DELIRIUM IN THE ELDERLY: A SURVIVAL ANALYSIS

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ABSTRACT

Mortality rates have consistently been shown to be greater in patients with delirium compared to those without. Published work over the last decade has revealed however, that several confounding factors play key roles in contributing to the excess mortality in the delirium population and that statistical adjustment for these factors in multivariate analyses minimizes, if not eliminates, the association between delirium and mortality. These factors include pre-existing dementia, advanced age, severe medical illness, diminished functional status, and intoxication or withdrawal from medications. However, studies on prognosis and prognostic indicators of delirium in the past have been limited to subjects admitted to the hospital where the sample may include both incident and prevalent cases of delirium.

Objective: To determine whether prevalent delirium is an independent predictor for mortality among elderly patients seen in the Emergency department. Potentially confounding factors were assessed to reveal their prognostic contributions in this population. Survival analysis was carried out using the Cox Proportional Hazards Modelling technique.

Methods: As part of a larger study, 268 patients seen in the Emergency department in two Montreal hospitals (107 delirium cases, 161 controls) were followed up in 6 month intervals for a total of 18 months. Dates of deaths for the deceased were obtained from the Ministère de la Santé et des Service Sociaux.

Results: The analysis revealed a non-significant association between delirium and mortality rate for the English speaking subjects, when adjusted for age, sex, pre-morbid cognitive decline (IQCODE), Basic ADL, Instrumental ADL, comorbidity, number of medication, education (years), eyesight, and hearing problems (p=0.752, HR=1.095, CI: 0.622-1.929). On the other hand, for the French speaking subjects, the same model revealed a highly significant association between delirium and death rate (p=0.001, HR=9.078, CI: 2.362-34.892). Possible explanations for the different results are discussed.

RÉSUMÉ

Il a été observé que le delirium est associé à une augmentation du taux de mortalité. Cependant, les études publiées au cours de la dernière décennie indiquent que plusieurs facteurs de confusion sont impliqués dans le mécanisme de cette surmortalité et que l'ajustement pour ces facteurs dans un modèle multivarié réduit, voire supprime, l'association entre delirium et mortalité. Ces facteurs de confusion incluent l'existence d'une démence prémorbide, un âge avancé, une pathologie médicale sévère, le déclin fonctionnel et l'intoxication ou le sevrage médicamenteux. Cependant, les études antérieures sur le pronostic du delirium ont étudié uniquement des sujets hospitalisés et ces échantillons incluent à la fois des cas incidents et des cas prévalents.

Objectif: De déterminer si le delirium prévalent (c'est-à-dire dont la symptomatologie est apparue avant l'arrivée à l'hôpital) était un facteur prédictif de la mortalité chez les sujets âgés vus aux urgences. Plusieurs facteurs de confusion potentiels ont été évalués pour prendre en compte leur contribution pronostique. L'analyse de survie a été réalisée en utilisant la méthode de Cox.

Méthodes: Dans le cadre d'une étude plus vaste, 268 sujets âgés ayant été vus dans les départements des urgences de deux hôpitaux montréalais (107 cas de delirium, 161 témoins) ont été réévalués tous les six mois pendant 18 mois. Les dates de décès pour les sujets décédés ont été obtenues du Ministère de la Santé de des Services Sociaux.

Résultats: Chez les sujets anglophones, il n'y avait pas d'association significative entre delirium et taux de mortalité après ajustement sur l'âge, le sexe, le statut cognitif prémorbide (IQCODE), le statut fonctionnel (Activités de la Vie Quotidienne de Base et Instrumentales), la comorbidité, le nombre de médicaments, le niveau d'éducation (années), l'acuité visuelle et les problèmes auditifs ($p = 0.752$; HR = 1.095; CI : 0.622-1.929). Pour les sujets francophones, le même modèle permettait d'observer une association très significative entre delirium et taux de mortalité ($p = 0.001$; HR = 9.078; CI : 2.362-34.892). Plusieurs explications possibles de ces différences sont discutées.

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CHAPTER 1. INTRODUCTION

OVERVIEW

Delirium, or acute confusional state, is an organic brain disorder seen most frequently in hospitalized elderly individuals and is characterized by an impairment in cognition, a disruption in perception, and a disturbance in consciousness with reduced ability to focus, sustain or shift attention[1]. Having an acute onset, with symptoms fluctuating over the course of the day, this disorder is generally believed to be the physiological consequence of an underlying general medical condition. Though relatively short in duration (hours to one month), it can be extremely distressing to both the individual as well as family and close friends. Furthermore, delirium has been estimated to account for excess annual health care expenditures of $1-2 billion[2].

Despite the fact that it is often difficult to distinguish delirium from psychiatric disorders such as dementia, psychotic depression and acute functional psychosis, there are clinical features that are specific to delirium (Table 1). For example, delirium is unique in exhibiting fluctuations of symptoms over the course of the day, having tendencies for lucid intervals surfacing during the day and disruptive symptoms at night and upon awakening[3-6]. Impairments in those afflicted with delirium include a reduction in awareness and attention, fluctuation in alertness, and a global deficit in attention. Delirium also presents itself through disorientation with respect to time, person and place, although disorientation to time is the most common. Memory impairment is selective to the immediate and recent memory while remote memory remains intact[3]. Concerning misperceptions, if hallucinations are present, they tend to be visual and/or auditory, and delusions, if present, tend to be of a persecutory nature[4,6,7]. Thoughts are also disorganized, which is evident from behaviours such as incoherent speech[5].

There are several overlapping symptoms between delirium and the above mentioned psychiatric disorders that give rise to the possibility of misdiagnosis. Global cognitive impairment for example, is characteristic of both delirium and dementia, and psychomotor activity is also symptomatic of acute functional psychosis. Disturbed sleep-wake cycle is also seen in dementia and depression although the nature of the disturbance differs, and poor judgement is evident in dementia as is in delirium. Furthermore,

disturbance in speech, impoverished thinking, and disorientation is symptomatic of all four psychiatric disorders.

Psychomotor activity is also altered in delirious individuals, in either or both directions. The direction of the abnormality is concordant with the abnormal change in EEG pattern that are present[7]. That is, individuals with an elevated EEG pattern exhibit hyperactivity, those with a reduced EEG pattern show hypoactivity, and those with both have a mix of the two. Delirium, based on the nature of the psychomotor abnormality, has therefore been categorized into three types: 1) Hyperactive, which is primarily described by agitation and perceptual disturbances, 2) Hypoactive, which is characterized chiefly by lethargy and reduced consciousness, and 3) Mixed, which includes both hyper- and hypoactive symptoms.

Table 1. Clinical Features of Delirium

Adapted from Chan 1999[3], Foreman 1996[4], Lipowski 1987[6], 1989[5], Beresin 1988[7], Bross 1994[8]

FEATURE	DELIRIUM	DEMENTIA	PSYCHOTIC DEPRESSION	ACUTE FUNCTIONAL PSYCHOSIS*
Onset	Acute/subacute, depends on cause, often in darkness (i.e. night)	Chronic, generally insidious, depends on cause	Acute, coincides with major life changes often abrupt	Sudden
Course over 24 hours	Fluctuating symptoms, with nocturnal exacerbation, lucid intervals, during the day, worse at night and on awakening	Stable over course of day, Static	Relatively stable – Diurnal effects, worse in morning, situational fluctuation but less than delirium	Stable
Progression	Abrupt	Slow but uneven	Variable, even	
Duration	Brief, hours to weeks	Chronic, months or years, unless reversible	Weeks to months to years	
Consciousness	Reduced	Clear	Clear	Clear
Awareness	Reduced	Clear	Clear	
Alertness	Fluctuation, abnormally low or high – always impaired	Usually normal	Normal	
Attention	Globally disordered, lacks direction and selectivity, distractibility, fluctuates over course of day	Normal, except in severe cases	Minimal impairment but easily distracted	May be disordered
Cognition	Globally disordered	Globally impaired		May be selectively impaired
Hallucinations	Visual, or visual & auditory	Often absent	Predominantly auditory	Predominantly auditory
Delusions	Fleeting, poorly systematized	Often absent	Sustained, systematized	Sustained, systematized
Orientation	Usually impaired for time, tendency to mistake unfamiliar for familiar place and persons	Often impaired, may be normal in mild cases	May be impaired Selective disorientation	May be impaired
Memory	Immediate and recent impaired (registration, retention & recall), remote memory intact	Immediate memory intact, recent and remote impaired, recent more than remote	Selective or 'patchy impairment, islands of intact memory	
Perception	Distorted, illusions, hallucinations (usually visual), difficulty distinguishing between reality & misperception Frequently disturbed, contents vivid	Misperceptions may be absent, contents less florid if present	Intact, delusions and hallucinations in severe cases	

(Continued)

*The DSM-IV equivalent of Acute Functional Psychosis is Brief Reactive Psychosis

Table 1. Clinical Features of Delirium - continued

FEATURE	DELIRIUM	DEMENTIA	PSYCHOTIC DEPRESSION	ACUTE FUNCTIONAL PSYCHOSIS
Psychomotor activity	Variable, increased, reduced, or shifting unpredictably	Often normal, maybe apraxia	Varies from retardation to hyperactivity (in agitated depression)	Varies from psychomotor retardation to severe hyperactivity, depending on the type of psychosis
Involuntary movements	Often asterixis or coarse tremor	Often absent		Usually absent
Sleep-wake	Disturbed, reversed	Fragmented	Disturbed, early morning waking	
Speech	Often incoherent, hesitant, slow or rapid	Patient has difficulty finding words, perseveration	Normal, slow, or rapid	Normal, slow or rapid
Thinking	Disorganized, distorted, fragmented, contents rich	Impoverished, contents empty and stereotypes, difficulty with abstraction	Relatively intact but with themes of hopelessness, helplessness or self-depreciation	
Judgement	Poor	Poor, frequent inappropriate social behavior		
Insight	May be present in lucid intervals	Absent	Present	
EEG	Invariably abnormal (slow, fast in withdrawal)	Normal or mild slowing		
Physical illness or drug toxicity	Either or both are present	Often absent, especially in senile dementia of the Alzheimer's type	Usually absent, but debatable	Usually absent
Associated features	Variable affective changes, symptoms of autonomic hyper-arousal, exaggeration of personality type	Superficial effect (inapprop & labile), try to conceal intellectual deficits, personality change, aphasia, agnosia	Depressed, dysphoric mood, exaggerated & detailed complaints, preoccupied with personal thoughts, verbal elaboration	
Assessment	Distracted from task, numerous errors	Frequent near miss answers, struggles with test, want to perform well	Frequently answer 'don't know', indifferent towards test	

*The DSM-IV equivalent of Acute Functional Psychosis is Brief Reactive Psychosis

OBJECTIVE OF THIS STUDY

The thesis research constitutes a secondary analysis of a longitudinal study of subjects initially recruited for a previous case-control study funded by the National Health Research and Development Programme (NHRDP) which examined the role of medication as a risk factor for delirium in the elderly (Galbaud du Fort G., Moride Y. et al. Drugs as a risk factor for delirium in the elderly: a case-control study). The objectives of the case-control study were 1) to detect the existence of delirium in the elderly seen for acute illness in the emergency departments of two hospitals (Jewish General Hospital, Montreal General Hospital), and 2) to compare the characteristics of recent exposure to drugs between subjects with and without delirium. The objective of this thesis research was to examine whether prevalent delirium is a predictor of mortality among elderly patients admitted through the Emergency department. Potential confounding and effect modifying variables were also assessed.

CHAPTER 2. DELIRIUM

EPIDEMIOLOGY

Prevalent cases of delirium in hospitalized patients refers to patients who are delirious at arrival to the hospital, whereas incident cases of delirium refers to patients who develop delirium during their hospital stay, or a specified time period. Rates of prevalent and incident delirium reported in the literature have been extremely variable, ranging anywhere from 0.74% to 43.8% and 3.3% to 31.3% respectively, as shown in Table 2. Such a variability can be due to numerous reasons. The diagnostic criteria, for instance, have evolved over the years (see Appendix 4), the target population and clinical setting being addressed have differed in different studies, and the ability of different screening tools to detect and distinguish the disorder from other similar disorders has been variable.

Detection and correct diagnosis of delirium has been shown to be difficult for several reasons. Although the study of delirium is relatively old, the diagnostic 'label' as well as standardized criteria for its diagnosis is quite young. As such, the disorder has been labelled in numerous ways making it difficult to review published work before 1980. Francis (1990)[9] and Liston (1982)[10] have identified up to 30 known labels for this disorder. To name a few, *acute brain failure*, *acute brain syndrome*, *acute organic psychosis*, *altered mental status*, *pseudosenility*, *reversible toxic psychosis*, *toxic encephalopathy*, and *toxic psychosis* have all been used as synonyms for delirium. Delirium first appeared as its own entity in the third version of the Diagnostic and Statistical Manual for Mental Disorders (DSM-III)[11], published by the American Psychiatric Association in 1980, but was not accompanied by standardized criteria, thereby resulting in inconsistencies in its application by clinicians and physicians. The DSM-III-R[12] was the first operationalized criteria for delirium, accompanied by change in two of the core features. Specifically, the clouding of consciousness and disorientation in DSM-III was replaced in DSM-III-R by reduced attention and disorganized thinking[13] When the DSM-IV[1] was published, the criteria for delirium had become broader under the stipulation that the DSM-III-R was too restrictive, and its use may result in missing individuals who were suffering from delirium. The prevalence and incidence rates

therefore, inevitably differ depending on which criteria the diagnosis of delirium is based. A review of the literature by Levkoff et al. (1991)[13] showed prevalence and incidence rates ranging from 10% to 30% and 4% to 53.2% respectively. When restricted to studies that used the DSM-III criteria however, the rate ranges reduced to 11.3%-16% and 4.2%-10.4% respectively, thus demonstrating the susceptibility of prevalence and incidence rates to the diagnostic criteria applied. Review of published work therefore necessitates the acknowledgement of the criteria used in defining the population to which the authors refer.

With regards to the population being studied, specifications such as settings (clinical or otherwise) and age groups affect the prevalence and incidence rates for delirium. If the population of interest is the elderly, aged 70 years and older, for instance, the prevalence ranges from approximately 30% to 50%[6]. If, on the other hand, the population of interest is elderly hospitalized medical patients, delirium is reported to occur in 14% to 56%[14]. Furthermore, focusing on post-operative hip fracture patients renders prevalence rates of 28% to 44%. And finally, shifting focus to community elderly individuals aged 55 years and older reveals a drastic decline in rates to approximately 1.1%[15]. Table 2 shows the different ranges of rates in different population and settings.

Since delirium is a disorder with symptoms that overlap those of other psychiatric disorders, as mentioned earlier, screening and diagnostic instruments need to be sufficiently sensitive and specific to the subtle differences between such disorders. The Mini-Mental State Exam (MMSE)[16] for example, has been used for the detection of cognitive impairment. This instrument however, is limited for the purposes of detecting delirium in that it is incapable of distinguishing delirium from dementia. Published works clearly demonstrate the variability in the use of tools of questionable validity for the detection of delirium.

Inouye (1994)[14] examined the utility of 18 published instruments specifically designed or used for the evaluation of delirium. The four criteria were 1) validated specifically for use in delirium; 2) capable of distinguishing delirium from dementia; 3) able to assess multiple features of delirium; and 4) feasible for use in delirious patients. Inouye found only two instruments that met all four criteria; the Confusion Assessment Method (CAM) and the Delirium Rating Scale (DRS). The Delirium Symptom Interview

(DSI) met three of the four criteria, with its ability to differentiate delirium from dementia still requiring validation. That 83% (15 of 18) of the existing screening instruments are potentially invalid, therefore, raises concerns as to whether subjects identified as having 'delirium' across studies that use different tools are truly comparable.

Lastly, there exists the problem of under-detection[2,10,14,17-21]. Though more an issue for clinical practice, under-detection can also be problematic in the realm of research. Delirium has consistently been shown to be under-detected by clinicians and nurses. Francis (1992)[17] for instance, reported that while physicians typically detect delirium in 30-50% of patients afflicted with delirium, nurses identify delirium in approximately 60-90%. Jacobson (1997)[2] also reported an under-detection of delirium by primary physicians in 32-67% of patients. Given its pattern of fluctuations and its tendency to occur mainly in physically ill patients, many clinicians and nurses may not observe the necessary symptoms to suspect delirium as a potential disorder, or may attribute the recognized symptoms to similar disorders such as dementia or depression. Proper detection and diagnosis is imperative because treatment will otherwise be lacking or inappropriate, and its consequences can be fatal[5,22]. This issue of under-detection becomes relevant for research purposes because delirium status in several studies has been determined through data obtained from medical charts that are completed by clinicians and nurses.

Table 2. Rates of Prevalent and Incident delirium

Study	Population	N	Mean age	Definition of delirium	Rates of Prevalent (P) and Incident (I)‡ delirium
Original Studies					
Berrios & Brook 1985[23]	Aged 75+, psychogeriatric unit with dementia	100	79	Among deluded, presence of disorientation, hallucination and hyperactivity	P: 37%
Cameron et al. 1987[18]	age 30+, general medical unit, not transferred from other services i.e. ICU	133	68.8 (32-97)	DSM-III; operational definitions not stated; rated by resident & intern	P: 13.5% I: 3.3%
Erkinjuntti et al. 1986[24]	age 55+, general medical unit	2000	NR	DSM-III (SPMSQ by trained nurse)	P: 11.5% P: 41.4% among dem, 12.4% among non-dem
Fields et al 1986[25]	med. service, no ICU	116	72.9 impaired 53.4 intact	MMSE < 24 =global impairment	P: 19.8%
Folks & Ford 1985[26]	age 60+ with psychiatric consultation	195	NR	Not specified	P: 23%
Francis et al. 1990[27]	age 70+, general med.	229	78	DSM-III-R (MMSE)	P: 36/229=16% I: 14/229=6%
Francis & Kapoor 1992[28]	age 70+, medical unit	229	78	DSM-III-R	P: 36/229=16% I: 14/229=6%
Golinger 1986[29]	adult surgical patient at psychiatric consultation-liaison service	128	47	DSM-III	P: 20.7% overall P: 43.8% among age 60+, 9.8% among age <60
Henker 1979[30]	psychiatry consults			DSM-II; Acute brain syndrome	P: 0.74%
Huang et al. (1998)[31]	psychiatric not dementia, withdrawal from alcohol, or substance	2512	73.2 (30-90)	DSM-III-R	P: 1.4% overall P: 9.6% among age 65+
Inouye et al. 1998[32]	age 70+, hospitalized patients	207	79	DSM-III-R (CAM)	P: 2%
Inouye et al. 1998[33]	age 65+	727	78.9	MMSE, CAM	P: 12%
Jitapunkul et al. 1992[34]	age 85+, acute geriatric ward, no rehab or respite care	184	81.7 (60-97)	DSM-III-R	P: 15%
Johnson et al. 1990[35]	age 70+, general medicine unit	235	78	DSM-III by psychiatrist (screened by nurse using MMSE<24, BPRS >25)	P: 16% I: 5%
Jolley & Baxter 1997[36]	All residents in contact with psychiatric services, aged 65+			OBD – Organic Brain Disorder[5]	I: 4.9%
Kolbeinsson & Johnsson 1993[37]	age 70+ admitted as emergency to med. dept	236		DSM-III-R (MMSE & MSQ)	P: 12.3%
Koponen et al. 1989[38]	psychogeriatric unit in mental hosp. ONE cohort, no comparison, not alcohol delirium	523	75 (60-88)	DSM-III (MMSE)	P: 13.4%
Levkoff et al. 1992[39]	age 65+, medical-surgical services	325	81.4	DSM-III (DSI)	P: 10.5% I: 31.3%
Murray et al. 1993[40]	Age 66+, hospitalized, community & NH elderly	291	80.5	DSM-III (DSI)	P: 19.9% I: 31.3%
O'Keeffe & Lavan 1997[41]	acute geriatric unit	225	82	DSM-III (DAS)	P: 18% I: 29%

Pompei et al. 1994[42]	age65+, med. & surgical	432	75	DSM-III-R (CAM, digit span, vigilance A test & clinical Assessment of Confusion)	P: 5% I: 13%
Rockwood 1989[43]	age 65+, 2 general medical unit, not coronary care or ICU admissions	80	76.8 (65-91)	DSM-III: "acute confusion"	P: 13/80=16% I: 12.5%
Rockwood 1993[44]	geriatric assessment unit in general med ward "frail" elderly	168	79	DSM-III (MMSE, DSRS)	P: 18% I: 7%
Rudberg et al. 1997[45]	age 65+, 2 med & 2 surgical services	432	65-95	DSM-III-R (digit span, vigilance A test, CAC, CAM, med charts, DRS)	P: 5% I: 14%
Thomas et al. 1988[46]	med unit, not from ICU or subspecialty med or surgical	133	del=68.8 non=62.8	DSM-III	P: 11.3% I: 3.8%
Weddington 1982[47]	med & surgical units with psychiatric consultation	116	---	DSM-III	P: 13%
Williams et al. 1985[48]	age 60+, no history of chronic mental impairment, occurrence of hip fracture by trauma	237	78.8 (60-96)	"Acute confusional state"[Φ], SPMSQ	P mild: 35.5% P mod/severe: 16%
Zubenko et al. 1997[49]	psychiatric patients	809	61.9	DSM-III-R criteria for organic mental, mood, or psychotic disorders	P: 7%

Review Articles – Prevalence/Incidence for various populations

Chan & Brennan 1999[3]	Medical: 15-20% Hip fracture: 30%
Devaul & Jervey 1981[22]	5-10% of all general medical & surgical services
Johnson 1990[50]	Medical and surgical: 10-15% Surgical: 15-40% Critical care: 20-40% Psychiatry, neurology, consultative services: 20-30% General medical: 15-20%
Inouye 1994[14]	elderly medical: 14-56%
Lipowski 1987[6]	70+ elderly: 30-50%
Liptzin 1995[15]	Age 70+ ED admission: 14% General hospital admission: 38.5% Community elderly age 55+: prev ~1.1% Post-op hip fracture: 28-44% Elective joint replacement: 26% Myocardial re-vascularization: 6.8% Geriatric unit with acute illness: 22%
Macdonald 1997[51]	elderly med: 30%
Rummans et al. 1995[52]	Elderly admission to hospital: P: 11-24%, I: 5-35%
Trzepacz 1996[53]	General hospital: 20%
Wattis 1996[54]	~20% in elderly

[§] Organic Brain Syndrome - includes dem., subacute del., epilepsy & other Dx (chronic organic hallucinosis, Korsakoff's Psychosis, apraxias, hemiplegia & preorganic change)

[Φ] "Acute confusional state" = disturbance in mental processes incorporating imp'd memory, thinking, attention, & orientation to time & place, there can be misperceptions of persons, objects, hallucinations & also may be accompanying hyper- or hypoactivity or emotional change. The state may be transient or prolonged.

‡ Incident delirium refers to the occurrence of delirium at any time during the hospital stay in all studies

RISK FACTORS AND ETIOLOGY

Delirium is an etiologically non-specific, wide-spread cerebral dysfunction that may be the result of a number of etiologic factors[6]. These etiologic factors can be classified into three main categories: predisposing, facilitating, and precipitating organic factors[55]. Predisposing factors are those that render an individual susceptible to the development of delirium in response to a wide range of causative agents and/or events. Facilitating or contributory factors are those that are neither necessary nor sufficient for the development of delirium, but can contribute in some way to the onset, severity and/or duration of delirium. And finally, precipitating organic factors are the 'causative' organic factors that are necessary for the development of delirium.

Predisposing Factors

Advanced age is one of the strongest known predisposing factors for the development of delirium[3,5,14,15,17,22,25,29,39,43,48,52,53,56-59]. The elderly are more likely to develop delirium in responses to events such as a mild infection or a therapeutic dose of medication that would not induce delirium in a younger individual. This susceptibility stems from the various physiologic changes that define the aging process which include their having less functional reserve to tolerate physiologic insults. Reduced efficiency in homeostatic regulation and immune mechanisms renders an elderly individual less resistant to diseases and stress such as surgery and anaesthesia, and age-related changes in brain neurochemistry and drug metabolism increase the likelihood of drug side effects[2,55]. As a consequence, the elderly have a higher prevalence of brain diseases, vision and hearing impairments[5], reduced synthesis of neurotransmitters, notably acetylcholine transmitters, increased frequency of chronic diseases and susceptibility to acute ones[5]. They also have reduced resistance to infection, proportionately less lean body mass, more body fat, and reduced glomerellar filtration rate and creatinine clearance. Under these conditions, therapeutic doses of commonly used drugs (especially those with anticholinergic effects) can, and frequently do, result in toxic side effects, including delirium[5,6,52,59].

Neurologically, aging affects the frontal lobe, hippocampus, locus ceruleus, and subsequent central cholinergic system[5]. The central cholinergic system is necessary for memory, learning, attention and wakefulness and is affected by use of anticholinergic

drugs[59]. The aging process is also associated with reductions in cortical brain cells, acetylcholine storage and muscarinic receptor plasticity, leading to reduced neurologic reserve and therefore increased susceptibility for developing delirium[52].

Brain damage and chronic brain disease (i.e. degenerative, vascular) are also common predisposing factors for delirium. Cognitive impairment has consistently been shown to be a strong risk factor for delirium[3,14,15,27,29,32,39,42,48,52,53,57,60], specifically pre-existing dementia[3,13,25,43,53,57,60]. Lipowski (1990)[55] reports that "a demented elderly individual has the highest general susceptibility to delirium, which increases with advancing age and progression of the dementing progress". Though uncommon for dementia to develop subsequent to delirium, delirium is often superimposed on dementia due to its strong predisposing effect. Elie and his colleagues (1998)[61] conducted a systematic review to examine risk factors of delirium in elderly hospitalized patients, and identified 61 risk factors from 27 studies. Dementia was found to be the most frequently studied (15 studies) and the strongest risk factor. Twelve of the 15 studies (80%) that examined and provided data on dementia as a risk factor found a positive correlation. Elie and colleagues further analyzed this correlation by synthesizing the data from the 12 studies having the positive correlations and found elderly hospitalized patients with dementia to be 5 times more likely to have delirium compared to those without dementia (odds ratio = 5.2; 95% confidence interval: 4.2-6.3).

Several other factors have been shown to predispose an individual to the onset of delirium. For instance, men have been shown in several studies to have a higher incidence of delirium[37,39,61], as have being unemployed[25], having few social interactions[3,7,53], and living in a nursing home or another form of long term care facility prior to hospitalization[39,57]. Addiction to alcohol or drugs, impaired vision or hearing, use of multiple medications, chronic illness resulting in functional weakness of vital organs, high frequency of episodic illnesses, impaired metabolism, reduced excretion and protein binding of drugs, reduced cerebral circulation and glucose metabolism with increased vulnerability to hypoxia have also been reported to be associated with delirium in a predisposing fashion[7].

Facilitating Factors

Psychological stress, emotional state, sensory deprivation/overload, sleep deprivation, and immobilization are five common conditions proposed to play contributory roles in the development, severity and duration of delirium, although none are believed to be necessary or sufficient individually.

Psychological stress poses emotional distress onto individuals, resulting in physiological changes that impose strain on homeostatic mechanisms[5-7,22,55]. Stress can result from various events, such as bereavement, transfer to an unfamiliar environment[9], medical illnesses, and as an emotional response to impaired cognition. The sustained elevation of plasma cortisol due to stress can exert a deleterious effect on both cerebral and mental function and hence interfere with selective attention and information processing such that an individual may be incapable of distinguishing between relevant and irrelevant inputs[5]. Plasma cortisol levels are abnormally high and sustained in the elderly population due to their reduced homeostatic capacities and consequently diminished resistance to stress.

