THE IMPACT OF ENVIRONMENTAL FACTORS ON THE DEVELOPMENT OF DELIRIUM

by

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ABSTRACT

Delirium. a confusional state characterized by acute onset and fluctuating symptoms. may be precipitated by virtually all physical illnesses. The personal and economic consequences of delirium highlight the importance of research in this field.

Two studies were undertaken that tried to address the limitations of previous delirium research. Study One. a prospective study of individuals 65 years of age and older, was conducted in an acute care facility. The primary purpose of Study One was t identify environmental risk factors for delirium in the acute care hospitalized elderly th were amenable to intervention. Environmental factors were defined as those factors th occur during hospitalization and are external to the individual. The secondary purpose Study One was to identify the negative consequences or outcomes associated with delirium that occur during hospitalization or at discharge. The primary purpose of Stud Two was to estimate the prevalence of delirium and identify possible risk factors for delirium in patients 65 years of age and older who were residents in a chronic care institution. The secondary purpose of Study Two was to assess the utility of the Minimum Data Set (MDS) for delirium research. The MDS is a comprehensive patient assessment tool mandated for use in chronic care hospitals in Ontario.

In Study One, one hundred and fifty six consecutive patients admitted to the hospital were followed for fourteen days or until discharge. Delirium developed in 28 individuals (17.4%) following hospital admission. Significant host risk factors include older age, surgery, a period in the intensive care unit and cognitive impairment. Significant environmental risk factors amenable to intervention included a high numbe

medications during hospitalization and a high number of procedures over the first four days. When the aggregate hospital medications variable was removed from the final model. Histamine$_2$ receptor antagonists and a combination of benzodiazepines and tricyclic antidepressants were significant independent risk factors for delirium. Deliriu independently contributed to an increased length of stay in hospital and the use of restraints other than siderails.

In Study Two, 230 patients were admitted to chronic care and met study criteria. There were 48 (20.9%) patients identified as potentially delirious according to MDS criteria. Eleven (4.8%) patients met the criteria for a diagnosis of delirium according The Diagnostic and Statistical Manual of Mental Disorders IV (DSMIV). Thus. future studies must be undertaken to assess the sensitivity and specificity of the MDS deliriu measure.

A number of host risk factors were identified for potential delirium (defined by MDS criteria). Host risk factors included (1) cognitive impairment, (2) not having a diagnosis of hemiplegia, (3) presence of an indicator of depression, anxiety or sad moc in last 30 days, (4) a deterioration in activities of daily living compared to status 90 da previously, (5) renal failure, (6) diagnosed with a terminal illness, (7) increasing bowe incontinence, (8) a wound infection, or (9) urinary tract infection.

One environmental variable was significant in the final model. Those patients w an increased number of daily physician order changes were at a higher risk for potenti delirium.

Host risk factors for DSMIV defined delirium (as opposed to potential delirium) included cognitive impairment, and a deterioration in urinary continence. Environmental risk factors included an acute care hospital admission in the previous 90 days and an increased number of medications.

With the exception of medical diagnoses, cognitive impairment and terminal illness the other risk factors identified in Study Two are susceptible to the limitations associated with a cross-sectional study, namely the difficulty in determining correct temporal sequence.

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Chapter 1. Introduction

Delirium has been described in the medical literature for over 2000 years; howev it remains relatively uninvestigated compared to other cognitive disorders such as dementia. The etymology of delirium is evocative: it is derived from the Latin *de*. meaning down or away from, and *lira*, a furrow or track in the fields; that is, to be "off track". Delirium is a mental impairment marked by confusion and sometimes hallucinations (perceptual disturbances). Although memory impairment occurs in both delirium and dementia, delirium is also characterized by a disorder of attention, an acu onset, and fluctuating symptoms, whereas the symptoms in dementia are relatively stab and attention is normal (American Psychiatric Association, 1994). Multiple cognitive deficits, including memory impairment that persist in an unchanged form for more than few months, suggest dementia rather than delirium (American Psychiatric Association, 1994). Delirium may coexist with dementia, causing an acute change in symptomatolo

Delirium can be considered a potential medical emergency in elderly individuals. Although delirium may be precipitated by virtually all physical illnesses, it may be the sole manifestation of a life-threatening illness such as sepsis, myocardial infarction, or pneumonia (Inouye, 1994). However, the etiology of delirium remains obscure. There little question that advanced chronological age is implicated in the brain's enhanced vulnerability to delirium (Miller & Lipowski, 1991). The majority of prospective studi have found age to be a significant predictor of delirium (Gustafson, Berggren, Brannstrom, et al. 1988; Marcantonio, Goldman, Mangione, et al. 1994; Rockwood,

1989: Schor. Levkoff. Lipsitz. et al. 1992: Williams. Campbell. Raynor. Musholt. Miynarczyk. & Crane. 1985). Although the reasons why aging predisposes an individ to delirium are poorly understood. deficits in the cholinergic system have been propose as a possible etiologic mechanism (Gibson. Blass. Huang. & Freeman. 1991). Similarl deficits in the cholinergic system may underlie the increased risk of delirium seen in individuals with cognitive impairment. However. delirium is not considered a normal aspect of aging.

Although delirium may occur in community populations. studies indicate that th prevalence is low. In a random sample of individuals 55 years of age and older (n=81(six persons received a diagnosis of delirium (Folstein. Bassett. Romanoski. & Nestadt. 1991). In contrast. prospective studies have identified the prevalence of delirium in hospitalized populations from .1% to 33%. while incidence ranged from 7% to 52%. variation in rates for elderly individuals within hospitals may be related to differences case ascertainment. diversity of settings and differences in patient selection criteria (e.g age, cognitive impairment). Delirium. therefore. appears to both precipitate and be precipitated by institutionalization. Given the progressive aging of the population. it is probable that the incidence of delirium in a hospitalized population will increase.

Prospective studies have identified a variety of host risk factors (intra-individual for delirium. including age and cognitive impairment. Although knowledge of some h risk factors may assist health care professionals to identify individuals at risk of deliriu such knowledge does not assist efforts to prevent delirium. One area that has not recei much attention is the role of environmental risk factors. those factors that occur during

hospitalization and are external to the individual. Medication use is the only consisten environmental risk factor examined in prospective studies. Findings have been inconsistent. implicating a number of medication classes. However. environmental factors other than medications may play a significant role in precipitating delirium. Fo example. admission to an acute care facility, with a concomittant decreased contact wi family or familiar persons. may place an individual at greater risk for delirium. The la of research on environmental risk factors is an important omission in research as environmental risk factors may be more easily amenable to intervention than host fact

Once delirium occurs. the consequences for the hospitalized elderly may be far reaching. Outcomes commonly attributed to delirium include increased morbidity and mortality, as well as an increased length of stay (Levkoff, Evans, Liptzin, et al. 1992). Close nursing and medical surveillance is required as delirious individuals may be at higher risk for injuries to self and others due to their mental impairment and perceptua disturbances. Increased duration of hospital stay and the increased attention required l to an increased health care cost. Yet the findings from prospective studies regarding t outcomes have been inconsistent. The variation in findings related to the negative consequences or outcomes of delirium may be attributed to the lack of control for potentially confounding or extraneous variables.

Less tangible, and yet perhaps the more important consequences of delirium incl the impact on quality of life and the adverse effects on significant others. Family members may become distraught if they mistake the sympromts of delirium for demen Similarly, when delirium is superimposed on dementia, family members may conclud

that the dementia is rapidly progressing, and decide to prematurely institutionalize an individual. An increased risk of institutionalization has been identified in a number of prospective studies (Marcantonio, Goldman, Mangione, et al. 1994; Francis, Martin, & Kapoor, 1990). Clearly, the accurate assessment of outcomes associated with delirium a meaningful undertaking.

The personal and economic costs of delirium combine to signify the importance continued research in this area. However, previous research was characterized by a number of limitations. First, previous studies of risk factors are limited by methodological weaknesses such as inclusion of prevalent cases, and by a focus on ho factors only. Second, prospective studies have been mainly conducted in an acute care environment, and yet many of the risk factors identified in previous research have a hi prevalence in chronic care hospitals. Thus, findings from studies conducted in acute c may not be generalizeable to chronic care. Third, studies examining the consequences delirium have been limited by inadequate control of confounding or extraneous variab

The primary purpose of Study One was to identify environmental risk factors tha are amenable to intervention while controlling for known risk factors for delirium. Th secondary purpose of Study One was to identify outcomes associated with delirium during hospitalization or at discharge. The study was conducted with individuals 65 y of age and older admitted to an acute care facility.

The primary purpose of Study Two was to estimate the prevalence of delirium in chronic care population and identify possible risk factors for consideration in future prospective studies. The secondary purpose of Study Two was to assess the research

utility of assessing delirium using a comprehensive patient assessment tool mandated fo

chronic care patients in Ontario.

Chapter 2. Literature Review

This chapter reviews the following: synonyms of delirium: diagnostic criteria f delirium: differentiation of delirium. depression and dementia: and the etiology of delirium. The following will be reviewed as background information for Study One: instruments used in the detection of delirium: the prevalence. incidence and onset of delirium; and predictors and outcomes of delirium for the hospitalized elderly. In this review, risk factors are divided into two main categories: host factors that are internal the individual; environmental factors that occur during hospitalization and are externa the individual.

2.1 Synonyms for Delirium

Many labels have been used to describe delirium (Table 1). Acute confusional state, organic brain syndrome (OBS) and acute cerebral insufficiency all represent the same diagnostic category. Currently, the diagnostic labels "acute confusional state" a "delirium" are the most frequent designations. The American Psychiatric Association adopted the term "delirium". Their rationale is that confusion. defined as a loss of one capacity to think with usual clarity and coherence, can be associated with several diffe psychiatric syndromes, and is therefore not helpful in developing a diagnostic or treatment plan (Lipowski. 1983). The term delirium will be used throughout this thesi

2.2 Criteria for Delirium

Although there is general agreement on the types of symptoms that characterize delirium, agreement on what combination of symptoms is required for a diagnosis, an how to measure these symptoms has evolved more slowly. In particular, consensus of

Table 1
Synonyms for Delirium

Synonyms for Delirium

Acute brain failure	Exogenous psychoses
Acute brain syndrome	Metabolic encephalopathy
Acute cerebral insufficiency	Pseudosenility
Acute confusional state	Reversible cognitive dysfunction
Acute mental status change	Reversible dementia
Acute organic psychosis	Reversible toxic psychosis
Acute organic reaction	Subacute befuddlement
Acute organic syndrome	Toxic confusional state
Agitated confusional state	Toxic delirious reaction
Altered mental status	Toxic encephalopathy
Cerebral insufficiency syndrome	Toxic-metabolic encephalopathy
Dysergastic reaction	Toxic psychosis

Reference: Francis, J. & Kapoor, W. (1990). Delirium in hospitalized elderly. Journal of General Intern Medicine, 5, 65-79.

opinion on the features that should be considered essential to the diagnosis and those that are secondary has been difficult to reach. The criteria developed by the American Psychiatric Association (APA) will be reviewed as this source is grounded in empirical research and was developed for clinical and research purposes. The following provides a brief description of the criteria that have evolved over time to culminate in the present criteria provided in Diagnostic and Statistical Manual (DSM) IV (American Psychiatric Association. 1994).

Statistical information on mental illnesses has been collected for some time. In the United States, an "idiocy/insanity" category was included in the 1840 census. The International Statistical Classification of Diseases and Related Health Problems (ICD) manual was developed to delineate categories that facilitate the collection of basic health statistics; therefore, diagnostic criteria were not included. It was not until 1952 that an official manual with a focus on clinical utility was developed for mental disorders. The APA published the Diagnostic and Statistical Manual (DSM) in an attempt to provide a standard classification of abnormal behaviour. The diagnostic criteria were developed by clinical consensus and evolved as knowledge from empirical research increased. Development of DSM occurred in tandem with development of the ICD. The DSM contained a glossary of descriptions of the diagnostic categories of mental disorders. The term "reaction" was used throughout the manual and reflected the influence of Meyer's psychobiological view that mental disorders represent reactions of the personality to psychological, social, and biological factors (American Psychiatric Association. 1994).

The next version. DSM II did not differ greatly from the first version except for the elimination of the term reaction. A number of important methodological innovations were introduced with the publication of DSM-III. including explicit diagnostic criteria. multiaxial system. and a descriptive approach that attempted to be neutral with respect theories of etiology (American Psychiatric Association. 1994).

Each version of DSM has contained slightly different criteria for a diagnosis of delirium (Appendix A). This refinement of criteria reflects the increased empirical evidence available to the consensus groups. The major DSM-III criterion for defining delirium was a "clouding of consciousness" (American Psychiatric Association. 1980). Operational criteria for symptoms were lacking in this version. thus it is not known exactly what "clouding of consciousness"entailed. DSM-III-R (American Psychiatric Association. 1987) attempted to provide some operational criteria for symptoms by including specific examples. It also redefined the core features of the syndrome. "Clouding of consciousness" in DSM-III was redefined in DSM-III-R as a reduced leve of consciousness, and became one of six criteria of which at least two had to be present (Liptzin, Levkoff, Cleary, et al. 1991). Disorientation and memory impairment were nc longer core criteria, as they had been in DSM-III (Liptzin, Levkoff, Cleary, et al. 1991) The major core criterion now became "attention". Literature reviews and studies usin successive versions of the DSM demonstrated the ambiguity of the criteria developed fc delirium, with practitioners and researchers experiencing considerable difficulty in attributing specific symptoms to delirium alone (Tucker. 1991). The most recent versic DSM-IV, specifies core criteria only, thus simplifying the diagnosis (American

Psychiatric Association. 1994). The criteria of acute onset and fluctuating course have remained constant throughout the revisions.

These DSM revisions contribute to the methodological difficulties associated with comparing studies over time. Albert et al. (1992) argue that the revisions do not substantially change the symptoms considered to be part of delirium. Unfortunately, however, cases of delirium detected by instruments based on the DSM-III criteria may differ from those detected by instruments based on later revisions. The additional criteria specified in DSM-III and DSM-III-R may make it more difficult to meet the full criteria and thus many cases of "partial" delirium may result. In a sample of 325, one hundred and ten patients experienced some symptoms of delirium without meeting the full criteria when assessed using a tool based on DSM-III criteria (Levkoff, Evans, Liptzin, et al. 1992). Liptzin et al (1991) found the DSM-III-R criteria more restrictive than the DSM-III criteria, with 125 patients meeting DSM-III criteria and only 106 meeting DSM-III-R criteria. This difference was partially accounted for by seven patients who spoke very little and could not be rated on the DSM-III-R criterion of disorganized thinking. Combined, these studies highlight the difficulty of comparing studies based on differing criteria.

In the development of a diagnostic algorithm for delirium, Inouye et al. (1990) retained only four of the nine elements of the DSM-III-R criteria because the remaining five clinical features did not increase the sensitivity or specificity of the instrument when compared to psychiatrists ratings. The four key elements identified include (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered

level of consciousness. These key elements are represented in the most recent version of DSM. the fourth edition. The essential feature of delirium is defined as a disturbance of consciousness that develops over a short period of time and tends to fluctuate during the course of the day. The disturbance includes a change in cognition. or the development of a perceptual disturbance that is not accounted for by dementia (American Psychiatric Association. 1994).

Summary.

In summary, although the criteria for delirium have evolved over the past few decades. the key features of acute onset and fluctuating course have remained constant throughout. The most recent criteria for delirium in DSM-IV contains core criteria only, thus eliminating much of the concern over specific elements.

2.3 Differentiating Delirium, Depression and Dementia

Delirium, depression & dementia represent three distinct diagnostic entities, and y overlapping symptomatology may lead to misdiagnosis. The treatment modalities required for each are very different, and thus it is important to accurately diagnose each condition. Further, depression and dementia have been implicated as risk factors for the development of delirium, and therefore are important to assess for research purposes.

Delirium is commonly thought of as a hyperactive-hyperalert form with visible confusion and agitation; however, elderly patients in particular may also exhibit a hypoactive-hypoalert form of delirium (Farrell & Ganzini. 1995). This hypoalert form is characterized by withdrawal, listlessness and quiet confusion, leading clinicians to conclude the patient is depressed. To illustrate, in those patients referred to a psychiatric

consultation-liason service with depressive symptoms. 6% received a final diagnosis of delirium. Patients with delirium were older than those diagnosed with depression. and more likely to be male (Nicholas & Lindsey. 1995). Distinguishing depression from delirium requires a careful history, including a family interview to ascertain duration of symptoms. The presence or absence of a psychiatric history is important. Major psychiatric disorders rarely develop in patients older than 40 (Dubin. Weiss. & Zeccard 1983). Further. while some symptoms such as sleep disturbances and psychomotor abnormalities are common to both delirium and depression, depression differs from delirium in that attention and cognitive disturbances are not pronounced. onset is more gradual. perceptual disturbances are uncommon. and the patient is alert (Farrell & Ganzini. 1995). Thus, the clinician must assume delirium when an elderly patient exhibits an acute change in cognitive status.

Delirium can also be differentiated from dementia. Like delirium. dementia may have prominent memory and cognitive deficits, but there is an insidious onset and chror course and it is stable over short periods of time. Individuals with dementia remain attentive and aware of their environment until very advanced stages, whereas a change i attention is a key feature of delirium. Delirium superimposed on dementia may result i what has been called "reversible dementia' wherein improvement in cognition occurs when the precipitants of delirium are treated (Francis & Kapoor. 1990).

Summary.

In summary, although delirium, depression and dementia share a number of symptoms, there are key features that differentiate delirium. Acute onset, changes in

attention and consciousness. and possibly perceptual disturbances are apparent in the delirious individual.

2.4 Etiology of Delirium

The etiology of delirium in the elderly is believed to be complex and multifactori involving the interaction of environmental factors superimposed on a vulnerable patien (Inouye. 1994). An important consequence of this etiological model is the possibility c intervening in order to prevent delirium. The precise processes by which delirium is mediated are unknown. As there appears to be heterogeneity within the diagnosis of delirium. it may be that different forms of delirium have specific molecular and anatom perturbations (Ross & Nisbett. 1991). This heterogeneity was exemplified in a study examining subtypes of delirium. Liptzin & Levkoff (1992) classified patients with delirium into three subtypes; hyperactive, hypoactive & mixed. The majority of patien (52%) were of the mixed type, consistent with the fluctuating criteria for delirium (Liptzin & Levkoff. 1992). They suggest. however, that hyperactive and hypoactive m not be distinct subtypes, but an interaction with physical well being. Those patients wh are physically well become agitated, in contrast with those who are physically ill and become lethargic (Liptzin & Levkoff. 1992). It is intriguing that hospitalized patients with hyperactive delirium had a length of stay comparable to individuals who did not experience delirium, and lower rates of in-hospital and six month mortality (Liptzin & Levkoff. 1992). Unfortunately, however, potential confounders for length of stay and mortality, such as severity of illness and physical function, were not controlled in this study.

Although a syndrome as clinically diverse as delirium might be expected to hav multitude of putative neurochemical mechanisms, only a few etiologic hypotheses ha been advanced. Aging in general, deficits in the cholinergic system in particular, and reduction in plasma tryptophan have been cited as contributing to the etiology of delirium. The following theories represent the current state of thinking regarding the etiology of delirium.

There is generally consistent support for the effect of age on the development of delirium (Gustafson, Berggren, Brannstrom, et al. 1988; Marcantonio, Goldman, Mangione, et al. 1994; Rockwood, 1989; Schor, Levkoff, Lipsitz, et al. 1992; William Campbell, Raynor, Musholt, Miynarczyk, & Crane, 1985). Little is known, however, about the changes with age in the systems thought to play a role in delirium. Several neurobiological processes may be involved. On a general level, the aging brain appea lose redundancy. As a result, relatively mild physiological insults may lead to the impairment of brain functioning that crosses the threshold into a clinically significant disability (Blass, Nolan, Black, & Kurita, 1991). Visual and hearing problems may re in sensory degradation, diminishing the quantity and quality of information received f the environment, and facilitating cognitive disorganization. Although the effects of a on drug metablism are complex and difficult to predict, there is evidence that the first phase of drug metabolism declines with increasing age, and may render the elderly m susceptible to drug-induced delirium (Kane, Ouslander, & Abrass, 1994).

Certain parts of the brain on whose integrity normal cognitive processes depend also susceptible to aging and show selective cell loss. There is loss of cells and reduc

in the dendritic tree in the cerebral cortex (Lipowski. 1983). The frontal cortex. hippocampus. and locus ceruleus are among the structures selectively involved (Lipowski. 1983). Destruction of locus ceruleus. or raphe nuclei. or both. has been blamed for the occurrence of nocturnal delirium in demented elderly patients (Lipowsk 1983). The normal elderly show reduction of cerebral blood flow and glucose metabolism. changes that are much greater in the presence of even mild and asymptomatic arteriosclerosis and are most pronounced in senile dementia (Lipowski. 1983). An inadequate supply of oxygen and glucose to the brain to meet the demands neuronal cells is hypothesized to be a common cause of delirium (Blass. Nolan. Black. Kurita. 1991).

Yet, the most compelling etiologic hypothesis is the anticholinergic hypothesis. The cholinergic system is known to be affected by aging, and even more so by degenerative brain disease (Antuono. 1995; Locascio. Growdon, & Corkin. 1995). Adequate functioning of the cholinergic system is needed for normal memory, learning attention, wakefulness, and the sleep-wake cycle. Deficiency in this system is therefor likely to be a predisposing factor for delirium. Animal and human studies support the hypothesis that deficits in the cholinergic system underlie many of the changes seen in delirium and Alzheimer's disease, particularly the diminished memory (Gibson, Blass, Huang, & Freeman. 1991). Anticholinergic medication intoxication can produce behavioral and electroencephalographic (EEG) changes consistent with delirium. Thes changes can be reversed with cholinesterase inhibitors such as physostigmine or tertrahydroaminoacridene (Francis & Kapoor. 1990). Case reports exist of individuals

who consumed large doses of anticholinergic medications and subsequently presented with delirium (Bernstein & Leff. 1967; Brizer & Manning. 1982). In clinical studies. higher serum anticholinergic activity has been reported in surgical patients who developed postoperative delirium (Tune. Holland. Folstein. Damloch. Gardner. & Coyl 1981: Golinger. Peet. & Tune. 1987). It is important to note. however. that there is a lo correlation of the actual dose of anticholinergic drugs with serum activity (Francis & Kapoor. 1992).

These findings have led to the hypothesis that anticholinergic medications may pl a significant role in the development of delirium. The risk of anticholinergic toxicity is high in the elderly as many medications have such activity including antipsychotics, antidepressants, anti-Parkinsonian agents, sedatives, hypnotics and antihistamines. Anticholinergic drugs are readily available over the counter as cold remedies, allergy formulations and sleeping pills. In addition, many drug classes not ordinarily viewed a anticholinergic binding can produce delirium that is reversible with physostigmine (Francis & Kapoor. 1990). Examples of such drugs include meperidine (Demerol), and Histamine$_2$ receptor antagonists, cimetidine and ranitidine (Francis & Kapoor. 1990).

Recently, a reduction in plasma tryptophan has been hypothesized as a contributi factor in the risk of post-operative delirium (Van der Mast, Fekkes, Moleman, & Pepplinkhuizen. 1991). Surgery, particularly after a prolonged illness, induces a catabc state. Plasma aminoacids in seven postcardiotomy delirious patients were compared wi two control groups (surgical and healthy). The mean plasma tryptophan concentrations were significantly lower in the delirious group than the two control groups (Van der Ma

Fekkes. Moleman. & Pepplinkhuizen. 1991). Tryptophan is the precursor of serotonin. Serotonin is a neurotransmitter involved in functions such as aggressive and impulsive behaviour. mood. motor activity and sleep. The amount of functional serotonin in the central nervous system is dependent on such factors as the transport of its precursor tryptophan across the blood-brain barrier. Van der mast et al. (1991) hypothesize that a catabolic state may reduce the transport of tryptophan because aminoacids that compete with tryptophan (i.e., valine. isoleucine. leucine. tyrosine. phenlalanine) for the transpor carrier at the blood-brain barrier are increased due to degradation of muscle proteins. Further. the concentration of tryptophan may be reduced because of induction of tryptophan pyrrolase (Van der Mast. Fekkes. Moleman. & Pepplinkhuizen. 1991). This theory of increased competition for the transport-carrier by competing amino-acids has recently been challenged. as the delirious and control groups did not differ in the circulating levels of these amino acids (Badawy. 1991). Others have suggested the decreased tryptophan concentrations may be due to immunostimulation caused. for example. by blood transfusions (Weiss. Werner. Werner-Felmayer. & Wachter. 1991). The role and impact of reduced tryptophan availability on the development of delirium remains unclear; however. replication of the study with larger groups of patients is warranted.

Summary.

Our present understanding of the etiology of delirium remains far from complete. Changes associated with aging, compounded by additional factors such as a high frequency of disease and prevalence of chronic diseases among the elderly, appear to

contribute to the increased risk of delirium in this age group. It is apparent, however, that many of these changes are not currently amenable to intervention. Thus, a focus o environmental risk factors could be the most worthwhile pursuit for an immediate imp

2.5 Detection of Delirium

The diagnosis of delirium is a clinical one that is based on direct observation of t patient, collateral sources of information, awareness of the patient's baseline mental st and current physical problems. Incorporating formal mental status testing into an evaluation may uncover subtle disturbances of attention, orientation and memory that might otherwise be missed (Kane, Ouslander, & Abrass, 1994).

Efforts to detect delirium have been hindered by several factors, including the fluctuating nature of delirium, the wide variety of clinical features (hyperactivity to hypoactivity), the importance of history to ascertain duration, and the wide variety of diseases and conditions that predispose an individual to delirium.

Researchers have used a variety of instruments to detect delirium. The primary methods have been the same ones used in the detection of cognitive impairment. Ment status questionnaires such as the Mini Mental State Examination (MMSE) have been found to be useful screens for dementia or delirium, but limited in the ability to yield a differential diagnosis between these conditions (Anthony, LeResche, Niaz, Vonkorff, & Folstein, 1982). While cognitive impairment is *necessary* for the diagnosis of delirium is not *sufficient*. Thus, use of a mental status questionnaire alone is not sufficient to differentiate between acute and chronic impairment. Core features of delirium, such as fluctuating behaviour, ability to maintain attention, and perceptual disturbances are not

tapped by such questionnaires (Levkoff. Liptzin. Cleary. Reilly. & Evans. 1991). An additional difficulty is that many delirious patients are not able to respond to the questio contained in a mental status questionnaire and must be assessed by observation.

The clinical interview remains the method most widely relied upon to detect delirium in research studies (Levkoff. Liptzin. Cleary. Reilly. & Evans. 1991). Unfortunately, observation bias is introduced by subjective opinions from clinical interviews. Unless an objective, formal method of assessment is undertaken. many episodes of delirium may be missed. For example, in a sample of 50 patients meeting DSM III-R criteria for delirium. there were 121 episodes of acute confusion (Francis. 1992). Physicians noted the confusion 61% of the time while nurses noted the confusio 74% of the time. It is not known how many of the 50 patients were diagnosed with delirium using a combination of medical records and nursing notes; however, in 22 episodes, only the nurse documented confusion (Francis. 1992). In a comparison of dail progress notes versus psychiatric interview results, it was found that physicians and nurses missed 28% of patients with postoperative delirium (Gustafson, Brannstrom, Norberg, Bucht. & Winblad. 1991). Diagnosis of delirium was frequently missed on the conventional workup of Emergency Departments, in that only 17% of delirium cases we properly diagnosed (Lewis, Miller, Morley, Nork, & Lasater. 1995). One hundred and thirty three consecutive admissions to an acute medical ward were assessed. Fifteen cas of delirium were diagnosed, but only one of these had been detected by the admitting physician. Thus, the standard clinical assessment or a review of medical records alone does not appear to be an effective case-finding method.

Since the publication of DSM-III criteria, studies typically have relied on this or DSM-III-R criteria; however, few studies have operationalized these criteria. In order to be useful in the diagnosis of delirium, a diagnostic instrument should be:

1. validated specifically for use in delirium;
2. capable of distinguishing delirium from dementia;
3. capable of assessing the multiple features of delirium;
4. feasible to use with delirious patients (Inouye, 1994).

Three published instruments developed to identify delirium fulfil this criteria - the Confusion Assessment Method (Inouye, VanDyck, Alessi, Balkin, Siegal, & Horwitz, 1990), the Delirium Rating Scale (Trzepacz, Baker, & Greenhouse, 1988), and the Delirium Symptom Interview (Levkoff, Liptzin, Cleary, Reilly, & Evans, 1991). These instruments will be examined in further detail. Two measures of the validity of a screening measure, sensitivity and specificity , will be described. Sensitivity is defined a the probability of being classified as delirious if delirium is truly present. Specificity is the probability of not being classified as delirious when delirium is absent.

The Confusion Assessment Method (CAM).

The CAM instrument consists of nine operationalized criteria from DSM-III-R. Some of the interview questions were designed to be answered on the basis of interviewers observations; therefore, a patient who is too sick or non-communicative can also be assessed through these behavioral observations. The CAM can be completed in less than five minutes, based on information obtained from the interview, a review of the

medical records. and an interview with the primary nurse. Although based on DSM-III-criteria. the CAM agrees closely with the current DSM-IV criteria.

The CAM was validated for use by physicians. although it is suggested that a trained lay or clinical interviewer can use the tool (Inouye. 1994). Subsequent studies used a trained lay interviewer (Marcantonio. Goldman. Mangione. et al. 1994) and train clinicians (Inouye. Viscoli. Horwitz. Hurst. & Tinetti. 1993). The prospective validatio study of the CAM was conducted in general medicine wards and an outpatient geriatric assessment center. Fifty six subjects were included. ranging in age from 65 to 98 years. The CAM was found to have a high sensitivity (100%. 94%) and specificity (95%. 90% in both settings when compared with psychiatrists ratings (Inouye, VanDyck. Alessi. Balkin. Siegal. & Horwitz. 1990). Convergent validity was established by comparing CAM ratings with the Mini Mental State Exam ($k = 0.59$), the Visual Analog Scale for Confusion ($k = 0.82$) and the digit span test ($k = 0.66$) (Inouye, VanDyck.Alessi, Balkin Siegal, & Horwitz. 1990). The lack of complete agreement reflects the fact that the CA measures aspects of delirium that are not tapped by the other indexes. Interobserver reliability was evaluated for 19 paired assessments. There was 100% agreement for the presence of absence or delirium. Inter-observer reliability of the CAM was tested in a separate study of surgical patients. Two independent investigators agreed on the presen or absence of delirium according to the CAM algorithm in 85 of 86 patients tested (k=0.90) (Marcantonio, Goldman, Mangione, et al. 1994).

The Delirium Rating Scale (DRS).

The DRS is a 10 item scale validated for use by psychiatrists. Information availa from the patient interview. mental status examination. medical history. laboratory tests nursing observations. family reports and other information is used to complete the tool (Trzepacz. Baker. & Greenhouse. 1988). Compared to patients with dementia. schizophrenia and normal control groups. 20 patients with delirium scored significantly higher on the DRS (Trzepacz. Baker. & Greenhouse. 1988). Unfortunately, the scoring relies on skilled clinical judgments based on unstructured clinical assessments from multiple sources. making the tool difficult to standardize and expensive to administer.

The Delirium Symptom Interview (DSI).

