Delirium

Focusing on intensive care patients

Het syndroom belicht bij patiënten op intensieve zorg

Proefschrift voorgelegd tot het behalen van de graad van doctor in de medische wetenschappen aan de Universiteit Antwerpen ter verdediging door

Bart Van Rompaey

Promotor : Prof. dr. L. Bossaert
Co-promotor: Prof. dr. M.J. Schuurmans
Artesis co-promotor: dr. S. Truijen

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Antwerpen, 2009

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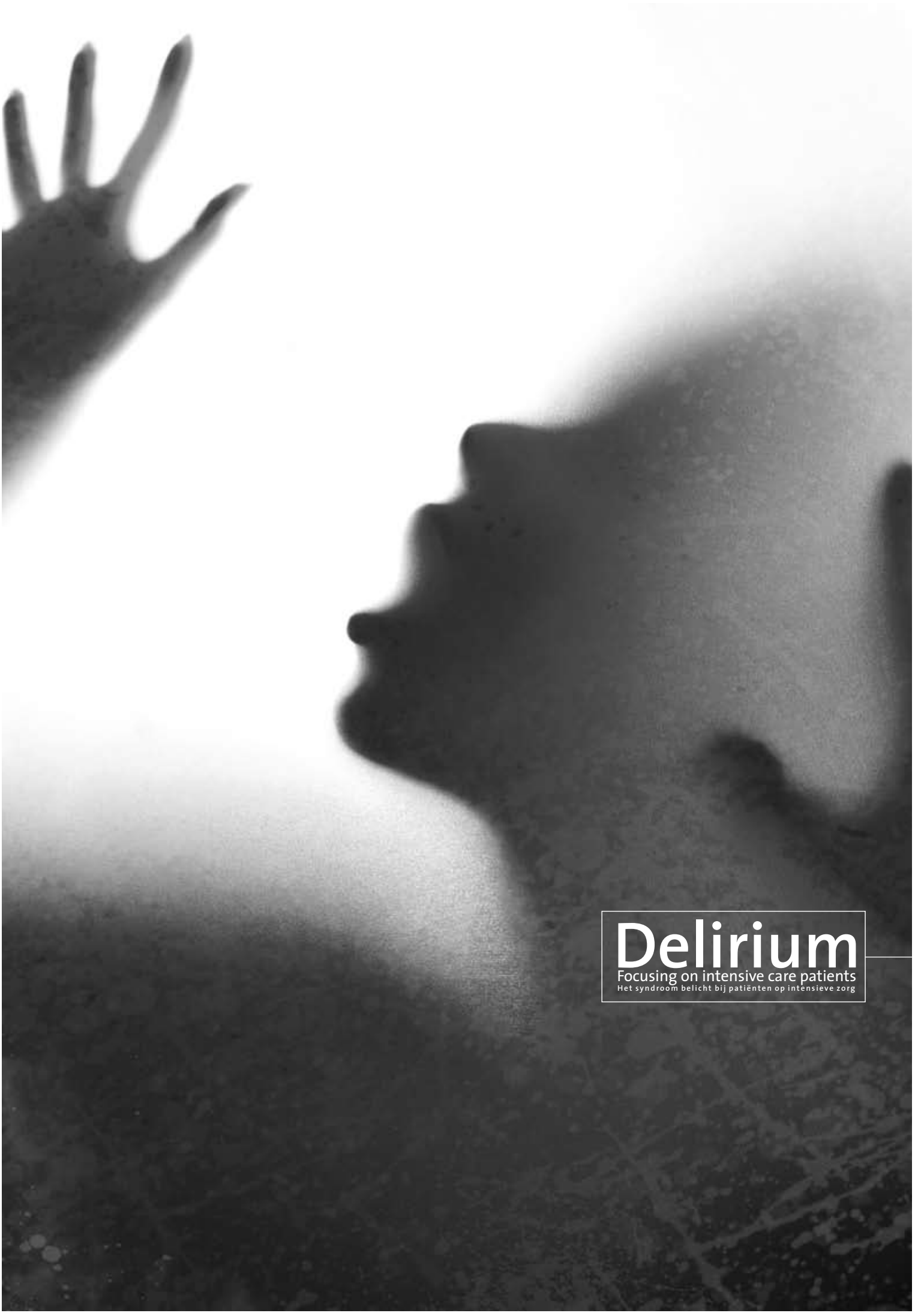
Co-promotor Prof. dr. M.J. Schuurmans

Artesis Hogeschool Antwerpen
Co-promotor dr. S. Truijen



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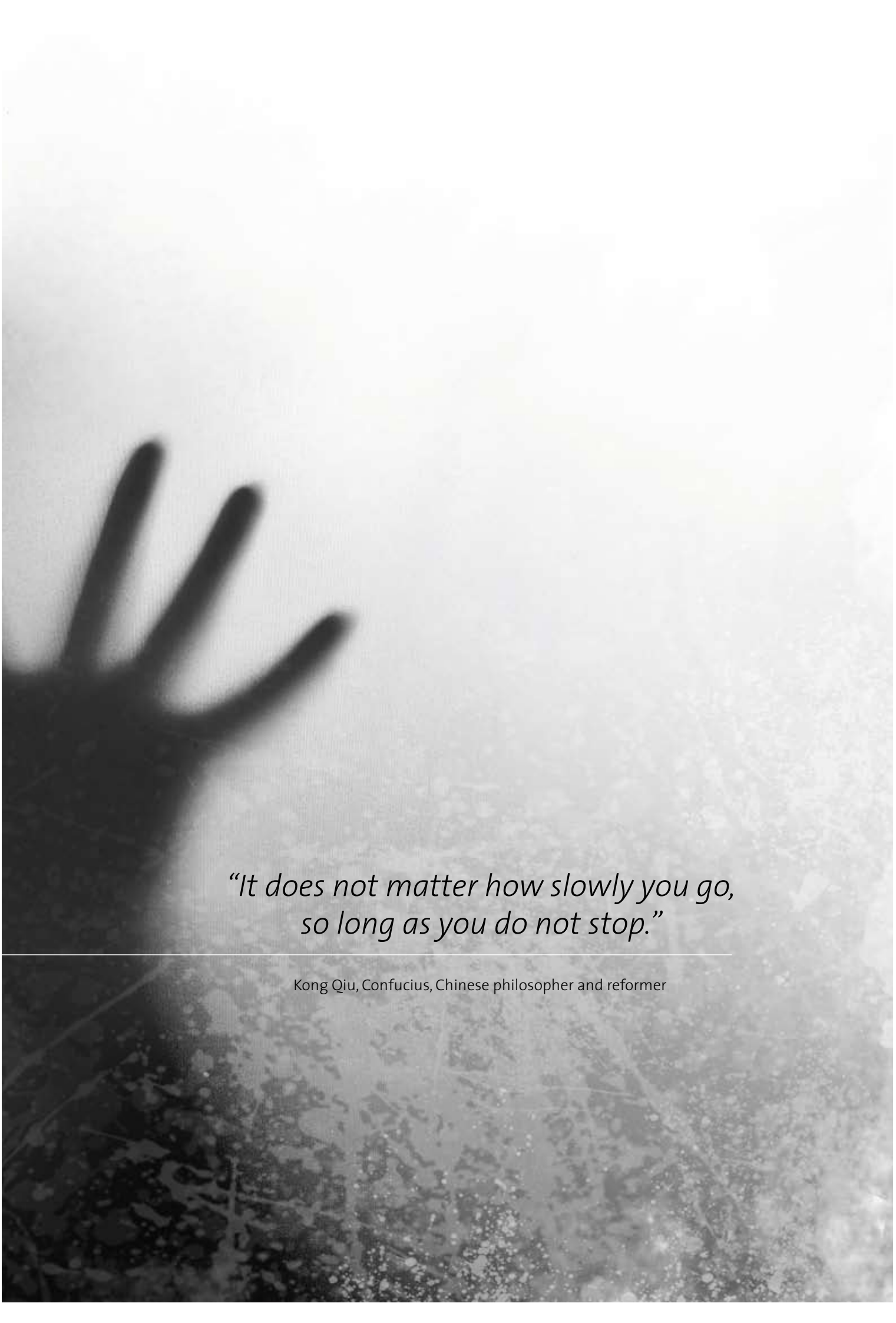

"It does not matter how slowly you go, so long as you do not stop."

Kong Qiu, Confucius, Chinese philosopher and reformer

Jury of the doctoral thesis

Members of the jury	Professor dr. P. Cras, Department of Neurosciences University of Antwerp, Belgium University Hospital of Antwerp, Belgium
	Professor dr. B. Sabbe Department of Neurosciences Collaborative Antwerp Psychiatric Research Institute University of Antwerp, Belgium
	Professor dr. P. Michielsen Department of Gastro-enterology University of Antwerp, Belgium University Hospital of Antwerp, Belgium
	Professor dr. K. Milisen, Centre for Health Services and Nursing Research Katholieke Universiteit Leuven, Belgium
	Professor dr. R. C. van der Mast Leids Universitair Medisch Centrum, Department of Geriatrics Universiteit Leiden, the Netherlands
Promotor	Professor dr. L. Bossaert Faculty of Medicine University of Antwerp, Belgium
Co-promotor	Professor dr. M. J. Schuurmans Professor of Nursing Science, Faculty of Medicine Utrecht University, the Netherlands
Artesis Co-promotor	dr. S. Truijen Department of Healthcare Sciences Artesis University College of Antwerp, Belgium

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Delirium
Focusing on intensive care patients

“He who speaks without modesty
will find it difficult to make his words good.“

Kong Qiu, Confucius, Chinese philosopher and reformer

1 Introduction

Partially based on:
Van Rompaey Bart, Intensief verward: het delirium op intensieve zorg, Chapter in Binnenste buiten, intensief bekeken, jaarboek 2006 Vlaamse Vereniging Intensieve *Zorgen Verpleegkundigen* (pp. 47-57), International Center for Reproductive Health Gent Belgium. (2006). (Dutch)

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1.1 Description of delirium

The word 'delirium' is derived from the Latin language and is etymologically related to a farmer taking an aberrant route off the furrow. Likewise, in medicine, the brain of a delirious patient creates an aberrant route. Consequently, in delirium cognitive and perceptual functions are impaired.

In common language delirium is mostly related to the extensive use or withdrawal of alcohol and drugs. Also in medicine, the term delirium is frequently used in this context. Additionally, delirium has been categorized by the European International Classification of Diseases and Related Health Problems-10 (ICD-10) as *a non-specific syndrome not induced by alcohol or psychoactive substances* (code F05). Likewise, the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) from the American Psychiatric Association classified delirium in the chapter cognitive disorders as *delirium due to a general medical condition* (293.0). Both slightly different descriptions characterise delirium as a syndrome not related to alcohol or drugs. The diagnosis is more specific using the DSM-IV criteria. Therefore, the majority of researchers accepted the DSM-IV criteria as the golden standard to define delirium. Consequently, the criteria for delirium in this thesis will be defined as an acute syndrome tending to fluctuate with periods of inattention, an altered level of consciousness and disorganised thinking (American Psychiatric Association, 2000).

1.2 A short history of delirium

Delirium has been studied since antiquity. Hippocrates described 'phrenitis', a state comparable to delirium in 500 BC. Antonius Cornelius Celsus used the word 'delirium' the first time in 58 BC in his De Medicina, Liber V: '*Quorundam sensus obtunduntur, appellatique ignorant; quorundam trux vultus est; quorundam oculi quasi resoluti huc atque illuc moventur; fereque tertio vel quinto die delirium accedit; multorum etiam nervi distenduntur... Ille aperniciosa est, quae vel levi vulneri supervenit, vel ultra tempus inflammationis durat, columna delirium movet; vel, si nervorum rigor aut distentio, quae ex vulnere orta est, eam non finit...Inter haec deinde febris acuta oritur ingensque sitis: quibusdam etiam delirium: alii, quamvis mentis suae compotes sunt, balbutiendo tamen vix sensus suos explicant; incipit adfici stomachus; fit foedi spiritus ipse odoris...*' (Thayer, 2006). Celsus associated delirium with brain injury, fever and excessive drinking. Through the millennia delirium has been described as a grave clinical situation often caused by fever and having a poor prognosis. The term confusion was widely used as a synonym. At the beginning of the nineteenth century, Greiner (1817) described the delirious state as a dream while awake. In the late nineteenth century the clouding of consciousness was the criterion to distinguish delirium from insanities. At that time, it was believed that the outcome of delirium was either full recovery or death. In the first half of the twentieth century, the organic cause of delirium was stressed. Different exogenous insults caused by illness were described. In the late part of the twentieth century, mental illnesses were defined and classified by either the ICD – 10 or the DSM criteria. Functional metabolism problems were considered to underlie delirium. The most important clinical feature was the disturbance in the cognitive functions. Nowadays, a change in consciousness is considered as the most important symptom distinguishing delirium from dementia or depression. Due to demographic changes, more elderly were hospitalised stimulating the attention on delirium. Researchers started to study the syndrome in detail. Among them, Lipowski is regarded as the father of modern research on the subject (Adamis *et al.*, 2007; Lipowski, 1983).

1.3 Aetiology of delirium

The exact aetiology of delirium is still unknown. Three major theories have been proposed. The first theory refers to the normal aging process of the neurons. Consequently, delirium is more a problem for elderly in this theory. A second theory seeks the explanation for delirium in a hypoxia in the brain, leading to a lower local oxidative metabolism. A third theory describes an imbalance of the neurotransmitters in the brain as a possible cause. This imbalance can be provoked either by a physical cause or the use of neuro-active medication. Each of these theories can be studied separately, but the answer is probably to be sought in a combination of the mentioned theories. (Maldonado, 2008; Seaman *et al.*, 2006)

1.4 Types of delirium

Three clinical subtypes of delirium can be distinguished. First, the most notable subtype is the *hyperactive* delirium, which is manifested as the agitated patient. Since these patients are restless and pull catheters and tubes, they are a serious risk to themselves, nurses and other staff members. Secondly, *hypoactive* patients are very quiet, and move scarcely. These patients are often overlooked, because they do not interfere with the normal procedures on the ward or do not appeal for extra attention. Nevertheless, they risk developing comorbid conditions, such as pneumonia or decubitus ulcers. The third subtype, the *mixed* delirium, originates from the typical fluctuating course of the syndrome. Hence, the patient will experience a mix of hyperactive and hypoactive periods (Granberg Axell *et al.*, 2001; Meagher *et al.*, 2000; Schuurmans *et al.*, 2001).

1.5 Delirium in different settings

Although most studies on delirium report on elderly, recent research showed possible implications for all ages, from children to elderly (Leentjens *et al.*, 2008; Turkel *et al.*, 2006).

The syndrome has been studied mainly in three settings. First, studies on general wards reported incidences in a range from 16 to 30 %. Risk factors were studied and multifactorial prevention programs were executed (Foreman, 1989; Francis *et al.*, 1990; Inouye *et al.*, 1999; Inouye, 2006). Second, research was done on patients after surgery. Incidences of the postoperative delirium ranging from 5 to 49 % were reported. The mental and physical condition of the patient, and the type of surgery were important predictors. Interdisciplinary prevention programs were studied (Amador and Goodwin, 2005; Eriksson *et al.*, 2002; Furlaneto and Garcez-Leme, 2006; Kalisvaart *et al.*, 2005; Milisen *et al.*, 2001; Yamagata *et al.*, 2005). The third setting is the intensive care unit. High incidences of delirium, ranging from 11 to 87 %, have been reported in this group of patients. Due to the large amount of possible risk factors and the typical setting, specific research is needed but mainly not performed as yet (Aldemir *et al.*, 2001; Bergeron *et al.*, 2002; Dubois *et al.*, 2001; Ely *et al.*, 2001d). No intervention programs have been studied or implemented. Delirium in the intensive care unit was accepted as a harmless process for years. Only recently, attention was focused on the possible worse outcome after a delirium (Angus and Carlet, 2002).

No distinction is made in the diagnostic criteria for delirium in general, postoperative delirium or delirium in the intensive care unit.

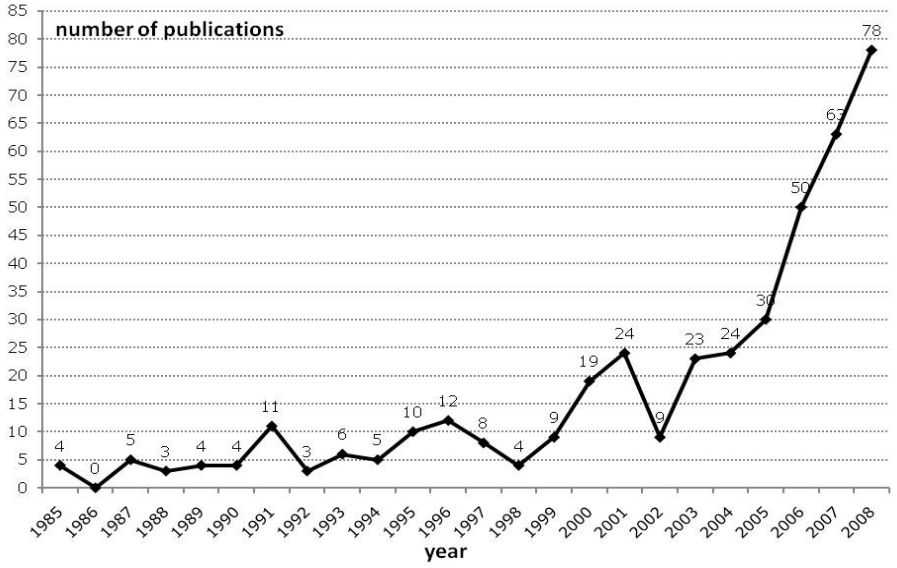
1.6 Definition of intensive care delirium

Many researchers have focused on the cognitive impairment of hospitalised patients in a high care unit. In literature more than 20 descriptions were given to name the phenomenon of a confused patient in the intensive care unit. The terms "intensive care unit confusion", "intensive care syndrome", "intensivitis", "acute confusional state" and others were used as a synonym to intensive care delirium. McGuire *et al.* stated that the confusion on terminology had obstructed standardised communication and research. Therefore, a consensus was established to exclusively use the term 'intensive care delirium', but other descriptions still appear in publications (McGuire *et al.*, 2000; Polderman and Smit, 2005).

Intensive care delirium is the presentation of the general picture of delirium in the specific setting of the intensive care unit with a patient encountering an acute confusional state, tending to fluctuate with periods of inattention, an altered level of consciousness and disorganised thinking.

Only during the last years, research and consequently publications on the topic have boomed. Figure 1.1 shows the number of hits in the PubMed database at the United States of America National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/pubmed) for the keyword 'intensive care delirium' selected by year from 1985 to 2008.

Figure 1.1: Number of hits in PubMed by year using the keyword 'intensive care delirium'



1.7 Risk factors for intensive care delirium

The onset of delirium is induced by a physical cause stimulated by predisposing and precipitating factors (Inouye *et al.*, 1993; Inouye and Charpentier, 1996). Predisposing factors exist in the patient before admittance to the intensive care unit. The precipitating factors challenge the patient's resistance. The higher the baseline vulnerability, the fewer challenging factors are required to push the patient into a delirium. Elderly patients in a general ward experience a more than 50 % higher potential for developing delirium when carrying more than three risk factors (Inouye and Charpentier, 1996). Ely *et al.* discovered a mean of 11 ± 4 risk factors in a population of intensive care patients (Ely *et al.*, 2001a). Therefore, an intensive care patient seems to be at major risk for the development of delirium.

For the typical clinical situation of the intensive care patient, there will always be a high vulnerability because of severe illness or trauma at the time of admittance. These illness and trauma provoke treatment with tubes, drains and psycho-active medication. The illness and the environment may cause disturbance of the circadian rhythm. Consequently, a patient encounters a cascade of predisposing and precipitating risk factors entering the intensive care unit.

Many risk factors for the onset of intensive care delirium have been mentioned by different researchers, but few have been studied thoroughly. Published risk factors were transferred from research outside the intensive care unit or from specific populations to intensive care patients. A factor, contributing to the development of delirium outside the intensive care unit, might not always have the same effect on the intensive care patient. Since none of the recent studies took the environment into account, there is no evidence that the intensive care environment causes delirium. Even so, the environment could exacerbate the development or the severity. Hence, research is urgently required focusing on the specific factors for intensive care delirium (Aldemir *et al.*, 2001; Dubois *et al.*, 2001; Sommer *et al.*, 2002).

1.8 Screening for intensive care delirium

For decades diagnosis for intensive care delirium was made by a consulting psychiatrist. The syndrome might often have been missed due to the absence of this specialist in the intensive care unit. The development of specific diagnostic tools for delirium has stimulated the assessment. Consequently, the use of validated instruments to screen for delirium facilitated the research in different cohorts and created the ability to compare results. Although different instruments have been developed, only a few have been used after their initial publication (Pandharipande *et al.*, 2005; Schuurmans *et al.*, 2003). Three assessment tools are commonly used to diagnose delirium in the intensive care unit: the Confusion Assessment Method for the Intensive Care Unit, the Neelon and Champagne Confusion Scale and the Intensive Care Delirium Screening Checklist. Neither of these tools is validated to indicate the severity of the delirium.

In 1990 Inouye et al. developed the Confusion Assessment Method (CAM) for delirium in general. The patient was assessed using an ad hoc assessment (Inouye *et al.*, 1990). Four years later, the instrument was used to screen patients for delirium in the intensive care unit (Marcantonio *et al.*, 1994). As the CAM required verbal interaction between patients and researchers, they are not easily applicable for ventilated or intubated patients. To overcome this problem, Ely and colleagues developed the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Ely *et al.*, 2001b). The verbal interactions were replaced by executing commands. The instrument has been translated in many languages. Although the translation and validation has not been published yet, the instrument is used in Dutch intensive care units and is considered as the golden standard in delirium assessment.

In addition, the Neelon and Champagne Confusion Scale (NEECHAM) (Neelon *et al.*, 1996; Neelon *et al.*, 1992) was developed to assess delirium based on standard nursing observations. In Belgium, Milisen et al. translated and validated the Flemish NEECHAM scale in a postoperative cohort of elderly hip fracture patients (Milisen *et al.*, 2005a). Immers et al. proved the NEECHAM Flemish translation to be valid in a Dutch intensive care unit (Immers *et al.*, 2005).

The third assessment tool, the Intensive Care Delirium Screening Checklist (ICDSC) (Dubois *et al.*, 2001) was developed to assess delirium in the specific intensive care situation. The instrument has been compared to the CAM-ICU giving high agreement rates (Plaschke *et al.*, 2008). A translation is used in Dutch intensive care units (Van Eijk *et al.*, 2008).

There seems no need in developing new tools to assess delirium in the intensive care unit. The existing tools, however, have to be studied thoroughly to refine them for the specific situation of the intensive care patient. Despite the existence of validated instruments, delirium remains unrecognized by nurses and clinicians in 66-84 % of the delirious patients. The hyperactive subtype is more likely to be discovered, but determines only 6 % of all the delirious cases in the intensive care unit. The hypoactive subtype remains unnoticed because patients undergo treatment without any resistance or complaint (Peterson *et al.*, 2006; Sanders, 2002; Truman and Ely, 2003). Nurses and clinicians might fail to recognize symptoms because of the lack of appropriate tools and knowledge on the subject.