On a related note, emotional states also have an influence on the potential for developing delirium. Mood disturbances[29] such as depression for instance, has been shown to be associated with delirium[32,42,52]. Such emotional states have commonalities in symptoms with delirium, including abnormal variability in psychomotor activity, impaired attention, cognition, and potential for hallucinations, delusions, and disorientation. In addition, Devaul (1981)[22] has indicated, without elaboration, that certain personality types are risk factors for delirium.

Sleep deprivation and fatigue[6,9,59], as a result of the disturbance in the sleep-wake cycle, have also shown strong links with delirium[22]. Sleep deprivation and sleep disorders are most commonly observed in the elderly stage of life, and its prevalence is reported to be greater in the hospitalized, physically ill elderly patients than in healthy elderly individuals. A disturbed and fragmented sleep-wake cycle can lead to excessive daytime somnolescence, and micro-sleeps, and sleep apnea, which can lead to hypoxemia, and may impair cognitive functioning. Awakening from REM sleep periods or occurrence of REM sleep without loss of muscle tone can also occur[5].

Sensory deprivation, either due to visual[2,3,5,53,59] or hearing impairment[2,5], has also been consistently shown to be associated with delirium[6,60] Delirious symptoms proposed to be associated with sensory deprivation include reduced intellectual efficiency, vivid imagery, visual and auditory hallucinations, delusions, mood shifts, and impaired directed thinking, to name a few. Sensory overload has also been shown to be related to cognitive impairment, hallucinations, illusions, disturbances in time sense, distortions of body image and delusions. Lipowski (1990)[55] reports various experimental and clinical evidence that indicate that sensory deprivation is associated with cognitive, perceptual and EEG pattern abnormalities that resemble delirium. Both an over- and under-stimulation relative to the individual's information processing capacity, therefore appears to play a facilitative role, rather than a causal role, with respect to delirium.

Disturbance in physical function has also been shown to be a risk factor for delirium. Immobilization[6], for instance, often due to surgery or other physical insults such as hip fractures, impaired physical function of increasingly frail elders[14,17], and impairment in instrumental activities of daily living[32] have all been shown to be associated with the delirium. Consequences of immobilization resemble those of sensory deprivation. That is, patients confined to prolonged bed rest have been reported to display impairments in intelligence tests, perceptual-motor functions, concentration, logical thinking[55].

Precipitating Organic Factors

A wide range of precipitating organic factors for delirium have been proposed, a subset of which are presented in Table 3. Given the susceptibility of the elderly population to delirium, even conditions that would not induce delirium in their younger counterparts could do so in the elderly. Physically traumatic events such as the occurrence of a disease (acute or chronic)[2], comorbidity[3,15,42,52,53,56], illness severity[3,9,14,15,25,43,62,63], reason of admission[25] and stability of medical condition[3,25,43], for instance, have all been shown to induce delirium in hospitalized elderly patients. Other traumatic events include surgery[52], pre-operative medical problems[64], complexity of surgical procedure from poor medical condition or metabolic stress of surgery itself[64], abnormal pre-operative serum sodium[27], potassium, calcium, chloride, glucose levels, high blood urea nitrogen/creatinine ratio[60], leukocytosis, alkolosis, hypoxemia,

hypoalbuminia[3,52], fracture on admission[57,65], infection[3,34,37,38,52,53,56,57,64-66], and metabolic disorders[3,45,52,53,57,64,66]

Cardiovascular and/or cerebrovascular conditions such as acute myocardial infarction[34,65], chronic cardiac failure[34], stroke[34,37,38,52,65,66], congestive heart failure[37,65], history of brain damage or disease[2,5,6,22,52,59,64,65], reduced blood flow[59,64,65], epilepsy[34], have been shown to precipitate delirium as have digestive and nervous system disorders[46,52], impaired glucose metabolism[59], and hepatic and renal dysfunction[52] Central Nervous System disease and systemic illnesses include diffuse cerebral disorder through inflammation or trauma, tumors[65], carcinoma[65], vascular, cardiovascular[45], endocrine imbalance, diabetes[65], thyroid disease, adrenal dysfunction and parathyroid disorders.

Increased risk for delirium has been seen in several physiological states as well, such as dehydration[9,56,60], fever[3,27,53], hypothermia[3,27,53], nutritional deficiency – Thiamine deficiency[5,53,64], hypoxaemia[64], electrolyte abnormalities[52,65], azotemia[9], increased dopamine[53,53]

Intoxication with exogenous substances and withdrawal from substances of abuse

Chan (1999)[3] reports that medication is the most common and reversible cause, followed by metabolic, cardiovascular and central nervous system (CNS) disorders, infections, and miscellaneous causes such as sleep or sensory deprivation, and post-operative states In the elderly population, the causes are frequently multifactorial.

Precipitating factors that are of pharmacological nature are polypharmacy[3,53], abrupt medicinal withdrawal[52], and drug intoxication[34,45,53,64,65] Due to changes in pharmacokinetic parameters and pharmacodynamic responses to medication that occur with age, virtually any drug or drug combination can lead to the onset of delirium in a susceptible individual[2,22] Specific drugs having deliriogenic effects include narcotics[57], neuroleptics[57], psychotropic drugs[15], and psychoactive drugs[3,27,53] The most common drugs known to induce delirium are alcohol, barbiturates, minor tranquilizers, sedatives, anticholinergic drugs and steroids. Furthermore, alcohol intoxication and withdrawalhave also been shown to induce delirium[15,42,64,65]

Exogenous substances, whether it be intoxication or withdrawal[22], are one of the most common precipitating factors for delirium in the elderly. The aging process increases susceptibility to the onset of delirium because of its association with 1) altered pharmacokinetics and pharmacodynamics; 2) drug-induced interactions resulting in synergism or potentiation of drug effects; 3) drug-induced nutritional deficiencies; 4) reduced thirst appreciation and thus a tendency toward hypovolemia; 5) excessive prescriptions and polypharmacy which is partly related to the greater tendency of comorbidity in the age; 6) non-compliance with and mismanagement of drug regimens by patients; and 7) inadequate drug monitoring by physicians[67].

Alcohol is highly associated with the onset of delirium in the elderly. Lipowski (1990)[67] reports that alcohol abuse is prevalent in approximately 18% of the elderly population and is frequently undetected. Physiologic effects of alcohol may differ in the elderly due to changes in absorption, hepatic metabolism, excretion, and sensitivity of the brain with age. Given its toxic effect to the brain, prolonged consumption could result in cognitive impairment. Alcohol can interact with drugs, including over-the-counter medications, as well as influence sleep quality and pattern, thereby accentuating susceptibility to delirium.

Table 3. Etiologic factors of delirium

Predisposing Factors

- Advance Age
- Male gender
- Unemployment
- Living in a nursing home or another form of long term care facility before hospitalization
- Cognitive Impairment – dementia
- Brain diseases
- Impaired vision or hearing
- Few socially interactions
- Poor medical status - chronic illness resulting in functional weakness of vital organs, high frequency of episodic illnesses, impaired metabolism, reduced excretion and protein blinding of drugs, reduced cerebral circulation and glucose metabolism with increased vulnerability to hypoxia
- Vitamin deficiency
- Alcohol and Benzodiazepine dependence
- Use of multiple medications

Facilitating Factors

- Psychological stress – Emotional state
- Sleep deprivation
- Sensory Deprivation
- Immobilization
- Depression

Precipitating Organic Factors

- Intoxication by Drugs and Poisons – Drugs, Alcohol, Illicit drugs, Addictive inhalants, Industrial poisons, Poisons of animal, plant, and mushroom origin
- Withdrawal Syndromes– Alcohol, Sedatives and hypnotics
- Physical Trauma - occurrence of a disease (acute or chronic), comorbidity, illness severity, reason of admission and stability of medical condition, rapidity of onset, metabolic stress of surgery, post-operative status, pre-operative medical problems, complexity of surgical procedure from poor medical condition
- Metabolic Disorders– Hypoxia, Hypoglycemia, Hepatic, pancreatic, pulmonary, or renal insufficiency (encephalopathy), Avitaminosis, Hypervitaminosis, Endocrinopathies, Disorders of fluid and electrolyte metabolism, azotemia, errors of metabolism diabetes, thyroid disease, adrenal dysfunction and parathyroid disorders, abnormal pre-operative serum sodium, potassium, calcium, chloride, glucose levels, high blood urea nitrogen/creatinine ratio, leukocytosis, alkolosis, hypoxemia, hypoalbuminia, fracture, increased dopamine, low serum albumin
- Infections– Intracranial, Systemic
- Head Trauma: concussion, contusion
- Epilepsy: ictal, interictal, postictal
- Neoplasm: extracranial, remote effects of tumors, carcinoma
- Vascular Disorders- Cerebrovascular, Cardiovascular (myocardial infarction: chronic cardiac failure, stroke, congestive heart failure, history of brain damage or disease, reduced blood flow, digestive and nervous system disorders, impaired glucose metabolism, and hepatic and renal dysfunction)
- Intracranial Space-Occupying Lesions– Abscess, Aneurysm, Neoplasm, primary or secondary, Parasitic cyst, Subdural haematoma
- Disorders of the Hematopoietic System- Severe anemia of any type, Erythremia, Thrombotic thrombocytopenic purpura, Macroglobulenemia
- Disorders due to Hypersensitivity - Serum sickness, Food allergy
- Injury by Physical Agents- Heat stroke (hyperthermia), Hypothermia, dehydration, fever, and nutritional deficiency – Thiamine deficiency, Radiation damage, Electrocution, gastrointestinal bleed, respiratory failure, pulmonary embolus, perforation of duodenal ulcer.

Pathogenesis

Several neurotransmitters have been found to be involved in delirium[52]. These include ACTH, dopamine, and gamma-aminobutric neurotransmitters. Some cases of delirium are caused by drug or toxins acting on specific neurochemical systems rather than producing a global disturbance in cerebral function. For instance, disturbance in the basal forebrain cholinergic pathways have been shown to have a specific effect on memory, whereas impairment to the pontine cholinergic pathway projecting to the frontal cortex and brain stem is reflected by an impairment in consciousness. There have been consistent evidence for the involvement of the cholinergic system in the development of delirium. A strong association has been found between the use of anticholinergic medication and the development of delirium. This hypothesis is supported by evidence showing that the anticholinergic drug use can induce delirium and that physostigmine, a cholinergic drug, can reverse the process. A chemical imbalance caused by an instability of central cholinergic and adrenergic mechanisms can lead to the onset of delirium, or an impairment of cerebral oxidative metabolism[6]. A general decline of cerebral metabolism can lead to the clinical manifestations of delirium and the associated slowing of EEG background activity[6]. Any disease or toxic agent leading to a decline of supply, uptake or utilization of substrates for brain oxidative metabolism could therefore result in delirium[5] Adequate level of these neurotransmitter is therefore necessary for normal cognitive functioning, attention, and sleep-wake cycle[5,53].

TREATMENT

In order to treat delirium, prompt identification and treatment of the underlying medical condition(s) inducing this disorder[2,7-9,15,50,64,68,69] and implementation of environmental and/or psychosocial support[68] is essential[2,64]. A comprehensive history should be obtained through interviews with family and caregivers, and physical examination should be carried out with particular attention to drug exposures and identification of physical and medical disorders[69]. A routine medical work up should also be performed which includes urinalysis, complete blood count, electrolytes, urea nitrogen and creatinine, calcium, liver chemistries, chest X-ray, and electrocardiogram[2,15,69].

While the comprehensive examination is being conducted however, several steps can be taken to ameliorate the symptoms. Medications should be reduced by discontinuing unnecessary medications[7], and adequate balance of fluid, electrolyte, nutrition, and vitamin supply should be restored and maintained[2,6-9,15,50,52,58,63,64,68,69].

Nonpharmacological Interventions

Nonpharmacological interventions can be employed for symptom management in the delirious patient, as shown in Table 4 (Adapted from Beresin 1988[7]). In addition to the reduction and discontinuation of unnecessary medications, some symptom management proposed include placing the individual near the nursing station for close observation[2,8,15,22,69] and orientation of patients during lucid periods[22]. Close family and friends should be encouraged and a light or radio should be on at night to prevent under-stimulation. Environmental interventions include monitoring of the amount of stimulation to maximize patients' abilities to perceive the environment accurately.

To minimize anxiety, comfort and reassurance should be provided, and reality testing should be promoted by conveying instructions, explanations, and coping strategies[7,8,52,64,69]. Rooms should be quiet and well-lit during the day[3,64] with a night light and soft music on at night[8,15,22]. Patients should be protected against physical harm by lowering beds, providing guard rails, and/or one-to-one supervision[7].

Familiarity and consistency is essential for reducing anxiety and/or agitation, and enhancing orientation[7,50]. Patients should be provided orienting stimuli such as a clock, calendar, labels, and photos[3,15,63] and familiar objects[6,8,50,68]. Visits by family and friends can promote orientation and reduce anxiety[3,7,8,15,22,52,64,68]. Frequent changes in bed location should be avoided[3].

Enhancing interpretation of surroundings is also essential. This can be done by correcting sensory deficits with eyeglasses and/or hearing aids[15,50,52,63], placing the patient in a room with a window for orientation, and avoiding over- or under-stimulation[2,52,68].

If confined to bed for long, physical activity or physiotherapy should be initiated as soon as possible to minimize adverse effects of immobility, such as pressure sores and contractures[52,68]. Physical restraints should be avoided as much as possible, since they may lead to fear, physical injury and thereby worsen delirium[2,3].

Therapy should not end when delirium clears. Patients may experience confusion of reality and fantasy as a result of the derangement of memory and perception, to the extent that post-traumatic stress disorder has been reported to occur after delirium in several cases[7]. Long-term care strategies may also need to be arranged for those dependent in physical or cognitive status[9].

Pharmacological Interventions

When agitation and psychotic behaviours are excessive, particularly when a patient poses harm to him/herself or others, pharmacological intervention may be necessary[3]. The choice of medication depends on the target symptoms, patients weight and frailty, level of arousal, and nature of medical disorder[7]. Elderly patients are sensitive to the side-effects of drugs, particularly anticholinergic agents, and care is therefore necessary to prevent iatrogenic delirium or worsening of pre-existing delirium [68]

Antipsychotic medications have been widely used to manage agitation and perceptual disturbances such as hallucinations, delusions, and paranoia[3,52]. Neuroleptic drugs are appropriate because they do not impair respiratory function and are less likely to aggravate cognitive impairment than benzodiazepines[64]. The most recommended antipsychotic medication is a high potency neuroleptic agent, haloperidol because of its minimal sedation, antipsychotic efficacy, low anticholinergic potency, low hypotensive effects, safety in cardiac and respiratory illness, and its ability to be administered intramuscularly or intravenously. Though thioridazine, droperidol, and chlorpromazine are other antipsychotic drugs that are as effective as haloperidol, they have a higher incidence of anticholinergic and cardiovascular side-effects that can accumulate in the elderly[51,52,64]. Despite it being the most recommended antipsychotic medication however, haloperidol also has some drawbacks that should be kept in mind. Specifically, it has strong extrapyramidal effects that can contribute to immobility and falling[7-9]and is therefore inappropriate for patient with pre-existing dementia or delirium. In such cases, a benzodiazepine can be administered along with haloperidol to blunt the extrapyramidal effects[9,52,64,69]. Though combining antipsychotic and benzodiazepine has short-term benefits, the end result may be further impairment of patients' sensorium and exacerbation of delirium symptoms. And some patients, especially with pre-existing cognitive impairment, have paradoxical responses to sedating, disinhibiting effects of

sedative-hypnotic drugs [52]. Further caution is also necessary since both haloperidol and benzodiazepine can cause or worsen delirium[8].

Physostigmine is a cholinergic agent which can temporarily reverse delirium caused by central anticholinergic toxicity. An excess level of physostigmine however, can lead to cardiac and respiratory side effects and since anticholinergic toxicity can be treated with its removal, use of physostigmine should be limited[9,64]

Benzodiazepine medication, such as lorazepam, temazepam, midazolam, chlormethiazole are the best drug of choice when delirium is the result of withdrawal from alcohol or sedative-hypnotic drugs, or if the patient with delirium also suffers from Parkinson's disease or hepatic failure[15,52,64,68]. Benzodiazepine drugs are effective for treating anxiety and sleeplessness[7] and useful adjuncts to haloperidol to blunt extrapyramidal side effects and promote sedation[9]. Lorazepam is the most frequently chosen option[52]. Midazolam (short-acting) is also effective but places the patient at higher risk of benzodiazepine-withdrawal symptoms upon its discontinuation and paradoxic agitation in patients with sedative-hypnotic withdrawal[52].

As is the case with midazolam, benzodiazepine drugs also have their drawbacks. They for instance, cannot relieve psychotic symptoms and can cause paradoxical excitement[7]. Sedatives may be essential for agitation and hallucination, but over-sedation can prolong delirium[64]. They worsen respiratory depression however, and can cause paradoxical excitement[64].

Lastly, when delirium is the result of withdrawal from a drug, then the same drug, or that of the same family, should be administered to the individual to reverse the process and then be weaned off gradually. In this situation, initial administration of the drug and subsequent gradual weaning can treat the condition[6].

Table 4. Treatment for Delirium

PHARMACOLOGICAL

Antipsychotic/Neuroleptic

- For management of agitation and perceptual disturbances
- Does not impair respiratory function and less likely to aggravate cognitive impairment than Benzodiazepines
- BUT can cause or worsen delirium

Haloperidol (Haldol)

- minimal sedation, antipsychotic efficacy, low anticholinergic potency, low hypotensive effects, safe in cardiac & respiratory illness, and able to be administered intramuscularly or intravenously.
- BUT extrapyramidal effects that can contribute to immobility and falling and is inappropriate for patient with pre-existing dementia

Thioridazine, Droperidol, Chlorpromazine are as effective as Haloperidol but have higher incidence of anticholinergic and cardiovascular side-effects that can accumulate in the elderly

Cholinergic

Physostigmine can temporarily reverse delirium due to central anticholinergic toxicity BUT an excess level of Physostigmine however, can lead to cardiac and respiratory side effects

ECT also reported to be effective BUT should only be used if agitation and/or psychosis is severe and Haloperidol and Benzodiazepine is not tolerated

Resperidone has also been shown to be effective for those with Parkinsonianism[5]

Benzodiazepines

- For withdrawal delirium, anxiety, sleeplessness, and As adjuncts to Haloperidol to blunt extrapyramidal side effects and promote sedation
- Best choice when delirium is the result of withdrawal from alcohol or sedative-hypnotic drugs, or if the patient with delirium also suffers from extrapyramidal disease or hepatic failure
- BUT can cause or worsen delirium, cause paradoxical excitement, cannot relieve psychotic symptoms, over-sedation can prolong delirium, and can worsen respiratory depression
- Midazolam however places the patient at higher risk of Benzodiazepine-withdrawal symptoms upon its discontinuation and paradoxic agitation in patients with sedative-hypnotic withdrawal

Lorazepam (intermediate-acting)

Midazolam (short-acting), Temazepam, Chlormethiazole also effective

Combination Antipsychotic and Benzodiazepine

- short-term benefits for agitation, psychotic symptoms.
- BUT the end result may be further impairment of patients' sensorium and exacerbation of delirium symptoms, and in some patients, especially with pre-existing cognitive impairment, have paradoxical responses to sedating, disinhibiting effects of sedative-hypnotic drugs

Table 4. Treatment for Delirium – continued

ENVIRONMENTAL AND PSYCHOSOCIAL SUPPORT - *adapted from Beresin E. 1988*
Environment • Sensory input: not excessive, inadequate, or ambiguous. Room should have adequate light and be quite. Some patients prefer radio or television for familiar background stimulation • Present one stimulus or task at a time • Medication schedules should not interrupt sleep
Orientation • Room should have a clock, calendar, and chart of the day's schedule • Keep the patient in the same surroundings • Verbal reminders of the time, day, and places should be used frequently • Evaluate the need for eyeglasses, hearing aids, and foreign language interpreters
Familiarity • Obtain familiar possessions from home to help orient the patient, particularly objects at the home bedside • Request family members to stay with the patient. They provide the basis for orientation, effective communication, support, and aftercare planning • Discuss familiar areas of interest, e.g. hobbies, occupation • Allow the same staff members to consistently care for the patient
Communication • Instructions and explanations should be clear, slow-paced, simple and repetitive • Use face-to-face contact • Convey an attitude of warmth and kind firmness • Consistently address the patient as he/she prefers • Begin each contact with orienting and identifying information • Acknowledge the patient's emotions and encourage verbal expression
Activities • Avoid physical restraining. Allow free movement, provided the patient is safe • Encourage self-care and other personal activities to reinforce competence and enhance self-esteem

PROGNOSIS

Research into the prognosis of delirium in the elderly population over the past few decades has shown relatively consistent results. For instance, full recovery is possible for many patients if delirium is recognized early and treated properly[2,6,9,22,52,59]. Once correctable factors are addressed, delirium improves within days and largely resolves within a few weeks[3]. In a hospitalized elderly population (age ≥ 65), Levkoff et al. (1992)[39] found complete resolution of delirium in 4% of patients at discharge, 20.8% at 3 months, and an additional 17.7% at 6 months after discharge. Similarly, Rockwood (1993)[44] found that 52% of survivors among the elderly with delirium in a general medical ward recovered fully. Furthermore, Cole et al. (1993)[70], using meta-analytic techniques, showed that mental state improved in 54.9% of delirious patients.

Although the identification and prompt treatment of the cause of delirium has been shown to result in the resolution of delirium in a majority of cases, a substantial proportion of subjects nevertheless experience negative, and often fatal, outcomes. Patients afflicted with delirium for instance, have a greater mean length of hospital stay, with reported hospital days across studies range from 12.1 to 31.5 days among delirium cases compared to a 7.2 to 25 day range among non-delirious controls[2,3,13,17,25,27,37,39,41-43,46,52,53,56,64-66,70]. In the elderly population, this excess in hospital days persists even when drug related group, illness severity and increased mortality are taken into account[52,53].

Residual impairment in cognitive and physical function have also been associated with delirium after hospitalization[2,15,53,63]. Despite controlling for confounding factors, impairment in physical function has been shown to persist[52]. Delirium has been identified as a predictor for decline in both activities of daily living and cognitive function both during and after hospitalization[3,40]. Francis and Kapoor (1992)[28] found in medical elderly patients aged over 70 years, that delirium is a predictor for greater decline in cognitive status and for decline in activities of daily living even after adjusting for confounding factors. Concordant with Francis (1992)[28], Inouye and her colleagues (1998)[33] also showed in individuals over 65 years of age, that the proportion of patients exhibiting functional decline in at least one of five activities of daily living was 67% in delirium cases and 34% in controls at discharge, and 53% and 26% respectively at 3 months post-discharge. Murray (1993)[40] has shown in 291 elderly community and institutionalized individuals that delirium is a strong predictor for functional decline (ADL) both at and three months after hospital discharge.

Other adverse outcomes associated with delirium include greater morbidity[2,3,25,52], post-operative complications[15], loss of independent community living[2,53], greater hospital re-admissions[65], and hospital-acquired complications[41]. George and colleagues (1997)[65] for instance, found that in an elderly population aged 65 years or older, the readmission rates of those with delirium and those without were 34% and 21% respectively at 6 months and 55% and 38% at 12 months post discharge. Hospital acquired complications were found in 60% of delirious patients and 34% of non-delirious controls[41].

Mortality

Published work in the past has consistently demonstrated an increased mortality rate among those afflicted with delirium compared to those not afflicted with the disorder[9,13-15,52,64]. Johnson (1990)[50] reported mortality rates ranging from 15% to 30%, while Inouye (1994)[14] and Francis (1990)[9] found rates as low as 10% and as high as 65%. Chan (1999)[3] also reported higher mortality rates in delirium patients than in those without, with 10-26% during index admission, 38% at 1 year, and 51% at 5 year follow up. Mortality rates have also been shown to be higher than in patients with dementia or depression during index admission[2]. Among those with delirium, some research has shown that the risk of mortality is highest for those with the mixed (having both hyper- and hypo-kinetic psychomotor activity) subtype[52]. These high rates of mortality among patients with delirium therefore represent a 2- to 20-fold increase relative to those without delirium.

More recent research however, has revealed that delirium may not be a risk factor for mortality. Though the increased rates of mortality among delirious patients has been shown to be up to 20-fold[17], once confounding factors are controlled for, delirium itself is no longer an independent contributor to the excess in deaths[2,6,9,15,17,28,53,68,71]. Taylor (1993)[68] for instance, found that successfully treating the underlying medical condition eliminated much of the excess mortality associated with delirium. The increase in mortality has also been attributed to functional decline rather than delirium[17,33,66].

The most consistent risk factors for the mortality however, appear to be sociodemographic and medical. These factors include age[15,33,39,41], sex[15,33,39], pre-existing cognitive impairment[15,28,39,41,66], medical diagnosis[6], medical stability[25], reason for admission[25], comorbidity[9,25,41], severity of the underlying illness[2], and physical function status[9,15,17,25,33,39,41,42,53].

Fields and colleagues (1986)[25] examined 116 hospitalized elderly patients receiving medical services, to assess the impact of global cognitive impairment on in-hospital mortality. The investigators employed the MMSE as their instrument to assess cognitive status. Despite the presence of significant differences in the proportions of in-hospital deaths between cognitively impaired and intact patients (17% impaired, 5% intact; $p=0.05$), the difference diminished once illness severity, medical stability, reason

for admission and comorbidity were accounted for. Among these confounding factors, illness severity was found to have the strongest predictive association with in-hospital mortality. Furthermore, follow up data revealed that mortality rates at 3 months post-discharge were not statistically significant even before the above factors were controlled for (30% impaired, 15% intact; p=.09). Thus, both during and after hospitalization, cognitive impairment was not found to be predictive of subsequent mortality.

Similarly, Francis and colleagues (1990)[27] conducted a study on elderly medical patients aged 70 and older, and found a significant difference in the mortality rates between cognitively impaired and intact patients during hospitalization (8% cognitively impaired, 1% cognitively intact; $p< 0.05$), but a lack of significance at 6 months post-discharge (14.3%, 10.1% respectively; $p>0.10$). Subsequent multivariate analyses revealed that the excess mortality among the cognitively impaired patients appeared to be attributable to the severity of their underlying illness rather than to delirium. Francis and Kapoor (1992)[28] then examined 229 medical elderly patients using the DSM-III-R criteria, and found a significant difference in mortality rates between delirious cases and non-delirious controls 2 years after discharge (37% cases, 23% controls, p=0.03). Once cancer, initial cognitive impairment, and baseline ADL were controlled for, however, this difference was no longer statistically significant. Delirium therefore was shown to be a predictor for ADL decline and cognitive decline, but not for death.

Pompei (1994)[42], on the other hand, showed in 432 medical and surgical patients aged 60 years and older, that delirium was significantly associated with in-hospital mortality even after adjusting for comorbidity. At three months post-discharge however, although there was still a significantly greater proportion of delirium patients who died compared to their non-delirious counterparts, (11% vs. 3% respectively, $p<0.01$), this association did not persist once comorbidity was taken into account.

Inouye and colleagues (1998)[33] examined mortality rates in hospitalized elderly patients and found a statistically significant in-hospital rate difference between patients with and without delirium. This difference disappeared however, once they adjusted for age, gender, illness severity (APACHE-II), and physical function (ADL and IADL). The same pattern of results were also found at 3 months after discharge. Koponen & Riekkinen (1993)[66] examined elderly patients in a psychogeriatric unit, and found that

level of cognitive function and ADL at admission were predictive of death, but that delirium was not.