The DSI is a tool based on approximately seventeen questions for the patient interview followed by the same number of questions to be completed by the research assistant following the interview. The DSI has been validated for use by a trained non-clinical interviewer. The DSI can be administered to a noncommunicative patient. an advantage many screening tests do not share (Levkoff. Liptzin. Cleary, Reilly, & Evan 1991). The DSI was found to be highly sensitive (90%) and specific (80%) in a sampl 50 patients when compared with assessments by a geriatric psychiatrist and a neurolog (Levkoff, Liptzin, Cleary, Reilly, & Evans. 1991). Interrater reliability with trained research assistants was high ($k=0.90$). The DSI is lengthy and detailed.

Summary.

In summary, there are three delirium assessment tools with evidence of psychometric reliability and validity. The DRS requires extensive resources, and is ba

on unstructured assessments. The CAM and DSI are standardized, easy to administer, and require approximately 5 to 15 minutes respectively to complete. In addition, the CAM fulfils the requirements for DSM-IV.

2.6 Prevalence, Incidence & Time of Onset of Delirium in the Hospitalized Elderly

Despite the number of studies undertaken, the incidence and prevalence of deliriur in the hospitalized elderly remains unclear. Prevalence quantifies the proportion of individuals in a population who have the disease at a specific point in time (Hennekens & Buring, 1987). In this case, prevalence is defined as those individuals experiencing delirium on admission to hospital. In contrast, incidence is the number of individuals without delirium on admission who go on to develop delirium at some point while in hospital. In prospective studies, prevalence of delirium in hospitalized populations ranged from .1% to 33% while incidence ranged from 7% to 52%. The variability regarding prevalence and incidence estimates can be related to imprecise diagnostic criteria, differing patient populations and different inclusion and exclusion criteria. Give the possible influence of these factors on the risk of delirium, it is not surprising that a range of prevalence and incidence rates are reported. The influence of these factors on th prospective studies that have been undertaken will be described. Prevalence and incidence rates, study population, study duration, age, and cognitive impairment status o patients in the prospective studies that have been undertaken are shown in Table 2.

Imprecise diagnostic criteria.

The imprecision in diagnostic criteria is related to the use of instruments to detect delirium that have not been validated for delirium. Most studies do not specify

Table 2

Prevalence and Incidence Rates of Delirium

Investigator	Population	Sample Size	Age	Study Duration (months)	Incidence	Prevalence	Cognitiv Impairm
Inouye & Charpentier (1996)	Medical	n=196	≥ 70 yrs	8	18%	5%	Yes
O'Keeffe & Lavan (1996)	Acute Geriatric Unit	n=100	*NS	18	28%	18%	Yes
Pompei et al. (1994)	Medical. Surgical	n=432	≥ 65 yrs	20	10%	5%	No
Marcantonio et al. (1994)	Surgical	n=876	≥ 50 yrs	17	9%	0.1%	No
Inouye et al. (1993)	Medical	n=107	≥ 70 yrs	10	25%	*NS	Yes
Rockwood (1993)	Geriatric Assessment Unit	n=168	*NS	12	7%	18%	Yes
Schor et al. (1992)	Medical/Surgical	n= 291	≥ 65 yrs	24	31%	10.5%	Yes
Williams-Russo et al. (1992)	Surgical	n=51	75% were ≥ 65 yrs	7	41%	*NS	No
Francis et al. (1990)	Medical	n=229	≥ 70 yrs	12	6%	15.7%	Yes
Johnson et al. (1990)	Medical	n=235	≥ 70 yrs	8	5%	16%	Yes
Foreman (1989)	Medical	n=71	≥ 60 yrs	*NS	38%	*NS	No
Rockwood (1989)	Medical	n=80	≥ 65 yrs	6	9%	16%	Yes
Rogers et al. (1989)	Orthopedic Surgery	n=46	≥ 60 yrs	17	28%	*NS	No
Gustafson et al. (1988)	Orthopedic Surgery	n= 111	≥ 65 yrs	15	28%	33%	Yes
Erikinjuntti et al. (1986)	Medical	n= 2000	≥ 55 yrs	15	*NS	15%	Yes
Williams et al. (1985)	Orthopedic Surgery	n= 170	≥ 60 yrs	24	51.5%	*NS	No

*NS= not specified

operational criteria for delirium. and those that do so use clinical interviews (Cameron. Thomas. Mudvihill. & Bronheim. 1987: Erkinjuntti. Wikstrom. & Palo. 1986: Francis. Martin. & Kapoor. 1990: Johnson. Gottlieb. Sullivan. et al. 1990: Rockwood. 1989) or clinician-rated scales (Trzepacz. Baker. & Greenhouse. 1988: Williams. Campbell. Raynor. Musholt. Miynarczyk. & Crane. 1985) that often lack standardization and may difficult to replicate. In one study, any error on the MMSE was considered evidence of potential impairment (Francis. Martin. & Kapoor. 1990). Similarly, 51.5% of patients undergoing orthopedic surgery evidenced "some" confusion post-operatively and were classified as delirious(Williams. Campbell. Raynor. Musholt. Miynarczyk. & Crane. 1985). Patients who were not able to state the exact date were included within this category. There was a 28% incidence of delirium in a study of elective orthopedic surgical patients (Rogers, Llang, Daltroy, et al. 1989). This included patients who wok up during the night and believed they were in a different place or situation for five to te minutes (Rogers, Llang, Daltroy, et al. 1989). The criteria used in these three studies would serve to elevate the estimate of incident delirium.

Differences in study populations.

Some of the differences in incidence and prevalence may be attributed to the population studied. For example, higher prevalence rates of delirium may be found in patients referred to psychiatry . However, due to the possibility of a referral bias inher in consultation service studies, an accurate denominator for calculating incidence and prevalence cannot be established.

Other studies with highly defined patient populations may be expected to have diverse estimates of prevalence and incidence compared with a more general medical surgical population. For example. 28% and 30% of patients admitted to an acute-care geriatric unit developed incident delirium (O'Keeffe & Lavan. 1996). Although this incidence appears high. only those who were frail and dependent in activities of daily living were admitted to the unit. As severity of illness and decreased activities of dail living scores have been found to be important risk factors in some studies (Francis. Martin, & Kapoor. 1990; Inouye, Viscoli. Horwitz. Hurst. & Tinetti. 1993), this may serve to elevate the incidence of delirium.

An incidence of 41% was found in patients undergoing bilateral knee replaceme surgery. This surgery is very lengthy, and associated with high postoperative pain anc morbidity (Marcantonio, Goldman, Mangione, et al. 1994) and thus may be different f findings in a general surgical population. Further, at least four patients were diagnose delirious in the recovery room immediately following surgery. More conservative stu of surgical patients did not assess for delirium for a minimum of eight hours post-operatively (Gustafson, Berggren. Brannstrom, et al. 1988; Marcantonio. Goldman. Mangione, et al. 1994; Rogers, Llang, Daltroy, et al. 1989) due to the effect of anesthe

Variations in inclusion and exclusion criteria.

Inclusion and exclusion criteria vary widely between studies. A combination of factors in the inclusion and exclusion criteria may influence the estimates of incidence and prevalence. In a study of elective surgical patients, individuals with cognitive impairment were excluded from the study (Marcantonio, Goldman, Mangione, et al.

1994). As cognitive impairment is a well-known risk factor for delirium, this criteria would decrease the incidence of delirium. In addition, patients were 50 years of age and older. Thus, the younger age groups would contribute to the denominator and yet, with such a low incidence, are not "at high risk". Further, emergent and urgent cases were excluded. This may exclude individuals with higher comorbid diseases or severity of illness, factors that have been found significant in some studies (Francis, Martin, & Kapoor, 1990; Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993; O'Keeffe & Lavan, 1996), thus lowering the incidence of delirium. Combined, these factors may explain the low (9%) incidence of delirium found in this study.

Other studies have included admissions from community only (Francis, Martin, & Kapoor, 1990), and thus may have lower rates. Two studies have included patients known to abuse alcohol, and can be expected to have a higher incidence rate of delirium related to the effects of alcohol withdrawal, often called "delirium tremens"(Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel, 1994; Williams-Russo, Urquhart, Sharrock, & Charlson, 1992).

One study is remarkable in that the definition of prevalent cases of delirium was notably different from all other studies. In this case, prevalence was defined as the number of patients developing delirium in the 72 hours following admission (Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel, 1994). Delirium is known to develop in the first few days of hospitalization, and therefore this definition would serve to elevate the prevalence and decrease the incidence.

Any combination of these factors may affect the prevalence and incidence rates found. Other factors, such as the high refusal rates noted in some studies (Johnson, Gottlieb, Sullivan, et al. 1990; Rogers, Llang, Daltroy, et al. 1989) decrease the generalizability of the findings. Further, a bias may be introduced as all studies have bee conducted in university teaching hospitals. It may be that these institutions receive cases different from those in a general population. Thus, findings regarding incidence and prevalence may not reflect those that would be found in a community based acute care facility. Given these limitations, the range of estimates for prevalence and incidence mu be viewed with some caution.

Onset of delirium.

When incident delirium does occur, the risk appears to be greatest in the first few days following hospitalization. Thus, risk of delirium in the hospitalized population decreases over time. Median onset for delirium following hospitalization was 4 and 6 days for patients admitted to a medical unit (Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993). Eighty three percent and 72% of patients admitted to a geriatric assessment unit and developing delirium met the diagnostic criteria for delirium within five days (O'Keeffe & Lavan, 1996). For patients admitted for elective surgery and experiencing delirium, 81% were diagnosed by day 3 in a surgical population (Marcantonio, Goldman Mangione, et al. 1994).

2.8 Predictors of Delirium: Overview & Methodological Limitations

Despite substantial variation in methods and terminology, there is some agreement concerning risk factors for delirium. Advanced age and pre-existing underlying

cognitive impairment have consistently been identified as risk factors for delirium. However, the majority of studies have important methodologic limitations for identifyin the risk factors. These include failure to separate prevalent cases from incident cases. retrospective design, imprecise diagnostic criteria, small sample size, referral bias, limitations associated with analytical technique, and confounding by indication. Although some of these limitations have influenced prevalence and incidence estimates and have been described previously, the importance of these limitations to the examination of risk factors for delirium will be discussed.

Separating incidence from prevalence.

A number of investigators examining risk factors for the development of delirium did not separate incident cases from prevalent cases (Gustafson, Berggren, Brannstrom, al. 1988; Francis, Martin, & Kapoor. 1990; Rockwood. 1989; Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel. 1994). Prevalence quantifies the proportion of patients who have delirium at a specific point in time (i.e., on admission) whereas incidence quantifies the number of new cases of delirium that develop over a specified time interval (i.e., following admission and until discharge or study end). The separatio of cases of incident delirium and cases of prevalent delirium is essential in order to evaluate the temporal sequence of the risk factors in relation to the onset of delirium. That is, does the risk factor precede the development of delirium, or is it an outcome of delirium? For example, although forced immobility through the application of restraints may increase the risk of delirium, restraints may be applied as a result of a delirious

episode. A number of examples from delirium studies serve to further illustrate this point.

In a study of medical patients, those individuals with delirium on admission wer found to have fluid and electrolyte imbalances which physicians believed to contribute 40% of the etiology of delirium (Francis, Martin, & Kapoor, 1990). This factor apparently did not contribute to the development of delirium during hospitalization. T fluid and electrolyte imbalance may be as a result of delirium. In another study combining individuals with incident and prevalent cases of delirium, the use of a urina catheter was thought to be an outcome of delirium (Gustafson, Berggren, Brannstrom, al. 1988). Temporal sequence is essential, however, as underscored by the findings of study using incident cases only. In this study population, urinary catheters were found be a risk factor for the development of delirium (Inouye & Charpentier, 1996).

Retrospective design.

Similar to the limitations noted with prevalent and incident cases, studies based retrospective design share the lack of ability to evaluate temporal sequence. In additio when a chart audit is used to determine the outcome (Levkoff, Safran, Cleary, Gallop, Phillips, 1988), the identification of delirium cases will usually be low, as delirium oft goes unrecognized by health care professionals (Francis, 1992; Gustafson, Brannstrom Norberg, Bucht, & Winblad, 1991).

Imprecise diagnostic criteria.

The imprecision in diagnostic criteria and the lack of well-defined operational definitions for symptoms have resulted in a great deal of variation between studies. A

valid and reliable instrument ensures that delirium is not combined with confusion in general (i.e., dementia). The majority of studies did not use a valid and reliable instrument for the detection of delirium (Foreman, 1989; Francis, Martin, & Kapoor, 1990; Gustafson, Berggren, Brannstrom, et al. 1988; Rockwood, 1989; Rogers, Llang, Daltroy, et al. 1989; Williams, Campbell, Raynor, Musholt, Miynarczyk, & Crane, 198 The use of an instrument with unknown sensitivity and specificity for the detection of delirium may not provide valid results. Some researchers have not used the DSM-III-R criteria as the basis for the detection of delirium, and instead have used instruments designed to detect "confusion" (Foreman, 1989). Scales developed to assess "confusion are limited because they do not address all the symptom domains required for delirium and may include unrelated diagnoses. Investigators that have used DSM-IIIR have developed operation definitions for study purposes. Some of these definitions would appear to be overly stringent. For example, disorientation and memory impairment wer assessed using MMSE, and any errors were considered evidence of potential impairmen (Francis, Martin, & Kapoor, 1990). The effect of this misclassification would be to increase the similarity between the exposed and nonexposed groups so that any true association between exposure and outcome would be underestimated(Hennekens & Buring, 1987). As a result, the observed relative risk estimate may be biased towards th null value of 1.0.

Small sample sizes.

In some studies, small sample sizes preclude the generalizability of findings. Rogers (1989) included 46 patients in a study, with only five patients definitely

experiencing delirium. and eight patients possibly experiencing delirium. Although the findings might be valid for this sample. it would be inappropriate to extrapolate the findings to other populations. Further. it may not be possible to detect a true association due to inadequate power.

Referral bias.

Referral bias is illustrated in a study of 100 cases of delirium referred for psychiatric consultation. In this study, men had an increased frequency of delirium (Sirois. 1988). Two types of referral bias may have occurred in this study. First. the hospital may admit more men than women. and second. males may be referred to a psychiatrist more frequently than females because they may not be so easily controlled if they become aggressive in delirium. Thus, individuals referred to a psychatrist may not be representative of patients in a more general medical or surgical population. and risk factors would not be generalizeable to this population.

Data analysis limitations.

Earlier studies were limited by an inability to control statistically for potential confounders, because sophisticated multivariate data analysis techniques were not used. For example, Wilson (1972) conducted bivariate analysis to determine risk factors for delirium. In a prospective study of 100 patients age 65 years and older admitted to a general surgical unit for elective surgery and assessed by a psychiatrist, factors found significant at a bivariate level included physical complications (i.e., abnormal lab values, cardiovascular problems, respiratory disease, wound infection) , use of morphine, use of intravenous, and insertion of urinary catheters (Millar. 1981). It is quite likely, however,

that not all of these factors would independently increase the risk of delirium when other factors significant at the bivariate level are controlled. A multivariate model allows for the estimation of measures of association while controlling for confounding and extraneous factors simultaneously.

Stepwise regression procedures have been utilized in the majority of prospective studies undertaken to determine risk factors for delirium (Inouye, Viscoli, Horwitz, Hurst & Tinetti, 1993; Inouye & Charpentier, 1996; Marcantonio, Goldman, Mangione, et al. 1994; O'Keeffe & Lavan, 1996; Schor, Levkoff, Lipsitz, et al. 1992; Rogers, Llang, Daltroy, et al. 1989). Caution is necessary when interpreting the results of stepwise solutions. Very slight differences among the correlations between dependent and independent variables can lead to major differences in which variables enter the final model using the stepwise approach. The importance of the variables may not be reflected in the final model obtained.

Confounding by indication.

This is of particular concern in the evaluation of the contribution of medications to the development of delirium. For example, neuroleptics have been found to be a significant risk factor for delirium, and yet physicians may recommend that a delirious patient requires a neuroleptic such as Haloperidol to protect the patients and staff, and to gain control (Barton, 1981). If medication exposure is not limited to those medications given prior to the development of delirium, medications given as a result of delirium may be identified as a risk factor. Antibiotic use provides an interesting situation. If antibiotic use was found to be associated with an increased risk of delirium, it would be difficult to

determine whether the associated infection or the antibiotic led to the increased risk of delirium.

Summary.

In summary, there are a number of methodological limitations associated with the previous studies of delirium. A prospective study, using a valid tool to assess for delirium, with a multivariate model for data analysis provides the strongest evidence concerning risk factors. Therefore, those studies with a prospective design, and utilizin reliable and valid assessment tool will be reviewed in greater detail.

2.9 Predictors of Delirium: Host Factors

Overall, prospective studies examining risk factors for delirium vary considerably in the definitions of delirium, the population studied (e.g., medical or surgical) and the method used for case-finding. Studies have been conducted for both explanatory and predictive purposes. Explanatory designs have described the interrelationships betwee delirium, host and environmental factors. Predictive studies (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; Inouye & Charpentier. 1996; Marcantonio, Goldman, Mangion et al. 1994; O'Keeffe & Lavan. 1996) have developed a prediction "rule" in one group patients and applied it to a separate group to evaluate the predictive ability of the identified risk factors. In these studies, findings from the group the prediction rule was developed from (typically called the derivation or developmental group) will be described. Table 3 describes the prospective studies undertaken to identify risk factors delirium.

Table 3
Prospective Studies of Delirium

AUTHORS	SAMPLE	DELIRIUM INSTRUMENT	ASSESSMENT DURATION	INCIDENCE	RESU
Williams et al. (1985)	Hip fracture patients age ≥ 60 n =170	Clinician Assessment	Postop days 1–5	51.5%	• Age • Poor perfor cognitive te operatively • Low pre-inj level
Gustafson et al. (1988)	Hip fracture patients age ≥ 65 n = 111	Modified Organic Brain Syndrome Scale - "in accordance with DSM-III criteria"	"Several times over 14 days"	*61%	• Age • Dementia
Foreman. M.D. (1989)	Medical patients age ≥ 60 n = 71	Presence of one of any 25 behaviors on the Clinical Assessment of Confusion checklist	daily 8 days	38%	• Hypernatrer • Hypokalem • Hypotensio • Azotemia • High numb medication • High confu nurses • High numb items in env • Low numbe interactions
Rockwood (1989)	Medical patients age ≥ 65 yr n = 80	Glasgow Coma Scale	daily- duration not specified	*25%	• Age • Dementia • Unstable co admission
Rogers et al. (1989)	Hip or Knee surgery age ≥ 60 yr n = 46	DSM III criteria	Post-op days 2, 3, 4, & 7	28%	Use of sco propanolol
Francis. J. (1990)	Medical patients age ≥ 70 yr n = 229	DSM IIIR criteria	Evaluation every 48 hrs. until discharge	*22%	• Abnormal s • Severe illne • Cognitive i • Fever/hypo • Psychoactiv • Azotemia
Schor. J. (1992)	Medical, surgical age ≥ 65 yr n = 291	DSI	daily 14 days	31%	• Age ≥ 80 y • Cognitive i • Fracture on • Institutiona • Neuroleptic • Infection • Narcotic us • Male gende
Williams-Russo, et al. (1992)	Surgical patients Majority ≥ 65 yr n= 51	DSM-111 Criteria	Daily 7 days	41%	• Age • Alcohol use • Male
Inouye, et al. (1993)	Medical patients age ≥ 70 yr n = 107	CAM	Daily Discharge	25%	• Vision imp • Severe illne • Cognitive i • High BUN/ (dehydratio
Marcantonio, et al. (1994)	Surgical patients age ≥ 50 yr n = 876	CAM/Medical Record	Postop days 2–5	9%	• Age ≥ 70 yr • Alcohol abu • Cognitive i • Poor functi • Abnormal N • Noncardiac aortic aneur

Table 3
Prospective Studies of Delirium (continued)

AUTHORS	SAMPLE	DELIRIUM INSTRUMENT	ASSESSMENT DURATION	INCIDENCE	RESU
Pompei et al. (1994)	Medical, surgical age ≥ 65 yr n=263	Clinical judgment/ Screening	Daily Unknown duration	*15%	• Alcohol abu • Cognitive i • Number of categories • Depression
Inouye & Charpentier (1996)	Medical Patients age ≥ 70 n=196	CAM	Evaluation every 48 hrs. for 9 days	18%	• Physical res • Malnutritio • > 3 meds • Use of blad • Iatrogenic e
O'Keeffe & Lavan (1996)	Medical Patients age not specified n=100	DSM-III	Evaluation every 48 hrs. until discharge	28%	• Dementia • Severe illne • Elevated se

* Incidence and Prevalence combined in analysis

In the development of a prediction rule for use in a surgical population. Marcantonio et al. (1994) used the CAM to determine the presence of delirium in a sample of 876 patients over 50 years of age admitted for major elective non-cardiac surgery. Patients were approached "non-selectively" based on the availability of study personnel with 65% of those eligible consenting and admitted to the study. Using a stepwise logistic regression model. age of 70 years or older. self-reported alcohol problems. cognitive impairment. lower physical function. abnormal pre-operative sodium potassium or glucose levels. aortic aneurysm surgery and noncardiac thoracic surgery were found to be independent correlates of post-operative delirium (Marcantonio. Goldman. Mangione. et al. 1994). The lack of a random sample is a serious limitation of this study, although the authors state that every attempt was made to approach a representative sample including old or sicker patients (Marcantonio, Goldman, Mangione et al. 1994). There was no attempt to evaluate the comparability of this convenience sample to those eligible, limiting the generalizability of these findings.

In a similar type of study, O'Keeffe & Lavan (1996) utilized the operational definitions of DSM-III criteria developed at the University of Pennsylvania in a prospective study of 184 patients admitted to an acute-care geriatric unit. One hundred patients were classified into a derivation group following recruitment but prior to data analysis. It was not stated how this classification occurred. Patients underwent cognitive assessment every 48 hours. Chronic cognitive impairment, severe illness and serum urea greater than 10mmol/l, were found to be significant predictors of delirium when analyzed in a stepwise logistic regression model (O'Keeffe & Lavan. 1996). The risk associated

with dependence in ADL could not be assessed as all patients admitted to the unit were dependent in ADL.

Inouye et al (1993) developed a predictive model for the occurrence of incident delirium in hospitalized elderly medical patients admitted from emergency (n= 107). Vision impairment, cognitive impairment, severe illness and a measure of dehydration were significant predictors of delirium (Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 19 Vision impairment was defined as corrected vision worse than 20/70 on both near and distant binocular tests. The low prevalence of vision impairment (n=6) results in unsta point estimates with widened confidence intervals, and therefore requires further evaluation to determine predictive ability. Although there is some support for the beli that dehydration is a risk factor for delirium (Seymour, Henschke, Cape, & Campbell, 1980), no absolute definition of dehydration exists and the evaluation of dehydration is problematic in the elderly (Weinberg & Minaker, 1995). In this study, a serum urea nitrogen (SUN)/creatinine ratio of 18 or more was defined as indicating dehydration(Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993). Clinically, a SUN/creatinine ratio of 25 or more is suggestive of dehydration; however, other conditions that occur in elderly patients such as renal vascular disease can increase this ratio even though dehydration may not be present (Weinberg & Minaker, 1995). Thus may be that dehydration is not the risk factor, but that a high SUN/creatinine ratio is a non-specific indicator. It is not known whether an increase in either SUN or creatinine independently increased the risk of delirium.

Contrary to other prospective studies. age was not found to be a significant predictor of delirium in the preceding study (Inouye. Viscoli. Horwitz. Hurst. & Tinetti 1993). The authors suggest the effect of age may have been removed by controlling for factors associated with aging, such as illness severity. Alternate explanations include t eligibility criteria with an age cutoff of ≥70 years resulting in a narrow age range represented. or the fact that age was analyzed as a binary variable. Age was dichotomiz at age>80 years which may have negated the independent contribution of age when analyzed as a continuous variable.

Two hundred and ninety one patients aged 65 years or older and admitted to gene medical or surgical wards were prospectively followed for 14 days or until discharge(Schor, Levkoff, Lipsitz, et al. 1992) in an exploratory study of risk factors fo delirium. Prior cognitive impairment, age over 80 years, fracture on admission, symptomatic infection, and being male were the admission characteristics found to be significant predictors of delirium (Schor, Levkoff, Lipsitz, et al. 1992). Although not labelled as delirious, a large number of individuals (n=110) partially met the criteria fo delirium in this study. It is not known what "partially met" entails. As this study was based on DSM-III criteria, it may be that the criteria were overly restrictive.

Summary.

In summary, the specification of host risk factors has been limited by the use of a wide variety of criteria to define delirium. Some of the differences in reported findings may be attributed to differences in casefinding methods. In addition, the wide variety o patient populations studied would be expected to contribute to variances in reported

findings since patient selection criteria such as age and cognitive impairment have been consistently associated with an increased risk of delirium. Factors such as severity of illness, functional impairment, abnormal laboratory values, specific surgery types, sensory impairment, a measure of dehydration, fracture on admission, infection and bei male have been found to be significant predictors of delirium in at least one of the prospective studies using a valid and reliable instrument.

2.10 Predictors of Delirium - Environmental Factors

Intoxication with medical drugs is hypothesized to be the most frequent single cause of delirium (Lipowski, 1983). Many other factors occurring during hospitalizatio have been proposed as environmental risk factors for delirium. Theoretically, it may be that unfamiliar sensory inputs from the hospital environment are not correctly perceivec as they cannot be adequately integrated with previous experience. However, there are only two prospective studies that have examined hospitalization-related risk factors in more detail (Foreman, 1989; Inouye & Charpentier, 1996). Only one study utilized a valid tool for delirium assessment (Inouye & Charpentier, 1996). In the present review, the evidence regarding delirium associated with medication use will be reviewed. The limited findings regarding hospitalization-related risk factors will be reviewed, briefly describing hypothesized factors followed by findings from the prospective studies.

Medications.

Medications are considered the most common reversible cause of delirium and ar believed to contribute to 22% to 39% of cases of delirium (Inouye, 1994). Medications are an important area of study, in that they are a potentially modifiable risk factor. In o

study. pharmacotoxic psychoses developed in 23% of elderly patients suffering from chronic cerebral disorders. however the retrospective design did not control other factor that may influence delirium (Danielczyk. 1984). In this case. confounding by indicatio may play an important role.

Anti-cholinergic medications are of particular interest as a risk factor for delirium failure of central nervous system cholinergic transmission is one of the postulated pathophysiological mechanisms for delirium. Several case reports and one study (Brize & Manning. 1982; Bernstein & Leff. 1967; Berggren. Gustafson. Eriksson, et al. 1987) have associated anticholinergics with delirium. In the only prospective study to identif this association, anticholinergic medications as a class significantly influenced post-operative delirium when compared to all "regular" medications ($p<.005$) (Berggren. Gustafson, Eriksson, et al. 1987). It is not known what constituted "regular" medicatio and the description of the analysis of the independent contribution of medication-relate risk factors is not well-defined. Anticholinergic medications as a class were not significant predictors of delirium in a number of prospective studies (Francis, Martin. & Kapoor. 1990; Marcantonio. Juarez. Goldman, et al. 1994; Schor, Levkoff, Lipsitz. et al 1992) and only weakly significant in one study combining patients with incident and prevalent delirium (Gustafson, Berggren, Brannstrom, et al. 1988). However, specific medications known to have an anticholinergic effect have been significantly associated with the development of delirium. In a large, prospective study of elderly patients admitted to a medical or surgical unit, the use of a neuroleptic during hospitalization wa

an independent risk factor for delirium(Schor. Levkoff. Lipsitz. et al. 1992). Some neuroleptics are known to have an anticholinergic effect.

In a study of elderly patients admitted for elective surgery, treatment with propranolol. scopolamine. and/or flurazepam was a significant predictor of delirium. Scopolamine is an anti-cholinergic medication: however. it is not known why these particular medications were combined as they do not belong to one medication class. may be that one of these medications had an independent contribution to the risk of delirium, however the small sample size (n=46) limited the power to detect a significa difference.

Although not prescribed as an anticholinergic. meperidine was originally develo as an anticholinergic agent and only later serendipitously found to have narcotic properties (Marcantonio, Juarez, Goldman, et al. 1994). Meperidine was found to hav significant association with delirium in a sample of surgical patients(Marcantonio, Juarez, Goldman. et al. 1994). Although previously associated with delirium in severa case reports (Eisendrath, Goldman, Douglas. Dimateo, & VanDyke. 1987; Bernstein & Leff. 1967), this was the first prospective study to find a significant association. The majority of previous studies analyzed medication classes, and not specific agents. Meperidine is a commonly used narcotic analgesic. The metabolite of meperidine, normeperidine, is active, has a long half-life, and is idiosyncratically metabolized by t liver, allowing the accumulation to toxic levels in patients receiving continuous meperidine (Marcantonio, Juarez, Goldman, et al. 1994). Thus, this specific narcotic analgesic is important to evaluate. Narcotic use as a group was not significant in this

study; however, because 94% of the study sample received a narcotic, this finding is n surprising. Narcotic use was found to be a significant predictor of delirium in a sampl 325 patients admitted to a medical or surgical unit (Schor, Levkoff, Lipsitz, et al. 199

Other medication classes found to increase the risk of delirium include psychoac drugs and benzodiazepines. Use of psychoactive drugs was found to be significantly associated with delirium in a sample of medical patients (Francis, Martin, & Kapoor, 1990). However, as both incident and prevalent cases were combined, it is unknown whether this medication class preceded the development of delirium. The use of benzodiazepines was significantly associated with delirium in a case-control study of elective surgical patients (Marcantonio, Juarez, Goldman, et al. 1994). The authors suggest that the longer acting benzodiazepines have a stronger association with deliriu compared with the short acting. However, the associated confidence interval includes indicating a null value and thus precludesthe significance of this finding.

Number and type of admission medications were not significant in those studies analyzing this variable (Francis, Martin, & Kapoor. 1990; Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996). However, number of medications received in-hospital has been found to be significantly associated with delirium in the studies analyzing this variable. In a sample of 71 medical patients, those patients receiving more medications were found to be at greater risk for developing delirium (Foreman. 1989). In a sample of 196 elderly patients admitted to a medical unit, the addition of more than three medication types prior to the onset of delirium significantl

increased the risk of delirium (Inouye & Charpentier. 1996). Thus it may be that risk of delirium increases with number of medications administered. regardless of specific class.

Summary.

In summary, the role of medications as a risk factor for the development of delirium is presently not clear . A synthesis of the evidence to date leads one to conclude that medications play a role in the development of delirium, however it may not be as large as originally hypothesized. Although medications with an anticholinergic effect have not been significantly associated with delirium when analyzed as a class, individual agents known to have anticholinergic effects have been found to be significant. Other medications found to be significant in prospective studies based on patients with incident delirium include narcotic analgesics and benzodiazepines. In addition, the number of medications received while in hospital may be a significant risk factor.

Psychosocial factors.

In an early study, postoperative delirium was significantly associated with sensory deprivation (Wilson. 1972). Unfortunately, this study did not control many of the factors known to influence delirium (i.e., age, underlying illness), delirium was not well defined, and a retrospective chart review was utilized. As the two sites involved in this study were staffed with different nursing staff, differences in charting may be a possible explanation of this finding. Other factors that have been identified in early studies using bivariate analyses or case studies include dehydration (Seymour, Henschke, Cape, & Campbell. 1980), acute urinary retention (Blackburn & Dunn. 1990)and room transfers during hospitalization (Mattice. 1989).