Before the start of this research project no incidences of intensive care delirium in Belgium were published. Table 1.1 demonstrates incidences of various cohorts. Specific cohorts, different instruments and different study protocols made it impossible to compare the data or to conduct a meta-analysis (Aldemir *et al.*, 2001; Bergeron *et al.*, 2001; Bergeron *et al.*, 2002; Dubois *et al.*, 2001; Ely *et al.*, 2001b; Ely *et al.*, 2001d; Ely *et al.*, 2001c; Granberg Axell *et al.*, 2002; Immers *et al.*, 2005; Kishi *et al.*, 1995; Lin *et al.*, 2004; McNicoll *et al.*, 2005; Roberts, 2004; Thomason *et al.*, 2005). With reported observation ranging from 11 to 87 %, screening for intensive care delirium in Belgium is worthwhile. Consequently, in order to compare Belgian data to international publications, an assessment tool has to be selected rigorously.

Table 1.1: Reported incidences of intensive care delirium. n: size of the cohort, NA: not available, APACHE: Acute Physiology and Chronic Health Evaluation II score; CAM-ICU: Confusion Assessment Method for the Intensive Care Unit; ICDSC: Intensive Care Delirium Screening Checklist; NEECHAM: Neelon and Champagne Confusion Scale

year	first author	n		assessment	country	
1995	Kishi	238	16%	psychiatric interview	Japan	NA
2001	Ely	38	87%	CAM-ICU	USA	17
2001	Ely	96	83%	CAM-ICU	USA	23
2001	Bergeron	93	16%	ICDSC	Canada	NA
2001	Ely	48	60%	psychiatric interview	USA	NA
2001	Aldemir	818	11%	psychiatric interview	Turkey	NA
2001	Dubois	198	20%	ICDSC & psychiatric interview	Canada	15
2002	Bergeron	96	83%	CAM-ICU	Canada	14
2002	Granberg - Axell	19	74%	interview, qualitative research	Sweden	23
2004	Lin	102	21%	CAM-ICU	Taiwan	NA
2004	Roberts	73	40%	observations	Australia	16
2005	Mc Nicoll	22	68%	CAM-ICU	USA	NA
2005	Thomasson	261	48%	CAM-ICU	USA	15
2005	Immers	263	35%	NEECHAM		NA

1.9 Outcome of delirium in the intensive care unit

The necessity to screen patients for intensive care delirium is sustained by a poor outcome for delirium. An older study by Levkoff et al. (Levkoff *et al.*, 1992) suggested that elderly in the hospital scarcely regained their cognitive functions after a delirious experience. Other research found a longer stay in the intensive care unit and the hospital, a higher cost of treatment, a higher morbidity and a higher mortality as a worse outcome for delirium (Inouye *et al.*, 1998; Jackson *et al.*, 2003; Lundstrom *et al.*, 2005; Marcantonio *et al.*, 2005; Thomason *et al.*, 2005). Therefore, the 2002 Brussels round table conference on intensive care suggested making the detection and prevention of intensive care delirium the main research topic for the upcoming year's conference (Angus and Carlet, 2002). Yet, the studied outcome of delirium in an intensive care patient was mainly limited to the intensive care unit or the hospital. Few data are available on long term outcome.

1.10 Prevention and treatment of delirium in the intensive care unit

Since admittance to the intensive care unit is often an urgent event or following major surgery, lowering the baseline vulnerability is not the first option to prevent delirium in the intensive care unit. The focus has to be on diminishing the noxious insults on the intensive care patient. In order to possibly develop interventions to lower the incidence of delirium in the intensive care unit, research and prevention must be concentrated on modifiable risk factors.

In studies on patients outside the intensive care unit, preventive nursing and medical activities, and curative actions were studied (Bogardus *et al.*, 2003; Breitbart *et al.*, 2005; Milisen *et al.*, 2005b; Milisen *et al.*, 2001). No evidence based treatment for delirium in the intensive care unit has been developed. Preventive administration of Haloperidol in a geriatric hip surgery population did not change the incidence of postoperative delirium. The mean number of days that patients stayed in the hospital, however, decreased. In addition, there was a positive effect on the duration and the severity of the delirium (Kalisvaart *et al.*, 2005). A retrospective cohort analysis in intensive care patients found a lower hospital mortality after admitting Haloperidol to mechanically ventilated patients. An effect on the incidence of delirium was not mentioned (Milbrandt *et al.*, 2005). Haloperidol is worldwide the most accepted treatment for hyperactive delirium. Adverse drug reactions were observed, and treatment with less adverse drug reactions was recommended (Ely and Dittus, 2004; Frankenburg, 2004; Lacasse *et al.*, 2006; Milbrandt *et al.*, 2005; Skrobik *et al.*, 2004).

This research project did not aim to develop a treatment for delirium in the intensive care unit. Risk factors will be studied to stimulate possible preventive actions.

1.11 Clinical and nursing relevance of the doctoral research

Literature demonstrates a lack of data on delirium in the Belgian intensive care population. Intensive care physicians and nurses need an uncomplicated assessment tool easy to use in daily practice. The implementation of such an instrument creates the opportunity to detect delirious patients in an intensive care unit. Then, besides the necessary lifesaving treatment nursing care can also focus on the cognitive revalidation of these patients.

Risk factors for delirium must be studied in the intensive care unit. Modifiable risk factors must be influenced without jeopardizing the necessary treatment of the current illness. Intervention programs could be developed to lower the incidence of delirium.

Although delirium was believed to be a harmless process for years, research pointed at the worse outcome for the patients. This outcome requires further study to help patients in regaining their normal cognitive functions.

1.12 Aim of the doctoral study

This research project aims to describe the incidence of intensive care delirium in a Flemish adult population. Consequently, patients will be included in a long term follow up study on the outcome of delirium. Additionally, risk factors, including those from the environment, will be studied to suggest interventions to lower the incidence of delirium in the intensive care unit.

1.13 Outline of the thesis

The first part of the thesis describes the selected assessment tools for delirium. Chapter 2 compared two tools including patients in a Flemish intensive care unit.
The second part focuses on the long term outcome of intensive care delirium. Chapter 3 studies mortality and quality of life three and six months after discharge of the intensive care unit for delirious and non delirious patients.
In the third part of this thesis, risk factors for intensive care delirium are studied. A systematic review of the literature is presented in Chapter 4. Next, a multi centre prospective cohort study reports on relevant risk factors in Chapter 5. Chapter 6 describes the sound levels in the included intensive care units and studies a possible relation with delirium.
Finally, the fourth part of this thesis includes the discussion, holding the relevance to the clinical practice, and the conclusions.

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Delirium
Focusing on intensive care patients

Part 1

The assessment of delirium in the intensive care unit

"We shall not fail or falter;
we shall not weaken or tire...
Give us the tools and we will finish the job."

Sir Winston Churchill, British politician

2 A comparison of assessment tools for delirium in the intensive care unit

Published as:

Van Rompaey B., Schuurmans M., Shortridge-Bagett L., Truijen S., Elseviers M. & Bossaert L. (2008) A comparison of the CAM-ICU and the Neecham Confusion Scale in intensive care delirium assessment: an observational study in non-intubated patients. *Critical Care* 12, R16, 1.

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Abstract

BACKGROUND

Several reports indicate a high incidence of intensive care delirium. To develop strategies to prevent this complication, validated instruments are needed. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is widely used. A binary result diagnoses delirium. The Neelon and Champagne (NEECHAM) Confusion Scale recently has been validated for use in the ICU and has a numeric assessment. This scale allows the patients to be classified in four categories: non-delirious, at risk, confused, and delirious. In this study, we investigated the results of the NEECHAM scale in comparison with the CAM-ICU.

METHODS

A consecutive sample of 172 non-intubated patients in a mixed ICU was assessed after a stay in the ICU for at least 24 hours. All adult patients with a Glasgow Coma Scale score of greater than 9 were included. A nurse researcher simultaneously assessed both scales once daily in the morning. A total of 599 paired observations were made.

RESULTS

The CAM-ICU showed a 19.8 % incidence of delirium. The NEECHAM scale detected incidence rates of 20.3 % for delirious, 24.4 % for confused, 29.7 % for at risk, and 25.6 % for normal patients. The majority of the positive CAM-ICU patients were detected by the NEECHAM scale. The sensitivity of the NEECHAM scale was 87 % and the specificity was 95 %. The positive predictive value and the negative predictive value were 79 % and 97 %, respectively. The diagnostic capability in cardiac surgery patients proved to be lower than in other patients.

CONCLUSIONS

In non-intubated patients, the NEECHAM scale identified most cases of delirium which were detected by the CAM-ICU. Additional confused patients were identified in the categorical approach of the scale. The NEECHAM scale proved to be a valuable screening tool compared with the CAM-ICU in the early detection of intensive care delirium by nurses.

2.1 Introduction

Delirium is a well-known acute syndrome in the intensive care unit (ICU). A physical cause induces a fluctuating disturbance of the cognitive processes in the brain. The patient encounters periods of inattention in combination with disorganized thinking or a changed level in consciousness. The process is observed as a hypoactive, hyperactive, or mixed type. The hyperactive type is the least frequent one although it is the easiest to detect (Miller and Ely, 2006; Palmieri, 2003). Incidence rates of intensive care delirium were reported in a range from 11 % to 87 % (Aldemir *et al.*, 2001; Ely *et al.*, 2001a). To develop strategies to prevent or cure this complication, validated instruments for diagnosing, screening, and quantifying are needed.

The standard assessment of delirium is performed when a psychiatrist uses the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria (Tucker, 1999). The development of internationally accepted diagnostic tools created the opportunity to compare and verify the onset and process of intensive care delirium without the need for consulting a psychiatrist. The Confusion Assessment Method (CAM) (Inouye *et al.*, 1990; Schuurmans *et al.*, 2003) is a well-validated and frequently used tool. The scale was designed to be used by non-psychiatric physicians and trained researchers. Because the patient in intensive care is not always able to communicate verbally, the CAM was adapted for screening intubated or artificially ventilated patients. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Ely *et al.*, 2001b) is widely accepted as the standard in intensive care delirium assessment. This assessment tool was based on the DSM-IV criteria and diagnoses the delirious state by a yes or no answer to a four-point algorithm (Appendix 2.1). A positive answer to this algorithm indicates delirium and a negative answer indicates a normal cognitive state. Nevertheless, the results of this scale are limited by its binomial approach of the evaluation of delirium and the fact that it is a one-point-in-time assessment.

The Neelon and Champagne (NEECHAM) Confusion Scale (Neelon *et al.*, 1996) was developed a few years later based on daily nursing practice. In this scale, the nurses' 24-hour assessment of the level of processing information, the level of behaviour, and the physiological condition rate the patient on a 30 to 0 scale classifying him or her in one of four categories (Appendix 2.2). The cut off values of 30 to 27 for 'non-delirious' (normal), 26 or 25 for 'at risk', and 24 to 20 for 'early to mild confusion' (mild confusion) were standardized. Validation for delirium against the DSM-III-R criteria was performed for the scores 19 to 0 ('moderate to severe confusion') in the original development of the scale. Consequently, the delirious state can be assessed and changes in the cognitive function of the patient can be monitored. The NEECHAM scale is reliable for the detection of delirium by nurses in the general hospital population (Matsushita *et al.*, 2004; Milisen *et al.*, 2005) and recently has been validated for use in the intensive care environment (Csokasy and Pugh, 1999; Immers *et al.*, 2005). In this study, we investigated the NEECHAM scale in comparison with the CAM-ICU in a non-intubated intensive care population.

2.2 Materials and methods

All patients were admitted to the intensive care department of the Antwerp University Hospital (625 beds). The department has a capacity of 39 beds and admits more than 2,000 patients each year. This department is divided in five units of seven or nine beds. These units are preferentially, but not exclusively, specialized in treating cardiosurgical, surgical, or medical intensive care patients. Patients are admitted to a separated space or an individual room with a clock, visual and auditive contact with the staff, and the possibility to listen to the radio or watch television. Most of the patients have a window with visible daylight. All non-intubated patients with a score of at least 10 on the Glasgow Coma Scale, a minimum age of 18 years, and a stay of at least 24 hours before the first assessment in the ICU were included. Patients of all units were included, resulting in a mixed intensive care population in this study.

A trained nurse researcher included the patients once daily in the morning. First, the patient was assessed with the NEECHAM scale without calculating the results and immediately afterwards with the CAM-ICU. A test with the CAM-ICU was regarded as positive for delirium scoring positive on the algorithm. The NEECHAM scale categories were used to classify the patient. A test score of lower than 20 (moderate to severe confusion) is defined as 'delirium'. Each patient scoring positive for delirium at least once on the CAM-ICU or the NEECHAM scale was identified as delirious for the calculation of the incidence rates.

The included patients were classified in three categories of admittance: cardiac surgery, non-cardiac surgery, and internal medicine. Age, gender, and Simplified Therapeutic Intervention Scoring System 28 (TISS 28) score (Miranda *et al.*, 1996) were collected for all included patients. The mean TISS 28 score was calculated for each patient based on all daily values obtained during the stay in the ICU. The Acute Physiology And Chronic Health Evaluation (APACHE) II score is not validated for calculating the severity of disease or risk prediction for a cardiac surgery group. This score was calculated at the first day of admittance for the internal medicine and the non-cardiac surgery groups only.

To compare the studied scales, diagnostic descriptives were calculated in a two-by-two table for all paired assessments. Sensitivity, specificity, negative predictive value, and positive predictive value of the NEECHAM scale refer to the CAM-ICU as the reference assessment tool (Altman and Bland, 1994a; Altman and Bland, 1994b). Subgroup analysis for age, gender, length of stay, and category of admittance was performed based on the most severe CAM-ICU and NEECHAM scale score of each patient.

The Statistical Package for the Social Sciences 14.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The different categories of admittance were compared using the chi-square test, the independent *t* test, and the one-way analysis of variance where applicable. Correlations were calculated using the Pearson correlation coefficient. Significance was calculated on a 0.05 level.

The protocol of this study was presented to the ethical board of the University Hospital of Antwerp, where it was approved. An informed consent was requested from the patient or his or her legal representative where appropriate.

2.3 Results

A first group of patients was included in July to August 2006 and a second group in February to March 2007, resulting in a consecutive sample of 172 patients and a total of 599 paired observations. The mixed intensive care population was composed of 23 % cardiac surgery, 37 % non-cardiac surgery, and 40 % internal medicine patients. The mean age of the included population was 60 years (range 20 to 90) and 59 % were male. The mean APACHE II score was 21 (range 7 to 47) and the mean TISS 28 score was 29 (range 2 to 46) (Table 2.1).

Table 2.1: Description of the included population

	n = 172 patients	Cardiac surgery 23.3%	Non-cardiac surgery 37.2%	Internal medicine 40.5%	*P* value
Age in years, mean (SD)	60 (14.9)	67 (10.2)	58 (14.4)	58 (16.4)	0.002[a]
Male gender	n = 102	28.4%	39.2%	32.4%	0.04[b]
Female gender	n = 70	15.7%	34.3%	50.0%	
APACHE II score, mean (SD)	20.6 (9.0)	-	20.1 (8.0)	21.1 (10.0)	0.65[a]
TISS 28 score, mean (SD)	28.6 (5.4)	32.7 (4.7)	28.4 (4.5)	26.5 (5.4)	<0.001[a]
Length of stay in days, mean (SD)	7.0 (8.9)	5.7 (8.5)	7.3 (10.2)	7.4 (7.9)	0.59[a]

[a]*P* value of difference calculated with one-way analysis of variance. [b]*P* value of difference calculated with the chi-square test. APACHE, Acute Physiology And Chronic Health Evaluation; SD, standard deviation; TISS 28, Simplified Therapeutic Intervention Scoring System 28.

The incidence of delirium assessed with the CAM-ICU was 19.8 % for the total population. The NEECHAM assessment showed 20.3 % with delirium, 24.4 % with 'mild confusion', 29.7 % as 'at risk', and 25.6 % as 'normal' (Figure 2.1). Most of the patients scoring positive for delirium on the CAM-ICU were classified in the NEECHAM scale category diagnosing delirium. Almost a third of the patients scoring negative on the CAM-ICU were positive on the NEECHAM scale, most in the 'mild confusion' group and fewer in the delirious group. All of the patients scoring 'normal' or 'at risk' on the NEECHAM scale were assessed as negative on the CAM-ICU (Table 2.2).

Figure 2.1 Incidence of intensive care delirium assessed with Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and Neelon and Champagne (NEECHAM) Confusion Scale (n = 172 patients)

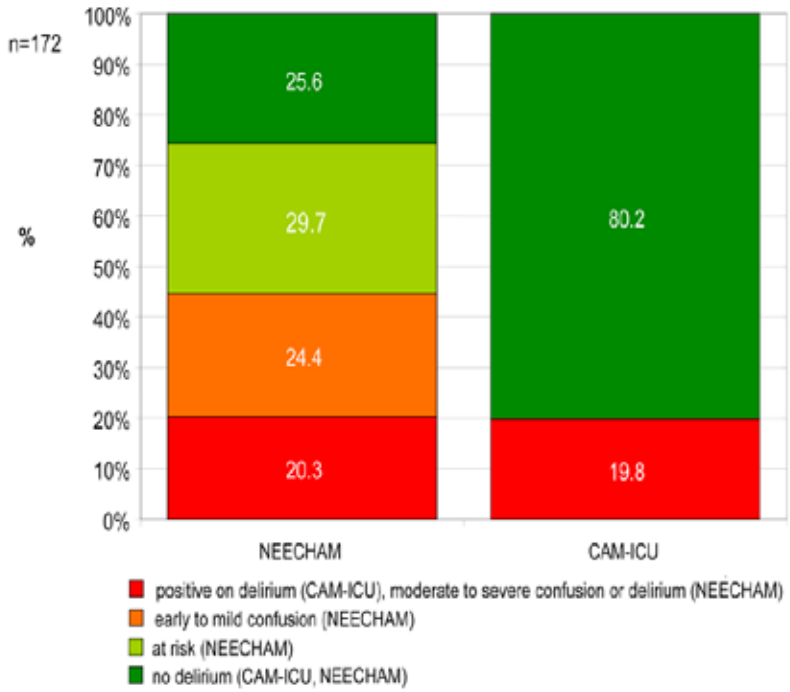


Table 2.2 Distribution of the total population in a NEECHAM Confusion Scale versus CAM-ICU matrix

n = 172 patients	NEECHAM scale			
CAM-ICU normal, n = 138		51		5
CAM-ICU delirious, n = 34	0	0	4	30

'Mild' is defined as early to mild confusion. CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; NEECHAM, Neelon and Champagne.

Positive delirium observations were obtained for 39 patients on 183 delirious days. Consequently, this resulted in a mean of 4.7 delirium days for each delirious patient, ranging from 1 to 18 days. Most of these patients suffered one (23 %), two (18 %), or three (13 %) delirious days. Most of the delirious patients (31 %) were positive for the first time within 3 days after admission to the ICU, and 57 % were positive for the first time after 4 days. Within 7 days, 77 % of the delirious patients were positive for the first time.

Subgroup analysis based on the most severe patient data (n = 172) showed similar results for the CAM-ICU and the NEECHAM scale. Both instruments agreed that there was no difference in the onset of delirium concerning age or gender (Table 2.3). Both showed a trend toward a higher incidence for the internal medicine patients. The length of stay in the ICU was higher for the delirious patients (Table 2.4). These results were significant regarding the CAM-ICU and the categories of the NEECHAM scale. Additionally, the NEECHAM scale scores showed a positive correlation with the length of stay in days (r = 0.61, P <0.01).

Table 2.3 Subgroup analysis for the incidence of delirium with CAM-ICU and NEECHAM Confusion Scale

n = 172 patients		CAM-ICU	*P* value	NEECHAM scale	*P* value
Age	Under 65 years, n = 98	22.4%	0.31	23.5%	0.24
	65 years or older, n = 74	16.2%		16.2%	
Gender	Male, n = 102	18.6%	0.65	19.6%	0.77
	Female, n = 70	21.4%		21.4%	
Category of admittance	Cardiac surgery, n = 40	15.0%	0.20	10.0%	0.08
	Other surgery, n = 64	15.6%		18.8%	
	Internal medicine, n = 68	26.5%		27.9%	

P value of the difference was calculated with the chi-square test. CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; NEECHAM, Neelon and Champagne

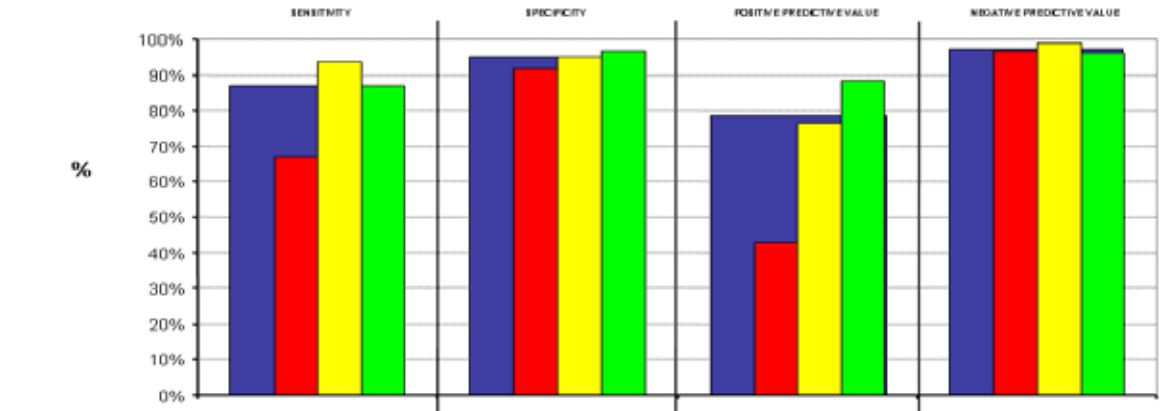
Table 2.4: Mean lengths of stay for delirious and non-delirious patients (CAM-ICU) and the four categories of the NEECHAM Confusion Scale

CAM-ICU	Mean length of stay in days (SD)	*P* value[a]	NEECHAM scale	Mean length of stay in days (SD)	*P* value[b]
Delirium	17.5 (14.5)	<0.001	Delirium	18.5 (15.1)	<0.001
			Mild confusion	7.0 (6.1)	
No delirium	5.0 (5.9)		At risk	4.0 (2.7)	
			Normal	2.8 (1.6)	

[a]*P* value was calculated with the independent *t* test. [b]*P* value was calculated with one-way analysis of variance. CAM-ICU, Confusion Assessment Method for the Intensive Care Unit; NEECHAM, Neelon and Champagne Confusion Scale; SD, standard deviation.

Each NEECHAM observation was compared with the paired CAM-ICU observation to calculate the diagnostic descriptives (Figure 2.2). Using the NEECHAM cut off value of less than 20 ('severe confusion'), test values were considered to be positive for delirium to calculate the diagnostic descriptives. The overall sensitivity was good but was lower in the cardiac surgery group (Figure 2.2). The specificity showed good results overall and in the different categories of admittance. Due to the lower sensitivity in the cardiac surgery group, the positive predictive value was poor for the assessment of this population but was higher in the other categories of admittance and was 79 % overall. The negative predictive value was good overall and in the different categories of admittance.

