional review board.

Abbreviations

AD: Alzheimer disease; AE: adverse event; ANCOVA: analysis of covariance; ChAT: choline acetyltransferase; ChEI: cholinesterase inhibitor; DLB: dementia with Lewy bodies; FAS: full analysis set; LOCF: last observation carried forward; MMRM: mixed-effect model for repeated measures; MMSE: Mini-Mental

State Examination; NPI: neuropsychiatric Inventory; PPS: per protocol set; RCT: randomized, double-blind, placebo-controlled; SAS: safety analysis set; SD: standard deviation; UPDRS: Unified Parkinson's Disease Rating Scale; ZBI: Zarit Caregiver Burden Interview.

Competing interests

EM received personal fees from Eisai during the conduct of the study; grants and personal fees from Eisai, Janssen, Daiichi Sankyo, Nihon Medi-Physics, and FUJIFILM RI; personal fees from Johnson & Johnson, Lundbeck, Novartis, Ono, and Medtronic outside the submitted work. All grants were for his department, and he received them as the director of the department. MI received personal fees from Eisai during the conduct of the study; grants and personal fees from Daiichi Sankyo, Eisai, FUJIFILM RI, Janssen, Nihon Medi-Physics, Novartis, Pfizer, Takeda, and Tsumura; and personal fees from MSD, and Ono Pharmaceutical outside the submitted work. All grants were for his department, and he received them as the director of the department. RM, KM, and MN are employees of Eisai. KK received personal fees from Eisai during the conduct of the study; and personal fees from Tsumura, Eisai, Janssen, FUJIFILM RI, Novartis, Nihon Medi-Physics, Daiichi Sankyo, Ono, Otsuka, and Dainippon Sumitomo outside the submitted work.

Authors' contributions

EM and MI designed the study, analyzed the data, and wrote the manuscript. RN and KM designed the study and analyzed the data. MN designed and conducted the study. KK designed and supervised the study. All the authors reviewed the manuscript and made final approval of the version to be published.

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References

- McKeith I, Mintzer J, Aarsland D, Burn D, Chiu H, Cohen-Mansfield J, et al. International Psychogeriatric Association Expert Meeting on DLB: Dementia with Lewy bodies. Lancet Neurol. 2004;3:19–28.
- McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996;47:1113–24.
- Ballard C, O'Brien J, Morris CM, Barber R, Swann A, Neill D, et al. The progression of cognitive impairment in dementia with Lewy bodies, vascular dementia and Alzheimer's disease. Int J Geriatr Psychiatry. 2001;16:499–503.
- Ballard C, Patel A, Oyebode F, Wilcock G. Cognitive decline in patients with Alzheimer's disease, vascular dementia and senile dementia of Lewy body type. Age Ageing. 1996;25:209–13.
- Olichney JM, Galasko D, Salmon DP, Hofstetter CR, Hansen LA, Katzman R, et al. Cognitive decline is faster in Lewy body variant than in Alzheimer's disease. Neurology. 1998;51:351–7.
- Walker Z, McKeith I, Rodda J, Qassem T, Tatsch K, Booij J, et al. Comparison of cognitive decline between dementia with Lewy bodies and Alzheimer's disease: a cohort study. BMJ Open. 2012;2:e000380.
- Imamura T, Hirono N, Hashimoto M, Kazui H, Tanimukai S, Hanihara T, et al. Fall-related injuries in dementia with Lewy bodies (DLB) and Alzheimer's disease. Eur J Neurol. 2000;7:77–9.
- Kudo Y, Imamura T, Sato A, Endo N. Risk factors for falls in communitydwelling patients with Alzheimer's disease and dementia with Lewy bodies: walking with visuocognitive impairment may cause a fall. Dement Geriatr Cogn Disord. 2009;27:139–46.
- Hanyu H, Sato T, Hirao K, Kanetaka H, Sakurai H, Iwamoto T. Differences in clinical course between dementia with Lewy bodies and Alzheimer's disease. Eur J Neurol. 2009;16:212–7.
- Ballard C, Walker M, O'Brien J, Rowan E, McKeith I. The characterisation and impact of 'fluctuating' cognition in dementia with Lewy bodies and Alzheimer's disease. Int J Geriatr Psychiatry. 2001;16:494–8.
- Boström F, Jönsson L, Minthon L, Londos E. Patients with dementia with lewy bodies have more impaired quality of life than patients with Alzheimer disease. Alzheimer Dis Assoc Disord. 2007;21:150–4.
- Lee DR, McKeith I, Mosimann U, Ghosh-Nodyal A, Thomas AJ. Examining carer stress in dementia: the role of subtype diagnosis and neuropsychiatric symptoms. Int J Geriatr Psychiatry. 2013;28:135–41.
- McKeith IG, Rowan E, Askew K, Naidu A, Allan L, Barnett N, et al. More severe functional impairment in dementia with lewy bodies than Alzheimer disease is related to extrapyramidal motor dysfunction. Am J Geriatr Psychiatry. 2006;14:582–8.
- Perry EK, Haroutunian V, Davis KL, Levy R, Lantos P, Eagger S, et al. Neocortical cholinergic activities differentiate Lewy body dementia from classical Alzheimer's disease. Neuroreport. 1994;5:747–9.
- Perry EK, Irving D, Kerwin JM, McKeith IG, Thompson P, Collerton D, et al. Cholinergic transmitter and neurotrophic activities in Lewy body dementia: similarity to Parkinson's and distinction from Alzheimer disease. Alzheimer Dis Assoc Disord 1993:7:69–79
- Edwards K, Royall D, Hershey L, Lichter D, Hake A, Farlow M, et al. Efficacy and safety of galantamine in patients with dementia with Lewy bodies: a 24-week open-label study. Dement Geriatr Cogn Disord. 2007;23:401–5.
- 17. Grace J, Daniel S, Stevens T, Shankar KK, Walker Z, Byrne EJ, et al. Long-Term use of rivastigmine in patients with dementia with Lewy bodies: an openlabel trial. Int Psychogeriatr. 2001;13:199–205.

- Mori S, Mori E, Iseki E, Kosaka K. Efficacy and safety of donepezil in patients with dementia with Lewy bodies: preliminary findings from an open-label study. Psychiatry Clin Neurosci. 2006;60:190–5.
- Rowan E, McKeith IG, Saxby BK, O'Brien JT, Burn D, Mosimann U, et al. Effects of donepezil on central processing speed and attentional measures in Parkinson's disease with dementia and dementia with Lewy bodies. Dement Geriatr Cogn Disord. 2007;23:161–7.
- Thomas AJ, Burn DJ, Rowan EN, Littlewood E, Newby J, Cousins D, et al. A
 comparison of the efficacy of donepezil in Parkinson's disease with
 dementia and dementia with Lewy bodies. Int J Geriatr Psychiatry.
 2005;20:938