Levkoff and colleagues (1992)[39] found in 325 medical-surgical elderly patients, that those with delirium had significantly excessive deaths compared to non-delirious patients at 6 months post-discharge, but this difference disappeared once adjustment was made for age, sex, pre-existing cognitive impairment and illness severity. Delirium was therefore not associated with increased mortality, but was associated with greater hospital length of stay and nursing home admissions. O'Keeffe and Lavan (1997)[41] found consistent results among 225 acute geriatric patients. In their study, despite initial difference in mortality at discharge, once age, illness severity, comorbidity, disability scores, and dementia were accounted for, the initially seen excess mortality in delirium disappeared. The same pattern of results were also found at 6 months post-discharge.

A study by Rabins and Folstein (1982)[72] compared mortality rates between delirious and demented patients. In their study, delirium was defined as deterioration in intellectual function, requiring a MMSE score of less than 24 and an abnormal level of consciousness. Demented controls were also required to have a MMSE score of less than 24, but their level consciousness to be normal. The investigators revealed a significantly excessive mortality rate among delirious patients at discharge (23% delirious, 4% demented, $p<0.02$; Mortality ratio = 5.8). Twelve-month data was a little less robust than at discharge in that changing the method of handling losses to follow-up affected the significance of the difference. When lost subjects were excluded from the analysis, mortality rates were not significantly different. When lost subjects were assumed to be alive however, the difference was significant. Rabins and Folstein therefore had relatively strong evidence for the excess mortality among delirium patients at discharge, but results at 12 months post-discharge were inconclusive. Furthermore, multivariate analyses were not carried out in this studies, which, if performed, could yield results consistent with the other, above mentioned studies.

Jolley et al (1997)[36] reported other factors that modified the association between delirium and mortality. For instance, men have been shown to have higher death rates than women. Low intake of vitamin C also increases the risk of developing cognitive impairment and subsequent mortality. Later age of onset and presence of co-existing

physical disability and illness are also associated with reduced survival following diagnosis of delirium. In addition to its association with delirium, cognitive impairment and its severity is also associated with shorter survival times. Family history of dementia, depressive mood, aphasia, parietal lobe dysfunction, psychotic features, and behavioral abnormalities at time of presentation or assessment have all been reported to have an association with survival times[36].

Published work is therefore very consistent in demonstrating the significant surplus in mortality among hospitalized elderly patients suffering from delirium relative to their non-delirious counterparts. They are also relatively consistent in demonstrating the elimination of this association once statistical adjustments are made for specific confounding factors such as illness severity, age, sex, comorbidity, initial physical function and the like.

However, several methodological characteristics of the above-mentioned studies are limiting in revealing the true association between delirium and mortality. First of all, the definition of delirium has changed over the past years and hence the tools used to assess delirium has changed as well. For example, the studies by Fields and colleagues (1986)[25] and Francis and colleagues (1990)[27] employed the MMSE as their tool to assess cognitive impairment but MMSE is not able to distinguish delirium and dementia. Rabins and Folstein (1982)[72] used the MMSE with or without abnormal level of consciousness as their definition for comparing delirium and dementia respectively. This too, is inconsistent with the current definition for delirium.

Secondly, recent studies have had numbers of delirious subjects ranging from 45-125 cases (Francis et al. (1990)[27], Francis and Kapoor (1992)[28]: 45; Pompei (1994)[42]: 64; Inouye et al. (1998)[33].: 88; Levkoff et al. (1992)[39]: 125, O'Keeffe and Lavan (1997)[41]: 94). However, all of these studies included both incident and prevalent delirium in their case definition. Literature on risk factors for delirium have indicated however, that incident and prevalent delirium are two distinct categories of delirium and as such, should be differentiated. Levkoff et al. (1992)[39], for example, reported having had 34 prevalent cases among the 125 cases, and O'Keeffe and Lavan (1997)[41] reported having had 41 among their 94 cases.

The suggestion to differentiate prevalent and incident delirium poses another issue of concern. In studies of subjects with prevalent delirium, delirium is often assessed after admission and therefore potentially include some incident cases (occurring between arrival to the emergency department and transfer to the department to which they are admitted). Also, delirium cases who are not admitted go undetected because they do not get assessed.

Furthermore, much of the evidence for the prognosis of delirium in hospitalized elderly patients is based on patients of specific divisions within the hospital setting, such as medical[27,28,39,42], surgical[39,42], psychiatric[36] and the like. Though these studies are relevant to patients in those particular divisions, there is uncertainty as to their applicability to all hospitalized elderly patients who suffer from delirium, and thereby giving rise to potential selection bias. Review of the literature reveals that there is, in fact, a knowledge gap in the prognosis of delirium patients in the Emergency Room settings. The distribution of the confounding variables in patients presenting to Emergency Departments and their association with delirium and mortality is yet unknown.

In this thesis research, the use of emergency department as the settings allowed us to avoid potential selection bias in that most of the studies in the past have focused on subjects in specific departments to which they were admitted. In addition to being able to detect delirious cases who are not admitted to the hospital, the emergency department setting allowed us to sample patients of all types. That is, sampling from the emergency department setting allows generalization of the results to all patients who access the hospital service rather than focussing on specific departments, which restrict applicability of the results to patients in that specific setting.

Furthermore, delirium was assessed using the CAM, which is a validated tool for diagnosing delirium[73]. The focus of the study was to examine mortality in patients with prevalent delirium. Assessing patients for delirium within six hours of arrival to the emergency department minimized the inclusion of incident cases and the exclusion of prevalent cases. This in turn allowed for a more homogeneous sample than previous studies. Despite the more restrictive case definition, we were able to recruit 107 delirious cases in this thesis research. Though the restriction to prevalent delirium prevents making

any inferences of incident delirium, the results are nevertheless more valid for prognosis of prevalent delirium.

Moreover, we used proxies in addition to the subjects themselves to allow for a better response rate than using subjects alone. Especially for delirium subjects who may or may not have been able to complete the baseline interview because of their delirious state or answer particular questions because of their impaired memory or attention, the use of proxy information renders itself to be an alternative source of information. As such, answers to items on the interviews for which we believed the proxy to be more reliable, information from the proxy was used. Having an alternative source of information therefore allowed us to increase accuracy by having the data more valid, and precision by reducing losses to follow up and the number of missing values for each of the items in the interviews.

Finally, assessment of cognitive status was carried out using the IQCODE[74], which is administered to a close relative or friend to examine changes in cognitive status over a specified time period. In this thesis research, the proxy was asked to report on any change in cognitive status over the preceding 6 months. The IQCODE is a preferred measure of cognitive status because responses given by subjects themselves are unreliable when they are in midst of their delirious state.

We believe that the methodological characteristics of this study allowed us to examine whether or not prevalent delirium is a predictor of mortality among elderly patients admitted through the Emergency department.

Table 5. Mortality Rates for delirious subjects

Study	Population	N	Mean age (range)	Delirium definition	Results*
RATES OF DEATHS AMONG DELIRIUM PATIENTS					
Farber 1959 *Dis Nerv Syst; 20:296-9*	general psychiatric ward	122	37 women 45 men	acute organic brain syndrome, no alcohol withdrawal or alcoholic hallucinations	MD 12%
Cole et al. 1994[illegible]	age 75+, medical unit	88	86	DSM-III-R (CAM)	MD 31.88 [illegible]
Huang et al. (1998)[11]	psychiatric	2512	73.2 (30-90)	DSM-III-R, not dementia, withdrawal from alcohol, or substance	M6 20.[illegible]% M12 36.5% M24 39.4%
Inouye et al. 1998	age 70+, hospitalized patients	207 dev't cohort 318 valid'n cohort	79	DSM-III-R (CAM) - not focus of study (results not specific to del)	MD 8% M3 14% M12 25% M24 36% MD 5% M3 [illegible]% MD12 32% M24 43%
Koponen et al. 1989	psychogeriatric unit in mental hosp (ONE cohort, no comparison	70	75 (60-88)	DSM-III & MMSE, not alcohol delirium	MD [illegible]% M1 [illegible]% M6 27% M12 37%
Sirois 1988	psychiatric consultation service of a general hospital	100	64.1 women 70.0 men	DSM-III	MD 27%
Bergmann 1974 *Age Ageing 3:174-88*	age 65+, general medical unit	100		acute confusion (del) diagnosed by using a semi-structured interview, specific criteria not stated	M1 [illegible] Mortality ratio 2.2
COMPARISON OF MORTALITY RATES AMONG DELIRIUM AND NON-DELIRIUM PATIENTS					
Cameron et al. 1987	age 30+, general medical unit not transferred from other services i.e. ICU	133	68.8 among del (32-97)	DSM-III, rated by resident & intern	MD 65% (A 3.3%) (p .001) (Mortality ratio [illegible])
Cole & Primeau 1993	age 60+	8 studies		Not specified	M1 14.2% (A 4.8%) [illegible] NS M6 22.2% (A [illegible]) (NS)
Dastoor et al. 1979	psychogeriatric unit	80	73	Functional vs organic brain disease	Organic dis. 40% Functional dis. [illegible]%
Fields et al. 1986	med. service, no ICU	316	72.9 imp'd 53.4 intact	MMSE [illegible] 24 (global cognitive impairment (rater NR (no differentiation between del. & dem	MD [illegible]% (A [illegible]%) [illegible] Mortality ratio [illegible] [illegible] after controlling for illness severity, medical stability, reason for admission & comorbidity, imp'd patients did not have a significantly higher mortality rate than intact patients
					M3 30% (A 15%) (p [illegible])
Francis et al. 1990	age 70+, general med	229	78	DSM-III-R (MMSE)	MH [illegible]% (A [illegible]) p [illegible] M6 14.3% (A [illegible]) p [illegible] Mortality due to illness severity, not del
Francis & Kapoor 1992	age 70+, medical unit	229 (205 with loss to F/U)	78	DSM-III-R	M24 37% (A 23%) p .03, RR [illegible] (NS when adjusted for cancer, initial cog imp't, baseline ADL) Del → decline in ADL (adjusted) → greater decline in cog status
George et al. 1997	age 65+, no terminal illness	266	80.6 (65-98)	DSM-III, confirmed by physician, no dementia	MD 11% (A [illegible]) (NS) M6 31% (A 13%) (p .001, OR 3.11 (1.82-5.77)) M12 38% (A 21%) (p .006, OR 2.30 (1.25-4.35))

Inouye et al 1993				3 risk groups (Low, Intermediate, High)	M: 9%, 16%, 42% dev't cohort M: 3%, 14%, 26% valid'n cohort
Inouye et al 1998	age 65+	727	78.9	MMSE, CAM	MD: 9% CA, 4% [illegible] BUT not signif when adjusted for age, gender, APACHE II score, ADL & IADL unadj'd OR 2.2 (NS) adj'd OR [illegible] M3: 30% CA, 12% [illegible] (p [illegible]) BUT not signif when adjusted for age, gender, APACHE II score, ADL & IADL Unadj'd OR [illegible] Adj'd OR [illegible]
Jitapunkul et al 1992	age 85+, acute geriatric ward, no rehab or respite care	184	81.7 (60-97)	DSM-III-R	MD: 35% CA, 16% [illegible] p [illegible]
Jolley 1997	All residents in contact with psychiatric services, aged 65+			Organic Brain Disorder*	SMR [illegible] RR [illegible]
Kolbeinsson & Jonsson 1993	age 70+ admitted as emergency to med. dept	236		DSM-III-R (MMSE & MSQ)	MD: 32% del, [illegible]% dem
Koponen & Riekkinen 1993	psychogeriatric unit ONE cohort, no comparison, not alcohol del	70	75	DSM-III (MMSE)	MD: 6% M12: 37% M48: 66% RF for mortality: cognitive function level & ADL at admission Prognosis: progression of basic CNS disease, cognitive decline & ADL decline
Koponen et al 1994	psychogeriatric unit ONE cohort, no comparison	67	75 (60-88)	DSM-III (MMSE)	M12: 23/67 (34%) M48: 43/67 (64%)
Levkoff et al 1992	age 65+, medical-surgical services	325	81.4	DSM-III (DSI)	M6: 26.4% CA, 13% [illegible] del NOT signif when adjusted for age, sex, pre-existing cog imp't & illness severity Del is NOT assoc'd with increased mortality but IS assoc'd with greater LOS & NH admission
Li & Wu 1999	Age 65+, 4 metropolitan districts	1434	NR	Cognitive Impairment via SPMSQ (5+ errors/10 = impaired) [CI] Physical function loss via ADL (1+ 6 disability = disabled) [PI]	[illegible] RR adjusted for age, sex, education, exercise, smoking, alcohol consumption, # chronic disease, depression score [illegible]
Marcantonio et al (1994) JAMA 271(2) 134-139	Age 50+, general surgery, orthopaedic surgery, and gynecologic services	876	68	DSM-III-R (CAM, medical chart and hospital nursing index)	4% CA, 0.3% [illegible] (p [illegible])
O'Keeffe & Lavan 1997	acute geriatric unit	225	82	DSM-III (DAS)	MD: 16% CA, 5% [illegible] signif but not when adjusted for age, illness severity, comorbid disease, disability score, & dem OR 3.4 (1.3-8.6) adj'd OR 2.6 [illegible] M6: 31% CA, 15% [illegible] signif but not when adjusted as above) OR 2.5 (1.3-4.7) adj'd OR 1.4 (0.7-2.8)

Pompei et al 1994[?]	age 65+, med & surgical	432	75	DSM-III-R (CAM - digit span, vigilance A test & clinical Assessment of Confusion)	MD: [illegible] p [illegible] 001) M3: 11% CA, [illegible] p [illegible] 01) In-hosp mortality & del Assoc'n persisted after adjusting for comorbidity, however, del Was not a signif with 90 day mortality after adjusting for comorbidity
Kabins & Folstein 1982		del 48 dem 25	del 54.5 dem [illegible]	Deterioration in intellectual function (MMSE 24 & abnormal level of consciousness [CA] Dementia - MMSE 24 & normal level of consciousness [illegible]	MD: 23% CA, [illegible] p [illegible] 02 Mortality ratio [illegible] M12a: 46% CA, 25% [illegible] NS) M12b: 38% CA [illegible] (p [illegible] 05) M1a not signif (excluding loss to FU n [illegible] & 1b) assuming loss as alive)
Rockwood 1989[?]	age 65+, 2 general medical unit, not coronary care or ICU admissions	80	76.8 (65-91)	DSM-III (acute confusion	M1: 29% higher in del
Rockwood 1993[??]	geriatric assessment unit in general med ward	168	[illegible]	DSM-III (MMSE, [illegible] SRS)	M12: 12% CA, [illegible]
Thomas et al 1988[?]	med unit, not from ICU or subspecialty med or surgical	133	del 68.8 non 62.8	DSM-III	MD: 65% CA, 4.4% [illegible] p [illegible] 0001
Weddington 1982[?]	med & surgical units with psychiatric consultation	116	---	DSM-III	M12: 33% in CA (Mortality ratio [illegible] 6.5)

med. - medical, del. - delirium, dem. - dementia, MMSE - Mini-Mental Status Exam.

* MD - in hospital mortality, M3 - mortality at 3 months post-discharge, M6 - mortality at 6 months, etc.

[?] Organic Brain Disorder - includes dem., subacute del., epilepsy & other Dx (chronic organic hallucinosis, Korsakoff's Psychosis, apraxias, hemiplegia & preorganic change)

CHAPTER 3. METHODS

STUDY DESIGN

Overview

The thesis research constitutes a secondary analysis of a longitudinal study of subjects initially recruited for a previous case-control study funded by the National Health Research and Development Programme (NHRDP) which examined the role of medication as a risk factor for delirium in the elderly (Galbaud du Fort G., Moride Y et al. Drugs as a risk factor for delirium in the elderly: a case-control study). The objectives of the case-control study were 1) to detect the existence of delirium in the elderly seen for acute illness in the emergency departments of two hospitals (Jewish General Hospital, Montreal General Hospital), and 2) to compare the characteristics of recent exposure to drugs between subjects with and without delirium. Ethics approval for this study is shown in Appendix 1.

Setting & Subject Recruitment Process.

This study was conducted in two hospitals in Montreal, Quebec, Canada. The two sites involved were the Montreal General Hospital (MGH) and the Jewish General Hospital (JGH). Subjects were recruited from the Emergency department on weekdays during the day and early evening shifts for 22 weeks (November 4, 1996-April 18, 1997) at the MGH and 36 weeks (November 1, 1996-June 27, and September 8-October 3, 1997) at the JGH. Two nurses and one research assistant recruited subjects at the JGH while one nurse recruited subjects at the MGH.

Figure 1 presents the recruitment process. The flow chart represents the size of the target population in the study time frame (subjects 66 years or older on stretcher in the emergency department), the number of patients screened for eligibility, the reasons for being ineligible and the corresponding number of subjects. Of the target population of 4998, 1614 individuals could not be located. The emergency department setting renders such situations because patients are often away from the emergency department for X-rays or other tests. In few cases, patients had left for home before they could be approached by one of the researchers in the study. Among the 1505 patients solicited for

consent, only 178 refused to participate, representing a response rate of 88.2%. Among the 1268 subjects enrolled, 107 (8.44%) fulfilled the CAM-DSM IV criteria for the diagnosis of delirium.

In order to maximize participation, consent consisted of verbal acceptance obtained from the subject. The rationale for this decision, as opposed to obtaining written consent, was that there was a potential for reluctance for signing forms when approached in the Emergency Department , and that patients were lying on stretchers when approached, which makes signing forms difficult. If verbal consent was obtained, the research assistant filled out a form indicating the name of the patient, a name of a witness and the date of consent. Participants were then given an information sheet describing the study and administered the short questionnaire. If the subject was shown to be cognitively in tact, as determined by a short assessment of cognitive status (BOMC, see below), then written consent was sought for administering a longer questionnaire, which included review of medical charts. If the subject was shown to be incapable of giving consent due to cognitively impairment, written consent was sought from a caregiver. For both cognitively impaired and in tact subjects who have agreed to participate (personally or through a caregiver), another consent was obtained for participation of a caregiver. Thus, for cognitively impaired subjects who had had a caregiver provide consent, a second consent was sought from the caregiver for his/her own participation in the study. All consent forms are attached in Appendix 2.

Eligibility Criteria

Those who met the following eligibility criteria were approached for inclusion in the study. The individuals needed to be 66 years of age or older visiting the emergency department. Patients were triaged by the triage nurse upon arrival at the Emergency room and classified as to the severity of their medical condition in two categories: those that could return to the waiting room were the ambulatory patients, those judged to require more immediate attention were placed on stretchers. Only the latter group of patients were approached for enrolment. Those who were blind, deaf, mute or aphasic were excluded from the study , as were those who: did not speak either English or French;

were residing in a nursing home or another form of long term care facility prior to the emergency department admission; were hospitalized or in emergency department for a 24 hour period in the last month; or were too sick or in too much pain to take part in the study.

Assessment of Delirium

Confusion Assessment Method (Inouye et al. 1990)[73]. The CAM is a standardized and structured instrument with sensitivity, specificity, positive and negative predictive values all being greater than 90%[73] that can be administered and completed within five minutes by a non-clinician. It consists of nine operationalized criteria based on the DSM-III-R, which are: 1) acute onset, 2) inattention, 3) disorganized thinking, 4) altered level of consciousness, 5) disorientation, 6) memory impairment, 7) perceptual disturbances, 8) psychomotor agitation or retardation, and 9) altered sleep-wake cycle and, in addition, the presence of fluctuation in items 1) to 4). The CAM algorithm requires the presence of both acute onset and inattention, and either disorganized thinking or an altered level of consciousness for the diagnosis of delirium. According to verbal communication with Dr. Inouye, the CAM algorithm was subsequently modified leading to a greater concordance with DSM-IV. The modified CAM is the version employed in this study for the determination of case-control status.

Validation of the CAM instrument by Inouye involved assessing the reliability of administration by a geriatrician with the use of diagnosis by a psychiatrist as a gold standard. To ensure that a trained interviewer who is not a physician has reliability comparable to a geriatrician, the validation for the CAM was carried out on 110 elderly patients. The agreement between the geriatrician's assessment and that of a non-physician interviewer resulted in a kappa coefficient of 0.91, a sensitivity of 1.00, a specificity of 0.97, a positive and negative predictive value of 0.86 and 1.00 respectively. According to the geriatrician assessment, 19% of subjects met the CAM criteria for delirium, 24% met the DSM-III-R criteria, 20% the DSM-IV criteria, and 21% had delirium according to the clinical impression of the geriatrician. The kappa statistics were the following: CAM vs. DSM-IV: = 0.97; CAM vs. DSM-III = 0.86; CAM vs. clinical impression = 0.94. This

validation study was therefore able to demonstrate high reliability of the CAM administered by a non-physician interviewer, and improved concordance rate between the CAM and DSM-IV than between the CAM and DSM-III.

Assessment of Outcome – Mortality

The outcome of interest for this thesis research was mortality. At each of the follow-up time points (2 weeks, 6, 12, and 18 months post-admission), all information was obtained either from the patient or a proxy. Vital statuses for the subjects were obtained by their proxy but dates were not always available (in situations where subjects were place in nursing homes, or if the respondent was a distant relative, etc.). Exact dates of deaths were obtained from the Ministère de la Santé et des Service Sociaux (MSSS) for all but six of the individuals.

Missing information with regards to both vital status and date of death or censoring were handled in the following way. For deceased subjects for whom exact dates were not obtainable, the median of the 6 month time interval during which the subject died were used as the date of death. This information was available from contact with proxies of the subjects. For subjects who either refused or withdrew, the date of refusal was taken as the date of censoring, since they were alive at the time of refusal or withdrawal. Lastly, for subjects who could not be reached, the date of the most recent participation or refusal/withdrawal was taken as their date of censoring, since that date is the most recent known information about vital status.

Assessment of Other Variables

The Blessed Orientation-Memory-Concentration Test (Katzman et al. 1983)[80]. The BOMC is a 6-item scale for the detection of cognitive impairment with a maximum error score of 28 (weighted) and a score greater than 10 indicating an impairment. It can easily be administered by a non-physician and has been shown to be able to discriminate between mild, moderate and severe cognitive deficits. This instrument was administered to assess for the subject's ability to provide consent for participation in the study.

Mini Mental Status Examination – ALFI (Folstein et al. 1975)[16]: The MMSE is a quantitative test that systematically evaluates cognitive function (spatio-temporal orientation, memory, concentration and attention). Inter-rater reliability is 0.83 and test-retest reliability is 0.89. The MMSE is sensitive for detecting moderate to severe cognitive deficits[81,82] but is recognized as not being able to distinguish delirium from dementia. Normative data to correct for the effect of age and level of education have been published[83]. The MMSE is short and easy to administer, and has also been translated into French[84]. The telephone version used in the ALFI (Adult Lifestyle and Function Interview; Fischbach, 1990)[85] study is a 14-item version of the MMSE with a maximum correct response score being 22 and a score of less than 17 indicating cognitive impairment. It has been tested by Roccaforte et al. (1992)[86] and the results are shown to be comparable to the original version of the MMSE. For the purposes of this study, the MMSE-ALFI was used to evaluate cognitive status and change at two weeks after discharge as well as at the 6, 12 and 18-month follow-up time points. Two items were the same as those appearing in the BOMC scale and therefore were not repeated (year and month). The serial 7s were used instead of spelling 'WORLD' backwards because of the lack of a satisfactory French equivalent for 'WORLD'.

The Informant Questionnaire on Cognitive Decline in the Elderly (Jorm et al. 1991)[74]
The IQCODE is a questionnaire that is administered to a close friend or family to evaluate the existence of change in course over the preceding 10 years, or a shorter time period, in principal cognitive functions and certain measure of activities of daily living[87]. The IQCODE was developed as a test to detect dementia. The validity of the IQCODE was evaluated in different contexts; the results have shown a high correlation with measures of actual cognitive function , a satisfactory concordance with the evaluation by a clinician on severity of dementia, and a global performance comparable to the MMSE as a test for the detection of dementia[88]. A French version of the IQCODE was established and validated by Law and Wolfson (1995)[87]. The short 16-item version of the IQCODE[89], with a performance demonstrated to be highly similar to the original version (26-item) of the instrument, was employed and administered to a proxy in this study for the detection of the existence of change in cognitive status. This shorter version was

chosen as a time saving measure considering the emergency room interview setting and medical condition of the subjects. For the purposes of this study, the initial administration of this instrument referred to the previous 10 years, while at the follow-up time points, the time frame to which the proxies were to refer was from the time of initial administration to the time of that follow-up.

The Older Americans Resources and Services (Duke University 1978)[90]: The OARS is a multidimensional functional assessment questionnaire designed to assess the overall functional status and service use of adults, particularly of the elderly. It consists of two parts, the individual functioning assessment and the services assessment. The former part includes five sections: social resources, economic resources, mental health, physical health, and activities of daily living[91]. This study used the Activities of Daily Living (Basic and Instrumental) section of the OARS questionnaire to measure physical function and change in functional abilities. Each item was dichotomized into dependent and independent, and the number of items on which subjects were dependent was used for the analysis in this study.

Sociodemographic– General sociodemographic information collected include age, sex, first language, marital status, education, having children, number of children, work, living alone, eyesight problems, and hearing problems, as well as general health (having a fever or visited the doctor in the month preceding the interview, surgery in the preceding 6 months), medications and alcohol consumption.

Medications/Chart Review – Each subject enrolled, or his/her proxy, was asked to provide written consent to release information on their prescribed medications back to one year prior to the interview. This information was to be obtained by using their Medicare number, a unique identifier issued by the Health Insurance Board (Régie de l'assurance maladie du Québec), a government agency, to all residents of the province of Quebec. A review of medical charts (68 at the MGH, 256 at the JGH) was also carried out for the cases as well as the controls from which a subset of information were examined in this research project. These include triage code, discharge diagnosis,

admission, service, and medications taken regularly (as noted in the emergency department notes and/or admission notes). This review was conducted by three medical archivists at the JGH and two medical archivists at the MGH.

Data Collection

Subjects were interviewed within 6 hours of their arrival in the emergency department in order to decrease the risk of including incident cases of delirium. Subjects were initially assessed for the presence of delirium using a short subject questionnaire which included questions about chronic disease, sociodemographics, two cognitive scales (BOMC, MMSE), and the Confusion Assessment Method (CAM). If the subjects were too ill to complete the questionnaire, attempts were made to administer the cognitive scales and the CAM of the subject questionnaire.

If subjects presented with at least one of the main symptoms of delirium, (i.e. inattention, disorganized thinking, or altered level of consciousness), a proxy (family member, caregiver) was sought to complete a short 'proxy' questionnaire, which included a proxy version of the CAM. The diagnosis of delirium was based on both the interviewer assessment and information obtained from the proxy. If the subject was not delirious but scored greater than 10 on the BOMC, or less than 17 on the MMSE-ALFI scale, then he or she was judged to be cognitively impaired. If the subject was neither delirious nor cognitively impaired, he or she was classified as normal. Once case-control status was established, proxies for all cases were sought and administered the long version of the questionnaire. Proxies for approximately one third of cognitively impaired control subjects were sought and administered the short version of the questionnaire.

The duration of the interview varied greatly as can be expected when interviewing in an emergency department setting but was generally approximately 20 minutes for a short subject questionnaire.

A case-control study was carried out within the enrolled subjects. The control subjects consisted of both those who were judged to be normal and those who were not delirious but were found to be cognitively impaired. As mentioned previously, impairment was defined as scoring greater than 10 on the BOMC or less than 17 on the

MMSE-ALFI. In assembling a control group, approximately one third of the cognitively impaired subjects and one fifteenth of the normal subjects were randomly selected in order to obtain an equal number of normal and cognitively impaired subjects. This 1:1 ratio was chosen because approximately 50% of individuals with delirium also have dementia, and we chose to control for dementia at the design rather than at the analysis level. A proxy was sought for each of the control subjects and administered the long proxy questionnaire. The long proxy questionnaire was also administered for a relatively small number (56) of normal subjects mostly for validation purposes. That is, the proxy questionnaire was a means for evaluating the comparability of responses to questions that were asked in both the subject and proxy questionnaires.