Figure 2.2: Diagnostic descriptives of the Neelon and Champagne Confusion Scale (NEECHAM) comparing to the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) as the reference tool. Values were calculated for n = 599 assessments.



	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
overall	87%	95%	79%	97%
cardiac surgery	67%	92%	43%	97%
non cardiac surgery	94%	95%	76%	99%
internal medicine	87%	97%	88%	96%

2.4 Discussion

In this study, the incidence of delirium assessed with the NEECHAM scale (20.3 %) was comparable to the results of the CAM-ICU (19.8 %). The diagnostic descriptives of the NEECHAM scale showed good results. Additionally, patients were classified in the different categories of the NEECHAM scale.

The research on intensive care delirium has taken a giant step forward since the development of assessment tools. A scale diagnosing delirium seems reliable when development was based on the DSM criteria. Hence, a confirmation by a psychiatrist is not necessary in daily practice. A gold standard for biological or physical tests, however, could be discussed (Claassen, 2005). A standard implies a level of perfection able to judge over all other tests. This perfection could hardly be attained by an individual assessing the patient.

Although the delirium assessment instruments have often been used in research, the implementation as a standard medical or nursing screening tool has just started in clinical practice. The CAM-ICU, the Intensive Care Delirium Checklist, and the NEECHAM scale are available to screen for delirium. Nowadays, there seems to be no need for the development of new tools, but the existing instruments should be studied thoroughly and refined to achieve a global understanding of the assessment of the delirium syndrome (Polderman, 2007).

The CAM-ICU was developed for physicians and researchers based on the DSM criteria (van Groos, 2004) but now is available to be used by intensive care nurses. The screening can be implemented in the daily nursing care after limited training. The instrument is translated and validated in 10 different languages. Therefore, the CAM-ICU usually is considered to be the 'gold standard' for the diagnosis of delirium. The incidence rates of delirium assessed with the CAM-ICU showed a wide range. Ely and colleagues (Ely *et al.*, 2001a; Ely *et al.*, 2001b) reported incidence rates of 83.3 % and 87.0 % in conscious medical or coronary care patients who were mechanically ventilated. McNicoll and colleagues (McNicoll *et al.*, 2003) detected 31.1 % delirium in medical intensive care patients older than 65 years, and Balas and colleagues (Balas *et al.*, 2007) reported 28.3 % in a surgical ICU. In our research, 19.8 % of the mixed

intensive care population developed delirium according to the CAM-ICU. The subgroup analysis of the internal medicine patients (Table 2.3) found an incidence of 26.5 % in our population, but the other categories of patients developed less delirium. Our incidence rates assessed with the CAM-ICU seem to be lower than those of the published reports. This could be explained by the absence of ventilated patients in our population. Moreover, the architecture of the studied ICUs might play a beneficial role in the prevention of delirium (for example, the presence of visible daylight and a clock). Further research has to focus on the onset of delirium and the precipitating risk factors in the studied ICU.

The NEECHAM scale was developed as a nursing screening instrument for the early detection of delirium and was validated against DSM criteria for use in an ICU (Immers *et al.*, 2005). In this validation research, 19.4 % delirium and 15.8 % mild confusion rates were found in a medium-sized ICU of a general hospital. The population in our study had a similar incidence for delirium but a higher incidence for 'mild confusion'. A report of Csokasy and Pugh (Csokasy and Pugh, 1999), also using the NEECHAM scale, showed a total score of 47 % for both categories taken together. The patients in their population (n = 19) were all older than 65 years and were admitted to an ICU of a smaller hospital. As already stated by Immers and colleagues (Immers *et al.*, 2005), the evaluation of the physiological condition may not be relevant to the delirium assessment of the patient in the ICU. Since there has been no research or validation study to verify this suggestion, the assessment of the physiological condition will be retained as a basic element of this tool. Additionally, further study is needed to adapt and validate the NEECHAM scale for the delirium assessment of the intubated or the ventilated patient. Also, a longitudinal study needs to inquire whether the numbered approach and the different categories of the NEECHAM scale have a predictive value against a binary approach. Consequently, the categories 'at risk' and 'mild confusion' could have an additional value. Preventive actions eventually could protect patients from becoming delirious. As Devlin and colleagues (Devlin *et al.*, 2007) in their excellent review of delirium instruments for the ICU already remarked, all evaluations are dichotomous and therefore do not measure delirium severity.

Besides the NEECHAM scale and the CAM-ICU, the Intensive Care Delirium Checklist is a commonly used screening tool for the detection of delirium in the ICU (Bergeron *et al.*, 2001). Incidence rates of 19.2 % and 31.8 % were reported in an adult population in a mixed ICU (Dubois *et al.*, 2001; Ouimet *et al.*, 2007). Many items in this scale can also be scored by a nurse during daily practice. This eight-item scale also provides a numeric approach to the delirium assessment. Each item scoring positive gets one point. A score of four points was considered to detect 99 % of the delirious patients. A definition of a population 'at risk' or with 'mild confusion' is not provided. A binary approach of the score was suggested. Given the four categories of the NEECHAM scale, the last one creates more opportunities to classify the patient.

Four positive CAM-ICU patients scored 'mild confusion'. Five patients scoring negative on the CAM-ICU scored delirious on the NEECHAM scale. Four of them had a borderline score on the NEECHAM scale. One patient had a score of 14 on the NEECHAM scale and was assessed as negative for delirium on the CAM-ICU. This patient received propofol (through a continuous intravenous infusion pump), which possibly influenced the results. The NEECHAM scale proved to be a good delirium screening instrument with a strong denial power. The specificity proved to be good in all categories. The diagnostic descriptives for the NEECHAM scale in the cardiac surgery group, in contrast to the results of the other categories of admittance, were low.

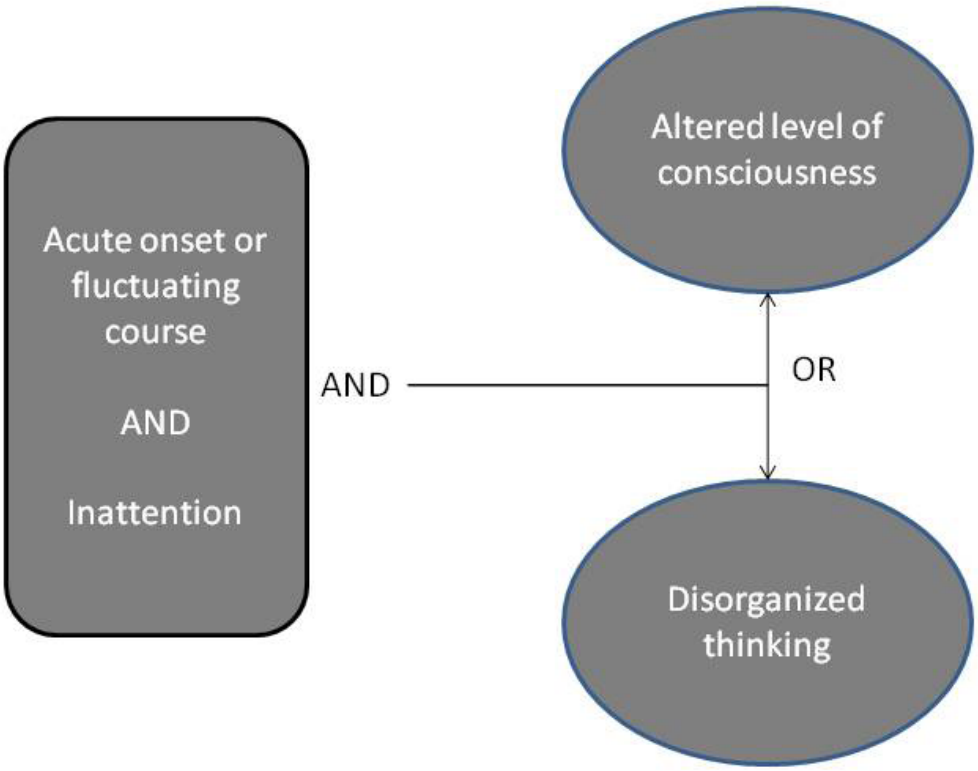
Nurses are the first caregivers to observe the patient and to detect an altering cognitive function. The NEECHAM scale uses the daily observation skills of nurses and their standard 24-hour monitoring of a patient in the ICU. The CAM-ICU needs a short visual or auditive test. Both scales, showing the same result in the diagnosis of delirium, could be considered for implementation in the standard nursing observation or monitoring in the ICU. The focus in research on intensive care delirium should shift from possible treatments to early prevention of the syndrome (Schuurmans *et al.*, 2001; van Gemert and Schuurmans, 2007). The detection of patients in an early stage of confusion and the classification in categories could become an important advantage of the NEECHAM Confusion Scale (Joshi, 2007; Polderman, 2007). Therefore, a longitudinal study is needed.

Our study is limited by the size of the population in the different categories of admittance. Each category could be the subject of a further study. Both studied scales were validated and verified for the intensive care setting. For the purpose of this study, a confirmation of the delirious state by a psychiatrist seemed unnecessary. The patient was assessed once in the morning. The simultaneous assessment of both scales could have created an interscale bias. The result of the NEECHAM scale, however, was calculated only after the paired assessment of the patient. Assessment of the patient at least three times a day could be recommended. A standardized screening for delirium should contain one observation during each nursing shift and an additional score on suspected events due to the fluctuating nature of the syndrome. The incidence in this study could have been higher when more daily assessments were completed. In addition, no ventilated or intubated patients were included. These categories of patients often develop delirium. There is a need to test the NEECHAM scale in this population.

2.5 Conclusions

The scales showed a comparable incidence of intensive care delirium in our population: 19.8 % for the CAM-ICU and 20.3 % for the NEECHAM scale. Additionally, patients could be classified as 'early to mild confused', 'at risk', or 'normal' using the NEECHAM scale. The studied scale showed acceptable sensitivity, specificity, and predictive values. The cut-off value of 20 of the NEECHAM scale is valuable in the assessment of intensive care delirium. The scale uses existing nursing skills to assess the patient and is easy to implement as a screening tool in standard nursing observation.

Appendix 2.1: The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
A detailed description is included in Chapter 12



Interaction required
Interview for four items
- Acute onset or fluctuating course
- Inattention (auditive or visual test)
- Disorganized thinking (questions)
- Altered level of consciousness

The score is dichotomous

-Positive: delirium

- Negative: no delirium

Appendix 2.2: The Neelon and Champagne (NEECHAM) Confusion Scale
A detailed description is included in Chapter 12

Observation on three levels

Level of processing information		*14 – 0*
	Attention	4 - 0
	Processing commands	5 - 0
	Orientation and memory	5 – 0
Level of behavior		*10 – 0*
	Appearance	2 – 0
	Processing commands	5 – 0
	Motor performance	4 – 0
Physiological condition		*6 – 0*
	Vital functions	2 – 0
	Oxygen saturation	2 – 0
	Urinary continence	2 - 0

Score 30 – 0

Normal	30 – 27
At risk	26 – 25
Early to mild confusion	24 – 20
Moderate to severe confusion	19 – 0

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Part 2

The outcome of delirium

"The goal is not to aim at the outcome,
but to develop the outcome"

Lillie M. Shortridge-Baggett, Professor, Lienhard School of Nursing, Pace University New York

3 Long term outcome after delirium in the intensive care unit

Published as:

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Abstract

AIMS AND OBJECTIVES

This research studied the long term outcome of intensive care delirium defined as mortality and quality of life at three and six months after discharge of the intensive care unit.

BACKGROUND

Delirium in the intensive care unit is known to result in worse outcomes. Cognitive impairment, a longer stay in the hospital or in the intensive care unit and a raised mortality have been reported.

DESIGN

A prospective cohort study.

METHODS

A population of 105 consecutive patients was included during the stay at the intensive care unit in July – August 2006. The population was assessed once a day for delirium using the NEECHAM Confusion Scale and the CAM-ICU. Patients were visited at home by a nurse researcher to assess the quality of life using the Medical Outcomes Study Short-Form General Health Survey at three and six months after discharge of the intensive care unit. Delirious and non delirious patients were compared for mortality and quality of life.

RESULTS

Compared to the non delirious patients, more delirious patients died. The total study population discharged from the intensive care unit, scored lower for quality of life in all domains compared to the reference population. The domains showed lower results for the delirious patients compared to the non delirious patients.

CONCLUSIONS

Mortality was higher in delirious patients. All patients showed lower values for the quality of life at three months. The delirious patients showed lower results than the non delirious patients.

RELEVANCE TO CLINICAL PRACTICE

Nurses are the first caregivers to observe patients. The fluctuating delirious process is often not noticed. Long term effects are not visible to the interdisciplinary team in the hospital. This paper would like to raise the awareness of professionals for long term outcomes for patients having experienced delirium in the intensive care unit.

3.1 Introduction

Delirium is a common syndrome in the intensive care unit with incidences ranging from 11 to 87 % (Aldemir *et al.* 2001, Bergeron *et al.* 2002, Ely *et al.* 2001, Immers *et al.* 2005). The definition is worldwide accepted using the Diagnostic and Statistical Manual of Mental Disorders criteria (American Psychiatric Association 2000). This acute, fluctuating disturbance in the cognitive or motoric functions is induced by a physical cause. The patient encounters periods of inattention in combination with disorganised thinking or a changed level of consciousness.

Delirium is observed as a hypoactive, hyperactive or mixed process. The hyperactive type is the least frequent one although it is the easiest to detect (Miller and Ely 2006, Palmieri 2003, Peterson *et al.* 2006). Recently, validated tools are worldwide available to assess patients for delirium in the intensive care unit without the need to consult a psychiatrist (Bergeron *et al.* 2001, Devlin *et al.* 2007, Ely *et al.* 2001, Neelon *et al.* 1996). Research showed, however, that delirium goes unrecognised in one third of the patients in the intensive care unit. The interdisciplinary team notices the hyperactive process, but fails in recognising the more frequent hypoactive syndrome (Peterson *et al.* 2006).

The attention of physicians and nurses is well focused on interventions for life threatening situations, but less on the poorly visible cognitive processes in the patient's brain (Pandharipande *et al.* 2005). Screening for delirium as a standard procedure was often criticised. The clinical relevance of detecting delirious patients has been questioned because defined guidelines for the treatment of the diagnosed patient are still not generally accepted or evidence based (Lacasse *et al.* 2006). In current years, researchers and intensive care physicians agreed to focus on the incidence, the treatment, the prevention and the outcome of the syndrome (Angus and Carlet 2002).

3.2 Background

Several studies reported a worse outcome for patients developing delirium during the stay in the intensive care unit. Attention has been given to the physical, cognitive and social outcome of patients leaving this unit. A higher morbidity, a higher mortality, a longer stay, a deterioration in the cognitive processes and a higher cost of treatment have been linked to the delirious process in the intensive care unit and the hospital (Jackson 2006, Jackson *et al.* 2003, Leslie *et al.* 2005, McCusker *et al.* 2001, McCusker *et al.* 2002, Thomason *et al.* 2005). The influence of delirium on the long term outcome of intensive care patients has been studied less.
The intensive care team has less contact with the patient once discharged from the intensive care unit or the hospital. Long term effects or complications are not visible to the interdisciplinary team. Therefore, the awareness of intensive care workers to the long term outcome of a delirious state developed during the stay in the intensive care unit must be stimulated.

One of the important aspects in the follow up of diseases is quality of life. The assessment of this outcome has been discussed as an indicator for the general health status of the patient. Most quality of life instruments assess several domains. Mental health and emotional well being are known to predict the quality of life. The general health status of a patient is more related to the physical functioning and the level of perceived pain. Quality of life and general health status are influenced by each other but are not synonyms. Therefore, an instrument covering several domains of the quality of life is advised to assess the status of patients after specific disorders or in specific situations (Smith *et al.* 1999). The choice for an instrument in research or in clinical practice depends on the situation, the availability and often the cost. The aim of this research is to study the long term outcome, defined as mortality

and quality of life, of patients having experienced intensive care delirium at three and six months after discharge of the intensive care unit.

3.3 Methods

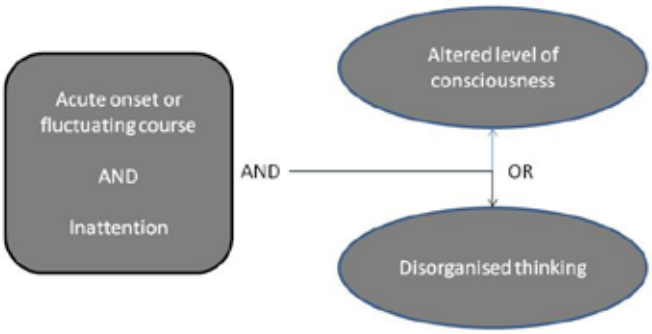
3.3.1 Study design

A sample of 105 patients was reached in an intensive care delirium study at the Antwerp University Hospital after a limited period of consecutive inclusion in July and August 2006. Non-intubated adult patients were included after a minimum stay of 24 hours in the intensive care unit and scoring a Glasgow Coma Scale greater than 10. All patients meeting the criteria and giving informed consent were included. The first objective of this study was to observe the incidence of delirium comparing two validated instruments. The recruitment of the patients was described in the original paper (Van Rompaey *et al.* 2008). Furthermore, the included patients were contacted by one nurse researcher for a follow up at three and six months after discharge of the intensive care unit to observe the long term outcome of delirium. A time span of two weeks before and after the exact date was accepted to visit the patient at home. The data collection was performed by a short questionnaire scoring mortality and quality of life.

3.3.2 Diagnosis of delirium in the intensive care unit

The diagnosis of delirium was established by nurse researchers. The mixed population was assessed once a day for delirium using both the Neelon and Champagne Confusion Scale (NEECHAM) (Immers *et al.* 2005, Neelon *et al.* 1996) and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Ely *et al.* 2001). The CAM-ICU diagnoses the delirious state by a yes or no answer to a four point algorithm. A positive answer to this algorithm indicates delirium, a negative indicates a normal cognitive state (Figure 3.1). The CAM-ICU was developed by Ely et al (Ely *et al.* 2001) based on de Confusion Assessment Method originally developed by Inouye et al (Inouye *et al.* 1990). The instrument is widely spread and translated in multiple languages. The assessment is based on an immediate assessment of the cognitive state of the patient (Fabbri *et al.* 2001, Laplante *et al.* 2005, Micek *et al.* 2005, Wei *et al.* 2008).The NEECHAM developed by Neelon (Neelon *et al.* 1996) and Champagne (Champagne *et al.* 1987) uses the nurses' twenty-four hour assessment of the level of processing information, the level of behaviour and the physiological condition to assess confusion. The instrument rates the patient on a 30-0 scale classifying him in one of four categories. The cut-off values, 30-27 'normal', 26-25 'at risk', 24-20 'early to mild confusion' were standardised (Figure 3.2). Delirium was diagnosed for the scores 19-0 'moderate to severe confusion' (Csokasy and Pugh 1999, Devlin *et al.* 2007, Matsushita *et al.* 2004, Milisen *et al.* 2005). The instrument was validated for assessing delirium in intensive care patients (Immers *et al.* 2005). The assessments of delirium scoring either positive on the CAM-ICU or scoring lower than 20 for the NEECHAM, resulted in the calculation of the incidence for delirium in the studied population (Van Rompaey *et al.* 2008). In this paper, patients having experienced a delirious period during the stay in the intensive care unit were indicated as the delirious patients, the others as the non delirious patients.

Figure 3.1:The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
The algorithm shows the assessment where at least three positive answers are required to diagnose delirium. The result of the CAM-ICU is dichotomous.



Interaction required Interview for four items - Acute onset or fluctuating course - Inattention (auditive or visual test) - Disorganized thinking (questions) - Altered level of consciousness	The score is dichotomous -Positive: delirium - Negative: no delirium

Figure 3.2: The Neelon and Champagne Confusion Scale (NEECHAM)
The assessment is based on standard nursing observations. The levels of the scores are described in the original instrument. The calculated result can be categorized.

Nursing observation results in a 30 - 0 score

Normal	30 – 27
At risk	26 – 25
Early to mild confusion	24 – 20
Moderate to severe confusion	**19 – 0**

delirium

Observation on three levels

Level of processing information		*14 – 0*
Attention	4 - 0	
Processing commands	5 - 0	
Orientation and memory	5 – 0	
Level of behavior		*10 – 0*
Appearance	2 – 0	
Processing commands	5 – 0	
Motor performance	4 – 0	
Physiological condition		*6 – 0*
Vital functions	2 – 0	
Oxygen saturation	2 – 0	
Urinary continence	2 - 0	

3.3.3 Observation of mortality

A patient who died in the intensive care unit scored positive for 'mortality in the intensive care unit'. A patient who died in the intensive care unit or between the discharge of the intensive care unit and the first visit at home was scored as 'died within three months'. Both mentioned groups and patients who died between the first and the second visit were mentioned as 'died within six months'.

3.3.4 Assessment of the quality of life

The quality of life was assessed using the Dutch Medical Outcomes Study Short-Form General Health Survey (SF-20) (Kempen *et al.* 1995). This tool, based on the RAND Health Insurance Study Questionnaire, was developed to decrease the burden on the patient using a shorter instrument (Stewart *et al.* 1988). The SF-20 assesses the quality of life in six domains: physical, role and social functioning, mental health, health perception and pain. The scale has been used in different groups of patients (Carver *et al.* 1999, Cooke *et al.* 1996, Hänninen *et al.* 1998). The 20 items of the questionnaire are computed to a 0 – 100 scale in each domain. A maximum score of 100 indicates the best possible functioning and a score of 0 the worst. Pain, however, scores 100 for a maximum possible pain and 0 for the total absence of pain. A total score for the quality of life is not calculated using the SF-20. The results obtained in this study were compared to the SF-20 reference scores for the Dutch population (Kempen *et al.* 1995). Differences in scores for delirious and non delirious patients were calculated.

3.3.5 Baseline data

Baseline data for the studied population were collected within the framework of the study in the intensive care unit. The Simplified Therapeutic Intervention Scoring System (TISS 28) (Reis Miranda *et al.* 1996, Reis Miranda *et al.* 2003) was collected daily for each patient during the stay in the intensive care unit. Based on these scores, a mean TISS 28 score was calculated for each individual patient. The Acute Physiology and Chronic Health Evaluation II (APACHE II) is a severity of disease baseline assessment tool in intensive care patients. The score, predicting mortality, is calculated once from the worst scores of routine measurements within 24 hours of admission to the intensive care unit (Knaus *et al.* 1985). Although the score has been studied recently in cardiac surgery or coronary care patients, the APACHE II was originally not developed to predict outcome in these patients (Knaus *et al.* 1985, Kramer and Zimmerman 2008, Sawchuk *et al.* 2003). Therefore, in our study the score was calculated for the internal medicine and non cardiac surgery patients only.