Few prospective studies conducted have included environmental risk factors. Thus, these studies will be reviewed in greater detail.

Seventy one medical patients over age 60 were followed and interviewed daily for eight days using a clinical assessment of confusion tool. Although the confusion tool was developed to assess delirium, only concurrent validity with a mental status questionnaire was evaluated. Delirium developed in 38% of patients. In addition to abnormal lab values and low blood pressure, Foreman (1989) identified two environmental factors as significant predictors of delirium. Patients with delirium had more orienting objects (newspapers, timepieces, radios, televisions, and the presence of personal belongings) in their immediate environment, and fewer interactions with significant others. The finding that confused patients had more orienting objects may have been an attempt by family and staff to orient the patient, and thus a consequence of the confusional state. Further, whether or not the orienting objects were actively used is not known. The second risk factor, interaction with significant others, was measured by the patient's nurse providing an estimate of the number of visitors and the length of visit (Foreman. 1989). Those individuals with fewer interactions with visitors were found to be at greater risk for developing delirium (Foreman. 1989). At a bivariate level, Inouye et al. (1993) found that individuals with six or fewer social supports, defined as the number of children, close relatives or friends seen at least once a month, were more likely to develop delirium. Individuals with either one type or no instrumental, emotional or confidante support types were more likely to develop delirium. Social support has been found to be protective for a variety of adverse events including institutionalization and mortality (Steinbach. 1992).

A study on the precipitating or environmental factors for delirium in hospitalized elderly persons admitted to a medical unit through the emergency service was recently published (Inouye & Charpentier. 1996). Potential environmental factors for delirium were *a priori* classified into four axes: immobility, medications, iatrogenic events and intercurrent illness (Inouye & Charpentier. 1996). Those variables with clinical relevance, a relative risk of 1.5 or greater and meeting the statistical selection criteria in forward and backward-stepping algorithms ($p \leq .10$) were selected as the optimal variables from each axis. Hospital day, categorized into three groups (1-3, 4-6 and 7-9) was included in each model to account for the declining risk of delirium over time. The inclusion of this variable within the predictive model is difficult to interpret. Although all prospective studies of delirium support the fact that, unlike most iatrogenic hospital-related events, the greatest risk of delirium appears to occur early in the hospital stay, the inclusion of day as an independent predictor of delirium is difficult to interpret. Included within this variable are those individuals who are discharged early (and presumably less likely to develop delirium). Hospital day also includes the day that delirium developed, and is, in fact, a response variable. It is important to note, however, that a logistic regression model and a proportional hazards model produced similar results, and the same final variables would have been selected using either strategy (Inouye & Charpentier. 1996).

Once the significant variables within each axis were identified, they were entered into the final model. At least one factor from each axis had to be included in the final model, as the researchers made an assumption that each axis is important in the

development of delirium (Inouye & Charpentier. 1996). Five independent risk factors for delirium were identified: use of physical restraints, malnutrition, more than three medications added, use of bladder catheter, and any iatrogenic event. The risk factor "malnutrition" was based on a serum albumin of less than 30g/L. However, 59% of study patients were missing serum albumin levels, and were classified as not at risk. Hypoalbuminaemia is also a non-specific marker of underlying disease, and therefore may not truly represent malnutrition.

This model did not control age, cognitive impairment or any of the factors determined as admission characteristics, because the authors were only interested in environmental factors. Given the current state of knowledge regarding hospitalization-related factors for delirium, determining *a priori* those factors that make an important contribution to delirium may not be a defensible position. It may be that it is a combination of factors that increase the risk of delirium, or factors that were significant at the bivariate level and were not included may have provided a better fit, and made an important contribution to our understanding.

Summary.

In summary, environmental risk factors other than medications that have been significantly associated with delirium in prospective studies include number of social contacts, number of orienting objects, use of restraints, malnutrition, use of a bladder catheter, and any iatrogenic event. An important limitation of the majority of prospective studies is that the interaction between environmental and host factors has not been assessed. The assumption is made that an environmental factor will have the same effect

regardless of host risk factors. It is probable that delirium is far more complex. and environmental factors may interact with host factors.

2.11 Outcomes of Delirium

Mortality, longer hospital stay, and risk for institutional placement continue to be cited as adverse outcomes associated with the diagnosis of delirium (see for example, Inouye & Charpentier, 1996). However, studies examining these outcomes are not consistent.

In an attempt to delineate the prognosis of elderly hospital patients with a diagnosis of delirium, Cole & Primeau (1993) undertook a meta-analysis of eight research studies. Overall, they note that no study controlled for treatments during delirious episodes in order to account for their effect on outcome, nor was the outcome assessment blind. It is advantageous to have blind outcome assessment to ensure that observation bias has not occurred. An observation bias may arise when the investigators elicit or interpret the information differentially knowing the delirium status. For example, it may be that knowing the delirium status of the individual, an investigator evaluates a functional assessment as lower, or seeks additonal information that would not have been sought if the individual did not have delirium.

Compared with unmatched control subjects, the meta-analysis revealed that patients with delirium had longer hospital stays, higher mortality rates at one month, and higher rates of institutionalized care at one and six months. This finding is at odds with the conventional clinical belief that delirium is a transient condition with a good prognosis. However, there are definite limitations to meta-analysis (Spitzer. 1991), and this analysis

is no exception. For example, the authors identified the fact that the eight studies chosen used different methods of determining delirium, with only one of the studies using a valid and reliable tool for assessing delirium(Cole & Primeau. 1993). Combining the findings from these studies may not be valid. Further, although the authors identified outcomes such as increased mortality and institutionalization, the most serious limitation with studies examining the effect of delirium on outcomes is the failure to adjust for confounding or modifying factors. Confounding occurs when an observed association (or lack of one) is due to a mixing of effects between the exposure, the disease, and a third factor that is associated with the exposure, and independently affects the risk of developing the disease (Hennekens & Buring. 1987). For example, although delirium has been found to increase mortality, a confounding factor is severity of illness. Severe illness has been found to increase the risk of delirium (Francis, Martin, & Kapoor. 1990; Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996) and also independently to increase the risk of mortality. Thus, confounding can lead to either the observation of apparent differences between groups when they do not truly exist, or conversely, the observation of no difference when there truly is a difference (Hennekens & Buring. 1987). In order to determine the independent contribution of delirium to the risk of mortality, independent predictors such as age, gender and severity of illness or comorbidity must be controlled. Only two of the studies included in the meta-analysis controlled for the influence of illness severity on prognosis. Thus, combining these studies for the purposes of meta-analysis may provide a misleading interpretation.

An alternative to meta-analysis may be to use a "best-evidence synthesis" (Slavin. 1986). In this case, one would consider the evidence from studies having the highest internal and external validity. The main outcomes associated with delirium will be reviewed with this consideration.

Mortality.

An often cited study of delirious patients found higher fatality rates for delirious patients as compared to demented, cognitively intact or depressed patients (Rabins & Folstein. 1982). Other studies using bivariate level analyses found similar results (Gustafson, Berggren, Brannstrom, et al. 1988; Guze & Cantwell. 1964). Unfortunately, confounding factors such as age and comorbidity or severity of illness were not controlled. This shortcoming is not limited to early studies, as more recent studies continue to report only bivariate level significant differences in mortality (Levkoff, Safran, Cleary, Gallop, & Phillips. 1988; Marcantonio, Goldman, Mangione, et al. 1994). Mortality rates may appear higher in patients with delirium as the presence of delirium may indicate significant underlying medical problems.

An increased risk of mortality was detected at the bivariate level in a large study (n=291) using a validated instrument to detect delirium (Levkoff, Evans, Liptzin, et al. 1992). When age, gender, pre-existing cognitive impairment and severity of illness were controlled, no independent increased risk of mortality (measured at six months) was associated with delirium (Levkoff, Evans, Liptzin, et al. 1992). Similarly, in a study using clinician assessment of delirium in a medical population of patients aged 70 years and older, an increased risk for mortality two years following discharge was found at the

univariate level (Francis & Kapoor. 1992). Once cancer, baseline ADL, and initial cognitive impairment were controlled, delirium failed to have a significant, independent effect on survival (Francis & Kapoor. 1992). In a sample of 225 elderly patients admitte to a geriatric unit, a higher mortality during hospitalization and at six months was observed (O'Keeffe & Lavan. 1997). Once again, in multivariate analysis controlling for age, illness severity, comorbid disease, disability, and dementia, delirium did not have a significant influence on either mortality measure (O'Keeffe & Lavan. 1997). In a sample of 216 elderly patients discharged from a medical unit, six month mortality was not significantly different once severity of illness was entered into the model (Francis, Martin, & Kapoor. 1990).

One study found an increased in-hospital mortality rate for patients admitted to a medical or surgical unit and who had delirium, even when comorbidity was controlled (Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel. 1994). However, delirium was not associated with and increased mortality rate at 90 days following discharge. Unfortunately, the measure used to assess comorbidity had not undergone any psychometric testing, and thus may not be a valid control for the independent contributio of comorbid disease. The authors counted the total number of discharge diagnoses and consolidated these into a major diagnostic category, corresponding to body systems (Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel. 1994). This method would not, therefore, take into account the seriousness of the disease. Further, the refusal rate of 46% seriously limits the generalizability of these findings.

It may be that the higher mortality rate found in other studies is, in fact, associated with uncontrolled extraneous or confounding factors, in particular, severity of illness. At present, there is little evidence to support the continued reference to an increased risk of mortality as an outcome of delirium. However, researchers continue to cite higher mortality rates even when their own previous studies have failed to support this finding (Inouye & Charpentier. 1996). There may be certain subpopulations that continue to have an increased risk of mortality.

Institutionalization.

At the bivariate level, patients with delirium have been found to have an increased risk for institutionalization (Marcantonio, Goldman, Mangione, et al. 1994; Francis, Martin, & Kapoor. 1990). However, other factors may better explain the increased risk. Complex interactions among risk factors elevate the risk of institutionalization (Shapiro. 1988). Age, cognitive impairment, decreased functional ability, and whether or not an individual lives alone have been found to be significant predictors of institutionalization (Shapiro. 1988). Other factors significant in some studies include socioeconomic status and marital status (not married) (Young, Forbes, & Hirdes. 1994). Shapiro and Tate (1988) found that a very elderly person with a spouse at home had only a 7% chance of admission to an institution, decreasing to 4% when no other risk factor was present. Thus whether or not the individual lives alone is an important risk factor to consider when evaluating risk of institutionalization. No study of delirium that has examined insitutionalization has controlled for this factor.

One study of medical/surgical patients found a sevenfold greater risk for institutional placement for patients with delirium after controlling for age, gender, preexisting cognitive impairment and illness severity (Levkoff, Evans, Liptzin, et al. 1992). The presence of delirium was the only significant predictor variable in the model (Levkoff, Evans, Liptzin, et al. 1992). This finding may be qualified, however, by the fact that functional status and whether or not the individual lived alone were not controlled.

In a recent study of geriatric patients admitted from the community and surviving to discharge, patients with delirium were more likely to be admitted to long term care within six months after discharge (O'Keeffe & Lavan. 1997). The multivariate model controlled for age, illness severity, comorbidity, cognitive impairment, and disability score. cognitive impairment was also identified as a significant risk factor for institutionalization (O'Keeffe & Lavan. 1997). Unfortunately, whether or not the individual lives alone was not included in the model.

Inouye (1993) suggests an inferential error may arise because patients who die in hospital can no longer be placed in an institution and recommends combining institutionalization and mortality to avoid this potential bias. Individuals with delirium were more likely to die or be placed in a nursing home (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993). However, it is difficult to justify combining institutionalization and mortality, particularly as delirium does not appear to have an independent influence on mortality.

Thus whether or not delirium makes an independent contribution to the risk of institutionalization is presently unclear, however findings from two studies suggest an increased risk. Further studies, controlling for known risk factors, must be undertaken.

Length of stay.

Delirium has been found to increase the average duration of hospital stay at the bivariate level (Erkinjuntti, Wikstrom, & Palo. 1986; Gustafson, Berggren, Brannstrom, et al. 1988; Marcantonio, Goldman, Mangione, et al. 1994; Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel. 1994; O'Keeffe & Lavan. 1997; Francis, Martin, & Kapoor. 1990; Levkoff, Evans, Liptzin, et al. 1992), and when possible confounders are controlled. Delirious medical patients stayed in the hospital an average of 12.1 days vs. 7.2 days, a difference that remained significant after controlling for illness severity, ADL status, prior cognitive impairment, and fever (Francis, Martin, & Kapoor. 1990). In support of this finding, Levkoff et al (1992) detected a significant difference in length of stay for those individuals with delirium after adjusting for age, gender, pre-existing cognitive impairment and illness severity. This difference was found in both the sample admitted for the community (n=203) and the sample admitted from an institution (n=88). The finding that the institutional based sample continued to have an increased length of stay is intriguing. It is possible that stay for the community based sample could be lengthened because patients lived alone at home without support. This same factor, presumably, would not influence the length of stay of the institutionalized population.

In a study combining prevalent and incident cases of delirium, patients with delirium remained in hospital longer than patients without delirium. This multivariate

model included age, severity of illness, comorbidity, disability score, and cognitive impairment (O'Keeffe & Lavan. 1997).

Length of stay was not significant at the bivariate level in two studies (Rogers, Llang, Daltroy, et al. 1989; Williams-Russo, Urquhart. Sharrock. & Charlson. 1992). In one study, the authors believed this was due to cost-containment pressures (Rogers, Llang, Daltroy, et al. 1989). Further, all cases defined as "delirium" were considered "mild" and thus may not have been serious enough to warrant an increased length of stay . Similarly, the definition of delirium in the second study included cases of confusion noted in the recovery room(Williams-Russo, Urquhart, Sharrock, & Charlson. 1992), such that the effects of anesthesia may have accounted for the confusion and presumably were short-term.

Thus, an increased length of stay for patients with delirium does appear to be a consistent outcome, even after controlling for known risk factors. This has economic implications for health care organizations because of the the increased financial burden on the system.

Physical function.

Recently, the effect of delirium on subsequent physical function was assessed (Murray, Levkoff, Wetle, et al. 1993; Foreman. 1989). In the first study, three hundred and twenty-five hospitalized elderly were followed to assess the impact of delirium on subsequent physical function. Physical function was measured by the Katz activities of daily living (ADL) index. ADL were assessed by interviewing the patient's primary caregiver upon hospital admission, and at 3 and 6 months after hospital discharge

(Murray, Levkoff, Wetle, et al. 1993). The dependent variable was adjusted change in function (mean physical dysfunction score after 3 months minus the physical dysfunction score on admission). Predictors included delirium, pre-existing cognitive impairment, age, sex, whether they were admitted from the community or from an institution, and comorbidity. Delirium was the only significant factor . This functional decline persisted to the 6 month follow-up (Murray, Levkoff, Wetle, et al. 1993). When data were analyzed using 3 month level of function as the outcome, delirium and initial level of function were significant predictors. Pre-existing cognitive impairment was significant for the community-based sample.

In a study of patients admitted to a geriatric unit, 47 patients who experienced incident delirium were compared at discharge with 124 patients who did not (O'Keeffe & Lavan. 1997). Patients with delirium were significantly more likely to experience a deterioration in functional status while controlling for age, severity of illness, comorbidity, cognitive impairment, length of stay, and admission disability score (O'Keeffe & Lavan. 1997).

In contrast, no significant differences were found in the rates of decline in ADL at six months for a sample of discharged medical patients (Francis, Martin, & Kapoor. 1990); however, patients with significant ADL dependency or severe dementia were excluded from this study. When analyses of the same subjects at a two year follow-up was conducted, delirium was associated with a 2.56 adjusted risk of loss of independent living among thos subjects who were previously independent. However, the sample size was small (n=20). In contrast, there were no differences between subjects with and

without delirium with respect to change in functional status from 2 weeks before admission to 90 days after discharge in a study of medical and surgical patients (Pompei, Foreman, Rudberg, Inouye, Braund, & Cassel. 1994). Unfortunately, the high refusal rate limits generalizability of this finding.

Another study found a significant difference in change scores on a physical function measure between thirteen delirious and thirteen non-delirious patients after controlling for surgery, age, and baseline score (Rogers, Llang, Daltroy, et al. 1989). However the control group may not have been comparable. Of the original control group, data could only be collected on three patients. To supplant the control group, the investigators selected thirteen controls from a study conducted two years previously. Failure to obtain information on the original control group and utilizaing a new control group with questionable comparability on key risk factors may be a major source of bias. Other than age and baseline function score, the comparability of the control group was not reported. This raises serious doubts about the validity of the study results.

There are a number of similarities between the majority of the preceding studies that may have had an important influence on findings. These include the length of time for follow-up, the use of a self-report physical function measure as compared to an observation based measure, and the influence of length of stay on the outcome.

Decisions regarding the appropriate length of the required time for follow-up are difficult in an elderly population. The longer the time for follow-up, the less confident one can be that the results are not related to intervening factors. For example, comorbid illness may have occurred that will impact the functional assessment conducted two years

later. Illnesses such as a stroke are particularly difficult to diagnose, and yet may have a substantial impact on physical functioning. Small cortical strokes are known to cause delirium (Kane, Ouslander, & Abrass. 1994). It is possible that such incapacitating illnesses differentially affect patients who have experienced delirium, and therefore exert a confounding influence.

Another limitation is that self-report measures of physical functioning were used in these studies. When one of the primary purposes of the study is to detect differences in function scores, it may be important to use a performance-based measure. There may be significant differences between patient or caregiver assessments and performance-based measurements of ADL (Sager, Dunham, Schwantes, Mecum, Halverson, & Harlowe. 1992) that could influence the sensitivity of these outcome measures. In a study comparing self-report with a performance-based measure, the rate of agreement between self-report and performance ADL measures was lowest in the areas of bathing and dressing (Sager, Dunham, Schwantes, Mecum, Halverson, & Harlowe. 1992). In a study of the possible biasing effects of different data sources on functional status scores, patients were found to overstate their functional abilities whereas significant others may understate the patients functional abilities (Rubenstein, Schairer, Wieland, & Kane. 1984). It is possible that some findings of significant differences in function status relate to the differences in data sources, rather than true differences.

An alternative explanation may be related to the increased length of stay associated with delirium. There is a decrease of independent physical functioning that occurs over the duration of hospitalization (Palmer, Landefeld, Kresevic, & Kowal. 1994). Thus, it

may be the decreased physical function associated with delirium in some studies is as a result of the longer hospital stay rather than delirium.

Overall, therefore, there is some question regarding whether or not delirium results in a long-term loss of functional ability. Only one study adjusted for important risk factors including length of stay, and thus provides preliminary support for an increased risk. Future prospective studies using performance based measures and adjusting for length of hospital stay may provide further information.

Morbidity.

Rogers et al (1989) found delirium to be strongly associated with post-operative complications. Unfortunately complications was operationalized to include patients "disrupting" the ward with "inappropriate behavior" and "danger to him or herself." As no patient with cognitive impairment was entered into this study, these behaviors would most likely characterize the delirious patient. "Complications" were classified as dichotomous and, therefore, would be significant because the predictor variable included the response variable.

Individuals who developed delirium had a 15% rate of major complications compared with a 2% rate among patients without delirium in a study of elective surgery patients (Marcantonio, Goldman, Mangione, et al. 1994). Unfortunately, the rate of complications following delirium was not differentiated from those preceding delirium.

Recently, patients with delirium were found to suffer significantly more complications during hospitalization (O'Keeffe & Lavan. 1997). Complications were defined as urinary incontinence, falls or pressure sores. At a bivariate level, only urinary

incontinence and falls were more likely to occur. The independent contribution of pressure sores to the overall model is unknown. The multivariate model combined these adverse events and adjusted for age, illness severity, comorbidity, cognitive impairment, disability and length of stay. Although many of the factors controlled are risk factors, other known risk factors were not included. For example, compromised nutritional status is an important risk factor for the development of pressure sores.

Overall, there is some initial evidence supporting an increased risk of adverse events during hospitalization for patients with delirium. These findings should be confirmed in future studies based on other study populations.

Summary.

It is apparent that studies evaluating the influence of delirium on outcomes such as mortality, institutionalization, length of stay, and physical functioning must control known risk factors. Findings from previous research suggest a number of adverse outcomes independently associated with delirium. There does not appear to be support for continuing to identify an increased risk of mortality associated with delirium. However, the seriousness of outcomes such as institutionalization, and increased hospital-associated complications, length of stay and loss of physical function warrant continued research into predictive and preventive measures of delirium.

2.12 Research Questions

In order to address the limitations of the previous studies of delirium in the hospitalized elderly, the primary focus of Study One was to identify hospitalization-related environmental factors that contributed to delirium and were potentially

modifiable. The secondary focus was to determine in-hospital outcomes while controlling for known risk factors. The research questions for this study were:

1. What are the host and environmental risk factors for delirium in hospitalized patients age 65 years or older?
2. Does delirium independently increase the risk of the following outcomes in the hospitalized elderly: in-hospital mortality, morbidity, restraint use, readmission within one month and institutionalization?

Chapter 4. Methods

This section of the paper describes the methods undertaken to address both the primary and secondary research questions. The study design and procedures followed to address both the risk factors and the outcomes associated with delirium will be described. The psychometric properties and methods of analysis of the research measures will be discussed. The statistical models employed to address both the primary and secondary research questions will be described.

4.1 Design

Sample size.

Sample size was based on the typical size from previous studies. Further, the financial resources available for this project precluded a larger sample size. This restriction is due to the detailed clinical follow-up required for each patient. Thus a target sample size of 150 patients was chosen.

Study population.

This prospective study was conducted at Grand River Hospital, Kitchener-Waterloo (K-W) site, a community, acute care facility. Potential study participants included all patients aged 65 years of age or older, who were admitted to a medical or surgical unit at the K-W site between Sunday at 0800 a.m. and Friday at 1200h from July 03, 1996 to September 18, 1996. These patients were identified through the use of a computerized data base. This time period was utilized so that the clinical research

assistants were able to obtain informed consent from all patients within 24 hours of admission (Appendix B).

Exclusion criteria were as follows.

1. unable to speak and understand English
2. undergoing a procedure that necessitated a stay in an intensive care unit (ICU) of greater than 2 days
3. admitted to an ICU or a palliative care unit
4. comatose, unconscious, or otherwise unable to communicate verbally
5. a known history of alchohol abuse
6. severe underlying dementia as determined by the admitting physician
7. evidence of delirium on admission

There were one hundred and sixty one patients meeting the study criteria from July 03, 1996 to September 18, 1996. Five individuals (3%) refused to participate, giving a final sample size of one hundred and fifty six patients. These patients were followed by two clinical research assistants for 14 days after admission or until discharge.

4.2 Procedure

The following sections describe the study procedures, including the procedure for obtaining informed consent, the initial interview, the daily patient assessment, the detection of delirium, reliability testing of the CAM, and the assessment of outcomes associated with delirium.

Informed Consent.

This study received ethics approval at the University of Waterloo and at the Ethical Research Committee, Grand River Hospital. All patient information was collected using a numeric identifier to ensure patient confidentiality.

All patients who met the study criteria were approached by the clinical research assistants within 24 hours of admission to obtain informed consent. The primary nurse of each potential study patient was asked to evaluate the patient's ability to answer questions and to understand the informed consent procedure. If the primary nurse thought the patient was competent to consent to the study, the clinical research assistant explained the study to the patient and sought written consent (Appendix B). If the patient was unable to provide consent, a relative or caretaker familiar with the patient's pre-hospital functioning was approached by the clinical research assistant to obtain informed consent. This person also answered questions regarding the patient's cognitive symptoms prior to admission and estimated duration of any cognitive impairment. In addition, family members were asked for informed consent (Appendix C) and to complete a measure of the patient's psychological well being (Appendix D).

Initial interview.

Once consent was given, an initial interview was conducted to establish baseline values for cognitive status, and to determine if the resident was free from delirium. The CAM instrument was utilized to assess whether the patient displayed evidence of delirium on admission. Thirty-two patients admitted from July 03, 1996 to September 18, 1996

were not eligible to participate in the study as they met the exclusion criteria of presence of severe dementia or delirium on admission.

Written protocols and uniform ways of probing for additional information were developed to aid standardized collection of information (Appendix E). The initial interview was completed for the 156 patients entered in the study. Baseline demographic and health information was obtained from the medical record and the initial patient interview (Appendix F). The interview also included completion of the depression measure (Appendix G), standard vision and hearing assessment (Appendix H), and an activity limitation assessment (Appendix I).

Daily assessment.

Subsequently, all participants were monitored daily in the hospital for the first 14 days of their stay or until discharge or death. Data on each symptom of delirium were collected. Laboratory data, available on the patient's medical record, were screened in order to identify abnormalities. The patients' environment was assessed daily, and objects that provided meaning and orientation were noted. Use of restraints and any invasive procedure that the individual underwent were recorded. Patient movement off the unit was noted (i.e., transports to radiology or other areas of the hospital).

Following completion of their involvement in the research project, research participants received a letter of thanks (Appendix J). In addition, a summary of the results of the study will be provided to those participants who indicated an interest.

Detection of delirium.

The characteristic shifting in quality and degree of symptomatology of delirium makes it necessary to obtain a longitudinal picture of a patient's illness, with repeated evaluations and close attention to observations made by hospital staff and family. In order to maximize the detection of symptoms of delirium, data were collected daily using several methods: a structured interview using the CAM; a brief interview with the primary nurse using a checklist similar to the CAM that documents whether any symptoms of delirium have been observed; and an examination of the patient's medical chart for the previous 24 hour period for any documented symptoms of delirium. Use of keywords such as agitated, confused, disoriented and delirious were followed up. If the patient met the CAM criteria based on any of these sources, the patient was classified as delirious.

Surgical patients were not assessed on the day of surgery in order to distinguish delirium from the effects of anesthesia. This period was considered adequate as recovery from the effects of anesthetic is usually complete after the first eight hours. In previous research designed to quantify the rate of mental recovery in elderly patients after general anaesthesia, there were no significant changes in the Mini-mental State Test or the Digit Span Test after the first post-operative day (Chung, Seyone, Dyck, et al. 1990).

Inter-rater reliability of the CAM.

Two clinical research assistants, registered nurses, received standardized training regarding the CAM algorithm based on the primer developed by the authors. Inter-rater reliability for the CAM instrument was assessed as follows: Independent ratings were

conducted simultaneously for fifteen patients, with one clinical research assistant conducting the interview while the other clinical research assistant observed. Both clinical research assistants had an opportunity to conduct the interview. Each clinical research assistant independently and blindly completed the confusion assessment questionnaire based on observations made during the interview. The observations were undertaken simultaneously due to the fluctuating nature of delirium. For assessing the presence or absence of delirium agreement was 100%.

Outcome assessment.

Outcome measures included in-hospital mortality, morbidity, restraint use, length of stay, readmission within 1 month following discharge, and placement at the time of discharge. In order to minimize the potential for bias, outcome assessment was blind for all variables with the exception of restraint use. Information regarding outcomes was received from a computerized data base through the health records department, with the exception of restraint use, evaluated on a daily basis by the clinical research assistants.

4.3 Measures

Delirium.

Delirium was measured by the CAM (Appendix K). The CAM is based on four criteria and has a high sensitivity (100%, 94%) and specificity (95%, 90%) (Inouye, VanDyck, Alessi, Balkin, Siegal, & Horwitz. 1990). Observations made during a brief structured patient interview, an interview with the primary nurse and medical record review are used to complete the CAM. As part of the CAM criteria, baseline mental status was assessed during the patient interview. Baseline mental status was evaluated through

the use of the digit span assessment (Appendix L) as a measure of attention, and the Mini Mental State Exam (MMSE), a short test of mental functioning (Appendix M).

The Digit Span is a subset of the Weschler Intelligence Test (WAIS-R). This test requires the accurate repetition of verbally presented random number strings both forward and backward. From memory, the subject must repeat number sequences of increasing length until two consecutive number strings are repeated incorrectly. This process is repeated with a different set of numbers recited from memory in reverse sequence to their original presentation until two number strings are again failed. The Digit span test requires one to hold information in the short-term memory and maintain it in an ordered sequence (Chung, Seyone, Dyck, et al. 1990).

The MMSE is easy to administer and generally can be completed in approximately ten minutes. In a mixed group of medical patients, a high alpha level (.96) was obtained for internal consistency for the MMSE (Foreman. 1989). Reliability coefficients for both cognitively intact and impaired subjects generally fall between r =.80 to .95 (Tombaugh & McIntyre. 1992). Sensitivity, or the ability of the MMSE to correctly identify those individuals classified as cognitively impaired was found to be 87% in a population of general medical ward patients (Anthony, LeResche, Niaz, Vonkorff, & Folstein. 1982). Similar levels of sensitivity have been reported elsewhere (Tombaugh & McIntyre. 1992). A score of less than 24 out of 30 was used to indicate cognitive impairment, which is a conventionally accepted criterion.

Independent variables.

Independent variables evaluated included host and environmental factors. The following section describes the host and environmental factors examined.

Host factors were defined as characteristics of the individual, and included sociodemographic and health factors (see Table 4). Sociodemographic factors included age, gender, marital status, education, whether the individual lived alone, admission type, entry classification, and where the patient was admitted from (Appendix F).

Age was estimated from date of birth available from patient records to create a continuous variable for age at admission to the study.

Gender was available from patient records, and analyzed as a binary variable (male=0, female=1).

Marital status was collapsed into a binary variable and coded as married (0) and other (never married/widowed/separated/divorced) (1).

Education was recorded on baseline assessment. Education was analyzed as a dummy variable with no schooling as the reference group, and as a binary variable coded as grade eight education or less (0) and greater than grade eight education (1).

Source of admission was available from health records. Admissions were collapsed into a binary variable coded as home (0) and retirement home, chronic care hospital, nursing home, or Home for the Aged (1).

Whether the patient lived alone was collected at initial interview. Lived alone was a binary variable (0=no, 1=yes).