For the follow up study, data were collected at four time points –at admission, 2 weeks, 6 months, 12 months and 18 months post-admission. Baseline information was collected for all 1268 subjects initially enrolled in the study, but follow-up data were collected only for a subset (n=268) of this sample, as indicated earlier. The follow up information was collected by telephone. Both subjects and proxies were interviewed at all time points, and the same proxy was sought as much as possible throughout the study.

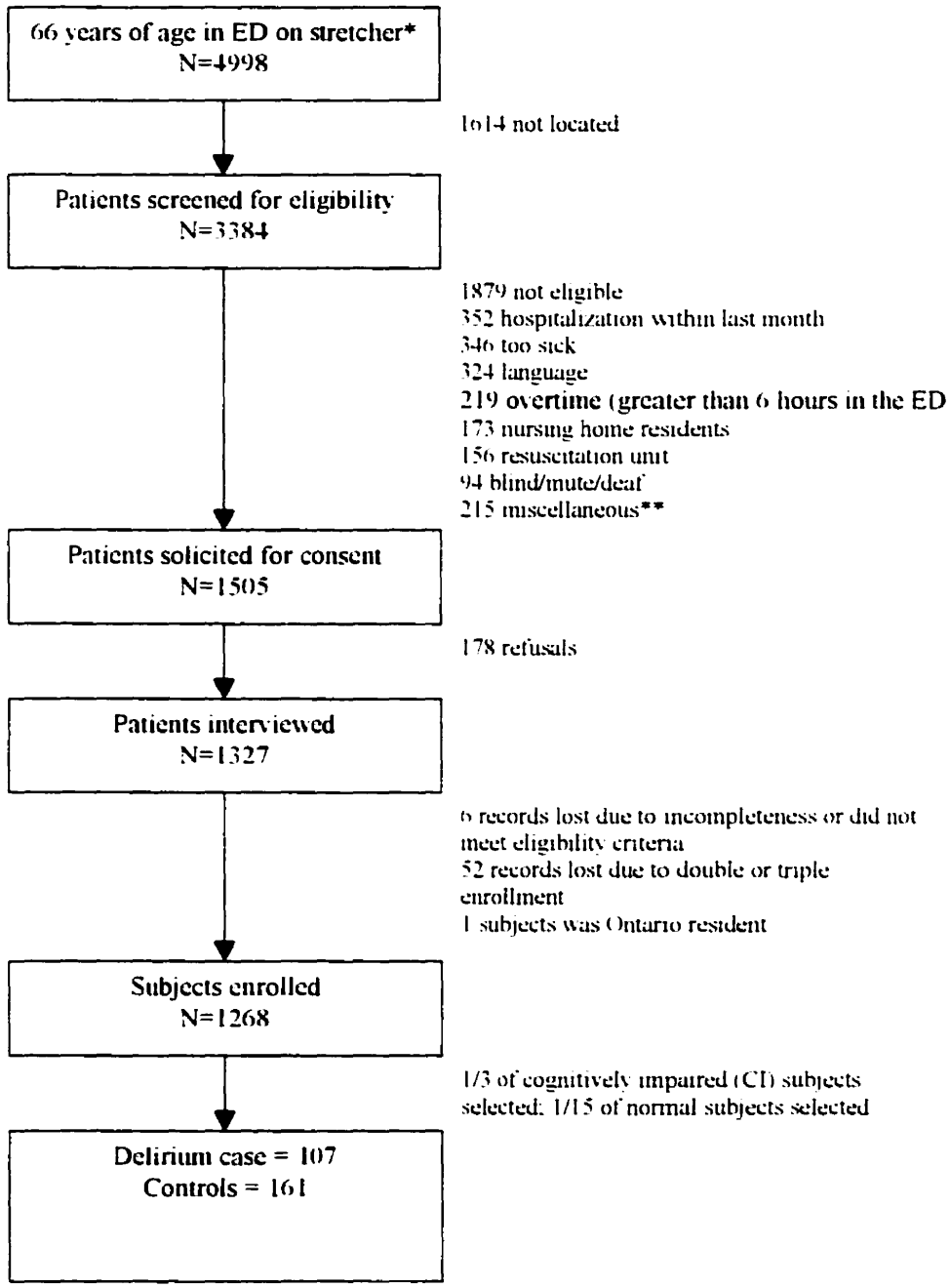
For the follow-up questionnaires, Table 6 shows the information collected at each time point. At 2 weeks, the MMSE-ALFI was administered to the subjects and the OARS, IQCODE, CAM and questions on frequency of contact with the subject, living location, and visits to doctors, were administered to the proxy. At 6, 12 and 18 months post-discharge, the MMSE, OARS, and questions on living arrangements and visits to doctors were administered to both subjects and proxies were administered. The purpose of the repeated measures was to assess physical and cognitive status at each time point as well as any change that may have occurred during the course of the follow up. This component of the follow up study was not addressed in this thesis research.

Table 6. Information collected from subjects and proxies at each time point

	Time of data collection		
	Baseline	2 wk	6, 12, & 18 mth
Sociodemographics	S/P		
BOMC	S		
MMSE-ALFI	S	S	S
CAM	S	P	
IQCODE	P	P	P
ADL/IADL (OARS)	S/P	P	S/P
Chronic Diseases	S/P		
General Health	S/P		
Health Problems (premorbid 2 wks)	S		
Living arrangements		P	S/P
Freq. of visits to GP, specialist, ED, hospitalization		P	S/P
How frequently proxy has seen/spoken to subject		P	P
Chart Data	X		

* Source of information: S = Subject, P= Proxy

Figure 1. Flowchart of subject recruitment



* or equivalent level of severity of illness

**including: 56 with MD or nurse, 43 not on stretcher, 38 not a Quebec resident, 27 previously enrolled, 17 sleeping/gone to X-ray, 10 in isolation unit, 9 unable to interview, 8 not registered on hospital computer, 4 deceased, 3 violent

ANALYSIS

The time until death was calculated as the number of days from the date of interview until date of death. Specific variables suspected of confounding or effect modification and hence examined include information on sociodemographic characteristics, comorbidity, number of medication, chronic diseases, discharge diagnosis, general health, premorbid health problems, physical functional status (ADL/IADL - OARS), living arrangements, cognitive functional status (IQCODE) and chart review information.

All data management and analyses were carried out with the SPSS statistical software version 10.1 for Windows 97.

Bivariate Analyses

Bivariate and stratified analyses, as well as examination of survival and log-minus-log curves were carried out to identify potential confounding and effect modifying variables. Pearson χ^2 tests were carried out for categorical variables and student's t-test for continuous variables. Additionally, variables suspected of confounding or effect modification based on past literature were tested in the multivariate analyses irrespective of results of the above-mentioned analyses.

Based on published works indicating associations of particular variables with both delirium and death, an a priori decision was made to enter specific factors into the Cox proportional hazards model irrespective of their bivariate association with delirium and with death in our sample. These include delirium status, age, sex, Basic ADL, Instrumental ADL, mean IQCODE score, comorbidity and number of medication.

Bivariate analyses were carried out to assess the associations of the available data with delirium and with death status. Variables having statistically significant associations with both delirium and death were identified as confounding variables and were therefore selected for inclusion in the multivariate modelling process.

Stratified bivariate analyses were also carried out to identify potential effect modifiers. Continuous variables were categorized to allow stratification. Associations between delirium and death status were examined for each category (stratum) of all of the

variables being examined for the analysis. All variables revealing a difference of greater than 10% between strata in the log of the odds ratios were selected for testing their interaction with delirium in the multivariate analysis.

Kaplan-Meier or product-limit method[92] was used to obtain the overall distribution of time to death as well as specific distribution over time for delirious cases and non-delirious controls. It was also used to obtain the distribution of death over time for levels of the variables. Survival and log minus log curves were plotted and examined for each variable to test the proportional hazards assumption, confounding and effect modification. To compare the time-to-death distributions, the log-rank statistic and significance were computed to test the equivalence of incidence curves.

Linearity of continuous variables were examined in two ways. Firstly, the continuous variables were transformed into categorical variables. Two Cox proportional hazards models were run, one including the categorical variable as dummy variables and the other including the continuous variable. Secondly, the continuous variables were transformed into its square, cubed, etc. (X, X^2, X^3, X^4) and again, various models were run, the first including the original continuous variable, the second including the squared variable, the third including the cubed variable, and the like. In each method, the −2 log likelihood statistics were compared. Lack of a significant difference in the −2 log likelihood statistics was taken as indicative of a linear association. All continuous variables included in this study were found to have linear effects on hazard.

Model Selection

The Cox proportional hazards model was employed to carry out the multivariate analysis because of its ability to determine the independent effect of numerous variables on time to death while adjusting for all other variables in the model. The Cox proportional hazards model was also employed because of its ability to handle censored data. There is no reason to suspect lack of independence between individual observations in this particular setting. The proportional hazards assumptions were tested by plotting and examining the parallelism of survival and log-log curves. All variables included in the analysis met the proportional hazards assumption.

Several variables were chosen as determinants of death irrespective of results from the bivariate and stratified analyses. These are delirium status, sex, age, physical function (ADL/IADL – OARS), cognitive status (IQCODE), number of comorbid conditions, and number of medication.

Crude and delirium-adjusted associations were computed to examine the predictability of variables with time to death. Interaction terms were examined in groups in the multivariate analyses. For example, all potential sociodemographic effect modifiers were tested together as a group, as were all chronic problems and all discharge diagnoses. Model performance were compared by examining the –2 log likelihood statistics and parameter estimates of delirium and effect modifying variables of models before and after including the interaction terms. Groups that showed a significant change were examined in further detail by testing the effect modifiers one at a time. If the change was not significant, then the group of effect modifiers were removed from the model.

Thus all variables significantly associated with both delirium and death, as well as significant interaction terms based on stratified analyses were selected for inclusion in the modelling process. The initial multivariable models included all potential confounders and effect modifiers. Variables were subsequently removed based on its lack of statistical significance, lack of change in the variables remaining in the model, and its overall impact on model performance which was determined by the change in –2 log likelihood statistic with and without the variable of interest. The degree of significant change was determined by the Likelihood Ratio Test, which is χ^2 test indicating the statistical significance of the difference in the –2 log likelihood statistics.

STUDY POWER

The following formula[93] was employed to compute the power of the study.

$$Z_{\beta} = \frac{\text{sqrt}(D) * (\text{lambda}(I)-\text{lambda}(C))}{\text{Phi}(\text{lambda}(I)) - \text{Phi}(\text{lambda}(C))} - Z_{\alpha}$$

where $D = 2 / ((1/d_{+A}) + (1/d_{+C}))$, and d_{+A} and d_{+C} are the number of subjects in each group

lambda(I) = -ln(0.5)/T(I), where T(I) is the median survival in the cases

lambda(C) = -ln(0.5)/T(C), where T(C) is the median survival in the controls

$\text{phi}(x) = x^2/(1-\exp(-xT))$

The analysis included 107 cases and 161 controls with the incidence of death being 40.2% and 26.1% over 18 months respectively. Although the actual median survival times could not be computed, evaluation of the data allowed estimation as 19 months and 24 months for cases and controls respectively. Given these numbers, the power of this study is 79.6% for death at 18-month follow-up

Friedman et al. also indicated that lambda can be estimated by taking the inverse of the mean survival time. The mean survival time for cases and controls were 16.38 and 19.70 months respectively. With this approach, the power is estimated to be 59.4% for death at 18-month follow-up.

CHAPTER 4. RESULTS

BASIC CHARACTERISTICS

Of the 1505 subjects eligible for inclusion in the case-control study, 1327 (88.2%) agreed to participate and were interviewed. Further examination identified 6 subjects with incomplete data, 52 subjects with double or triple enrolment, and one subject was an Ontario resident. A total of 1268 subjects were enrolled in the case-control study, of which a subset (n=268) were selected for the current research.

The average follow-up period was 13.4 months overall (SD=7.30), with the delirium cases having a shorter follow-up time than controls (11.9 months (SD=8.07) vs. 14.4 months (SD=6.57), p=0.005). Twenty subjects, 10 cases and 10 controls, were lost to follow-up during the 18 months. At 2 weeks post-discharge (PD), three cases and one control refused to participate. At 6 months PD, two controls and two cases withdrew and one case could not be reached. At 12 months PD, four controls and three cases withdrew, and at 18 months PD, two controls and one case withdrew. For the purposes of this study however, these subjects remained in the analysis because baseline information was available and outcome status could be determined. That is, the fact that subjects were alive to refuse or withdraw provided information about vital status, and date of censoring (last known vital status) was taken as the date of refusal or withdrawal.

Of the original 1268 subjects enrolled in the case-control study, 107 (8.4%) subjects were suffering from delirium when they arrived at the emergency department. The study sample for this research study consisted of these 107 delirious cases and 161 (60.1%) non-delirious control subjects. The overall mean age was 80.66 years, ranging from 66 to 103, and women comprised 59.70% of the study sample. The subjects were predominantly English speakers (219 vs. 49). Only 5% of the subjects were never married, with the remaining 95% being equally distributed between those who were married or common-law, and those who were either separated, divorced or widowed. Approximately 30% of subjects lived alone, the remaining 70% living with either their spouse, children, or friends. Forty-two subjects (15.7%) did not have any children, while among those who did, the subjects had an average of 2.6 children, ranging from one to eleven. A total of 86 deaths occurred during the study period.

ASSOCIATIONS WITH DELIRIUM

Occurrence of Delirium by socioeconomic characteristics

Table 7 provides the delirium status according to sociodemographic factors. Among the delirious cases, there were 63 (58.9%) women and 44 (41.1%) men, and among the non-delirious controls, there were 97 (60.3%) and women 64 (39.7%) men. The mean age was 80.3 years among the cases and 80.9 years among the controls. The subjects were predominantly English speakers among both cases and controls (84% and 80% respectively). Slightly fewer subjects with delirium lived alone compared to non-delirious subjects (24% vs. 33%, p=0.105) Delirious subjects had an average of 2.07 children, ranging from one to 11, while control subjects had an average of 2.24 children, ranging from one to 10. These differences however, were not statistically significant. Examination of alcohol consumption behaviour showed no significant differences in whether or not subjects drink, frequency of drinking, or change in drinking habits.

Delirious cases were less likely to be working than non-delirious controls (8.4% vs. 16.8%, p=0.049, OR=0.456, CI: 0.205-1.012). By the end of the 18-month follow-up, 43 (40.2%) cases and 43 (26.7%) controls had died (p=0.021, OR= 1.8544, CI: 1.095-3.104).

Occurrence of Delirium by functional status at baseline

Table 8 provides delirium status according to cognitive and physical functional status. Cases were slightly more cognitively impaired according to their mean IQCODE score than controls (3.84 vs. 3.59, p=0.006). With respect to physical function, delirious subjects were more dependent than non-delirious subjects but these differences did not reach conventional levels of statistical significance.

Occurrence of Delirium by general health at baseline

Table 9 provides delirium status according to general health factors. A dichotomized triage code (potentially life-threatening vs. not life-threatening) also revealed that delirious subjects were less likely to have had a potentially life-threatening

illness (25% vs. 42.36%, p=0.005, OR=0.454, CI: 0.259-0.794) than non-delirious controls. Two possible explanations for this finding appear likely. Perhaps patients who are identified as having life-threatening conditions receive different (more intensive) care, which may be preventive or reversing of delirium, such that by the time they were interviewed for this study, their cognitive status was in the normal range. The other possibility is that the diseases recognized as potential risk factors for delirium are the non-life-threatening illnesses. Supported for this view is given by the known risk factors for delirium such as urinary tract infections, which are not labelled as life-threatening by the triage nurses. Delirious subjects were also more likely to have started taking a new medication (43.75% vs. 31.58%, p=0.059, OR=1.685, CI: 0.978-2.904) as well as stopped taking a medication (40.86% vs. 15.49%, p<0.001, OR=3.769, CI: 2.039-6.967) compared to control subjects in the month preceding the baseline interview. Finally, though of marginal significance, delirious subjects were more likely to have visited a doctor in the month preceding the interview compared to control subjects (76.0% vs. 67.79%, p=0.161, OR=1.505, CI: 0.848-2.670).

There were however, no associations found for delirium with having a fever in the two weeks preceding the baseline interview, vision or hearing problems. We also failed to find any association for delirium with other treatment factors, such as the number of medications, having started, or changed any medications.

Occurrence of Delirium by chronic problems at baseline

Table 10 provides delirium status according to chronic problems. None of the chronic problems, including the number of chronic problems (comorbidity), were found to be associated with delirium.

Occurrence of Delirium by discharge diagnoses

Table 11 provides delirium status according to discharge diagnoses. Among the various discharge diagnoses, statistically significant differences in the occurrence of delirium were found with delirium, dysrythmia and respiratory illnesses. Because of its high correlation with the case-control status however, delirium as a discharge diagnosis

was excluded from the multivariate analysis. In both dysrythmia and respiratory illnesses, the direction of association was opposite to that expected. None of the subjects with delirium had had either dysrythmia or respiratory illnesses, whereas 12 and 6 control subjects had had dysrythmia (p=0.004) and respiratory illnesses (p=0.042) respectively.

Table 7. Delirium status by Socioeconomic Characteristics

	Case (n=107)		Control (n=161)		P-value	OR	95% CI
	N	%	N	%			
Age (yr)	80.30 (66-99)	SD=6.48	80.90 (66-103)	SD=7.57	0.501		
Sex							
Women	63	58.88	97	60.25	0.823	1.0	
Men	44	41.12	64	39.75		1.059	(0.643-1.742)
Language							
English	90	84.11	129	80.12	0.408	0.761	(0.399-1.454)
French	17	15.89	32	19.88		1.0	
Education (yr)	9.18 (0-20)	SD=4.52	8.78 (0-23)	SD=4.06	0.488		
Work							
Yes	9	8.41	27	16.77	0.049	0.456	(0.205-1.012)
No	98	91.59	134	83.23		1.0	
Marital Status							
Single	6	5.61	8	4.97	0.473	1.0	
Married/Common-law	54	50.47	70	43.48	0.961	1.029	(0.337-3.141)
Divorced, Separated or Widowed	47	43.93	83	51.55	0.622	0.755	(0.247-2.308)
Having Children							
yes	88	82.24	138	85.71	0.444	0.772	(0.397-1.499)
no	19	17.76	23	14.29		1.0	
# children	2.07		2.24		0.431		
Living alone							
yes	26	24.30	54	33.54	0.105	0.636	(0.367-1.102)
no	81	75.70	107	66.46		1.0	
Alcohol consumption							
Yes	31	31.63	59	39.86	0.189	0.698	(0.408-1.195)
No	67	68.37	89	60.14		1.0	

(continued)

Table 7. Delirium status by Socioeconomic Characteristics - continued

	Case (n=107)		Control (n=161)		P-value	OR	95% CI
	N	%	N	%			
Alcohol consumption							
Everyday	7	22.58	10	17.86	0.489	1.257	(0.460-5.075)
4-6 times a week	--	--	4	7.14	0.726	0.0	N/A
2-3 times a week	3	9.8	2	3.57	0.228	3.273	(0.447-22.463)
Once a week	5	16.13	7	12.50	0.520	1.558	(0.403-6.020)
Once / twice a month	5	16.13	9	16.07	0.773	1.212	(0.329-4.472)
< once a month	11	35.48	24	42.86		1.0	---
Change in drinking habit							
Drinking more now	--	--	2	3.51	0.801	0.0	N/A
Drinking less now	3	10.00	2	3.51	0.252	2.944	(0.464-18.693)
No change	27	90.00	53	92.98		1.0	---

Table 8. Delirium status by Functional Characteristics

	Case (n=107)	Control (n=161)	P-value*
Mean IQCODE	3.84	3.59	0.006
BADL score	3.22	2.90	0.249
IADL score	1.92	1.51	0.105
Total ADL	5.12	4.38	0.140

* P-value for difference in means using t-test (2-sample)

Table 9. Delirium status by General Health Factors

	Case (n=107)		Control (n=161)		P-value	OR	95% CI
	N	%	N	%			
# Medication	5.15		4.58		0.165		
Eyesight problems							
yes	21	19.81	24	15.09	0.316	1.390	(0.729-2.650)
no	85	80.19	135	84.91		1.0	
Hearing problems							
yes	18	16.98	20	12.58	0.316	1.422	(0.713-2.836)
no	88	83.02	139	87.42		1.0	
Triage							
Life-threatening	1	1.00	1	0.69	0.532	2.667	(0.123-57.620)
Potentially life-threatening	24	24.00	60	41.67	0.928	1.067	(0.261-4.364)
Non-life-threatening	72	72.00	75	52.08	0.177	2.560	(0.653-10.032)
Stretcher/mobility problem/minor injuries	3	3.00	8	5.56	0.019	1.00	--
Triage dichotomized							
Potentially life-threatening	25	25.00	61	42.36	0.005	0.454	(0.259-0.794)
Not life-threatening	75	75.00	83	57.64		1.0	
Fever recently? (2wk)							
Yes	13	14.44	20	14.18	0.956	1.021	(0.480-2.172)
No	77	85.56	121	85.82		1.0	
Visit to Doctor?							
Yes	76	76.00	101	67.79	0.161	1.505	(0.848-2.670)
No	24	24.00	48	32.21		1.0	
New medication							
Yes	42	43.75	42	31.58	0.059	1.685	(0.978-2.904)
No	54	56.25	91	68.42		1.0	

(Continued)

Table 9. Delirium status by General Health Factors - continued

	Case (n=107)		Control (n=161)		P-value	OR	95% CI
	N	%	N	%			
Change in medication	19	20.88	19	15.32	0.291	1.458	(0.722-2.946)
Yes	72	79.12	105	84.68		1.0	
No							
Non-prescription medication							
Yes	26	28.00	39	28.26	0.960	0.985	(0.549-1.768)
No	67	72.00	99	71.74		1.0	
Stop medication							
Yes	38	40.86	22	15.49	0.000	3.769	(2.039-6.967)
No	55	59.14	120	84.51		1.0	

Table 10. Delirium status by Chronic Problems

	Case (n=107)		Control (n=161)		P-value	OR	95% CI
	N	%	N	%			
Morbidity*							
yes	106	99.07	159	98.76			
no	1	0.93	2	1.24	0.815	1.333	(0.119-14.890)
Comorbidity**	6.05		5.91		0.668		
Chronic problems							
Heart and/or Circulation problems	51	49.51	94	60.26	0.088	0.647	(0.392-1.069)
High blood pressure	44	41.12	66	40.99	0.863	1.045	(0.636-1.715)
Stroke or effects of stroke	20	18.69	28	17.39	0.786	1.092	(0.579-2.059)
Migraines	14	13.08	20	12.42	0.873	1.061	(0.511-2.205)
Arthritis/Rheumatism/Osteoporosis	56	52.34	97	60.25	0.200	0.724	(0.442-1.187)
Allergies	25	23.36	41	25.47	0.696	0.892	(0.504-1.580)
Colds	13	12.15	19	11.80	0.931	1.034	(0.487-2.193)
Eye trouble	56	52.34	76	47.20	0.411	1.228	(0.753-2.004)
Ear trouble	45	42.06	76	47.20	0.407	0.812	(0.496-1.329)
Chest problems	24	22.43	43	26.71	0.428	0.793	(0.447-1.407)
Stomach or digestive troubles	12	11.21	28	17.39	0.132	0.574	(0.278-1.189)
Kidney or urinary problems	40	37.38	61	37.89	0.933	0.979	(0.591-1.621)
Skin problems	21	19.63	36	22.36	0.592	0.848	(0.463-1.551)
Trouble with nerves	48	44.86	69	42.86	0.746	1.085	(0.663-1.775)
Fatigue/Lack of energy	55	51.40	88	54.66	0.601	0.877	(0.538-1.432)
Sleep problems	62	57.94	76	47.20	0.085	1.541	(0.941-2.523)
All fractures	11	10.28	21	13.04	0.494	0.764	(0.352-1.657)
Parkinson's	16	14.95	17	10.56	0.284	1.489	(0.717-3.095)
Infections	10	9.35	9	5.59	0.241	1.741	(0.683-4.439)
Cancer	20	18.69	20	12.42	0.158	1.621	(0.825-3.183)
Diabetes/thyroid problems	32	29.91	38	23.60	0.250	1.381	(0.796-2.396)
Other	22	20.56	23	14.29	0.178	1.553	(0.816-2.957)

* Morbidity – having at least one chronic condition
** Comorbidity – Number of chronic conditions

Table 11. Delirium status by Discharge Diagnoses

	Case (n=101)*		Control (n=152)		P-value	OR	95% CI
	N	%	N	%			
GI infections	1	0.99	2	1.32	0.808	0.743	(0.066-8.298)
Cancer	8	7.92	10	6.58	0.700	1.209	(0.460-3.174)
Endocrine/Metabolic	9	8.91	11	7.24	0.645	1.240	(0.495-3.110)
Anemia	0	0.00	2	1.32	0.245	--	N/A
Dementia	7	6.93	4	2.63	0.104	2.726	(0.777-9.565)
Delirium**	20	19.80	3	1.97	0.000	12.114	(3.495-41.989)
Psychiatric/ Neurologic	5	4.95	6	3.95	0.714	1.254	(0.372-4.224)
Hypertensive/ Ischaemic	4	3.96	11	7.24	0.272	0.523	(0.162-1.691)
Cardiologic illnesses NOS/Veins	2	1.98	4	2.63	0.730	0.740	(0.133-4.117)
Dysrythmia	0	0.00	12	7.89	0.004	0.579	(0.520-0.644)
Congestive Heart failure	1	0.99	7	4.61	0.105	0.205	(0.025-1.693)
Cerebrovascular	10	9.90	12	7.89	0.596	1.268	(0.526-3.026)
Respiratory not otherwise specified	0	0.00	6	3.95	0.042	--	N/A
Pneumonia	6	5.94	3	1.97	0.099	3.104	(0.758-12.707)
Gastro-hepatic	5	4.95	11	7.24	0.453	0.661	(0.223-1.962)
Nephro-urologic NOS	3	2.97	3	1.97	0.619	1.505	(0.298-7.608)
Urinary Tract Infection	3	2.97	3	1.97	0.619	1.505	(0.298-7.608)
Dermatological	0	0.00	3	1.97	0.153	--	N/A
Rheumatological	5	4.95	5	3.29	0.517	1.515	(0.427-5.374)
Syncope	1	0.99	5	3.29	0.235	0.291	(0.034-2.529)
Dizziness	2	1.98	6	3.95	0.374	0.487	(0.096-2.460)
Symptoms not otherwise specified	4	3.96	3	1.97	0.354	2.027	(0.444-9.255)
Pain	2	1.98	8	5.26	0.185	0.360	(0.075-1.731)
Fracture/Trauma	2	1.98	10	6.58	0.089	0.284	(0.061-1.324)
Intoxication	2	1.98	1	0.66	0.346	3.020	(0.270-33.750)

* Numbers differ due to missing data

** Delirium reported on medical chart as the diagnosis at discharge

ASSOCIATIONS WITH DEATH

Occurrence of Death by Socioeconomic characteristics

Table 12 shows the occurrence of death according to discharge diagnoses. Men were more likely to have died than women (48.84% vs. 36.26%, p=0.050, OR=1.678, CI: 0.998-2.821). No differences were found with age, language, education, working status, marital status, having children, living alone, or alcohol consumption habits.

