

ORIGINAL ARTICLE

DEVELOPMENT OF CLINICAL PATHWAY FOR MILD COGNITIVE IMPAIRMENT AND DEMENTIA TO QUANTIFY COST OF AGE-RELATED COGNITIVE DISORDERS IN MALAYSIA

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ABSTRACT

As the Malaysian population ages, the burden of age-related cognitive disorders such as dementia and Alzheimer's disease will increase concomitantly. This is one of the sub-study under a research project titled by quantify the cost of age-related cognitive impairment in Malaysia, which was undertaken to develop a clinical pathway for Mild Cognitive Impairment (MCI) and Dementia. The clinical pathway (CP) will be used to support the costing studies of MCI and Dementia. An expert group discussion (EGD) was conducted among selected experts from six (6) government hospitals from different states of Malaysia, Ministry of Health, and United Nations University, International Institute for Global Health, UKM and UPM. The expert group includes psychiatrist specialists and public health medicine specialists. A total of 15 participants took part in the EGD. The group was presented with the different approach in managing MCI and Dementia. Finally, the group came to the consensus agreement on the most appropriate and efficient ways of managing the two conditions. In the EGD, an operational definition for MCI and Dementia was agreed upon and a pathway was developed for the usual practice in the Malaysian health system. A typical case used, as a reference is a 60-year-old patient referred to a memory clinic with complaint of "forgetfulness". After three outpatient visits in the clinic, the diagnosis of MCI and Dementia could be clinically established. The clinical pathways covered all active clinical and non-clinical management of the patient over a period of one year. The experts identified the additional resources required to manage these patients for the whole spectrum of lifetime based on the expected life expectancy. The Clinical pathway (CP) for MCI and Dementia was successfully developed in EGD with strong support from practitioners in the health system. The findings will help the researchers to identify all-important clinical activities and interventions that will be included in the costing study.

Key words: Mild Cognitive Impairment, Dementia, Clinical pathway, Cost, Malaysia

INTRODUCTION

Mild cognitive impairment (MCI) is a clinical term describing the transitional state between normal aging and dementia¹. The MCI is becoming an increasingly recognized clinical entity. Most clinicians are aware of patients who appear to have a mild deficit in memory or some other aspect of cognition but who are not demented. There are important differences between clinical practice setting and research setting. For example, researchers use comprehensive neuropsychologist testing to document that memory loss in clinical significant cognitive impairment that might mimic criteria for mild common of which is Alzheimer's disease. Other common forms include vascular dementia, Lewy Body dementia, and fronto-temporal dementia³. Today, 5.4 million Americans are living with

Alzheimer's disease (AD). Clinicians should be wary about designating a patient as having MCI in absence of specific criteria. Although therapies are being developed that might prevent progression of amnesic MCI to AD, there is no evidence to support prescribing therapeutic agents to patients with MCI at this time².

The term "dementia" refers to symptoms typically characterized by a loss of cognitive and intellectual ability, impairment in memory, and brain changes affecting areas such as language, reasoning, and judgment severe enough to interfere with everyday functioning. Dementia can be caused by many conditions, the most common of which is Alzheimer's disease in the United States – 5.2 million aged 65 and over, and 200,000 under the age of 65. By 2050, up to 16 million will have the disease. Currently, one in every 8 Americans age

65 and older has Alzheimer's, and nearly half of people age 85 and older have the disease. Providing services and supports for people with Alzheimer's and other dementias was estimated to cost the United States about \$200 billion in 2012 alone; \$140 billion of which is paid by Medicare and Medicaid. In 2011, 15.2 million family and friends provided 17.4 billion hours of unpaid care to those with dementias – valued at \$210.5 billion³.