Table 4
List of Study Variables

Outcome Variables:

- Delirium
- Length of Stay
- Mortality
- Readmission Within 1 month
- Restraint Use
- Intercurrent Illness
- Institutionalization

Host Variables:

- Age
- Gender
- Marital Status
- Education
- Lives Alone
- Admission Type
- Entry Classification
- Source of Admission
- Prior Hospital Admission within 1 Year
- Surgical Status
- Surgical Risk
- Major Clinical Category
- Medical Diagnosis
- Comorbidity
- Illness Severity
- Intercurrent Illness
- Abnormal Lab Values
  - Creatinine, Urea, Na, K, Glucose, Oxygen, Hemoglobin, White Blood Cell
- Hearing
- Communication Devices/Techniques
- Vision
- Visual Limitations/Difficulties
- Visual Appliances
- Activity Limitation
- CES-D (Depression)
- MIDAS (Psychological Well Being)
- Pain
- Fever

Table 4
List of Study Variables (continued)

Environmental Factors:
- Number of Visitors
- Restraint Use
- Number of Procedures
- Number of Invasive Procedures
- Catheterization
- Number of Orienting Objects
- Telephone Availability
- Contact with Health Care Disciplines
  - Occupational Therapy
  - Physiotherapy
  - Respiratory Therapy
  - Medical Specialist
  - Discharge & Planning
  - Nutrition & Food Services
  - Other Staff
- Room Type
- Number of Room Transfers

Medications:
- Number of Medications on Admission to Hospital
- Number of Medications in Hospital
- Patient Controlled Analgesic
- Classes (Based on AHFS codes)
  - Adrenals
  - Anti-Infective Agents
  - Anticoagulants
  - Antidepressants
  - Antidiabetic Agents
  - Antiemetics
  - Antihistamine Drugs
  - Antilipemic Agents
  - Antimuscarinics/Anitspasmodics
  - Antiparkinsonian Agents
  - Antithyroid Agents
  - Antitussives
  - Benzodiazepines (Long Acting)
  - Benzodiazepines (Short Acting)

Table 4
List of Study Variables (continued)

Classes (Based on AHFS codes) continued
- Cardiac Drugs
- Diuretics
- Estrogens
- Histamine$_2$ Antagonists
- Hydantoins
- Hypotensive Agents
- Misc. Anxiolytics, Sedatives & Hypnotics
- Miscellaneous Analgesics & Antipyretics
- Miscellaneous GI Drugs
- Nonsteroidal Anti-Inflammatory Agents
- Opiate Agonists (Codiene)
- Opiate Agonists (Demerol)
- Opiate Agonists (Dilaudid)
- Opiate Agonists (Leritine)
- Opiate Agonists (Morphine)
- Opiate Agonists (Percocet)
- Opiate Antagonists
- Opiate Partial Agonists
- Parasympathomimetic (Cholinergic) Agents
- Progestins
- Smooth Muscle Relaxants
- Thyroid Agents
- Tranquilizers
- Unclassified Therapeutic Agents
- Vasodilating Agents

Type of admission was available from health records and coded as a binary variable, emergent (1) and elective (0).

Entry classification was available from health records and analyzed as a binary variable coded as emergency room (1) and direct (0).

Health variables included surgical or medical status, surgical risk, number of previous hospital admissions, medical diagnosis, comorbidity, severity of illness, intercurrent illness, abnormal lab values, hearing, communication device/techniques use, vision, visual limitations, visual appliance use, pain, fever, activity limitation, and psychological well-being, including a measure of depression.

Surgical status was a binary variable representing whether the patient was surgical (1) or medical (0).

Surgical risk is based on the American Society of Anesthesiologists (ASA) physical status class and was measured by the surgeon and recorded on the patient chart. Scores range from 1-5, with 5 indicating a high risk . Surgical risk scores were analyzed as a continuous variable.

Previous hospital admissions over the preceding year were available from health records. Prior admissions were analyzed as yes (1) or no prior admissions (0).

Medical Diagnosis was the diagnosis recorded by the physician as "most responsible" for hospitalization. Due to the small numbers of patients with the same medical diagnosis at admission, diagnoses were grouped according into Major Clinical Categories (MCC). MCCs are utilized by the Canadian Institute of Health Information as

the most basic classification scheme. This scheme is based on organ systems. There are twenty three MCCs.

Comorbidity was assessed through the use of the Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie. 1987). This weighted index is a method of classifying comorbid conditions and takes into acount both the number and the seriousness of the comorbid diseases (Appendix N). The comorbidity index was tested in a large cohort for its ability to predict risk of death from comorbid disease at one year and 10 years. The index was shown to be a valid method of estimating risk of death from comorbid disease (Charlson. Pompei, Ales, & MacKenzie. 1987).

Illness Severity was assessed using a subjective overall rating by the responsible physician based on the Charlson method, a 9 point ordinal scale (Appendix O) (Charlson, Sax, MacKenzie, Fields, Braham, & Douglas. 1986). In previous research, the physician's rating of illness severity was found to be the most significant predictor of mortality in 604 patients admitted to a medical service in a one month period (Charlson. Sax, MacKenzie, Fields, Braham, & Douglas. 1986). In a comparison of three diagnosis-independent measures of illness severity, the Charlson method was found to have the highest sensitivity (66.7%) and specificity (87.3%) for predicting mortality during hospitalization(Young & Barer. 1995). Illness severity was analyzed as a continuous variable and as a binary variable, mild to moderate illness (0), and severe illness (1). A binary classification was comparable with other studies.

Intercurrent Illnesses included any acute illness that the patient was not admitted with. This was assessed during the patient interview and in chart reviews, and included

urinary tract infections, respiratory infections and more serious complications such as myocardial infarctions. When utilized as an outcome measure, intercurrent illness information was collected following the initial incidence of delirium or until discharge. Intercurrent illness was coded as yes (1) and no (0).

Abnormal Laboratory Values: As the mean values and standard deviations for many blood lab values do not show variation with age or sex (Leask, Andrews, & Caird, 1973), the following standard abnormal values were utilized:

Hemoglobin: 135>Males>180g/L 116 >Females>160

130<**Sodium** >150 mmol/L

3.3<**Glucose**>6.0mmol/L

3.0<**Potassium**>6.0 mmol/L

Oxygen PCO_2 >45 mmHg or PO_2<50mmHg or O_2 saturation <80%

White blood count greater than $13.0 \times 10^9/l$

Serum urea nitrogen/creatinine ratio defined as 25 or more

Normal levels for serum urea does show an age-related increase, and thus the upper limits of normal for individuals age 75 and older were used as the cut-off (Leask, Andrews, & Caird, 1973). Serum urea levels greater than 10mmol/l was abnormal. Abnormal lab values were analyzed separately as continuous and as dichotomous variables (normal=0 and abnormal=1) and in combination.

Dehydration was based on an abnormal creatinine/urea ratio of 25 or more and collapsed into a binary variable (normal=0 and abnormal=1).

Vision and hearing were assessed using the Minimum Data Set (MDS) items (Appendix H). Vision was assessed as the ability to see in adequate light with glasses if used. In previous research, vision patterns had an average reliability (r =.66). Vision was analyzed both as a continuous variable and as a dichotomous variable (adequate or slightly impaired coded as 0, and moderately impaired, highly impaired, or severely impaired coded as 1). Hearing was assessed with a hearing appliance if used. The clinical research assistant evaluated hearing ability through the inital assessment. Hearing was found to have an excellent reliability (r >.80) in previous research.. Hearing was analyzed both as a continous variable and as a dichotomous variable (hears adequately or minimal difficulty coded as 0, and hears in special situtations only and highly impaired coded as 1).

Visual limitations, a measure of whether the individual saw "halos" around lights or experienced decreased peripheral vision, was analyzed as a dichotomous variable (any limitation coded as 1, and no limitation coded as 0).

Communication devices were assessed at the initial interview and included the use of a hearing aid or other receptive communication technique such as lip reading. Communication devices were analyzed as a dichotomous variable (hearing aid, present & used, or other receptive communication techniques used coded as 1, and hearing aid, present and not used regularly, or none coded as 0).

Visual appliances was a dichotomous variable coded as 1 for the use of glasses, contact lenses, or magnifying glass.

Pain was assessed utilizing nursing and physician notes documenting that the patient was spontaneously or upon movement complaining of pain or exhibiting pain. Pain was evaluated as a binary variable no pain (0) or pain (1).

Fever was defined as a temperature greater than 37.5 degrees Celsius. and analyzed as fever present (1) or absent (0).

Activity Limitations were assessed using the Activity Limitation scale included in the SENOTS battery (Appendix I) (Stones & Kozma. 1989). Activity Limitation achieved an internal consistency of alpha =.90, and was able to discriminate community and institutional residents (Appendix I). The Activity Limitation measure consists of seven ADL questions covering shopping, spare time activities, regular chores, getting about, dressing, getting shoes on and off, and cutting toenails. Each question is scored 1 for no and 2 for yes with a total possible score on the measure of 14 indicating impairment on all ADL areas assessed.

Psychological Well-Being was evaluated using the Measure of Intensity and Duration of Affective States (MIDAS) (Appendix J). The MIDAS is a twelve item measure of positive and negative affectivity. Coefficient alpha reliability estimates for the MIDAS all exceeded .85 in self-rated and third party rated forms (Martin & Stones, 1996). The MIDAS was completed by family members. The respondent utilized a 6 point scale to provide a rating of the frequency with which the subject has demonstrated each characteristic in the past month before admission to hospital (never=1, almost never=2, occasionally=3 usually=4, almost always=5, & always=6). The positive (Items

1, 2, 6, 7, 9 & 10) and negative items are summed separately to a total possible of 36 each. The positive and negative MIDAS variables were analyzed as continuous variables.

Depression was assessed using the Center for Epidemiological Studies Depression Scale (CES-D) (Appendix K). Coefficient alpha for the CES-D was .90 in a patient population (Sawyer Radloff. 1977). The CES-D has been found to discriminate well between psychiatric inpatients and a general population (Sawyer Radloff. 1977). The scale contains twenty statements both positive (Items 4, 8, 12 & 16) and negative with a total possible score of 60. The patient is asked to rate how often they have felt this way during the past week (rarely, some of the time, occasionally, or most of the time). The negative questions are scored from 0 to 3 (rarely=0, some of the time=1, occasionally=2 and most of the time=3). The scoring for the positive questions is reversed. The CES-D variable was analyzed as a continuous variable.

Environmental variables were defined as those factors that occur during hospitalization and are external to the individual. Environmental factors included social contacts, restraint use, patient movement throughout the hospital, invasive and non-invasive procedures, objects that provided meaning and orientation, telephone use, formal health care contacts, and medications. All variables were measured until delirium developed or until discharge for the non-delirious group.

Social contacts were assessed through the use of a guest book. Visitors were asked to sign in, and specify their relationship to the patient. The number of visitors was summed daily. The number of visitors was analyzed as the mean number of visitors up to day 4. To control for the differential effects of length of stay between delirious and non-

delirious patients the mean onset of delirium (Day 4) was utilized as a cut-off point for variables collected each day the patient was in the study. As such, number of visitors was averaged over the patient's first four days.

Restraints were defined as any device that restricts patient movement regardless of intent. Restraint use was examined both as a risk factor for delirium and as an outcome of delirium. Restraint use and type of restraint were monitored daily through observation and chart review. As an independent variable, use of restraints included use of siderails, except on the day of surgery. When analyzed as an outcome variable, only the use of a belt or lap restraint was coded as a restraint. Restraint variables were coded as no restraints (0) and restraints (1).

Patient movement within the hospital was assessed daily through a combination of information sources. The patient was asked to describe events of the previous day. In addition, the primary nurse was asked if the patient was transported to other areas. Finally, information was sought from the patient chart. The number of times the patient left their unit was summed daily. The number of times off the unit was averaged up to and including day 4 and analyzed as a continuous variable.

Room type was recorded as ward (1) or semi/private (0). If an individual had been transferred during hospital stay, the room that they spent the most time in during the first five days of hospitalization was recorded.

Number of room transfers during study period was recorded. Data were collapsed into a dichotomous variable (no transfers=0 and transfers=1).

Invasive procedures such as insertion of an intravenous, catheter insertion, blood tests, and scans requiring invasive preparation were monitored daily through interview, observation and chart information. The number of invasive procedures a patient underwent was recorded daily. The number of invasive procedures were averaged over the first 4 days and analyzed as a continuous variable.

Procedures was a general category including invasive and non-invasive procedures. This included procedures such as x-rays, electrocardiogram and ultrasound, in addition to the invasive procedures previously defined. The number of procedures the patient underwent was recorded daily. The number of procedures were averaged over the first 4 days and analyzed as a continuous variable.

Catheterization was evaluated daily through interviews and chart reviews. Catheterization, defined as the insertion of a foley or suprapubic catheter, was analyzed as a binary variable (no catheter=0 and catheter=1).

Objects that provide meaning and orientation included newspapers, timepieces, radio, television and personal belongings such as pictures. The number of these objects was assessed and recorded daily. Number of orienting objects was averaged over the first 4 days and analyzed as a continuous variable.

Telephone use represented a proxy of whether or not the individual had some form of social contact. As significant others may not be able to visit, the use of the telephone may represent an important way that the patient and significant other(s) maintains contact. Telephone use was initially monitored through the use of a call logbook, however when this proved too much of a burden for patients and staff, a list of those individuals within

the study who had telephone hook-up was obtained. The use of a telephone is an additional expense, and thus only those who would actually use it would have one. Telephone availability was recorded as telephone present (1) or absent (0).

Consults were the number of contacts with formal health care providers and was measured by number of consults to occupational therapy, medicine, physiotherapy, respiratory therapy, discharge planning, nutrition and food services staff, social work and others recorded in individual discipline documentation. These records were validated during chart review. Number of health care discipline contacts were analyzed individually as dichotomous variables (no=0 and yes=1) and as a continuous variable (the number of consultations to different services).

Medications were assessed on admission and then daily. Only medications administered up to and including the period prior to incident delirium or until discharge were entered. Medication information was available on the patient's chart. Medications were classified utilizing the American Hospital Formulary Service Pharmacologic-Therapeutic (AHFS) classification. If the AHFS classification codes did not identify individual medications and classses of medications separately that have been found in previous literature to be associated with delirium, then new codes based on the AHFS codes were created to identify these medications. Each medication class was analyzed, and detailed analyses on anticholinergics, neuroleptics, narcotics, Histamine-2 (H_2) antagonists, digoxin and benzodiazepines as specific agents were conducted as these medications have been found to be risk factors for delirium in previous studies. Exposure to anticholinergic agents was defined as administration of antihistamines, tricyclic

antidepressants, antiemetics and neuroleptics. Benzodiazepines were classified into long-acting (Librium,Rivotril, Valium, Mogadon and Dalmane) and short-acting (Halcion, Ativan, Serax, and Versed).

Medication combinations predicted to lead to moderate or severe adverse events (Hansten & Horn. 1996) were analyzed. In addition, a clinical pharmacist reviewed medication classes to determine likely interactions leading to a negative impact on mental function.

Number of medications in hospital was the total number of different medications the patient was taking during hospitalization. This information was obtained from the medication administration record in the patient chart. Number of medications in hospital was analyzed as a continuous variable.

Number of medications on admission was the number of different medications the patient was taking in the week preceding their admission to hospital. This was recorded on admission to hospital and was analyzed as a continuous variable.

Patient Controlled Analgesia (PCA) was whether or not a surgical patient used a self-controlled pump that dispensed a preset amount of intravenously administered narcotics. This information was analyzed as a binary variable, absent (0) or present (1).

Outcome variables.

In addition to the use of restraints, the following outcome variables were examined:

Length of Stay was defined as the number of days from the time the patient was admitted to a medical or surgical unit until the day of discharge. This information was

available through the health records department. Length of stay was analyzed as a continuous variable.

Mortality included all patient deaths during hospitalization. This information was available through health records. Mortality was coded as a binary variable, expired (1) and discharged alive (0).

Readmission within one month was collected through the admitting department. Patients are tracked from the day of discharge until the day of readmission. Readmission status was coded as a binary variable, no readmission (0) and readmission (1).

Institutionalization information was available through health records. Where the patient was discharged to was coded as a dichotomous variable representing institutionalization. Patients who were discharged to an institution and who had not been admitted from an institution, were coded as institutionalized (1), and patients who were not discharged to an institution or who were admitted back to an institution were coded as not institutionalized (0).

4.4 Data Analysis

Logistic regression.

Logistic regression is a statistical model appropriate for binary outcomes (i.e., those outcomes with only two responses). In this study, the logistic regression model provided an estimate of the probability of delirium occuring given a set of continuous or dummy-coded variables. Specifically, the dependent variable (in this case delirium) is defined as the natural logarithm (ln) of the odds of disease, or the logit (Hennekens & Buring, 1987).

Given the probability of delirium occurring (represented by Y=1), the logistic regression model can be expressed as:

$$\log \frac{p(Y=1)}{1-p(Y=1)} = a + \sum bx_i$$

or

$$p(Y=1) = \frac{e^{a+\sum bixi}}{l+e^{a+\sum bixi}}$$

where a represents the intercept term and $\sum b_i x_i$ represents the effects of the set of independent variables. The coefficients obtained through logisitic regression denote the magnitude of the increase or decrease in the log odds produced by one unit of change in the value of the independent variable, while controlling for the effects of the other variables in the model (Hennekens & Buring. 1987). An odds ratio can be calculated by exponentiating the beta coefficients. An odds ratio of 1.0 indicates that the incidence rate of delirium in the exposed and nonexposed groups is identical, therefore there is no association between the exposure and the incidence of delirium in the data. A value greater than 1.0 indicates a positive association or increased risk of delirium among those exposed. Conversely, an odds ratio less than 1.0 means there is an inverse association or a decreased risk among those exposed. Odds ratios provide a valid estimate of relative

risk when the cases of disease are newly diagnosed, and prevalent cases are not included (Hennekens & Buring. 1987).

Confidence limits around this estimate of relative risk can be obtained using the beta coefficient and its related standard error.

$$95\% \text{ Confidence interval} = e^{(b_i \pm 1.96 SE_{b_i})}$$

The confidence interval provides information on whether the association is significant at the specified level. For example, if a 95% confidence interval includes the null value (i.e., 1.0), then the corresponding p value is, by definition, greater than 0.05 (Hennekens & Buring. 1987). The confidence interval provides additional information by indicating the amount of variability inherent in the estimate (i.e., the narrower the confidence interval, the more stable the estimate).

In this study, only the initial episode of delirium (as defined by the CAM) for each subject was included in the analysis. Information on subsequent delirious episodes was not included.

Unadjusted odds ratios (O.R.) were calculated as the ratio of number of incident cases of delirium when the host or environmental factor was present versus the number when the factor was absent. Similar to other delirium studies, bivariate correlations significant at $p<.10$ were entered into a multiple logistic regression model. Non-significant variables were removed sequentially until all the variables were significant ($p<0.05$). Those variables removed were added back into the model sequentially to ensure there were no other significant variables. Variables that were significant in

previous studies but not significant in this study (eg. activity limitation, severity of illness) were entered into the final model to assess contribution. Interaction terms between the main effects in the final model were examined in order to determine whether the effect of an independent variable is modified by a second variable.

Coefficient of determination.

The use of R^2, the coefficient of determination, is well established in classical regression analysis (Rao. 1973). It is defined as the proportion of variance "explained" by the regression model, and therefore useful as a measure of success of predicting the dependent variable from the independent variables (Nagelkerke. 1991). In more general binary response models, the concept of residual variance cannot be easily defined. The following generalization has been proposed (Maddala. 1983)

$$R^2 = 1 - \left[\frac{L(0)}{L\left(\hat{\beta}\right)} \right]^{\frac{2}{n}}$$

where L(0) is the likelihood of the intercepts-only model, $L\left(\hat{\beta}\right)$ is the likelihood of the specified model, and *n* is the sample size. This measure achieves a maximum of less than 1 for discrete models, with maximum given by

$$R^2_{max} = 1 - \left[L(0)\right]^{\frac{2}{n}}$$

Nagelkerke (1991) proposed an adjusted coefficient, which can achieve a maximum value of 1:

$$R^2_{adj} = \frac{R^2}{R^2_{max}}$$

The coefficient of determination is given for the full models.

Analysis of Outcomes.

Data on outcomes associated with the development of delirium were examined using logistic regression models for the dependent binary variables mortality, restraint use, morbidity and institutionalization. To analyze length of stay as a dependent continuous variable, a multiple linear regression model was used. Factors identified in previous research as risk factors for these outcomes were included in the models to determine the independent contribution of delirium.

To reiterate, there were one hundred and sixty one patients meeting the study criteria from July 03, 1996 to September 18, 1996. Five individuals (3%) refused to participate leading to a final sample size of one hundred and fifty six patients. These patients were followed for 14 days after admission or until discharge. Characteristics of the study sample are shown in Table 5.

The mean age of the study population was 76.4 years (SD 6.48). Approximately 61% (n=95) were female and 61% (n=95) were medical as compared to surgical admissions. The majority (94%) of admissions were directly from home. 47% (n=74) were married. Almost half the study population (49%) had a grade 8 education or less. The majority of the admissions were either urgent or emergency, and had no prior admissions to this hospital in the previous year. Scores on the MMSE ranged from 12 to 30 on admission, with twenty seven (17%) research participants classified as cognitively impaired according to the MMSE.

Incident delirium occurred in 28 patients (17.4%) in the study population. The median onset of delirium was hospital day 3 (range, day2-day14) . The majority (79%) of patients developed delirium within six days. Of those individuals with incident delirium, one-half (n=14) had an episode of delirium lasting at most twenty four hours, typically occurring at night. The remainder experienced delirium for two or more days, with three individuals experiencing delirium for six days (Table 6).

Table 5
Characteristics of Study Population (n=156)

Age, mean (± SD)	76.4 yrs (± 6.48)	
	% of Total Sample	
Female	61%	(n=95)
Prior Residence		
Home	94%	(n=146)
Marital Status		
Married	47%	(n=74)
Widowed	38%	(n=59)
Single	15%	(n=23)
Education		
< 8 yrs	49%	(n=77)
9 - 12 yrs	32%	(n=49)
Post-secondary	16%	(n=25)
University	3%	(n=5)
Admission		
Emergent/Urgent	62.2%	(n=97)
Elective	37.8%	(n=59)

Table 6
Patient Days of Delirium

# Days With Delirium	# Patients
1	14
2	3
3	3
4	3
5	1
6	3

5.1 Bivariate Analyses: Host Factors

Unadjusted risk factors significant at $p<.10$ included age, cognitive impairment, abnormal hemoglobin value, diseases of the musculoskeletal system, and visual limitations (Table 7). Other than age, no demographic variable was a statistically significant risk factor for delirium. Therefore, marital status, gender, education, whether or not they lived alone, and type of admission were not significant predictors of delirium.

No single diagnostic category was found to significantly increase the risk of delirium, however as there were so few individuals with the same diagnoses, it was important to group diagnoses into larger clinical categories. The major clinical category, diseases of the musculoskeletal system and connective tissue, was significant. As this category was significant, the disease diagnostic category of osteoarthritis was examined in further detail, but was not significant at the bivariate level.

Measures of positive and negative affectivity, and depression were not predictive of delirium. Interestingly, illness severity was not significant either as a continuous or dichotomous variable.

Activity limitation, measured as a continuous variable or as a binary score (severe (1) and mild to moderate (0)) was not a significant predictor of delirium.

Other variables that were not significant at the bivariate level included dehydration ratio, the individual values for creatinine or urea, abnormal lab values, (with the exception of hemoglobin), fever, and intercurrent illnesses.

Table 7

Unadjusted Odds Ratios for Delirium (p < .1): Host & Environmental Factors

	% Without Delirium (n= 128)	% With Delirium (n=28)	Unadj. OR	CI (95%)		β	SE
Host Factors							
Age (Continuous variable)			1.1	>1.0	1.1	0.07	0.03
Musculoskeletal Diseases	14.1	32.1	2.9	1.1	7.4	1.06	0.48
Visual Limitation	10.9	28.6	3.3	1.2	8.8	1.18	0.51
Hemoglobin	32.0	60.7	3.3	1.4	7.6	1.19	0.43
Cognitive Impairment	10.6	33.3	4.2	1.6	11.3	1.44	0.50
Environmental Factors							
Catheterization	8.6	28.6	4.3	1.5	11.9	1.45	0.52
Surgery	35.2	57.1	2.5	1.1	5.7	0.90	0.42
ICU Stay	0.8	21.4	34.6	4.0	301.8	3.54	1.11
Mean Number of Procedures (Day 4 inclusive) (Continuous variable)			2.0	1.1	3.8	0.69	0.32
Mean Number of Invasive Procedure (Day 4 inclusive) (Continuous variable)			2.7	1.2	6.2	1.0	0.42

5.2 Bivariate Analyses: Environmental Factors

Medications.

The number of medications received while in the hospital was a significant risk factor at the bivariate level. Information concerning the number of admitting medications was not available for 47 patients and thus could not be analyzed. Medication classes found to be significant at the bivariate level ($p<.10$) included opiate agonists coded as a continuous variable, long acting benzodiazepines, and H_2 Antagonists (Table 8). Combinations found to be significant included demerol and H_2 Antagonists, morphine and H_2Antagonists, antidepressants and short-acting benzodiazepines, long-acting benzodiazepines and cardiac drugs, long acting benzodiazepines and H_2 Antagonists, and benzodiazepines and opiate agonists (Table 8). Although demerol was borderline for the statistical significance cut-off for inclusion in the model ($p<.11$), it was included as it has previously been found to be a risk factor for delirium (Marcantonio, Juarez, Goldman, et al. 1994). Findings related to medication classes hypothesized to increase the risk of delirium, based on the previous literature, are presented in Table 9.

Environmental factors.

A number of environmental factors were found to be significant at the bivariate level (Table 7). Significant environmental factors analyzed as binary variables included the use of a foley or suprapubic catheter, an intensive care unit (ICU) stay, and undergoing surgery. Continuous variables include average number of procedures calculated over the first four days, and average number of invasive procedures calculated over the first four days. To control for the differential effects of length of stay between

Table 8
Unadjusted Odds Ratios for Delirium (p < .1): Medications

	% Without Delirium (n= 128)	% With Delirium (n= 28)	Unadj. OR	CI (95%)		β	SE
Medications							
Number of Hospital Medications (Continuous variable)			1.2	1.1	1.4	0.19	0.07
Opiate Agonists (Continuous variable)			1.6	1.0	2.5	0.47	0.22
Demerol	27.3	42.9	2.0	0.9	4.6	0.69	0.43
Morphine	19.5	35.7	2.3	0.9	5.6	0.83	0.45
Benzodiazepines (Long Acting)	4.7	14.3	3.4	0.9	12.9	1.22	0.68
Histamine$_2$ Antagonists	12.5	32.1	3.3	1.3	8.6	1.20	0.48
Demerol & Histamine$_2$ Antagonists	3.1	14.3	5.2	1.2	22.1	1.64	0.74
Morphine & Histamine$_2$ Antagonists	0.8	7.1	9.8	0.9	111.8	2.28	1.24
Antidepressants & Benzodiazepines (Short Acting)	0.8	7.1	9.8	0.9	111.8	2.28	1.24
Antidepressants & Benzodiazepines (Short & Long Acting)	0.8	10.7	15.2	1.5	152.5	2.72	1.18
Benzodiazepines (Long Acting) & Cardiac Drugs	2.3	10.7	5.0	1.0	26.2	1.61	0.85
Benzodiazepines (Long Acting) & Histamine$_2$ Antagonists	0.8	7.1	9.8	0.9	111.8	2.28	1.24
Benzodiazepines (Short & Long Acting) & Opiate Agonists (Continuous variable)			1.6	1.1	2.3	0.47	0.19

Table 9

Unadjusted Odds Ratios for Medications Predictive of Delirium in Previous Literature

	% Without Delirium (n= 128)	% With Delirium (n= 28)	Unadjusted OR	CI (95%)		β	SE
Therapeutic Classification							
Anticholinergic							
Atimuscarinics / Antispasmodics	0.8	3.6	4.7	0.3	77.6	1.55	1.43
Antihistamine	3.1	0	–	–		–	–
Antiemetics	45.3	60.7	1.9	0.8	4.3	0.62	0.43
Antidepressants	5.5	14.3	2.9	0.8	10.6	1.06	0.67
Tranquillizers	4.7	7.1	1.6	0.3	8.2	0.45	0.84
Cardiac Drugs	43.0	35.7	0.7	0.3	1.7	-0.30	0.43
Adrenals (Steroids)	5.5	3.6	0.6	0.1	5.4	-0.45	1.09
Non-Steroidal Anti-inflammatory Agents	28.1	21.4	0.7	0.3	1.9	-0.36	0.50
Benzodiazepines							
Short Acting	35.9	46.4	1.6	0.7	3.5	0.43	0.42
Long Acting	4.7	14.3	3.4*	0.9	12.9	1.22	0.68
Narcotics							
Opiate Agonists (Continuous)			1.6**	1.0	2.5	0.47	0.22
Demerol	27.3	42.9	2.0	0.9	4.6	0.69	0.43
Histamine$_2$ Antagonists	12.5	32.1	3.3**	1.3	8.6	1.20	0.48

Note * $p<.10$
** $p<.05$

delirious and non-delirious patients the mean onset of delirium (Day 4) was utilized as a cut-off point for variables collected each day the patient was in the study. As such, number of procedures, number of invasive procedures, number of visitors, and number of orienting objects were averaged over the first four days.

Variables that were not significant at the bivariate level included mean number of orienting objects over the first four days, room type (ward versus semi or private), prior admissions over the preceding year, number of transfers during during hospitalization, consults to professional staff analyzed in combination and singly, and the presence of a telephone. The mean number of visitors over the first four days was not significant, although no information was available for twenty six individuals. Individuals who lived alone were compared with those who did not to determine if they were more likely to have this information missing. There was no significant difference. Those variables that were significant in previous studies but not significant in this study are included in Table 10.

Use of restraints (including use of siderails, except on the day of surgery) was not predictive of the development of delirium. However, no patients were recorded as having trunk or pelvic restraints applied prior to the onset of delirium. In addition, use of patient controlled analgesia was not significant for surgical patients.

5.3 Multivariate Analyses

Variables significant at $p<.10$ were entered into the mutivariate model, and those significant at $p<.05$ were retained. The full multivariate logistic regression model included age (OR=1.1), cognitive impairment (OR= 6.3),a high average number of

Table 10

Selected Non-Significant Unadjusted Odds Ratios for Delirium (p> .10): Host & Environmental Factors

	Unadj. OR	CI (95%)		β	SE
Host Factors					
Severe Activity Limitation	1.3	.8	2.1	1.8	1.3
Severity of Illness	1.0	.8	1.3	.01	.1
Abnormal Lab Values					
Abnormal Sodium	2.3	.2	26.7	.85	1.2
Abnormal Potasium	3.2	.5	20.2	1.2	.9
Elevated serum urea	1.9	.8	4.6	.62	.5
Fever	.7	.2	2.5	-0.37	.7
Depression (CES-D)	1.3	.1	15.9	.24	1.3
Male Gender	.7	.3	1.7	-0.34	.4
Dehydration	1.2	.5	2.9	.15	.5
Environmental Factors					
Mean Number of Orienting Objects (4 days)	.7	.3	1.4	-0.38	.4
Visitors (summary - 4 days)	1.0	.9	1.1	-.003	.04

procedures over the first four hospital days (OR=3.1), a high number of medications received during hospitalization (OR=1.2), surgery (OR=7.6), and a period in the intensive care unit (OR= 22.4) (Table 11). No significant ($p<0.05$) interactions between main effects were found. The coefficient of determination for this model was 41%.

The variable for average number of procedures was further analysed utilizing various cut-off points from day 3 to day 14 and was found to be significant in the full model regardless of the cut-off point utilized.

Although number of hospital medications may be of interest in allowing comparisons to previous literature, it may be more helpful to clinicians to identify specific pharmacological agents that increase risk for delirium. When the variable number of hospital medications was removed from the model, two drug variables became significant, H_2 Antagonists, and a combination of benzodiazepines and tricyclic antidepressants (Table 12). The coefficient of determination for this model was 46%

To provide a direct comparison with the only other study of the effects of environmental variables on the development of in-hospital delirium, a multivariate model that included hospital days (a variable representing days to the development of delirium or discharge from the study) was examined. Variables significant in the full multivariate model remained significant. In the previous study, catheterization was an important risk factor. To evaluate the independent contribution of catheterization, average number of procedures was removed from the full model and replaced with catheterization. This variable approached significance ($p=.06$) (Table 13).