Occurrence of Death by functional characteristics at baseline

The occurrence of death according to functional characteristics are shown in Table 13. Subjects who died were more physically disabled than those that survived in Basic activities of daily living (BADL), Instrumental ADL, and total ADL. Subjects who died were dependent on a mean of 3.4 Basic ADL items compared to a dependence on 2.8 items (p=0.037), and subjects who died were dependent on 2.32 Instrumental ADL items compared to 4.36 items in subjects who survived (p<0.001). When Basic and Instrumental ADL items were combined, subjects who died were dependent on 5.72 items compared to 4.16 items in subjects who survived (p=0.002). As for cognitive status, measured by the IQCODE, no difference was found between survivors and non-survivors.

Occurrence of Death by general health factors

Table 14 provides the occurrence of death according to general health factors. Subjects who died were found to have been more likely to report eyesight problems compared to survivors (24.7% vs. 13.3%, p=0.021, OR=2.133, CI: 1.109-4.102). Subjects who died were less likely to have visited a doctor in the month preceding the interview than survivors (20.51% vs. 32.75%, p=0.048, OR=1.887, CI: 0.999-3.563). With respect to medications, non-survivors were more likely to have started a new medication (77.14% vs. 84.83%, p=0.038, OR=1.812, CI: 1.030-3.187), less likely to have stopped taking a medication (65.33% vs. 78.52%, p=0.028, OR=1.966, CI: 1.071-3.621), and had been taking a greater number of medications (5.71 vs. 4.38, p=0.002).

Occurrence of Death by chronic problems

Table 15 shows the occurrence of death according to chronic problems. Subjects who died had a greater number of comorbid conditions compared to those who survived (6.50 vs. 5.71. p=0.019). Among the chronic problems, ear trouble, chest problems, fatigue or lack of energy, and cancer were all associated with death at a statistically significant level. Specifically, subjects who died were more likely to have had ear trouble compared to controls (54.65% vs. 40.66, p=0.032, OR=1.759, CI: 1.048-2.951), to have had chest problems (33.72% vs. 20.88%, p=0.023, OR=1.928, CI: 1.088, 3.147), to have suffered from fatigue or lack or energy (67.44% vs. 46.70%, p=0.001, OR=2.364, CI: 1.382-4.044), and to have had cancer (30.23% vs. 7.69%, p<0.001, OR=5.200, CI: 2.548-10.613). Diabetes or thyroid problems were found to have a marginal association with death as well (33.72% vs. 22.53%, p=0.051, OR=1.750, CI. 0.996-3.083).

Occurrence of Death by discharge diagnoses

Table 16 shows the occurrence of death according to discharge diagnoses. Cancer, dysrythmia and pain were statistically significantly associated with death. Subjects with cancer were more likely to have died compared to those without cancer (18.75% vs. 1.73%, p<0.001, OR=12.879, CI: 3.610-45.940). An unexpected direction of association was found with pain and dysrythmia however, in that subjects with pain were less likely to have died (0% vs. 5.78%, p=0.027), as were subjects with dysrythmia (0% vs.6.94%, p=0.015).

Table 12. Death status by Socioeconomic Characteristics

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
Delirium							
Yes	43	50.0	64	35.16	0.021	1.844	(1.095-3.104)
No	43	50.0	118	64.84			
Age	81.43 (68-103)	SD=7.53	80.30 (66-99)	SD=6.94	0.226		
Sex							
Women	44	51.16	116	63.74	0.050	1.0	
Men	42	48.84	66	36.26		1.678	(0.998-2.821)
Language							
English	65	75.58	154	85.56	0.074	1.0	
French	21	24.42	28	15.56		1.777	(0.941-3.356)
Education (yr)	9.10 (0-23)	SD=4.59	8.85 (0-22)	SD=4.08	0.677		
Work							
Yes	10	11.63	26	14.29	0.551	0.789	(0.362-1.721)
No	76	88.37	156	85.71		1.0	
Marital Status							
Single	4	4.65	10	5.56	0.959	1.00	---
Married/Common-law	40	46.51	84	46.67	0.779	1.190	(0.352-4.029)
Divorced, Separated or Widowed	42	48.84	88	48.89	0.776	1.193	(0.354-4.027)
Having Children							
yes	76	88.37	150	82.42	0.211	1.621	(0.757-3.473)
no	10	11.63	32	17.58			
Living alone							
yes	25	29.07	55	30.22	0.848	0.946	(0.539-1.661)
no	61	70.93	127	69.78		1.0	

(continued)

Table 12. Death status by Socioeconomic Characteristics - continued

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
Alcohol consumption							
Yes	24	30.77	66	39.29	0.197	0.687	(0.388-1.217)
No	54	69.23	102	60.71		1.0	
Alcohol consumption							
Everyday	4	16.67	13	20.63	0.433	0.590	(0.158-2.208)
4-6 times a week	1	4.17	3	4.76	0.711	0.639	(0.060-6.823)
2-3 times a week	--	--	5	7.94	0.780	0.0	N/A
Once a week	3	12.50	9	14.29	0.553	0.639	(0.145-2.810)
Once / twice a month	4	16.67	10	15.87	0.700	0.767	(0.198-2.967)
< once a month	12	50.00	23	36.51		1.0	---
Change in drinking habit							
Drinking more now	2	8.00	--	--	0.753	∞	N/A
Drinking less now	1	4.00	4	6.45	0.716	659	(0.070-6.226)
No change	22	88.00	58	93.54		1.0	--

Table 13. Death status by Functional Characteristics

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
Mean IQCODE	3.7543		3.6640		0.345		
OARS							
No problems	9	10.59	31	18.45	0.019	1.00	---
Mild problems	25	29.41	53	31.55	0.280	1.625	(0.673-3.923)
Moderate problems	8	9.41	26	15.48	0.916	1.060	(0.358-3.139)
Severe problems	9	10.59	21	12.50	0.479	1.476	(0.503-4.335)
Total problems	34	40.00	37	22.02	0.010	3.165	(1.318-7.601)
BADL score	3.43		2.83		0.037		
IADL score	2.32		1.36		0.000		
Total ADL	5.72		4.16		0.002		

Table 14. Death status by General Health Factors

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
# Medication	5.71		4.38		0.002		
Eyesight problems							
Yes	21	24.71	24	13.33	0.021	2.133	(1.109-4.102)
No	64	75.29	156	86.67		1.0	
Hearing problems							
Yes	11	12.94	27	15.00	0.655	0.842	(0.396-1.790)
No	74	87.06	153	85.00		1.0	
Triage dichotomized							
Potentially life-threatening	27	34.62	59	35.54	0.888	0.960	(0.546-4.688)
Not life-threatening	51	65.38	107	64.46		1.0	
Fever recently? (2wk)	14	19.44	19	11.95	0.132	1.779	(0.836-3.785)
Yes	58	80.56	140	88.05		1.0	
No							
Visit doctor recently							
Yes	62	79.49	115	67.25	0.048	1.887	(0.999-3.563)
No	16	20.51	56	32.75		1.0	
New medication							
Yes	35	46.05	49	32.03	0.038	1.812	(1.030-3.187)
No	41	53.95	104	67.97		1.0	
Change in medication							
Yes	16	22.86	22	15.17	0.166	1.657	(0.807-3.400)
No	54	77.14	123	84.83		1.0	
Non-prescription drugs							
Yes	18	23.68	47	30.32	0.292	0.713	(0.380-1.339)
No	58	76.32	108	69.68		1.0	
Stop medication							
Yes	26	34.67	34	21.25	0.028	1.966	(1.071-3.612)
No	49	65.33	126	78.75		1.0	

Table 15. Death status by Chronic Problems at baseline

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
Morbidity*							
yes	84	97.67	181	99.45	0.197	0.232	(0.021-2.595)
no	2	2.33	1	0.55		1.0	
Comorbidity**	6.50		5.71		0.016		
Chronic problems							
Heart and/or Circulation problems	52	60.47	93	51.10	0.184	1.433	(0.842-2.437)
High blood pressure	37	43.02	74	40.66	0.714	1.102	(0.656-1.852)
Stroke or effects of stroke	12	13.95	36	19.78	0.246	0.658	(0.323-1.339)
Migraines	8	9.30	26	14.29	0.253	0.615	(0.266-1.422)
Arthritis/Rheumatism/Osteoporosis	45	52.33	108	59.34	0.279	0.752	(0.449-1.260)
Allergies	20	23.26	46	25.27	0.720	0.896	(0.491-1.635)
Colds	12	13.95	20	10.99	0.485	1.314	(0.610-2.828)
Eye trouble	40	46.51	92	50.55	0.537	0.851	(0.509-1.422)
Ear trouble	47	54.65	74	40.66	0.032	1.759	(1.048-2.951)
Chest problems	29	33.72	38	20.88	0.023	1.928	(1.088-3.147)
Stomach or digestive troubles	14	16.28	26	14.29	0.650	1.178	(0.580-2.395)
Kidney or urinary problems	34	39.53	67	36.81	0.668	1.122	(0.662-1.901)
Skin problems	19	22.09	38	20.88	0.821	1.075	(0.577-2.002)
Trouble with nerves	36	41.86	81	44.51	0.684	0.898	(0.534-1.508)
Fatigue/Lack of energy	58	67.44	85	46.70	0.001	2.364	(1.382-4.044)
Sleep problems	50	58.14	88	48.35	0.134	1.484	(0.884-2.490)
All fractures	11	12.79	21	11.54	0.764	1.124	(0.516-2.451)
Parkinson's	8	9.30	25	13.74	0.302	0.644	(0.278-1.494)
Infections	6	6.98	13	7.14	0.961	0.975	(0.358-2.659)
Cancer	26	30.23	14	7.69	< 0.001	5.200	(2.548-10.613)
Diabetes/thyroid problems	29	33.72	41	22.53	0.051	1.750	(0.996-3.083)
Other	18	20.93	27	14.84	0.213	1.520	(0.785-2.943)

* Morbidity – having at least one chronic condition
** Comorbidity – Number of chronic conditions

Table 16. Death status by Discharge Diagnoses

	Died (n=86)		Censored (n=182)		P-value	OR	95% CI
	N	%	N	%			
Discharge Diagnosis							
GI infections	0	0.00	3	1.73	0.233	0.0	N/A
Cancer	15	18.75	3	1.73	<0.001	12.879	(3.610-45.940)
Endocrine/Metabolic	7	8.75	13	7.51	0.756	1.164	(0.446-3.038)
Anemia	1	1.25	1	0.58	0.581	2.150	(0.133-34.811)
Dementia	2	2.50	9	5.20	0.319	0.461	(0.097-2.186)
Delirium	10	12.50	13	7.51	0.211	1.733	(0.726-4.140)
Psychiatric/ Neurologic	1	1.25	10	5.78	0.097	0.204	(0.026-1.619)
Hypertensive/ Ischaemic	4	5.00	11	6.36	0.655	0.765	(0.236-2.480)
Cardiologic illnesses NOS/Veins	2	2.50	4	2.31	0.939	1.070	(0.192-5.963)
Dysrythmia	0	0.00	12	6.94	0.015	0.0	N/A
Congestive Heart failure	3	3.75	5	2.89	0.729	1.292	(0.301-5.544)
Cerebrovascular	5	6.25	17	9.83	0.335	0.604	(0.215-1.698)
Respiratory not otherwise specified	1	1.25	5	2.89	0.418	0.420	(0.048-3.655)
Pneumonia	5	6.25	4	2.31	0.121	2.780	(0.726-10.641)
Gastro-hepatic	5	6.25	11	6.36	0.955	0.969	(0.325-2.887)
Nephro-urologic NOS	3	3.75	3	1.73	0.335	2.179	(0.430-11.042)
Urinary Tract Infection	3	3.75	3	1.73	0.335	2.179	(0.430-11.042)
Dermatological	1	1.25	2	1.16	0.957	1.069	(0.096-11.960)
Rheumatological	3	3.75	7	4.05	0.896	0.912	(0.230-3.622)
Syncope	1	1.25	5	2.89	0.418	0.420	(0.048-3.655)
Dizziness	1	1.25	7	4.05	0.232	0.296	(0.036-2.450)
Symptoms not otherwise specified	4	5.00	3	1.73	0.143	2.944	(0.643-13.472)
Pain	0	0.00	10	5.78	0.027	0.0	N/A
Fracture/Trauma	3	3.75	9	5.20	0.600	0.701	(0.185-2.661)
Intoxication	1	1.25	2	1.16	0.957	1.069	(0.096-11.960)

STRATIFIED ASSOCIATION OF DELIRIUM WITH DEATH

A difference of more than 10% in the log of odds ratios for the association between delirium and death across strata was taken as being indicative of potential interactions. The stratified analyses revealed numerous potential effect modifiers. Among sociodemographic variables, language, marital status, having children, living alone, working, alcohol consumption, frequency of alcohol consumption, and having changed drinking habits showed associations between delirium and death to indicate potential effect modification.

Among functional characteristics, cognitive status (dichotomized IQCODE) was found to be a potential effect modifier. We assessed cognitive status using two different cut-off points because the author of the IQCODE[74] indicated a range within which the cut-off should fall rather than a specific number. Rather than taking a mid-point of the range, we thought it best to examine the variable at both extremes of the range. Consequently, both methods showed that cognitive status may be an effect modifier.

Regarding general health factors, eyesight problems, hearing problems, triage, having started new medications, having changed medications or doses of medications, having taken non-prescription substances, and having stopped taking medication showed different stratified associations between delirium and death.

With regards to chronic problems, heart or circulation problems, stroke or effects of stroke, migraines, arthritis/rheumatism/osteoporosis, allergies, eye trouble, ear trouble, chest problems, stomach or digestive troubles, kidney or urinary problems, skin problems, trouble with nerves, fatigue or lack of energy, sleep problems, all fractures, Parkinson's disease, cancer, and diabetes showed a difference of greater than 10% in the log of odds ratios of delirium for death.

Among discharge diagnoses, potential effect modifiers were cancer, endocrine or metabolic disorders, dementia, hypertensive or ischaemic illnesses, unspecified cardiologic illnesses or veins, cerebrovascular disorders, pneumonia, gastro-hepatic illnesses, Unspecified Nephro-urologic, urinary tract infections, rheumatological disorders, symptoms not otherwise specified, and fractures or trauma.

KAPLAN-MEIER & PROPORTIONAL HAZARDS ASSUMPTIONS

Kaplan-Meier survival and log-minus-log curves were examined for all variable to test the proportional hazards assumption, confounding, and effect modification. The crude survival and log-minus-log curves are shown in Figure 2. Consistent with previous evidence, survival is worse in subjects with delirium than those without. All potential explanatory variables were found to have met the proportional hazards assumption.

Table 17 provides the cumulative mortality rates in 6-month intervals. Delirious subjects showed higher hazard rates at 6 and 18months compared to non-delirious subjects, though slightly lower at 12 months (p=0.007). French speakers were also found to have higher hazard rates at 6 months relative to English speakers (p=0.031). All other socioeconomic characteristics showed similar hazard rates between categories. A marginal difference was also found between men and women (p=0.076).

For functional status, survival distributions were found to be different between the different levels of dependence (p=0.046). Among general health factors, subjects having sight problems, having started a new medication and subjects having stopped taking a medication showed higher mortality rates compared to those not having them (p=0.023, p=0.044, p=0.031, respectively). Having had a fever recently initially showed a higher hazard rate, although this did not persist (p=0.101).

With regards to chronic problems, subjects having had ear problems, chest problems, fatigue or lack of energy and cancer, all consistently showed higher mortality rates over the 18-month interval compared to those not having these conditions (p=0.032, p=0.020, p=0.002, p<0.001, respectively).

Among discharge diagnoses, subjects with psychological or neurological disorders were found to have lower mortality rates compared to those not having these conditions (p=0.083). All subjects with dysrythmia, pain and urinary tract infection survived the 18-month follow up. Subjects with cancer, on the other hand, showed greater mortality rates at 6 and 18 months (p<0.001). Patients with pneumonia also showed a greater mortality rate initially, but this excess rate did not remain at 12 and 18 months post-discharge (p=0.055).

Figure 2. Crude survival and log-minus-log curves for cases and controls

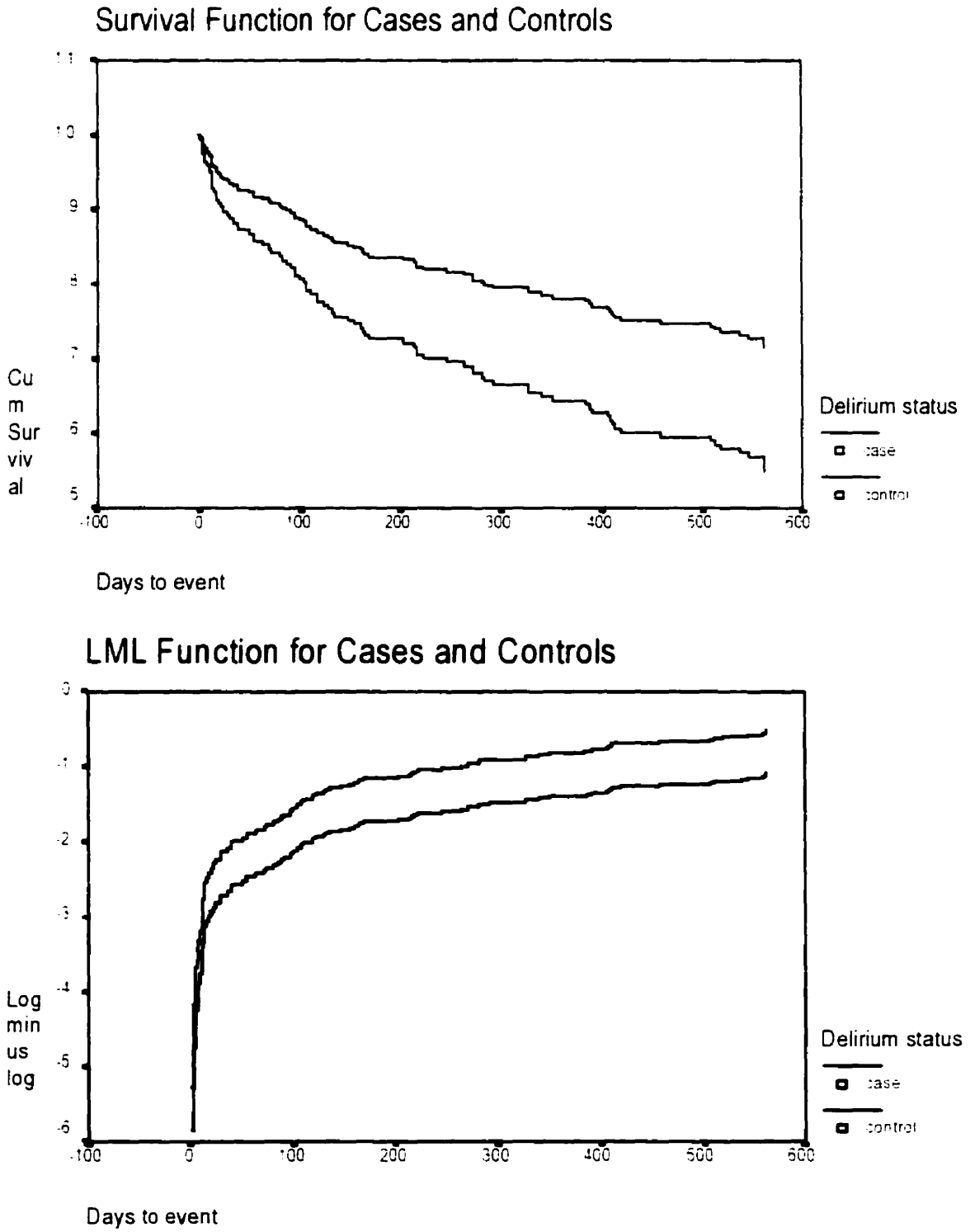


Table 17. Cumulative mortality rates

Variable	6 mth hazard rate	(SE)	12 mth hazard rate	(SE)	18 mth hazard rate	(SE)	P†
Socioeconomic characteristics							
Delirium							
Yes	0.0177	(0.0067)	0.0122	(0.0061)	0.0550	(0.0094)	
No	0.0119	(0.0040)	0.0138	(0.0046)	0.0033	(0.0033)	0.0067
Language							
English	0.0124	(0.0036)	0.0132	(0.0040)	0.0078	(0.0045)	
French	0.0219	(0.0109)	0.0133	(0.0094)	0.0000	(0.0000)	0.0312
Sex							
Women	0.0113	(0.0040)	0.0081	(0.0036)	0.0068	(0.0048)	
Men	0.0180	(0.0064)	0.0219	(0.0077)	0.0062	(0.0062)	0.0761
Functional status							
ADL problems							
None	0.0108	(0.0076)	0.0060	(0.0060)	0.0000	(0.0000)	
Mild	0.0112	(0.0056)	0.0160	(0.0072)	0.0071	(0.0071)	
Moderate	0.0065	(0.0065)	0.0152	(0.0107)	0.0000	(0.0000)	
Severe	0.0317	(0.1580)	0.0000	(0.0000)	0.0000	(0.0000)	
Total	0.0194	(0.0087)	0.0249	(0.0111)	0.0222	(0.0157)	0.0461
General Health							
Sight Problems							
No	0.0123	(0.0035)	0.0106	(0.0035)	0.0076	(0.0044)	
Yes	0.0238	(0.0019)	0.0310	(0.0154)	0.0000	(0.0000)	0.0320
New medication							
No	0.0108	(0.0041)	0.0110	(0.0045)	0.0122	(0.0070)	
Yes	0.0278	(0.0092)	0.0148	(0.0074)	0.0000	(0.0000)	0.0872
Stop medication							
No	0.0113	(0.0038)	0.0149	(0.0047)	0.0065	(0.0046)	
Yes	0.0315	(0.0119)	0.0053	(0.0053)	0.0108	(0.0107)	0.1176
Fever							
No	0.0124	(0.0037)	0.0160	(0.0046)	0.0058	(0.0041)	
Yes	0.0310	(0.0154)	0.0095	(0.0095)	0.0000	(0.0000)	0.1014

(continued)

† Logrank test for equality of survival distribution

Table 17. Cumulative mortality rates - continued

	6 mth hazard rate	(SE)	12 mth hazard rate	(SE)	18 mth hazard rate	(SE)	P†
Chronic Problems							
Ear							
No	0.0093	(0.0038)	0.0105	(0.0043)	0.0037	(0.0037)	
Yes	0.0198	(0.0063)	0.0170	(0.0064)	0.0108	(0.0076)	0.0318
Chest							
No	0.0114	(0.0036)	0.0093	(0.0035)	0.0084	(0.0049)	
Yes	0.0217	(0.0089)	0.0267	(0.0109)	0.0000	(0.0000)	0.0199
Fatigue/Lack of energy							
No	0.0105	(0.0043)	0.0079	(0.0040)	0.0042	(0.0042)	
Yes	0.0173	(0.0055)	0.0189	(0.0063)	0.0091	(0.0065)	0.0022
Cancer							
No	0.0125	(0.0035)	0.0113	(0.0036)	0.0048	(0.0034)	
Yes	0.0263	(0.0151)	0.0323	(0.0185)	0.0238	(0.0237)	< 0.001
Discharge Diagnoses							
Psychological/ Neurological							
No	0.0154	(0.0038)	0.0136	(0.0390)	0.0074	(0.0042)	
Yes	0.0000	(0.0000)	0.0196	(0.0196)	0.0000	(0.0000)	0.0828
Dysrythmia							
No	0.0155	(0.0039)	0.0151	(0.0042)	0.0076	(0.0044)	
Yes	0.0000	(0.0000)	0.0000	(0.0000)	0.0000	(0.0000)	N/A
Pain							
No	0.0153	(0.0038)	0.0147	(0.0041)	0.0073	(0.0042)	
Yes	0.0000	(0.0000)	0.0000	(0.0000)	0.0000	(0.0000)	N/A
Urinary tract infections							
No	0.0147	(0.0037)	0.0140	(0.0039)	0.0070	(0.0040)	
Yes	0.0000	(0.0000)	0.0000	(0.0000)	0.0000	(0.0000)	N/A
Cancer							
No	0.0130	(0.0035)	0.0142	(0.0039)	0.0047	(0.0033)	
Yes	0.0741	(0.0511)	0.0000	(0.0000)	0.1111	(0.1048)	< 0.001
Pneumonia							
No	0.0140	(0.0036)	0.0143	(0.0040)	0.0072	(0.0042)	
Yes	0.0370	(0.0368)	0.0000	(0.0000)	0.0000	(0.0000)	0.0545

† Logrank test for equality of survival distribution

COX PROPORTIONAL HAZARDS MODELLING RESULTS

After assessing bivariate associations of the explanatory variables with both delirium and death status, and ensuring that the proportional hazards assumption is met by all variables of interest, Cox proportional hazard models were carried out for time to death. Tests for linearity was carried out for all of the continuous variables and all were found to meet the linearity assumption. Before modelling a multivariate model however, crude and delirium-adjusted Cox models were carried out to examine the association of variables with time to death. All of the results of crude and delirium-adjusted Cox modelling were consistent with the bivariate analyses carried out with death status.

Crude and Delirium-adjusted Cox Models by Socioeconomic Characteristics

Table 18 provides the crude and delirium-adjusted associations between various socioeconomic characteristics and time to death. Subjects with delirium showed an increased rate of mortality compared to non-delirious controls (HR=1.781, CI: 1.116-2.718, p=0.008). Advanced age was shown to have a slight elevation in the hazard rate (HR=1.020, CI: 0.990-1.051; HR_{adj}=1.023, CI: 0.992-1.055). Men had a higher mortality rate in both crude (HR=1.473, CI: 0.965-2.249) and delirium-adjusted (HR_{adj}=1.483, CI: 0.971-2.264) models. French speakers also showed higher mortality rates in both models, with the association becoming stronger once adjusted for delirium (HR_{adj}=1.754, CI: 1.066-2.885).

Crude and Delirium-adjusted Cox Models by Functional Characteristics

Table 19 provides the crude and delirium-adjusted associations between physical and cognitive function and time to death. A statistically significant association was found between death and increased dependence in basic ADL in both the crude and delirium-adjusted models (HR=1.118, CI: 1.012-1.235; HR_{adj}=1.105, CI: 0.99-1.221). Similarly, increased dependence in instrumental ADL was statistically associated with increased mortality rate in both models (HR=1.191, CI: 1.085-1.308; HR_{adj}=1.171, CI: 1.067-1.286). The association between cognitive status and time to death, on the other hand, was not statistically significant.

Crude and Delirium-adjusted Cox Models by General Health Factors

Table 20 provides the crude and delirium-adjusted associations between various general health factors and time to death. Subjects with eyesight problems were found to have a higher hazard rate at both the crude and delirium-adjusted level (HR=1.809, CI: 1.104-2.964; HR_{adj}=1.707, CI: 1.047-2.818). Having visited the doctor in the preceding month also elevated the hazard rates in both models (HR=1.750, CI: 1.009-3.003; HR_{adj}=1.635, CI:0.941-2.842). Having been prescribed a new medication was increased the hazard rate at the crude level but this association disappeared once adjusted for delirium (HR=1.577, CI: 1.004-2.477; HR_{adj}=1.492, CI: 0.947-2.350). The same result was found with having stopped taking a medication (HR=1.718, CI: 1.068-2.766; HR_{adj}=1.486, CI:0.902-2.448). A statistically significant association was also found with the number of medication the subjects were taking, with increasing numbers increasing the hazard rate (HR=1.097,CI: 1.033-1.165; HR_{adj}=1.094, CI: 1.029-1.163).