3.3.6 Statistical analysis

The scores for the NEECHAM, APACHE II, TISS 28 and age were explored for their relation with the six domains of the SF-20. The standard variation in the SF-20 scores of delirious and non delirious patients and the way those scores are computed, necessitated the use for non parametric statistics. Other data were analyzed with the Students T-test, One Way ANOVA or the Chi^2 test where appropriate. Odds Ratio's (Bland and Altman 2000) were calculated for mortality in the intensive care unit, at three months and six months using binary logistic regression with adjustment for age and gender. Correlations were calculated using the non parametric Spearman's Rho. A significance level of 0.05 was accepted. All statistics have been calculated using the Statistical Package for the Social Sciences 15.0 (SPPS Inc.).

3.3.7 Ethical considerations

The ethical board of the University Hospital of Antwerp approved the study design and an informed consent was obtained from all patients or their legal representative. Before the first and the second interview patients were formally asked if they did agree to continue their collaboration to the study.

3.4 Results

3.4.1 Characteristics of the studied population

A group of 105 consecutive patients was included in this study. Almost two third of the patients was male (63 %), the mean age was 62 years (20-90). The population was admitted to the intensive care unit for 'cardiac surgery' (35 %), 'other surgery' (32 %) and 'internal medicine' (32 %). The incidence of delirium was 19 % during the stay on the intensive care unit. The CAM-ICU and the NEECHAM assessed each 18 % of the patients as positive for delirium. The Kappa of the assessment of delirium for the used scales was 0.94 (p<0.001). The mean TISS 28 score for all patients was 30 (18-41). The mean APACHE II score for the 'other surgery' and the 'internal medicine' group was 20 (7-47) (Table 3.1).

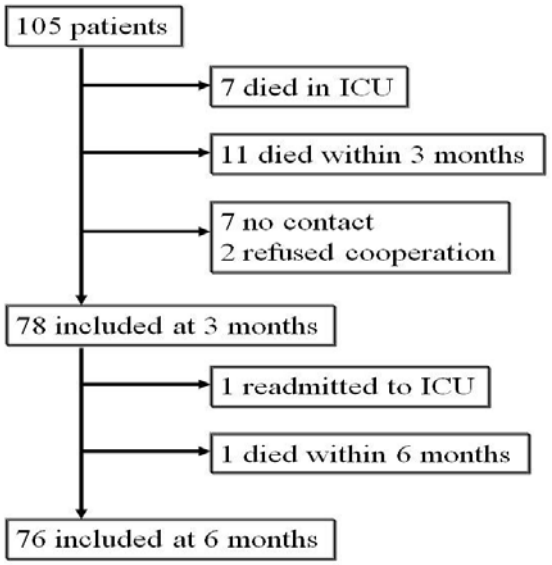
Table 3.1: Description of the included population

			non delirium	delirium	p**
			n=85	n=20	
age	years	(range)	61.5 (20-86)	64.3 (32-90)	0.46
APACHE II*	n=62	(range)	19.7 (7-47)	22.3 (9-36)	0.47
TISS 28		(range)	29.5(18-41)	31.1 (23-31)	0.28
length of stay ICU	days	(range)	2.5 (1-14)	13.4 (2-49)	<0.001
gender	male		64.7 %	55.0 %	0.42
reason of admittance	cardiac surgery		37.6 %	35.2 %	
	non-cardiac surgery		35.3 %	32.4 %	
	internal medicine		27.1 %	32.4 %	0.06

*: The APACHE II score was not calculated for cardiac surgery patients
**: p-value of difference

For the follow up of this cohort, two patients refused further cooperation to the study and seven patients could not be located at the address registered in the hospital (Figure 3.3). Mortality during the stay in the intensive care unit was 15 % (n = 3) in the delirious population and 5 % (n = 4) in the non delirious population. A sample of 78 patients was interviewed at three months. Only one patient in this population was readmitted to the intensive care unit between the interview at three and six months. Therefore, this patient was excluded for further follow up (Figure 3.3).

Figure 3.3 Inclusion of patients
The diagram shows the inclusion of patients in the intensive care unit, at three months and at six months. ICU: intensive care unit



3.4.2 Mortality after delirium

Three delirious and four non delirious patients died in the intensive care unit. After three months, seven delirious and 11 non delirious patients did not survive. Additionally, one non delirious patient died after six months. More included patients died in the delirium group compared to the non delirium group: 41 % and 15 % respectively (Table 3.2).

Table 3.2 Odd Ratio's for cumulative mortality after delirium, Odds Ratio (OR) adjusted for age and gender

cumulative mortality	non delirium	delirium	p**	OR	95 % CI*
study population	n=85	n=20			
mortality in the intensive care unit	4.7 %	15.0 %	0.097	3.03	0.57 – 16.19
mortality within 3 months	13.9 %	41.2 %	0.009	4.31	1.26 – 14.68
mortality within 6 months	15.4 %	41.2 %	0.016	3.80	1.11 – 13.05

*: CI: confidence interval
**: p-value of difference

The Odds Ratio for mortality in the intensive care unit was 3.03 (0.57-16.19) after experiencing a delirium (Table 3.2). After discharge of the intensive care unit 11 patients died before the first interview at three months. The Odds Ratio for mortality within three months after a delirious period increased to 4.31 (1.26-14.68) after correction for age and gender. One patient died before the interview at six months. He had not experienced delirium during the stay in the intensive care unit. This influenced the Odds Ratio for mortality within six months after delirium to 3.80 (1.11-13.05) after correction for age and gender (Table 3.2).

3.4.3 Quality of life of the total study population

At three months the total intensive care unit study population scored lower in all domains of the SF-20 than the reference population (Table 3.3). Physical function, role function and health perception showed significant lower values. The social function and the mental health showed a trend towards a lower score. At six months, only the perception of pain was significantly different from the reference population.

Table 3.3: SF-20 scores for the study group compared to the reference population

domain		at 3 months		at 6 months	
	SF-20* (SD)	mean (SD)	p**	mean (SD)	p**
physical function	67.8 (29.6)	56.8 (35.1)	0.01	72.9 (31.2)	0.16
role function	73.7 (41.3)	58.3 (58.3)	0.01	73.3 (43.8)	0.94
social function	80.9 (25.7)	72.3 (41.1)	0.07	78.9 (36.2)	0.64
mental health	76.0 (18.9)	71.4 (23.3)	0.09	74.0 (22.8)	0.44
health perception	67.6 (24.8)	54.6 (31.5)	<0.001	64.8 (28.3)	0.40
pain	30.4 (31.1)	34.0 (36.0)	0.38	22.3 (32.8)	0.04

*: mean scores for the Dutch reference population (Kempen et al. 1995)
**: p-value of difference

3.4.4 Quality of life after intensive care delirium

At three months, the delirium group showed lower values than the non delirium group in all domains of the SF-20 (Figure 3.4). Only the role function scored significantly lower than the non delirium group (Table 3.4). At six months, all domains had lower results for the delirious patients than the non delirious patients also. The role function persisted in a significantly lower score. The non delirious patients had lower SF-20 values than the reference population at three months. In contrast to the delirious patients, the non delirious patients reached the values of the reference population at six months in five domains.

Figure 3.4: SF-20 scores for the Dutch population, delirium and non delirium
The number on top of the bar indicates the mean value of the domain of the SF-20 calculated for a group (reference value, delirium, non-delirium).

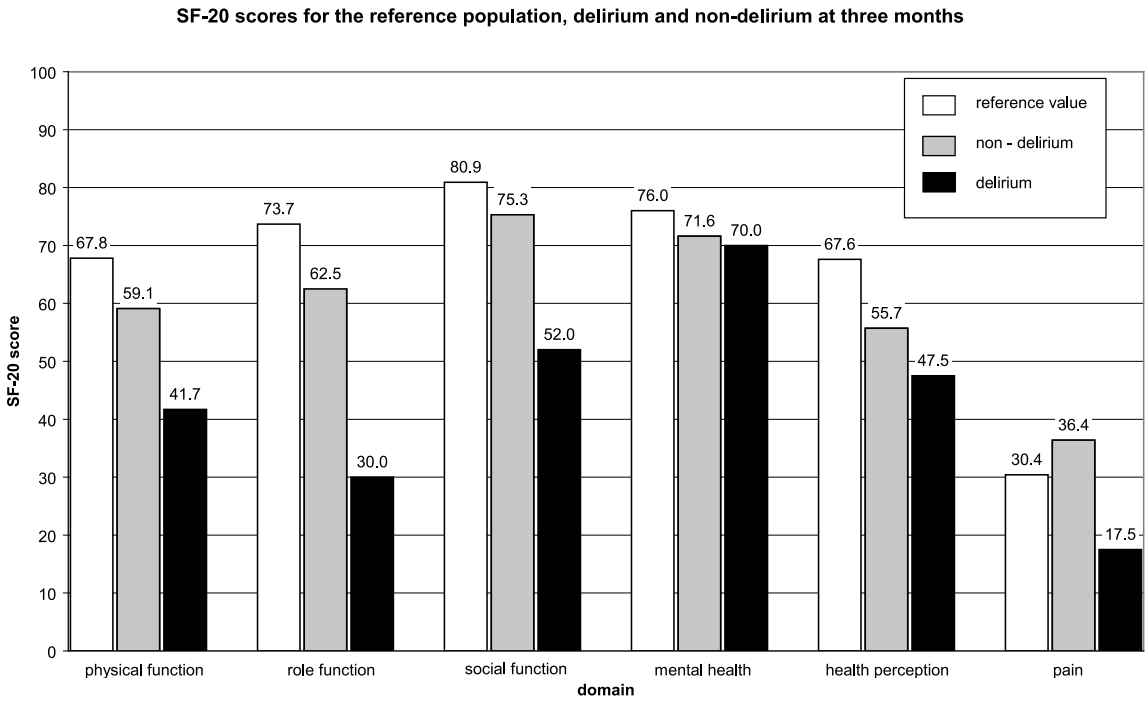


Table 3.4: mean SF-20 scores, compared with Mann Whitney U test for difference between delirium and non delirium

domain	SF-20*	at 3 months			at 6 months		
		non delirium	delirium	p**	non delirium	delirium	p**
physical function	67.8	59.1	41.7	0.13	73.8	66.7	0.56
role function	73.7	62.5	30.0	0.05	78.5	40.0	0.01
social function	80.9	75.3	52.0	0.20	81.5	62.0	0.24
mental health	76.0	71.6	70.0	0.48	74.9	68.0	0.21
health perception	67.6	55.7	47.5	0.40	68.9	57.5	0.42
pain	30.4	36.4	17.5	0.14	20.8	32.5	

*: mean scores for the Dutch reference population (Kempen et al. 1995).
**: p-value of difference

3.4.5 Relation between quality of life scores and patient and clinical characteristics

Age was negatively related to most domains at three and six months (Table 3.5). The physical function at six months, however, was the only domain significantly related. Mental health showed a weak positively relation at three and at six months. The Spearman's Rho showed a significant positive relation between the results of the NEECHAM Confusion Scale and the SF-20's physical function, role function and the health perception at three months. At six months, the social function was additionally positively related. A higher degree of confusion, indicated by a lower a NEECHAM score, seemed related to lower values for the quality of life. The APACHE II score in the intensive care unit was significantly related to four domains at three months and to three domains at six months. The APACHE II score was still linked to the physical, the role and the social functioning at six months.

The TISS 28 score in the intensive care unit seemed not related to the scores in the different domains at three months. At six months, only the domain mental health showed a significant relation. Multivariate analysis, taking into account delirium and possible confounding factors, did not find any relevant or significant relationship with the quality of life scores.

Table 3.5: Relation between the six domains of the SF-20, age, NEECHAM, APACHE II and TISS 28 using Spearman's Rho

3months	Physical function	Role function	Social function	Mental health	Health perception	Pain
Age	- 0.21	- 0.17	- 0.19	0.03	- 0.13	- 0.10
NEECHAM	0.35*	0.31*	0.20	0.19	0.25*	- 0.05
APACHE II[X]	- 0.34*	- 0.38*	- 0.40*	- 0.31*	- 0.19	- 0.08
TISS 28	- 0.01	0.00	0.06	0.13	0.09	- 0.16
6 months	Physical function	Role function	Social function	Mental health	Health perception	Pain
Age	- 0.31*	- 0.16	- 0.15	0.11	- 0.11	- 0.01
NEECHAM	0.27*	0.34*	0.30*	0.28*	0.20	- 0.18
APACHE II[X]	- 0.33*	- 0.34*	- 0.40*	- 0.27	- 0.13	- 0.04
TISS 28	0.14	0.06	0.06	0.25*	0.12	- 0.13

*: significant at 0.05 level

[X]: APACHE II is calculated for non cardiac surgery and internal medicine patients only

3.5 Discussion

3.5.1 Long term outcome

In this study delirious patients showed a higher mortality within six months after discharge of the intensive care unit. At three months non delirious patients scored higher on the SF-20 as the delirious patients, but showed lower values than the reference population. At six months the delirious patients still scored significantly lower for the role function.
There seems no doubt that mortality is an important outcome after an intensive care unit delirium. In this study a larger amount of delirious patients died before and after the discharge of the intensive care unit. In spite of the small population, the calculated Odds Ratio's showed a higher risk for mortality after delirium. This confirmed research on outcome of delirium outside the intensive care unit. Leslie (Leslie *et al.* 2005) and McCusker (McCusker *et al.* 2002) calculated hazard ratios of 1.62 and 2.11 for mortality in delirious patients after 12 months. Intensive care nurses and physicians should be aware that the life threatening situation of a patient could be extended for months by a delirium.

The scores in the six domains of the SF-20 in this study showed lower values for the included patients compared to the reference population. The results suggest the impact of critical illness on the quality of life. For non delirious patients this situation seems to normalise after six months. In contrast, delirious patients showed a delayed improvement of the situation.

Delirious patients scored lower at three and at six months for all domains. Jackson and colleagues (Jackson *et al.* 2003) did not find differences in quality of life at hospital discharge and at a six month follow-up after cognitive impairment in the intensive care unit. This should be verified in a larger cohort. The major problem for delirious patients in this study seems to be situated in the role function. This domain reflects on functioning in daily life activities such as work, housekeeping or daily activities (Kempen *et al.* 1995). Therefore, delirious patients seem to rehabilitate more difficult in the society after discharge of the intensive care unit. This was supported by the lower trend in the domain social function. The quality of life scores of the Dutch reference population were given separately for different decades for age, differences in education or specific chronic diseases in the original instrument (Kempen *et al.* 1995). Due to the small population, the findings in this study were not compared to this categorised SF-20 values.

The Spearman's Rho pointed at two important factors explaining the scores in the different domains. First, the NEECHAM demonstrated a long term effect on the quality of life. A lower score, indicating more confusion or delirium, was correlated to a lower score in all domains. Second, the APACHE II might balance the long term effect of delirium. A higher APACHE II score resulted in lower scores for several domains also. It might be questioned whether either delirium or the severity of illness influenced the quality of life most. The severity of illness, however, was not calculated for the total population leaving a multivariate analysis for a smaller population not appropriate.

The SF-20 was selected for this research based on availability without cost and low burden for the patient. The instrument has proven to be a valid tool in the past (Carver *et al.* 1999, Cooke *et al.* 1996, Hänninen *et al.* 1998). The physical functioning is based on six questions, the mental health and health experience on five. The role function, however, is based on two questions and the social function and perceived pain on one. The transformation of a limited number of questions to a percentage results in a low number of available scores. The range of scores between 0 and 100 resulted in an interrupted scaling where only a few scores were possible within that range. Therefore, non parametric statistics were chosen to handle the scores of the SF-20.

3.5.2 Limitations

As already mentioned, the small population of this study limits the conclusions. The results must be confirmed in a larger population. Additionally, this research was confronted with a lack of total score of the quality of life limiting the analytical possibilities.

3.6 Relevance to clinical practice

In spite of standardised screening protocols, intensive care delirium remains mainly undetected. Nurses are always present at the bedside of a patient and therefore best placed to observe and report. A long term effect on the outcome of the patient has been reported. This worse outcome, however, is not visible to the intensive care nurse or physician. Since delirium might be a preventable complication in the intensive care unit, preventive or therapeutic action must be developed. Therefore, this paper would like to raise the awareness of all caregivers for delirium in the intensive care unit.

3.7 Conclusions

Non delirious patients were more likely to survive three months after discharge of the intensive care unit. All included intensive care patients showed lower SF-20 results than the reference population three months after discharge. Moreover, the delirious patients still showed lower results than the non-delirious patients at six months. Further research in larger intensive care unit populations is needed to confirm the long term outcome of a delirium in the intensive care unit.

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Delirium
Focusing on intensive care patients

Part 3

Risk factors for delirium in the intensive care unit

"Everything should be made as simple as possible, but not one bit simpler."

Albert Einstein, US (German-born) physicist

4 A systematic review on risk factors for intensive care delirium

Published as:

Van Rompaey B., Schuurmans M., Shortridge-Bagett L., Truijen S. & Bossaert L. (2008) Risk factors for intensive care delirium: a systematic review. *Intensive and Critical Care Nursing* 24, 2, 98-107.

Abstract

Delirium has been a recognised syndrome in the intensive care unit for years. This systematic review reports risk factors for delirium studied in the intensive care unit. Four predisposing and 21 precipitating factors, including nine laboratory blood values and seven items relating to the use or the administration of medication, were found to influence the onset of delirium in the intensive care unit in six publications. The APACHE II score and hypertension were the only factors reported twice. Risk factors for the development of intensive care delirium were understudied and underreported in the literature.

4.1 Introduction

Delirium is a disturbance of the cognitive processes in the brain induced by a physical cause and presented as an acute syndrome characterized by a fluctuating course. The patient encounters periods of inattention in combination with disorganized thinking or a changed level in consciousness. The process is observed as a hypoactive, hyperactive or mixed type. The hyperactive type is the least frequent one although it is the easiest to detect (Miller and Ely, 2006; Palmieri, 2003).

The syndrome has not been well recognized for years. In addition, it has been accepted as a harmless process. Recent evidence, however, highlights the poor clinical outcomes (Inouye *et al.*, 1998; Inouye, 2006; Jackson , 2006; Jackson *et al.*, 2003; Leslie *et al.*, 2005; Rockwood *et al.*, 1999; Thomason *et al.*, 2005; Treloar and Macdonald, 1997b; Treloar and Macdonald, 1997a). A higher morbidity, a higher mortality, a longer stay in the hospital or in the intensive care unit, a deterioration in the cognitive processes and a higher cost of treatment have been linked to the delirious process. Delirium has been described as a general syndrome, but has been described in specific settings as "postoperative delirium" in the surgical patient and as "intensive care delirium" in the intensive care unit (Roberts, 2004).

The standard assessment of delirium is performed by a psychiatrist using the DSM-IV criteria (Tucker, 1999). Diagnostical tools for physicians and nurses were developed during the last decade (Schuurmans *et al.*, 2003). The Confusion Assessment Method (CAM) (Inouye *et al.*, 1990) and the NEECHAM Confusion Scale (NEECHAM) (Neelon *et al.*, 1996) proved to be well validated and regularly used tools to assess the delirious patient. Since the intensive care patient is not always able to communicate verbally, these scales have been adapted for screening intubated or ventilated patients. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (Ely *et al.*, 2001c) was used most commonly in the published research concerning delirium in the intensive care unit. This scale diagnoses the delirious state by a yes or no answer to a four point algorithm based on the DSM-IV criteria. The NEECHAM rates the patient on a 30-0 scale assessing the level of processing information, the level of behaviour and the physiological condition. The patient can be classified into four categories: 30-27 normal, 26-25 at risk, 24-20 early to mild confused and 19-0 moderate to severe confused. The Intensive Care Delirium Checklist (Bergeron *et al.*, 2001) and the Organic Brain Syndrome Scale (Björkman Björkelund *et al.*, 2006) were also common used diagnostical tools for delirium in the intensive care unit. The development of worldwide accepted diagnostic tools created the opportunity to compare and to verify the onset and the process of intensive care delirium without the need for consulting a psychiatrist.

The intensive care patient seems to be at high risk for the development of delirium with reported incidences ranging from 11 to 87 % (Bergeron *et al.*, 2002; Ely *et al.*, 2001b; Ely *et al.*, 2001c; Immers *et al.*, 2005; Lin *et al.*, 2004; McNicoll *et al.*, 2005; Thomason *et al.*, 2005; Aldemir *et al.*, 2001). The wide range in reported incidences could be explained by the different study designs, a difference in the method of assessing delirium and the differences in the studied population. Evidence is growing, however, that delirium is a common problem in all intensive care units.

Screening for delirium as a standard procedure was often criticized. The clinical relevance of detecting delirious patients was questioned because defined guidelines for the treatment of the diagnosed patient are still not generally accepted (Lacasse *et al.*, 2006). Multifactorial intervention programs were developed and tested in different settings (Inouye *et al.*, 1999; Lundstrom *et al.*, 2005; Marcantonio *et al.*, 2001; Milisen *et al.*, 2005; Milisen *et al.*, 2001) albeit not in the intensive care unit. Consequently, there seems to be an urgent need for an evidence-based development on a treatment or preventive action for delirium in the intensive care unit.

Inouye *et al.* created a predictive model for the development of delirium in elderly patients in the hospital (Inouye *et al.*, 1993; Inouye and Charpentier, 1996). This simple model was very useful outside the intensive care unit. Risk factors could be classified as predisposing or precipitating. The predisposing factors e.g., age, gender, hearing or visual impairment, are acquired baseline characteristics and are patient dependent. The precipitating e.g., disturbed laboratory blood values, surgical interventions, drugs or intercurrent illness, are dependent of the kind of disease and the type of admittance to the hospital. These factors are modifiable to decrease the risk a patient encounters. The onset of delirium in each individual patient is caused by an interaction of predisposing and precipitating factors. A higher number of factors encountered by a patient will increase the risk on intensive care delirium. Ely *et al.* (Ely *et al.*, 2001a) reported a heavy burden on intensive care patients having at least 10 risk factors. Outside the intensive care unit Inouye *et al.* stated that three or more of these factors increased the risk for delirium with 60 %.

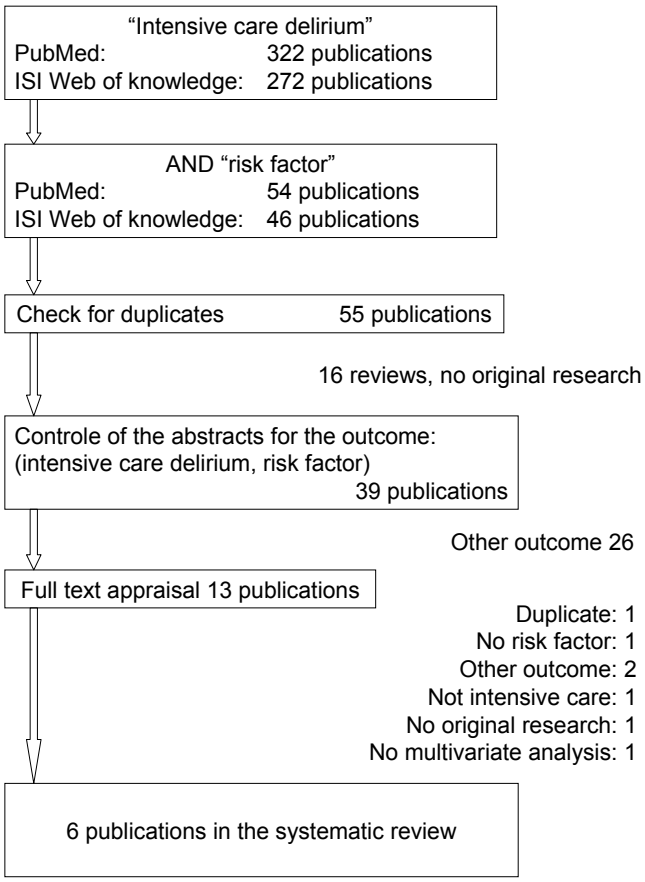
Hence, not all factors may be applicable to intensive care patients or have the same effect as in the onset of delirium outside the intensive care unit. Therefore the aim of this systematic review was to explore the reported risk factors for the development of delirium in the intensive care unit.