Table 11

Adjusted Odds Ratios for Delirium: Multivariate Model with Number of Hospital Medications

Variable	Adjusted OR	β	SE	95% CI	
Age (continuous)	1.1**	0.13	0.04	1.0	1.2
Hospital Medication (continuous)	1.2*	0.20	0.10	1.0	1.5
Cognitive Impairment	6.2**	1.83	0.68	1.6	23.7
Surgery	7.6**	2.03	0.68	2.0	28.7
Mean Number of Procedures to Day 4 (continuous)	3.1*	1.12	0.45	1.3	7.5
ICU	22.4*	3.11	1.24	2.0	252.4

Note: * $p<.05$
** $p<.01$

Adjusted RSquare = 41%

Table 12

Adjusted Odds Ratios for Delirium: Multivariate Model with Medication Classes

Variable	Adjusted OR	β	SE	95% CI	
Age (continuous)	1.1**	0.13	0.05	1.0	1.
Antidepressants and Benzodiazepines	35.2*	3.56	1.57	1.6	764.
Histamine$_2$ Antagonists	4.2*	1.43	0.62	1.2	14.
Cognitive Impairment	5.6*	1.71	0.67	1.5	20.
Surgery	10.0**	2.31	0.71	2.5	40.
Mean Number of Procedures to Day 4 (continuous)	3.8**	1.34	0.47	1.5	9.
ICU	20.8*	3.03	1.30	1.6	264.

Note: * p<.05
** p<.01
*** p<.001

Adjusted RSquare = 46%

Table 13
Adjusted Odds Ratio for Delirium: Multivariate Model with Catheterization

Variable	Adjusted OR	β	SE	95% CI	
Age (continuous)	1.1*	0.09	0.04	1.0	1.2
Hospital Medication (continuous)	1.3*	0.23	0.10	1.0	1.5
Cognitive Impairment	4.6*	1.54	0.66	1.3	16.8
Surgery	3.3*	1.20	0.59	1.0	10.6
Catheterization	3.1 (p=.06)	1.14	0.62	0.9	10.5
ICU	31.0**	3.44	1.21	2.9	335.0

Note: * $p<.05$
** $p<.01$

Adjusted RSquare = 39%

5.4 Outcomes Associated With Delirium

Mortality.

Seven patients died, four of these individuals had experienced delirium. Delirium was a significant risk factor for mortality ($p<.05$) at the bivariate level. Other variables significant at the bivariate level ($p<.10$) included increased comorbidity scores, older age, increased severity of illness, and cognitive impairment. In a multivariate logistic regression model, individuals with higher comorbidity scores (OR=1.7) and cognitive impairment (OR=18.4) were more likely to die (Table 14). Once these variables were entered in the model, delirium was not an independent predictor of mortality.

Institutionalization.

There were seven individuals admitted to a higher level of care following discharge (e.g., retirement home to chronic care hospital). There were no significant ($p<.10$) predictors of institutionalization. Variables examined at the bivariate level included activity limitations, whether or not the individual lived alone, increasing age, gender, severity of illness, comorbidity, education, marital status, increased number of hospital medications, and delirium.

Combined institutionalization and mortality.

For purposes of comparison, institutionalization and mortality were combined as an outcome variable. Significant predictors at the bivariate level ($p<.10$) included individuals who lived alone, had higher comorbidity scores, were cognitively impaired, had an increased severity of illness score, had higher activity limitation scores, had a grade eight education or less, and had experienced an episode of delirium during

Table 14
Significant Unadjusted and Adjusted Odds Ratios for Mortality

Variable	Unadjusted Odds Ratio	Adjusted Odds Ratio	95% C.I.		Adjusted β	Adjusted SE
Age (Continuous variable)	1.1*					
Cognitive Impairment	19.3****	18.4***	2.9	118.0	2.91	0.95
Comorbidity (Continuous variable)	1.8***	1.8**	1.1	2.8	0.58	0.23
Delirium	6.9**					

Note: * p<.1
** p<.05
*** p<.01
**** p<.001

hospitalization. In a multivariate logistic model, individuals who had higher comorbidity scores (OR= 1.4), cognitive impairment (OR= 7.5), and lived alone (OR=3.7) were more likely to die or become institutionalized ($p<.05$) (Table 15). Delirium was not an independent significant predictor.

Length of stay.

Individuals experiencing delirium during their hospital stay had an average length of stay of 20 days (SD 20) with a range of 2-82 days. One individual with delirium was taken out of the hospital by family members on day 2, against medical advice. Individuals free of delirium had an average length of stay of 8 days (SD 8.58), with a range of 2-52 days.

Variables significantly correlated with length of stay included increased severity of illness, increased activity limitation, and experiencing delirium.

In a multiple linear regression model, individuals with higher severity of illness ($p=.0001$), having an episode of delirium ($p=.0001$), and a higher activity limitation score ($p=.01$) were significantly more likely to have a longer length of stay in the hospital (Table 16). These three predictors explained 26% of the variance in length of stay.

Restraint use.

Seven individuals were restrained using a trunk or lap belt. All seven had developed delirium, and restraints were an intervention by staff. No individual not experiencing delirium was restrained in this manner.

Table 15
Significant Unadjusted and Adjusted Odds Ratios for Institutionalization or Death

Variable	Unadjusted Odds Ratio	Adjusted Odds Ratio	95% Conf. Interval		Adjuste β	
Activity Limitation (Continuous variable)	55.2**					
Cognitive Impairment	8.4****	7.5***	2.2	26.0	2.02	0.6
Comorbidity (Continuous variable)	1.4**	1.4**	1.1	1.9	0.35	0.1
Delirium	4.1**					
Education	0.4*					
Lived Alone	2.8*	3.7**	1.0	13.2	1.30	0.6

Note: * p<.1
** p<.05
*** p<.01
**** p<.001

Table 16
Linear Regression Model for Length of Stay

Variable	Parameter Estimate	Standard Error
Activity Limitation (Continuous variable)	14.3*	5.8
Delirium	12.0**	2.4
Illness Severity (Continuous variable)	2.0**	0.5

Note: * $p<.05$
**$p<.0001$

$R^2 = 26\%$
$F_{3,152} = 18.24$

Morbidity.

There were 14 cases of intercurrent illnesses during hospitalization. In seven cases, the individual was classified as delirious. Of these seven cases, only three cases experienced an intercurrent illness following the delirious episode. In order to examine the outcomes associated with delirium, the four cases experiencing an intercurrent illness prior to the incidence of delirium were coded as "0" , not experiencing an intercurrent illness. A high number of hospital medications, having less than grade 8 education, and experiencing delirium were significant at the bivariate level ($p<.10$). In a multivariate logistic model, an increased number of hospital medications (OR= 1.2) and education less than grade 8 (O.R= 4.3) were weakly predictive ($p<.10$) of developing an intercurrent illness (Table 17) Delirium was not an independent significant predictor of morbidity.

Readmission.

There were ten individuals re-admitted to the hospital up to one month following discharge. Severity of illness, comorbidity, having less than grade eight education, a previous emergent/urgent admission, and increased number of hospital medications were significant predictors of readmission at the bivariate level ($p<.10$). In a logistic regression model, higher comorbidity scores (OR= 1.4), greater than grade 8 education (OR=6.5) and a high number of hospital medications (OR= 1.3) were significant predictors of readmission (Table 18). Delirium was not an independent predictor of readmission.

Table 17

Significant Unadjusted and Adjusted Odds Ratios for Intercurrent Illness

Variables	Unadjusted Odds Ratio	Adjusted Odds Ratio	95% Conf. Interval		Adjusted β	Adjusted SE
Education	0.2*	0.2*	0.1	1.1	-1.47	0.81
Number of Hospital Medications (Continuous variable)	1.2*	1.2*	1.0	1.4	0.17	0.10

Note: * p<.1
** p<.05

Table 18

Significant Unadjusted and Adjusted Odds Ratios for Readmission Within 1 Month

Variables	Unadjusted Odds Ratio	Adjusted Odds Ratio	95% C.I.		Adjus β
Comorbidity (Continuous variable)	1.3*	1.4*	1.0	2.0	0.32
Education	4.2*	6.5**	1.2	36.5	1.87
Entry Classification	4.2*				
Number of Hospital Medications (Continuous variable)	1.3**	1.3**	1.1	1.6	0.28

Note: * $p<.1$
** $p<.05$

The incidence of delirium was 17.4%, which falls within the range noted in previous studies. Median time to onset of delirium confirms the findings of all other prospective studies, in that risk for delirium is greatest during the first few days of hospitalization. Over one-half of the patients developing delirium did so at night. Nocturnal exacerbation has long been recognized as a hallmark of delirium, possibly secondary to a decrease in sensory cues by which a patient may orient himself or herself (Nicholas & Lindsey. 1995).

There are a number of limitations associated with this study that must be considered. Despite biological plausibility for the associations found in this study, a true etiologic link between these factors and delirium cannot be determined from a descriptive study such as this. Other factors such as the strength of the association, consistency of the findings and presence of a dose-response relationship are important and should be examined in future studies. Further, it is unclear to what extent the results based on one hospital are generalizable to experiences in other settings. However, K-W Hospital does not differ dramatically with respect to funding, staff characteristics, or patient population compared with other community based acute care hospitals in Ontario of similar size. Finally, relatively small numbers of patients developing delirium and exposed to some of the risk factors caused wide confidence intervals. However, as this is an exploratory study designed to detect possible areas for intervention, the results provide a basis for future studies.

There are a number of methodological advances for this study compared to most previous studies of risk factors for delirium. These include a prospective design, the use of a valid and reliable instrument to detect delirium, daily structured interviews, and daily assessment for symptoms of delirium

6.1 Predictors of Delirium

In a multivariate model, age, number of in-hospital medications, cognitive impairment, having surgery, number of procedures and a stay in the icu were significant risk factors for delirium. Two medication classes, Histamine$_2$ receptor antagonists and a combination of benzodiazepines and tricyclic antidepressants were found to be significant when hospital medications as a general variable was removed.

Findings from previous studies conducted on risk factors for delirium are consistent with two of the risk factors found in this study, age (Gustafson, Berggren, Brannstrom, et al. 1988; Marcantonio, Goldman, Mangione, et al. 1994; Rockwood. 1989; Schor, Levkoff, Lipsitz, et al. 1992; Williams, Campbell, Raynor, Musholt, Miynarczyk, & Crane. 1985) and cognitive impairment (Francis, Martin, & Kapoor. 1990; Gustafson, Berggren, Brannstrom, et al. 1988; Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996; Rockwood. 1989; Schor, Levkoff, Lipsitz, et al. 1992). These factors are important clinically as they provide health care professionals with a basis for the development of screening assessments. Unfortunately, knowing that advancing chronological age increases the risk of delirium does not further our understanding of the etiology of delirium or our ability to intervene and possibly prevent delirium. Age can be considered the ultimate confounder as the precise changes that occur with increasing age

that confer a greater risk for delirium are unknown. It is known that aging affects the cholinergic activity within the brain (Francis & Kapoor. 1990). If such a link between delirium and the cholinergic system were confirmed, this may be the process by which age influences the development of delirium.

Decreasing sensory ability has also been hypothesized as being associated with both aging and delirium. In the present study, hearing ability was not associated with delirium. nor was vision impairment. This finding is in contrast with that of Inouye et al. (1993) wherein an increased risk of delirium was found for individuals classified as having impaired vision. However, the small number of individuals classified as visually impaired (n=6) makes it difficult to replicate this finding. The difference in findings may also be associated with the sensitivity of the assessment, as the present study assessed ability to see reading material, while the previous study clinically evaluated vision. O'Keefe & Lavan (1996) operationalized impaired vision as occurring when activities of daily living were affected, but did not find this measure to be a risk factor for delirium. Of interest, however, is that individuals in this study with side vision problems or experiencing "halos" around lights were at an increased risk for delrium at the bivariate level.

It is widely accepted that chronic cognitive impairment increases the risk of developing delirium (Francis, Martin, & Kapoor. 1990; Gustafson, Berggren, Brannstrom, et al. 1988; Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996; Rockwood. 1989; Schor, Levkoff, Lipsitz, et al. 1992). Once again, the specific mechanism underlying this increased risk is poorly understood. The consistency of the

finding may provide some support for the anticholinergic hypothesis related to the etiology of delirum.

Additional support for the anticholinergic hypothesis is provided by the finding that Histamine$_2$ (H_2) receptor antagonists were a significant risk factor for the development of delirium. H_2 receptor antagonists included cimetidine and ranitidine. These drugs block the stimulant action of histamine on the acid-secreting cells of the stomach, thus inhibiting gastric acid secretion. H_2 receptor antagonists are commonly prescribed for gastroesophageal reflux disease (heartburn), peptic ulcers.and for prophylactic treatment of patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs). Although there have been case reports of delirium associated with the use of H_2 receptor antagonists (Weddington, Muelling, & Moosa. 1982; Mogelnicki, Wallen, & Finlayson. 1979), this is the first prospective study to find an increased risk. H_2 receptor antagonists are not classified as an anticholinergic medication, however the delirium associated with their use has been shown to be reversible with the use of physostigmine (Goff, Garber, & Jenike. 1985; Mogelnicki, Wallen, & Finlayson. 1979). The effect of physostigmine is to increase the amount of acetylcholine available at receptor sites in the central nervous system and elsewhere. Physostigmine is considered an antidote for cholinergic blocking agents as it prolongs and exaggerates the effects of acetylcholine. The fact that the use of physostigmine reversed the delirium suggests a possible anticholinergic action of cimetidine. Alternatively, the effects of physostigmine could be due to a non-specific stimulation of the central nervous system. Of interest, however, is that physostigmine therapy has been used with variable results in a limited number of patients with

Alzheimer's disease. In some patients, the drug has improved cognitive and/or behavioral function (American Society of Health-System Pharmacists. 1996). A double-blind, placebo-controlled study of patients with Alzheimer's disease demonstrated that velnacrine, another cholinesterase inhibitor, produced modest but significant benefits(Antuono. 1995). It may be that drug intervention may ultimately be possible for the treatment of delirium. Unfortunately, medications such as physostigmine have serious side effects, such as seizures.

A combination of benzodiazepines and tricyclic antidepressants increased the risk of delirium compared to those individuals not taking this combination. These medications are known to individually precipitate delirium as reported in case studies (Gomolin & Melmed. 1983). Although this combination is known to cause side effects, delirium was not listed as one of those effects. Long-acting benzodiazepines all require phase I oxidative metabolism and therefore have prolonged half-lives in older patients. Tricyclic antidepressants have a moderate to high affinity at muscarinic cholinergic and H_2 histaminergic receptors that is probably related to the untoward effect of delirium (Goodman & Gilman. 1991). However, the small number of individuals (n=4) taking this particular combination of medications precludes generalizability of this finding. Yet, future studies may need to assess the contribution of medication combinations rather than single medication classes.

Some medications found previously to increase the risk of delirium were not significant in the multivariate model in this study. The use of narcotic analgesics have been associated with delirium in two large prospective studies (Francis, Martin, &

Kapoor. 1990; Schor, Levkoff, Lipsitz, et al. 1992) and were significant at the bivariate level in this study. However, narcotic analgesic use was not a significant predictor of delirium in the multivariate model. Also, neuroleptics and psychoactive drugs were not found to be significant.

In contrast to the the findings of Schor et al., patients in this study undergoing a surgical procedure were found to be at higher risk for delirium then patients admitted to medical units. It is worth noting however, that there was a non-significant trend towards an increased risk in the previous study (Schor, Levkoff, Lipsitz, et al. 1992). It is possible that differences between the two populations account for this discrepancy. Schor et al. (1992) studied a university-based teaching hospital that may differ dramatically from community based hospitals in population characteristics. The increased risk of delirium for surgical patients in this study may be related to factors such as immunostimulation hypothesized by Weiss et al to lead to a decrease in plasma tryptophan, which in turn increase the risk of delirium (Weiss, Werner, Werner-Felmayer, & Wachter. 1991).

The finding that a high number of procedures increased the risk of delirium is an important hospitalization-related finding. Although Inouye & Charpentier (1996) did not include this variable, their related finding that any iatrogenic event increased the risk of delirium provides compatible evidence. Their definition of iatrogenic event included such factors as urinary tract infection following instrumentation, phlebitis, and transfusion reactions (Inouye & Charpentier. 1996). In order to incur an iatrogenic event, individuals typically must first undergo a procedure. The greater the number of procedures that an individual undergoes, the higher the associated risk of experiencing an adverse outcome.

It is interesting that catheterization was of borderline significance as a risk factor for delirium in this study when average number of procedures was removed from the model. However, inclusion of the average number of procedures that an individual underwent during hospitalization was associated with a higher explained variance in delirium. Thus, it may be the number of procedures that an individual undergoes is important, regardless of what the procedures actually are.

A high number of hospital medications was a risk factor for delirium. This confirms the findings from two previous prospective studies (Foreman, 1989; Inouye & Charpentier, 1996). Risks associated with the use of multiple medications is important for the elderly. In a recent study of acutely hospitalized male veterans aged 65 and older, 42% reported use of five or more prescription drugs (Satish, Hutner Winograd, Chavez, & Bloch, 1996). Further, elderly community residents using three or more prescription drugs compared with one or two, were more likely to be taking an inappropriate medication(Stuck, Beers, Steiner, Aronow, Rubenstein, & Beck, 1994). The increased risk of adverse events associated with the use of multiple medications (often referred to as polypharmacy) in the elderly is well known (see for example, (Stuck, Beers, Steiner, Aronow, Rubenstein, & Beck, 1994; Carr & Michele, 1994). In Ontario, one-third of all reported adverse drug reactions were on people older than sixty (Gowdey & Brennan, 1985). In a previous study, polypharmacy was found to be a significant predictor of nursing home placement (Satish, Hutner Winograd, Chavez, & Bloch, 1996). In a prospective study of 9651 admissions through an emergency department resulting in a stay of more than 24 hours, 5.7% of all admissions were drug-related (Dartnell, Anderson,

Chohan, et al. 1996). Unfortunately, the multiple comorbid conditions experienced by the elderly may necessitate higher prescription practices. However, the variety of risks associated with multiple medication use highlights the significance of judicious use of medications for the elderly.

A stay in an intensive care unit was found to increase significantly the risk of incident delirium. This may be related to the nature of the environment, with multiple invasive and non-invasive procedures, numerous consults, noise and lighting. The number of procedures that each patient underwent while in ICU could not be determined, as not all procedures would have been recorded on the patient record. It is probable that a combination of factors increases the risk of delirium for patients in the ICU. It is important to note, however, the wide confidence interval associated with this finding. Only seven individuals had a stay in icu. Of these, six individuals developed delirium.

6.2 Non-Significant Findings

A number of variables previously noted to be a risk factor for delirium were not found to be significant at the bivariate or multivariate level in this study. Further, some of the environmental variables identified as possible risk factors were not significant. In some cases this may be due to low rates of exposure to the risk factor. For example, although fracture on admission was a significant risk factor for delirium in a previous study, only two patients were admitted with a fracture during this study period. In this situation, the independent contribution of fractures could not be assessed. However, for other potential risk factors, non-significant associations may be due to other reasons. It is important to discuss a number of these variables to provide a basis for future studies.

Delirium was not associated with severity of illness, in contrast to the findings from the majority of studies conducted in teaching hospitals. This may reflect a difference in severity of illness for admissions to teaching hospitals and community hospitals. In this study population, the highest severity designation was an "8" (n=2) on a 9 point ordinal scale. Physicians rated the severity of illness for 12 (7.6%) patients in the severe range (7-9), with only two of these patients developing delirium. In comparison, the two other studies using the same tool rated 27% (O'Keeffe & Lavan. 1996) and 19% (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993) of the study population as severely ill. There may also be some differences according to who rated the patients. In this study, the admitting physician rated the patient. Other studies have used the primary nurse (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993) and the study physician (O'Keeffe & Lavan. 1996).

Activity Limitation was not a significant risk factor for delirium, whether as a continuous measure or for individuals with the most limitations. Some studies have found decreased physical function to be a significant risk factor for delirium (Williams, Campbell, Raynor, Musholt, Miynarczyk, & Crane. 1985; Marcantonio, Goldman, Mangione, et al. 1994) while others have not (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996). It may be that baseline activity levels are significant for certain subpopulations, for example surgical patients. Those studies identifying activity limitation as a significant risk factor were conducted with patients undergoing surgery. However, future studies using an observation-based measure of physical function are necessary to determine the contribution of activity limitation.

Fever, measured as a temperature greater than 37.5 was not a significant predictor of delirium. Fever is a predictor of infection. In the elderly population, the evaluation of fever is difficult. Several studies have shown that significant infections may be present in the elderly with an altered or no febrile response (Gleckman & Hibert. 1982; Finkelstein. Petkun, & Freedman. 1983). It may be that delirium occurs only at higher temperatures. and thus in future studies, body temperature should be measured as a continuous variable rather than as a dichotomous variable.

The evaluation of risk associated with admissions from institutions was not possible in this study, as only six percent (n=10) of the study sample were admitted from an institution. Of those admitted from an institution, three developed delirium.

Abnormal lab values were not a significant risk factor for delirium, either singly or in combination. The only exception was a low hemoglobin, significant at the bivariate level. This finding may have been confounded with surgery, explaining why it was not significant in multivariate analyses. As many of the abnormal lab values occurred in only a few individuals, this study may have lacked sufficient power to adequately assess their contribution to the development of delirium.

Social contacts was assessed through the use of a guest book. Unfortunately, almost 17% did not have information available. This may have indicated either that they did not have visitors, or that people did not sign in. Further, any estimate of the number of visitors is probably an underestimate, as not every visitor would sign in. It may be that it is not the number of visitors, but the type of support they are able to offer the patient, or perhaps the length of the visit, that is important.

Room Type (e.g. ward versus private or semi-private) was not a significant risk factor for delirium. It may be that the room type is not an important factor per se, but perhaps the level of noise has more relevance. However, this is difficult to measure due to the variability. Further, patients were moved to quieter locations if the noise was too disturbing, particularly at night. Because it is possible that cognitive impairment differentially affects the risk associated with room type, an interaction between cognitive impairment and room type was analyzed, however was not significant. The amount of noise and number of disturbances throughout the night may be an important environmental variable to include in future studies

Number of room transfers has been hypothesized to be a risk factor for delirium, and yet was not confirmed in this study. Patients had as many as three transfers during their hospital stay. Individuals receiving rehabilitation therapy following surgery were transferred at least once during their stay. It may be that certain subpopulations (e.g. cognitively impaired) are at greater risk for delirium following transfers; however, that interaction was not significant in this study.

Those individuals who had been admitted to the hospital during the previous year may have been more familiar with the surroundings, and perhaps at a decreased risk of delirium. However, this hypothesis was not confirmed in this study. It is possible that familiarity with the surroundings is only important for certain subpopulations of patients.

The number of consults to medical specialists and allied health professionals was not a significant predictor of delirium. This variable was intended as an indirect measure of the number of different staff in contact with the patient. A number of intervention

studies have attempted to limit the number of different staff in contact with the patient, and yet no prospective study has identified this variable as a risk factor. Initially, staff were asked to initial a door sheet each time they had some form of contact with the patient. Unfortunately, this proved too great a burden for hospital staff. As allied health professionals must record each visit, departmental records were used to determine the number of consults. This area warrants further investigation, however a method involving little compliance from staff needs to be developed.

Implications for Clinical Practice

The focus of this study was to identify iatrogenic, hospitalization-related factors that contribute to delirium and are potentially remediable. As such, the significant finding that the average number of procedures that an individual undergoes during the first few days of hospitalization is important. While many of the procedures identified in this study may have been essential, a number may not have been. For example, blood tests are ordered routinely, and often many blood samples are drawn throughout the day. It may be useful to evaluate this routine, decreasing both the number of tests ordered, and the number of blood draws that are required. While the procedure itself may be important, the frequency may be decreased without a concommitant decrease in sensitivity. For example, how frequently do x-rays need to be taken in order to evaluate clinical progress? Further, it may not be the procedure itself that is critical, but something associated with the procedure. It may be that there are different staff coming in to do each procedure, that the procedure itself is not being fully explained, or some other related factor.

The other factor identified in this study that is amenable to intervention concerns the increased risk of delirium associated with a greater number of medications given during hospitalization, Histamine$_2$ receptor antagonists and the combination of tricyclic antidepressants and benzodiazepines. Recently the value of prophylactic treatment with an Histamine$_2$ receptor antagonists was questioned, as a prospective study found patients taking these in combination with NSAIDS experienced a significantly higher risk for serious gastrointestinal complications (Singh, Ramey, Morfeld, Shi, Hatoum, & Fries. 1996). It may be beneficial for elderly hospitalized patients to have pharmacists directly involved with the physician to review medication interactions and potential adverse effects. Further, a process could be developed whereby admitting medications and in-hospital medications are reviewed on an ongoing basis. Physicians need to seriously consider every additional medication ordered in light of the increased risk of adverse interactions.

Research Recommendations

1. Intervention studies aimed at decreasing the incidence of delirium should be undertaken. Possibilities include:
    - Does a reduction in the number of procedures decrease the risk of delirium?
    - Are there different approaches to procedures that may decrease the risk of delirium?
    - Is there a temporal factor associated with procedures? That is, if all procedures were undertaken at once, does this decrease risk of delirium?

2. Would a joint initiative between pharmacy and medicine designed to reduce the number of medications that a patient is prescribed during hospitalization decrease the incidence of delirium?
3. The association between Histamine$_2$ receptor antagonists and the development of delirium requires further study. In particular, is there a dose-response relationship between Histamine$_2$ receptor antagonists and delirium? As doseage may be standard, is duration of use significant?
4. Are there specific combinations of medications that lead to an increased risk of delirium?
5. Does early discharge with home care lead to a decreased incidence of delirium?
6. Does a stay in the ICU result in an increased risk of delirium? If so, what are the contributing factors associated with the increased risk?
7. Does decreased physical function measured by observation lead to an increased risk of delirium?
8. Does the type of social contact influence the development of delirium?

6.3 Outcomes Associated With Delirium

The secondary purpose of this study was to examine the outcomes or consequences of delirium while controlling for confounding or extraneous variables. Despite the numerous outcomes frequently associated with delirium, an increased length of stay and use of trunk or pelvic restraints were the only significant outcomes at the multivariate level in this study. It is important to recognize, however, that the frequency of any of the outcomes was low, and thus the power to detect a significant difference may be

diminished. This study does, however, highlight the importance of controlling for risk factors known to influence the outcome examined.

An increased length of stay for individuals with delirium is an important finding, confirming the results of other prospective studies (Francis, Martin, & Kapoor. 1990; Levkoff, Evans, Liptzin, et al. 1992). Delirium is an independent risk factor for increased length of stay, while controlling for severity of illness and activity limitations. This is of considerable consequence for health care planners. As length of stay increases. so does the risk of other iatrogenic events. For example, in a population already compromised. the increased length of stay may have a significant influence of physical function. As our ability to detect, prevent and intervene in cases of delirium improves, the expected impact includes a reduced length of stay.

The use of restraints other than siderails was an adverse outcome associated with delirium. Rationale for restraint use documented in the patient record was to prevent injury to the patient. There is no basis to support the efficacy of restraints to safeguard a patient from injury. In fact, as early as 1885, in an early nursing test, Weeks cautioned "in violent delirium, restraint must be effectual or it only aggravates the trouble...With proper attendance physical restraint is seldom necessary and should be avoided if possible..." (p. 302). In a review of the literature regarding restraints, Evans & Strumpf (1989) found a wide variety of adverse effects associated with restraint use in the elderly, including accidental death, functional decline, skin abrasions and cardiac stress. This review cited a number of studies supporting the finding that restraining a delirious patient serves to increase panic and fear, and produce angry, belligerent, or combative behaviour

(Evans & Strumpf. 1989). Unfortunately, research is lacking on satisfactory alternatives to restraint. In a prospective study of patients with a hip fracture who were experiencing delirium, Williams et al (1985) identified environmental manipulations related to six problems: strange environment; altered sensory input; loss of control and independence; disruption in life pattern; immobility and pain; and disruption in elimination patterns. Interventions included, for example, correcting sensory deficits by ensuring glasses and hearing aids were used, keeping the number of hospital personnel who interact with the patient to a minimum, and providing a rationale for all procedures (Williams, Campbell, Raynor, Mlynarczyk, & Ward. 1985).

The findings regarding mortality are important for two reasons. One, delirium was a significant predictor of mortality at the bivariate level. This confirms the results of many of the previous studies (Gustafson, Berggren, Brannstrom, et al. 1988; Guze & Cantwell. 1964; Levkoff, Evans, Liptzin, et al. 1992; Rabins & Folstein. 1982). Second, and most importantly, delirium was not a significant predictor of mortality when comorbidity and cognitive impairment were controlled, a finding supported by others (Francis & Kapoor. 1992; Francis, Martin, & Kapoor. 1990; Levkoff, Evans, Liptzin, et al. 1992).

There were no significant risk factors identified for institutionalization following discharge, however in order to compare with a large prospective study, institutionalization and mortality were combined. In this model, several variables were significant predictors. Individuals who lived alone were 3.4 times more likely to die or be institutionalized compared to individuals who lived with others. This is a well-known

risk factor for institutionalization, and highlights the importance of adjusting for this factor in studies examining the relationship between delirium and institutionalization. Individuals with cognitive impairment were 7.5 times more likely to die or become institutionalized compared with individuals not classified as having cognitively impairment. Although Inouye et al (1993) believes combining institutionalization and mortality may increase the accuracy concerning the independent contribution of delirium by avoiding the inferential bias that occurs when evaluating the risk of delirium to institutionalization alone, this procedure remains controversial.

Patients who had experienced delirium were at an increased risk of morbidity during hospitalization when analyzed at the the bivariate level; however, delirium was not a significant risk factor in a multivariate model. Unlike the study by Rogers et al. (1989) behaviours consistent with delirium (e.g., psychiatric consult, disrupting the ward with inappropriate behaviour) were not classified as cases of morbidity. Even at the bivariate level, delirium could only be considered weakly significant (p=.08). When education and increased number of hospital medications were entered into the model, delirium was no longer significant. A paper published after this study was completed identified a combined variable representing urinary incontinence, pressure sores and falls as a significant risk factor for delirium. Thus, it may be that delirium does not have an independent contribution to the risk of morbidity, but does lead to an increased risk of adverse events.

The findings from this study highlight the importance of controlling for those factors known to influence the outcome. For example, future studies on the risk of

delirium associated with institutionalization should control for whether or not the individual lives alone, in addition to other well known risk factors such as age, cognitive impairment, and activity limitation.

Clinical implications.

Restraint use is not generally recommended for use with the delirious elderly, and definitely should not be used as a substitute for surveillance. Interventions such as companionship during the night, changing treatment to a less aggravating form (e.g., oral feedings rather than nasogastric or intravenous), and interventions designed to increase the safety of the environment (e.g., low bed, bed alarm systems) may serve to decrease or eliminate the need for restraints.

Decreasing length of stay is currently a significant trend in health care. Interventions designed to decrease the risk of delirium should therefore be undertaken, as length of stay will be impacted.

Research Implications

In order to provide valid estimates of the independent contribution of delirium to adverse outcomes, it is critical to control for known risk factors. Future studies aimed at evaluating outcomes in delirium will also need to consider appropriate follow-up periods. Is a follow-up period of six months appropriate to assess outcomes such as physical function, considering the possible influence of other intervening factors that may differentially affect patients with delirium.