Clinical pathways are tools used to guide evidence-based healthcare that have been implemented internationally since the 1980s⁴. A clinical pathway is method for patient care management of a well-defined group of patients during a well defined period of time. A clinical pathway explicitly states the goals and key elements of care based on evidence based medicine guidelines, best practice and patient expectations by facilitating the communication, coordinating roles and sequencing the activities of the multidisciplinary care team, patients and their relatives; by documenting, monitoring and evaluating variances and providing the necessary resource and outcome⁵. According to the last national census, there are 2.2 million older Malaysians aged 60 years or over in 2010, making up about 8.4% of the total population⁶. As the Malaysian population ages, the burden of age-related cognitive disorders such as dementia and Alzheimer's disease will increase concomitantly. There is no clinical pathway for MCI and Dementia in Malaysia yet. Aim of this study to develop a clinical pathway for Mild Cognitive Impairment (MCI) and Dementia. The clinical pathway (CP) will be used to support the costing studies of MCI and Dementia.

METHODOLOGY

An EGD was conducted among selected experts from Hospital Kuala Lumpur; Hospital Alor Setar, Kedah; Hospital Queen Elizabeth, Sabah; Hospital Raja Perempuan Zainab II, Kelantan; Hospital Umum Sarawak; Ministry of Health, United Nations University, International Institute

for Global Health; Hospital UKM and UPM to develop a clinical pathway in management of MCI and Dementia in Malaysia. The EGD was initiated for three days in Kuala Lumpur City in September 2013. The expert group includes psychiatrist specialists and public health medicine specialists. A total of 15 participants took part in the EGD. The whole session was recorded. This

clinical pathway is used as a reference in imputing the total cost of managing MCI and Dementia. This study was approved by Ministry of Health Malaysia (NMRR-13-1023-14660).

RESULTS

In the EGD, an operational definition for MCI and Dementia was agreed upon and a pathway was developed for the usual practice in the Malaysian health system. A typical case used, as a reference is a 60-year-old patient referred to a memory clinic with complaint of "forgetfulness". After three outpatient visits in the clinic, the diagnosis of MCI and Dementia could be clinically established. The clinical pathways covered all active clinical and non-clinical management of the patient over a period of one year. The experts identified the additional resources required to manage these patients for the whole spectrum of lifetime based on the expected life expectancy.

Operational definition of MCI and Dementia

Operational definition of MCI and Dementia were developed by psychiatrist during the EGD.

MCI: patient with Evidence of memory impairment, Preservation of General Cognitive and functional Abilities and Absence of Dementia.

Dementia: Evidence of memory impairment, Decline in Cognitive function and Decline in functional and social abilities

Referred case

Reasons for referring cases

Case referred to psychiatrist for screening of MCI or Dementia due to following reasons; Depression, Delirium, Alcohol Abuse, Alzheimer's Disease, Frontotemporal Dementia (all types of Dementia), Encephalitis & Meningo-Encephalitis, Parkinsonism and Stroke/Cerebrovascular Accident.

Proportion of MCI and Dementia

Around 15-20% of referred cases are MCI and Dementia out of all referred case at psychiatric department. Among the MCI and Dementia cases around 95% of cases are 60 years and more only 5% cases less than 60 years old. Proportion of MCI and Dementia; around 60-70% cases are MCI and 30-40% cases are Dementia among all referred case to psychiatric department.