4.2 Methods

The first author searched the PubMed databases and the ISI Web of Knowledge for original research publications. Furthermore, the references of the retrieved papers were searched for additional links. The papers had to be published in English, Dutch, French or German. Due to the tremendous ongoing technical, medical and nursing evolution in intensive care, publications have been taking limited to those published during the last 10 years (Feb 1997-Mar 2007). Moreover, most researchers have only used validated delirium assessment tools during the last decade to screen for the syndrome in intensive care patients. The papers were included if they reported on original research in an intensive care unit, limited to randomized clinical trials, prospective or retrospective studies, containing at least one risk factor for delirium. The outcome of the delirium assessment in the study had to be focused on the incidence or the onset of delirium. The risk factors were selected if they reached the significance level of 95 % in a multivariate analysis.

'Intensive care delirium' was entered as the first keyword in the databases to focus on the intensive care population. Subsequently, 'risk factor' was added. The results from both searches were similar, adding MESH terms or manual input by the researcher did not reveal any further results. After the systematic search 13 publications met all of the inclusion criteria to be appraised by reading the full text. After further reading only six original research papers were included in the systematic review (Figure 4.1).
The risk factors were presented as odds ratio (OR) with a 95 % confidence interval if possible (Bland and Altman, 2000).

Figure 4.1: Presentation of the bibliographic research



A short review of the literature showed a lack of an appropriate tool for evaluation of cohort studies. A standardized form was developed based on the appraisal of cohort studies as published in the British Medical Journal (Rochon *et al.*, 2005; Mamdani *et al.*, 2005; Normand *et al.*, 2005). The general guidelines for the review of these studies were combined into six items in this systematic review. The quality of the studies was evaluated scoring one point for each item, resulting in a maximum score of six points for the best paper (Table 4.2).

4.3 Results

Table 4.1 presents a description of the included publications. All papers were published from 2001 to 2007. No randomized clinical trials concerning risk factors on intensive care were retrieved. Five papers reported on a prospective cohort study and one on a retrospective record analysis. The critical appraisal resulted in the maximum score for

Table 4.1: Description of the included papers (NA: not available, ICU: intensive care unit)

Author, year, country Period of data collection	Type of research	Included population	Delirium assessment tool	
Aldemir et al., 2001 Turkey January 1996 - 1997		N=818 - general surgery patients admitted to the ICU - age: NA - no history of dementia - no history of drug or alcohol abuse	- daily psychiatric interview by trained researchers - consult by psychiatrist for patients with changes in state of consciousness	11.0 %
Dubois et al., 2001 Canada November 1998 - April 1999		N=198 - medical and surgical ICU patients - age: ffl 18 years - ffl 24 hours in the ICU - likely to survive ffl 24 hours	- diagnosis by an intensivist - confirmation by psychiatrist - Intensive Care Delirium Screening Checklist	19.2 %
Sommer et al., 2002 USA September 1997 – September 1998		N=3308 ICU admissions - research on 20689 hospital patients - selection of medical and surgical ICU patients (severe illness) - age: NA - haloperidol was administrated	- Haloperidol administration as an indicator of delirium occurrence(IDO) - 5.3 % IDO (in 20689 hospital patients)	NA
McNicoll et al., 2003 USA December 2000 - July 2001		N=118 - medical ICU patients - age: ffl 65 years	- CAM-ICU	31.1 %
Pandharipande et al., 2006 USA February 2000 -May 2001		N=198 - medical or coronary ICU patients - age: ffl 18 years - mechanically ventilated	- CAM-ICU	
Ouimet et al., 2007 Canada December 2003 - August 2004		N=764 - medical and surgical ICU patients - age: ffl 18 years - ffl 24 hours in the ICU - likely to survive ffl 24 hours	- Intensive Care Delirium Screening Checklist	31.8 %

four publications, whereas two publications scored intermediate (Table 4.2). In one of the latter, the description of the selected patients could not exclude a possible bias and no validated instrument was used to assess delirium (Sommer *et al.*, 2002). Similarly, a validated instrument was not used in the other publication and neither the statistical analysis, nor the results were clearly formulated (Aldemir *et al.*, 2001).

Table 4.2: Critical appraisal of the included papers

Author,	Study Design	Selection of patients	Delirium	Multi-variate analysis	Plausible	Clinically relevant	Total
Aldemir et al., 2001	1	1	0	1	0	0	3
Dubois et al., 2001	1	1	1	1	1	1	6
Sommer et al., 2002	1	0	0	1	1	0	3
McNicoll et al., 2003	1	1	1	1	1	1	6
Pandharipande et al., 2006	1	1	1	1	1	1	6
Ouimet et al., 2007	1	1	1	1	1	1	6

Criteria of appraisal:1) the *study design*. The description of the aim, the design and the methods were evaluated. The size of the sample was large enough to answer the formulated research question, 2) the *selection of patients* was clearly formulated and sustained. A severe selection bias could not be detected. *3*) The *delirium assessment* was able to retrieve all delirious patients. A psychiatric interview or a validated assessment tool was used to diagnose the delirious state. 4) *Multivariate* analysis was used to minimize possible confounding factors. 5) The statistical analysis made the results plausible. 6) The results were *clinically relevant* to medical or surgical ICU patients

The reported incidence for intensive care delirium ranged from 11 to 83 %. The lowest number of included patients was 118, whereas the largest sample considered 3308 patients in the intensive care unit. The data were collected in medical, surgical, coronary or mixed intensive care units. The CAM-ICU and the Intensive Care Delirium Screening Checklist were both used in two publications as the delirium assessment tool. In one research, trained researchers carried out a daily psychiatric interview with a psychiatric consultation for patients with a change in the state of consciousness.

The review identified 25 risk factors in the six publications that proved to be significant in a multivariate analysis. The OR of the risk factors was presented with a 95 % confidence interval in Table 4.3. Four factors could be classified as predisposing risk factors, 21 were precipitating factors related to the actual disease of the patient. An overview of the published factors is synthesized in Figure 4.2.

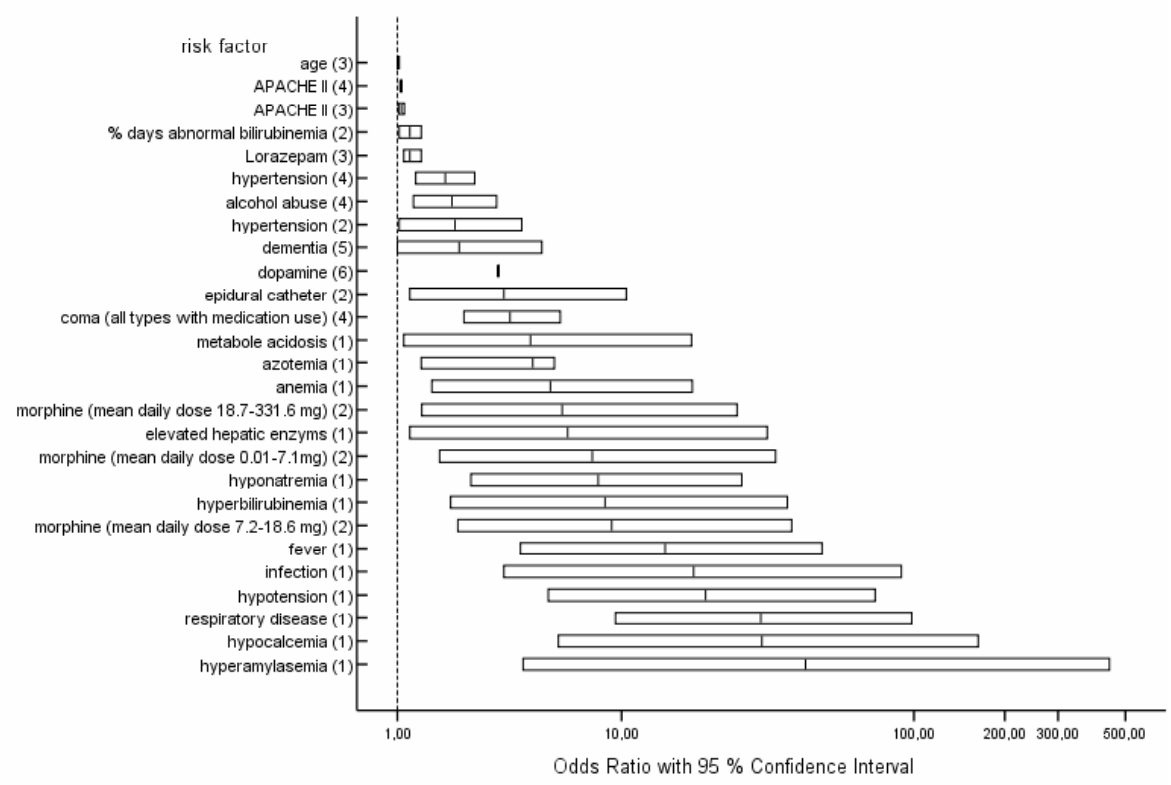
The predisposing risk factors reported were respiratory disease, age, alcohol abuse and dementia. A respiratory disease in the medical history scored the highest OR. Pre-existing dementia and alcohol abuse are risk factors to be considered, whereas the effect

Table 4.3: Multivariate risk factors (95 % CI). All multivariate risk factors were presented as Odds Ratios (OR) with 95 % confidence interval. Sommer et al. did not report a confidence interval for dopamine administration after multivariate analysis. McNicoll calculated a relative risk ratio (RR) for dementia, NA: not available

Risk factor OR (95 % confidence interval)	Aldemir et al., 2001 n=818	Dubois et al., 2001 n=198	Sommer et al., 2002 n=3308	McNicoll et al., 2003 n=118	Pandharipande et al., 2006 n=198	Ouimet et al., 2007 n=764
Age					1.02 (1.00-1.03)	
Alcohol abuse						2.03 (1.26-3.25)
Anemia	5.40 (1.60-17.80)					
APACHE II					1.06 (1.02-1.11)	1.05 (1.05-1.07)
Azotemia	4.60 (1.40-5.60)					
Coma (with the use of medication)						3.71 (2.32-5.90)
Dementia				2.2 (1.0-5.0) RR!		
Dopamine			3.31 (NA)			
Elevated hepatic enzymes	6.30 (1.20-32.20)					
Epidural catheter use		3.50 (1.20-10.39)				
Fever	14.30 (4.10-49.30)					
Hyperamylasemia	43.40 (4.20-442.70)					
Hyperbilirubinemia	8.70 (2.0-37.70)					
% Days with abnormal bilirubinemia		1.20 (1.03-1.40)				
Hypertension		2.60 (1.14-5.72)				1.88 (1.30-2.60)
Hypocalcaemia	30.90 (5.80-163.20)					
Hyponatremia	8.20 (2.50-26.40)					
Hypotension	19.80 (5.30 -74.30)					
Infections	18.00 (3.50-90.80)					
Lorazepam					1.20 (1.10-1.40)	
Metabolic acidosis	4.50 (1.10-17.70)					
Morphine daily dose 0.01-7.1 mg		7.80 (1.76-34.40)				
Morphine daily dose 7.2-18.6 mg		9.20 (2.17-39.00)				
Morphine daily dose 18.7-331.6 mg		6.00 (1.41-25.40)				
Respiratory disease	30.60 (9.50-98.40)					

of age on the onset of delirium in the intensive care unit has been mentioned, although with a limited influence.

Figure 4.2: Odds ratio for the multivariate risk factors with 95 % CI, The Odds ratio is presented on a logarithmic scale. The 95 % confidence interval is presented by bars. Dementia is presented as a relative risk score.
(1) Aldemir et al., 2001 (2) Dubois et al., 2001 (3) Pandharipande et al., 2006 (4) Ouimet et al., 2007 (5) McNicoll et al., 2003 (6) Sommer et al., 2002



Among the 21 precipitating factors, the APACHE II score and hypertension were identified as significant in two publications. The calculated OR's were comparable. Hyperbilirubinaemia and the percent of days with abnormal bilirubinaemia proved to be significant in one publication each.
Nine laboratory blood values were reported as a possible risk factor for intensive care delirium. Hyperamylasaemia, hypocalcaemia, hyperbilirubinaemia and hyponatraemia were reported as the strongest risk factors.

Seven factors concerning the type or the administration of medication in the intensive care unit were identified. Three different levels of administration of morphine influenced the onset of delirium. The highest OR was reached for the intermediate daily dose between 7.2 and 18.6 mg. Different types of coma were studied for their correlation with intensive care delirium. The iatrogenic coma induced by medication was the only significant contributor after multivariate analysis. The administration of lorazepam and dopamine also invoked a higher risk.

4.4 Discussion

Six original research papers, including five prospective cohort studies and one retrospective record analysis, were selected in the systematic review resulting in the identification of 25 risk factors. Two factors were mentioned twice. The different settings and the different study designs may have caused possible factors not always to be evaluated as a risk factor. A meta-analysis was not performed due to the different context of the possible risk factors were identified.

The incidence of delirium in the selected papers ranged from 11 to 87 % for populations ranging from 118 to 3308 intensive care patients. The included patients differed in age, medical condition and the type of the intensive care unit. Intensive care delirium, however, was a severe problem in all studied units.

The diagnosis of intensive care delirium can be questioned in two of the selected papers. Sommer et al. (2002) assumed the record of haloperidol in the patient's database as an 'indicator of delirium occurrence'. A pilot pharmacy study in their hospital stated that 69 % of the administered haloperidol was prescribed for the treatment of delirium after excluding patients with a psychiatric history. Underestimation can be expected since delirium has been reported to be largely undetected, thus untreated (Angus and Carlet , 2002; Inouye *et al.*, 2001; Maldonado and Dhami, 2003; Young and Inouye, 2007). In the research of Aldemir et al. (2001) the psychiatric consultation was only carried out when the state of consciousness of the patient had changed. The hyperactive delirium was the most prevalent type in this study (47 %). This contradicted reports of the clinical subtypes of intensive care delirium (Peterson *et al.*, 2006). The assessment by trained researchers might have missed hypoactive patients.

The authors used different covariates in the multivariate analysis. Some factors proved to be significant in research outside the intensive care unit (Benoit *et al.*, 2005; Gaudreau *et al.*, 2005; McCusker *et al.*, 2001; Minden *et al.*, 2005). Despite the evidence in other settings, retrieved factors cannot be automatically projected to the intensive care setting; the environment, the severity of disease and the treatment are different from the total hospital population.

Outside the intensive care unit age is considered as an established risk factor. In this review age was an important item in all papers as a selection criterion or a possible risk factor. Patients were included from 65 years in McNicoll et al. and most of the patients in Aldemir et al. aged under 60. Whereas this factor proved to be a covariate for Pandharipande et al. and Ouimet et al., it was not a significant contributor for two other researchers. After this systematic review it still can be questioned if age is a strong predictor for the onset of delirium in the intensive care unit.

The severity of disease, measured by the APACHE II score (Knaus *et al.*, 1985), is an important management tool in the intensive care unit. In this review, the APACHE II score was mentioned twice as a risk factor. The score however was not found significant in one research (Dubois *et al.*, 2001) and two researchers used the factor as a adjusting covariate in the multivariate analysis (Ouimet *et al.*, 2007; Pandharipande *et al.*, 2006). Severity of disease could be an important risk factor to be considered in future research.

The drug related factors in this review stressed on the risk of morphine, lorazepam or the medication used for inducing a coma. Psychoactive drugs seem to have an active role in the onset of delirium. The use of an epidural catheter could be an additional factor either due to the extra manipulations of the staff or the admitted medication.

The largest group of factors was the laboratory blood values. All except one were reported in one publication (Aldemir *et al.*, 2001). In this research hyperamylasaemia was found in only 2.2 % of the population. The other factors occurred in a range of 5.5-26.7 %. This could explain the high OR's with a very wide confidence. The presentation of the results or the analysis did not create the opportunity to verify the findings making them statistically doubtful. Dubois et al. included several laboratory blood values in the data collection. They were found not to relate to delirium. Very recently an additional retrospective chart review on different risk factors (Watts *et al.*, 2007) was published. Neither laboratory values nor medication were significant risk factors. Continuous venovenous haemodiafiltration was the only significant risk factor in this research. The question remains if abnormal laboratory values must be considered as independent risk factors or as part of the clinical picture of a more severe ill patient.

Until to now, the attention of researchers seems to be most focused on disease or treatment related markers. Research outside the intensive care unit focused on other predictive factors for the development of delirium (Blondell *et al.*, 2004; Elie *et al.*, 1998; Inouye *et al.*, 1993; Korevaar *et al.*, 2005; Voyer *et al.*, 2006; Yamagata *et al.*, 2005). In this systematic review particularly, environmental risk factors were not retrieved (Dyson, 1999; Granberg *et al.*, 1999; McCusker *et al.*, 2001). Noise, sleep deprivation, nursing and architectural characteristics of the intensive care unit were discussed, but the effects have not been studied recently in a prospective cohort study or a randomized clinical trial (McGuire *et al.*, 2000; Pandharipande and Ely, 2006; Tanios *et al.*, 2004).

4.5 Conclusions

Twenty five risk factors, 21 precipitating and 4 predisposing, were found to influence the onset of delirium in the intensive care unit. The impact of the different predisposing and precipitating risk factors need further investigation. Additional risk factors should be explored in the intensive care unit with special attention to the environment and nursing related factors. Hence, a tool for physicians and nurses could be developed to stratify patients in different risk categories and to develop preventive actions.

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5 A prospective cohort study on risk factors for delirium in intensive care patients

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Abstract

INTRODUCTION

Delirium is a common complication in the intensive care unit. The attention of researchers has shifted from the treatment to the prevention of the syndrome necessitating the study of associated risk factors.

METHODS

In a multicenter study at one university hospital, two community hospitals and one private hospital, all consecutive newly admitted adult patients were screened and included when reaching a Glasgow Coma Scale greater than 10. Nurse researchers assessed the patients for delirium using the NEECHAM Confusion Scale. Risk factors covered four domains: patient characteristics, chronic pathology, acute illness and environmental factors. Odds ratios were calculated using univariate binary logistic regression.

RESULTS

A total population of 523 patients was screened for delirium. The studied factors showed some variability according to the participating hospitals. The overall delirium incidence was 30 %. Age was not a significant risk factor. Intensive smoking (OR 2.04), daily use of more than three units of alcohol (OR3.23) and living single at home (OR 1.94), however, contributed to the development of delirium. In the domain of chronic pathology a pre-existing cognitive impairment was an important a risk factor (OR 2.41). In the domain of factors related to acute illness the use of drains, tubes and catheters, acute illness scores, the use of psychoactive medication, a preceding period of sedation, coma or mechanical ventilation showed significant risk with odds ratios ranging from 1.04 to 13.66. Environmental risk factors were isolation (OR 2.89), the absence of visit (OR 3.73), the absence of visible daylight (OR 2.39), a transfer from another ward (OR 1.98) and the use of physical restraints (OR 33.84).

CONCLUSIONS

This multicenter study indicated risk factors for delirium in the intensive care unit related to patient characteristics, chronic pathology, acute illness and the environment. Particularly among those related to the acute illness and the environment, several factors are suitable for preventive action.

5.1 Introduction

Delirium is a common complication in the intensive care unit. The acute syndrome, caused by a disturbance of the cognitive processes in the brain, is characterized by a reduced ability to focus, sustain or shift attention, disorganized thinking or a changed level in consciousness. The pathophysiology is based on different neurochemical processes induced by a physical cause. Multiple factors seem to stimulate abnormal processes in the human brain (Maldonado, 2008).
Despite the international efforts, no evidence based treatment or management of delirium in the intensive care unit has been established (Lacasse *et al.*, 2006). Proposed guidelines or a existing delirium protocol might not be available or not known by the intensive care staff (Van Eijk *et al.*, 2008). Nurses and physicians should assess patients for delirium. A standardized screening for delirium, however, is not common in most intensive care units.

The attention of researchers has shifted from the treatment to the prevention of the syndrome necessitating the study of associated risk factors. Delirium is never caused by a single factor, but is always the consequence of multiple factors. Inouye et al. (Inouye and Charpentier, 1996) conceived a risk model for patients outside the intensive care unit based on predisposing and precipitating factors. Predisposing factors are patient dependent or related to chronic pathology. These factors are limited or not modifiable. Precipitating factors are related to the acute illness or the environment. In the intensive care unit current illness and aggressive treatment generate different impacts.
More than 60 variables have been studied for their relation with delirium in the general hospital population. A patient encountering three or more of these factors has a 60 % increased risk for the development of delirium (Inouye and Charpentier, 1996; Inouye, 2006). Ely et al. (Ely *et al.*, 2001) stated that a patient in the intensive care unit accumulates ten or more of these factors. Since not all patients in the intensive care unit may develop delirium, it seems obvious that not all factors studied in general patients or elderly may be extrapolated to the intensive care patient. Therefore, each factor must be studied in the concept of the intensive care unit. Earlier research on risk factors for delirium in the intensive care unit, using different methods and populations, showed sometimes conflicting results (Aldemir *et al.*, 2001; Dubois *et al.*, 2001; Ouimet *et al.*, 2007; Pandharipande *et al.*, 2006; Pisani *et al.*, 2007). Additionally, environmental factors are poorly studied in the intensive care unit.

An intervention on relevant factors could influence the incidence of delirium in the intensive care unit. To prevent delirium, precipitating factors are more modifiable than predisposing factors. This research studied factors related to patient characteristics, chronic pathology, acute illness and the environment for their contribution to the development of delirium in the intensive care patient.

5.2 Materials and methods

5.2.1 Study design

A prospective cohort study included patients at different locations based on a single protocol. All consecutive patients in the intensive care units of four hospitals, two community hospitals, one private hospital and one university hospital were screened for delirium and associated risk factors by trained nurse researchers under supervision of the first author.

All consecutive patients with a minimum age of 18 years and a stay of at least 24 hours in the intensive care unit were included when reaching a Glasgow Coma Scale of at least 10. None of the patients was intubated at the time of the assessments. All patients were able to communicate with the nurse researchers. Patients or their relatives gave informed consent to the study. The ethical board of the hospitals approved the study.

The data were obtained in a first period of data collection from January to April 2007 in the university hospital and in a second period from January to April 2008 in separate studies in the community hospitals, the private hospital and the university hospital again. The separate studies used the same methodology and all nurse researchers used the same standardised list to screen possible factors. Not all factors, however, were scored identically at the different locations. Non identical data were deleted from the database. One hospital did not report on all factors. Therefore, the studied factors showed some variability according to the participating hospitals (Table 5.1). For the non delirious patients the highest score of the possible risk factors of the entire observation period was selected. For delirious patients the highest score before the onset of delirium was registered.
The databases were joined based on depersonalised coded data. Patients from the different units were included using the same criteria resulting in a mixed intensive care population.