Crude and Delirium-adjusted Cox Models by Chronic Problems

Table 21 shows the crude and delirium-adjusted associations between various chronic problems and time to death. Hazard rates were found to be statistically significantly higher among subjects with ear trouble (HR=1.522, CI: 0.995-2.328; HR_{adj}=1.601, CI: 1.045-2.452), chest trouble(HR=1.610, CI: 1.029-2.518; HR_{adj}=1.696, CI: 1.082-2.657), fatigue or lack of energy (HR=1.945, CI: 1.238-3.054; HR_{adj}=2.002, CI: 1.274-3.146) cancer (HR=3.249, CI: 2.047-5.155; HR_{adj}=3.149, CI: 1.982-5.004) in diabetes/thyroid problems (HR=1.451, CI: 0.928-2.369; HR_{adj}=1.411, CI: 0.902-2.208) both the crude and delirium-adjusted models.

Crude and Delirium-adjusted Cox Models by Discharge Diagnosis

Table 22 provides the crude and delirium-adjusted associations between various discharge diagnoses and time to death. Cancer and pneumonia both showed a statistically significant association with time to death in both models. Cancer patients showed a much greater hazard rates than non-cancer patients (HR=6.380, CI: 3.608-11.281; HR_{adj}=6.470,

CI: 3.645-11.488). Patients with pneumonia also had a increased hazard rate compared to patients without pneumonia (HR=2.536, CI: 1.025-6.227; HR_{adj}=2.358, CI: 0.925-5.842). Cox models for gastrointestinal infections, dysrythmia, and pain could not be computed due to the lack of deaths in delirium cases. Consequently, these variables will not be tested in the multivariate model.

Table 18. Crude and Delirium-adjusted Cox Models by Socioeconomic Characteristics

	Crude Cox Model			Delirium adjusted Cox Model		
	HR	95% CI	p-value	HR	95% CI	p-value
Delirium	1.781	(1.166-2.718)	0.008	---	---	---
Age (yr)	1.020	(0.990-1.051)	0.195	1.023	(0.992-1.055)	0.149
Sex (men=1)	1.473	(0.965-2.249)	0.072	1.483	(0.971-2.264)	0.068
Language (French=1)	1.594	(0.974-2.609)	0.063	1.754	(1.066-2.885)	0.027
Education (yr)	1.018	(0.962-1.078)	0.529	1.021	(0.966-1.080)	0.458
Work – yes	0.741	(0.383-1.432)	0.372	0.821	(0.422-1.596)	0.561
Marital Status						
Single	1.000			1.000		
Married/Common-law	1.112	(0.398-3.108)	0.840	1.100	(0.393-3.074)	0.856
Divorced, Separated or Widowed	1.140	(0.409-3.179)	0.803	1.187	(0.425-3.313)	0.743
Having Children	1.486	(0.768-2.874)	0.239	1.583	(0.818-3.067)	0.173
Living alone	0.878	(0.554-1.398)	0.583	0.923	(0.579-1.473)	0.738
Alcohol consumption	0.706	(0.437-1.142)	0.706	0.726	(0.448-0.175)	0.192
Alcohol consumption						
Everyday	1.000			1.000		
4-6 times a week	0.940	(0.105-8.417)	0.956	1.252	(0.132-11.836)	0.845
2-3 times a week	0.000	---	0.983	0.000	---	0.983
Once a week	1.096	(0.245-4.898)	0.905	1.151	(0.257-5.157)	0.854
Once / twice a month	1.395	(0.348-5.585)	0.639	1.499	(0.372-6.034)	0.569
< once a month	1.511	(0.487-4.688)	0.475	1.705	(0.541-5.379)	0.362
Change in drinking habit						
Drinking more now	1.000			1.000		
Drinking less now	0.185	(0.017-2.053)	0.169	0.113	(0.009-1.363)	0.086
No change	0.292	(0.068-1.249)	0.097	0.224	(0.050-1.004)	0.051

Table 19. Crude and Delirium-adjusted Cox Models by Functional characteristics

	Crude Cox Model			Delirium adjusted Cox Model		
	HR	95% CI	p-value	HR	95% CI	p-value
IQCODE	1.189	(0.883-1.600)	0.254	1.096	(0.808-1.486)	0.558
Basic ADL	1.118	(1.012-1.235)	0.028	1.105	(0.999-1.221)	0.051
Instrumental ADL	1.191	(1.085-1.308)	0.000	1.171	(1.067-1.286)	0.001

Table 20. Crude and Delirium-adjusted Cox Models by General Health Factors

	Crude Cox Model			Delirium adjusted Cox Model		
	HR	95% CI	p-value	HR	95% CI	p-value
Eyesight problems	1.809	1.104-2.964)	0.019	1.717	(1.047-2.818)	0.032
Hearing problems	0.818	(0.434-1.541)	0.534	0.784	(0.416-1.478)	0.452
Triage						
Life-threatening	3.927	(0.356–43.350)	0.264	3.901	(0.353–43.113)	0.267
Potentially life-threatening	1.986	(0.471-8.369)	0.350	1.964	(0.466-8.276)	0.358
Non-life-threatening	2.177	(0.529-8.956)	0.281	1.904	(0.430-7.860)	0.375
Stretcher/mobility problem/minor injuries	1.000			1.000		
Triage: life-threatening	0.972	(0.610-1.551)	0.906	1.096	(0.679-1.767)	0.708
Fever recently	1.601	(0.893-2.871)	0.114	1.621	(0.904-2.907)	0.105
Visit to Doctor	1.750	(1.009-3.003)	0.046	1.635	(0.941-2.842)	0.081
New medication	1.577	(1.004-2.477)	0.048	1.492	(0.947-2.350)	0.085
Change in medication	1.446	(0.827-2.527)	0.196	1.448	(0.828-2.531)	0.194
Non-prescription medication	0.728	(0.429-1.236)	0.240	0.745	(0.439-1.266)	0.277
Stop in medication	1.718	(1.068-2.766)	0.026	1.486	(0.902-2.448)	0.120
Number of medications	1.097	(1.033-1.165)	0.003	1.094	(1.029-1.163)	0.004

Table 21. Crude and Delirium-adjusted Cox Models by Chronic Problems

	Crude Cox Model			Delirium-adjusted Cox model		
	HR	95% CI	p-value	HR	95% CI	p-value
Heart and/or Circulation problems	1.282	(0.825-1.991)	0.270	1.352	(0.869-2.105)	0.181
High blood pressure	1.149	(0.750-1.761)	0.524	1.164	(0.759-1.784)	0.487
Stroke/effects of stroke	0.697	(0.379-1.284)	0.247	0.690	(0.375-1.270)	0.233
Migraines	0.614	(0.396-1.271)	0.189	0.599	(0.289-1.240)	0.168
Arthritis/Rheumatism/ Osteoporosis	0.705	(0.462-1.077)	0.106	0.712	(0.466-1.088)	0.116
Allergies	0.918	(0.557-1.514)	0.738	0.950	(0.576-1.568)	0.841
Colds	1.241	(0.674-2.284)	0.489	1.268	(0.689-2.334)	0.446
Eye trouble	0.867	(0.538-1.325)	0.509	0.848	(0.555-1.296)	0.447
Ear trouble	1.522	(0.995-2.328)	0.053	1.601	(1.045-2.452)	0.031
Chest problems	1.610	1.029-2.518)	0.037	1.696	(1.082-2.657)	0.021
Stomach / digestive troubles	1.162	(0.656-2.069)	0.603	1.316	(0.735-2.357)	0.355
Kidney/urinary problems	1.081	(0.701-1.666)	0.724	1.084	(0.704-1.671)	0.714
Skin problems	1.049	(0.603-1.747)	0.853	1.087	(0.653-1.811)	0.749
Trouble with nerves	0.911	(0.594-1.399)	0.671	0.894	(0.582-1.373)	0.609
Fatigue/Lack of energy	1.945	(1.238-3.054)	0.004	2.002	(1.274-3.146)	0.003
Sleep problems	1.316	(0.858-2.020)	0.209	1.238	(0.804-1.906)	0.332
All fractures	1.112	(0.590-2.095)	0.742	1.139	(0.604-2.146)	0.687
Parkinson's	0.673	(0.625-1.393)	0.285	0.615	(0.296-1.277)	0.193
Infections	0.916	(0.400-2.101)	0.837	0.860	(0.375-1.975)	0.723
Cancer	3.249	(2.047-5.155)	< 0.001	3.149	(1.982-5.004)	< 0.001
Diabetes/thyroid problems	1.451	(0.928-2.269)	0.103	1.411	(0.902-2.208)	0.131

Table 22. Crude and Delirium-adjusted Cox Models by Discharge Diagnoses

	Crude Cox Model			Delirium-adjusted Cox Model		
	HR	95% CI	p-value	HR	95% CI	p-value
GI infections	did not	converge				
Cancer	6.380	(3.608-11.281)	< 0.001	6.470	(3.645-11.488)	< 0.001
Endocrine/Metabolic	1.138	(0.524-2.471)	0.744	1.076	(0.495-2.338)	0.854
Anemia	1.644	(0.229-11.822)	0.622	2.151	(0.295-15.669)	0.450
Dementia	0.613	(0.151-2.494)	0.494	0.512	(0.133-2.212)	0.394
Delirium	1.353	(0.698-2.624)	0.370	0.974	(0.484-1.962)	0.941
Psychiatric/ Neurologic	0.221	(0.031-1.588)	0.133	0.202	(0.028-1.456)	0.113
Hypertensive/Ischaemic	0.764	(0.279-2.088)	0.599	0.865	(0.315-2.375)	0.778
Cardiologic illnesses NOS/Veins	1.327	(0.326-5.406)	0.693	1.602	(0.390-6.581)	0.514
Dysrythmia	did not	converge				
Congestive Heart failure	1.304	(0.411-4.131)	0.652	1.691	(0.523-5.465)	0.380
Cerebrovascular	0.629	(0.254-1.554)	0.315	0.603	(0.244-1.493)	0.274
Respiratory NOS	0.441	(0.061-3.168)	0.416	0.570	(0.078-4.146)	0.578
Pneumonia	2.536	(1.025-6.271)	0.044	2.358	(0.952-5.842)	0.064
Gastro-hepatic	0.901	(0.364-2.227)	0.821	0.907	(0.367-2.244)	0.833
Nephro-urologic NOS	1.599	(0.505-5.066)	0.425	1.585	(0.500-5.022)	0.434
Urinary Tract Infection	2.507	(0.788-7.980)	0.120	2.449	(0.769-7.804)	0.130
Dermatological	1.011	(0.141-7.269)	0.991	1.318	(0.181-9.596)	0.785
Rheumatological	0.804	(0.254-2.548)	0.711	0.745	(0.235-2.365)	0.618
Syncope	0.456	(0.063-3.280)	0.436	0.508	(0.071-3.666)	0.502
Dizziness	0.341	(0.048-2.454)	0.286	0.378	(0.052-2.719)	0.378
Symptoms NOS	2.110	(0.771-5.774)	0.146	1.830	(0.665-5.033)	0.242
Pain	did not	converge				
Fracture/Trauma	0.749	(0.236-2.372)	0.623	0.873	(0.274-2.785)	0.819
Intoxication	0.883	(0.123-6.345)	0.901	0.750	(0.104-5.406)	0.775

* NOS = Not otherwise specified

MULTIVARIATE COX PROPORTIONAL HAZARD MODEL

The results of the Cox proportional hazards modelling revealed that survival differed according to the language of interview. Specifically, subjects interviewed in French showed a slightly higher mortality rate compared to those interviewed in English. As shown in Table 23, the interaction term has a large impact on the model, specifically on the delirium parameter estimate. Inclusion of the language interaction term resulted in a change in the hazard ratio of the main variable of interest, delirium, which changed from significantly increasing the hazard rate ratio (HR=1.865, CI: 1.116-3.117) to having a non-statistically significant effect (HR=1.141, CI: 0.620-2.099) when adjusted for age, sex, language, mean IQCODE score, Basic ADL, Instrumental ADL, number of comorbid conditions, number of medications, sight, hearing and education. Thus when restricted to English-speaking subjects, as is the case when the interaction term is included in the model, the magnitude of the impact of having delirium on time to death is smaller than when including all subjects in the analysis.

Most of the explanatory variables other than delirium however, remained relatively stable between the two models. For example, cognitive status was not significantly predictive of time to death in either model, nor was age, number of comorbid conditions, and level of education. The number of medications taken (Model 1 HR=1.109, CI: 1.022-1.203; Model 2 HR=1.082, CI: 1.003-1.168) and sight problems (Model 1, HR=1.955, CI: 1.049-3.643; Model 2 HR=2.099, CI: 1.088-3.710) both remained statistically significantly in increasing the hazards ratio. For physical function, the Basic ADL remained insignificant in both models, but Instrumental ADL was significant in the model adjusted for the interaction of delirium and language. Sex and language were also significant once adjusted for the interaction. Unexpectedly, subjects with hearing problems appeared to have a lower hazard of death compared to subjects without hearing problems (Model 1, HR=0.445, CI: 0.176-1.124; Model 2 HR=0.499, CI: 0.202-1.234). Because of the strong impact of the language interaction term on the model, the model was stratified by language.

Table 23. Cox proportional hazards models for all subjects

	Model 1. Adjusted for interaction				Model 2. Not adjusted for interaction			
Variable	**β**	**p-value**	**HR**	**95% CI**	**β**	**p-value**	**HR**	**95% CI**
Delirium	0.132	0.671	1.141	(0.620, 2.099)	0.623	0.017	1.865	(1.116, 3.117)
Sex	0.504	0.053	1.656	(0.994, 2.758)	0.590	0.024	1.803	(1.081, 3.007)
Age	0.027	0.179	1.028	(0.988, 1.070)	0.022	0.251	1.023	(0.984, 1.063)
Language	-0.452	0.415	0.636	(0.214, 1.889)	0.702	0.020	2.018	(1.119, 3.641)
IQCODE	-0.156	0.588	0.855	(0.486, 1.505)	-0.135	0.630	0.873	(0.503, 1.515)
Basic ADL	-0.048	0.690	0.953	(0.751, 1.208)	-0.089	0.455	0.915	(0.725, 1.155)
Instrumental ADL	0.134	0.140	1.143	(0.957, 1.365)	0.182	0.045	1.199	(1.004, 1.433)
Comorbidity	0.004	0.953	1.004	(0.890, 1.131)	0.017	0.776	1.017	(0.903, 1.146)
Number of medication	0.104	0.013	1.109	(1.022, 1.203)	0.079	0.043	1.082	(1.003, 1.168)
Delirium*Language	2.047	0.003	7.748	(2.020, 29.712)	---	---	---	---
Sight	0.670	0.035	1.955	(1.049, 3.643)	0.698	0.026	2.009	(1.088, 3.710)
Hearing	-0.810	0.087	0.445	(0.176, 1.124)	-0.695	0.132	0.499	(0.202, 1.234)
Education (yr)	0.015	0.618	1.015	(0.958, 1.075)	0.003	0.931	1.003	(0.946, 1.063)

Final Model for English Speakers

For the English speaking subjects, adjustment for age, sex, IQCODE, Basic ADL, Instrumental ADL, comorbidity, number of medication, education (years), sight problems, and hearing problems revealed a non-significant association between delirium and mortality rate (p=0.710, HR=1.125, CI: 0.605-2.092) as shown in Table 24.

Increasing age showed a marginally statistically significant association with time to death (HR=1.039, CI: 0.994-1.086). Sex, on the other hand, did not show a significant association with time to death when adjusted for all other variables in the model.

Increasing dependence for instrumental ADL had a significantly increased hazard rate (HR=1.27, CI: 1.016-1.589) when adjusted for all other variables in the model. Neither dependence in basic ADL nor cognitive impairment was found to be predictive of death.

Although the number of comorbid conditions was not significantly associated with death rate, increasing number of medications increased the hazard of death significantly (HR=1.136, CI: 1.036-1.247). Having eyesight problems significantly increased the hazard of death (HR=2.32, CI: 1.12-4.806), whereas having hearing problems revealed a protective effect for death (HR=0.212, CI: 0.048-0.945).

Final Model for French Speakers

As shown in Table 24, the French-speaking subjects have a very different pattern of the same model. Adjustment for age, sex, IQCODE, Basic ADL, Instrumental ADL, comorbidity, number of medication, education (years), sight problems, and hearing problems revealed a highly significant association between delirium and death rate (p=0.002, HR=9.231, CI: 2.313-36.829). All other variables in the model were not statistically significant in predicting the mortality rate.

Among the non-significant variables, some showed a change in the direction of effect. For instance, increasing age and higher dependence on instrumental ADL were predictive of increased hazard rate among the English speakers but of decreased hazard rate among the French-speaking subjects. On the other hand, increasing cognitive

problems and number of comorbid conditions were decreasing of hazard in the English speakers but increasing for the French speakers.

The Cox model for this sub-sample indicate that though the final model may be appropriate for the English speakers, a different model might be more fitting for the French speaking subjects. Important to note here is that there were much fewer French speaking subjects in this study relative to the English speakers. Equal number of English and French speakers may show more comparable results than that found here.

Table 24. Cox proportional hazards model for English and French speakers

	English speakers				French speakers			
Variable	**β**	**p-value**	**HR**	**95% CI**	**β**	**p-value**	**HR**	**95% CI**
Delirium	0.118	0.710	1.125	(0.605, 2.092)	2.223	0.002	9.231	(2.313, 36.829)
Sex	0.322	0.296	1.380	(0.755, 2.524)	0.538	0.516	1.713	(0.337, 8.697)
Age	0.038	0.094	1.039	(0.994, 1.086)	-0.018	0.713	0.982	(0.893, 1.080)
IQCODE	-0.350	0.322	0.704	(0.352, 1.410)	0.218	0.656	1.243	(0.477, 3.238)
Basic ADL	-0.090	0.521	0.914	(0.695, 1.202)	-0.007	0.975	0.993	(0.633, 1.558)
Instrumental ADL	0.239	0.036	1.270	(1.016, 1.589)	-0.102	0.573	0.903	(0.634, 1.286)
Comorbidity	-0.020	0.783	0.980	(0.849, 1.131)	0.008	0.957	1.008	(0.745, 1.365)
No. of medications	0.128	0.007	1.136	(1.036, 1.247)	0.016	0.871	1.016	(0.841, 1.227)
Sight	0.842	0.023	2.320	(1.120, 4.806)	0.256	0.778	1.292	(0.218, 7.661)
Hearing	-1.551	0.042	0.212	(0.048, 0.945)	0.355	0.671	1.426	(0.277, 7.343)
Education (yr)	-0.010	0.807	0.991	(0.917, 1.069)	0.116	0.117	1.123	(0.971, 1.299)

CHAPTER 5. DISCUSSION

DETERMINANTS OF MORTALITY RATE

Consistent with many of the previously published work, statistical adjustment for particular explanatory variables such as age, sex, basic and instrumental activities of daily living, cognitive status, comorbidity, number of medications, sight, hearing and education diminished the statistically significant association initially found between the occurrence of delirium and time to death among the English speakers in this sample. The positive association found between age and time to death was consistent with that found in the studies by Levkoff et al. (1988)[19] and O'Keeffe and Lavan (1997)[41]. Similarly, increased dependence in the instrumental ADL being associated with time to death was also found by Inouye et al. (1998)[33]. However, although statistical adjustments were made for comorbidity, defined as the number of chronic problems endured by the subject, based on existing evidence[41,42], we did not find it to be predictive of mortality in this study. No other studies, other than this thesis research, found the number of medication and eyesight problems to have a statistically significant positive association with mortality. Furthermore, the significant protective effect found with hearing problems was surprising as well as contrary to existing evidence[33], which have shown that hearing problems marginally increase the risk for the occurrence of delirium.

In the French speaking subset however, delirium was still significantly associated with time to death despite adjustment for the above-mentioned variables. No other statistically significant predictor was found. It appears evident that a different model is necessary to predict mortality rates among this population.

Although it did not remain in the final model, the protective effect found with dysrythmia was an unexpected finding. One explanation might be that patients diagnosed with dysrythmia receive treatment, which in turn may be protective against death. Similarly, the problem may be that of underdetection. Though the presence of dysrythmia may be in fact associated with increased risk of death, the underdetection may be masking a potential association. Consequently, the lack of detection may also result in subsequently occurring illnesses to be detected and identified as being associated with death - competing risks of death.

Furthermore, statistically significant associations between delirium and death were found among subjects who, in the month preceding the interview, were sick (OR=2.594, CI: 1.362-4.941), visited the doctor (OR=1.905, CI: 1.019-3.562), had a change in their medication (OR=6.429, CI: 1.517-27.244), or were taking non-prescription drugs (OR=3.352, CI: 1.084-10.365). Although none remained in the final model, all of these factors may be markers of overall morbidity.

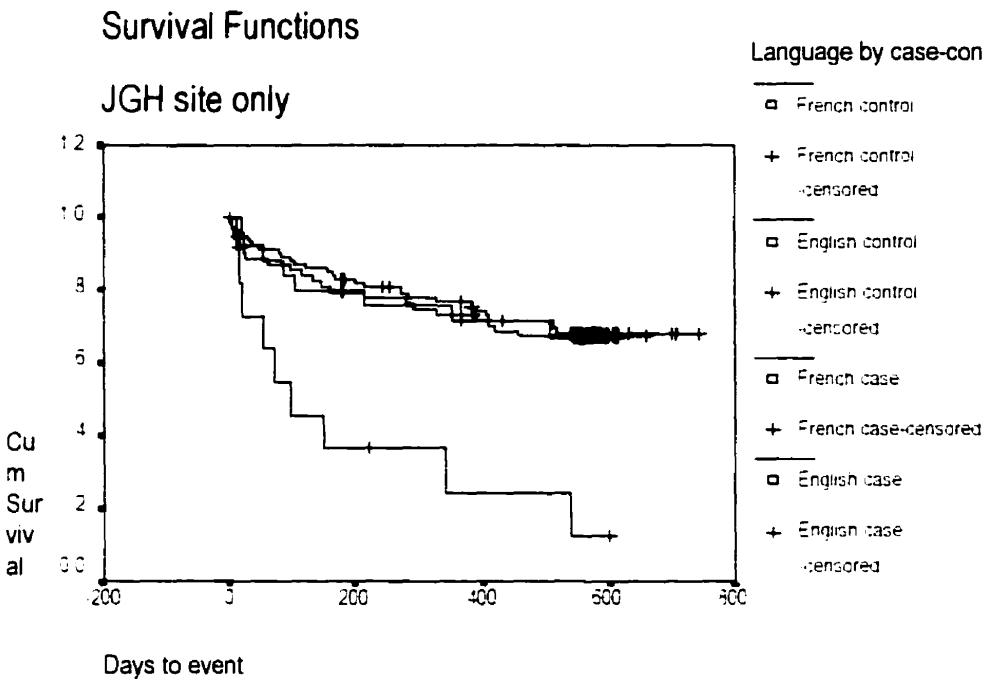
EFFECT MODIFICATION BY LANGUAGE

The analysis revealed a drastic difference in the mortality rates between the English and French speaking subjects. Specifically, the French speakers were found to have a higher mortality rate compared to the English speakers. At the bivariate level, irrespective of statistical significance, there was an evident trend for higher mortality among the French-speaking subjects. The multivariate analyses diminished the statistical significant effect of delirium on time to death in the English speaking population although it remained statistically significant in the French speaking population. Thus among the English speakers, as shown in previous studies prognostic, delirium may be a marker for other factors such as those we adjusted for, which in turn may be predictive of mortality. On the other hand, among the French speaking population, the factors for which we adjusted for do not seem to be the contributing factors for mortality and therefore delirium remained predictive of mortality. Some unmeasured and unknown factors may be playing a role in the excess mortality seen in delirious patients and that statistical adjustment for these factors may diminish the association between delirium and time to death among the French speakers. Potential explanations were therefore sought to explain this finding through further analysis of the data.

Stratification of the data revealed that at the bivariate level, delirium was significantly associated with death for the French speakers (61.9% vs. 14.3%, p=0.001, OR=9.750, CI: 2.430-38.639) but not for the English speakers (43.2% vs. 38.9%, p=0.323, OR=1.343, CI: 0.748-2.411). When the association of delirium with death was further stratified by hospital site, we found that the association between delirium and death among the English speakers at the Jewish General Hospital was distinct from the

rest of the study sample. Specifically, delirium was associated with death in all but the English speakers of the Jewish General Hospital. Exploratory analysis was therefore carried out only on the subjects from the Jewish General Hospital. The survival curves of the French- and English-speaking cases and controls at the Jewish General Hospital (shown in Figure 3) revealed that the French cases have a much higher mortality rate than the rest of the subjects at the Jewish General Hospital.

Figure 3. Survival curves showing the difference in rates of delirium by language of interview



Among the subjects at the Jewish General Hospital, the English speakers were more likely to have children compared to French speakers (86.2% vs. 73.9%, p=0.039, OR=0.455, CI: 0.212-0.975), but among those having children, the English speakers had fewer numbers of children (2.0 vs. 2.7 children, p=0.015). As for marital status, French speakers had a higher proportion of subjects who were single (13% vs. 4%) as well as divorced, separated or widowed subjects (52% vs.49%).

Regarding functional status, the French speakers were significantly more dependent than English speakers (p=0.007). The significant difference appears to stem from the greater dependence in the basic ADL, where English speakers were dependent on an average of 3.15 items while the French speakers were dependent on 3.98 items (p=0.020).

As for chronic problems, English speakers were more likely to have had allergies (p=0.014, OR=0.282, CI: 0.097-0.823), while French speakers were more likely to have had chest problems (p=0.014, OR=2.318, CI: 1.170-4.594). Moreover, among the discharge diagnoses, cancer was found to be more prevalent among the French speakers (p=0.023, OR=3.027, CI: 1.118-8.198).

Several post-discharge information were also compared between English and French speakers at the Jewish General Hospital. No statistically significant associations were found between language and who the proxy or caregiver was, the frequency in which the subjects saw or spoke with the proxy, who they lived with, pattern of use of the emergency department, use of services (i.e. re-hospitalization, institutionalization, etc.), morbidity, comorbidity, physical and cognitive functional change over time, and living location (i.e. institutionalization, respite care, foster home etc.).

In a verbal communication with Dr. Johanne Monette, a geriatrician at the Jewish General Hospital, it was pointed out that whereas all of the English speakers in the vicinity go to the Jewish General Hospital when necessary, among the French speakers in the same vicinity, those in the lower socioeconomic status go to the Jewish General Hospital and those in the higher socioeconomic status tend to go to the Montreal General Hospital. This pattern of hospital use therefore systematically places the French speaking patients of the Jewish General Hospital at a disadvantage with respect to access to care.

financial independence and the like compared to the English speakers at the Jewish General Hospital. This in turn may result in a higher proportion of individuals at risk of the occurrence of both delirium and death.

Thus, exploratory analyses and communication with Dr. Monette revealed that the French speaking subjects at the JGH tend to be more functionally dependent, have poorer social support networks, have a higher prevalence of cancer, are less financially secure, and perhaps have less access to care, which may all put them at greater risk of death.

On the other hand, it may be that the English speaking subjects of the Jewish General Hospital that are distinct from the rest of the sample. In this light then, the English speakers may have different accessibility to care, social support, community support, availability of care providers, or a different lifestyle, including cultural factors, that may be protective against both delirium and death. Examination into religious beliefs or cultural background may also shed light into the difference found in the occurrence of both delirium and mortality among this subset of subjects.

Since none of the above-mentioned possibilities were pre-specified hypotheses and the number of French speaking subjects were small in this sample, further research is necessary for verification. While it is striking, it is possible that it is a Type I error.

STRENGTHS OF THE STUDY

There are several characteristics that are considered to be strengths of this study. Fist of all, when sampling from the case-control study from which the follow-up sample was formed, there was an over-sampling of dementia subjects in the controls as a means to control for dementia at the design level. Existing literature indicated that approximately 50% of elderly individuals with delirium are also afflicted with dementia. Accordingly, efforts were made to ensure that approximately 50% of controls subjects had dementia. In doing so, we were able to isolate delirium from dementia to improve our ability to obtain a true association between delirium and mortality.