Table 1: Outpatient visits

1st outpatient visit	
Duration of 1st visit	1-2 hours
Assessment	<ul style="list-style-type: none"> -Psychological assessment -Physical examination -Human Resource: Psychiatrist and clinic Nurse <ul style="list-style-type: none"> • Nurses taking vital signs <p>Assessment done by nurses</p> <ul style="list-style-type: none"> - ECAQ (Elderly Cognitive Assessment Questionnaire) - MMSE (Mini Mental State Examination) - BPRS (Brief Psychiatric Rating Scale) - Instrumental ADL-(Lawton & Brody) /Activities of Daily Living (Barthel Index/ Modified Barthel) - GDS (Geriatric Depression Scale) - NPI- Neuropsychiatric Inventory <p>Assessment done by Doctors</p> <ul style="list-style-type: none"> - MoCA (Montreal Cognitive Assessment) - CSDD (Cornell Scale for Depression and Dementia) - Blessed dementia scale - ADL and cognition - HIS (Hachinski Ischaemic Scale) - Verbal Fluency - Staging of MCI/Dementia: Clinical Dementia Rating Scale or Global Deteriorations Scale
Investigation	<ul style="list-style-type: none"> - Full blood account - Renal profile - Liver function test - Thyroid functional test - B12 and Folate - Random Blood Sugar - CT Scan (70%) ; MRI (10%)
Medication	<p>Treatment for depression</p> <ul style="list-style-type: none"> • 60-70% of case • Drugs: Generics <ul style="list-style-type: none"> - SSRI ((Selective Serotonin Reuptake Inhibitor) (60%) <ul style="list-style-type: none"> ➢ Sertraline (80%) ➢ Escitalopram (15%) ➢ Fluvoxamine (5%) - SNRI (Selective Norepinephrine Reuptake Inhibitor) (40%) <ul style="list-style-type: none"> ➢ Mirtazapine (80%) ➢ Duloxetine (20%) <p>Treatment every day until next visit (one month)</p>
2nd outpatient visit; One month after the first visit	
Duration of 2nd visit	30 minutes to 1 hour
Activity	<ul style="list-style-type: none"> - Review the result - Around 80% of cases diagnosis can be established either MCI or Dementia - Around 20% cases need further visit to establish diagnosis <ul style="list-style-type: none"> ➢ Need further investigation ➢ Further psychiatric assessment (repeat 1st visit assessment tool) <p>No further physical investigations</p>
Establishment of Diagnosis	<p>Typical MCI and Dementia patients age over 60 years old, the patients are seen as outpatient at psychiatric clinics or Memory clinic. The patients complain of forgetfulness and the patients are mostly are referred.</p>

After 2-3 outpatient visit diagnosis can be established as MCI or Dementia. Ever visit one moth apart. MCI has two types which are Amnestic and Non-Amnestic. The Dementia has three sub types which are Neurodegenerative, Vascular and Medical. The Neurodegenerative dementia has also four types which are Alzheimer’s (AD), Frontal-Temporal Dementia (FTD), Dementia Lewy Bodies (DLB) and Parkinsonism (PDD). The table 1 describes duration and activities at outpatient visits of MC and Dementia. The duration of the first outpatient takes around one to two hours and second visit only takes around half an hour (Table 1). After three visits diagnosis of MCI and Dementia can be established. Treatment pathway for MCI and Dementia are different. MCI and Dementia are chronic disease need to follow up.

MCI

MCI patients included two groups Amnestic and non-Amnestic. Amnestic group is around 60-70% of cases and non -amnestic group is around 30-40%. The amnestic group includes two groups such as with and without depression. Cases without depression around 30-40%, the cases need follow up every 6 to 12 month and with depression cases around 60 -70%, the cases need to follow up every 2 to 3 months.

Non-amnestic group includes Non- ADL Impaired which is around 40-50% and ADL impaired around 50-60%. Non-ADL impaired considers FTD. ADL impaired possible VaD or LBD disease, this need to be followed up other specialities such as Medical/primary care or Neurologist. The table 2 presents duration of visit, activity and medication of amnestic and non-amnestic MCI.

Table 2: Amnestic and Non- Amnestic MCI

Amnestic MCI Group	
Duration	1 hour per visit
Assessment	<ul style="list-style-type: none"> - MOCA - MMSE - CDR - Psychiatric counselling
Investigation	None
Medication	<ul style="list-style-type: none"> - Antidepressants around 80% will be needed. drugs are generics <ul style="list-style-type: none"> • SSRI (Selective Serotonin Reuptake Inhibitor) (60%) <ul style="list-style-type: none"> ➢ Sertraline (80%) ➢ Esertalopram (15%) ➢ Fluoxetine (5%) • SNRI (Selective Norepinephrine Reuptake Inhibitor)(40%) <ul style="list-style-type: none"> ➢ Mirtazapine (80%) ➢ Duloxetine (20%) ➢ Treatment every day until next visit (one month) - No cognitive drug prescribed normally
Admission	Might be due to other medical condition
Non-Amnestic MCI Group	
Duration	30 minutes to 1 hour every visit
Assessment	<ul style="list-style-type: none"> - MMSE - GDS (Geriatric Depression Scale) - ADL - Psychiatric counselling
Investigation	None
Medication	Drug for specific co-morbidity e.g. Parkinson