 44.
- McKeith I, Del Ser T, Spano P, Emre M, Wesnes K, Anand R, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet. 2000;356:2031–6.
- Mori E, Ikeda M, Kosaka K. Donepezil-DLB Study Investigators: Donepezil for dementia with Lewy bodies: a randomized, placebo-controlled trial. Ann Neurol. 2012;72:41–52.
- Ikeda M, Mori E, Kosaka K, Iseki E, Hashimoto M, Matsukawa N, et al. Donepezil-DLB Study Investigators: Long-term safety and efficacy of donepezil in patients with dementia with Lewy bodies: results from a 52week, open-label, multicenter extension study. Dement Geriatr Cogn Disord. 2013;36:229–41.
- Ikeda M, Mori E, Matsuo K, Nakagawa M, Kosaka K. Donepezil for dementia with Lewy bodies: a randomized placebo-controlled, confirmatory phase III trial. Alzheimers Res Ther. in press.
- Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology. 1997;48:S10–6.
- Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology. 1994;44:2308–14.
- Hashimoto M, Manabe Y, Mori E, Hirono N, Kosaka K, Ikeda M. Content validity and inter-rater reliability of the Cognitive Fluctuation Inventory. Brain Nerve [in Japanese]. 2014;66:175–83.
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967;17:427–42.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state. a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189–98.
- Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist. 1980;20:649–55.
- Fahn SER: UPDRS Development Committee. Unified Parkinson's disease rating scale. In: Fahn SMC, Calne D, Goldstein M, editors. Recent developments in Parkinson's disease, vol. 2. New York: Macmillan Healthcare Information; 1987. p. 153–63. 293–304.
- Tohgi H, Homma A, Imai Y, Udaka F, Takeda M, Nishimura T, et al. Longterm safety and efficacy of acetylcholinesterase inhibitor E2020 in patients with Alzheimer-type dementia: 52-week open label study. Clin Eval. 2000;28:97–126.
- Homma A, Imai Y, Tago H, Asada T, Shigeta M, Iwamoto T, et al. Long-term safety and efficacy of donepezil in patients with severe Alzheimer's disease: results from a 52-week, open-label, multicenter, extension study in Japan. Dement Geriatr Cogn Disord. 2009;27:232–9.

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(in press)

Integrating Psychiatric Services into Comprehensive Dementia Care in the Community*

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Abstract

Purpose: This study was conducted to clarify the utility of patient-held records as an integrated care approach for patients with dementia in the community.

Method: We analysed the family-held/patient-held records of patients with dementia in the community. The inclusion criteria in the study were as follows: (1) patient-held/family member-held records of patients with dementia in the community, (2) patient-held records designed to share information across different professionals, direct-care staff members, and local government staff, and (3) the continuous participation of psychiatrists in the development and use of the patient-held records.

Results: We identified eight sets of family-held/patient-held records in Japanese communities of various sizes, all of which were aimed at integrating information from various services, including information provided by medical and psychiatric professionals to the family and patient. Innovative tools have been available in the areas of the hopes and preferences of the patient, medication and monitoring, sharing information, and the use of information technology.

How to cite this paper: Author 1, Author 2 and Author 3 (2014) Paper Title. ********, *, **-**. http://dx.doi.org/10.4236/ojpsych.2014.***** Conclusion and Discussion: Family-held/patient-held records have potential as a tool to enhance the integrated care of people with dementia in the community.

Keywords

Dementia; Integrated care; Patient-held medical record; Psychiatry

1. Introduction

Dementia has become a major public health concern worldwide due to the aging populations in many countries [1]. Among the developed countries, Japan is facing a "super-aging" society with an increasing number of elderly individuals [2]. As the number of aged people increases, so does the number of people with dementia. According to the results of a multicentre epidemiological study in Japan, the numbers (prevalence per population) of individuals aged 65 and over with dementia and mild cognitive impairment were 4.6 million (15%) and 4.0 million (13%), respectively [3]. In brief, in 2013 one-fourth of the population of Japan was aged 65 and over (with a projected estimate of 40.5% in 2055), and one-fourth of the people aged 65 and older (with a projected estimate of one-tenth of the total population in 2055) were estimated to be cognitively impaired.

Integrated care is an essential concept for caring for people with dementia in the community. People with dementia often suffer from multiple chronic conditions, including diabetes [4], stroke [5] and heart disease such as atrial fibrillation [6], and thus they need to receive multiple forms of treatment from many professionals. It is also necessary for them to receive nonmedical community social services.

Family members and informal carers may play important roles in integrating these multiple services to share information about the diagnosis and individual treatment plans for people with dementia in their community. The importance of family members' roles in transition from one care service to another has been highlighted [7,8].

Patient-held medical records have been used as a tool to share care information with patients and professionals [9,10]. However, people with cognitive impairment often have difficulty in understanding and remembering to use their patient-held records, and the utility of these records for family member and informal caregivers is not clear.

This study was conducted to clarify the utility of patient-held or family-held care records as an integrated care approach for patients with dementia in the community.

2. Method

2.1. Materials

We analysed the family-held/patient-held records of patients with dementia in communities that meet our criteria in Japan. Since psychiatry is part of dementia care in Japan, we included only family-held/patient-held records that were developed in collaboration with psychiatric services. Although dementia care comprises more than psychiatry alone, it is necessary to consult with a psychiatrist when behavioural and psychological symptoms of dementia appear. The inclusion criteria in the study were as follows: (1) patient-/family member-held records for the individual with dementia, (2) the patient-held care records were designed to share information across professionals, direct-care staff members, and local government staff, and (3) psychiatrists continuously participated in the development and use of the patient-held records of patients.

2.2. Search Strategy

^{*}Special description of the title. (dispensable)

In Japan, the government's health policy promotes the use of family-held/patient-held records of patients with dementia in each prefecture, based on the Regional Health Care Strategic Plan implemented in 2013 [12]. The National Center of Neurology and Psychiatry, a government-funded national institute, helps local governments and healthcare organisations develop and use family-held/patient-held records of patients with dementia in the community. The National Center of Neurology and Psychiatry created a website with materials that are easy to access and download regarding current government health policy, emphasising the importance of family-held/patient-held records of patients with dementia. Using this website, we encouraged individuals to send us family-held/patient-held records of patients with dementia in each community, for sharing model activities with staff of other communities.

Between 2012 and 2014, we also conducted workshops on the Regional Health Care Strategic Plan with staff from local governments and healthcare organisations, in collaboration with the national-level government and that of Nagano Prefecture. Participants brought their family-held/patient-held records of patients with dementia to the workshop, the records was described to the participants.

In addition to the nationwide systematic search strategy, we searched for articles in academic communities between 2012 and 2014 in Japan, to find family-held/patient-held records of patients with dementia.

2.3. Analysis of the contents of family-held/patient-held records of patients with demen-

After searching for family-held/patient-held records of patients with dementia in Japan, our research group shared and analysed all records. We first broke down elements of each record and made a table of elements. Nine elements were categorized based on previous research [12–16] on family-held/patient-held records of patients, as follows: (1) patient profile [13,14], (2) hopes/preferences, (3) daily planner (e.g., appointments) [14–16], (4) resources [13,15,16], (5) diagnosis and treatment [14–16], (6) monitoring [14], (7) exchange note-book with multiple services [14], (8) referral, and (9) use of information technology. The elements of hopes/preferences, referral, and use of information technology were included because they are regarded as essential to the integration of care services for people with dementia in the community.

We asked staff members who use family-held/patient-held records of patients with dementia in each community to provide case descriptions of these records.

3. Results

3.1. Overview

Eight sets of family-held/patient-held records of patients with dementia met the criteria in this study. Figure 1 shows the coversheet of the records and characteristics of each of the eight communities. The populations in these communities ranged from 55,000 in Arao City to 764,000 in Tokushima Prefecture. The coversheets were unique, and Arao City (Kumamoto), Kawanishi City (Hyōgo), the Jyoetsu area (Niigata), and the Nakasorachi area (Hokkaido) also used local mascots.

Figure 1.

The contents of each family-held/patient-held record are shown in Table 1. All records were A5-sized, and four of these were presented in binders. The first set of family-held/patient-held records (Gifu) was developed primarily in 2011 by Ogaki Hospital. The records focused on the diagnosis, treatment and monitoring of symptoms, and is distributed to hospitals that are members of the Japanese Association of Psychiatric Hospitals. The Ogaki City model is currently in the feasibility study stage, aimed at connecting the family-held/patient-held records and information technology to allow information to be shared in a more flexible way. For the first (Gifu) and third (Kumamoto) sets of family-held/patient-held records of patients, there is a plan to use three standardized scales for monitoring cognitive impairment, instrumental activities of daily living, and behavioural and psychological symptoms of dementia using information technology.

The second set of family-held/patient-held records (Nagano) was developed in 2012 during a multicentre,



multidisciplinary meeting including Saku Hospital, Saku Public Health Center, and Ueda City in the area. Ueda City (population 157,000) officially distributes these records to resident family members/patients who come to the city office.

The third set of family-held/patient-held records (Kumamoto) was developed in 2012 by the Department of Neuropsychiatry at Kumamoto University. The department took a central part in dementia care planning in Kumamoto Prefecture. Family-held/patient-held records are distributed to all areas in Kumamoto Prefecture. This third set of records is focused on the four components of schedule, diagnosis and treatment, monitoring, and referral.

The referral formats are designed to be reimbursed by the fee schedule of the national insurance system. Arao City, one of 10 catchment areas in Kumamoto Prefecture, actively participates in using the third set of records. The black bear mascot, 'Kuma-mon' (kuma means 'bear' in Japanese), is a formal brand of the Kumamoto local government. Residents and staff of Kumamoto Prefecture are freely permitted to use the Kuma-mon after registration. This set of records is shared not only with staff of dementia care services, but also with dental care practitioners. In Arao City, one dentist is responsible for dental care for people with dementia in the community in addition to the patients who visit her office. She visits residential facilities and hospitals, and even visits the homes of people with dementia. She notes essential information regarding dental care in the family-held/patient-held records. A psychiatrist asked this dentist for patients' dental care records. Challenges regarding the personal and diagnostic information to be shared may be encountered; for example, sharing diagnostic information sometimes results in conflicts among various healthcare providers. In the third set of family-held/patient-held records of patients (Kumamoto Prefecture), a unique approach was developed to simplify prescriptions from multiple physicians. In this set of records, it was suggested that each physician enters information in a prescription list sheet. Items on the list include drug name, usage, the start date of the prescription, the target of the treatment, and the name of healthcare organisation. An example of the sheet is as follows:

Donepezil hydrochloride, 5 mg after breakfast, since February 10, 2014, improving forgetfulness, clinic A.

The fourth set of family-held/patient-held records (Hyōgo) was originally developed by the Department of Psychiatry at Osaka University and implemented in Kawanishi City. The records were designed primarily to share information on patient care with all multicentre staff and family members. Staff members of Kawanishi City take a central role to using the records in collaboration with the Kawanishi Medical Association. In Kawanishi City there is a unique practice whereby family members participate in a training program to use the records every month. The program facilitates information sharing not only for professionals but also with family members. The record functions as a source of important information to change prescriptions. In one case, the staff of an elder day care service noted an individual's dizziness and a high risk of falling after the administration of newly prescribed benzodiazepine. After checking the information in the records, the physician changed the individual's prescription from the benzodiazepine to another drug.

Another example was recorded with regard to the behavioural and psychological symptoms of patients with dementia. Public sector staff noted in the family-held/patient-held records that a family member reported the emergence of behavioural disturbances in persons with dementia. The physician checked the documentation and gave these patients an additional, new medication, which resulted in improvement in the behavioural problems.

The fifth set of family-held/patient-held records (Niigata Prefecture) was originally developed by a psychiatric hospital in the area. The records are designed to focus on sharing the patient's hopes and preferences in regard to their treatment and lifestyle. The record is summarized in the first person. The sections in these records include the following: (1) the patient's own preferences about where he or she wanted to live, (2) the patient's personal history and preferences, and (3) advance directives for medical decisions. This section sheet is revised periodically if necessary.

The sixth set of family-held/patient-held records (Kanagawa Prefecture) was developed in 2013 based on the experience of keeping records on depression by the Department of Psychiatry at Kitasato University East Hospital (2011). The records are unique in including monitoring the family/caregiver burden of caring for patients with dementia.

The seventh set of family-held/patient-held records (Hokkaido Prefecture) was originally developed at

Sunagawa City Medical Centre, and currently an independent non-profit organization is responsible for the distribution of the records. The records are primarily designed for referrals among services. An apple (Supporter) is the formal mascot of Sunagawa City.

The eighth set of family-held/patient-held records (Tokushima Prefecture) is the formal records of the prefecture. The prefecture started distributing the records in 2014.

Table 1.

4. Discussion

The results of our analysis showed that family-held/patient-held medical records for patients with dementia in the community are widespread in Japan. All of the integrated care programs being used are aimed at integrating information from various services, including medical and psychiatric professionals, to give to the family and patient. Innovative tools have been developed in the areas of the hopes/preferences of the patient, medication and monitoring, sharing information, and the use of information technology. In addition, we also found that family-held/patient-held records of patients are designed using local mascots.

The aims of the integrated care programs were reducing fragmentation and improving continuity and coordination of care [17]. Based on a systematic review of integrated care programs, Owens et al. (2005) categorized seven components of integrated care programs as follows: (1) self-management support and patient education, (2) clinical follow-up, (3) case management, (4) multidisciplinary patient care team, (5) multidisciplinary clinical pathway, (6) feedback, reminders and education for professionals, and (7) a supportive clinical information system and other additional requirements such as leadership [17]. The use of family-held/patient-held records of patients may primarily function as a multidisciplinary clinical pathway, and these records promote other components such as self-management support, clinical follow-up, case management, and a supportive clinical information system.

4.1. Hopes/preferences

Respecting the hopes and preferences of each patient is a critical element in the enhancement of dementia patients' self-management. Some family-held/patient-held records include a sheet for the patient's hopes and preferences, including advance directives. Recently, the concept of decisional capacity has been changing from a categorical and exclusionary concept to a dimensional and inclusionary concept [18]. Professionals need to assess what type of support is needed by people with decision-making disabilities in order for them to be involved in decision making [18]. Family-held/patient-held records of patients with dementia also function as the documentation of patient hopes and preferences from a time when the patient had a better level of decisional capacity and less cognitive impairment [19].

4.2. Follow-up

In the first (Gifu Prefecture) and third (Kumamoto Prefecture) sets of records, a follow-up plan is discussing using standardised scales: (1) The Mini-Mental State Examination (MMSE), which is a widely used questionnaire test to screen for cognitive impairment [20]; (2) Instrumental Activities of Daily Living (IADL) [21], and (3) The Neuropsychiatric Inventory (NPI), developed by Cummings et al. (1994), which is a scale consisting of 10 subdomains of behavioural function that are used to assess dementia-related behavioural symptoms [22]. Sharing the scores of the scales helps monitor changes in the clinical symptoms of patients with dementia.

4.3. Case management

Case management, or the explicit allocation of coordination tasks to an appointed individual [17], is a promising but costly component of integrated care programs. Some family-held/patient-held records of dementia patients



alternatively function as part of case management in relation to symptom monitoring and revising care plan. Case descriptions of the third (Kumamoto Prefecture) and fourth (Hyōgo Prefecture) sets of family-held/patient-held records show a coordinating function in the prescribing of medication by each physician. The healthcare system in Japan does not have a formal gate-keeping system, which means that people in their communities do not have a formal (or mandated) general practitioner, and patients with multiple chronic conditions often receive multiple prescriptions from several physicians. Family-held/patient-held records of patients may contribute to improvements in sharing information about medication changes.

4.4. Information technology

Information technology plays an important role in integrating care. A challenge of family-held/patient-held records of patients is how to share current information with multidisciplinary team members. This is important when a patient becomes sicker or unstable, when a patient shows nonadherence, and when a patient drops out. If the family-held/patient-held records of a patient is connected to a cloud server in part, care staff can check the current status of the patient using documentation from other services. At the same time, there are a number of issues to be solved with regard to the use of information technology, including confidentiality, information to be shared, and the personnel who use the information technology. Gifu Prefecture, which produced the first set of family-held/patient-held records of patients, plans to produce information about the appropriate uses of information technology with these records, based on a feasibility study.

4.5. Confidentiality

Ideally, family-held/patient-held records could be integrated using a cloud storage system on computers. However, those who are concerned about protecting individual personal information are resistant to using a cloud storage system. In addition, personal identification numbers have not been integrated in the public system in Japan. Therefore, some areas have started to use information technology for family-held/patient-held records without including the name of the patient. Another unsolved challenge regards who shares what types of information for dementia care. The Personal Information Protection Law in Japan restricts access to personal information. It is necessary to set criteria for varying levels of sharing information, and the consents of family and patients to share their information in different care settings should be required.

In the Ogaki area, the first set of family-held/patient-held records of patients was assigned an anonymous 15-digit identification number before being distributed to patients with dementia or their family members. Only staff members responsible for the direct care of the patient have access to the patient identification number table. The Ogaki area is now at the feasibility study stage, connecting the first set of family-held/patient-held records of patients and a database of cloud servers using the identification numbers. The database functions to share minimum patient information with direct care staff at multiple facilities, using three subsystems (monitoring, a social service network, and reminders) [23]. The monitoring information includes the results of assessments using the MMSE [20], IADL [21] and NPI [22], and adherence.

4.6. Healthcare system

It is surprising that family-held/patient-held records for people with dementia have been independently developed in local communities since 2011, because individuals with dementia have cognitive impairment and are often have difficulty in using patient-held records. There are three possible reasons for the community-level development, the first of which relates to the traditional family involvement in caring for patients in Asian countries [24]. Family members usually take responsibility for the informal care of patients. The family-held/patient-held records of patients enable family members to actively participate in the medical care as a 'team' caregiver.

Second, the healthcare system in Japan lacks gate-keeping tools to share medical information among staff members, patients, and family members because there is no formal gate-keeping system [25]. Countries such as

Japan have difficulty in integrating medical information among team members of various organisations. Family-held/patient-held records of patients enable the team members to share this information and functions as a gate-keeping tool. Third, since 2013 the dementia care policy and related health policies in Japan have promoted the development of care pathways for people with dementia in the community [11]. The local government of each prefecture facilitates the development and use of the pathway. All family-held/patient-held records of patients in this study are categorized as care pathways.

4.6. Limitations

The present study has several limitations. First, though our research group conducted extensive investigations to gather family-held/patient-held records of patients for 2 years, other such records do exist. Second, most of the family-held/patient-held records of patients we found are at the stage of distribution to residents of each community. Although we showed case examples, further research is necessary to assess the effectiveness of the family-held/patient-held records for caring for patients with dementia in the community.

Despite the limitations, our results highlight the new challenges of family-held/patient-held records for people with dementia in their communities, and we have identified several innovative tools for integrating care. Japan has experience in reducing infant mortality using a child and maternal health handbook that was originally developed in 1947 [26]. The handbook is currently exported to more than 20 developing and developed countries [26]. In addition, since 2008 the care pathway in the community has been promoted for patients with cancer, stroke, acute myocardial infarction, and diabetes by Japan's government. The dementia care pathway was added in 2013 [11]. This trend may help care staff develop and use family-held/patient-held records of dementia patients in Japan. Family-held/patient-held records of patients have potential as a tool to integrate the care of people with dementia in the community.

4. Conclusions

Family-held/patient-held records for dementia patients have been developed in various local communities all over Japan, aimed at the integration of information from various services. Innovative tools have been available in the areas of hopes and preferences of the patient, medication and monitoring, sharing information, and the use of information technology. Family-held/patient-held records have potential as a tool to enhance the integrated care of people with dementia in the community.

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References

- [1] Reitz C, Brayne C, Mayeux R. (2011) Epidemiology of Alzheimer disease. Nat Rev Neurology 7, 137-152.
- [2] Kaneko R, Ishikawa A, Ishii F, Sasai T, Iwasawa M, Mita F, et al. (2008) Population projections for Japan: 2006–2055 outline of results, methods, and assumptions. *The Japanese Journal of Population* **6**, 76–114. http://www.ipss.go.ip/webj-ad/webjournal.files/population/2008_4/05population.pdf.
- [3] Asada. (2014) Prevalence of people with dementia in city area and care for impairment in daily living. Final report of Health and Labor Sciences Research Grant. Available at



- http://www.tsukuba-psychiatry.com/wp-content/uploads/2013/06/H24Report Part1.pdf.
- [4] Cheng G, Huang C, Deng H, et al. (2012) Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Intern Med J* 42, 484-491.
- [5] Pendlebury ST, Rothwell PM. (2009) Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol* 8, 1006-1018.
- [6] Santangeli P, Di Biase L, Bai R, et al. (2012) Atrial fibrillation and the risk of incident dementia: a meta-analysis. *Heart Rhythm* 9, 1761-1768.
- [7] Coleman EA, Smith JD, Frank JC, et al. (2004) Preparing patients and caregivers to participate in care delivered across settings: the Care Transitions Intervention. *J Am Geriatr Soc* **52**, 1817-1825, 2004.
- [8] Elliott J, Forbes D, Chesworth BM, et al. (2014) Information sharing with rural family caregivers during care transitions of hip fracture patients. *Int J Integr Care* 14, e018, 2014
- [9] Ko H, Turner T, Jones C, et al. (2010) -held medical records for patients with chronic disease: a systematic review. *Qual Saf Health Care* 19, 1-7.
- [10] Gysels M, Richardson A, Higginson IJ. (2007) Does the patient-held record improve continuity and related outcomes in cancer care: a systematic review. *Health Expect* 10, 75-91.
- [11] Ito H, Frank RG, Nakatani Y, Fukuda Y. (2013) Regional healthcare strategic plan: growing impact of mental disorder in Japan. *Psychiatric Services* **64**, 617-619.
- [12] Farrelly S, Brown GE, Flach C, Barley E, Laugharne R, Henderson C. (2013) User-held personalised information for routine care of people with severe mental illness. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD001711. DOI: 10.1002/14651858.CD001711.pub2.
- [13] Brunero S, Lamont S, Myrtle L, et al. (2008) The Blue Card: a hand-held health record card for mental health consumers with comorbid physical health risk. *Australasian Psychiatry* 16, 238-243.
- [14] Lester H, Allan T, Wilson S, et al. (2003) A cluster randomized controlled trial of patient-held medical records for people with schizophrenia receiving shared care. *Br J Gene Practice* **53**, 197-203.
- [15] Stafford A, Hannigan B. (1997) Client-held records in community health. Nursing Times 93, 50-51.
- [16] Warner JP King M, Blizard R, et al. (2000) Patient-held shared care records for individuals with mental illness. *Br J Psychiatry* 177, 319-324.
- [17] Ouwens M, Wollersheim H, Hermens R, et al. (2005) Integrated care programmes for chronically ill patients: a review of systematic reviews. *Int J Qual Health Care* 17, 141-146, 2005.
- [18] Peisah C, Sorinmad OA, Mitchell L, et al. (2013) Decisional capacity: toward an inclusionary approach. International *Psychogeriatrics* **25**, 1571-1579.
- [19] Campbell LA, Kisely SR. (2009) Advance treatment directives for people with severe mental illness. *Cochrane Database Syst Rev* 2009.
- [20] Folstein MF, Folstein SE, McHugh PR (1975). ""Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". *Journal of Psychiatric Research* 12,: 189-198.
- [21] Lawton MP, Brody EM. (1969) Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 9, 179-186.
- [22] Cummings, J., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 44, 2308-2314.
- [23] Ito H, Sugiura S, Noda H, Higuchi T. (2013) Creating an online patient follow-up system. *Shakai Hoken Jyunpo* **2531**, 10-14 (in Japanese). Available at http://mhcnp.jp/pdf/130513_syakaiHokenJunpo.pdf. Accessed on September 30, 2014.
- [24] Ito H, Setoya Y, Suzuki Y (2012) Lessons learned in developing community mental health care in East and South East Asia. *World Psychiatry* 11, 186-190.
- [25] OECD 2010, "Health care systems: Getting more value for money", OECD Economics Department Policy

- Notes, No. 2. Available at http://www.oecd.org/eco/growth/46508904.pdf. Accessed on September 30, 2014
- [26] Nakamura Y. (2010) Maternal and Child Health Handbook in Japan. *JMAJ* 53, 259-265. Available at https://www.med.or.jp/english/journal/pdf/2010 04/259 265.pdf. Accessed on September 30, 2014.

Fig. 1. Coversheets of family-held/patientheld records of patients



Orange handbook Ogaki city, *Gifu prefecture* Population: 163,000



Support handbook Sagamihara city, Kanagawa prefecture Population: 722,000



Warm handbook Toshin area, *Nagano prefecture* Population: 256,000



Worry Free Notebook for people with dementia Arao city, *Kumamoto prefecture* Population: 55,000



Connected notebook Kawanishi city, *Hyogo prefecture* Population: 156,000



Smile notebook Jyoetsu area, *Niigata prefecture* Population: 279,000



Support and joint notebook Nakasorachi area, *Hokkaido prefecture* Population: 118,000



Next to you notebook Tokushima prefecture Population: 764,000 Table 1. Contents of family-held/patient-held records

		1	2	3	4	5	6	7	8
Prefecture		Gifu	Nagano	Kumamoto	Hyōgo	Niigata	Kanagawa	Hokkaido	Tokushima
Year (first	version)	2011	2012	2012	2013	2013	2013	2013	2014
Style	Size	A5	A5	A5	A5	A5	A5	A5	A5
Style	Binder			×	×	×	×		
Patient pro	file	×	×	×	×	×		×	×
Hope/prefe	rence		×		×	xx	×	×	×
Daily planner (appointment)			×	××	××	××	××		
Resources		×	×	×	×	×	×	×	×
Diagnosis and treatment (dementia)		×	×	×	×	×	×	×	×
Diagnosis a (other disea	and treatment ases)	×		××	×	×	×	×	×
Monitoring	5	xx	×	xx	×	×	××	×	
Exchange notebook with multiple services			×	××	××	××	×	×	
Referral				××				xx	××
Use of info nology	rmation tech-	xx		×					

^{×:} The element is included. ××: The included element is evaluated as rich and innovative.

ORIGINAL RESEARCH

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Clinical Features of Delusional Jealousy in Elderly Patients With Dementia

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ABSTRACT

Objective: Delusional jealousy is a psychotic syndrome characterized by a belief in the infidelity of one's spouse that reaches delusional intensity. Although delusional jealousy has been described in relation to organic psychosis, little is known concerning the actual role of delusional jealousy in dementia. The aim of the present study was to investigate the clinical features of delusional jealousy and possible mechanisms whereby delusional jealousy arises in patients with dementia.

Method: We studied 208 consecutive outpatients with dementia (diagnosis based on DSM-III-R criteria; mean [SD] age of 77.0 [8.0] years; study period: September 2011– August 2012). Delusional jealousy was defined as a false belief derived from a pathological jealousy that makes the patient believe that his or her spouse is unfaithful. The prevalence of delusional jealousy was compared between Alzheimer's disease, dementia with Lewy bodies, and vascular dementia. Patients with and without delusional jealousy were compared in terms of general characteristics. In addition, each patient with delusional jealousy and their primary caregivers were interviewed about the clinical features of the syndrome.

Results: Of the 208 patients with dementia, 18 (8.7%) showed delusional jealousy. The prevalence of delusional jealousy in patients who had dementia with Lewy bodies (26.3%) was significantly higher than that in patients with Alzheimer's disease (5.5%) (P<.01). There were no significant differences between patients with and without delusional jealousy in regard to gender (P=1.00), age (P=.81), educational attainment (P=.29), presence of other persons living with the couple (P=.22), and Mini-Mental State Examination score (P=.47). On the other hand, delusional jealousy was preceded by the onset of serious physical diseases in nearly half of the patients. Delusional jealousy resolved within 12 months after treatment in 15 of 18 patients (83%).

Conclusions: Although delusional jealousy is a considerable problem in dementia, the prognosis of delusional jealousy in demented patients appears to be relatively benign. In dementia, delusional jealousy may develop more easily in patients who have dementia with Lewy bodies and those with coexisting serious physical disorders.

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Submitted: January 24, 2014; accepted July 30, 2014. Online ahead of print: April 28, 2015 (doi:10.4088/JCP.14m09018). Corresponding Author: Mamoru Hashimoto, MD, PhD, Department of Neuropsychiatry, Faculty of Life Sciences, Kumamoto University, Honjo1-1-1, Chuo-ku, Kumamoto, 860-8556, Japan (m-hashi@kumamoto-u.ac.jp).

elusional jealousy, also known as Othello's syndrome, is a psychotic disorder characterized by the belief in the infidelity of one's spouse or lover that reaches delusional intensity. Delusional jealousy may be observed in many psychiatric disorders, but previous clinical reports have noted the association of this morbid condition in several organic psychoses, including stroke, 3,4 Parkinson's disease, 5,6 traumatic brain injury, 7 and dementia. 8 Soyka et al 9 found that the prevalence of delusional jealousy was highest in organic psychoses (7.0%), followed by paranoid disorders (6.7%), alcohol psychosis (5.6%), and schizophrenia (2.5%); whereas in affective disorder, delusional jealousy was found in only 0.1% of patients. These findings suggest that neurologic elements very likely combine with psychodynamic factors to produce this specific condition. 10

In dementia, delusions constitute one of the most prominent psychiatric complications.¹¹ Delusional jealousy was described as the initial clinical symptom in the first clinical Alzheimer's disease case reported by Alois Alzheimer.⁸ Tsai et al¹² comprehensively investigated the clinical features of delusional jealousy in patients with dementia within a psychiatric ward and identified delusional jealousy in as many as 15.6% of demented patients. Furthermore, with respect to individual delusional symptoms, delusional jealousy has been identified as a risk factor for aggression and homicide, especially against one's partner. 13 These findings suggest that evaluation and treatment of delusional jealousy are of considerable importance in practice for demented patients. However, to our knowledge, there have been few systematic studies about the clinical features of delusional jealousy in persons suffering from dementia, 12 and little is known concerning the actual role of delusional jealousy in dementia. The aim of this study was to investigate the clinical features of delusional jealousy and possible mechanisms whereby delusional jealousy arises in patients with dementia.

METHOD

All procedures followed the Clinical Study Guidelines of the Ethics Committee of Kumamoto University Hospital, Kumamoto, Japan, and were approved by the internal review board. Informed written consent was obtained from patients and their caregivers in compliance with the research standards for human research for all participating institutions and in accordance with the Helsinki Declaration.

Subjects

A total of 208 patients (mean [SD] age of 77.0 [8.0] years) were selected according to the following inclusion/exclusion criteria from a consecutive series of 327 demented patients who attended 1 of 2 dementia clinics from September 2011 to August 2012 at Kumamoto University Hospital or Heisei Hospital, which is a mental hospital. All patients were examined comprehensively by senior

- Among diagnostic categories of dementia, delusional jealousy develops more easily in patients with dementia with Lewy bodies.
- In addition to cognitive decline, coexisting serious physical illness is a significant risk factor of delusional jealousy in demented patients.
- Although delusional jealousy is often accompanied by violent behavior and can add to the stress experienced by the patient's spouse, the prognosis of delusional jealousy in demented patients is relatively benign.

neuropsychiatrists with sufficient experience in examining patients with dementia, and all patients underwent routine laboratory tests and standard neuropsychological examinations including the Mini-Mental State Examination (MMSE). ¹⁴ Brain magnetic resonance imaging (MRI) or computed tomography (CT) was also performed. Exclusion criteria consisted of the following: (1) patients with serious psychiatric diseases such as schizophrenia or major depression before the onset of dementia and (2) patients without a spouse.

The diagnosis of dementia was based on *DSM-III-R* criteria. ¹⁵ The diagnosis of each dementia was established according to the international consensus criteria. Diagnostic categories consisted of probable Alzheimer's disease (n=127), ¹⁶ probable dementia with Lewy bodies (n=38), ¹⁷ vascular dementia (n=21), ¹⁸ frontotemporal lobar degeneration (n=7), ¹⁹ possible idiopathic normal pressure hydrocephalus (iNPH) (n=6), ²⁰ probable progressive supranuclear palsy (n=4), ²¹ probable corticobasal degeneration (n=3), ²² and unspecified etiology (n=2).

Assessments of Delusional Jealousy

In the present study, delusional jealousy was defined as a false belief derived from a pathological jealousy that makes the patient believe that his or her spouse is unfaithful.¹² Specifically, the delusion had to be clearly and repeatedly stated some time during the follow-up period and had to require therapeutic intervention. Patients with these characteristics were assigned to the delusional jealousy group. Thus, the delusional jealousy group did not include patients with mild or episodic delusional jealousy without therapeutic intervention. The remaining patients were assigned to the non-delusional jealousy group. In each case in the delusional jealousy group, the patient and primary caregiver were interviewed by the authors, senior neuropsychiatrists, about the presence of the following features: (1) coexisting psychiatric symptoms such as hallucinations, other types of delusions, or depression; (2) coexisting severe physical disorder of the patient (severe physical disorder was defined as present if the disorder was severe enough to require hospitalization or to interfere with the patient's activities of daily living); (3) violent behavior by the patient; (4) past history of infidelity by the spouse;

Table 1. Demographics of Demented Patients With and Without Delusional Jealousy

Delusional Jealousy Group (n = 18)	Non–Delusional Jealousy Group (n=190)	P Value
77.4 (5.6)	76.9 (8.2)	.81
9/9	95/95	1.00
10.1 (2.7)	10.9 (2.9)	.29
6 (33)	92 (48)	.22
18.7 (5.9)	17.5 (6.8)	.47
	Jealousy Group (n = 18) 77.4 (5.6) 9/9 10.1 (2.7) 6 (33)	Jealousy Group (n=18) Non-Delusional Jealousy Group (n=190) 77.4 (5.6) 76.9 (8.2) 9/9 95/95 10.1 (2.7) 10.9 (2.9) 6 (33) 92 (48)

(5) health condition of the spouse; and (6) spouse's frequent absence in the home (*frequent absence* was defined as present if the spouse went out alone a few times a week or more).

Statistics

The prevalence of delusional jealousy was compared against each diagnostic category that comprised 10 or more patients. Fisher exact probability test was utilized. In addition, to examine risk factors for delusional jealousy, gender, age, educational attainment, presence of other people living with the couple, and MMSE scores were compared between the delusional jealousy and non–delusional jealousy groups. Student t test and χ^2 test were used when appropriate. The significance level was set at P < .05 for all analyses.

RESULTS

Of the 208 demented patients with a spouse, 18 (8.7%) met the inclusion criteria for having delusional jealousy. Patients with delusional jealousy were found to have various types of dementia; 7 patients had Alzheimer's disease, 10 patients had dementia with Lewy bodies, and 1 patient had vascular dementia. The prevalence of delusional jealousy in patients with dementia with Lewy bodies (26.3%) was significantly higher than that in patients with Alzheimer's disease (5.5%) (P < .01), and patients with dementia with Lewy bodies tended to have a higher prevalence of delusional jealousy than patients with vascular dementia (4.8%) (P = .08). Nine patients already had delusional jealousy at the initial visit; in the other 9 patients, delusional jealousy developed during the follow-up period. Table 1 shows the clinical characteristics of the delusional jealousy and non-delusional jealousy groups. We found no significant differences between the 2 groups in regard to gender, age, educational attainment, presence of other people living with the couple, and MMSE scores. However, 10 of the 18 patients with delusional jealousy had mild dementia; these patients' MMSE scores were 20 or

Table 2 shows a comparison of coexisting psychiatric symptoms among dementia with Lewy bodies, Alzheimer's disease, and vascular dementia. All but 1 patient with dementia with Lewy bodies had at least 1 other psychotic symptom. Eight patients with dementia with Lewy bodies exhibited visual hallucinations. The contents of the visual hallucinations included images of the patient's spouse in a

Table 2. Number of Patients With Coexisting Psychiatric Symptoms and Violence

	Dementia With Lewy Bodies (n=10)	Alzheimer's Disease (n=7)	Vascular Dementia (n=1)	Total (N = 18)
Hallucinations				
Visual	8	0	0	8
Auditory	1	1	0	2
Delusions				
Misidentification	8	0	0	8
Theft	2	0	0	2
Persecution	2	2	0	4
Depression	2	1	0	3
Violence	6	5	0	11

Table 3. Period Between Initiation of Therapy and Disappearance of Delusional Jealousy^a

	Dementia With	Alzheimer's	Vascular	
	Lewy Bodies	Disease	Dementia	Total
	(n=10)	(n=7)	(n=1)	(N = 18)
1–3 months	3	3	1	7
4-12 months	4	4	0	8
Intractable	3	0	0	3
^a Values represe	nt the number of pa	atients (n).		

sexual situation (2 patients), the spouse having an affair in the house (3 patients), and the spouse having a child with his or her lover (2 patients). Six patients with dementia with Lewy bodies misidentified his or her spouse as another person in a delusional manner. In 1 patient with dementia with Lewy bodies, delusional jealousy persisted after the death of the spouse. Two patients with dementia with Lewy bodies were noted to have increased sexual desire after the onset of dementia. Two patients with Alzheimer's disease had other psychotic symptoms. One patient with Alzheimer's disease suffered from auditory hallucinations, including hearing knocking at the door that the patient attributed to the spouse's lover. In this series, 7 of 9 males and 4 of 9 females committed actual physical assault on their spouse. We found no significant gender differences in regard to the prevalence of violent behavior (P = .15).

Several precipitating or predisposing factors for delusional jealousy were identified. Delusional jealousy was preceded by the onset of serious physical diseases, such as cancer, aortic aneurysm, or femoral neck fracture in 8 patients (44%). In contrast, all the spouses, except for 1, who suffered from iNPH, were active and in good health. Eight of 18 spouses (44%) frequently spent time away from home without the patient. In the present study, only 1 spouse (5.6%) was confirmed to have a previous history of infidelity. Although delusional jealousy has been described in Parkinson's disease patients on dopaminergic therapy, 23,24 only 1 patient who had dementia with Lewy bodies was treated with antiparkinson medication in this series; this patient had undergone dopaminergic therapy 3 years prior to the development of delusional jealousy.

All 10 patients who had dementia with Lewy bodies were treated with donepezil medication. In addition to donepezil, treatment for 6 of the patients with dementia

with Lewy bodies also included atypical neuroleptics such as quetiapine, olanzapine, and aripiprazole. All 7 patients with Alzheimer's disease were treated with neuroleptic medications: 6 were treated with risperidone, and 1 was treated with sulpiride. In 3 of the 7 patients with Alzheimer's disease, donepezil was discontinued or decreased. One patient who suffered from vascular dementia improved with risperidone medication for a couple of months. Delusional jealousy resolved after treatment in 15 of 18 patients (83%) (Table 3), and all of the 7 patients with Alzheimer's disease experienced complete resolution of delusional jealousy within 12 months, although antipsychotic therapy continued for over 12 months after delusional jealousy disappearance in all patients. In 3 patients with dementia with Lewy bodies, delusional jealousy showed no response to treatment. In 1 female patient with dementia with Lewy bodies, delusional jealousy improved with donepezil administration for 8 months; however, she had a relapse in delusional jealousy after an improvement in her husband's health following an operation for iNPH. Two of the 3 recalcitrant patients exhibited visual hallucinations of their spouses in sexual acts, and the remaining patient recurrently mistook her husband for her father-in-law. Only 1 patient with dementia with Lewy bodies was placed in a nursing home due to active delusional jealousy.

DISCUSSION

Although delusional jealousy is a known risk factor for violence and homicide, ¹³ it has been considered a rare syndrome. Soyka et al⁹ studied the prevalence of delusional jealousy in over 8,000 psychiatric inpatients and found an overall low prevalence of 1.1%. However, the authors also found that delusional jealousy was most frequently seen in patients with organic psychoses, in whom its prevalence reached 7.0%. In the present study, we reported that 8.7% of demented patients exhibited delusional jealousy, which was well within the 2.3%²⁵ to 15.6%¹² range reported in previous studies. These findings suggest that delusional jealousy is a frequent symptom in dementia and that neurologic elements including cognitive decline quite likely produce delusional jealousy in combination with psychosocial factors.

The most remarkable finding of the present study was the fact that as many as 26.3% of patients with dementia with Lewy bodies exhibited delusional jealousy, and the prevalence of delusional jealousy in patients with dementia with Lewy bodies was significantly higher than that in patients with Alzheimer's disease. Although delusional jealousy has been observed in neurologic patients, particularly in those with Parkinson's disease,⁵ little is known about the association between delusional jealousy and dementia with Lewy bodies. In a recent case series of 105 patients with delusional jealousy, Graff-Radford et al²⁶ reported that 29 of 56 patients with a neurodegenerative disorder had Lewy body disease, which was seen with a higher frequency than Alzheimer's disease (n = 22). Both the findings of Graff-Radford et al and the present study indicate the possibility that patients with dementia with

Lewy bodies exhibit a higher frequency of delusional jealousy as compared to other demented patients, including those with Alzheimer's disease.

Most of the patients with dementia with Lewy bodies in the present study presented with visual hallucinations with concrete contents suggesting spousal infidelity. This phenomenon had been reported elsewhere. Graff-Radford et al²⁶ reported that 4 of 20 patients with dementia with Lewy bodies had visual hallucinations specific to spousal infidelity resulting in delusional jealousy. Although visual hallucinations and delusions are common symptoms in patients with dementia with Lewy bodies, 27,28 the underlying mechanisms of these symptoms have not been fully clarified. Nagahama et al²⁹ investigated the association between psychotic symptoms in dementia with Lewy bodies and brain perfusion using single-photon emission computed tomography and revealed that delusions and visual hallucinations were served by distinguishable cerebral networks. On phenomenological grounds, it is not clear whether visual hallucinations pertaining to a sexual theme induced the thought of the spouse's infidelity or whether suspicion about the spouse's infidelity induced hallucinations involving the spouse committing sexual indiscretions. Nevertheless, the common theme of visual hallucinations with delusional jealousy may suggest a potential link between these symptoms in dementia with Lewy bodies.

Low self-esteem and feelings of insecurity and inferiority have been considered central to many psychological theories of delusional jealousy in the literature. 1,2,30 According to Sibisi,³¹ the accusation of infidelity develops in parallel with deteriorating cognitive function. However, we found no significant differences between the delusional jealousy and non-delusional jealousy groups in regard to MMSE score. Rather, in 10 of the 18 patients with delusional jealousy, MMSE score was greater than 20, suggesting that the occurrence of delusional jealousy may require a certain level of cognitive function. In dementia, especially in mild cases, cognitive decline can give the patient a feeling of inferiority compared to his or her spouse. Numerous studies have reported that awareness of deficits decreased with disease progression in patients with dementia,³² meaning that impaired intellect in the later stages of dementia could weaken the patient's feelings of inferiority. Thus, delusional jealousy in patients in earlier stages of dementia may be strengthened by the fact that the patient has considerable remaining intellectual ability, and is thus more likely to have feelings of inferiority.

Disparities in health between the patient and spouse have also been proposed as specific and distinct risk factors for delusional jealousy in the elderly.³³ In the present study, 8 patients (44%) had serious physical diseases before the onset of delusional jealousy; as a result, these patients became more dependent upon their spouses for daily living and activities. In contrast, all but 1 of the spouses were active and in good health. In addition, nearly half of the spouses in our study often spent time away from the home alone. Physical

disorders of the patient and good health of the spouse could therefore contribute to the patient's feelings of inferiority with regard to the spouse. In addition to cognitive decline, coexisting serious physical disorders may be a significant risk factor of delusional jealousy in demented patients.

Most catamnestic studies have shown that delusional jealousy in older patients usually has a poor prognosis. 2,34,35 Jørgensen and Munk-Jørgensen³⁴ followed up with patients over 60 years of age who were diagnosed with paranoid psychosis over 5-15 years and reported that only 2 of 24 patients with delusions comprising sexual ideas or jealousy achieved full remission. In contrast, in the present study, delusional jealousy disappeared within 1 year after treatment in as many as 83% of the patients with dementia. In addition, all but 1 patient with dementia with Lewy bodies who was placed in a nursing home due to active delusional jealousy continued outpatient treatment without institutionalization or hospitalization. These findings suggest that delusional jealousy in patients with dementia may have a much better prognosis than those with other psychiatric disorders. It is noteworthy that all of the patients with treatment-resistant delusional jealousy in the present study had dementia with Lewy bodies. In addition, 1 patient with recurrent episodes of delusional jealousy had dementia with Lewy bodies. Generally, the prognosis for delusional jealousy is considered to depend on the existence of comorbid mental disorders.³⁶ The existence of other psychotic symptoms, such as visual hallucinations, may result in a worse prognosis in patients with dementia with Lewy bodies.

Several methodological issues limit the interpretation of the present results. First, psychiatric symptoms were assessed by a clinical interview without using a structured assessment scale, such as Neuropsychiatric Inventory (NPI).³⁷ In addition, delusional jealousy can be difficult to diagnose because of the reluctance of patients and caregivers to discuss personal matters. These methodological problems can make the current prevalence of delusional jealousy seem lower than it is. In the present study, senior neuropsychiatrists investigated the contents of delusional jealousy and coexisting psychiatric symptoms using both the patient and their primary caregiver. Moreover, this research excluded subjects with mild or episodic delusional jealousy and focused on clinically relevant delusional jealousy, allowing us to obtain robust observations about delusional jealousy. Second, the statistical evaluation was limited by the small sample size of the delusional jealousy group. Third, premorbid personality of demented patients was not considered in the present study. Specific types of premorbid personality (passive personality, borderline personality, or paranoid personality) have been hypothesized to be significant factors in the development of delusional jealousy.³⁸ In future studies, the relationship between delusional jealousy and premorbid personality in people with dementia should be evaluated.

Drug names: aripiprazole (Abilify), donepezil (Aricept and others), olanzapine (Zyprexa and others), quetiapine (Seroquel and others), risperidone (Risperdal and others).

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Author contributions: Dr Hashimoto designed this study, worked on data analysis, and drafted the article. Dr Sakamoto helped to collect the data and analyzed and interpreted the data. Dr Ikeda supervised this study and was responsible for the statistical design of the study.

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REFERENCES

- 1. Shepherd M. Morbid jealousy: some clinical and social aspects of a psychiatric symptom. *J Ment Sci.* 1961;107(449):687–704. Cobb J. Morbid jealousy. *Br J Hosp Med.* 1979;21(5):511–518.
- 3. Richardson ED, Malloy PF, Grace J. Othello syndrome secondary to right cerebrovascular infarction. J Geriatr Psychiatry Neurol. 1991;4(3):160-165.
- 4. Luauté JP, Saladini O, Luauté J. Neuroimaging correlates of chronic delusional jealousy after right cerebral infarction. J Neuropsychiatry Clin Neurosci. 2008;20(2):245-247.
- 5. Cannas A, Solla P, Floris G, et al. Othello syndrome in Parkinson disease patients without dementia. Neurologist. 2009;15(1):34-36.
- 6. Poletti M, Perugi G, Logi C, et al. Dopamine agonists and delusional jealousy in Parkinson's disease: a cross-sectional prevalence study. Mov Disord. 2012;27(13):1679-1682.
- Butler PV. Reverse Othello syndrome subsequent to traumatic brain injury. Psychiatry. 2000;63(1):85-92.
- 8. Alzheimer A. Uber eine eigenartige Erkrankung der Hirnrinde. Allg Z Psychiat Psych Gerichtl Med. 1907;64:146-148.
- Soyka M, Naber G, Völcker A. Prevalence of delusional jealousy in different psychiatric disorders: an analysis of 93 cases. Br J Psychiatry. 1991; 158(4):549–553.
- 10. Malloy PF, Richardson ED. The frontal lobes and content-specific delusions. J Neuropsychiatry Clin Neurosci. 1994;6(4):455-466.
- 11. Finkel SI. Behavioral and psychological symptoms of dementia: a current focus for clinicians, researchers, and caregivers. J Clin Psychiatry. 2001;62(suppl 21):3-6.
- 12. Tsai SJ, Hwang JP, Yang CH, et al. Delusional jealousy in dementia. J Clin Psychiatry. 1997;58(11):492-494.
- 13. Silva JA, Derecho DV, Leong GB, et al. Stalking behavior in delusional jealousy. J Forensic Sci. 2000;45(1):77-82.
- 14. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189-198.
- 15. American Psychiatric Association. Diagnostic and Statistical Manual on

- Mental Disorders, Third Edition-Revised. Washington, DC: American Psychiatric Association; 1987.
- 16. McKhann G, Drachman D, Folstein M, et al. 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. 1984;34(7):939-944.
- McKeith IG, Dickson DW, Lowe J, et al; Consortium on DLB. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology. 2005;65(12):1863-1872.
- Chui HC, Victoroff JI, Margolin D, et al. Criteria for the diagnosis of ischemic vascular dementia proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers. Neurology. 1992;42(3, pt 1):473-480.
- Neary D, Snowden JS, Gustafson L, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology. 1998;51(6):1546-1554.
- Ishikawa M, Hashimoto M, Kuwana N, et al. Guidelines for management of idiopathic normal pressure hydrocephalus. Neurol Med Chir (Tokyo). 2008;48(suppl):S1-S23.
- 21. Litvan I, Mangone CA, McKee A, et al. Natural history of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome) and clinical predictors of survival: a clinicopathological study. J Neurol Neurosurg . Psychiatry. 1996;60(6):615–620.
- Boeve BF, Lang AE, Litvan I. Corticobasal degeneration and its relationship to progressive supranuclear palsy and frontotemporal dementia. Ann Neurol. 2003;54(suppl 5):S15-S19.
- Marsh L, Williams JR, Rocco M, et al. Psychiatric comorbidities in patients with Parkinson disease and psychosis. Neurology. 2004;63(2):293-300.
- Chou KL, Messing S, Oakes D, et al. Drug-induced psychosis in Parkinson disease: phenomenology and correlations among psychosis rating instruments. Clin Neuropharmacol. 2005;28(5):215-219.
- Mendez MF, Martin RJ, Smyth KA, et al. Psychiatric symptoms associated with Alzheimer's disease. J Neuropsychiatry Clin Neurosci. 1990;2(1):28-33.
- Graff-Radford J, Whitwell JL, Geda YE, et al. Clinical and imaging features of Othello's syndrome. Eur J Neurol. 2012;19(1):38-46.
- Ballard C, Holmes C, McKeith I, et al. Psychiatric morbidity in dementia with Lewy bodies: a prospective clinical and neuropathological comparative study with Alzheimer's disease. Am J Psychiatry. 1999;156(7):1039–1045.
- Hirono N, Cummings JL. Neuropsychiatric aspects of dementia with Lewy bodies. Curr Psychiatry Rep. 1999;1(1):85-92.
- Nagahama Y, Okina T, Suzuki N, et al. Neural correlates of psychotic symptoms in dementia with Lewy bodies. Brain. 2010;133(pt 2):557-567.
- Seeman MV. Pathological jealousy. Psychiatry. 1979;42(4):351-361.
- Sibisi CD. The phenomenology of delusional jealousy in late life. Int J Geriatr Psychiatry. 1999;14(5):398-399.
- Kashiwa Y, Kitabayashi Y, Narumoto J, et al. Anosognosia in Alzheimer's disease: association with patient characteristics, psychiatric symptoms and cognitive deficits. Psychiatry Clin Neurosci. 2005;59(6):697-704.
- Breitner BCC, Anderson DN. The organic and psychological antecedents of delusional jealousy in old age. Int J Geriatr Psychiatry. 1994;9(9):703-707.
- Jørgensen P, Munk-Jørgensen P. Paranoid psychosis in the elderly: a followup study. Acta Psychiatr Scand. 1985;72(4):358-363.
- Soyka M. Delusional jealousy in psychiatric disorders of later life. *Int J* Geriatr Psychiatry. 1992;7(8):539-542.
- Kingham M, Gordon H. Aspects of morbid jealousy. Adv Psychiatr Treat. 2004;10(3):207-215.
- 37. Cummings JL, Mega M, Gray K, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology. 1994;44(12):2308-2314.
- Cipriani G, Vedovello M, Nuti A, et al. Dangerous passion: Othello syndrome and dementia. Psychiatry Clin Neurosci. 2012;66(6):467-473.

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Correlation between cognition and symptomatic severity in patients with late-life somatoform disorders

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