Secondly, the use of proxies allowed for a better response rate than using subjects alone. Especially for delirium subjects who may or may not have been able to complete the baseline interview because of their delirious state or answer particular questions because of their impaired memory or attention, the use of proxy information rendered

itself to be an alternative source of information. As such, answers to items on the interviews in which we believed the proxy to be more reliable, information from the proxy was used. Subsequent examination of the data showed that, consistent with our expectations, information regarding chronic problems, general health factors, and many of the socioeconomic information was more complete and reliable in the proxies than subjects. Having an alternative source of information therefore allowed us to increase accuracy and precision by having the data more valid and reducing losses to follow up and the number of missing values for each of the items in the interviews.

On a related note, losses to follow up were extremely low in this thesis research. Of the 268 subjects enrolled in this study, only 20 subjects (7.5%, 10 cases and 10 controls) were lost to follow up over the 18 months. As mentioned earlier in this report, we did not exclude these 20 subjects from the analysis because we were able to estimate the time of loss.

Also, existing literature on risk factors for delirium have indicated that incident and prevalent delirium are two distinct categories of delirium and as such, should be differentiated. This suggestion to differentiate the two categories of delirium posed another issue of concern. In studies of subjects with prevalent delirium, delirium is often assessed after admission and probably includes some incident cases (occurring between arrival to the emergency department and transfer to the department to which they are admitted). Also, delirium cases who are not admitted go undetected. In this thesis research, assessing patients for delirium within six hours of arrival to the emergency department minimized the inclusion of incident cases and the exclusion of prevalent cases. This in turn allowed for a more homogeneous sample than previous studies. Though the restriction to prevalent delirium prevents making any inferences of incident delirium, the results are nevertheless more valid for prognosis of prevalent delirium.

Furthermore, recent studies have had numbers of delirious subjects ranging from 45-125 cases (Francis et al. (1990)[27] & Francis and Kapoor (1992)[28]: 45; Pompei (1994)[42]: 64; Inouye et al. (1998)[33].: 88; Levkoff et al. (1992)[39]: 125, O'Keeffe and Lavan (1997)[41]: 94). However, all of these studies included both incident and prevalent delirium in their case definition. Levkoff et al. (1992)[39], for example, reported having had 34

prevalent cases among the 125 cases, and O'Keeffe and Lavan (1997)[41] reported having had 41 among their 94 cases. This thesis research focused on prevalent cases of delirium, of whom we were able to identify 107. This greater number of cases allowed for greater precision in the results.

Additionally, the use of emergency departments as the setting allowed us to avoid potential selection bias in that most of the studies in the past have focused on subjects in specific departments to which they were admitted. In addition to being able to detect delirious cases who are not admitted to the hospital, the emergency department setting allowed us to sample patients of all types, thereby allowing generalization of the results to all patients who access the hospital service rather than focussing on specific departments.

The use of the CAM to identify patients with delirium in the emergency department has been shown by Lewis et al. (1995)[20] to be effective in overcoming the problem of underdetection. They compared the rates of recognition of delirium between the use of conventional evaluation methods of emergency physicians and the CAM administered by a study nurse and found that only 17% (n=6) of the 35 CAM-identified patients were detected by conventional methods. In our study sample, only 20 (18.7%) of the 107 CAM-identified delirious patients were given the diagnosis of delirium in their medical charts, hence supporting the stance of Lewis et al..

Finally, the MMSE is also very difficult to administer over the telephone to subjects who are already impaired, resulting in a high rate of refusals. The assessment of cognitive status was therefore carried out using the IQCODE, which is administered to a close relative or friend to examine changes in cognitive status over a specified time period. The IQCODE is a preferred measure of cognitive status because responses given by subjects themselves are unreliable when they are in midst of their delirious state.

WEAKNESSES OF THE STUDY

During the study, realizations were made as to particular information that would have been helpful to have in trying to explain the results. For example, information about socioeconomic status, cultural backgrounds, religious beliefs, and perceived levels of

psychological distress would have been useful to explore as potential predictors for mortality among this sample of subjects. Also, the role of depression would have been worthwhile examining since it has been shown to be a risk factor for delirium and a possible risk factor for delirium. Finally, more detailed information regarding chronic pain may have also been shown to be predictive of mortality. This information may have helped explain the role of education as well as the differential effect of delirium on mortality found in the English and French speakers.

In this study, the burden of comorbidity was defined as the number of chronic conditions the subjects were experiencing at the time of the interview. This method is not as comprehensive as existing indices of comorbidity, such as the Charlson's weighted comorbidity index[94]. Using an index may have shown comorbidity to be a stronger predictor than was found in this study.

Finally, because of the large number of analyses that were carried out in this thesis research, verification of the results in a different sample is necessary.

CHAPTER 6. CONCLUSION

This thesis research revealed very interesting findings with regards to the prognosis of elderly patients with delirium. Some of the differences found between this thesis research and previous work may be attributed to different methodological characteristics. For example, that we employed the emergency department setting rather than particular departments to which patients are admitted may account for particular differences in the association between death and comorbidity, which was significant in the study by O'Keeffe and Lavan (1997)[41] who employed an acute geriatric unit, and Pompei et al. (1994)[42] who sampled from medical and surgical wards. The differences may also be attributed to the restricted case definition for delirium used in this study. The results of this study may not be comparable to studies including both incident and prevalent delirium.

It was evident that functional, general health, perceptual impairment and sociodemographic characteristics all play a role in the prognosis of elderly individuals with or without delirium. It would be insightful to examine some of these further to try to pinpoint what, among these factors are particularly contributing to mortality. For example, further examination into the specific drug that the subjects recently started taking or from which subjects were withdrawn may reveal that specific drugs are associated with mortality. It would also be interesting to examine whether different assessment scales for physical and cognitive status would influence results.

Interaction between language and delirium suggests that level of support and patterns of use of health services may influence the prognosis of delirium. This may have potential implications for prevention of negative outcomes after an episode of delirium. Further research is therefore necessary to obtain a better understanding of the prognosis of elderly individuals who experience delirium.

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APPENDIX 1. ETHICS APPROVAL LETTER

APPENDIX 2. CONSENT

Appendix 2.1 Protocol for obtaining verbal consent

Appendix 2.2 Verbal Consent for Short Questionnaire

Appendix 2.3 Written Consent Form for Long Questionnaire

DRUGS AS A RISK FACTOR FOR ACUTE CONFUSION IN THE ELDERLY
Principal investigators: Dr. G. Galbaud du Fort, Dr. Y. Moride

PATIENT INFORMATION

Medication can have some side effects in the elderly. This study will examine the relationship between use of medication and the ability to function on a daily basis. The results of this research study may help prevent certain side effects of medication in the elderly in the future.

If you participate, a Research Assistant may ask you to complete a short questionnaire, on health, medications you have taken and alcohol consumption in the past week. This will require approximately 30 minutes.

If you consent, a relative or caregiver will also be asked similar questions about your health and your medication use and alcohol consumption in the past week. The amount of time required from you relative or caregiver will be approximately 20 minutes.

As well, two weeks after your discharge from hospital an interviewer may telephone you to ask you to answer a short 15 minute questionnaire. As well as the above mentioned relative or caregiver will also be contacted. If you agree, this phone interview will be similar to today's, dealing with health, medication, etc.. This would take place again at 6, 12, and 18 months after your discharge.

If you refuse to participate, your care will not be affected in any way. All information collected from you and your relative or caregiver will be kept strictly confidential.

If you have any further questions, you can contact the project coordinator: Louise Arsenault at the Jewish General Hospital at 340-8222 ext 4316 or the principal investigators: Dr. Guillaume Galbaud du Fort at the Jewish General Hospital at 340-7563 or Dr. Yola Moride at 340-8222 ext 4667 or the patient representative: Ms. Roslyn Davidson at 340-5833.

DRUGS AS A RISK FACTOR FOR ACUTE CONFUSIO IN THE ELDERLY
Principal investigators: Dr. G. Galbaud du Fort, Dr. Y. Moride

PATIENT CONSENT (1) (Short Questionnaire)

Medication can have some side effects in the elderly. This study will examine the relationship between use of medication and the ability to function on a daily basis. The results of this research study may help prevent certain side effects of medication in the elderly in the future.

If you participate, a Research Assistant may ask you to complete a short questionnaire, on health, medications you have taken and alcohol consumption in the past week. This will require approximately 30 minutes.

If you consent, a relative or caregiver will also be asked similar questions about your health and your medication use and alcohol consumption in the past week. The amount of time required from you relative or caregiver will be approximately 20 minutes

As well, two weeks after your discharge from hospital an interviewer may telephone you to ask you to answer a short 15 minute questionnaire. As well as the above mentioned relative or caregiver will also be contacted. If you agree, this phone interview will be similar to today's, dealing with health, medication, etc.. This would take place again at 6, 12, and 18 months after your discharge.

If you refuse to participate, your care will not be affected in any way. All information collected from you and your relative or caregiver will be kept strictly confidential.

You will be give a copy of the details of this study (Patient Information).

If you have any further questions, you can contact the project coordinator: Louise Arsenault at the Jewish General Hospital at 340-8222 ext 4316 or the principal investigators: Dr. Guillaume Galbaud du Fort at the Jewish General Hospital at 340-7563 or Dr. Yola Moride at 340-8222 ext 4667 or the patient representative: Ms. Roslyn Davidson at 340-5833.

Verbal consent by: _____ (patient)

_____ (witness)

Date: _____

DRUGS AS A RISK FACTOR FOR ACUTE CONFUSIO IN THE ELDERLY
Principal investigators: Dr. G. Galbaud du Fort, Dr. Y. Moride

PATIENT CONSENT (2) (Prescription medication and chart review)

Medication can have some side effects in the elderly. This study will examine the relationship between use of medication and the ability to function on a daily basis. The results of this research study may help prevent certain side effects of medication in the elderly in the future.

If you participate, a Research Assistant may ask you to complete a short questionnaire, on health, medications you have taken and alcohol consumption in the past week.

We would like you to participate in an additional part of the study: if you agree to participate your medical charts will be reviewed and your Medicare number will be used to obtain information on medication prescriptions from the Regie de l'Assurance Maladie du Quebec. Since all information will be grouped it will not be possible to identify you individually.

If you refuse to participate, your care will not be affected in any way. All information collected from you and your relative or caregiver will be kept strictly confidential.

You will be give a copy of the details of this study (Patient Information).

If you have any further questions, you can contact the project coordinator: Louise Arsenault at the Jewish General Hospital at 340-8222 ext 4316 or the principal investigators: Dr. Guillaume Galbaud du Fort at the Jewish General Hospital at 340-7563 or Dr. Yola Moride at 340-8222 ext 4667 or the patient representative: Ms. Roslyn Davidson at 340-5833.

Signature: _____ (patient)

Signature: _____ (witness) Date: _____

SUBSTITUTED CONSENT (2) (Prescription medication and chart review)

SECTION A: **PATIENT ASSENT**

The patient cannot presently given an informed consent to participate in the study due to his/her medical condition. However, the patient has not refused to co-operate in this study

_____ _____
Patient's assent acknowledged by: Date

_____ _____
Signature of investigator or his/her delegate Date

SECTION B: **SUBSTITUTED CONSENT**

A representative for the patient _____. has been contacted on _____to give substituted consent as soon as possible under the same conditions as the patient's consent form. The representative has reviewed the patient's consent form and understands that the patient is not opposed to participating in the study.

The representative's questions concerning the study have been answered to her/her satisfaction.

_____ _____
Substituted consent of patient's representative Date

_____ _____
Signature of witness Date

_____ _____
Signature of investigator or his/her delegate Date

SECTION C: **TELEPHONE CONSENT**

_____ _____
Patient's verbal consent Date

_____ _____
Patient's representative's verbal consent Date

_____ _____
Investigator's delegate (person calling) Date

_____ _____
Witness (other than person calling) Date

APPENDIX 3. QUESTIONNAIRES

Appendix 3.1 Subject short questionnaire

Appendix 3.2 Additional items for the Subject long questionnaire

Appendix 3.3 Proxy short questionnaire

Appendix 3.4 Additional items for the Proxy long questionnaire

Appendix 3.5 Chart data

STUDY ID |__|__|__|__|__|__|__|__|

RAMQ #:

Sex: F M __

Lang: E F __

DOB: __ __ / __ __ / __ __

Age: __ __ __

Outcome: __

SUBJECT
SHORT QUESTIONNAIRE

(CHRONIC DISEASES / SOCIODEMOGRAPHICS
BOMC / MMSE / CAM)

Interview date: ____ / ____ / ____
d m y

Registration Time: __ __ : __ __
Interview began: __ __ : __ __
Interview ended: __ __ : __ __

For Office Use Only

BOMC > 10 |__|
MMSE < 17 |__|
CAM pos+ |__|

Proxy contacted: |__|
F/U at 2 wks: |__|

Drugs as a Risk Factor for Delirium in the Elderly **STUDY ID** |_|_|_|_|_|_|_|_|

PERSONAL DATA

Date of Interview: (d/m/y) _____

Hospital chart # _____ RAMQ #: _____

Subject's name: _____, _____
Family name at birth (then married name) First

Sex: 1 F 2 M _

Language: 1 English 2 French _

D.O.B. ____/____/____ _____
d m y

Age: _____ ___

Address: _____

_____ _____

(____) _____-_____
telephone number

_____

Proxy (caregiver/informant)

Relationship to subject: _____ _

1 spouse	4 other kin	7 neighbor
2 daughter	5 sibling	8 formal service provider
3 son	6 friend	9 other _____

Name: _____, _____
Family First

Address: _____

_____ _____

H: (____) _____-_____ W: (____) _____-_____
telephone number telephone number

PERSONAL DATA - cont'd

Other person to contact: _____ |_|
Relationship

1 spouse	4 other kin	7 neighbor
2 daughter	5 sibling	8 formal service provider
3 son	6 friend	9 other _____

Name: _____, _____
Family First

Address: _____

_____

H: (_____)_____-_____ W: (_____) _____ - _____
telephone number telephone number

Name of Family physician and (or physician that most often sees patient):

_____
Name

_____
Street City

A. CHRONIC DISEASES

STUDY ID |__|__|__|__|__|__|__|__|

1a. What brings you here today? (What seems to be the problem?) |__|__|__|

_____

1b. When did these symptoms begin ? (# of days ago) _____

Let me begin with me reading a list of health problems that may or may not apply to you. All information will be kept strictly confidential.

2. Do you have the following? (How long have you had this? Do you take any medication for this?)

1=Yes 2=No; 1= 1 year + 2=less than 1 yr; 1=Yes 2=No 9= N/A

	Problem	**Onset**		**Taking Meds**	
2a. High Blood Pressure _____	Y N	+1yr	-1yr	Y	N
2b. Heart and/or circulation problems _____	Y N	+1yr	-1yr	Y	N
2c. Stroke or effects of stroke _____	Y N	+1yr	-1yr	Y	N
2d. Migraines _____	Y N	+1yr	-1yr	Y	N
2e. Arthritis or rheumatism, osteoporosis _____	Y N	+1yr	-1yr	Y	N
2f. Allergies _____	Y N	+1yr	-1yr	Y	N
2g. Colds, sinusitis, laryngitis _____	Y N	+1yr	-1yr	Y	N
2h. Eye trouble (cataracts, glaucoma) _____	Y N	+1yr	-1yr	Y	N
2i. Ear trouble (hearing loss) _____	Y N	+1yr	-1yr	Y	N
2j. Chest problems (asthma, pneumonia, TB,____ emphysema, bronchitis, breathing problems)	Y N	+1yr	-1yr	Y	N
2k. Troubles with your stomach or digestive _____ system, nausea	Y N	+1yr	-1yr	Y	N
2l. Kidney / urinary trouble _____	Y N	+1yr	-1yr	Y	N
2m. Skin problems _____	Y N	+1yr	-1yr	Y	N
2n. Trouble with your nerves (including all _____ psychiatric or emotional problems such as depression, anxiety)	Y N	+1yr	-1yr	Y	N
2o. Fatigue, lack of energy _____	Y N	+1yr	-1yr	Y	N
2p. Sleep problems _____	Y N	+1yr	-1yr	Y	N
2q. Any fractures (if Yes, specify) _____	Y N	+1yr	-1yr	Y	N
2r. Parkinson's disease (other neurological problems) _____	Y N	+1yr	-1yr	Y	N
2s. Infections (if Yes, specify) _____	Y N	+1yr	-1yr	Y	N
2t. Cancer (if Yes, specify) _____	Y N	+1yr	-1yr	Y	N
2u. Diabetes or thyroid problems _____	Y N	+1yr	-1yr	Y	N
2v. Other (specify) _____	Y N	+1yr	-1yr	Y	N

B. SOCIODEMOGRAPHICS STUDY ID |__|__|__|__|__|__|__|__|

These are some questions about you and your family. As I mentioned before, all information will be kept strictly confidential.

1. How many years of schooling have you completed? _____ (actual # of years) __|__
   That means that you ... (have completed grade school, part or all of high school...? __|__
   (Choose the most accurate category)

   1 No schooling
   2 Part of grade school
   3 Completed grade school
   4 Part of high school completed
   5 Completed high school
   6 Part of college, or trade school, CEGEP, or nursing studies
   7 Completed college, or trade school, CEGEP, or nursing studies
   8 Part of a university program
   9 A bachelors degree
   10 A masters degree
   11 A doctorate
   12 Other
   77 DK

2. Are you working outside the home now? (Paid or volunteer) __
   1 Yes, paid 2 Yes, volunteer 3 No

3. What type of work did you do for <u>most</u> of your life?
   Principal occupation: _____

   If worked outside the home, how long ago did you stop working? _____(# yrs) __|__

4. Are you single, married, divorced, separated, or widowed? __

   1 single
   2 married
   3 common law spouse
   4 divorced
   5 separated
   6 widowed

5. Do you have any children? (actual #):____ ___

6. Do you live alone? 1 Yes 2 No __
   If NO, with whom?

   1 spouse
   2 daughter
   3 son
   4 other kin
   5 sibling
   6 friend
   7 neighbor
   8 formal service provider
   9 other _____ __

C. BOMC – (Blessed Orientation-Memory-Concentration Test) |__|__|__|__|__|__|__|__|

		(Max. Err.)	Score		Weight	Subscore
1	What *year* is this?.	(1)	|__|	X	4=	__
2	What *month* of the year is this?	(1)	|__|	X	3=	__
Memory Phase	**'Repeat this phrase after me':** ***John Brown, 42 Market Street, Ottawa*** Number of trials ( )	**'Keep this sentence in mind, I will ask you what it is in a few minutes'**				
3	Without looking at your watch, about what *time* is it?	(1)	__	X	3=	__
4	*Count* backwards 20 to 1 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1	(2)	__	X	2=	__
5	Say the *months* in reverse order D N O S A Jl Jn M A M F J	(2)	__	X	2=	__
6	**'Can you repeat the sentence I asked you to remember?'** *John Brown, 42 Market Street, Ottawa* ____ _____ __ _____ ____ _____	(5)	__	X	2=	__ __
					Total	__ __

Score 1 for each incorrect response: maximum weighte derror score = 28; Impairment score >10

D. MMSE– (ALFI) |__|__|__|__|__|__|__|__|

Section 1		Max.	Subscore
1.	(Same as BOMC Q.1)	(1)	___
2.	What season is this?	(1)	___
3.	(Same as BOMC Q.2)	(1)	___
4.	What is today's *date*?	(1)	___
5.	What *day* of the week is this?	(1)	___
6.	Which *country* are we in?	(1)	___
7	What *province* are we in?	(1)	___
8.	What *city* are we in?	(1)	___
9.	Where are you now?	(1)	___

Section 2

10. I am going to say 3 words for you to remember. Please repeat them after I have said all 3. Remember what they are because I am going to ask you to name them again in a few minutes.

REPEAT	**BALL**	**CAR**	**MAN**	(3)	___
11.	Subtract 7 from 100 and so on	(93 - 86 - 79 - 72 - 65)		(5)	___
12.	Now what were the three words that I asked you to remember?				
RECALL	**BALL**	**CAR**	**MAN**	(3)	___
13.	Tell me, what is the thing called that you are speaking into as you talk to me?	(Telephone)		(1)	___
14.	I'd like you to repeat this phrase after me: *"no if's, and's or but's"*			(1)	___

Total ___

Score correct responses: maximum 22 ; impairment score < 17

E. CAM– (CONFUSION ASSESSMENT METHOD) STUDY ID |__|__|__|__|__|__|__|__|

Scoring: 1 = Absent 1 = Present, Mild 3 =Present, Severe 7 = Don't know 9 = Not applicable

Onset & Fluctuation 1 =No 2 = YES 9 = N/A

	Abs.	Mld.	Sev.	D/K	N/A
1. ACUTE ONSET (PROXY)	1	2		7	9
2a. Inattention	1	2	3	7	
Proxy	1	2	3	7	
2b. Inattention/Fluctuation	1	2		7	9
Proxy	1	2		7	9
3a. Disorganized Thinking	1	2	3	7	9
Proxy	1	2	3	7	9
3b. Disorganized Thinking/Fluctuation	1	2	3	7	9
Proxy	1	2	3	7	9
4a. Altered Level of Consciousness	1	2	3	7	9

	Alert	Vigilant	Lethargic	Stupor	Coma	D.K.
	1	2	3	4	5	7
Proxy	1	2	3	4	5	7

4b. Altered level of consciousness/Fluctuation	1	2	7	9
Proxy	1	2	7	9

SCORE

1 – Acute Onset (1) OR Fluctuating course (2b, 3b, 4b)	1 Yes	2 No
2 – Inattention (2)	1 Yes	2 No
3 – Disorganized Thinking (3) OR Altered level of Consciousness (4)	1 Yes	2 No
DELIRIUM	1 Yes	2 No

E. CAM– con'td **STUDY ID** |__|__|__|__|__|__|__|__|

Acute Onset (Proxy)

1. Course of symptoms ___

1) appeared very abruptly (occurring over 7 days) (Abrupt)
2) appeared fairly suddenly (occurring over 1 month?) (Acute)
3) appeared gradually (occurring within a 6-month period)
4) was always like that (no significant change)

(IF response is 1 OR 2, code as ACUTE ONSET CAM)

Onset of symptoms ___

1) over the past 2 weeks
2) over the last month
3) over 1 to 6 months
4) over the last six months to 1 year
5) more than 1 year

IF during the last 2 weeks, when exactly (date)? ___/___/___ ___:___

E. CAM– cont'd **STUDY ID** |__|__|__|__|__|__|__|__|

	Abs.	Mld.	Sev.	D/K	N/A
5a. * Disorientation *	1	2	3	7	
Proxy	1	2	3	7	9
5b. Disorientation\Fluctuation	1	2		7	9
Proxy	1	2		7	9
6a. Memory Impairment	1	2	3	7	
Proxy	1	2	3	7	9
6b. Memory Impairment\Fluctuation	1	2		7	9
Proxy	1	2		7	9
7a. * Perceptual Disturbances *	1	2	3	7	
Proxy	1	2	3	7	9
7b. Perceptual Disturbances\Fluctuation	1	2		7	9
Proxy	1	2		7	9
8a. Psychomotor Agitation	1	2	3	7	
Proxy	1	2	3	7	9
8b. Psychomotor Agitation\Fluctuation	1	2		7	9
Proxy	1	2		7	9
8c. Psychomotor Retardation	1	2	3	7	
Proxy	1	2	3	7	9
8d. Psychomotor Retardation\Fluctuation	1	2		7	9
Proxy	1	2		7	9
9a. Altered Sleep-Wake Cycle	1	2	3	7	
Proxy	1	2	3	7	9

*10. IF Disorientation: what type	1- time	2- place	3- person	9- NA	__ __ __
*11. IF Hallucinations: what type	1-auditory	2- visual	3- tactile		__ __ __ __ __
	4- olfactory	5- gustatory	9- NA		

FOR PROXY ONLY

12a. Has _____ had previous episodes of confusion? 1 Yes 2 No __

12b. How many? __

12C. WHEN WAS THE FIRST TIME? HOW LONG AGO? (# YRS) __|__

STUDY ID |__|__|__|__|__|__|__|__|

RAMQ #:

Sex: F M __

Lang: E F __

DOB: |__|__|__|__|__|__|

Age: __ __ __

SUBJECT
LONG QUESTIONNAIRE

Interview date: ____/____/____
d m y

Registration Time: __ __ : __ __
Interview began: __ __ : __ __
Interview ended: __ __ : __ __

For Office Use Only

BOMC > 10 |__|
MMSE < 17 |__|
CAM pos+ |__|

Proxy contacted: |__|
F/U at 2 wks: |__|

F. GENERAL HEALTH

STUDY ID |__|__|__|__|__|__|__|__|

Now we come to some questions on your general health.

1. How is your eyesight (with glasses or with contacts)? __

1 Excellent 2 Good 3 Fair 4 Poor 5 Unable to see

2. How is your hearing (with a hearing aid if you wear one)? __

1 Excellent 2 Good 3 Fair 4 Poor 5 Unable to see

3. In the last 6 months, did you have an operation? 1 Yes 2 No __

If Yes, describe

4.

Reason for operation	When (m / y)	Days Hospitalized	
a.			__|__ __|__|__ __|__|__|__ a
b.			__|__ __|__|__ __|__|__|__ b
c.			__|__ __|__|__ __|__|__|__ c

G. HEALTH PROBLEMS - LAST MONTH STUDY ID |__|__|__|__|__|__|__|__|

Now I'm going to ask you some questions about health problems you may have had in the last week or two.