MCI comorbidities of in-patient MCI cases; Most common comorbidity of admitted MCI cases are delirium which is about 50% followed by

depression 30%, stroke/CVA 10%, parkinsonism 5%, alcohol 3%, encephalitis meningo-

encephalitis 1% and other comorbidities around 1%.

Dementia

There are three sub type of dementia namely Neurodegenerative, Vascular and Medical dementia. The Neurodegenerative dementia has four types Alzheimer’s disease (AD), Frontal-Temporal (FTD), Demntia Lewy Bodies (DLB) and Parkinsonism (PDD). The proportion of neurodegenerative dementia around 80% while vascular 20%. The AD is the most common type of

neurodegenerative dementia which is about 60% followed by FTP 10%, DLP 5% and PDD 5%.

Dementia cases potentially need for institutionalization for long term care. Around 55% of neurodegenerative dementia FTD type needs to long care institutionalisation, AD around 20%, DLB 10% and PDD 10%. About 30% vascular dementia is also need to require long term institutionalization care.

Potential need for episodic admission

If the disease is mild level no need to admit, if moderate level once per year for 1 to 2 weeks per admission, if sever level 2 to 3 times per year for 1 to 2 weeks per admission. Around 30 % of cases are mild level, around 50% of cases are moderate level and around 20% of cases are sever level.

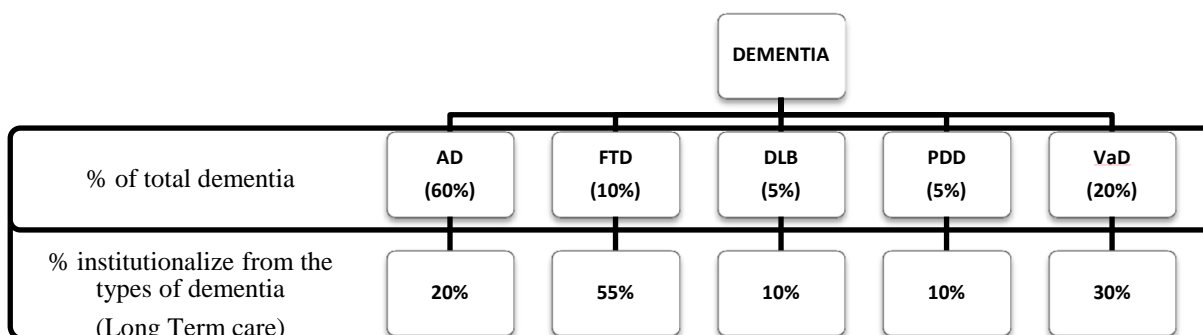


Figure 1 proportion of total dementia and institutionalization dementia Dementia Home Care

Community nurse visit Patients that living within 30-40km from hospitals. The visit 3 to 4 times per year, each visit takes 1 hour. Physiotherapist/ Occupational therapist/ Dietician/ Pharmacists visit the patient one a year, they follow the community nurse during the home visit.

Life expectancy

Life expectancy of subtype of dementia is different. Life expectancy of Alzheimer’s dementia patient ‘s 6-8 years, frontal Temporal Dementia patient’s 6 years, stroke/vascular dementia patient’s 5 years, Lewy Body Dementia patient’s 5-7 years and Parkinson Dementia patient’s 6-7 years. Table 3 describes visits, duration, activities and medication of subtypes of dementia.

DISCUSSION

Issues related to patient safety, quality of care and efficiency are of serious concerns for the healthcare managers all over the world. New interventions, approaches and tools are introduced to better address these concerns and improve quality of patients’ care. Clinical pathway (CP) is a multidisciplinary plan of care based on best clinical practice for a specified group of patients with a particular diagnosis. A

CP is designed to integrate care, minimize delays, optimize resource utilization, and maximize quality of care.

Healthcare professionals and workers have used CP as a clinical management tools to define the best treatment, procedures and duration of treatment for patients with specific diagnoses according to Evidence Based Medicine (EBM). The aim of EBM is to bring research and practice close together and reduce the time lag between the development of clinically proven treatments and their use in everyday medical practice and the clinical pathways can be used as a tool to implement EBM practices^{7, 8}.

According to Campbell et al (1998), previous studies on integrated pathways into the clinical care have shown the benefits such as the ability to complementing the introduction of local protocols based on research evidence into clinical practice, establishing explicit and well defined standards for care, reduction in variations of patient care, improve clinical outcomes, improve multidisciplinary teamwork, and help improve patient documentation⁹. Other studies have also demonstrated that the development and implementation of Clinical Pathways have resulted in improvements of care delivery process^{10, 11}.

Table 3: Alzheimer’s Dementia

Outpatient visit	<ul style="list-style-type: none"> - Monthly for first 3-4 months - 3 monthly for 6-9 months - 6 monthly for rest of life (mostly 6-8 years)
Duration	Every visit takes 30 minutes to 1 hour
Assessment	<ul style="list-style-type: none"> - MMSE, GDS (Geriatric Depression Scale) - every visit - IADL/MBI; CDR/GDS (Global Deterioration Scale); BPRS- every year
Dementia Psycheducation	<ul style="list-style-type: none"> - Patient and career - 30 to 45 minutes - Once at the beginning
Medication	<p>Proportion of Medication by severity level</p> <ul style="list-style-type: none"> - Mild (30%) - Moderate (50%) - Severe (20%) <p>Drugs for Cognitive Function</p> <ul style="list-style-type: none"> - Antidemential Drugs - Three types of drugs <ul style="list-style-type: none"> ➢ Donapezil (Mild and Moderate) ➢ Rivastigmine (Mild and Moderate Cases) ➢ Memantine (Severe) <p>Drugs for Behavioural</p> <ul style="list-style-type: none"> - Agitation- Antipsychotic - Depression- Antidepressant - Anxiety- Anti-anxiety - Insomnia- Sedative hypnotics <p>In patient care: around 20% admitted for in-patient care at end of their life.</p>

FRONTAL TEMPORAL DEMENTIA

Outpatient Visit	Follow up every 3-6 month
Duration	Every visit takes 30 minutes to 1 hour
Assessment	<ul style="list-style-type: none"> - Frontal Assessment Battery (FAB) - All other Test -
Behaviour management	<ul style="list-style-type: none"> - Home visit by Psychiatric Nurse (in community) - 3 to 4 visits per year -
Medication	<p>Drugs for Cognitive Function</p> <ul style="list-style-type: none"> - No drugs <p>Drugs for Behavioural</p> <ul style="list-style-type: none"> - Anti-depressant - Anti-psychotic

Malaysian population dynamic is evolving rapidly with increasing proportion of ageing population and resultant increase in the Cognitive related disorders. With this rationale, project was conceived to develop the Clinical Pathway for the Minor Cognitive Impairment (MCI) to ensure not only to reduce the variation of care but at the same time to estimate the resources needed to manage MCI effectively and efficiently.

Mild cognitive impairment (MCI) is a clinical term describing the transitional state between normal aging and dementia. In MCI patient do not have significant functional deficits; presence of functional deficits suggest instead a diagnosis of dementia¹². The consensual definition of MCI developed during this study is “patient with Evidence of memory impairment, Preservation of General Cognitive and functional Abilities and Absence of Dementia”. The definition adopted

comply with Petersen who define mild cognitive impairment (MCI) as a memory impairment beyond that expected for age and education yet are not demented.