The previous prospective study identified risk factors for delirium in an acute care setting. Yet, many of the risk factors for delirium, such as advanced age, cognitive impairment and decreased functional ability have a high prevalence in an institutionalized population. However, few studies of delirium have been undertaken in long term care settings. Prevalence of delirium in United States nursing homes range from 6% to 12% (Katz, Parmelee, & Brubaker. 1991), yet the prevalence and risk factors associated with delirium for patients in a chronic care setting remains unknown. Studies undertaken in American nursing homes may not be directly comparable to data from Canada due to differences in admission criteria.

Although prospective studies of delirium provide the strongest evidence, they are also expensive to conduct. In the previous study, hospital employees and physicians contributed valuable time to answer questions and run reports. Two research assistants, a study coordinator, and a data-entry clerk were hired for three months. In addition, there was secretarial support. Thus, even for a relatively small scale study, there are significant costs. An economic alternative may be a cross-sectional study based on existing data. This type of study would identify possible risk factors for delirium and provide a basis for future prospective studies. One of the major limitations of this type of study is the reliance on adequate detail from pre-existing records. However, the chronic care setting provides a unique opportunity to overcome this limitation, as a standardized assessment tool is currently in use. The Minimum Data Set (MDS) was mandated for use with all

patients in a chronic care setting in Ontario on July 01, 1996. The MDS is a comprehensive patient assessment covering 16 specific areas, including items designed to assess delirium. The MDS contains an assessment of many of the risk factors for delirium identified in previous studies such as functional status, cognitive impairment, and infections. The comprehensiveness of the information, and the objective, standardized assessment of the MDS may provide researchers with a feasible, cost-effective method of identifying possible risk factors to provide a basis for future research. The purpose of this study was to identify the prevalence of delirium and potential delirium in a chronic care population. Multivariate models of risk factors for patients identified by the MDS as potentially delirious were developed. Reliability of specific items included in the MDS was assessed, and reliability of the delirium items were evaluated. Finally, the utility of the MDS as a research tool for delirium is discussed.

Chapter 8: Literature Review

This chapter describes the development of the MDS and the procedure for completion of the MDS. The psychometric properties of the MDS will be described. A description of the Resident Assessment Protocols (RAPs) triggered by MDS items, including the delirium RAP will be discussed. A comparison of the MDS items specific to delirium and the DSMIV criteria will be undertaken.

8.1 The Minimum Data Set (MDS)

Description and Development

The MDS is a standardized assessment of a patient's functional, medical psychosocial and cognitive status (Appendix P) (Hartmaier, Sloane, Guess, Koch, Mitchell, & Phillips. 1995). The MDS highlights resident needs relevant to current function and to the potential for maximizing functioning. The MDS instrument is designed to be minimal in its content, yet capture the core elements needed for a comprehensive assessment(Morris, Hawes, Fries, et al. 1990).

The MDS was developed and initially tested in the United States under contract with the Health Care Financing Administration with four fundamental goals:

1. to replace nonuniform and cursory assessment
2. to stimulate learning and facilitate assessment and care planning
3. to lead to improved care planning and care provision and enhance quality of life
4. to serve as a model for the method by which the MDS would continue to be updated(Morris, Hawes, Fries, et al. 1990).

The development of the MDS occurred in several stages. Initially, over 60 patient assessment instruments were reviewed to identify common domains, definitions, responses and scoring patterns (Morris, Hawes, Fries, et al. 1990). The next stage consisted of clinical deliberations, extensive review and revisions. In addition to project clinicians and researchers, professionals from a variety of clinical disciplines and additional experts were assembled into a clinical consultant panel and advisory committee (Morris, Hawes, Fries, et al. 1990). Following this, the MDS was tested in U.S. nursing facilities, and the reliability of individual items was evaluated.

The use of the MDS in Medicaid-certified nursing facilities is now mandated by federal regulation in the U.S. Recently, completion of the MDS has been mandated for all chronic care patients in Ontario.

MDS Procedure

The MDS is structured so that health care professionals are required to directly observe and assess patient performance over all shifts during a specified time period. Generally, this time period is seven days, although for some areas the assessment period may occur for up to 90 days. Information required to complete the MDS is acquired through chart review, interview with other health care professionals, and interaction with and observation of patients. The MDS requires 60 to 90 minutes to complete. A Registered Nurse is responsible for co-ordinating this assessment.

MDS assessments are completed at regular intervals. The initial MDS is completed within 14 days of the patient's admission to a chronic care hospital. Following this, an

assessment is undertaken if there is a significant change in the patient's status, and annually. In addition, eight of the sixteen assessment areas are updated quarterly.

MDS Reliability & Validity

In order to examine the inter-rater reliability (agreement among raters) of items included in the MDS, dual patient assessments were completed for 187 patients in twenty facilities in the United States (Morris et al., 1997). Weighted Kappa coefficients ranged from .19 to 1.0.

The range of reliabilities obtained highlights the need for future studies designed to evaluate the sources of unreliability. Further, as differential reliabilities exist across domains within the MDS, site-specific reliabilities need to be examined. In addition, reliability of the MDS when used by facility staff under usual conditions (as opposed to research) has not been assessed.

Despite the enormous potential of the MDS, few studies have assessed the validity of the measures within the MDS. Areas that have received some attention include cognition (Morris, Fries, Mehr, et al. 1994; Rowe-Sleeman. 1996), ADL (Williams, Fries, & Warren. 1997), incontinence (Crooks, Schnelle, Ouslander, & McNees. 1995; Resnick, Brandeis, Baumann, & Morris. 1996; Brandeis, Baumann, Hossain, Morris, & Resnick. 1997) and a measure of social engagement (Mor, Branco, Fleishman, et al. 1995). In general, measures within the MDS have been found comparable to other measures assessing similar area (criterion validity); however, some areas of concern have been noted. For example, when compared to "wet checks", MDS recordings regarding incontinence were valid in determining whether a resident was continent or incontinent.

Unfortunately, however, MDS items were not sensitive in identifying even marked changes in the frequency of incontinence in response to prompted voiding (Crooks, Schnelle, Ouslander, & McNees. 1995). Thus, the MDS is still relatively new, and further studies must be undertaken to assess the validity of the measures included.

Reliability of the Delirium Measure

Reliability of the delirium measure was assessed in two ways - as a trichotomous rating and as a dichotomous rating. When delirium was assessed as a trichotomous measure, weighted Kappa coefficients ranged from .63 to .77, indicating moderate agreement. However, how well does the measure assess behaviour associated with delirium as opposed to chronic behaviour or no behaviour indicators? When Kappa coefficients were calculated for a dichotomous measure (0-1 versus 2), the results obtained were much lower. Kappa coefficients ranged from .24 to .65. Four of the six measures did not attain even moderate agreement (ie. kappa coefficient $\geq .40$). Thus, although the nurse evaluators were able to differentiate between behaviour present or not, their ability to assess recent behaviour changes was far less reliable. In a previous paper evaluating the reliability of an earlier version of MDS, the authors felt that the problem did not lie with the assessors understanding of the instrument, but rather that facility staff were unable to accurately and consistently recognize changes in the patient's condition (Hawes, Morris, Phillips, Mor, Fries, & Nonemaker. 1995). Despite low reliabilities, the seriousness of delirium warranted continued inclusion of the items in the final MDS (Hawes, Morris, Phillips, Mor, Fries, & Nonemaker. 1995).

In a study of the effects of cognitive impairment on reliability of MDS measures. assessment of individuals with cognitive impairment were significantly less reliable than assessments of cognitively intact in four of the five indices assessed (Phillips. Chu. Morris, & Hawes. 1993). It may be that the influence of cognitive impairment is significant for delirium. Unfortunately, however. the indicators of delirium were not assessed.

8.2 Resident Assessment Protocols (RAPS)

Although the MDS provides a form of preliminary screening, resident assessment protocols. or "RAPs" are frameworks for additional assessment. Individual items or combinations of items on the MDS trigger further assessments on the basis of one of the 18 Resident Assessment Protocols (RAPS) (Ouslander. 1994). For example, if a patient was assessed as having a pressure ulcer, the pressure ulcer RAP would be triggered. Once a RAP is triggered, the next step is to initiate clinical reviews (possibly requiring additional data gathering and assessment), care planning and patient monitoring to reduce or manage risks to the patient's well-being (MDS manual, 1996). RAPS were developed by clinical experts, and cover a broad range of conditions common in nursing home populations. The goal of the RAP is to identify potential health risks, and guide the interdisciplinary team through a structured, comprehensive assessment of the patient's functional status (MDS manual, 1996). In addition, RAPs have been promoted as an outcome measure to be used in longitidunal research to evaluate interventions strategies (Hirdes. 1995).

Each RAP is composed of four sections. Section I provides an overview of the condition and may include the focus of the protocol. Section II specifies the MDS triggers that suggest the possibility of the condition. Section III describes guidelines to facilitate care planning. These guidelines assist staff to evaluate the "triggered" condition (MDS manual, 1996). Information is provided in order to evaluate factors that may cause, contribute to, or exacerbate the condition. Section IV is a RAP key, providing a summary of the triggers and guidelines.

Delirium RAP

The delirium RAP was developed to identify potentially delirious patients and is constructed from nine MDS items (Appendix Q). Six items are captured under the MDS heading "indicators of delirium" and include the following:

1. Easily distracted
2. Periods of altered perception or awareness of surroundings
3. Episodes of disorganized speech
4. Periods of restlessness
5. Periods of lethargy
6. Mental function varies over the course of the day

When any of these indicators are present over the last seven days and appear different from the resident's usual functioning, the delirium RAP is triggered.

In addition to these specific indicators, three general indicators are also included within the RAP. These three general indicators include a deterioration in cognitive status,

mood or behavioural symptoms compared to status of 90 days ago. Any one of these items will trigger the delirium RAP.

8.3 MDS Indicators of Delirium compared to DSM criteria

Although six items are identified within the MDS as indicators of delirium, no sensitivity and specificity is described. Thus, it is useful to compare these items with four features of delirium that have been found to have the highest sensitivity and specificity for diagnosing delirium as compared to psychiatrist's ratings (Inouye, VanDyck, Alessi, Balkin, Siegal, & Horwitz. 1990). Sensitivity ranged from 94 -100% and specificity ranged from 90 to 95%. These four features are based on DSM criteria and include:

1. acute onset and fluctuating course
2. inattention
3. and either disorganized thinking
4. or altered level of consciousness.

In comparison with features known to have high sensitivity and specificity, the MDS indicators encompass the majority of these criteria. Acute onset (as behaviour is assessed over previous seven days), and fluctuating course (mental function varies over the course of the day) are assessed. Further, although not labelled as inattention, the operational definition for "easily distracted" is comparable. Disorganized thinking may be evidenced in the MDS by "episodes of disorganized speech". The last item, altered level of consciousness is not assessed completely. The MDS identifies "Periods of lethargy" as an indicator of delirium; however, that is only one aspect of altered level of consciousness. The delirious patient may also present as hyperalert.

The MDS includes two additional indicators. "Periods of restlessness" is defined in the MDS as an indicator of delirium, and yet this item is not included in DSM IV criteria. Periods of restlessness is defined as fidgeting or picking at skin, clothing, napkins, etc.; frequent position changes, repetitive physical movements or calling out (MDS manual. 1996). The MDS manual discusses the difficulties of assessing delirium in patients with pre-existing cognitive impairment or pre-existing behaviours such as restlessness. Therefore, the "periods of restlessness" indicator may be designed to aid in the detection of delirium for these individuals. However, there is currently no valid assessment of delirium for the severely cognitively impaired. and the usefulness of this item as an indicator of delirium is open to debate.

Also included in the MDS is the item " perods of altered perception or awareness of surroundings". The operational definition for this item is similar to that identified in DSM IV as the development of a perceptual disturbance. In previous research, the individual clinical feature of perceptual disturbance was found to have a high specificity, but low sensitivity for the diagnosis of delirium (Inouye, VanDyck, Alessi. Balkin, Siegal, & Horwitz. 1990). When added alone or in combination with other items to the four indicators, perceptual disturbance did not increase the sensitivity or specificity of the delirium measure (Inouye, VanDyck, Alessi, Balkin, Siegal, & Horwitz. 1990).

Summary

The MDS is a comprehensive assessment tool mandated in the province of Ontario for all chronic care patients. The standardized, objective information combined with the completion of assessments at regular intervals represent enormous research

potential. Despite this, the wide range of reliability coefficients, and the low reliability coefficients obtained for the delirium measure suggest site-specific reliability assessments are required. The majority of items required to suggest a diagnosis of delirium are included within the MDS, although level of consciousness is only partially assessed. Therefore, estimates regarding prevalence of delirium can be obtained. As assessors are not trained specifically to detect delirium, many patients with delirium may be missed. The delirium RAP, a tool developed to identify potentially delirious patients, includes broad, general indicators, and therefore may be useful as a screening measure. The delirium RAP also includes possible risk factors for delirium within the guidelines, providing a framework for the development of multivariate models.

8.4 Research Questions

The primary focus of Study Two was to identify prevalence of delirium in the chronic care population and possible risk factors. The secondary focus was to evaluate the utility of the MDS for delirium research. The research questions for Study Two were:

1. What is the prevalence of delirium in patients admitted to a chronic care institution? What are the possible risk factors for delirium in patients admitted to chronic care?
2. What is the utility of the MDS for delirium research?

Chapter 9. Methods

This section of the paper describes the methods undertaken to address both the primary and secondary research questions for Study Two. The study design and procedures followed to address reliability of the MDS, the prevalence of delirium and potential delirium, and the identification of risk factors associated with the MDS delirium RAP in a chronic care population will be described. The definitions and methods of analysis of the research measures will be discussed. The statistical models employed to address both the primary and secondary research questions will be described. In keeping with the previous study, risk factors are divided into two main categories; host, factors that are internal to the individual; and environmental, factors that occur during hospitalization and are external to the individual.

9.1 Design

Sample size.

All patients admitted to or residing in the chronic care institution between July 01, 1996 and September 30, 1996 and meeting the inclusion and exclusion criteria were included in the analysis, leading to a total sample size of 230 patients.

Study population.

This cross-sectional study was conducted at Grand River Hospital, Freeport site, a chronic care hospital. Potential study participants included all patients aged 65 years of age or older. Patients who were identified as comatose (n=4) were excluded from the analysis.

Training on the Minimum Data Set.

Data were obtained by registered nurses (R.N.s) who performed direct assessments of patients based on version 2.0 of the MDS. R.N.s underwent a two-day standardized training program in assessment based on the MDS. In addition, the R.N.s received a manual providing detailed instructions on all MDS 2.0 protocols.

Reliability Testing

Twenty eight patients were randomly chosen to have dual assessments of sections E (Mood and Behavior Patterns), G (Physical Functioning and Structural Problems) and P (Special Treatments and Procedures). One nurse assessor was the usual staff R.N. assigned to complete the MDS, and the second assessor was the staff R.N. who provided the MDS training within the facility. This individual had the most experience completing MDS assessments and participated in the initial training of nurse assessors in Ontario. Each nurse completed the assessment blindly and independently for the same 7 day period, and was prohibited from discussing the resident or their assessments with each other.

9.2 Measures

Delirium.

The MDS-2 Delirium Rap (Appendix Q) was utilized as the measure of delirium. Two versions of delirium were created from the Delirium Rap items. A dichotomous variable (1=yes, 0=no) representing whether or not the Delirium Rap was triggered, and a continuous variable constructed from the presence of any of the MDS delirium RAP triggers. Therefore, the continuous dependent variable ranges from 0 to 9, with 9

representing an individual who was positive on each item. For purposes of comparison. a delirium variable based on DSMIV criteria was constructed based on the following items in the MDS assessed as " behaviour present over last 7 days appears different from the resident's usual functioning" :

1. Easily distracted, and fluctuating mental function and either

2. periods of altered perception or episodes of disorganized speech or periods of lethargy.

Independent variables.

Previous studies and variables identified in the delirium RAP guidelines provided a reasonable framework for choosing variables representing broad clinical domains and reducing the more than 350 MDS variables to those most useful as risk factors for delirium. The independent variables available in the MDS assessment included both host and environmental factors as defined in section 4.3 of the Methods Chapter. The following section describes the host and environmental factors examined. The variable name in square brackets represents the MDS-2 variable/item identifier (see Appendix P).

Host factors included both sociodemographic and health factors. Sociodemographic factors included age, gender and marital status.

Age [aa3] was estimated from the date of birth and represented a continuous variable for age as of Sept. 30th, 1996.

Gender [aa2] was analyzed as a dichotomous variable (male=0, female=1).

Marital Status [a5] was dichotomized as married=1 and not married=0 (includes never married/widowed/separated/divorced).

Health variables included cognitive functioning, vision and hearing, mood, depression and mood, Activities of Daily Living (ADL) measure, bowel and bladder continence, disease diagnosis, comorbidity, infection, pain, dehydration, abnormal lab values, fever and stability of condition.

Cognitive Impairment : was assessed through the use of the Cognitive Performance Scale (CPS) (Morris, Fries, Mehr, et al. 1994). The CPS combines five MDS items (comatose status, decision-making, short-term memory, making self understood, and eating performance) into a single, hierarchical cognitive rating scale creating 7 categories of cognitive impairment. The CPS showed substantial agreement with the MMSE in the identification of cognitive impairment; sensitivity was .94 and specificity was .94 (Hartmaier, Sloane, Guess, Koch, Mitchell, & Phillips. 1995). As comatose status was utilized as an exclusion criteria for this study, it was not included in the CPS variable used in this study. To represent cognitive impairment, patients with a CPS score of 2 or more were coded as 1 (cognitively impaired). Patients with severely impaired decision-making skills [b4] were classified as severe cognitive impairment.

Vision [d1] was assessed as the ability to see in adequate light with glasses if used. Vision was analyzed both as a continuous variable and as a dichotomous variable (adequate or slightly impaired coded as 0, moderately/highly/severely impaired coded as 1).

Visual limitations [d2], a measure of whether the individual saw "halos" around lights or experienced decreased peripheral vision, was analyzed as a dichotomous variable (any limitation coded as 1, no limitation coded as 0)

Hearing [c1] was assessed with a hearing appliance if used. Hearing was analyzed both as a continuous variable and as a dichotomous variable (hears adequately or with minimal difficulty coded as 0, and hears in special situations only and highly impaired coded as 1).

Depression was assessed directly and indirectly, based on a diagnosis of depression [i1ee] or whether or not the Mood State Rap Key (Appendix R) was triggered. Both indicators were analyzed as binary, with 1 representing depression or possible depression.

Activities of Daily Living (ADL) [g1] was based on the scores from individual ADL items. When used as a clinical measure, raters are able to score an item as '8' for activity did not occur. For the purposes of this study, '8' was recoded as '4' for total dependence. In addition, a more general variable, change in ADL [g9] was analyzed as a binary variable, with 1 representing a deterioration in ADL.

Continence status was assessed for both bladder [h1b] and bowel [h1a]. Urinary and bowel incontinence were analyzed as a continuous variable and as a dichotomous variable (1 represented frequently or always incontinent). An overall assessment of a change in urinary continence [h4] was analyzed, with 1 representing a deterioration in urinary continence.

Disease diagnoses [i1] were examined as a binary variable (Appendix S).

Comorbidity score was constructed through the use of the Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie. 1987) applied to those disease diagnoses identified [I1]. Comorbidity was analyzed as a continuous variable.

Infection was analyzed as a dichotomous variable. Individuals with any of the infections listed in items i2a - i2l were coded as 1. Individual infections affecting greater than 3% of the population were also assessed separately. These include antibiotic resistant infection. urinary tract infection and wound infection.

Dehydration was analyzed as a dichotomous based on whether or not the Dehydration/Fluid Maintenance Status Rap (Appendix T) was triggered or a positive response to [j1c].

Fever [j1h] was analyzed as a binary variable. with 1 representing fever.

Pain was assessed as pain frequency [j2a] and pain intensity [j2b]. Pain frequency was analyzed as a continuous and dichotomous variable, with patients 1 if pain occurred daily. A second dichotomous variable was created based on pain intensity. Individuals experiencing pain daily and rating the intensity as moderate to excruciating were coded as 1.

Abnormal lab values [p9] was analyzed as a dichotomous variable.

Stability of Condition [j5] was assessed as two variables. Whether or not the patient was experiencing an acute condition as analyzed as a binary variable. with 1 representing an acute condition. The second variable was whether or not the patient was terminally ill, with 1 representing 6 or fewer months to live.

Environmental factors included activity involvement, medications, physician's orders and visits, treatments & procedures, falls, consults with other health care professionals, social support, social engagement, restraint use, and prior hospital stays..

Activity [n2], the time the patient was involved in activities. was assessed as a continuous variable and as a dichotomous variable with little or no time involved in activities coded as a 1..

Medications included the number of medications used in the last 7 days [o1], any new medications initiated during the last 90 days [o2], and receipt of the following medications; antipsychotic [o4a], antianxiety [o4b], antidepressant [o4c], and hypnotics [o4d]. Number of medications was analyzed as a continuous variable, and as a dichotomous variable. Whether or not the patient had received a new medication was analyzed as a dichotomous variable. Individual medication classes were analyzed as dichotomous variables, individuals who had received the medication during the last 7 days were coded as 1.

Physician Orders [p8] were examined as a continuous variable. This item is assessed as the number of days in the previous 14 that the physician changed the patients orders.

Physician Visits [p7] were examined as a continuous variable. This item is assessed by the number of days the physician has examined the patient over the previous 14 days.

Procedures were assessed indirectly by the receipt of treatments[p1a and k5a]. Treatments were analyzed individually as dichotomous variables (1 representing received treatment), and as a continuous variable constructed from the following: chemotherapy, dialysis, monitoring acute medical condition, ostomy care, oxygen therapy, suctioning, tracheostomy care and intravenous fluid administration. Radiation, transfusions and

ventilators were not used within this facility, and therefore were not included. The use of a foley catheter [h3d] was analyzed separately as a dichotomous variable.

Falls [j4a, j4b, j4c, j4d] were assessed individually as dichotomous variables.

Consults were the number of contacts with formal health care providers [p1b]. Contacts with any of the health care disciplines were analyzed individually as dichotomous variables (no=0 and yes=1) and as a continuous variable (the number of consultations to different services).

Social Support was assessed indirectly by the item 'absence of personal contact with family/friends' [f2e]. This was analyzed as a binary variable, with 1 representing absence of contact. A second variable was also evaluated 'recent loss of close family member/friend [f2f] and analyzed as a binary variable (1=yes).

Social Engagement was analyzed as a continuous variable based on six items [f1]. In a sample of 2175 residents of nursing homes, internal consistency for the six items was Cronbach's alpha= .79 (Mor, Branco, Fleishman, et al. 1995).

Restraint use [p4]was analyzed as a dichotomous variable, with 1 representing the daily use of any of the restraints listed with the exception of the half rail [p4b].

Prior hospital stay in the last 90 days [p5] was analyzed as a continuous variable, and as a dichotomous variable with 1 representing any acute care hospitalization.

9.3 Data Analysis

Reliability

Reliability of the MDS items were assessed by comparing the dual MDS assessments completed by the two nurses. Kappa coefficients were calculated in order to

compare the findings with the weighted kappa coefficients from the U.S. reliability study. Kappa coefficients assess how well two raters agree - that is to what extent different raters classify a subject into an identical category. The kappa coefficient is defined as:

$$k = \frac{II_o - II_e}{I - II_e}$$

When there is perfect agreement, k equals 1. When the agreement equals that expected by chance, k is 0. Thus, the closer the value is to 1, the higher the level of agreement between the two raters.

Multivariate Models

Variables identified in previous research as potential risk factors for delirium and environmental variables hypothesized as risk factors and included in the MDS were analyzed at the bivariate level. As there were so many possible predictors, only those variables significant at $p<.05$ and affecting 3% (n=7) of the population or greater were entered into the multivariate model. Two variables consistently identified as significant risk factors for delirium in previous studies were entered into the multivariate model regardless of bivariate significance. These were age and cognitive impairment. Variables significant at $p<.05$ were retained in the final model.

Logistic regression was used to examine the binary delirium variable, whether or not the individual triggered the delirium rap. Logistic regression has been previously described.

Multiple linear regression was the statistical model used to examine the relationship between the continuous delirium dependent variable, a continuous measure of items from

the delirium RAP, and potential risk factors. However, Pearson correlation coefficients (r) between the predictor variables and the continuous measure of delirium were first examined. Bivariate correlations significant at $p<.05$ were entered into a multiple linear regression model.

Independent or predictor variables in non-experimental data sets are often correlated with one another. If these correlations are moderate to high, then the regression coefficients are greatly affected. The present data showed no excessive intercorrelations among the predictors with the exception of the association between bowel incontinence and activities of daily living. In this case, only one variable was entered into the final model at a time.

The equation for a multiple linear regression model is represented by:

$$y = \alpha + \beta_1 x_1 + \beta_2 x_2 + \ldots \beta_k x_k + e$$

wherein Y is the response variable, in this case a continuous variable representing items from the delirium RAP, $\beta_k x_k$ represents the predictor variables, and e is the random deviation. The value of β_1 gives the average change in y when x_i increases by 1 unit while the values of all other predictors are held fixed.

Non-significant variables were removed sequentially until all the variables were significant ($p<0.05$). Those variables removed were added back into the model sequentially to ensure there were no other significant variables. Interaction terms between the main effects in the final model were examined in order to determine whether the effect of an independent variable was modified by a second variable.

There were 230 patients who met the study criteria and were assessed using the MDS between July 01, 1996 and September 30, 1996. The average age was 79.8 years (SD 7.8). Of these, approximately 67% were female. The majority (54%) of patients were widowed. 145 (63%) of the patients were classified as cognitively impaired, 87 of those patients classified as cognitively impaired were severe or very severely impaired according to the cognitive performance scale. The median score on the ADL measure was 35 on a scale ranging from 0-44 with 44 indicating the most disability. Approximately 74% (n=171) of the patients triggered the moodrap, indicating mood distress. Variables not examined because prevalence was less than 3% included dehydration [j1c] and whether or not the patient had a hip or other fracture in last 6 months [j4c].

10.1 Reliability

Section E: Mood and Behaviour Patterns

Kappa coefficients were calculated for 25 items in Section E (Table 19). In some cases, coefficients were not calculated as the table was not symmetrical (eg. only one rater coded patients as a "4"). The coefficients obtained for section E ranged from a low of k= .26 to 1.0 (Table 19). Of the 25 items assessed, 13 (52%) items achieved a reliability coefficient of $k \geq .75$. For those items without a kappa coefficient, all had high levels of inter-rater agreement.

Table 19
Kappa Coefficients for Section E: Mood and Behaviour Patterns

Section E Item	Kappa Coefficient	U.S. Weighted Kappa Coefficient
e1a	.79	.70
e1b	(25/28)*	.76
e1c	.80	.69
e1d	.68	.72
e1e	.71	.76
e1f	.89	.80
e1g	1.0	.65
e1h	.80	.58
e1i	.72	.69
e1j	.53	.69
e1k	.46	.53
e1l	.69	.85
e1m	.83	.82
e1n	.92	.73
e1o	.80	.65
e1p	.77	.65
e2	.44	.93
e4aa	(25/28)*	.83
e4ab	.46	.72
e4ba	.89	.68
e4bb	1.0	.65
e4ca	.59	.60
e4cb	.63	.51
e4da	.54	.68
e4db	.26	.75
e4ea	.86	.64
e4eb	.78	.37

* Unable to calculate Kappa as coding is assymetrical. Value ( ) indicates frequency of perfect agreement.

Section G: Physical Functioning and Structural Problems

Kappa coefficients were calculated for 15 items in Section G . Kappa coefficients ranged from k=.28 to k=.94 (Table 20). Of the items assessed, 8 (53%) achieved a reliability coefficient of $k \geq .75$. Levels of agreement ranged widely for those measures without kappa coefficients calculated.

Section P: Special Treatments and Procedures

Section P had coefficients ranging from k=.19 to k = 1.0 (Table 21). Of the 12 items assessed, 5 (42%) achieved a reliability of $k \geq .75$.

10.2 Prevalence of Delirium

There were 48 (20.9%) patients identified as potentially delirious, as they had triggered one or more items included in the delirium RAP. Eleven (4.8%) patients met the criteria for a diagnosis of delirium according to DSMIV.

The frequency for each of the indicators included within the delirium rap is described in Table 22 . Thus, a deterioration in mood was one of the items most frequently triggered within the RAP. Patients were assessed as having from one to eight of the items included within the RAP (Table 23). Only three patients triggered eight items, and no patient triggered all nine items.

Although the majority of individuals triggered a combination of items in the delirium RAP, it is of interest to note the number of individuals triggering the RAP due to a single variable. Of those patients identified as potentially delirious, 15 (31%) triggered a single variable within the Delirium RAP, typically one of the more general indicators

Table 20

Kappa Coefficients for Section G: Physical Functioning and Structural Problems

Section G Item	Kappa Coefficient	U.S. Weighted Kappa Coefficient
g1aa	.80	.91
g1ab	.68	.86
g1ba	1.0	.91
g1bb	1.0	.91
g1ca	(24/28)*	.92
g1cb	.79	.92
g1da	.84	.89
g1db	.84	.90
g1ea	(21/28)*	.92
g1eb	(21/28)*	.84
g1fa	.68	.89
g1fb	(21/28)*	.81
g1ga	(23/28)*	.90
g1gb	(21/28)*	.81
g1ha	.73	.94
g1hb	(22/28)*	.88
g1ia	.77	.93
g1ib	(16/28)*	.85
g1ja	(5/28)*	.87
g1jb	(3/28)*	.79
g2	.52	.86
g3a	.77	.86
g3b	.71	.76
g4aa	.51	.60
g4ab	(20/28)*	.76
g4ba	.79	.78
g4bb	.88	.86
g4ca	.78	.78
g4cb	.88	.67
g4da	.69	.62
g4db	.94	.65
g4ea	.75	.72
g4eb	.94	.73
g4fa	.50	.84
g4fb	.55	.81
g7	.28	.67

*Unable to calculate Kappa as coding is assymetrical. Value ( ) indicates frequency of perfect agreement.

Table 21
Kappa Coefficients for Section P: Special Treatments and Procedures

Section P Item	Kappa Coefficient	U.S. Weighted Kappa Coefficient
p3a	(21/28)**	.73
p3b	(24/28)**	.64
p3c	(27/28)**	.60
p3d	.65	.64
p3e	.65	.53
p3f	.65	.73
p3g	(25/28)**	.59
p3h	.47	.65
p3i	1.0	*
p3j	(25/28)**	*
p3k	1.0	*
p4a	.89	.80
p4b	.78	.69
p4c	.39	.76
p4d	.89	.95
p4e	.58	.61
p7	.19	.53
p8	(15/28)**	.66

* not calculated

* *Unable to calculate Kappa as coding is assymetrical. Value ( ) indicates frequency of perfect agreement.

Table 22
Frequency of MDS Delirium RAP indicators

MDS Indicator	Frequency
Easily Distracted	12 (5.2%)
Periods of Altered Perception	8 (3.5%)
Episodes of Disorganized Speech	15 (6.5%)
Periods of Restlessness	12 (5.2%)
Periods of Lethargy	13 (5.7%)
Mental Function Varies	16 (7.0%)
Deterioration in Cognitive Status	25 (10.9%)
Deterioration in Mood	31 (13.5%)
Deterioration in Behavioral Symptoms	22 (9.6%)

Table 23
Frequency of Patients Triggering Delirium RAP Indicators

Number of Delirium Rap Indicators	Number of Patients triggering
1	15
2	9
3	7
4	4
5	3
6	4
7	3
8	3

(Table 24) . Thus, six patients were included as potentially delirious due to being assessed as having had a "deterioration of mood status".

Of the 48 patients who triggered the delirium RAP. 10 were also assessed as "rarely/never understood". Therefore, approximately 21% of the individuals assessed as being potentially delirious were able to communicate to staff using at best, resident-specific sounds or body language. Further, for the seventeen patients triggering from 4 to 8 items on the delirium RAP, 6 patients were also classified as rarely or never understood. Approximately 42% (n=20) of the patients triggering the delirium RAP were severely cognitively impaired.

10.3 Significant Bivariate Risk Factors: Logistic Regression Model

Host Factors

There were a number of variables significant ($p<.05$) at the bivariate level based on whether or not the delirium RAP was triggered (Table 25). These included cognitive impairment, triggering the Mood RAP, deterioration of ADL, deterioration in urinary continence, triggering the dehydration RAP, a fall in previous 30 days, an abnormal lab value, an acute episode, and experiencing a terminal illness. In addition, there were four disease diagnoses significant at the bivariate level, including cardiac dysrhythmias, heart failure, hemiplegia and renal failure.

Environmental Factors

A continuous variable measuring number of treatments was significant at the bivariate level. In addition, use of a foley catheter, receiving a new medication within the

Table 24
Frequency of Single RAP Indicators

DSMIV criteria only	2
Any of the specific indicators only*	5
Deterioration of cognitive status only	5
Deterioration of mood status only	6
Deterioration in behavioural symptoms only	2

*includes DSMIV criteria, may be more than one of the indicators

Table 25
Unadjusted Odds Ratios for Potential Delirium

Host Factors	Unadj. OR	CI (95%)		β	SE
Cognitive Impairment	2.7	1.3	5.7	.98	.39
Mood RAP	6.6	1.9	22.4	1.9	.62
Deterioration of ADL	9.3	4.1	21.1	2.23	.42
Deterioration in urinary continence	8.7	3.0	25.1	2.2	.54
Disease Diagnoses					
Cardiac Dysrhythmias	3.8	1.4	10.6	1.4	.52
Heart Failure (CHF)	2.6	1.01	6.7	.96	.48
Hemiplegia	.22	.07	.8	-1.5	.62
Renal Failure	8.5	2.1	35.5	2.1	.73
Dehydration (RAP)	2.4	1.3	4.6	.88	.33
Fell in past 30 days	10.5	2.0	55.8	2.3	.85
Abnormal Lab Value	2.4	1.3	4.6	.88	.33
Stability of Condition					
Acute episode	2.9	1.1	8.2	1.1	.52
Terminal illness	7.7	2.6	22.5	2.0	.55
Environmental Factors					
Procedures	1.7	1.1	2.6	.53	.22
Foley Catheter	2.7	1.2	6.5	1.0	.44
New Medication within past three months	2.4	1.2	4.9	.88	.36
Number of times Physican changed orders in 2 weeks	1.3	1.1	1.4	.23	.06

previous 90 days, and an increased number of days the physician changed the patient's orders were significant at the bivariate level.

10.4 Significant Bivariate Risk Factors: Linear Regression Model

Host Factors

When the dependent variable was continuous, a number of variables were significant (Table 26). Significant bivariate associations included female gender, cognitive impairment, triggering the Mood RAP, increased dependence in ADL, a deterioration in ADL, a deterioration in urinary continence, increasing bowel incontinence, triggering the dehydration RAP, experiencing an acute condition or terminal care, any infection, and specifically a urinary tract infection or wound infection. Significant medical diagnoses included cardiac dysrhythmias, congestive heart failure, hemiplegia, cancer and renal failure.

Environmental Factors

Significant environmental factors included an increased number of medications, new medications in the previous 90 days, use of a foley catheter, a fall in the previous 30 days, an increased number of days the physician changed the patient's orders, and an acute care hospital admission in the previous 90 days.

10.5 Significant Bivariate Risk Factors DSM IV

When the dependent variable was delirium as defined solely by DSMIV criteria, significant ($p<.05$) host risk factors included a deterioration in ADL, deterioration in urinary continence, and experiencing a terminal illness (Table 27). Significant medical diagnoses included congestive heart failure, cancer, and renal failure. Cognitive

Table 26

Significant Bivariate Correlations with the Continuous Delirium Measure and Predictor Variables

MDS Variable	r	p
Host Factors		
Gender (Female)	.13	.05
Cognitive Impairment	.19	.004
Mood RAP	.20	.003
ADL		
(continuous)	.15	.02
(bivariate)	.42	.0001
Deterioration in Continence	.38	.0001
Bowel Continence (cont.)	.13	.04
Disease Diagnoses		
Cardiac Dysrhytmias	.14	.04
Congestive Heart	.15	.02
Hemiplegia	.14	.03
Cancer	.19	.003
Renal Failure	.34	.0001
Dehydration Rap	.16	.02
Stability of Condition		
Acute episode	.17	.01
Terminal Illness	.30	.0001
Infection	.18	.006
Urinary Tract	.27	.001
Wound infection	.15	.03
Fall in previous 30 days	.14	.03
New Physician orders	.29	.0001
Environmental Factors		
Number of medications	.19	.005
New medications	.16	.02
Foley catheter	.17	.009
Prior hospital stay	.16	.02

Table 27

Unadjusted Odds Ratio for Delirium Based on DSMIV criteria

	Unadj. OR	CI (95%)	β	SE
Cognitive impairment	6.2*	.78 49.5	1.8	1.1
Deterioration in ADL	6.2****	1.8 21.7	1.8	.64
Deterioration in urinary continence	14.4****	3.8 53.9	2.7	.67
Diagnoses				
CHF	4.2**	1.02 17.2	1.4	.72
Cancer	4.1**	1.1 14.8	1.4	.66
Renal Failure	13.3***	2.8 63.1	2.6	.79
Terminal Illness	5.9**	1.4 25.1	1.8	.74
Number of Medications	1.2***	1.04 1.3	.16	.06
Number of New Orders	1.2**	1.01 1.4	.17	.08
Previous hosp stay	16.0***	2.4 108	2.8	.97

* p<.10
** p<.05
***p<.01

impairment was significant at p=.08. Significant environmental risk factors included an increased number of medications, an increased number of days the physician changed the patient's orders, and an acute care admission in the previous 90 days.

10.6 Multivariate Model: Logistic Regression

Those variables significant at the bivariate level (p<.05) were entered into a multivariate model (Table 28). Host factors significant in whether or not the delirium RAP was triggered included: cognitive impairment (OR=3.5), triggering the Mood RAP (18.9), and a deterioration in ADL compared to status 90 days ago (OR=6.6). A diagnosis of hemiplegia exerted a protective effect (O.R.=.07). Further, an interaction between the main effects of cognitive impairment and deterioration in ADL was significant. The only significant environmental variable was an increased number of days the physician changed the patient's orders in the previous 14 days (OR=1.5).

10.7 Multivariate Model: Continuous Delrap: Multiple Linear Regression

Significant factors (p<.05) for the continuous dependent variable included cognitive impairment, a deterioration in ADL compared to status 90 days ago, renal failure, experiencing a terminal illness, increasing bowel incontinence, and a wound or urinary tract infection (Table 29). In addition, there was a significant interaction between cognitive impairment and terminal illness. Once again, the only significant environmental variable was an increased number of days the physician changed the patient's order over the previous two weeks. Approximately 42% of the variance in the continuous measure of delirium was explained by this combination of variables.

Table 28

Logistic Regression Model for Potential Delirium

Variable	Adjusted OR	β	SE	95% CI
Hemiplegia	.07**	-2.65	.96	.01 .47
Cognitive Impairment	3.5*	1.26	.53	1.2 9.9
Mood RAP	18.9***	2.94	.85	3.6 99.8
Deterioration in ADL	6.6**	1.89	.63	1.9 22.7
Number of New Orders	1.5***	.39	.09	1.2 1.8
Interaction between cognitive impairment and deterioration in ADL	**	3.55	1.39	

Note: * p<.05
** p<.01
*** p<.001

R^2 adjusted= 47%

Table 29
Linear Regression Model for Potential Delirium

Variable	Parameter Estimate	Standard Error
Cognitive Impairment	.61**	.20
Deterioration in ADL	.91***	.28
Renal Failure	1.44*	.46
Urinary Tract Infection	.79*	.37
Wound Infection	1.32*	.44
Terminal Illness	1.93**	.42
Number of new orders	.13***	.04
Bowel Incontinence	.12*	.06
Interaction between cognitive impairment and terminal illness	3.65***	.72

Note: * p<.05
** p<.01
*** p<.001

$R^2 = .44$
$R^2_{adj} = .42$

$F_{9,220} = 19.13$ (p<.0001)

10.8 Multivariate Model: Delirium based on DSM IV

When the dependent variable was delirium based on DSMIV criteria, cognitive impairment (OR=52.2) and a deterioration in urinary continence (OR=24.5) were significant host risk factors. Significant environmental risk factors included an increased number of medications (OR=1.3), and an acute care hospital admission in the previous 90 days (OR=18.9) (Table 30).

Table 30
Multivariate Model with DSMIV as Dependent Variable

MDS Variable	OR	CI		β	SE
Cognitive Impairment	52.2*	1.7	999	4.0	1.8
Deterioration in urinary continence	24.5***	4.0	149.3	3.2	.92
Number of medications	1.3**	1.1	1.5	.25	.09
Previous hospitalization	18.9*	1.6	222	2.9	1.3

* p<.05
** p<.01
***p<.001

R^2 adj = 44%

Chapter 11. Discussion

Approximately 21% (n=48) of the patients in chronic care were defined as potentially delirious when assessed according to the MDS. This prevalence probably overestimates the number of patients who would be diagnosed with delirium as it is based on a screening measure. When DSMIV criteria were applied, 4.8% (n=11) of the chronic care patients would be diagnosed with delirium. As assessors were not trained to detect delirium, the true prevalence probably falls somewhere between these two figures. Regardless, the range falls within the prevalence previously noted within acute care settings, and is similar to that found in U.S. nursing homes.

11.1 Risk Factors for Potential Delirium

Multivariate Logistic Regression Model

Cognitive impairment, a risk factor identified in the previous study and also consistently identified in other delirium research, was found to be a significant predictor of potential delirium. Individuals with cognitive impairment were 3.5 times more likely to trigger the delirium rap compared to individuals without cognitive impairment. The rationale for the significance of the association between cognitive impairment and delirium has been described previously.

One disease diagnosis was significant in the final model. Those individuals with a medical diagnosis of hemiplegia/hemiparesis were less likely to develop delirium than those individuals without this diagnosis. This variable remains significant while controlling for a deterioration in activities of daily living. The rationale for this finding is puzzling. No other study has found a medical diagnosis to be significant; however,

because previous studies were conducted with acute care populations. hemiplegia/hemiparesis may not be as prevalent. Most of the patients in a chronic care setting would have a long-standing diagnosis. Hemiplegia is obviously associated with decreased functional ability, a significant risk factor for delirium in previous studies and yet in this study, individuals with hemiplegia were at less risk of being assessed as potentially delirious. It may be that some other factor is confounding this association.

Those individuals who had a deterioration in their ADL self-performance status compared to 90 days ago were 6.6 times more likely to trigger the delirium RAP compared to individuals with an unchanged or improved ADL status over the previous 90 days. Previous research has identified a decreased functional ability at baseline as a risk factor for delirium (Williams, Campbell, Raynor, Musholt, Miynarczyk, & Crane. 1985; Marcantonio, Goldman, Mangione, et al. 1994). However, in a prospective study of patients admitted to a geriatric assessment unit, patients with delirium were significantly more likely to experience a deterioration in functional status (O'Keeffe & Lavan. 1997). As this study is cross-sectional, it is impossible to determine if the deterioration in ADL preceded or is as a result of the potential delirium. However, a deterioration in ADL (as opposed to baseline ability) may be an important risk factor to assess in future prospective studies.

Those individuals who triggered the Mood RAP were approximately 19 times more likely to trigger the delirium RAP than those individuals who did not trigger the Mood RAP. The Mood RAP is intended to screen for mood distress, and is assessed based on mood during the previous 30 days. These mood states may occur anywhere from once in

the past 30 days to daily. The Mood RAP includes indicators of depression, anxiety, sad mood, and mood persistence. Of the 48 individuals who triggered the delirium RAP, 45 triggered the Mood rap. The previous prospective study did not find a significant association between psychological well being and delirium, and only one prospective study has found depression to be significant. It is difficult to determine the relationship between potential delirium and the mood RAP, particularly as the Mood RAP can be triggered by even one occurrence of distress in the past 30 days. The significance of the Mood RAP may in part be related to the association between this measure and the deterioration in mood included in the delirium RAP. However, the correlation between the two variables, while significant, is only r=.25, and thus only 7% of the variation in deterioration in mood can be explained by the variation in the moodrap.

Once again, temporal order is problematic, as it may be that the indicators of mood are as a result of potential delirium. For example, patients experiencing delirium may be more likely to ask repetitive questions or verbalizations, items which would trigger the Mood RAP.

Those individuals with an increased number of days that the physician changed the patient's orders were more likely to trigger the delirium RAP. It may be that the constant order changes affected the patients medications, or the order changes may have disrupted the patients usual routines. Alternatively, the increased number of orders may have been the physician's attempt to decrease the symptoms associated with the potential delirium.

In this model, the effect of cognitive impairment was modified by the effect of a deterioration in ADL. Thus, individuals with cognitive impairment who experienced a

deterioration in ADL over the previous 90 days were at greater risk than patients with cognitive impairment who improved or maintained ADL. However, effect modification detected at the analysis stage is often measured less precisely than overall exposure effects, and although important, may be regarded as best suited for hypothesis generation requiring confirmation in subsequent studies.

Linear Regression Model

Similar to the previous model, cognitive impairment and a deterioration in ADL were significant risk factors. As the rationale underlying the association between these variables and potential delirium have been described, only variables unique to the linear regression model will be discussed in detail.

Those individuals with renal failure were at an increased risk of delirium. Renal failure causes an increase in urea and creatinine levels (Ganong. 1995), and leads to mental deterioration and confusion in addition to other symptoms. It may not be the accumulation of urea and creatinine per se but the accumulation of other toxic substances, possibly organic acids or phenols, that produce the symptoms (Ganong. 1995).

Individuals who had a wound or urinary tract infection were significantly more likely to trigger one of the delirium items. A previous prospective study found infection was a significant risk factor for delirium (Schor, Levkoff, Lipsitz, et al. 1992). Fever occurs concurrently with many infections, and there are experimental data to support a causal link between fever and delirium (Siesjo, Carlsson, & Hagerdal. 1976; Bilbert. 1968). However, delirium may occur in infected patients without fever. It may be some feature of infection other than fever that underlies the development of delirium in patients

with infections. Cytokines or bacterial products have been suggested as possible links in the association between infection and delirium (Dinarello. 1984; Kadlecova, Masek, & Rotta. 1974).

Those individuals experiencing a terminal illness were more likely to trigger an increased number of delirium indicators. The increased risk associated with terminal illness is comparable to the increased risk of delirium associated with severe illness noted in previous studies (Francis, Martin, & Kapoor. 1990; Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996).

Increased bowel incontinence led to an increased risk of delirium items triggered. Although urinary incontinence has been assessed in previous studies, the risk associated with bowel incontinence has not. Bowel incontinence is associated with increased levels of cognitive impairment. In this study, bowel incontinence and severe cognitive impairment were significantly correlated (r=.46), thus 21% of the variance in bowel continence can be explained by the variance in severe cognitive impairment. However, bowel incontinence is significant even when cognitive impairment is controlled. The independent contribution of bowel incontinence is unknown; however, it may be that the relationship between bowel incontinence is confounded by another factor such as functional status. Although ADL was not significant in the multivariate model even when the variable representing bowel incontinence was removed, the correlation between ADL and bowel incontinence was strong (r=.71). Thus, 50% of the variance in bowel incontinence is explained by the variance in ADL. It may be that ADL has an indirect influence on delirium.

Once again, a significant interaction was identified between the main effects. The effect of cognitive impairment was modified by the effect associated with a terminal illness. No similar interaction has been found in other studies; however, palliative patients were typically excluded (Inouye, Viscoli, Horwitz, Hurst, & Tinetti. 1993; O'Keeffe & Lavan. 1996). Thus, those individuals with cognitive impairment who were experiencing a terminal illness were at greatest risk. However, as previously described, this interaction would need to be confirmed in future prospective studies.

11.2 Risk Factors for Delirium

DSM Model

When the dependent variable was based on DSMIV criteria for a diagnosis of delirium as opposed to potential delirium, cognitive impairment and a deterioration in urinary continence compared to status 90 days ago were significant host factors. Significant environmental factors included an increased number of medications and a recent acute care hospitalization in the previous 90 days. It is of interest to note that with the exception of cognitive impairment, the other significant variables were not included in either the logistic or linear regression models when the dependent variable was "at risk" rather than a diagnosis of delirium. Unfortunately, however, this model must be interpreted with caution, as there were only 11 individuals classified as delirious. The small proportion of patients experiencing delirium results in a greater potential for unstable predictive estimates. Yet it may be that the models based on the delirium RAP are including diagnoses other than delirium, and thus are capturing risk factors that are not specific for delirium.

Summary of Multivariate Model Risk Factors

Cognitive impairment was consistently identified as a risk factor, whether the dependent variable was potential delirium or delirium. Surprisingly, age was not identified as a risk factor in any of the multivariate models. With the exception of medical diagnoses, cognitive impairment and terminal illness, the other risk factors identified are susceptible to the limitations associated with a cross-sectional study, namely knowledge of temporal sequence. Further, when the dependent variable was the DSMIV criteria for a diagnosis of delirium, significant risk factors differed. Future prospective studies should be undertaken in chronic care to confirm that these are risk factors, and not outcomes of delirium. It may be useful at this point to examine the utility of the MDS as a research instrument for delirium, integrating knowledge gained from this study with previous MDS literature.

11.3 The MDS as a Research Instrument for Delirium

The accessibility of a mandated, standardized, comprehensive measure is appealing to researchers. Yet initial enthusiasm for the ease of access must be tempered with concerns regarding the psychometric properties of the MDS as a research instrument. This section will review the reliability of the MDS in general and the reliability of the delirium indicators. The validity of the delirium indicators and of other measures within the MDS will be examined. The limitations associated with a cross-sectional study design will be discussed.

Reliability

In order for a measure to be valid, it must first be reliable. Hawes et al. (1992) argue that the reliability results from the final testing of the MDS $^{+}$ demonstrated that excellent research quality data can be gathered with the MDS. Kappa coefficients obtained in the U.S. study ranged from .19 to 1.0. At this site, kappa coefficients also ranged from .19 to 1.0. Unfortunately, coefficients could not be calculated for some items. Although many of the items tested indicated excellent reliability, the range of coefficients obtained indicates a continued need for site specific testing.

Reliability testing for MDS 2.0 relied on weighted kappa coefficients. Weighted coefficients give more weight to those scores that are closer together (ie. one rater assesses the patient as a '3' while the other assesses the patient as a '4'). While this scheme may be applicable to some areas, such as physical functioning, it may not be appropriate for other sections. In particular, the nominal categories assessed in the delirium section. It is difficult to understand why a difference of '1' in the patient's score should be weighted more heavily. For example, why would a patient coded by one rater as 'behaviour not present' and the second rater as 'behaviour present but not recent' receive a higher weighting than a patient coded as 'behaviour not present' and 'behaviour present and recent'? Further, the use of a trichotomous scoring scheme is misleading. The intent of the delirium section is to assess for delirium. The use of a trichotomous score for reliability inflates the kappa coefficients obtained due to the fact that the reliability coefficient obtained from the assessment of "behaviour not present" vs "behaviour present" should be very high. However, what is of interest is whether or not

the behaviour is of recent onset. The kappa coefficients obtained in the U.S. data support this hypothesis. When the score is trichotomized, kappa coefficients range from .62 to .77. However, a dichotomous score (behaviour not present or not recent versus behaviour recent) reveals much lower scores : .24 to .65. Thus, as with the original delirium measure in MDS$^+$, reliability remains a problem. In fact, using a conservative $k \geq .40$, only two of the six items assessing delirium could be considered to have adequate reliability.

The potential for unreliability of the MDS in general has been noted previously. Teresi & Holmes (1992) point out the considerable potential for variance in sources of information, as MDS protocols require assessors to complete the form using multiple information sources. Hawes et al (1992) argue that the explicit use of multiple sources of information strengthens the validity and reliability of MDS data. However, particularly for areas that require some subjective interpretation or when the patient is cognitively impaired, explicitly defining the necessary information chain from data collection to form completion may improve the reliability(Crooks, Schnelle, Ouslander, & McNees. 1995). The MDS manual offers only general instructions relevant to the way in which the assessor is to gather information.

Validity of the Delirium RAP

The MDS delirium RAP is intended as an initial care planning guide, developed to identify potential health risks. Thus, all patients identified should have clinical reviews to determine whether or not delirium is actually present. Yet, as with any research measure, validity is important. Validity concerns the crucial relationship between the

concept and the indicator (Carmines & Zeller. 1979). Sensitivity and specificity are two measures of the validity of a screening tool. In order for the MDS delirium screening measure to be considered valid, it must be sensitive, that is, able to detect patients who actually have delirium. Further, the tool must be specific, that is able to identify patients who do not have delirium. At present, there are no published studies examining the validity of the delirium RAP or the derivation of the specific delirium indicators used within the MDS. A paper describing the development of the MDS discusses the use of experts, and the review of many other assessment instruments (Morris, Hawes, Fries, et al. 1990). Presently, one can only postulate the sensitivity and specificity of the tool in comparison to "gold standard" measures. The items contained within the MDS delirium RAP measure suggest a high sensitivity, as most DSMIV criteria are included. Unfortunately, however, this comes at the expense of specificity, as a number of the measures included are not included in the DSMIV definition of delirium. Individuals who do not have delirium will still trigger the delirium RAP. There are a number of areas that may contribute to decrease the specificity of this measure including the ability of a single item to trigger the RAP, vague general indicators and the inclusion of specific indicators not included in the DSMIV definition. These concerns will be addressed in more detail.

Recall that a combination of items are required for an actual diagnosis of delirium, and the delirium RAP will be triggered even if only one item is positive. In fact, in this study, fifteen patients triggered the RAP on the basis of one item. For 13 patients, the single item triggered was one of the three general indicators. As previously discussed,

health care professionals may not have the education required to detect delirium, and therefore the use of more general indicators to screen for delirium may be of some benefit. The inclusion of such broad indicators may assist health care professionals to detect the more subtle changes that the specific indicators may not assess. In this study, six individuals triggered the delirium RAP on the basis of "deterioration of mood status". As previously described, this measure compares the patient's "mood" (items from e1 or e2) to the mood status 90 days ago. Although it is well-known that delirium can be misdiagnosed as depression (Nicholas & Lindsey. 1995), a deterioration in mood status does not screen for depression, but instead assesses an increase in the frequency, numbers or intensity of any of the mood items. As such, the inclusion of this measure is difficult to support as a general indicator of delirium, and probably serves to decrease the specificity of this measure. The other two general indicators are also broad. For example, a deterioration in behavioural symptoms not only includes an increase in the numbers, frequency or intensity of behavioural symptoms, but also the alterability of symptoms. Although a deterioration in cognitive status and behaviour may indicate delirium, they are not specific for delirium. Further, the contribution that "alterability" of behaviour makes to risk of delirium is questionable.

An additional item included within the delirium RAP is the measure of "periods of restlessness". This non-specific indicator would not appear to increase the sensitivity of the Delirium RAP, but may decrease the specificity.

Obviously, it is desireable to have a screening test that is both highly sensitive and highly specific; however, there is generally a trade-off between the sensitivity and

specificity of any given screening test (Hennekens & Buring. 1987). Yet, clarifying the broad indicators and excluding "periods of restlessness" as a delirium indicator would be unlikely to affect the sensitivity of the measure and would serve to increase the specificity.

An additional concern regarding the validity of the delirium measure is that 21% of individuals who triggered the Delirium RAP were patients who were rarely or never able to make themselves understood. Almost half (42%) of the patients triggering the delirium RAP were severely cognitively impaired. At present, there is no valid method of assessing delirium in patients with severe cognitive impairment.

Careful consideration needs to be given to the impact of the choice made for the dependent variable. By choosing to use the broader definition, and thus perhaps aggregating unrelated disease, the likelihood of detecting a significant associated is decreased. Therefore, many risk factors specific to the chronic care population may have been missed. Risk factors not significant in this study may prove to be significant in future prospective studies.

The development of an adequate screening measure for research purposes is a high priority. Researchers are interested in a measure with known sensitivity and specificity. Future studies will need to focus on this important area.

Temporal Ordering

Although there is some variation in specific criteria recommended for determining causality with non-experimental data, one criterion, temporal ordering, is obviously important. Ensuring correct temporal sequence, that is the suspected cause precedes the

disease, is difficult using the MDS data. The screening measure for delirium requires the nurse to assess the patient based on the previous seven days. Many of the possible risk factors occur anywhere from seven to ninety days prior to the assessment date. Thus, a "change in activities of daily living as compared to ninety days ago" may have occurred immediately following the development of delirium, and certainly would not be an unexpected finding. Similarly, once the individual has delirium, the patient may display items that would trigger the moodrap or physician's orders may increase. Thus, these "predictor" variables may in fact be consequences of delirium. This limitation is not specific to the MDS, as any study based on a cross-sectional design shares this limitation. Yet the MDS data is particularly problematic in this regard, as there is no data available concerning dates when changes occurred. As such, this design can only be thought of as hypothesis generating.

Summary

The MDS represents enormous potential for researchers with an interest in chronic care. At present however, reliabilities associated with the MDS are variable, and must be examined within each potential research site prior to conducting studies. Future studies conducted to identify variances within reliability should be undertaken. Further, future studies must be conducted to validate the delirium RAP as a screening measure prior its use as a research measure. As previously described, few studies have been undertaken to validate other measures within the MDS. Presently, only one of the RAPs has been validated (Resnick, Brandeis, Baumann, & Morris. 1996). As such, research aimed at

improving reliability and evaluating the validity of the MDS must be considered a high priority.

11.4 Research Recommendations

1. Reliability of the MDS indicators of delirium
2. Validity of the MDS Delirium RAP when recorded under normal field utilization conditions. Criterion validity of the MDS delirium items must be established prior to its usefulness as a research tool.
3. Validity of other measures within the MDS, including the predictive ability of ADL measures and the validity of a depression screen based on MDS 2.0 items.

Chapter 12. Summary & Conclusion

Thirty years ago, delirium was termed the Cinderella of American psychiatry due to the paucity of research conducted in the area (Lipowski. 1967). Since then. a number of prospective studies have been conducted to explore the factors that contribute to an increased risk of delirium. Two studies were undertaken to contribute to this body of knowledge. Study One had considerable methodological strength. using a prospective design, a valid and reliable instrument to detect delirium, structured interviews, and daily patient assessment. The intent of Study One was to identify those hospitalization-related factors that may be amenable to intervention, and to evaluate the contribution of delirium to in-hospital outcomes. Outcomes included mortality, morbidity, length of stay, use of restraints and also to discharge to an institution. Study Two was undertaken to examine the prevalence of delirium in a chronic care population, to explore possible risk factors for delirium and to assess the utility of the MDS as a research instrument for delirium. To evaluate the utility of the MDS, assessments of inter-rater reliability for three large sections and the specific delirium indicators included within the MDS was undertaken. In addition the MDS was compared with DSMIV criteria for delirium. As Study Two was an initial exploratory study, the use of a cross-sectional design was justified.

12.1 Study One

In Study One, one hundred and fifty six patients over the age of 65 and admitted to an acute care environment were followed for two weeks or until discharged. Assessments occurred daily. A number of factors amenable to intervention were identified as significant risk factors for delirium. As such, these risk factors are important for clinical

and research purposes. Individuals undergoing a high number of procedures within the first four days of hospitalization or receiving a high number of medications during hospitalization significantly increased the risk of delirium. In addition, Histamine$_2$ receptor antagonists and a combination of benzodiazepines and tricyclic antidepressants contributed to an increased risk of delirium once the more general variable representing number of medications was removed from the model.

Consistent with previous research, a number of host characteristics were also significant. Increased age and cognitive impairment have been identified in the majority of prospective studies, and were significant in this model. Undergoing a surgical procedure and a period in the intensive care unit were also significant in the multivariate model.

In-hospital outcomes associated with delirium included an increased length of stay and the use of restraints. Individuals developing delirium in the hospital were more likely to have a longer length of stay even while controlling severity of illness and activity limitations. Thus, interventions designed to reduce delirium can be expected to impact length of stay.

The second in-hospital outcome associated with delirium, restraint use, is an important finding for clinicians. Only individuals with delirium were restrained. As restraints may contribute to an increased risk of adverse effects, practical alternatives should be identified.

There has been considerable controversy regarding whether or not delirium independently increased the risk of mortality. In this study, there was not an increased

risk of mortality associated with delirium. Although an increased risk of mortality is repeatedly described in papers discussing delirium, this risk was based on bivariate models. In multivariate models, controlling for factors such as age, severity of illness and comorbidity, delirium does not appear to have an independent effect.

12.2 Study Two

In Study Two, 230 patients admitted to chronic care were assessed using the MDS. There were 48 (20.9%) patients identified as "potentially" delirious according to items assessed within the MDS and included in the Delirium Resident Assessment Protocol. Eleven (4.8%) patients met the criteria for a diagnosis of delirium according to DSMIV. As nurses were not specifically trained to assess for delirium, the true prevalence probably lies within these two estimates.

Host risk factors for potential delirium identified in either the logistic regression or linear regression models included cognitive impairment, triggering the Mood Rap (indicating potential depression, anxiety or sad mood) , a deterioration in ADL compared to status 90 days ago, renal failure, experiencing a terminal illness, increasing bowel incontinence and a wound or urinary tract infection. In order to provide a comparison, a multivariate model based on DSMIV criteria for delirium was developed. Similar to the models for potential delirium, cognitive impairment was a significant risk factor. A deterioration in urinary continence, an increased number of medications and an acute care hospital admission in the previous 90 days were also significant. These variables were not included in the two models developed for potential delirium. However, the number of individuals experiencing delirium was small, and thus findings must be viewed with some

caution. It may be that the delirium RAP aggregates unrelated diagnoses, and thus captures risk factors not specific for delirium. Further, the cross-sectional design precludes the assessment of correct temporal sequence. Potential risk factors for delirium idenitified in this study should be confirmed in future prospective studies.

The utility of the MDS as a research instrument for delirium was assessed. Kappa coefficients ranged k =.19 to k = 1.0 for Sections E, G, and P of the MDS. Based on a dichotomous score, the The U.S. study revealed kappa coefficients ranging from k = .24 to k = .65. Thus,as with the original delirium measure in MDS$^+$, reliability of the measure remains an issue. In fact, using a conservative $k \geq .40$, only two of the six items assessing delirium could be considered to have adequate reliability.

The range of reliability coefficients noted in the U.S. study suggest continued site-specific studies must be undertaken. Further studies to increase the reliability of some items should be undertaken.

The items contained within the MDS Delirium RAP suggest a high sensitivity, as most DSMIV criteria are included. However, specificity may be low. A number of items included within the delirium RAP probably serve to decrease specificity. These include the use of only one item to trigger the Delirium RAP, vague broad indicators and inclusion of periods of restlessness as a specific indicator of delirium. Future studies must be conducted to validate the delirium RAP as a screening measure prior to undertaking research studies based on this measure. Further, as few studies have been undertaken to validate other measures within the MDS, substantial work is required prior to recommending the MDS as a research tool.

12. 3 Comparison of Findings in Study One and Study Two

The two studies were undertaken to contribute to the body of knowledge regarding delirium. A comparison of the general model in Study One and the DSMIV model in Study Two yields some similarities. Consistent with the findings in Study One, Study Two identified cognitive impairment as a risk factor for delirium. This finding has been confirmed in previous delirium research. Further, number of medications received during hospitalization continued to be a risk factor for patients in acute and chronic care institutions. This finding is not surprising, as the risk associated with a higher number of medications in the elderly is well known. Study Two also identified a deterioration in urinary continence as a risk factor. Although this factor was not assessed in Study One. the use of a foley catheter has been identified as a risk factor in a prospective study (Inouye & Charpentier, 1996). In contrast with findings from Study One, acute care hospitalization was identified as a risk factor in Study Two. It is possible that underlying factors that were not measured (eg. severity of illness) contributed to this increased risk. Consistent with research in other fields, age was no longer a significant risk in the chronic care environment.

In conclusion, as evidence regarding risk factors for delirium increases, a focus on those factors that may be amenable to intervention is a worthwhile pursuit. Although identifying host risk factors provides health care professionals with a basis for screening, identifying a patient as high risk is not enough. Currently, research has not provided health care professionals with evidence to support practices that may decrease the incidence of delirium. A recent review of the few studies undertaken to evaluate the

effectiveness of interventions to prevent delirium revealed a broad spectrum of possible interventions that may be modestly effective (Cole, Primeau, & McCusker. 1996). Unfortunately intervention studies were plagued by methodolgical problems (Cole, Primeau, & McCusker. 1996). A logical approach may be to first identify risk factors that are amenable to intervention, and then develop specific strategies targetting these risk factors. Reducing the incidence of delirium must continue to be a high priority for research, as patients continue to suffer the personal and economic costs associated with delirium.

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Appendix A

Diagnostic & Statistical Manual (DSM) Criteria for Delirium

III:

Diagnostic criteria for Delirium

A. Clouding of consciousness (reduced clarity of awareness of the environment),with reduced capacity to shift, focus, and sustain attention to environmental stimuli.

B. At least two of the following:
   (1) perceptual disturbances: misinterpretations, illusions, or hallucinations;
   (2) speech that is at times incoherent;
   (3) disturbance of sleep-wakefulness cycle, with insomnia or daytime drowsiness;
   (4) increased or decreased psychomotor activity

C. Disorientation and memory impairment (if testable).

D. Clinical features that develop over a short period of time (usually hours to days) and tend to fluctuate over the course of a day.

E Evidence, from the history, physical examination, or laboratory tests, of a specific organic factor judged to be etiologically related to the disturbance.

IIIR:

A. Reduced ability to maintain attention to external stimuli (e.g., questions must be repeated because attention wanders) and to appropriately shift attention to new external stimuli (e.g., perseverates answer to a previous question).

B. Disorganized thinking, as indicated by rambling, irrelevant, or incoherent speech.
   (1) clouding of consciousness

C. At least two of the following:
   (1) reduced level of consciousness, e.g., difficulty keeping awake during examination
   (2) perceptual disturbances: misinterpretations, 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 of current episodes of illness

D. Clinical features develop over a short period of time (usually hours to days) and tend to fluctuate over the course of a day.

E Either (1) or (2):
   (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 ccounting for agitation and sleep disturbance

Appendix A
Diagnostic & Statistical Manual (DSM) Criteria for Delirium

IV:

Diagnostic criteria for Delirium

A. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
B. 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 dementia.
C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
D. 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.

Appendix B
Patient Cover Letter & Consent

[Letterhead]

Dear Patient,

Admission to hospital is often a stressful experience for persons of all ages. New patients may experience a response to this stress. For example, some older persons show temporary confusion while others do not.

The Research Department of Grand River Hospital is interested in studying what factors may contribute to this temporary confusion in some but not all new patients. The aim of this research is to understand and develop ways to minimize this type of response. In addition to being conducted with the support of Grand River Hospital, the study also represents the doctoral thesis of Nancy Martin and is conducted under the supervision of Professor Michael Stones, University of Waterloo.

We would greately appreciate your involvement in this project. As a participant, you would have an initial assessment (one time only) of:

- vision
- hearing
- daily activities

and a daily 10–15 minute interview (at a time convenient to you) where you will be asked:

- some general questions (e.g., date, season)
- events of previous day
- and to repeat a series of numbers.

As a participant in this study, you should know that your involvement is voluntary. All information you provide will be held in confidence and neither you or any member of your family will be identified in any report, publication or thesis based on this study. You may also decline answering any question you prefer not to answer. Further, you may withdraw your consent for participation at any time simply by telling the research assistant that you no longer wish to continue. This decision will in no way affect the medical care you receive at the Grand River Hospital.

Appendix B
Patient Cover Letter & Consent

This project has been reviewed by, and received ethics approval from the Office of Human Research at the University of Waterloo (phone number 519-885-1211, ext. 6005) and the Grand River Hospital Committee on Ethical Research. If after receiving this letter, you have any questions about this study, or would like additional information to assist you in reaching a decision about participation, please feel free to contact Nancy Martin at 519-894-8360, extension 7187 or the Office of Human Research at 519-888-4567, extension 6005. Thank you for your interest in this project.

Yours Sincerely,

Nancy Martin, Director of Research,
Grand River Hospital

Appendix B
Patient Cover Letter & Consent

Patient Consent to Participate

I agree to participate in this study. I have made this decision based on the information I have received in the Information Letter and have had the opportunity to receive any additional details I wanted about the study. As a participant in this study, I realize that I will be asked to take part in a daily fifteen minute interview and that I may decline answering any of the questions, if I so choose. All information provided will be held in confidence and I will not be identified in any report or publication. I understand that I may withdraw this consent at any time by asking that the interview be stopped. I also understand that this project has been reviewed by and received ethics approval through the Office of Human Research at the University of Waterloo and at Grand River Hospital. I am aware that I may contact this office if I have any concerns or questions about my participation in this study.

Participant's Name:

_____

Participant's Signature:

_____

Name of Witness:

_____

Signature of Witness:

_____ Date:_____

Appendix C
Family Member Cover Letter & Consent

[Letterhead]

Dear Family Member,

Admission to hospital is often a stressful experience for persons of all ages. New patients may experience a response to this stress. For example, some older persons show temporary confusion while others do not.

The Research Department of Grand River Hospital is interested in studying what factors may contribute to this temporary confusion in some but not all new patients. The aim of this research is to understand and develop ways to minimize this type of response. In addition to being conducted with the support of Grand River Hospital. the study also represents the doctoral thesis of Nancy Martin and is conducted under the supervision of Professor Michael Stones. University of Waterloo.

Consent to participate has been obtained from _____. We would also greatly appreciate your involvement in this project. You would be asked to:

- answer a few brief questions regarding preadmission health of your family member
- and complete a brief questionnaire on the usual mood of your family member.

The time committment is not expected to exceed 15 minutes.

As a participant in this study, you should know that your involvement is voluntary. All information you provide will be held in confidence and neither you or any member of your family will be identified in any report, publication or thesis based on this study. You may also decline answering any question you prefer not to answer. Further, you may withdraw your consent for participation at any time simply by telling the research assistant that you no longer wish to continue. This decision will in no way affect the medical care your family member will receive at the Grand River Hospital.

This project has been reviewed by, and received ethics approval from the Office of Human Research at the University of Waterloo (phone number 519-885-1211, ext. 6005) and the Grand River Hospital Committee on Ethical Research.

Appendix C
Family Member Cover Letter & Consent

If after receiving this letter, you have any questions about this study, or would like additional information to assist you in reaching a decision about participation, please feel free to contact Nancy Martin at (519)-894-8360, extension 7187 or the Office of Human Research at (519)-888-4567, extension 6005. Thank you for your interest in this project.

Yours Sincerely,

Nancy Martin,
Director of Research,
Grand River Hospital

Appendix C
Family Member Cover Letter & Consent

Family Member Consent to Participate

I, the family member of the patient _____, agree to participate in this study. I have made this decision based on the information I have received in the Information Letter and have had the opportunity to receive any additional details I wanted about the study. As a participant in this study, I realize that I will be asked to answer a few brief questions regarding the preadmission health of my hospitalized family member and complete a brief questionnaire on the usual mood of my hospitalized family member. The time committment is not expected to exceed 15 minutes. I know that I may decline answering any of the questions, if I so choose. All information provided will be held in confidence and I will not be identified in any report or publication. I understand that I may withdraw this consent at any time by asking that the interview be stopped. I also understand that this project has been reviewed by and received ethics approval through the Office of Human Research at the University of Waterloo and at Grand River Hospital. I am aware that I may contact this office if I have any concerns or questions about my participation in this study.

Family Member's Name:

_____

Family Member's Signature:

_____

Name of Witness:

_____

Signature of Witness:

_____ Date:_____

Appendix D
MIDAS

Patient ID

Date:

(mm/dd/yy)

MIDAS

NEVER	ALMOST NEVER	OCCASIONALLY	USUALLY	ALMOST ALWAYS
1	2	3	4	5

		Score
1.	The person was enthusiastic.	
2.	When cheerful, the person remained cheery for a long time.	
3.	When agitated, the person remained restless for a long time.	
4.	When distressed, the person appeared tense.	
5.	His/her feelings of uneasiness persisted for long periods.	
6.	This person got really happy.	
7.	When having a good day, the person acted cheerfully.	
8.	When angry, the person looked tense.	
9.	This person remained happy about things longer than most others.	
10.	His/her feelings of delight persisted for long periods.	
11.	He/she got upset easily.	
12.	The person was often tense for extended periods.	

Appendix E
Protocols

INITIAL PATIENT PROTOCOL

Note:

- Patient ID# must be written on all materials that are used to collect information for this study.
- Please initial all assessment materials in the top right hand corner & staple the assessment package.
- Check that your initials, patient ID, and the date are on all assessment packages
- Please return all lists and completed initial patient assessment packages to Donna at the end of each day. (Donna updates the study participant lists daily from the information you provide).

1. Review study criteria and determine whether the patient meets the criteria.

2. Obtain patient consent (leave letter with patient, keep consent form only)

IF patient is cognitively impaired:

- complete initial patient assessment and when able to contact family, confirm patient consent with family member
- obtain family member consent and complete family member assessment including:
    - MIDAS instrument

IF evidence of delirium contact family member to confirm that confusion is of acute onset:

- If it at time of initial assessment you are unable to confirm that confusion is of acute onset, complete the steps listed above for cognitively impaired patients and follow-up with the family to confirm if acute onset confusion.

3. Complete the CAM instrument (includes MMSE, Digit span : record digit span score on initial patient interview form following activity limitation)

4. Complete initial patient interview form:

- demographics
- telephone list (record frequently called numbers on orange list)
- devices and restraints
- medications
- assessment of vision & hearing
- activity limitation
- depression

5. Post Study Materials

- Tape visitor sign to wall
- Guest book: attach string and pencil. fill in bed number on front of guest book. fill in patient id on sign in sheets & tape guest book to wall next to the patient's bed
- Insert orange notification card into kardex by patients name (ie. research subject)
- Severity of illness: complete patient id and clip to front of patient chart -(ask charge nurse to ask doctor to complete)

Appendix E
Protocols

DAILY PATIENT PROTOCOL

- Patient ID# must be written on all materials that are used to collect information for this study.
- Please initial all assessment materials in the top right hand corner & staple the assessment package.
- Check that your initials, patient ID, and the date are on all assessment packages
- Please update the Active Study Participant List and return all lists to Donna at the end of each day (e.g. check if forms posted, severity of illness completed, consent obtained, daily assessment completed, etc.)
- File daily assessment, family consent & assessment materials (after checking that you have recorded the necessary information on the Active Study Participant List).

- **Review chart** according to chart review document

- **Complete the CAM instrument** (includes MMSE, Digit span : record digit span score on the daily patient information form

- **Review the "follow-up structured client interview"** sheet attached to this protocol

- **Complete the daily patient information form:**
  - orienting objects
  - record digit span

- **Update Guest Book:**
  - Check guest book - if filling up, replace with new form. (retaining the previous form)

- Record any patient movement off unit in the space provided in the chart review document, and note whether staff sign in sheet agrees (ie. if went to xray, did a porter initial form).
- Contact nursing staff and review CAM criteria. If no positive responses, do not record. If positive, add to CAM assessment and indicate source.
- Check for completed severity of illness measure on chart, and follow-up with physician if not completed.
- If the patient is being discharged - Complete thank-you letter information, and remind staff to place all study materials (e.g., telephone list, staff sign in sheet, guest book, etc.) in the orange folder at the nursing station when the patient is discharged.

Appendix F
Initial Patient Interview

Patient Identification Number: ☐

Date: ☐ (mm/dd/yy)

Date of Admission: ☐ (mm/dd/yy)

Please fill in the box next to each question the number that corresponds to the most appropriate response.

Demographic Information

Marital Status: ☐
1. Never married
2. Married
3. Widowed
4. Separated
5. Divorced

Education (Highest Level Completed): ☐
1. No schooling
2. 8th grade/less
3. 9-11 grades
4. High school
5. Technical or trade school
6. Some college/university
7. Diploma
8. Bachelor's degree
9. Graduate degree

Admitted from ☐
0. Home
1. Chronic care hospital
2. Nursing home/Home for the Aged
3. Retirement home
4. Other, please specify

Lived Alone (Prior to Admission): ☐
0. No
1. Yes

Appendix F
Initial Patient Interview

List the phone numbers that you call most frequently.
(LIST ON TELEPHONE SHEET and below in the space provided)

Area Code	Phone Number

Devices & Restraints
Are there any restraints presently being used? ☐

0. No
1. Yes

If yes, what type: **(Please place a check mark in the box for each that applies)**

1. Full bed rails on all sides ☐
2. Other types of side rails (half rail, one side) ☐
3. Trunk restraint ☐
4. Limb restraint ☐
5. Chair prevents rising ☐
6. Other, specify ☐

Appendix F
Initial Patient Interview

Prescribed, Over the Counter and Naturopathic Medications (also check chart)
Have you taken any prescribed, over the counter or naturopathic medications in the last 7 days? ☐

0. No
1. Yes

List all prescription, over the counter and naturopathic medications taken during the last 7 days. (Include medications that are used regularly but less than weekly).

Medication Name	Dosage	Route	Number Taken	Frequency

Note: **Route of Administration:**

1. by mouth	2. sublingual	3 intramuscular	4. intravenous
5.subcutaneous	6.rectally	7. topical	
8. inhalation	9. enteral tube	10. other (please specify)	

Frequency (choose the most appropriate category)

1D=once daily	1W=once each wk	QO=every other day
2D=two times daily	2W=twice each week	1M=once every month
3D=three times daily	3W=3 times each week	2M=twice every month
4D=four times daily	4W=four times each week	
5D=five + times daily	5W=five times each week	
	6W=six times each week	

Appendix G
CES-D

Below is a list of the ways you might have felt or behaved. Please tell me how often you have felt this way during the past week.

1. I was bothered by things that usually don't bother me.
2. I did not feel like eating; my appetite was poor.
3. I felt that I could not shake off the blues even with help from my family or friends.
4. I felt that I was just as good as other people.
5. I had trouble keeping my mind on what I was doing.
6. I felt depressed.
7. I felt that everything I did was an effort.
8. I felt hopeful about the future.
9. I thought my life had been a failure.
10. I felt fearful.
11. My sleep was restless.
12. I was happy.
13. I talked less than usual.
14. I felt lonely.
15. People were unfriendly.
16. I enjoyed life.
17. I had crying spells.
18. I felt sad.
19. I felt that people dislike me.
20. I could not get "going".

Appendix G
CES-D

Please write the number of the most appropriate response (see below) next to each question on the following depression sheet.

Rarely or none of the time (Less than 1 day)

Some or little of the Time (1 to 2 days)

Occasionally or a Moderate Amount of Time (3 to 4 days)

Most or All of the Time (5 to 7 days)

Appendix H
MDS

Assessment of Vision & Hearing

Unless otherwise specified, enter the number for the most appropriate response in the box next to the question

Hearing: (With hearing appliance, if used) ☐

0. HEARS ADEQUATELY—normal talk, TV, phone
1. MINIMAL DIFFICULTY when not in quiet setting
2. HEARS IN SPECIAL SITUATIONS ONLY—speaker has to adjust tonal quality and speak distinctly
3. HIGHLY IMPAIRED/absence of useful hearing

Communication Devices/Techniques: **(Check all the boxes that apply during last 7 days)**

Hearing aid, present and used ☐
Hearing aid, present and not used regularly ☐
Other receptive comm. techniques used (e.g., lip reading) ☐
NONE OF ABOVE ☐

Vision: (Ability to see in adequate light and with glasses if used) ☐

0. ADEQUATE—sees fine detail, including regular print in newspapers/books
1. IMPAIRED—sees large print, but not regular print in newspapers/books
2. MODERATELY IMPAIRED—limited vision; not able to see newspaper headlines, but can identify objects
3. HIGHLY IMPAIRED—object identification in question, but eyes appear to follow objects
4. SEVERELY IMPAIRED—no vision or sees only light, colors, or shapes; eyes do not appear to follow objects

Visual Limitations/Difficulties: **(Check all that apply)**

A. Side vision problems–decreased peripheral vision ☐
(e.g., leaves food on one side of tray, difficulty travelling, bumps into people and objects, misjudges placement of chair when seating self)

B. Experiences any of following: ☐
sees halos or rings around lights;
sees flashes of light;
sees "curtains" over eyes

C. None of the Above

Visual Appliances: ☐

Glasses; contact lenses; magnifying glass ☐
(0=No 1=Yes)

Appendix I
Activities of Daily Living

Activity Limitation
Please fill in the box next to each question the number that corresponds to the most appropriate response.

The next questions are about activities that might cause you problems.

1. Health problems prevent me from doing my shopping. ☐
   1=no
   2=yes

2. I have difficulty cutting my toenails. ☐
   1=no
   2=yes

3. I have difficulty getting my shoes on and off. ☐
   1=no
   2=yes

4. Health troubles limit my spare time activities. ☐
   1=no
   2=yes

5. Health troubles stop me from doing regular chores. ☐
   1=no
   2=yes

6. Health troubles stop me from getting about. ☐
   1=no
   2=yes

7. I sometimes have problems dressing myself. ☐
   1=no
   2=yes

Appendix J
Thank-You Letter

[Letterhead]

Dear Study Participant:

I would like to thank you for your participation in this study on delirium (acute confusion). The results that you have provided will assist us in identifying those factors that place individuals admitted to the hospital at greater risk than others. Depending on the results from this study, we hope to introduce interventions designed to decrease this risk.

If you would like to receive a summary of the results from this study, please complete the information on the bottom of this form.

Once again, thank you for your participation.

Yours Sincerely,

Nancy Martin
Grand River Hospital

If you desire a summary of the findings pertaining to the study on delirium (acute confusion), please complete the following information and leave it with the research assistant or at the nursing station.

(Please Print)

Name.: _____

Mailing Address:

Street _____

City _____

Postal Code _____

Confusion Assessment Method (CAM) Questionnaire

Patient ID #_____
DATE:_____

OBSERVATIONS BY INTERVIEWER

Interviewer: *Immediately after completing the interview, please answer the following questions based on what you observed during the interview.*

ACUTE ONSET

1. a. Is there evidence of an acute change in mental status from the patient's baseline?

Yes	– 1
No	– 2
Uncertain	– 8

b. (IF YES) Please describe change and source of information:

_____
_____
_____

INATTENTION

2. a. Did the patient have difficulty focusing attention, for example being easily distractible, or having difficulty keeping track of what was being said?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	– 1
No	– 2
Uncertain	– 8
Not Applicable (NA)	– 9

c. (IF PRESENT) Please describe this behavior:

_____
_____
_____

DISORGANIZED THINKING

3. a. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes– 1
No– 2
Uncertain– 8
NA – 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

ALTERED LEVEL OF CONSCIOUSNESS

4. a. Overall, how would you rate this patient's level of consciousness?

GO TO Q5 ← Alert (normal) – 1
Vigilant (hyperalert, overly sensitive to environmental stimuli, startled very easily – 2
Lethargic (Drowsy, easily aroused) – 3
Stupor (Difficult to arouse) – 4
Coma (Unarousable) – 5
Uncertain – 8

b. (IF OTHER THAN ALERT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes – 1
No – 2
Uncertain – 8
NA – 9

c. (IF OTHER THAN ALERT) Please describe this behavior:

_____

_____

_____

_____

DISORIENTATION

5. a. Was the patient disoriented at any time during the interview, such as thinking he/she was somewhere other than the hospital, using the wrong bed, or misjuding the time of day?

Not present at any time during interview – 1
Present at some time during interview, but in mild form – 2
Present at some time during interview, in marked form – 3
Uncertain – 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes – 1
No – 2
Uncertain – 8
NA – 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

MEMORY IMPAIRMENT

6. a. Did the patient demonstrate any memory problems during the interview, such as inability to remember events in the hospital or difficulty remembering instructions?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	– 1
No	– 2
Uncertain	– 8
NA	– 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

PERCEPTUAL DISTURBANCES

7. a. Did the patient have any evidence of perceptual disturbances, for example, hallucinations, illusions, or misinterpretations (such as thinking something was moving when it was not)?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	– 1
No	– 2
Uncertain	– 8
NA	– 9

c. (IF PRESENT) Please describe these perceptual changes:

_____

_____

_____

Appendix K
Confusion Assessement Method (CAM) Questionnaire

PSYCHOMOTOR AGITATION

8. a. (Part 1) At any time during the interview, did the patient have an unusually increased level of motor activity, such as restlessness, picking at bedclothes, tapping fingers, or making frequent sudden changes of position?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	– 1
No	– 2
Uncertain	– 8
NA	– 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

PSYCHOMOTOR RETARDATION

8. a. (Part 2) At any time during the interview, did the patient have an unusually decreased level of motor activity, such as sluggishness, staring into space, staying in one position for a long time, or moving very slowly?

Not present at any time during interview	– 1
Present at some time during interview, but in mild form	– 2
Present at some time during interview, in marked form	– 3
Uncertain	– 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	– 1
No	– 2
Uncertain	– 8
NA	– 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

ALTERED SLEEP-WAKE CYCLE

9. a. Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness with insomnia at night?

Yes	– 1
No	– 2
Uncertain	– 8

(IF YES) Please describe the disturbance:

Appendix L
Digit Span Assessment

Digit Span Assessment

The research assistant tells the subject three one-digit numbers. The subject is asked to repeat these numbers back. This process is repeated with increments of one until the subject fails to correctly repeat the numbers. Subjects are given two attempts to correctly repeat each set of numbers. The score is the total number of successful repetitions.

Following this, the subject is asked to repeat two one-digit numbers in reverse order. For example, the research assistant will state "5, 2". A correct response by the subject would be "2,5". This process is repeated with increments of one until the subject fails to correctly repeat the numbers. Subjects are given two attempts to correctly repeat each set of numbers. The score is the total number of successful repetitions.

1, 7, 9
1, 7, 9, 2
1, 7, 9, 2, 5
1, 7, 9, 2, 5, 6
1, 7, 9, 2, 5, 6, 8
1, 7, 9, 2, 5, 6, 8, 2
1, 7, 9, 2, 5, 6, 8, 2, 1
1, 7, 9, 2, 5, 6, 8, 2, 1, 3
1, 7, 9, 2, 5, 6, 8, 2, 1, 3, 2
1, 7, 9, 2, 5, 6, 8, 2, 1, 3, 2, 5
1, 7, 9, 2, 5, 6, 8, 2, 1, 3, 2, 5, 4

3, 7
3, 7, 1
3, 7, 1, 2
3, 7, 1, 2, 5
3, 7, 1, 2, 5 4
3, 7, 1, 2, 5, 4, 1
3, 7, 1, 2, 5, 4, 1, 5
3, 7, 1, 2, 5, 4, 1, 5, 3
3, 7, 1, 2, 5, 4, 1, 5, 3, 2
3, 7, 1, 2, 5, 4, 1, 5, 3, 2, 1

Appendix M
Standardized Mini-Mental State Exam (MMSE)

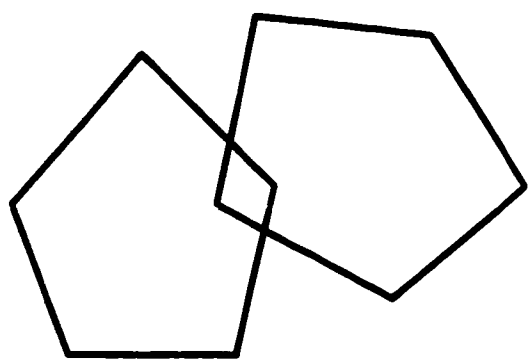
Patient ID:

Date:

(mm/dd/yy)

Standardized Mini-Mental State Exam (MMSE)

			Maximum Score	Cl Sc
1	a)	What year is this?	1	
	b)	What season is this?	1	
	c)	What month of the year is this?	1	
	d)	What is today's date?	1	
	e)	What day of the week is this?	1	
2	a)	What country are we in?	1	
	b)	What province are we in?	1	
	c)	What city/town are we in?	1	
	d)	What is the name of this hospital?	1	
	e)	What is this room number?	1	
3		I am going to name three objects. After I have said all three objects, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes. *(Say them slowly at approximately 1 second intervals.)* APPLE TABLE PENNY Please repeat the three items for me.	3	
4		Spell the word "WORLD" Now spell it backwards please.	5	
5		Now what were the three objects that I asked you to remember? APPLE TABLE PENNY	3	
6		Show wristwatch. Ask: "What is this called?"	1	
7		Show pencil. Ask: "What is this called?"	1	
8		I'd like you to repeat a phrase after me: "NO IF'S, AND'S OR BUT'S"	1	
9		Read the words on this page and then do what it says. *(Hand the client a sheet with : "CLOSE YOUR EYES")*	1	
10		Ask if the client is right or left-handed. Alternate right/left hand in statement, "Take this paper in your right/left hand, fold the paper in half once with both hands, and put the paper down on the floor."	3	
11		Ask client to write a sentence.	1	
12		Visual-spatial drawing	1	
		TOTAL	30	



Appendix N
Comorbidity Index[1]

Assigned weights for diseases	Conditions
1	Myocardial infarct
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumor
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
4	Metastatic solid tumor
	AIDS

Assigned weights for each condition that a patient has. The total equals the score. Example: chronic pulmonary (1) and lymphoma (2) = total score (3)

[1] Table from Charlson, M. E.; Pompei, P.; Ales, K. L.; MacKenzie, C. R. (1987) A New Method of Classifying Prognostic Comorbidity in Longitudinal Studies: Development and Validation. *Journal of Chronological Diseases* 40 (5) pp. 373-383.

Appendix O
Illness Severity

Patient ID#:_____

Attending Physician: **Please circle the appropriate number on this continuum**

SEVERITY OF ILLNESS MEASURE

How sick is this patient *now* ?

Not ill	Mildly		Moderately		Severely		Moribund
1	2	3	4	5	6	7	8	9

Appendix Q

The Delirium RAP (Key)

TRIGGER

Delirium problem suggested if one or more of following present:

- Easily Distracted [B5a = 2]
- Periods of Altered Perception or Awareness of Surroundings [B5b = 2]
- Episodes of Disorganized Speech [B5c = 2]
- Periods of Restlessness [B5d = 2]
- Periods of Lethargy [B5e = 2]
- Mental Function Varies Over the Course of the Day [B5f = 2]
- Deterioration in Cognitive Status [B6 = 2]
- Deterioration in Mood [E3=2]
- Deterioration in Behavioral Symptoms [E5 = 2]

Appendix R

Mood State Rap Key

TRIGGER

A mood problem suggested if one or more of following present:

- Resident made negative statements [E1a = 1,2]
- Repetitive questions [E1b = 1,2]
- Repetitive verbalizations [E1c = 1,2]
- Persistent anger with self or others [E1d = 1,2]
- Self deprecation [E1e = 1,2]
- Expressions of what appear to be unrealistic fears [E1f = 1,2]
- Recurrent statements that something terrible is about to happen [E1g = 1,2]
- Repetitive health complaints [E1h = 1,2]
- Repetitive anxious complaints/concerns [E1i = 1,2]
- Unpleasant mood in morning [E1j = 1,2]
- Insomnia/change in usual sleep pattern [E1k = 1,2]
- Sad, pained, worried facial expressions [E1l = 1,2]
- Crying, tearfulness [E1m= 1,2]
- Repetitive physical movements [E1n = 1,2]
- Withdrawal from activities of interest [E1o = 1,2]
- Reduced social interaction [E1p = 1,2]
- Mood Persistence [E2 = 1,2]

Appendix S
Disease Diagnoses

Diabetes Mellitus
Arterosclerotic heart disease
Cardiac dysrhythmias
Congestive heart failure
Hypertension
Peripheral vascular disease
Arthritis
Cerebrovascular accident
Hemiplegia/hemiparesis
Parkinson's disease
Seizure disorder
Transient ischemic attacks
Depression
Emphysema/COPD
Anemia
Cancer
Renal Failure

Appendix T

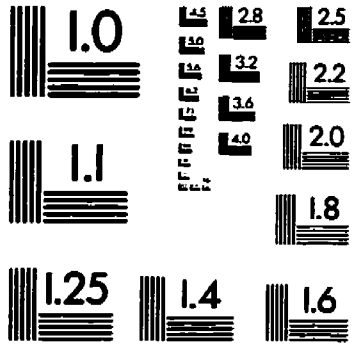
The Dehydration RAP

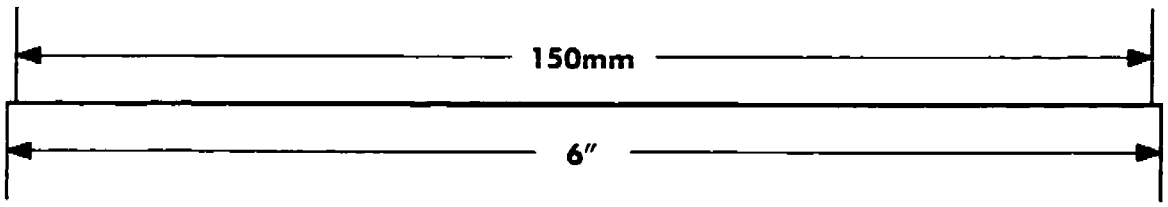
TRIGGER

Dehydration suggested if one or more of following present:

- Dehydrated [J1c = checked]
- Insufficient fluid/did not consume all liquids provided [J1d = checked]
- UTI [I2j = checked]
- Weight fluctuation of 3+ pounds [J1a = checked]
- Fever [J1h = checked]
- Internal bleeding [J1j = checked]
- Parenteral/IV [K5a = checked]
- Feeding tube [K5b = checked]
- Taking diuretic [O4e = 1-7]

TEST TARGET (QA-3)





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