1. During the last 2 weeks, did you have fever? 1 Yes 2 No 7 D/K __
   What was your temperature? _____(Centigrade) __ __ . __

2. Have you been sick or not feeling well in the last 2 weeks? 1 Yes 2 No __
   What was the problem? _____ __ __ __
   When? (# of days ago) _____ __ __

3. Did you see or speak to a doctor in the last 2 weeks? 1 Yes 2 No __
   IF NO, Go to Q.6
   If Yes, When? _____(# of days ago) __ __
   What was the problem? _____ __ __ __

4a. Did the doctor prescribe any new medication for you to take? 1 Yes 2 No __
   Medication: _____ __ __ __
   Dose: _____ _____ __ __ __ __
   When did you begin the medication (# of days ago) _____ __ __

4b. Medication: _____ __ __ __
   Dose: _____ _____ __ __ __ __
   When did you begin the medication (# of days ago) _____ __ __

4c. Medication: _____ __ __ __
   Dose: _____ _____ __ __ __ __
   When did you begin the medication (# of days ago) _____ __ __

5a. Did the doctor change the dose of any of your medication ? 1 Yes 2 No __
   Medication: _____ __ __ __
   Dose: _____ _____ __ __ __ __
   When did this change in medication begin (# of days ago) _____ __ __

5b. Medication: _____ __ __ __
   Dose: _____ _____ _____ __ __ __ __
   When did this change in medication begin (# of days ago) _____ __ __

6a. During the last 2 weeks, did you take any medication, not prescribed by a doctor?
   (Ex. aspirin, pills for allergies, sleeping pills, something bought at phcy, etc.)
   1 Yes 2 No __
   Medication: _____ __ __ __
   Dose: _____ __ __ __ __
   When (# of days ago): _____ __ __

6b. Medication: _____ __ __ __
   Dose: _____ __ __ __ __
   When (# of days ago): _____ __ __

G. HEALTH PROBLEMS - LAST MONTH cont'd STUDY ID |__|__|__|__|__|__|__|__|

7a. During the last 2 weeks, did you stop taking any medication that you usually take? 1 Yes 2 No __
Medication(s): _____ __|__|__
When (# of days ago): _____ __|__
Why? _____ __

7b. Medication(s): _____ __|__|__
When (# of days ago): _____ __|__
Why? _____ __

7c. Medication(s): _____ __|__|__
When (# of days ago): _____ __|__
Why? _____ __

8. In the past 12 months, have you taken any beer, wine, liquor or other alcoholic beverages? 1 Yes 2 No
If NO, go to **next page** __

9. In the past 12 months, how often did you take alcoholic beverages? __

1 Everyday
2 4 to 6 times a week
3 2 to 3 times a week
4 Once a week
5 Once or twice a month
6 Less than once a month
7 DK

10. Have your drinking habits changed over the past month? __

1 Yes, drinking more now
2 Yes, drinking less now
3 No, same as before
7 DK

If YES, Any special reason? _____ __

H. OARS – IADL STUDY ID |__|__|__|__|__|__|__|__|

Now I'd like to ask you about some of the activities of daily living, things that we all need to do as a part of our daily lives. I would like to know if you can these activities - without any help at all, or if you need some help to do them, or if you can't do them at all.
(Be sure to read all answer choices (if applicable in questions 1 to 14)

1 Can you use the telephone...
- 2 without help, including looking up numbers and dialling
- 1 with some help (can answer phone or dial operator in an emergency, but need a special phone or help in getting the number or dialing
- 0 or are you completely unable to use the telephone?
- - not answered

2 Can you get to places out of walking distance...
- 2 without help (can travel alone on buses, taxis, or drive your own car)
- 1 with some help (need someone to help you or go with you when travelling) or
- 0 are you unable to travel unless emergency arrangements are made for a specialized vehicle or like an ambulance?
- - not answered

3 Can you go shopping for groceries or clothes (assuming subject has transportation)...
- 2 without help (taking care of all shopping needs yourself, assuming you had transportation)
- 1 with some help (need someone to go with you on all shopping trips)
- 0 or are you completely unable to do any shopping?
- - not answered

4 Can you prepare your own meals...
- 2 without help (plan and cook full meals yourself)
- 1 with some help (can prepare some things but unable to cook full meals yourself)
- 0 or are you completely unable to prepare any meals?
- - not answered

5 Can you do your housework...
- 2 without help (can scrub floors, etc)
- 1 with some help (can do light housework but need help with heavy work)
- 0 or are you completely unable to do any housework?
- - not answered

6 Can you take your medicine...
- 2 without help (in the right doses at the right time)
- 1 with some help (able to take medicine if someone prepares it for you and/or reminds you to take it)
- 0 or are you completely unable to take your medicines?
- - not answered

7 Can you handle your own money...
- 2 without help (write checks, pay bills, etc.)
- 1 with some help (manage day-to-day buying but need help with managing checkbook and paying your bills)
- 0 or are you completely unable to handle money?
- - not answered

H. OARS - ADL

STUDY ID |__|__|__|__|__|__|__|__|

8 Can you eat..
- 2 without help (able to feed yourself completely)
- 1 with some help (need help with cutting, etc.)
- 0 or are you completely unable to feed yourself?
- - not answered

9 Can you dress and undress yourself...
- 2 without help (able to pick out clothes, dress and undress yourself)
- 1 with some help
- 0 or are you completely unable to dress and undress yourself?
- - not answered

10 Can you take care of your own appearance, for example combing your hair and (for men) shaving
- 2 without help
- 1 with some help
- 0 or are you completely unable to maintain your appearance yourself?
- - not answered

11 Can you walk ..
- 2 without help (except from a cane)
- 1 with some help (either from a person or with the use of a walker, or crutches, etc.)
- 0 or are you completely unable to walk?
- - not answered

12 Can you get in and out of bed..
- 2 without any help or aids
- 1 with some help (either from a person or with the aid of some device)
- 0 or are you totally dependent on someone else to lift you?
- - not answered

13 Can you take a bath or shower ..
- 2 without help
- 1 with some help (need help getting in and out of the tub, or need special attachments on the tub)
- 0 or are you completely unable to bathe yourself?
- - not answered

14. Do you ever have trouble getting to the bathroom on time?
- 2 No
- 0 Yes
- 1 Have a catheter or colostomy
- - not answered

(If 'Yes' ask a.)

a. How often do you lose control of your bladder or bowels? (either day or night)?
- 1 once or twice a week
- 0 three times a week or more
- - not answered

15. Is there someone who helps you with such things as shopping, housework, bathing, dressing and getting around?
- 1 Yes
- 0 No
- - not answered

COMMENTS:

STUDY ID # |__|__|__|__|__|__|__|__|

PROXY
SHORT QUESTIONNAIRE

Proxy Relationship __

Interview date: ___ ___ ___
d m y

Interview began: ___ : ___

Interview ended: ___ : ___

Record of calls made until contacted: ___

Date (d/m/y)	Time (24 hr clock)	Comments

Location: ER __

phone __

Drugs as a Risk Factor for Delirium in the Elderly **STUDY ID #**|_|_|_|_|_|_|_|_|

PERSONAL DATA (PROXY)

Date of interview: (d/m/y) |_|_|_|_|_|_|

Hospital chart # _____ RAMQ #: |_|_|_|_|_|_|_|_|_|_|_|_|

Subject's name: _____, _____
Family name at birth (then married name) First

Sex: 1 F 2 M _

D.O.B. ____/____/____ _ _ _ _ _ _ _ _
d m y

Age: _____ _ _ _

Address: _____

_____ _____

(____)_____-_____
telephone number

==========

Proxy (caregiver/informant)

Relationship to subject: _____

1	spouse	4	other kin	7	neighbor
2	daughter	5	sibling	8	formal service provider
3	son	6	friend	9	other _____

Name: _____, _____
Family First

Address: _____

_____ _____

H: (_____)_____-_____ W: (_____) _____ - _____
telephone number telephone number

Name of Family Physician (or physician that most often sees patient):

_____
Name

_____
Street City

A. CHRONIC DISEASES STUDY ID |__|__|__|__|__|__|__|__|

1a. What brings him/her here today? (What seems to be the problem?) __|__|

_____

1b. When did these symptoms begin? (# of days ago) __|__|__|

Let me begin with a list of health problems that or may not apply to *All information will be kept strictly confidential.*

2. Does she/he have the following? (How long has she/he had this? Does she/he take any medication for this?)

1=Yes 2=No; 1= 1 year + 2=less than 1 yr; 1=Yes 2=No 9=N/A

	Problem	Onset		Taking Meds
2a. High Blood Pressure _____	Y N	+1yr	-1yr	Y N
2b. Heart and/or circulation problems _____	Y N	+1yr	-1yr	Y N
2c. Stroke or effects of stroke _____	Y N	+1yr	-1yr	Y N
2d. Migraines _____	Y N	+1yr	-1yr	Y N
2e. Arthritis or rheumatism, osteoporosis _____	Y N	+1yr	-1yr	Y N
2f. Allergies _____	Y N	+1yr	-1yr	Y N
2g. Colds, sinusitis, laryngitis _____	Y N	+1yr	-1yr	Y N
2h. Eye trouble (cataracts, glaucoma) _____	Y N	+1yr	-1yr	Y N
2i. Ear trouble (hearing loss) _____	Y N	+1yr	-1yr	Y N
2j. Chest problems (asthma, pneumonia, TB, emphysema, bronchitis, breathing problems) ____	Y N	+1yr	-1yr	Y N
2k. Troubles with your stomach or digestive system, nausea _____	Y N	+1yr	-1yr	Y N
2l. Kidney / urinary trouble _____	Y N	+1yr	-1yr	Y N
2m. Skin problems _____	Y N	+1yr	-1yr	Y N
2n. Trouble with your nerves (including all psychiatric or emotional problems such as depression, anxiety) _____	Y N	+1yr	-1yr	Y N
2o. Fatigue, lack of energy _____	Y N	+1yr	-1yr	Y N
2p. Sleep problems _____	Y N	+1yr	-1yr	Y N
2q. Any fractures (if Yes, specify) _____	Y N	+1yr	-1yr	Y N
2r. Parkinson's disease (other neurological problems) _____	Y N	+1yr	-1yr	Y N
2s. Infections (if Yes, specify) _____	Y N	+1yr	-1yr	Y N
2t. Cancer (if Yes, specify) _____	Y N	+1yr	-1yr	Y N
2u. Diabetes or thyroid problems _____	Y N	+1yr	-1yr	Y N
2v. Other (specify) _____	Y N	+1yr	-1yr	Y N

B. SOCIODEMOGRAPHIC (PROXY) STUDY ID |__|__|__|__|__|__|__|__|

I will be asking you some questions about _____, her/his family, and her/his health. As I mentioned before, all information will be kept strictly confidential. Let me start by asking a couple of questions about your relationship to _____.

1. Do you live with _____? 1 Yes 2 No __

2. How often do you see _____? __
   1 Daily 4 Several times a month
   2 Several times a week 5 Once a month
   3 Once a week 6 Several times a year

3. How often do you speak to _____? __
   1 Daily 4 Several times a month
   2 Several times a week 5 Once a month
   3 Once a week 6 Several times a year

4. How well do you feel you know _____? __
   1 Very well 2 Well 3 Not very well

5. How many years of schooling has __ completed? (actual # of years) ____ ____
   That means that she/he ... (has completed grade school, part or all of high school...? ___
   (Choose the most accurate category)
   1 No schooling
   2 Part of grade school
   3 Completed grade school
   4 Part of high school completed
   5 Completed high school
   6 Part of college, or trade school, CEGEP, or nursing studies
   7 Completed college, or trade school, CEGEP, or nursing studies
   8 Part of a university program
   9 A bachelors degree
   10 A masters degree
   11 A doctorate
   12 Other
   77 DK

6. Is she/he working outside the home now? 1 Yes, paid 2 Yes, volunteer 3 No __

7. What type of work did she/he do for the greater part of her/his life?
   Principal occupation: _____ __
   If worked outside the home, how long ago did she/he stop working? __(#yrs) ____

8. Is she/he single, married, divorced, separated, or widowed? __
   1 single 4 divorced
   2 married 5 separated
   3 common law spouse 6 widowed

9. Does she/he have children? # :_____ ____

10. Does she/he live alone? 1 Yes 2 No __
    If NO, with whom? __
    1 spouse 4 other kin 7 neighbor
    2 daughter 5 sibling 8 formal service provider
    3 son 6 friend 9 other _____

STUDY ID # |__|__|__|__|__|__|__|__|

PROXY
LONG QUESTIONNAIRE

Proxy Relationship: __

Interview date: ___/___/___
d m y

Interview began: __ __ : __ __

Interview ended: __ __ : __ __

Record of calls made until contacted: __ __

Date (d/m/y)	Time (24 hr clock)	Comments

Location: ER __

phone __

F. GENERAL HEALTH (PROXY)

STUDY ID |__|__|__|__|__|__|__|__|

These are a few questions on _____'s general health.

1. How is her/his eyesight (with glasses or with contacts)? __

1 Excellent 2 Good 3 Fair 4 Poor 5 Unable to see

2. How is her/his hearing (with a hearing aid if you wear one)? __

1 Excellent 2 Good 3 Fair 4 Poor 5 Unable to see

3. In the last 6 months, did she/he have an operation? 1 Yes 2 No __

If Yes, describe

4.

Reason for operation	Date (m / y)	Days Hospitalized	
1.			|__|__|__|__|__|__| a
2.			|__|__|__|__|__|__| b
3			|__|__|__|__|__|__| c

G. HEALTH PROBLEMS - LAST MONTH (PROXY) STUDY ID |__|__|__|__|__|__|__|__|

Now I'm going to ask you some questions about some health problems _____ may have had in the last month.

1. During the last month, did she/he have any fever? 1 Yes 2 No __
   What was the temperature? _____ (Centigrade) __.__

2. Has she/he been sick or not feeling well in the last month? 1 Yes 2 No __
   What was the problem? _____ ___
   When? (# of days ago) _____ __

3. Did she/he see a doctor in the last month? 1 Yes 2 No __
IF NO, Go to Q.6
   If Yes, When? _____ __
   What was the problem? _____ ___

4a. Did the doctor prescribe any new medication for her/him to take? 1 Yes 2 No |__|
   Medication: _____ ___
   Dose: _____ _____ ____
   When did she/he begin the medication? _____ __

4b. Medication: _____ ___
   Dose: _____ ____
   When did she/he begin the medication? _____ __

4c. Medication: _____ ___
   Dose: _____ ____
   When did she/he begin the medication? _____ __

5a. Did the doctor change the dose of any of her/his medication? 1 Yes 2 No __
   Medication: _____ |__|__|__|
   Dose: _____ ____
   When did she/he begin the change in medication? _____

   __

5b. Medication: _____ ___
   Dose: _____ ____
   When did she/he begin the change in medication? _____ __

6a. During the last 2 weeks, did she/he take any other medication, not prescribed by a doctor? (Ex. a decongestant, pills for allergies, sleeping pills, etc.) 1 Yes 2 No |__|
   Medication: _____ ___
   Dose: _____ ____
   When (# of days ago): _____ __

6b. Medication: _____ |__|__|__|
   Dose: _____ ____
   When (# of days ago): _____ __

G. HEALTH PROBLEMS - LAST MONTH (PROXY) cont'd STUDY ID |__|__|__|__|__|__|__|__|

7a. During the last month, did she/he stop taking any medication that she/he usually takes? 1 Yes 2 No__
Medication(s): _____ __
When (# of days ago): _____ __
Why? _____ __

7b. Medication(s): _____ __
When (# of days ago): _____ __
Why? _____ __

7c. Medication(s): _____ __
When (# of days ago): _____ __
Why? _____ __

IF **NO** delirium **Go. To Q.9**

DELIRIUM cases only ask Q8a to 8e

8a. Was a medication (prescribed OR OTC) started, changed, or stopped around the time the symptoms began? 1 Yes 2 No 9 NA
|__|

IF NO. **Go to Q.9**
IF Yes.

8b. Was it a _____ in medication? __
1 start 2 change 3 stop 9 NA

8c. Which medication was it? _____ __

8d. IF another medication, which one? _____ __

8e. Did the symptoms begin _____ the start/change/stop of medication ? __
1 before 2 after 7 DK 9 NA

---

9. In the past 12 months, has she/he taken any beer, wine, liquor or other alcoholic beverages? 1 Yes 2 No If NO. **Go to next page** __

10. In the past 12 months, how often did she/he take alcoholic beverages? __
1 Everyday
2 4 to 6 times a week
3 2 to 3 times a week
4 Once a week
5 Once or twice a month
6 Less than once a month
7 DK

11. Has she/he drinking habits changed over the past month? __
1 Yes, drinking more now
2 Yes, drinking less now
3 No, same as before
7 DK
If YES. Any special reason? _____ __

H. OARS – IADL

STUDY ID |__|__|__|__|__|__|__|__|

Now I'd like to ask you about some of the activities of daily living, things that we all need to do as a part of our daily lives. I would like to know if you can these activities - without any help at all, or if you need some help to do them, or if you can't do them at all.
(Be sure to read all answer choices (if applicable in questions 1 to 14)

1 Can you use the telephone..
- 2 without help, including looking up numbers and dialling
- 1 with some help (can answer phone or dial operator in an emergency, but need a special phone or help in getting the number or dialing
- 0 or are you completely unable to use the telephone?
- - not answered

2 Can you get to places out of walking distance..
- 2 without help (can travel alone on buses, taxis, or drive your own car)
- 1 with some help (need someone to help you or go with you when travelling) or
- 0 are you unable to travel unless emergency arrangements are made for a specialized vehicle or like an ambulance?
- - not answered

3 Can you go shopping for groceries or clothes (assuming subject has transportation)
- 2 without help (taking care of all shopping needs yourself, assuming you had transportation)
- 1 with some help (need someone to go with you on all shopping trips)
- 0 or are you completely unable to do any shopping?
- - not answered

4 Can you prepare your own meals..
- 2 without help (plan and cook full meals yourself)
- 1 with some help (can prepare some things but unable to cook full meals yourself)
- 0 or are you completely unable to prepare any meals?
- - not answered

5 Can you do your housework..
- 2 without help (can scrub floors, etc)
- 1 with some help (can do light housework but need help with heavy work)
- 0 or are you completely unable to do any housework?
- - not answered

6 Can you take your medicine..
- 2 without help (in the right doses at the right time)
- 1 with some help (able to take medicine if someone prepares it for you and/or reminds you to take it)
- 0 or are you completely unable to take your medicines?
- - not answered

7 Can you handle your own money...
- 2 without help (write checks, pay bills, etc.)
- 1 with some help (manage day-to-day buying but need help with managing checkbook and paying your bills)
- 0 or are you completely unable to handle money?
- - not answered

H. OARS - ADL

STUDY ID |__|__|__|__|__|__|__|__|

8 Can you eat...
- 2 without help (able to feed yourself completely)
- 1 with some help (need help with cutting, etc.)
- 0 or are you completely unable to feed yourself?
- - not answered

9 Can you dress and undress yourself...
- 2 without help (able to pick out clothes, dress and undress yourself)
- 1 with some help
- 0 or are you completely unable to dress and undress yourself?
- - not answered

10 Can you take care of your own appearance, for example combing your hair and (for men) shaving...
- 2 without help
- 1 with some help
- 0 or are you completely unable to maintain your appearance yourself?
- - not answered

11 Can you walk...
- 2 without help (except from a cane)
- 1 with some help (either from a person or with the use of a walker, or crutches, etc.)
- 0 or are you completely unable to walk?
- - not answered

12 Can you get in and out of bed...
- 2 without any help or aids
- 1 with some help (either from a person or with the aid of some device)
- 0 or are you totally dependent on someone else to lift you?
- - not answered

13 Can you take a bath or shower...
- 2 without help
- 1 with some help (need help getting in and out of the tub, or need special attachments on the tub)
- 0 or are you completely unable to bathe yourself?
- - not answered

14 Do you ever have trouble getting to the bathroom on time?
- 2 No
- 0 Yes
- 1 Have a catheter or colostomy
- - not answered

(If "Yes" ask a.)

a. How often do you lose control of your bladder or bowels? (either day or night)?
- 1 once or twice a week
- 0 three times a week or more
- - not answered

15 Is there someone who helps you with such things as shopping, housework, bathing, dressing and getting around?
- 1 Yes
- 0 No
- - not answered

STUDY ID |__|__|__|__|__|__|__|__|

I. IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly)

Now we want you to remember what your friend or relative was like 10 years ago and compare it with what she/he was like before the illness that brought her/him to the hospital. (10 years ago was in 1986). Below are situations where this person has to use her/his memory or intelligence and we want you to indicate whether this has improved, stayed the same, or got worse in that situation over he past 10 years. Note the importance of comparing her/his performance with 10 years ago. So if 10 years ago this person always forgot where she/he had left things, and she/he still does, then this would be considered "Not much change".

Compared with 10 years ago, how is this person at:

1 Much improved	**2** A bit improved	**3** Not much change	**4** A bit worse	**5** Much worse	**9** Don't know

1	Remembering things about family and friends e.g. occupations, birthdays, addresses	1	2	3	4	5	9
2	Remembering things that have happened recently	1	2	3	4	5	9
3	Recalling conversations a few days later	1	2	3	4	5	9
4	Remembering her/his address and telephone number	1	2	3	4	5	9
5	Remembering what day and month it is	1	2	3	4	5	9
6	Remembering where things are usually kept	1	2	3	4	5	9
7	Remembering where to find things which have been put in a different place from usual	1	2	3	4	5	9
8	Knowing how to work familiar machines around the house	1	2	3	4	5	9
9	Learning to use a new gadget or machine around the house	1	2	3	4	5	9
10	Learning new things in general	1	2	3	4	5	9
11	Following a story in a book or on TV	1	2	3	4	5	9
12	Making decisions on everyday matters	1	2	3	4	5	9
13	Handling money for shopping	1	2	3	4	5	9
14	Handling financial matters, e.g. the pension, dealing with the bank	1	2	3	4	5	9
15	Handling other everyday arithmetic problems e.g. knowing how much food to buy, knowing how long between visits from family and friends	1	2	3	4	5	9
16	Using her/his intelligence to understand what's going on and to reason things through	1	2	3	4	5	9

I. IQCODE - cont'd

IF ANY CHANGES HAS BEEN REPORTED.

17. With regards to the differences you have observed in your relative or friend, in general, when did you first notice these changes?

    ___

    1 Within the past year
    2 between 1 and 2 years ago
    3 between 2 and 3 years ago
    4 between 3 and 4 years ago
    5 between 5 and 5 years ago
    6 more than 5 years ago

MEMORY COMPLAINTS

HAS _____ EVER COMPLAINED ABOUT HIS/HER MEMORY?

___

1 Yes 2 No
If Yes, when was the first time?

___

1 3 months ago
2 6 months ago
3 1 year ago
4 more than 1 year ago
5 D/K
6 N/A

CHART DATA (1) **STUDY ID** |__|__|__|__|__|__|__|__|

Hospital Chart # _____

1) ER Date: _____/_____/_____
d m y

2) Triage code: **JGH** 01) 1 02) 2 ____
03) 3 04) A2S
05) A1 06) A2
07) A3

MGH 08) 1 - red 09) 2 - yellow
10) 3 - green 11) 4 - blue

3) Admission: 1) Yes 2) No ___

4) # days admitted (if in ER only, # of days in ER) _____

5) Discharge Dx (from ER or ward) ICD-9 _____ _____

Specify _____
_____

6) Discharge Date____/____/____
d m y

Discharged from Service:
01) Geriatrics 02) Medicine 03) Surgery ____
04) Neurology 05) Cardiology 06) GI
07) Hematology 08) Respirology 09) Psychiatry
Other (Specify) _____

(For either discharged from ER or Ward)

8) Disposition: 1) discharged home 2) foster home ___
3) LTC 4) deceased
5) other hosp 6) rehab
7) respite care

DIAGNOSTIC TEST RESULTS

(At ER visit or within 2 days of visit; 3 days for Endocrinology & Radiology)

Date: ____/____/____
d m y

Vital Signs: **Temp**: |__|__|.|__|

BP: |__|__|__| / |__|__|__| mg/Hg

Pulse: |__|__|__|/min.

Resp: |__|__| /min

HEMATOLOGY	Reference Range (JGH)	(actual values where applicable)
WBC	4.6-11.0	|__|__|.|__|
RBC	M:4.50-5.90F: 4.10-5.10	|__|.|__|__|
HGB (Hemoglobin)	M:140-175F:120-152	|__|__|__|
HCT (Hematocrit)	M:0.420-0.500F: 0.360-0.450	|__|.|__|__|__|
PLAT (Platelets)	150-400	|__|__|__|
ESR (Westergren)	M: 0 - 15F: 0 - 20	|__|__|
Serum Vitamin B12	80 - 600	|__|__|__|
Serum Folate	5.0 - 36.3	|__|__|.|__|
PT	10.0-13.0	|__|__|.|__|
PTT	25.0-37.0	|__|__|.|__|
INR	2.0-3.0	|__|.|__|
BIOCHEMISTRY		
Urea (BUN)	2.9-8.2	|__|.|__|
Creatinine	M: 70-125F: 56-108	|__|__|__|

		STUDY ID _____
BIOCHEMISTRY - cont'd		
Glucose (random)	3.6-6.1	___.___
Calcium	2.12-2.62	__.___
Phosphorus	0.81-1.45	__.___
Bilirubin	3-17	___
AST (SGOT)	5-40	___
ALT (SGPT)	5-40	___
LD (LDH)	100-210	___
Magnesium	0.74-1.23	__.___
Potassium	3.8-5.5	__.__
Chloride	98-108	___
Sodium	135-148	___
Albumin	35-51	___
CK (cardiac enzyme)	M:30-200F:25-150	___
BACTERIOLOGY / MICROBIOLOGY		
Blood – Culture	1=done 2=not done **If done**, (results) organism	__ __ (Specify _____)
Urine - Culture	1=done 2=not done **If done**, (results) organism	__ __ (Specify _____)
BLOOD GAS		
pH		_.__
PCO_2		__
HCO_3 (Bicarb)		__
PO_2		__._

		STUDYID |__|__|__|__|__|__|__|__|
ENDOCRINOLOGY		
TSH	0.4-4.5	|__|.|__|
CARDIOLOGY		
ECG (EKG)	1=done 2=not done	|__|
NEUROLOGY		
EEG	1=done 2=not done	|__|
RADIOLOGY / NUCLEAR MED.		
CXR	1=done (<= 3 days) 2=not done 3= done (>3 - 15 days)	|__|
CT Scan (brain)	1=done 2=not done 3= done (>3 - 15 days)	|__|
Doppler - echo (carotid arteries)	1=done 2=not done 3= done (>3 - 15 days)	|__|

CHART DATA (3)

STUDYID	MEDICATION (taken)	CODE (obtain from meds list or new code to be generated	SOURCE 1=ER 2=Adm 3=both

CHART DATA (3) **EXTRA**

STUDYID	**MEDICATION (taken)**	**CODE** (obtain from meds list or new code to be generated	**SOURCE** 1=ER 2=Adm 3=both

APPENDIX 4. DIAGNOSTIC AND STATISTICAL MANUAL VERSIONS III, III-R, AND IV.

Appendix 4. Diagnostic and Statistical Manual versions III, III-R, and IV.

DSM-III criteria[11]

- Clouding of consciousness (reduced clarity of awareness of the environment), with reduced capacity to shift, focus, & sustain attention to environmental stimuli.
- At least 2 of the following:
  1) Perceptual disturbance: misinterpretation, illusions, or hallucinations
  2) Speech that is at time incoherent
  3) Disturbance of sleep-wakefulness cycle, with insomnia or daytime drowsiness
  4) Increased or decreased psychomotor activity
  5) Disorientation & memory impairment (if testable)
  6) Clinical features that develop over a short period of time (usually hours to days) & tend to fluctuate over the course of the day
  7) Evidence, from the history, physical examination, or laboratory tests, of a specific organic factor judged to be etiologically related to the disturbance

DSM-III-R criteria[12]

Core problem = attention which stems out to 1) awareness of surroundings, 2) easily distracted, 3) have trouble following commands & concentrating, 4) disorganized thinking (rambling, incoherent speech), 5) behavioral changes (reduced consciousness, perceptual disturbances, sleep/wake disturbances, hyper/hypo psychomotor activity, disorientation, memory impairment)

- Reduced ability to maintain attention to external stimuli (e.g., questions must be repeated because attention wanders) & to appropriately shift attention to new external stimuli (e.g., perseverates answer to a previous question)
- Disorganized thinking, as indicated by rambling, irrelevant, or incoherent speech
- Presence of at least 2 of the following:
  1) Reduced level of consciousness e.g., difficulty keeping wake during examination
  2) Perceptual disturbance: misinterpretation, illusions, or hallucinations
  3) Disturbance of sleep-wake cycle, with insomnia or daytime sleepiness
  4) Increased or decreased psychomotor activity
  5) Disorientation to time, place or person
  6) Memory impairment, e.g., inability to learn new material, such as the names of several unrelated objects after five minutes, or to remember past events, such as history or current episode of illness
- Development of acute clinical features over a short period of time (usually hours to days) & tend to fluctuate over the course of the day
- Either one of the following:
  1) Evidence from the history, physical examination, or laboratory tests of a specific organic factor (or factors) judged to be etiologically related to the disturbance.
  2) In the absence of such evidence, an etiologic organic factor can be presumed if the disturbance cannot be accounted for by any nonorganic mental disorder, e.g., Manic Episode accounting for agitation & sleep disturbance

DSM-IV criteria[1]

Impairment of attention, disorganized thinking with incoherent speech, reduced level of consciousness, illusions or hallucinations, disturbed sleep-wake cycle, increased or decreased psychomotor activity, disorientation, & memory impairment WITH acute/subacute onset, with fluctuations in clinical signs during the course of the day

- Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention
- A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dem.
- The disturbance develops over a short period of time (usually hours to days) & tends to fluctuate during the course of the day
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition