



Dementia Still Diagnosed Too Late – Data from the Czech Republic

**Jan LUZNY^{1,2}, Iva HOLMEROVA³, Petr WIJA³, Igor ONDREJKA⁴*

1. Dept. of Psychogeriatry, Mental hospital Kromeriz, Kromeriz, Czech Republic
2. Dept. of Social Medicine and Public Health, Faculty of Medicine, Palacky University, Olomouc, Czech Republic
3. Center of Longevity, Faculty of Humanities, Charles University in Prague, Czech Republic
4. Dept. of Psychiatry, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Slovak Republic

***Corresponding Author:** Tel: +420 573314111 Email: luznyj@plkm.cz

(Received 09 May 2014; accepted 15 Aug 2014)

Abstract

Background: The goal of the study is to evaluate the sensitivity of Czech physicians to the early diagnosis of dementia in patients with memory impairment.

Methods: A retrospective observational study was designed. We have reviewed the electronic medical records of patients who have been hospitalized for the first time due to dementia of any type at the Kromeriz Mental hospital from January 1, 2012 to December 31, 2013 (24-month period). Pluralistic methods combining the qualitative and quantitative approach were used in this study.

Results: Dementia of any type was diagnosed in 125 patients in the monitored period. The mean time between patient memory complaints and his / her admission to our facility for their first hospitalization due to dementia was 7.1 years (+- 3.7 years). Most patients with dementia had no prior outpatient treatment of their memory impairment (56.2%); a minority of patients (43.8%) had treatment of their memory impairment by an outpatient physician.

Conclusion: The sensitivity of Czech physicians to the early diagnosis of dementia is very low. Any delay in starting the treatment of dementia means a worsened effectiveness of this treatment, a worsened quality of life of patients with dementia and their caregivers. Our recommendations for both the early diagnosis and treatment of dementia should be involved in guidelines and should become a part of the pregraduate and postgraduate education of all physicians.

Keywords: Dementia, Cognitive enhancers, Electronic medical records, Content analysis

Introduction

Dementia of any type belongs to the new non-communicable pandemic of these days. The increasing incidence of dementia is the result of the demographic aging of the population in well-developed countries (1). The improved quality of health care services are prolonging life expectancy - many patients with somatic diseases are surviving heart attacks, strokes, cancer or diabetes mellitus, so that there is a chance for developing age-related neurodegenerative disorders including de-

mentia (2, 3). The prevalence of dementia is estimated from 5% prevalence at the age of 65 to 40% prevalence at the age of 80 (4, 5). Dementia is an incurable neurodegenerative disorder with a natural course leading to the worsening of both the mental and somatic state and death (6-8). In the case of severe dementia, the loss of autonomy usually reaches a critical level and the affected individual is usually unable to carry out the basic activities of daily living (such as ingesting food

and liquids, maintaining personal hygiene). Incontinence usually develops in this stage of dementia, together with accessory neurological symptoms such as dysphagia, motor function abnormalities or immobility (7, 9). Dementia at the caregiver level leads to the risk of developing burnout syndrome and the risk of a lowered quality of life in both patients with dementia and their caregivers. Dementia at the national level means increasing financial expenditures spent on health and social care systems (10).

The preventive role of medicine comes to the forefront in dementia. The primary prevention of dementia should decrease all known risk factors closely linked to etiopathogenesis of neurodegenerative dementia – smoking habits, early detection and treatment of hyperlipidemia, arterial hypertension, hyperglycemia and hyperuricemia. On the contrary, protective factors should be promoted – healthy nutrition and the lifelong promotion of motor and mental activity (sports and memory training) (11). The secondary prevention of dementia means the early detection and early treatment of memory impairment. Early treatment with anti-dementia drugs (inhibitors of cholinesterase, memantine) together with non-pharmacological modalities may stop the development of dementia symptoms for a long time and may delay the progression of dementia to severe stages. Modern diagnostic tools may be helpful in this early diagnostics – including genetic tests (apo E4 polymorphism tests, early markers of neurodegeneration tests), liquor tests of early neurodegenerative markers (tau / phospho protein levels, neuron specific enolase levels) or neuroimaging methods (functional MRI, SPECT, PET) (12-14). Tertiary prevention in dementia means early and effective treatment of all accessorial complications linked to dementia (uroinfections, respiratory infections, bedsores management, malnutrition, dehydration) (6, 15).

Theoretically, nothing impedes clinicians now from providing better medical care to patients with dementia – we have better diagnostic tools (new diagnostic criteria, neuropsychological tests, laboratory checks, neuroimaging methods etc.), efficient drugs (cognitive enhancers and other substances), nonpharmacological approaches

(reminiscence therapy, cognitive behavioral approaches, memory training) – but the question is – what are we actually doing for patients with dementia? Are physicians sensitive enough to early diagnostics and management of dementia?

The aim of the study was to evaluate the sensitivity of Czech physicians to the early diagnosis of dementia in patients with memory impairment.

Material and Methods

Design of the study

A retrospective observational study was designed. We have reviewed the electronic medical records of patients who have been hospitalized for the first time due to dementia of any type at Kromeriz Mental Hospital from January 1, 2012 to December 31, 2013 (24-months period). The Hospital is the most prominent psychiatric facility in the Moravian region of the Czech Republic (Europe). This psychiatric facility has 1,000 psychiatric beds, 248 beds are dedicated to the treatment of seniors with dementia or related organic disorders.

Research questions

Several research questions were expected to be answered by this study:

- (1) At which stages of dementia were patients admitted to Kromeriz Mental hospital for their first hospitalization due to memory impairment?
- (2) What was the average time between patient memory complaints and his/her first hospitalization due to dementia in Kromeriz Mental hospital?
- (3) How many patients were treated for memory complaints by outpatient physicians before their admission for their first hospitalization due to dementia in Kromeriz Mental hospital?

Methods

Pluralistic methods combining qualitative and quantitative approach were used in this study. We focused on a content analysis of electronic medical records (qualitative approach) followed by a

quantitative analysis of the studied categories (quantitative approach).

The content analysis of electronic medical records was used as the fundamental qualitative method in our research. The use of the content analysis of electronic medical records is recommended by many authors (16, 17). Content analysis is used to construct concepts or theories and this method has been used in biomedical and sociological research since 1960 (18). Content analysis, when used for the analysis of documents or interviews, determines inductively fundamental elements which can be used for further conceptual interpretation (qualitative interpretation) and/or these elements can be counted in the frequency of their appearance within the text or transcribed interview (quantitative interpretation). There are different rules for identifying and recording these fundamental elements, usually specific to the level of content analysis of such analytic elements – most often the rule is open code. In open coding, the text is analyzed for the presence of the studied category (18).

In our study, the fundamental elements, which were studied within the electronic medical records, were:

[1] Variables describing the patients (categories: sex, age)

[2] Type of dementia (three categories within this fundamental element were studied: dementia of Alzheimer's type, vascular dementia, other / unspecified dementia)

[3] The severity of dementia (three categories within this fundamental element have been studied: mild stage, moderate stage, severe stage of dementia)

[4] Time between patient memory complaints and his/her first hospitalization due to dementia (a single category has been studied – the time between patient memory complaints and his/her first hospitalization)

[5] The previous treatment of memory impairment by outpatient physicians such as general practitioners, neurologists, psychiatrists before the first hospitalization in our facility (two categories have been studied: YES – when patient *was* treated for memory complaints or NO – when a pa-

tient *was not* treated for memory complaints by an outpatient physician).

Specification of the studied categories and selected criteria

Dementia of Alzheimer's type (DAT) – the diagnosis DAT was given by a licensed psychiatrist when fulfilling the diagnostic criteria for DAT according to the International classification of Diseases, 10th version (8) and was obligatorily recorded in the electronic medical records (this is an internal rule of our Mental hospital) (2).

Vascular dementia (VD) – the diagnosis VD was given by a licensed psychiatrist when fulfilling the diagnostic criteria for VD according to the International classification of Diseases, 10th version (8) and was obligatorily recorded in the electronic medical records (this is an internal rule of our Mental hospital).

Other / unspecified dementia (OUD) – the diagnosis OUD was given by a licensed psychiatrist when fulfilling the diagnostic criteria for OUD according to the International classification of Diseases, 10th version (8) and was obligatorily recorded in the electronic medical records (this is an internal rule of our Mental hospital).

Stages of dementia – dementia is always tested for severity in the Czech Republic when examining anyone with dementia. The screening tool used for such a severity estimation is the Mini mental-State Examination (MMSE). This screening tool was developed by Folstein et al. (19) and the total score reached by a patient in this screening tool is measured. The total score ranks from 0 points (extremely severe dementia) to 30 points (cognitively intact patients with no evidence of dementia) (8). The total score in MMSE was obligatorily recorded in the electronic medical records (this is an internal rule of our Mental hospital).

Mild stage of dementia – this stage of dementia can be diagnosed when the total MMSE score is from 18 – 25 points), the classification of the severity of dementia was obligatorily recorded in electronic medical records.

Moderate stage of dementia - this stage of dementia can be diagnosed when the total MMSE score is from 7-17 points), the classification of the severity

of dementia was obligatorily recorded in the electronic medical records.

Severe stage of dementia - this stage of dementia can be diagnosed when the MMSE total score is 0-6 points), the classification of the severity of dementia was obligatorily recorded in the electronic medical records.

The time between patient memory complaints and his/her first hospitalization – the period between the initial memory complaints of the patient and admission to the first hospitalization in Kromeriz Mental Hospital. This category was obligatorily recorded in the electronic medical records (compulsory part of the examination - patient history that is taken by the psychiatrist when the patient is admitted to our mental hospital). This period is counted in years (total time in months divided by twelve).

The patient *was* treated for memory complaints by an outpatient physician before the first hospitalization in our facility (category YES) – this is obligatorily noted in the electronic medical records in our facility by the psychiatrist when a patient is admitted to our mental hospital).

The patient *was not* treated for memory complaints by an outpatient physician before their first hospitalization in our facility (category NO) – this is obligatorily noted in the electronic medical records in our facility by the psychiatrist when patient is admitted to our mental hospital).

Statistical analysis

When the content analysis of the electronic medical records has been finished, fundamental elements - variables describing the sample, type of dementia, severity of dementia, time between patient memory complaints and his/her first hospitalization due to dementia, previous treatment of memory impairment by outpatient physicians, and all the selected categories related to them were transcribed in an Excel-chart. The transcription of data is crucial for the ensuing quantitative analysis. The Excel 2007 program was used for all calculations (descriptive statistic calculations have been done – the total count of selected categories, the calculation of the relative count of selected categories, calculation of the mean and standard deviation).

With respect to the goal of the study and research questions, only descriptive statistics were used in these calculations.

Results

Variables describing the patients and type of dementia

Patients

Dementia of any type was diagnosed in 125 patients (mean age 76.4 +- 6.1 years) according to the selected criteria (diagnostic criteria ICD-10) in the studied time-period. 72 of them (57.6%) were women (mean age 78.4 +- 6.6 years), 53 of them (42.4%) were men (mean age 75.2 +- 5.8 years).

Types of dementia

According to the electronic medical records, dementia of Alzheimer's type (DAT) was diagnosed in 53 (42.4%) patients (mean age 76.1 +- 7.9 years), vascular dementia (VD) was diagnosed in 62 (49.6%) patients (mean age 82.8 +- 8.4 years) and the category "other and unspecified dementia" (OUD) was diagnosed in 10 (8.4%) patients (mean age 72.2 +- 5.4 years).

Severity of dementia

Globally, most patients were admitted to our facility at a moderate stage of dementia (49.6% of patients), this stage is characterized by a total MMSE score from 7 to 17 points. The second most common category was the severe stage of dementia (42.4% of patients), this stage is characterized by a total MMSE score from 0 – 6 points. A mild stage of dementia was detected in only 8.0% of admitted patients due to dementia. These results answer the first research question (At which stages of dementia were patients admitted to Kromeriz Mental Hospital for their first hospitalization due to memory impairment?).

Respecting the type of dementia, the most frequent categories were a severe stage of dementia followed by the moderate stage of dementia (DAT), the moderate stage of dementia followed by a severe stage of dementia (VD), and a severe stage of dementia followed by a moderate stage of dementia (OUD) (Table 1).

Table 1: Severity of dementia

Severity of dementia	DAT		VD		OUD		Dementia – total	
	n	(%)	n	(%)	n	(%)	n	(%)
Mild stage	2	(3.8)	8	(12.9)	0	(0.0)	10	(8.0)
Moderate stage	21	(39.6)	37	(59.7)	4	(40.0)	62	(49.6)
Severe stage	30	(56.6)	17	(27.4)	6	(60.0)	53	(42.4)
Total	53	(100.0)	62	(100.0)	10	(100.0)	125	(100.0)

DAT – dementia of Alzheimer's type

VD – vascular dementia

OUD - other and unspecified dementia

n – number of patients with certain type of dementia

% - relative proportion of patients with certain type of dementia

Time between patients memory complains and his/her first hospitalization due to dementia

Globally, the mean time between patient memory complains and his / her admission to the first hospitalization due to dementia to our facility was 7.1 years (+ 3.7 years). These results answer the second research question (What was the average time between patient memory complains and his/her first hospitalization due to dementia at Kromeriz Mental hospital?).

Respecting the type of dementia, the mean time between patient memory complains and his / her admission to the first hospitalization due to dementia at our facility differs from 2.7 years + 1.3 years (OUD), to 6.2 years + 4.1 years (DAT) and 8.5 years + 2.8 years (VD) (Table 2).

Former treatment of memory impairment by outpatient physicians before first hospitalization in Mental Kromeriz Hospital

Globally, most patients with dementia had no prior outpatient treatment of their memory impairment (56.2%), a minority of patients (43.8%) had treatment of their memory impairment by an outpatient physician. These results answer the third research question (How many patients were treated for memory complains by outpatient physicians before their admission for their first hospitalization due to dementia at Kromeriz Mental hospital?). Respecting the type of dementia, most patients with VD and OUD had no prior outpatient treatment of their memory impairment; only a majority of patients with DAT underwent treatment of their memory impairment by an outpatient physician (Table 3).

Table 2: Time from first memory complains to first psychogeriatric hospitalization

	DAT	VD	OUD	Dementia - total
Mean time	6.2	8.5	2.7	7.1
(standard deviation)	(4.1)	(2.8)	(1.3)	(3.7)

DAT – dementia of Alzheimer's type/ VD – vascular dementia/ OUD - other and unspecified dementia

Table 3: Former outpatient treatment for memory complains or dementia

Category	DAT		VD		OUD		Dementia – total	
	n	(%)	n	(%)	n	(%)	n	(%)
YES	35	(67.30)	15	(25.4)	3	(30.0)	53	(43.8)
NO	17	(32.7)	44	(74.6)	7	(70.0)	68	(56.2)
TOTAL	52	(100.0)	59	(100.0)	10	(100.0)	121	(100.0)

DAT – dementia of Alzheimer's type

VD – vascular dementia

OUD - other and unspecified dementia

n – number of patients with certain type of dementia

% - relative proportion of patients with certain type of dementia

Discussion

To fulfill the goal of our study we may summarize that diagnosis of dementia as being too late in our country. Although we have all the diagnostic and therapeutic modalities for the management of dementia in the Czech Republic (all are fully paid by insurance), we don't make full use of them. The consequences of the low awareness of Czech physicians about patients' memory impairment are serious: any delay in starting treatment of dementia means a worsened effectiveness of treatment, including a higher economic burden on health care for the management of dementia at the national level.

What is even worse is that it will not be better in the future. The pandemic of dementia is becoming a problem for public health right now (20, 21). Because of the increasing prevalence of dementia, the global economic burden of dementia is becoming and will become a serious problem for public health expenditures in many countries (22-24). Both direct and indirect costs associated with dementia increase from the mild to the severe stage of dementia (23). The total annual costs according to Swedish research increases from 172,000 Swedish Crowns (equal to 9,045 USD) in mild dementia to 375,000 Swedish Crowns (equal to 55,815 USD) in severe dementia (23). The economic implications of dementia are now being discussed in many countries. According to López-Pousa et al. (24), costs can be linked to the total score achieved in the Mini-Mental State Examination (MMSE). The total costs in patient scoring 19 points and more in MMSE are estimated to be 419.3 Euro monthly (equal to 7,040 USD annually), the total costs in patients scoring 11-19 points are estimated to be 641.9 Euro monthly (equal to 10,770 USD annually) and the total costs in patient scoring below 11 points in MMSE are estimated to be 1,150.6 Euro monthly (equal to 19 320 USD annually). A decrease in the total MMSE score by one point corresponds to an increase of the total costs for treatment by 2,000 USD. (24) This finding encourages struggling for any point scored in MMSE by a patient – and the early diagnosis of dementia and early treatment by

cognitive enhancers is the best way in such a struggle (25, 26). The NADES study was done in Belgium by Scuvee-Moreau et al. (27) to estimate the economic impact of dementia and the results are similar – higher costs were measured in patients with severe dementia (and patients with dementia staying in institutions) whereas lower costs were measured in patients with mild dementia living in a community. (27)

The correlation between the stages of physical dependence, co-morbidities and total costs of treatment was described by many researchers (7, 27). According to our previous research, we should add to this finding that a better physical status and higher quality of life in patients with dementia correlates with the early treatment of dementia (10). This supports arguments for the early diagnosis and treatment of dementia. Thanks to early treatment with cognitive enhancers, any gain in the MMSE score or any stopping of the deterioration of dementia means a lot for a patient, for his or her caregivers and for public health expenditures (28-30).

Our study shows there is a low sensitivity of physicians to the early diagnosis of dementia although all the diagnostic and therapeutic means are available and can be used in clinical practice. What should be done for global improvement? This should be a key message for the postgraduate education of physicians – the tasks of dementia should be involved both in the pregraduate and postgraduate education of physicians. The role of general practitioners seems to be crucial thanks to their close contact with patients living in community as well as the role of secondary care specialists. Some countries have started such changes in education (31) and we should adopt this experience too.

Contribution to scientific knowledge

There are many fields of interest in dementia research now – new guidelines and new drugs are being researched in order to ensure the better management of dementia. Unfortunately, no new drugs are expected for dementia treatment and cognitive enhancers may stay a standard in treatment for a long time. We should make the best use of the current means that we have for demen-

tia treatment. Just a small amount of attention is paid to routine clinical practice – especially to the sensitivity of physicians for the early diagnosis of dementia. Our findings point out this omitted area of scientific attention, which may be called as the sensitivity of physicians to the secondary prevention of dementia.

Limits of the study

The simple design of the proposed study is the most obvious limit of the proposed study (the results are based on an estimation of memory impairment by means of the MMSE screening tool, and medical records analysis). No deeper statistical analysis was performed; only basic statistical descriptive data has been shown. Another limit of the study is the gender selective group of patients (only women were included in the study), because of doing research among patients hospitalized in women psychogeriatric wards. Nevertheless, the results of this study are challenging for both better early diagnostics and early treatment of memory impairment among seniors.

Conclusion

The sensitivity of Czech physicians to early diagnosis of dementia is very low despite the fact that we have all the diagnostic and therapeutic modalities for the management of dementia in our country. These modalities are achievable in routine clinical practice, but we don't use them as we should. For a patient and his or her caregivers, this means a worsened quality of life and worsened life expectancy of both patients and caregivers. For public health policy it means higher total expenditures. Our recommendations for both early diagnostics and the treatment of dementia should be involved in guidelines and should become a part of pregraduate and postgraduate education of all physicians.

Ethical considerations

There was no direct participation of any patient in this study, only a retrospective analysis of electronic medical records was performed. Intimacy

and anonymity was guaranteed in all steps of the research process accordingly. However, the agreement of the local ethical commission with the study has been assigned.

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgement

No financial interest promoted the study. No grant was awarded to the study. The authors declare that there is no conflict of interests.

References

1. Halley LJ, Smyth KA (2013). Human culture and the future dementia epidemic: crisis or crossroads? *Neurology*, 80(20):1824-5.
2. Hampel H, Prvulovic D, Teipel S et al. (2011) The future of Alzheimer's disease: the next 10 years. *Prog. Neurobiol*, 95(4):718-28.
3. Holmerová I, Vanková H, Jurasková B (2011). Biogerontology in the Czech Republic. *Biogerontology*, 12(1): 31-5.
4. Azam B, Whitfield TJ, Radford D, Dontham SG, Stevens T, Dannhauser T, Walker Z (2014). Trends in referred patient profiles in a memory clinic over 20 years. *Dementia (London)*, 2014 Jun 16. pii: 1471301214539691. [Epub ahead of print].
5. Dorsey ER, George BP, Leff B, Willis AW (2013). The coming crisis: obtaining care for the growing burden of neurodegenerative conditions. *Neurology*, 80(21):1989-96
6. Holmerová I, Jurasková B, Kalvach Z, Rohanová E, Rokosová M, Vanková H (2007). Dignity and palliative care in dementia. *J Nutr Health Aging*, 11(6): 489-94.
7. Vanková H, Holmerová I, Andel R, Veleta P, Janecková H. (2008). Functional status and depressive symptoms among older adults from residential care facilities in the Czech Republic. *Int J Geriatr Psychiatry*, 23(5):466-71.
8. Luzny J. (2012). *Gerontopsychiatrie*. [Textbook of Psychogeriatrics in Czech language]. 1st ed. Triton, Prague, pp. 28-29.

9. Holmerová I, Koopmans R, Skela Savič B, Egervári A, Hermann B, Ruseckiene R, Tolson D (2012). Advancing long term care: central European perspectives. *J Am Med Dir Assoc*, 13(7):578-80.
10. Luzny J (2013). Quality of life in patients with dementia. [Article in Czech language]. *Cesk Slov Neurol N*, 76/109(1): 90-95.
11. Pandiani L, Souètre A (2009). Latest trends in preventive medicine: highlights of the PreMed 2008 meeting, 6 - 7 June 2008, Monza, Italy. *Expert Opin Med Diagn*, 3(2):207-10.
12. Fiedler U, Wiltfang J, Peters N, Benninghoff J (2012). Advances in the diagnostics of Alzheimer's disease. *Nervearzt*, 83(5):661-73.
13. Wolz R, Julkunen V, Koikkalainen J, Niskanen E, Zhang DP, Rueckert D, Soininen H, Lötjönen J (2011). Multi-method analysis of MRI images in early diagnostics of Alzheimer's disease. *PLoS One*, 6(10):213-19.
14. Mosconi L, Berti V, Glodzik L, Pupi A, De Santi S, de Leon MJ (2010). Pre-clinical detection of Alzheimer's disease using FDG-PET, with or without amyloid imaging. *J Alzheimers Dis*, 20(3):843-54.
15. Lužný J. Staging in neurodegenerative dementias. [Article in Czech language]. *Geri Gerontol*, 2(3): 142.
16. Makoul G, Curry RH, Tang PC (2001). The use of electronic medical records: communication patterns in outpatient encounters. *J Am Med Inform Assoc*, 8(6): 610-615.
17. Weitzman EA, Miles MB (1995). *Computer programs for qualitative data analysis*. 1st ed. CA Sage, Thousand oaks, pp. 65-78.
18. Miles MB, Huberman MA (1994). *Qualitative analysis: an expanded sourcebook*. 2nd edition. CA Sage, Thousand oaks, pp. 655- 683.
19. Folstein MF, Folstein SE, McHugh PR. (1975). A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*, 12(3): 189-98.
20. Viscogliosi G, Marigliano V (2013). Alzheimer's disease: how far have we progressed? Lessons learned from diabetes mellitus, metabolic syndrome, and inflammation. *J Am Geriatr Soc*, 61(5):845-6.
21. Sokol EW (2013). National plan to address Alzheimer's disease offers hope for new home care and hospice provisions. *Caring*, 32(1):24-7.
22. Feldman H, Gauthier S, Hecker J, Vellas B, Hux M, Xu Y, Schwam EM, Shah S, Mastey V (2004). Economic evaluation of donepezil in moderate to severe Alzheimer disease. *Neurology*, 63(4): 644-50.
23. Jönsson L, Eriksdotter Jönhagen M, Kilander L, Soininen H, Hallikainen M, Waldemar G, Nygaard H, Andreassen N, Winblad B, Wimo A (2006). Determinants of costs of care for patients with Alzheimer's disease. *Int J Geriatr Psychiatry*, 21(5): 449-59.
24. López-Pousa S, Garre-Olmo J, Turon-Estrada A et al. (2004). Cost relation between severity of Alzheimer's disease and cognitive and functional impairment. *Med Clin (Barc.)*, 122(20): 767-72.
25. Wimo A, Ballard C, Brayne C, Gauthier S, Handrle R, Jones RW, Jonsson L, Khachaturian AS, Kramberg M (2014). Health economic evaluation of treatments for Alzheimer's disease: impact of new diagnostic criteria. *J Intern Med*, 275(3):304-316.
26. Vilorio A (2011). Predementia Alzheimer's disease. Benefits of early diagnostics. *Rev Esp Geriatr Gerontol*, 46 Suppl 1:47-54.
27. Scuvee-Moreau J, Kurz X, Dresse A; National Dementia Economic Study Group (2002). The economic impact of dementia in Belgium: results of the National Dementia Economic Study (NADES). *Acta Neurol Belg*, 102(3): 104-13.
28. de Vugt ME, Verhey FR (2013). The impact of early dementia diagnosis and intervention on informal caregivers. *Prog Neurobiol*, 110:54-62.
29. Phung TK, Waltoft BL, Kessing LV, Mortensen PB, Waldemar G (2010). Time trend in diagnosing dementia in secondary care. *Dement Geriatr Cogn Disord*, 29(2): 146-53.
30. Villars H, Oustric S, Andrieu S et al. (2010). The primary care physician and Alzheimer's disease: an international position paper. *J Nutr Health Aging*, 14(2):110-20.
31. Iliffe S, Koch T, Jain P, Lefford F, Wong G, Warner A, Wilcock J (2012). Developing an educational intervention on dementia diagnosis and management in primary care for the EVIDEM-ED trial. *Trials*, 22; 13:142-49.