This research was about the inpatient care of the MCI & Dementia patients, so it includes all the patients admitted in the selected hospitals during the research period. Most of the patients were admitted in the wards other than the Psychiatric ward, and need Psychiatric

evaluation by the primary Physicians. During the research it was documented that the MCI and Dementia constitute about 15 to 20 % of all the inpatient referral to Psychiatric department. Within this MCI and Dementia group 60 - 70 % cases were diagnosed as MCI whereas Dementia constitute about 30 - 40 % of these referrals. The frequency of inpatient referrals for MCI is not documented in the literature, but ambulatory referrals are frequently documented in the literature and ranges from 20 - 25 %^{13, 14}.

Table 4: Parkinsonism, Lewy Body Dementia and Vascular Dementia/Stroke

Parkinsonism Dementia & Lewy Body Dementia	
Outpatient visit	- 3-6 month follow up
Duration	Every visit takes 30 minutes to 1 hour
Assessment	- Same as all other Az Dementia - (inc: Hoehn and Yar Scale) -
Medication	Drugs for Cognitive Function - Rivastigmine - Donapezil (less common) Drugs for Behavioural - Psychotic ➢ QTP (Quetiapine) or ➢ Clozapine (less common) - Depression ➢ Antidepressant - Motor Symptoms ➢ Antiparkinson medication
Vascular Dementia/Stroke	
Outpatient visit	- 3-6 month follow up
Duration	Every visit takes 30 minutes to 1 hour
Assessment	Same as all other Az Dementia -
Medication	Drugs for Cognitive Function - Donapezil (first line) - Rivastigmine (If cannot tolerate Donapazil) - Memantine (third line) Drugs for Behavioural - Depression → Antidepressant - Maniac/Affective → Anti-Epileptic: Na Valproate, lamotrigine - Aggressive / Agitation → Short term anti-psychotic Stroke Prophylaxi and Co-morbidity - Aspirin or equivalent

About 95 % of the patients referred to the Psychiatric department were more than 60 years of age whereas the remaining 5 % were less than 60 years of age, and the most common complain of these patients include 'forgetfulness'. Once attended at the psychiatry or memory clinic, it

require 2- 3 visits (each visit 1 to 2 months apart lasting for 1 to 2 hours) to establish the diagnosis of MCI or Dementia.

Once diagnosed, Minor Cognitive Impairment can be divided into Amnestic MCI or Non-Amnestic

MCI. Whereas the Dementia can be divided into 3 different types, these include; Neurodegenerative Dementia, Vascular Dementia and Medical Dementia. It is important to differentiate and establish the MCI and Dementia diagnosis because both of these are chronic diseases and the way these are clinically managed is different.

Within the MCI group, the 60 - 70 % of patients can be grouped as Amnesic MCI and 30 - 40 of patients as Non-Amnesic MCI patients. Within the Amnesic MCI group the patients can be divided into Depressive Amnesic MCI (60 - 70 %) and Non-Depressive Amnesic MCI (30 - 40 %). It is important to establish this distinction because Depressive Amnesic MCI require follow up every 2 - 3 months whereas the patients with Non-Depressive Amnesic MCI requires follow up every 6 - 12 months.

Non-Amnesic Minor Cognitive Impairment is further divided into Non- ADL (Assisted Daily Living) impaired (40 - 50 % of the patients in this group) and ADL - Impaired group (50 - 60 % patients). The Non-ADL impaired is also called Fronto Temporal Dementia. ADL impaired can be due to Vascular Diseases or Diffuse Lewy Body (DLB) disease, and these need to be followed up by other specialities such as Medical/primary care or Neurologist.

Patients of MCI are not admitted due to their core morbidity i.e. MCI, but are admitted due to other co-morbidities such as delirium (50% of time) followed by depression (30% of time), stroke/CVA (10%), parkinsonism (5%), alcohol (3%), encephalitis meningo- encephalitis (1%) and other co-morbidities around (1%).

Dementia in general can be divided into three sub-types namely; Neurodegenerative Dementia, Vascular Dementia and Medical Dementia. The Neurodegenerative dementia has four types Alzheimer's disease (AD), Frontal-Temporal (FTD), Demntia Lewy Bodies (DLB) and Parkinsonism (PDD). The proportion of neurodegenerative dementia around 80% while vascular 20%. The AD is the most common type of neurodegenerative dementia which is about 60% followed by FTP 10%, DLP 5% and PDD 5%.

Dementia cases potentially need institutionalization for long term care. Around 55% of neurodegenerative dementia and FTD type needs long care institutionalization, AD around 20%, DLB 10% and PDD 10%. About 30% vascular dementia is also need to require long term institutionalization care.

CONCLUSION

MCI and Dementia are the group of diseases mostly affecting patients with more than 60 years of age. Both diseases affect the quality of life of the patients as well as the care givers. Understanding and standardizing can not only efficiently manage these disease groups but also can improve the quality of lives of these patients. The Clinical pathway (CP) for MCI and Dementia was successfully developed in EGD with strong support from practitioners in the health system. The findings will help the researchers to identify all-important clinical activities and interventions that will be included in the costing study.

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REFERENCE

1. Petersen, R.C., Doody, R., Kurz, A., Mohs, R.C., Morris, J.C., Rabins, P.V., Ritchie, K., Rossor, M., Thal, L., Winblad, B. Current concepts in mild cognitive impairment. *Arch. Neurol.* 2001,58, 1985-1992.
2. Ronald C. Petersen, Rachele Doody, Alexander Kurz et al. Current concept in Mild Cognitive impairment. *Arch Neurol.* Dec 2001, Vol 58.
3. The Alzheimer's association .The journal of the Alzheimer's association, Vol,8 No. 6 November, 2012 P.463-598
4. Leigh Kinsman, Thomas Rotter, Erica James, Pamela Snow and Jon Willis. What is a clinical pathway? Development of a definition to inform the debate. *BMC Medicine* 2010, 8:31.
5. Leentje De Bleser, Roeland Depreitere, Katrijn De Waele, Kris Vanhaecht, Joan Vlayen M D And Walter Sermeus. Defining pathways. *Journal of Nursing Management*, 2006, 14, 553-563
6. Department of Statistics, Malaysia, 2011. <http://www.statistics.gov.my/main/main.php>
7. Cheah J: Development and implementation of a clinical pathway programme in an acute care general hospital in Singapore. *International journal for quality in health care* 2000, 12(5):403-12.

8. Rotter T, Kinsman L, James EL, Machotta A, Gothe H, Willis J, Snow P, Kugler J: Clinical pathway: effect on professional practice, patient outcomes, and length of stay and hospital costs. The Cochraen Collaboration, (John Wiley & Sons Ltd.) 2010.
9. Campbell H, Hotchkiss R, Bradshaw N, Proteous M: Integrated clinical pathway. J British Medical 1998, 316:133-147.
10. Panella M, Marchisio S, Stanislaio FD: Reducing clinical variations with clinical pathways: do pathways work 2003. J Quality Health Care 2003,15(6):509-521.
11. Cheah J: Clinical pathway - An evaluation of its impact on the quality of care in an acute care general hospital in Singapore. Singapore Medical Journal 2000,41(7):335-346.
12. Paul B. Rosenberg, Deirdre Johnston, Constantine G. Lyketsos. A Clinical Approach to Mild Cognitive Impairment. Am J Psychiatry, November 2006, 163:11,
13. Jane A. Lonie, Lucie L. Herrmann, Claire L. Donaghey and Klaus P. Ebmeier. Clinical referral patterns and cognitive profile in mild cognitive impairment. BJP 2008, 192:59-64.
14. Lehrner J, Gufler R, Guttman G, Maly J, Gleiss A, Auff E, Dal-Bianco P. Annual conversion to Alzheimer disease among patients with memory complaints attending an outpatient memory clinic: the influence of amnesic mild cognitive impairment and the predictive value of neuropsychological testing. Wien Klin Wochenschr 2005; 117: 629-35.