Table 5.1: number of the factors scored with indication of the site where the factor was included	n	community hospital (n=210)	private hospital (n=123)	university hospital (n=190)
domain patient characteristics				
age in years (mean, SD)	523	X	X	X
age more than 65	523	X	X	X
gender masculine	523	X	X	X
living single at home	182	X		X
units of alcohol per day	230	X		X
daily use of alcohol	496	X	X	X
daily use of more than 3 units of alcohol	230	X		X
number of cigarettes per day	221	X		X
daily smoking	519	X	X	X
daily smoking of more than 10 cigarettes	217	X		X
domain chronic pathology				
predisposing cognitive impairment	384	X	X	X
predisposing cardiac disease	265	X		X
predisposing pulmonary disease	262	X		X
domain acute illness				
length of stay in the ICU before inclusion	523	X	X	X
length of stay in the ICU before inclusion > 1 day	523	X	X	X
length of stay in the ICU before inclusion > 2 days	523	X	X	X
admission for internal medicine	523	X	X	X
high risk of mortality (SAPS >40; APACHE > 24)	212	X		X
APACHE II	120	X		X
SAPS II	108	X		
highest TISS 28 score	179	X		X
mean TISS 28	179	X		X
TISS 28 cut off 30 (318 minutes)	279	X		X
psychoactive medication	424	X	X	X
benzodiazepine	283	X	*X(low response)*	X
morphine	287	X	*X(low response)*	X
sedation	228	X	*X(low response)*	X
endotracheal tube or tracheastomy	390	X		X
gastric tube	395	X		X
bladder catheter	400	X		X
arterial catheter	398	X		X
number of perfusions	400	X		X
more than 3 perfusions	398	X		X
number of vascular catheters	400	X		X
no normal food	395	X		X
fever	397	X		X
domain environmental factors				
admission via emergency room	377	X		X
admission via transfer	377	X		X
open room in intensive care	508	X	X	X
isolation	523	X	X	X
no visible daylight	523	X	X	X
no clock present or visible	523	X	X	X
number of visitors	256	X	X	X
no visit	269	X	X	X
physical restraints	292	X		X

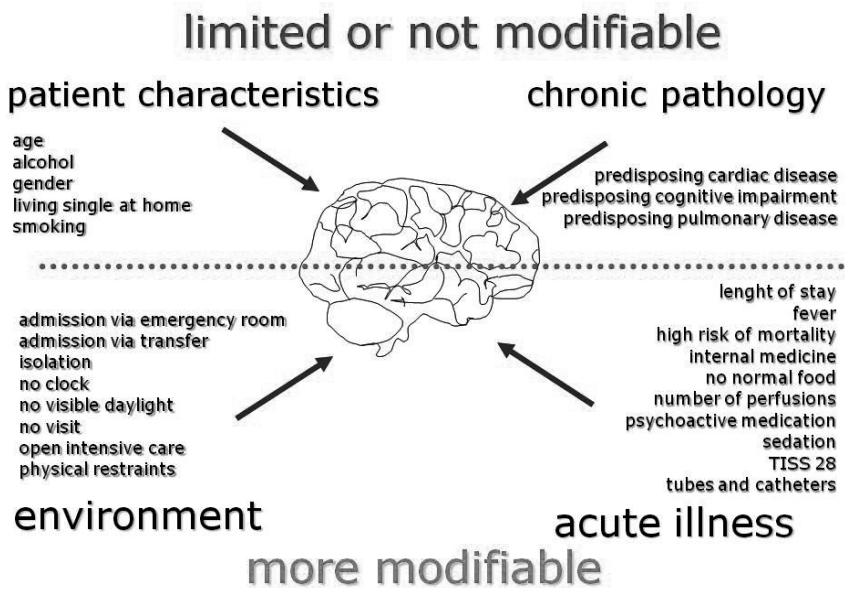
5.2.2 Delirium assessment

All patients were screened for delirium using the Neelon and Champagne Confusion Scale (Immers *et al.*, 2005; Milisen *et al.*, 2005; Neelon *et al.*, 1996). Earlier research indicated this scale as a valuable tool for screening delirium in the intensive care unit by trained nurses (Van Rompaey *et al.*, 2008). This tool uses standard nursing observations to rate the patient on a 0-30 scale. A score 0-19 indicates delirium, where scores between 20-24 indicate mild or beginning confusion, 25-26 a patient at risk for confusion and 27-30, a normal patient, respectively.

5.2.3 Assessment of the risk factors

Factors were grouped in four domains based on the predisposing and precipitating model of Inouye et al. (Inouye and Charpentier, 1996), the remarks of Ely (Ely, 2006) and the experience of intensive care staff: patient characteristics, chronic pathology, acute illness and environmental factors (Figure 5.1). The first two domains contain predisposing or achieved factors being less modifiable through preventive actions. The last two domains apply to the current situation and are probably more modifiable to reduce the incidence of intensive care delirium.

Figure 5.1: Four domains of risk factors for intensive care delirium



In the domain of the patient characteristics age, gender and daily smoking or alcohol usage habits were scored in almost all patients. Patients or their relative reported less on the number of cigarettes or units of alcohol daily used. These data were not reported by the private hospital. At two locations, the community hospital and one study in the university hospital, supplementary data on the social and matrimonial status, profession and education of the patient were obtained.

In the domain of the chronic illness the main focus was on a pre-existing cognitive impairment. This item was scored as positive when an established diagnosis of dementia was recorded in the medical record of the patient. All hospitals, except the private hospital, mentioned chronic cardiac or pulmonary diseases reported in the patient's record.

In the domain of the acute illness, factors were studied relating to the current diagnosis or treatment. All patients could be classified as either a surgical or an internal medicine patient. Since patients were included at the time they scored a Glasgow Coma Scale of ten or more, the length of stay in the intensive

care unit before inclusion was observed as an indicator for coma or induced coma. Fever, temperature over 38.5 °C, nutrition, the use of drains, tubes and catheters were observed at four locations. The number of infusions was transformed in a dichotomous factor 'more than three infusions' based on the relative risk for 'more than three medications added' (RR, 2.9; 95 % CI, 1.6 to 5.4) described by Inouye et al. (Inouye and Charpentier, 1996). The admittance of psychoactive medication before delirium, including the use of morphine and benzodiazepines, was scored in all studies. A risk of mortality score, the Simplified Acute Physiology Score (SAPS II) (Le Gall *et al.*, 1993) or the Acute Physiology And Chronic Health Evaluation (APACHE II) (Knaus *et al.*, 1985), was observed in the university hospital and one community hospital. The two scores were transformed in a binary scoring factor 'high risk for mortality' indicating an APACHE II of at least 24 or a SAPS II score of at least 40. The Therapeutic Intervention Scoring System-28 (TISS 28) was scored in patients at the same locations (Reis Miranda *et al.*, 1996). A cut off value of 30 was used indicating a nursing time workload of 318 minutes during each nursing shift.

Factors from the fourth domain relate to architectonical items or the interaction between the patient and the environment. Admission characteristics, the presence of visible daylight, the presence of a visible clock and the architectonical structure, e.g. an open space with several patients or a closed room, were scored at all locations. Three studies reported on the use of physical restraints and relatives visiting the patient.

5.2.4 Statistical approach and analysis

Continuous or categorical data were transformed to factors with a binary score. Cut-off values were based on literature or the variance of the data. For the non delirious patients the most severe score of the possible risk factors of the entire observation period was selected. For delirious patients the most severe score before the onset of delirium was taken for the analysis.

The tables present the data for delirious and non-delirious patients. For each factor, the number of patients in both groups is mentioned. Continuous data are presented using mean and standard deviation. Categorical data are presented in percentages indicating the prevalence of the factor in either the delirium or the non-delirium group. Differences between delirious and non-delirious patients were calculated using the independent t-sample test or the Pearson Chi^2 where appropriate.

Odds ratio's (OR) with a confidence interval of 95 % were calculated for all factors using univariate binary logistic regression. To facilitate reading, the text does not mention the confidence intervals. The tables of the different domains (Table 5.2-5.5), however, show the OR and the confidence interval. Only factors with a prevalence of 10 % in the delirious group and with a significant increased risk for delirium after univariate analysis were used in a multivariate forward conditional (0.05) regression analysis. Factors showing a wide confidence interval after univariate analysis were not used in the multivariate analysis. The Nagelkerke regression coefficient was used to explain the variation in delirium predicted by the factors in the different domains.
A level of significance of 0.05 was used for all analysis. All statistics were calculated using SPSS 16.0 ®.

5.3 Results

A total population of 523 patients was screened for delirium and associated risk factors (Table 5.2). The overall incidence of delirium was 30 %. Of 155 delirious patients, 75 % was delirious on the first day of inclusion, more than 90 % after the third day. The incidence in the community hospitals was higher than the incidence in the private hospital or the university hospital. The mean age was 64 years and most of the population was male. The surgical and internal patients are equally represented, but the participating hospitals showed some variety.

Table 5.2: baseline characteristics; p-value for difference between groups was calculated with the independent samples T-test for continuous data and Chi^2 for categorical data.

		total population	community hospital	private hospital	university hospital	p-value
n		523	210	123	190	
age in years	mean (range)	64 (19-90)	65 (19-90)	67 (26-87)	60 (20-90)	<0.001
gender	male	59%	61%	54%	62%	0.34
admission	surgery	49%	26%	73%	59%	<0.001
	internal medicine	51%	74%	27%	41%	
length of stay in days	mean (range)	8 (1-68)	11 (2-68)	7 (2-43)	8 (1-54)	0.01
length of stay before inclusion in days	mean (range)	3.6 (1-63)	3.9 (1-63)	3.5(1-34)	3.2 (1-47)	0.62
NEECHAM	delirium	29.6%	38%	29%	21%	<0.001
	early to mild confused	25.8%	23%	33%	24%	
	at risk	19.7%	10%	21%	30%	
	normal	24.9%	29%	17%	26%	
APACHE II	mean (range)	--------	15 (19-23)	--------	19 (7-47)	0.04
SAPS II	mean (range)	--------	31 (4-73)	--------	--------	
TISS 28	mean (range)	--------	34 (19-48)	--------	32 (17-49)	0.19
Capacity of the intensive care units			25 beds	24 beds	34 beds	

Patients tended to stay longer in the intensive care unit of the community hospital, but the length of stay in the intensive care unit before inclusion was the same for all hospitals. More than 60 % of the patients had an immediate inclusion in the study regarding to the protocol (24 hours after admission to the intensive care unit). After 48 hours of admission to the intensive care unit, almost 80 % of the population was included.

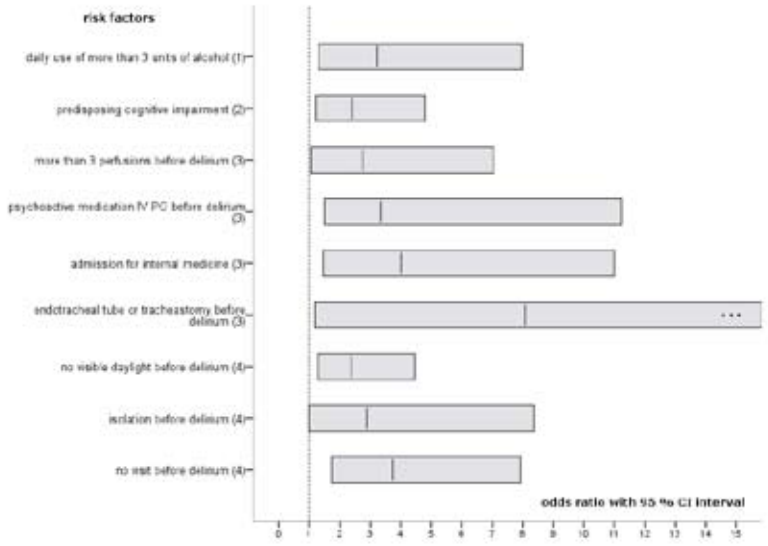
5.3.1 Factors related to patient characteristics

Neither age, age over 65 years nor gender showed a relation to the onset of delirium in this study. Patients living single at home had a higher risk to develop delirium (OR 1.94) (Table 5.3). The use of alcohol was a significant risk factor for delirium when a patient consumed more than three units each day. Moreover, this factor showed a higher risk after multivariate analysis (OR 3.23) (Figure 5.2). Each cigarette increased the risk for delirium, showing a significant OR for patients smoking ten cigarettes or more each day (OR 2.04).

Table 5.3: factors related to patient characteristics; D=delirium group; ND=non delirium group; continuous variables are presented in number, mean and standard deviation (SD); categorical variables are presented in number per group and percentage; *: p value of difference in groups, calculated with independent samples T-test for continuous variables, with Chi^2 for categorical variables.

	n		mean (SD) or %			univariate	multivariate
	D	ND	D	ND	p*	OR (CI)	OR (CI)
age in years (mean, SD)	155	368	65.0 (16.4)	63.7 (14.6)		1.01 (0.99-1.02)	
age more than 65	91/155	202/368	55%	59%		1.17 (0.80-1.71)	
gender masculine	90/155	220/368	58%	60%		0.93 (0.64-1.36)	
living single at home	45/114	38/68	56%	40%		1.94 (1.06-3.57)	
units of alcohol per day	58	172	3.2 (5.2)	2.1 (3.9)		1.05 (0.99-1.12)	
daily use of alcohol	44/142	94/354	31%	27%		1.24 (0.81-1.90)	
daily use of more than 3 units of alcohol	21/58	32/172	36%	19%		2.48 (1.29-4.80)	3.23 (1.30-7.98)
number of cigarettes per day	46	175	11.4 (13.6)	6.4 (9.6)		1.04 (1.01-1.07)	
daily smoking	33/153	98/366	22%	27%		0.75 (0.48-1.18)	
daily smoking of more than 10 cigarettes	22/46	54/174	48%	31%		2.04 (1.05-3.95)	

Figure 5.2: multivariate risk factors for intensive care delirium; odds ratio with 95 % confidence interval, the number behind the factor indicates the domain: (1) patients characteristics; (2) chronic pathology; (3) acute illness; (4) environment



5.3.2 Factors related to chronic pathology

In the domain chronic pathology only a predisposing cognitive impairment, indicating an established diagnosis of dementia, was a risk factor (Table 5.4).This factor remained significant after correction with the non-significant factors in the domain (OR 2.41) (Figure 5.2). Pre-existing cardiac or pulmonary diseases were no risk factors in the studied cohort.

Table 5.4: factors related to chronic pathology; D=delirium group; ND=non delirium group; categorical variables are presented in number per group and percentage; *: p value of difference in groups, calculated with independent samples T-test for continuous variables, with Chi^2 for categorical variables.

	n		%		p*	univariate	multivariate
	D	ND	D	ND		OR (CI)	OR (CI)
predisposing cognitive impairment	19/107	25/277	18%	9%	0.02	2.18 (1.14-4.14)	2.41 (1.21-4.79)
predisposing cardiac disease	36/72	112/193	50%	58%	0.15	0.72 (0.42-1.25)	
predisposing pulmonary disease	18/72	47/190	25%	25%	0.54	1.01 (0.54-1.90)	

5.3.3 Factors related to acute illness

The prevalence of abnormal blood values in the delirium group was too low to be considered in this study.

The length of stay in the intensive care unit before inclusion showed to be a relevant factor in the onset of delirium. Based on the length of stay before inclusion as a risk factor, the risk for delirium increased with 26 % each day (Table 5.5). Patients admitted for internal medicine had a higher risk to develop delirium than surgical patients, even after multivariate analysis (OR 4.01) (Figure 5.2). The high risk of mortality score indicated that patients scoring an APACHE II higher than 24 or a SAPS II higher than 40 were at risk for delirium (OR 2.50). The TISS 28 score showed significant odds ratio's in all calculations. The cut-off value of 30 showed to be a relevant marker in the onset of delirium (OR 2.81). Yet, none of those scores for the intensive care unit showed to be a risk factor after multivariate analysis (Table 5.5).

The use of different psychoactive medications was a multivariate significant risk factor (OR 3.34) (Figure 2). Detailed observations generated an increased risk for benzodiazepines generated (OR 2.89). Patients having an endotracheal or trachea cannula were at greater risk, even after multivariate analysis (OR 8.07). A gastric tube (OR 7.80) and a bladder catheter (OR 5.37) were significant factors after univariate analysis. The risk for the onset of delirium increased with the number of infusions (OR 1.35). Moreover, more than three infusions

Table 5.5: factors related to acute illness; D=delirium group; ND=non delirium group; continuous variables are presented in number, mean and standard deviation (SD); categorical variables are presented in number per group and percentage; *: p value of difference in groups, calculated with independent samples T-test for continuous variables, with Chi^2 for categorical variables.

	n		mean (SD) or %			univariate	multivariate
	D	ND	D	ND	p*	OR (CI)	OR (CI)
length of stay in the ICU before inclusion*	155	368	7,9 (11,5)	1.7 (2.3)	<0.001	1.26 (1.17-1.35)	
length of stay in the ICU before inclusion > 1 day*	87/155	116/368	56%	32%	<0.001	2.78 (1.89-4.09)	
length of stay in the ICU before inclusion > 2 days*	70/155	46/368	45%	13%	<0.001	5.77 (3.71-8.97)	
admission for internal medicine	91/155	175/368	48%	59%	0.013	1.57 (1.07-2.29)	4.01 (1.46-11.01)
high risk of mortality (SAPS >40; APACHE > 24)	29/73	29/139	40%	21%	0.003	2.50 (1.31-4.66)	
APACHE II	33	87	19.7 (7.3)	18.6 (7.5)	0.47	1.02 (0.97-1.08)	
SAPS II	54	54	33.4 (12.6)	28.6 (10.7)	0.04	1.04 (1.01-1.08)	
highest TISS 28 score	88	191	34.9 (5.7)	31.9 (6.6)	<0.001	1.08 (1.04-1.13)	
mean TISS 28	88	191	30.8 (3.9)	29.1 (5.6)	0.004	1.07 (1.02-1.13)	
TISS 28 cut off 30 (318 minutes)	68/88	104/191	77%	55%	<0.001	2.81 (1.60-5.05)	
psychoactive medication	103/135	146/289	76%	51%	<0.001	3.15 (1.99-4.99)	3.34 (1.50-11.23)
benzodiazepine	18/68	24/215	27%	11%	0.003	2.89 (1.44-5.69)	
morphine	24/70	54/217	34%	25%	0.09	1.58 (0.88-2.82)	
sedation	65/88	24/140	74%	17%	<0.001	13.66 (7.15-26.10)	
endotracheal tube or tracheastomy	27/118	11/272	23%	4%	<0.001	7,04 (3.36-14.76)	8.07 (1.18-55.06)
gastric tube	44/120	19/275	37%	7%	<0.001	7.80 (4.30-14.16)	
bladder catheter	115/120	227/280	96%	81%	<0.001	5.37 (2.09-13.80)	
arterial catheter	108/120	231/278	90%	83%	0.05	1.83 (0.93-3.59)	
number of perfusions	120	280	4.2 (2.0)	3.1 (1.7)	<0.001	1.35 (1.20-1.52)	
more than 3 perfusions	65/120	81/278	54%	29%	<0.001	2.87 (1.85-4.47)	2.74 (1.07-7.05)
number of vascular catheters	120	280	1.2 (0.5)	1.3 (0.6)	0.18	0.74 (0.47-1.17)	
no normal food	92/120	127/275	77%	46%	<0.001	3.83 (2.36-6.22)	
fever	10/119	16/278	8%	6%	0.222	1.50 (0.66-3.42)	

*: the only reason for later inclusion of patients was a score on the Glasgow Coma Scale below 10

(OR 2.74) showed a higher risk after multivariate analysis (Figure 5.2). Patients who were not able to have a regular meal, showed a higher risk (OR 3.83) for the development of delirium. Fever before delirium and an arterial catheter could not be identified as risk factor in this research.

5.3.4 Factors related to the environment

The isolation of a patient (OR 2.39), not having visible daylight and not having a visit from relatives (OR 3.73) showed a higher risk after multivariate analysis (Figure 2) (Table 5.6). Admittance through the emergency room showed no higher risk for the development of delirium. A transfer from another ward, however, was a significant risk factor (OR 1.98).

The use of physical restraints before the onset of delirium showed a very high risk (OR 33.84). The confidence interval (11.19-102.36), however, is very wide leaving this factor not appropriate for multivariate analysis.

The absence of a visible clock was no risk factor. Although more delirious patients were admitted in a bed in an open shared room, this factor showed no higher risk (Table 5.6).

Table 5.6: environmental factors; D=delirium group; ND=non delirium group; continuous variables are presented in number, mean and standard deviation (SD); categorical variables are presented in number per group and percentage; *: p value of difference in groups, calculated with independent samples T-test for continuous variables, with Chi^2 for categorical variables.

	n		mean (SD) or %			univariate	multivariate
	D	ND	D	ND	p*	OR (CI)	OR (CI)
admission via emergency room	60/118	119/259	51%	46%	0.22	1.22 (0.79-1.88)	
admission via transfer	36/118	47/259	31%	18%	0.006	1.98 (1.20-3.28)	
open room in intensive care	52/149	98/359	35%	27%	0.055	1.43 (0.95-2.15)	
isolation	*16/155*	*11/368*	10%	3%	0.001	3.74 (1.69-8.25)	2.89 (1.00-8.36)
no visible daylight	70/155	118/368	45%	32%	0.003	1.75 (1.19-2.56)	2.39 (1.28-4.45)
no clock present or visible	19/155	36/368	12%	10%	0.243	1.29 (0.71-2.33)	
number of visitors	88	168	2.4 (1.9)	2.5 (2.0)	0.70	0.97 (0.85-1.11)	
no visit	27/96	21/173	28%	12%	0.001	2.83 (1.50-5.36)	3.73 (1.75-7.93)
physical restraints	25/66	*4/226*	38%	2%	<0.001	33.84 (11.19-102.36)	

5.3.5 Multivariate model in the four domains

The significant factors in the different domains were studied using the Nagelkerke R . The significant risk factors in the domain of the patient characteristics were responsible for 20 % of delirium. The predisposing cognitive impairment, the only risk factor in the domain of the chronic diseases, was responsible for 2 % of delirium. The risk factors in the domain of the acute illness were responsible for 48 % of delirium and the fourth domain with factors related to the environment for 53 %.

5.4 Discussion

The overall incidence of delirium in this research was 30 %. Risk factors for delirium were divided in four domains: patient characteristics, chronic pathology, acute illness and environmental factors. Particularly in the latter domains an important number of significant risk factors were identified.

5.4.1 Factors related to patient characteristics

As in our research, most studies on risk factors for delirium in the intensive care unit did not mention age as a significant factor (Aldemir *et al.*, 2001; Ouimet *et al.*, 2007). Research outside the intensive care unit often pointed at the relevant effect of age on the onset of delirium (Inouye, 2006; Maldonado, 2008). In this specialized unit, the cascade of other risk factors possibly overrules the obvious effect of age. Also, gender had no effect on the development of delirium.

The best-known type of delirium is delirium tremens. The withdrawal of alcohol causes a delirious state. The daily use of three units of alcohol is an important multivariate factor in our study. Alcohol abuse, in the study of Ouimet et al. (Ouimet *et al.*, 2007), defined as the daily use of more than two units, also showed to be a multivariate risk factor. Therefore, in order to prevent delirium, patients or their relatives must be interviewed as soon as possible to detect daily use of alcohol.

In our research, the risk to develop delirium was elevated after smoking 10 cigarettes each day. Ouimet et al. (Ouimet *et al.*, 2007) also indicated an effect of active tobacco consumption and Dubois et al. (Dubois *et al.*, 2001) calculated a comparable odds ratio after consumption of 20 or more cigarettes each day. The sudden stop in the consumption of nicotine may have caused a withdrawal delirium. Public health data of the World Health Organization revealed that smoking is common in 24 % of the adults in the United States and 37 % in Europe and 27 % in the Belgian population (World Health Organization, 2005). It might be justifiable to study the effect of nicotine surrogates to prevent delirium in patients with a high consumption of cigarettes. Additionally, patients smoking more than ten cigarettes are more vulnerable to chronic pulmonary diseases. Lower oxygen saturation in the brain might influence the onset of delirium in these patients.

In our study, patients living single at home showed a higher risk to develop delirium. This factor possibly interfered with 'no visit before delirium', a significant environmental risk factor. The group of patients 'not living single at home' did not receive visit for 8 %; patients 'living single at home' for 28 %. Further research has to identify the individual effect of this factor.

In our research, neither education, nor profession was a risk factor for the onset of delirium.

5.4.2 Factors related to chronic pathology

This study had a limited approach to factors related to chronic pathology. Research outside the intensive care unit showed possible relations with diabetes, AIDS or other chronic pathology (Cole, 2005; Inouye, 2006).

A previously diagnosed dementia showed to be an important risk factor. Research in the intensive care unit on elderly by McNicoll et al. (McNicoll *et al.*, 2003) found a relative risk of 2.2 (1.0-5.0) and by Pisani et al. (Pisani *et al.*, 2007) an odds ratio of 6.3 (2.9-13.8). Our research, focusing on adult patients, found a similar effect. Patients with an established diagnosis of dementia were at risk for delirium. It can be advised to screen newly admitted intensive care patients with a dementia screening instrument to detect vulnerable patients.

5.4.3 Factors related to acute illness

The factors most studied for a possible relation with the onset of delirium in the intensive care unit are related to either abnormal serum values or the use of psychoactive medication (Aldemir *et al.*, 2001; Dubois *et al.*, 2001; Marcantonio *et al.*, 2006; Ouimet *et al.*, 2007; Pandharipande *et al.*, 2006). The prevalence of the studied abnormal blood values was too small to include in our study.

Psychoactive medication may disturb the neurotransmission in the brain provoking a delirious state. The total group of this medication, either benzodiazepines or morphine showed to be a risk factor in this study. As in other research, a more detailed view pointed at the delirious effect of benzodiazepines (Dubois *et al.*, 2001; Ouimet *et al.*, 2007; Pandharipande *et al.*, 2006; Pisani *et al.*, 2007). After the administration of morphine to the patient, the risk for delirium is higher, although not significant. Literature pointed at a higher risk, but only Dubois et al. (Dubois *et al.*, 2001) found significant results concerning the use of morphine. The effect of psychoactive medication on the onset of delirium appeals for prudence in the prescription and the administration.

Most of the patients were included after a stay of 24 hours in the intensive care unit. Later inclusion in the study was caused by a Glasgow Coma Scale below 10. A longer period where patients did not reach this criterion for inclusion resulted in a higher risk for delirium. Ouimet et al. (Ouimet *et al.*, 2007) also showed that patients were at higher risk after sedation or coma. Other research pointed to the possible relation between the length of stay in the intensive care unit and the development of delirium (Aldemir *et al.*, 2001; Granberg Axell *et al.*, 2002). The length of stay, however, has been discussed as a time-dependent risk factor or outcome after delirium (Girard *et al.*, 2007; Ouimet *et al.*, 2007; Skrobik *et al.*, 2007). Since, most of the patients in this study developed delirium within three days after inclusion, the use of a Cox proportional hazard model, as suggested by Girard et al., did not seem necessary in this research. When studying the length of stay as a risk factor, the clinical relevance of a time-correcting analysis can be questioned. A study on the short term outcome of delirium can use this method to address the time-dependent bias.

A high risk of mortality at admission indicates a patient with more severe pathology. Although an elevated APACHE II score showed no significant higher risk in our research, as in Dubois et al. (Dubois *et al.*, 2001), the combined factor 'higher risk of mortality' showed a significant univariate risk for delirium. In the studies of Pandharipande et al. (Pandharipande *et al.*, 2006) and Ouimet et al. (Ouimet *et al.*, 2007), this higher risk was significant after multivariate analysis. Similarly, the TISS 28 score, indicating the nursing time needed for each individual patient on a certain day, was related to the onset of delirium. A patient requiring about five hours of nursing care in each shift was at high risk for delirium. Although the interpretation of mortality or severity of illness scores has been discussed for individual patients, higher values indicate a greater illness burden. Patients with these higher scores are at higher

risk for delirium. Future research could study cut off values of risk scores and nursing workload scores as for patients at risk for delirium.

The number of infusions is a significant risk factor in multivariate analysis. Most likely it is not the infusion itself being linked to the delirious process, but the number of medications administered. This is comparable to the results of Inouye et al. (Inouye, 2006) in older patients outside the intensive care unit. Also, a treatment with more drugs indicates a more severely ill patient.
Furthermore, many patients in the intensive care unit will not receive normal food, have an endotracheal tube, a gastric tube, a bladder or other catheters when necessary for a more invasive treatment. A more ill patient generates more factors. Consequently, the cascade of different significant factors in the third domain is related to the degree of illness and consequent treatment. The mentioned factors, however, are often not modifiable due to current pathology and current treatment. Nevertheless, intensive care staff should pay special attention to the removal of tubes and catheters when no longer needed. Prudence with medication is advised and the intensive care staff must have extra attention for more ill patients.

5.4.4 Factors related to the environment

As in our study, earlier research did not describe the architectonical structure of the intensive care unit as a possible risk factor. Patients did show a higher incidence of delirium after a stay in an isolation room. The absence of visible daylight, however, is very important. The presence of daylight in the patient's room should be stimulated where possible. This complies with research stating that the disturbance of the circadian rhythm might cause delirium (Jacobson *et al.*, 2008; Taguchi *et al.*, 2007).
The use of physical restraints was studied before the onset of delirium. Patients were not observed as agitated when restrained before the onset of delirium. The preventive use of soft wrist restraints to protect the position of catheters, tubes and drains seems to evoke delirium. Likewise, research pointed at a possible relation between restraints and self-extubation (Tung *et al.*, 2001; Curry *et al.*, 2008). The low prevalence of the factor in non delirious patients impeded interpretation. The high incidence of delirium in patients after physical restraints, however, showed a strong relation. This indicates that the unnecessary use of physical restraints in the intensive care unit must be banned. Inouye et al. also showed a higher relative risk for delirium for restrained patients outside the intensive care unit (Inouye and Charpentier, 1996). Further research is needed to study the effect of physical restraints in the onset of delirium.
Admission via the emergency room was not a significant risk factor, whereas the transfer from another ward to the intensive care unit was. The transport of a critical patient is an urgent decision most of the time. This abrupt change of environment seems to influence the onset of delirium.
Patients without visit were at greater risk for developing delirium. Recent literature pointed at the possible beneficial effects of visit in the intensive care unit (Gonzalez *et al.*, 2004). The prevention of delirium could be an argument in the discussion towards a more open visitor policy.
Visible daylight, where available, and a policy to allow more visits to the patient are factors easy to influence to study the possible beneficial effect on the onset of delirium.

5.4.5 Domains of factors

The individual effect of a single factor in the onset of delirium is hard to study. Multivariate analysis excluded many related factors. The cumulative presence of factors always causes a combined effect. Moreover, one factor may cause others. Therefore, the design of a mathematical predictive model based on single factors might not be the best solution. Patients are vulnerable due to patient characteristics or chronic pathology. Multivariate analysis showed the importance of patient characteristics. Additional factors should be studied in the domain of the chronic pathology. The noxious insults, however, are related to the acute illness or situated in the environment. The Nagelkerke regression coefficient showed a high prediction of delirium based on the factors in the last domains. Interventions on these noxious insults seems be the best action to prevent delirium.

The use of factor analysis for the assignment of risk factors to different domains could improve the insight in an overall delirium model. Such a model could be useful to consider delirium as the sixth vital sign (Flaherty *et al.*, 2007).

5.4.6 Study limits

The patients included in this study are only a segment of the intensive care population. The inclusion criteria and the selected assessment tool resulted in a subgroup of less sick or recovering intensive care patients. Nevertheless, this research showed that risk factors are also predominant in this specific population.

Not all factors were registered in all participating hospitals reducing the sample size in the joined database, particularly in multivariate analysis. The differences in case mix and the incidence in delirium provided a heterogeneous sample of intensive care patients from the different hospitals. Further research using a more robust method will focus on the differences in the onset of delirium within each hospital.

Factors were assigned to their domain based on experience of different physicians and nurses. Statistical techniques might split factors otherwise. Our model tried to be logical and comprehensive based on known precipitating and predisposing factors.

This study only included an Antwerp population. The results should be confirmed in an international research.

5.5 Conclusion

This multicenter study indicated risk factors for delirium in the intensive care unit related to patient characteristics, chronic pathology, acute illness and the environment. Multivariate risk factors were the use of more than three units of alcohol each day, a predisposing cognitive impairment, more than three infusions, an admission for internal medicine, an endotracheal tube or tracheastomy, no visible daylight, isolation and no visit. Particularly among those related to the acute illness and the environment, several factors are suitable for preventive action.

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6 Sound levels and delirium in the intensive care unit

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Abstract

INTRODUCTION

Sound in the intensive care unit has been a subject of research for years. Although the impact on sleep has been studied, contradicting results require the study of the direct impact of sound on the patient's outcome. This study assessed different sound levels and the sound level changes in the intensive care unit and related them to the onset of delirium.

METHODS

Three different approaches in a university and a private hospital assessed sound by counting alarms or using sound level meters. Delirium was assessed using the NEECHAM Confusion Scale.

RESULTS

All registered sound levels were over 40 decibels. The maximum noise level was 66 decibels in the private hospital and 68 decibels in the university hospital. The 27 % audible sound changes during the night in the university hospital were related to the onset of delirium ($p=0.05$). A higher amount of alarms in the private hospital was also related to delirium ($p=0.008$).

CONCLUSIONS

During the night, the same sound levels were registered, but a lower amount of sound changes was observed than during the day. This research pointed to a possible relation between the amount of alarms and sound changes during the night and the onset of delirium.

6.1 Introduction

The intensive care unit (ICU) is a rapidly changing ward designed to admit severely ill patients. The typical character and the health care process in this unit induce heavier care sustained by high technological equipment. This equipment and the higher intensity of care produce augmented sound levels (MacKenzie and Galbrun, 2007).

Sound is a vibration within the perception of hearing (Gelfand, 1997). The physical phenomenon is characterised by frequency, amplitude and intensity. Sound can be assessed using a sound level meter. The assessed frequencies are weighted in a logarithmic calculation. The result of this calculation can be weighted in different formats. The A–weighting refers close to the human hearing. The result is an amount of A-weighted decibels (dB(A)). An elevation of three decibels is just perceptible for most people. An elevation of five decibels is clearly audible. An elevation of ten decibels indicates a doubled sound volume. Noise refers to unwanted sound, possibly in combination with a high sound volume. Noise is always influenced by an individual perception.

The World Health Organisation recommends maximum 30 dB(A) for continuous background noise in a sleeping room. Individual events should not exceed 45 dB(A). Guidelines suggest 40 dB(A) as the maximum limit for night-time sound levels in hospitals and stated that 60 dB(A) should never be exceeded in any case, particularly in ICU's (WHO European Centre for Environment and Health, 2005).

Sound in the ICU has been a subject of research for years. Most studies report on a possible relation with sleep or on architectural improvements. Sleep disturbance in the ICU is often related to the environmental noise. Sound, however, is not always the most important factor in sleep disturbance in the ICU. Pain, discomfort and medication seem to have a higher impact on sleep (Freedman *et al.*, 1999; Freedman *et al.*, 2001; Frisk and Nordstrom, 2003; Otenio *et al.*, 2007). A recent review pointed at contradictory results of the impact of noise on sleep in the ICU (Xie *et al.*, 2009).
Peak noise is not the main determinant in sleep disruption in the ICU (Stanchina *et al.*, 2005). Sound changes from the baseline might have a higher impact on the patient. Further research with objective instruments is needed to clarify a possible relation between noise and sleep in the ICU. Therefore, research on the direct effect of environmental sound on the intensive care patient is necessary. Additionally, assessments on the perception of sound by patients are needed. Earlier research already showed a difference between the energy produced by sound levels and the perception of noise (Robinson, 1971). Patients indicated people talking and telephones ringing as the most disturbing sounds in the ICU. Alarms generating high peak sounds were mostly not referred to as disturbing (Gabor *et al.*, 2003; Kahn *et al.*, 1998; MacKenzie and Galbrun, 2007).

Delirium is a common complication in the ICU caused by a malfunction of the cognitive processes in the brain. The syndrome is characterized by a fluctuating course, shifting attention, disorganized thinking and a changed level of consciousness. Risk factors related to patient characteristics, chronic pathology, acute illness and the environment have been studied (Van Rompaey *et al.*, 2009; Van Rompaey *et al.*, 2008b). Although the impact on the onset of delirium was often suggested, sound has not been studied as a risk factor for delirium yet.

The first goal of this research was to study the sound levels and the sound level changes in the included ICU's. Secondly, the environmental sound was studied as a possible risk factor for the onset of delirium in the ICU.

6.2 Methods

6.2.1 Study design

The first part of this study was based on cross-sectional sound assessments near occupied beds in two ICU's. In a second prospective part patients were consecutively included in the same ICU's. Both parts were executed in the ICU of a university hospital and a private hospital with a capacity of 34 beds and 24 beds, respectively.
All beds in the ICU in the private hospital were situated in individual closed rooms. The ICU of the university hospital has, besides the closed rooms, bed spaces open to the central passageway and the desk where nurses and physicians are located.

6.2.2 Sound assessment

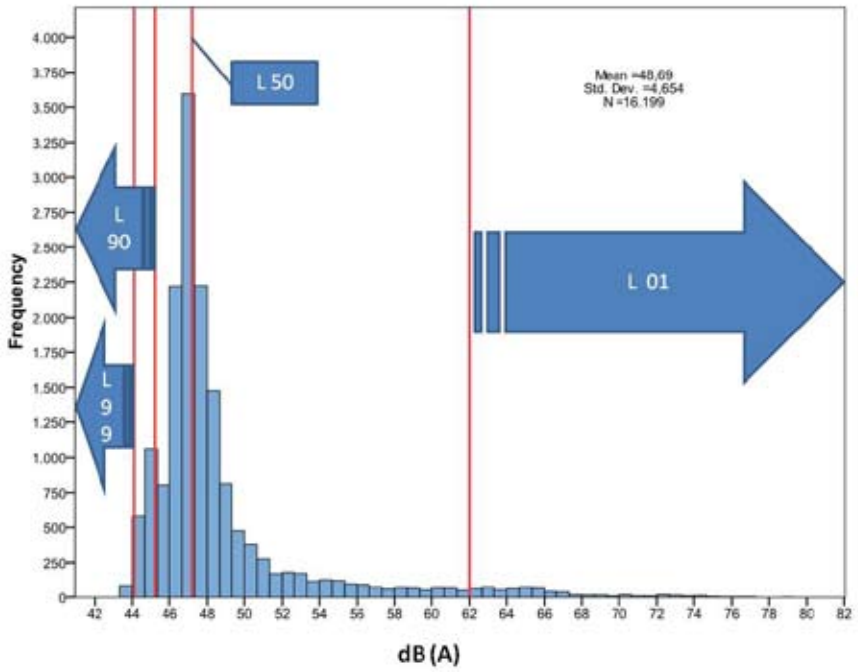
In a first approach in the university hospital (university A), the sound level was recorded every hour during one minute from 10:00 PM till 07:00 AM from February 2007 until April 2007. In this approach a sound level meter (Center 320IEC651 Type II) with maximum-hold function was used to observe the maximum sound volume in dB(A) for each observed minute. The researcher, holding the sound level meter, was positioned within one meter of the occupied bed.

A second approach in the private hospital (private A) retrieved data from the patient and technical alarms in the ICU from December 2007 until March 2008. Alarms from technical equipments in the patient's room were registered on a checklist by the nurses. Monitoring alarms were manually counted from generated listings of the automatically stored alarm data. Both types of alarm within the same minute, remaining for at least three seconds, were counted for one alarm-minute. The alarm-minutes were summed for each day.

In a third approach, in the university hospital (university B) from February 2008 until April 2008 and the private hospital (private B), from September 2008 until October 2008, the sound level was recorded every two seconds during 24 hour using five calibrated sound level meters with a data logger function (Center 322 datalogger sound level meter). The sound level meter was positioned at one meter of the patient's head. The observations were divided in nighttime, from 10:00:00 PM till 06:59:59 AM, and daytime, from 7:00:00 AM till 09:59:59 PM, resulting in 16,199 sound assessments for each patient during the night and 26,999 during the day. Adult patients were included on a first come first include basis, having a Glasgow Coma Scale of at least 10 and a length of stay in the ICU of minimum 24 hours.
Standard sound assessment is based on a dual approach, either representing equivalent sound levels based on cumulated energy in a limited period, or in the assessment of fluctuation in the environmental sound (Kahn *et al.*, 1998; Krueger *et al.*, 2007). Based on the recorded decibel assessments, equivalent continuous sound levels (Lxx) were calculated for daytime and nighttime based an algorithm dividing

the integrated sound pressure by the total presence of the sound level. The minimum sound level L99 is based on the 1 % lowest observations showing the equivalent silence level. The sound level L90, based on the 10 % lowest observations shows the equivalent ambient sound level. The median sound level L50 was calculated from all observations. The maximum sound level L01 was calculated from the 1 % highest observations showing the equivalent maximum sound level a patient encountered during the day or the night (Figure 6.1). The equivalent sound levels were expressed in dB(A).
The percentage clearly perceptible changes (+ 5 dB(A)) and the percentage changes being twice as loud (+10 dB(A)) from the ambient sound level were calculated to study the fluctuation of sound in the environment.

Figure 6.1: Histogram of sound recording presenting the sound levels; arrows showing the area for calculation of the sound levels (Leq L99 showing the minimum noise level, L90 the ambient sound level, L50 the median sound level and L1 the maximum sound level)



6.2.3 Sound during the night and delirium

All consecutively included patients were screened for delirium and associated risk factors by trained nurse researchers under supervision of the first author (Van Rompaey *et al.*, 2009). All patients with a minimum age of 18 years and a stay of at least 24 hours in the ICU were included when reaching a Glasgow Coma Scale of at least 10. All patients were able to communicate with the nurse researchers.

Delirium was assessed using the Neelon and Champagne Confusion Scale (NEECHAM). Earlier research indicated this scale as a valuable tool for screening delirium in the ICU (Immers *et al.*, 2005; Van Rompaey *et al.*, 2008a). This tool uses standard nursing observations to rate the patient on a 0-30 scale. A score 0-19 indicates delirium, where scores between 20-24 indicate mild or beginning confusion, 25-26 a patient at risk for confusion and 27-30, a normal patient, respectively.

In the private A study, the lowest NEECHAM score of a patient during his stay in the ICU was related to the number of alarm-minutes from the preceding night.
To study the relation between sound and delirium the lowest score on the NEECHAM scale and the worst dichotomous score, delirious or not delirious, of each patient were related to the sound

assessments from the night before. The equivalent sound levels L50 and L01 were related to delirium for the university A and university B studies. The L99 and the L90 level were not calculated for the university A since only maximum sound levels were registered. The percentage in perceptible sound level changes and the percentage in doubled sound level changes resulting from the university B study were compared for delirious and non delirious patients.

6.2.4 Statistical analysis

The number of alarm-minutes in the private A study was related to the NEECHAM scores using the Pearson correlation. An odds ratio was calculated using logistic regression with the dichotomous delirium score. Combined data from the university A and the university B studies were analysed using parametric statistics (Independent Samples T-test, Pearson correlation). When data from the university B were considered, non parametric statistics were used due to the small sample size (Mann Whitney U-test, Spearman correlation). Mean sound levels and sound level changes were compared using the dichotomous delirious or non delirious score. The continuous NEECHAM scores were used to search the possible relations with the sound assessments. Binary logistic regression was used to calculate the odds ratio with 95 % confidence interval of a possible risk factor where appropriate (Bland and Altman, 2000). SPSS 16.0 was used for all analysis with a 0.05 level of significancy.

6.2.5 Ethical considerations

The ethical board of both hospitals approved the study designs. Patients or their relatives gave informed consent to the study in both ICU's.

6.3 Results

A total of 278 sound assessments were executed in the university and the private hospital, 97 during the day and 181 during the night. A total of 209 patients admitted to the ICU's was included in the study, 29 % developed delirium (Table 6.1). The mean age of patients in the university hospital and the private hospital was 59 years (24-79) and 67 years (26-87), respectively. More male patients were admitted in the university hospital (66 %) as in the private hospital (54 %). Also, more internal medicine patients were admitted in the university hospital (42 %) compared to the private hospital (27 %).

Table 6.1: Number of sound assessments and included patients in each approach

approach	Sound assessments			included patients		method
	day	night	total	n	delirium	
private A	------	--------	-----	123	28%	counting alarms
private B	49	48	97	------	-------	data logger function
university A	0	85	85	60	30%	maximum hold function
university B	48	48	96	26	31%	data logger function
Total	97	181	278	209	29%	

6.3.1 Sound levels in the intensive care unit

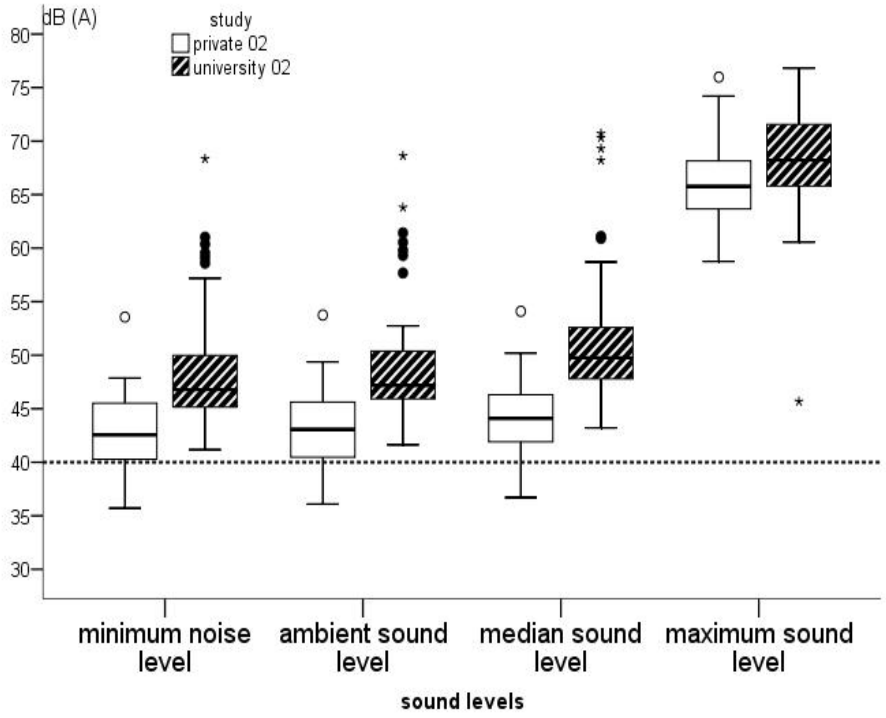
The minimum noise level in both studied ICU's was over 40 dB(A) and did not show a clearly perceptible difference of 5 dB(A) with the ambient sound level (Table 6.2). The median sound levels during the night was 44 dB(A) in the private hospital and 52 dB(A) in the university hospital. The peak sound during the night, illustrated by the maximum sound level, was 66 dB(A) in the private hospital and 70 dB(A) in the university hospital. All equivalent noise levels for day and night showed to be significantly higher in the university hospital as in the private hospital (Figure 6.2). In none of the ICU's a significant difference between the mean sound levels of day and night was found.

Table 6.2: Mean sound levels and mean sound level changes for each approach; p-value (indicating the difference between day and night for the specific sound level or percentage in changes in the studied hospital) was calculated using the independent samples T-test or One-Way ANOVA.

		private B		*university A*		university B	
Sound assessments			p				p
DAY minimum noise level L 99	dB(A) (range)	42.5 (35.5-53.7)	0.82	---		49.4 (41.6-72.2)	0.58
NIGHT minimum noise level L 99	dB(A) (range)	42.6 (35.7-53.6)		---		48.7 (41.2-68.3)	
DAY ambient sound level L 90	dB(A) (range)	43.2 (36.6-54.1)	0.79	---		50.3 (42.5-72.3)	0.66
NIGHT ambient sound level L 90	dB(A) (range)	43.2 (36.1-53.8)		---		49.2 (41.6-68.6)	
DAY median sound level L 50	dB(A) (range)	45.1 (39.5-54.5)	0.74	---		54.4 (47.0-72.3)	0.42
NIGHT median sound level L 50	dB(A) (range)	44.3 (36.7-54.1)		---		51.7 (43.2-70.7)	
DAY maximum sound level L 01	dB(A) (range)	67.7 (54.0-76.5)	0.23	---		69.9 (61.9-72.4)	0.83
NIGHT maximum sound level L 01	dB(A) (range)	65.7 (58.8-76.0)		61.4 (44.9-87.9)	---	68.4 (45.7-76.8)	
DAY % higher than L90 (+ 5 dB(A), audible change)	% (range)	21.5 (2.7-61.8)	0.04	---		36.5 (0.0-92.3)	0.02
NIGHT % higher than L90 (+ 5 dB(A), audible change)	% (range)	10.7 (2.2-61.4)		---		26.8 (0.2-83.2)	
DAY % higher than L90 (+ 10 dB(A), double sound)	% (range)	9.12 (0.8-28.5)	0.03	---		16.4 (0.0-65.8)	0.08
NIGHT % higher than L90 (+ 10 dB(A), double sound)	% (range)	4.8 (0.2-22.8)		---		10.7 (0.0-75.7)	

The + 5 dB(A) change in environmental sound indicated a clearly audible change. Significantly more sound changes were registered during the day as during the night in both ICU's (Table 6.2). More than one third of the sound changes in the university hospital were clearly perceptible by the patient during the day. During the night, the percentage of sound changes from the L90 level was significantly lower than the changes during the day. The doubled sound, an elevation of + 10 dB(A), was present in almost 10 % of the registrations in the private hospital and 16 % in the university hospital. During the night double sound level changes were lower in both ICU's. All sound level changes were significantly lower in the private hospital than in the university hospital (Figure 6.2).

Figure 6.2: Sound levels at night in the university B and the private B study, the dashed line at 40 dB(A) shows the maximum limit from the World Health Organization sound recommendation in hospitals. The independent samples T-test for difference between the university and the private hospital showed a p-value < 0.01 for all sound levels.



6.3.2 Sound levels and delirium

The private A study included 123 patients. The incidence of delirium in the private hospital study was 28 %. Delirious patients showed significantly more alarm minutes the day before the onset of delirium (Table 6.3).

The university A and university B studies included 60 and 26 patients respectively. The incidence of delirium was 30 % and 31 % (Table 6.3). None of the calculated sound levels showed a significance difference for delirious or non delirious patients. The percentage perceptible changes from the L90 ambient sound level, however, was significantly higher for delirious patients. The double sound changes were non significantly higher for delirious patients. The odds ratio describing the percentage audible elevation during the night as a risk factor for delirium was 1.06 (0.98-1.15). Also, the odds ratio describing the double sound changes during the night was 1.14 (0.92-1.40).

Table 6.3: Mean sound levels at night for delirious and non delirious patients. P-Value for difference calculated with the independent samples T-test for alarm-minutes and maximum sound volume and with Mann-Whitney U-test for minimum noise level, ambient sound level, median sound level, audible sound changes and double sound changes. P-Value showing difference between delirious and non-delirious patients. Sound levels are expressed in dB(A).

	patients	mean (SD)	mean (SD)	p
private A study:				
alarm-minutes	(n=123)	31.9 (26.6)	49.2 (36.3)	0.008
university B study:				
minimum noise level L 99	(n=26)	47.8 (3.3)	46.2 (1.4)	0.08
ambient sound level L 90	(n=26)	47.5 (4.2)	46.7 (2.7)	0.55
median sound level L 50	(n=26)	52.4 (4.2)	52.6 (2.7)	0.74
university A and university B study:				
maximum sound level L 01	(n=86)	65.5 (7.4)	66.4 (6.3)	0.60
university B study:				
% higher than L90 (+ 5 dB(A), audible change)	(n=26)	17.3 % (12)	39.8 % (29.1)	0.045
% higher than L90 (+ 10 dB(A), double sound)	(n=26)	6.8 % (6.0)	11.6 % (5.9)	0.08

6.4 Discussion

All sound levels in the ICU, including the minimum and the ambient sound level, exceeded de WHO guidelines. The mean sound levels were 44 dB(A) and 52 dB(A) in the studied ICU's. Maximum sound levels during the night, were 66 dB(A) in the private hospital and 70 dB(A) in the university hospital. None of the sound levels showed a relation with the onset of delirium, but the changes in sound from the ambient sound level were higher for delirious patients. Also, the amount of alarms in the private A study was higher for delirious patients.

6.4.1 Sound levels during day and night

Peak sounds are created by the numerous alarms and the activity in the ICU. Although this activity seemed to diminish during the night, no significant differences in the sound levels were found between day and night. The changes from minimum to ambient or median sound level were almost not audible. The audible fluctuation in sound is originated by higher peak sounds. MacKenzie et al. stated that that 34 % of the peak sounds were totally avoidable and 28 % were partially avoidable (MacKenzie and Galbrun, 2007). Sound modification programs have been developed based on architectonical, structural or staff behavioural interventions (Kahn *et al.*, 1998; Monsen and Edell-Gustafsson, 2005). Conversation between staff seemed one of the major sources. Therefore, a staff education program could already affect 14 % of the peak sound sources (Kahn *et al.*, 1998; MacKenzie and Galbrun, 2007). The study in the private hospital showed lower sound levels than the levels in the university hospital. Most likely, the architectural structure based on closed rooms reduced the sound at the bedside as described by Gabor et al. (Gabor *et al.*, 2003).

During the night, a significantly lower amount of audible sound changes was registered. The double sound changes lowered also, but significantly in the private hospital only. Although the sound levels were not significantly different between day and night, this study showed that the changes from the ambient sound level were less frequent during the night.

This study used different approaches in the evaluation of sound in the ICU. The sound level meter with data logger function provided the most detailed relevant information. All sound levels were too high according to the WHO guidelines. The ambient sound level in the ICU is comparable to the sound in a living room. The maximum sound level is comparable to a business office or average street traffic. Staff intervention programs have been developed to reduce sound in the ICU.

6.4.2 Sound levels and delirium

The incidence of delirium scored by the NEECHAM Confusion scale was almost identical in all settings. The different sound levels were not related to the onset of delirium. Research already pointed at the perception of patients indicating high peak alarms as less disturbing (Gabor *et al.*, 2003; Kahn *et al.*, 1998; MacKenzie and Galbrun, 2007). If high sound pressure in the ICU is accepted by the patient, then high level sounds generating high sound pressure will not be registered as noise.
As yet, the relation between sound, sleep and the onset of delirium is not well established. More sound changes and more alarms resulted in more delirium in our study. Stanchina et al. (Stanchina *et al.*, 2005) added baseline noise to an artificial intensive care environment. The augmented baseline resulted in less sound level changes. The subjects showed an improved sleep pattern. Therefore, the change in sound pressure seems more important than the intensity of the level itself in disturbing sleep or generating delirium.

6.4.3 Study limits

In the private A study automatic and manual scoring systems had to be combined. Therefore, nurses possibly missed a number of technical alarms resulting in underscoring of the total number of alarm-minutes.
The different approaches in this study resulted in a different number of included patients. The included patients in the university B study were low, limiting the conclusions of this research. Recent research showed delirium is caused in a context where factors origin from the patient characteristics, the chronic illness, the acute disease and the environment (Van Rompaey *et al.*, 2009). Sound may contribute as an environmental factor. Further research has to study the impact of sound, focusing on changes in sound levels, in a larger population using multivariate analysis including other risk factors.

6.5 Conclusions

Sound level meters with data log function can be advised to study sound changes in the ICU. During the night, the same sound levels were registered, but a lower amount of sound changes was observed than during the day. All registered sound levels were too high regarding the WHO guidelines. This limited research pointed to a possible relation between sound changes during the night in the ICU and the onset of delirium.

Conflict of interests
The authors declare no conflict of interest.

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Part 4

Discussion and conclusions

"Whoever in discussion adduces authority uses not intellect but memory."

Leonardo da Vinci, Italian engineer, painter, and sculptor

7 General discussion and prospects for further research

7.1 Summary of the results

The nurse-oriented Neelon and Champagne Confusion Scale (NEECHAM) was selected as the assessment tool for delirium in the different studies of this research project. Using this tool, measured incidences for delirium ranged from 18 % to 50 % in the non intubated intensive care populations of the Antwerp region. Patients included in a long term follow up study showed a higher mortality and a worse quality of life after a delirious period in the intensive care unit. A systematic review identifying 25 risk factors for delirium in the intensive care unit was followed by a prospective cohort study. Risk factors were investigated related to patient characteristics, chronic pathology, acute illness and the environment. Among them several factors were found to be suitable for preventive action. Additionally, the direct impact of different sound levels and the sound level changes in the intensive care unit were studied and related to the onset of delirium. Although, a higher degree of illness is probably related to a higher number of alarms and a higher risk for delirium, environmental factors showed to be important in the onset of the syndrome.

7.2 Incidences for intensive care delirium

The reported incidences of delirium for non intubated patients assessed with the NEECHAM ranged from 18 % to 50 % in the different chapters. The incidence in the university hospital ranged from 18 % to 31 %. The assessment of delirium in the intensive care unit of the community hospitals in chapter 5 included two different intensive care wards. Although both units seemed comparable regarding to pathology and included patients before the study, delirium showed an incidence of up to 50 % in one of them. Insufficient data on the case mix of the different wards limited the possibility to compare the results of the intensive care units, as yet. The higher incidence has been verified in a limited prospective study from February to April 2009, showing again an incidence of 51 % in 67 patients. A follow-up study in 2010 will focus on specific characteristics of the unit and the population to determine modifiable risk factors for delirium in this population.

All studies indicated an important incidence of delirium in the included intensive care units. Although the different units might not be comparable, delirium showed to be present in a large number of patients in each of them. Neither an evidence based treatment, nor a preventive program has been developed for this group of patients. Symptomatic pharmacological treatments were advised but have not been adequately tested yet (Lacasse *et al.*, 2006; Milbrandt *et al.*, 2005; Skrobik *et al.*, 2004).

7.3 The Neelon and Champagne Confusion Scale

Although most researchers worldwide use the Confusion Assessment Method for the Intensive Care Unit (CAM – ICU), guided by the famous 'ICU Delirium and Cognitive Impairment Study Group' at the Vanderbilt University Medical Center, Nashville, the NEECHAM was selected in this research project to assess patients for delirium in the intensive care unit. The NEECHAM has several advantages.

First of all, the instrument was developed to assess patients using standard nursing observations. Since these professionals are almost continuously present at the bedside of the critical patient, interactions

creating an additional burden to the patient are minimized. This is contrast with other delirium assessment tools, e.g. the CAM-ICU. Moreover, a scale requiring additional actions might encounter more resistance when implemented. The NEECHAM seems to fit more naturally in the standard intensive care nursing task. Research already compared the implementation and the use of different instruments outside the intensive care unit (Schuurmans *et al.*, 2003; van Gemert and Schuurmans, 2007). Since few intensive care units screen for delirium in the standard observation of their patients, further research is needed to optimally implement the NEECHAM in the routine intensive care nursing task. This research can reveal barriers for the use of such a scale by intensive care staff. Consequently, an implementation strategy can be developed.

Secondly, the 30 to 0 score on the NEECHAM scale enables the evaluation of the course of the patient's cognitive status and patients can be classified in four categories from normal over at risk to delirious. Nor the course of the patients through the scores, neither the predictive value of the different categories has been studied yet. Besides the larger spectrum of statistical possibilities of a continuous scale and derived categories, a predictive value could be developed based on consecutive measurements.

A first disadvantage of the NEECHAM is the absence of a published validated version for intubated patients. A NEECHAM for the Intensive Care Unit (NEECHAM-ICU), including intubated patients, has been validated in a Dutch intensive care unit, but has not been published yet. Consequently, researchers and intensive care staff are waiting for this publication for further implementation.

A second disadvantage of the NEECHAM is related to the structure of the scale. Three items assess the level of processing information, three items score the level of behaviour and four items observe the physiological condition of the patient. The physiological condition score is based on oxygen saturation, urinary continence, physiological and vital parameters of the patient. Temperature or hemodynamic scores, however, are often impaired in an intensive care population. The assessment of this physiological condition may be redundant and possible exclusion from the scale needs to be considered. Further research on the NEECHAM-ICU must focus on the two remaining levels. Then, the cut-off score of 19 indicating delirium has to be reconsidered.

The sensitivity and the specificity of the NEECHAM studied in chapter 2 indicated this tool valuable to screen for delirium in the intensive care unit. There seems no need to develop new tools to assess delirium but revision of the NEECHAM for the intensive care unit is recommended. The publication of the validation report of the NEECHAM-ICU, useful for the total intensive care population, can eliminate critiques on the instrument.

7.4 The onset of delirium

Delirium was not the main issue for intensive care staff for years. Nursing and medical actions have been focused on life threatening situations and severe acute illness. In this view, delirium was considered a harmless symptom. Only recently, it has been accepted as an important syndrome affecting a large number of patients in the intensive care unit.

In chapters 2 and 5, an early onset of delirium was demonstrated with 80 % of the intensive care patients scoring positive within 48 hours after inclusion. Most of them were included on admission in the intensive care unit. The remaining was included after gaining consciousness, meeting the inclusion criteria of a Glasgow Coma Scale more than 10. The later inclusion in the study was observed and

reported as a risk factor for delirium in chapter 5. The eventual length of stay in the hospital before admittance to the intensive care unit was not yet studied as an additional risk factor. A more definite description of the case mix might reveal a relation between the onset of delirium and an earlier admittance to the hospital.

A later onset of delirium in the intensive care unit was observed in 20 % of the patients. Probably, for these patients the onset of delirium can be considered as the sixth vital sign. In this context, the syndrome is considered as a marker of underlying hemodynamic instability or upraising illness in recent publications (Bellelli and Trabucchi, 2008; Boockvar *et al.*, 2008).

Patients who do not develop delirium in the intensive care unit, often showed a shorter length of stay in this unit. Observation of these patients during the first period after discharge of the intensive care unit might find them positive for delirium later in the medium care unit or the general ward. A longitudinal study including patients for an observation during a week after admittance in the intensive care unit is suggested, regardless their localization.

The fluctuating character of delirium appeals for a minimal screening three times a day or once in each nursing shift. Eventually, a score can be added when patients are suspected of cognitive changes or when suspicious events occur. Standardized screening is advised to detect delirious patients in the early onset or to warn for underlying physical changes.

7.5 The outcome of delirium

Jackson et al. suggested that the worse cognitive outcome of delirium might be caused by a reduced brain reserve capacity (Jackson *et al.*, 2004). Neuroimaging of the brain showed a lower blood flow and a lower oxygenation during the delirious episode. The cerebral blood flow became normal when the patient was not delirious anymore (Alsop *et al.*, 2006). This period of lower oxygenation might have caused damage to the brain tissue. Also, the disturbance of the neurotransmitters in the brain might result in neuronal injury in some cases of delirium (Marcantonio *et al.*, 2006). The serum anticholinergic activity was compared with electroencephalography as a biomarker for delirium. The first did not show differences for delirious and non delirious patients, the latter did (Milbrandt and Angus, 2005;Plaschke *et al.*, 2007;Thomas *et al.*, 2008). Research on biomarkers indicating neuronal damage was suggested (Marcantonio *et al.*, 2006). The biomarker S-100 beta already showed to be predictive in postoperative cognitive decline in cardiac surgery patients (Shaaban *et al.*, 2000).

The short term outcome of delirium has been studied in the intensive care unit and in general wards. Delirious patients showed a higher trend for mortality. Additionally, a higher morbidity has been observed in agitated patients, e.g. by pulling on catheters and tubes.

For long term outcome, recent research showed a higher amount of patients with cognitive impairment, even two years after delirium. Also, patients seem to have higher odds to develop dementia or mild cognitive impairment. Although research on long term outcome was implied by several authors, few studies have been reported (Hopkins and Jackson , 2006;Jackson *et al.*, 2003). There seems to be a general agreement that delirium causes a long term effect on the cognitive impairment of intensive care patients. The findings in this thesis were adjacent showing a lower quality of life and a higher mortality in a delirious population.

The length of stay in the intensive care unit was significantly related to delirium. In chapter 2 and chapter 3 delirious patients had a length of stay of 18 and13 days respectively. Non delirious patients showed a length of stay of five days in chapter 2 and three days in chapter 3. The question remains, however, if patients with an increased length of stay in the intensive care unit have a higher risk for delirium or if delirious patients have a higher length of stay as a worse outcome. Future research using time dependent analysis can study the length of stay after a delirious period as an outcome.

Today, the sequelae of delirium in the brain are unclear. When the brain tissue is permanently damaged, delirium results in a negative long term outcome. Further research on serum markers or using neuroimaging has to define this permanent damage. The exact aetiology and the causal relation between delirium and the negative outcome are still unknown and consequently need further study. Since no evidence based treatment is available to avoid the worse long term outcome, the aspects of an interdisciplinary cognitive revalidation program must be studied.

7.6 Risk factors

Since the focus in delirium research has shifted from treatment and outcome to prevention, research on risk factors gained importance. In this research project a wide screening was used to identify a broad range of risk factors in different domains: patient characteristics, chronic pathology, acute illness and environment. The wide screening created opportunities to refine the questionnaires and to study several risk factors in detail. Differences in the characteristics of the included populations or hospital sites were not compared.

In contrast with published observations, abnormal blood values were not observed as a risk factor in this research project. Blood values in the studied patients were probably normal or were already balanced by adequate treatment. Moreover, the inclusion of risk factors was not definitive. The factors studied in this thesis showed the top of the iceberg. APACHE or SAPS scores should be included to describe the severity of illness at admission. The evolution of the patient's severity of illness needs to be tracked by a daily score, e.g. the SOFA or SAPI score. A detailed description of disease and treatment related factors, e.g. the use of medication including dopamine, dialysis or insulin therapy, must be studied in a larger population. The absence of these data caused a gap in our knowledge.

Recently, the use of time dependent statistics in delirium research was suggested (Adamis, 2009). Patients might encounter a first delirious period at different moments during the stay in the intensive care unit. Since most positive cases in this research project were observed in a very short period after inclusion, time dependent analysis was not used. Not all patients, however, developed delirium in an early onset. In this context, delirium and the subsequent risk factors must be considered as time dependent. Future research using survival analysis enables the study of risk factors for the late onset delirium or the fluctuating patterns of the syndrome.

A discussion on the length of stay in the intensive care unit questioned delirium as a cause or an outcome (Ely, 2006; Skrobik *et al.*, 2007). In chapter 5, the length of stay before inclusion was studied as a risk factor revealing that a longer period before inclusion showed a higher risk for the development of delirium.

The high number of factors and the fluctuating character of many of them seem to limit the use of a mathematical risk model in daily intensive care practice. A predictive model might be calculated,

but is related to factors originating from the treatment or the illness. Therefore, a risk for delirium score calculated once on admittance is not definite due to the changing precipitating factors. Clinical practice might have a higher benefit from an analysis of the predictive value of the scores and the four categories of the NEECHAM, normal, at risk for delirium, mild or beginning confusion and delirium. Then, the course of patients through the scores or the categories can be observed during the delirious episode. A standardised screening for delirium using the NEECHAM causes a lower burden on the intensive care staff than the observation of numerous risk factors.

In this project, the four domains were not joined in a model. The aim was to detect modifiable risk factors stimulating the research on prevention programs in the intensive care unit. Further studies developing a scientific model seem useful in a more detailed description of the individual factors and the relation between them. The development might focus on modifiable factors in the domains of the acute illness and the environment, corrected by the less or not modifiable factors in the domains related to patient characteristics or chronic pathology.

7.7 Assessment of sleep and sleep perception in delirious patients in the intensive care unit

The impact of disturbed sleep on the onset of delirium in the intensive care unit has been discussed in literature. Several studies showed severe fragmentation, arousals and awakenings in the sleep of ICU patients and pointed at the absence of slow wave and REM sleep. Researchers hypothesized this disturbance of sleep to be an important role player in the onset of the delirious syndrome (Drouot *et al.*, 2008; Mistraletti *et al.*, 2008). Within the context of this research project, efforts have been made to select appropriate assessment tools to investigate sleep disturbance related to delirium.

First, the use of polysomnography has been discussed with physicians and specialists of the intensive care unit and the sleep laboratory of the University Hospital of Antwerp. This technique showed to be very expensive to implement in a large scale research. Additionally, the presence of numerous electric devices in the immediate surroundings of the patient in the intensive care unit caused an unacceptable level of electrical interference. Also, specific medication or illness can influence the interpretation of the registration. Actigraphy systems have been evaluated as an alternative. Since intensive care patients are limited in their movements, these instruments do not provide sufficient data to assess the patient's sleep. The ICU Delirium and Cognitive Impairment Study Group' at the Vanderbilt University Medical Center, Nashville USA, was consulted. Similar problems, however, were encountered in recent studies reporting on the assessment of sleep in the intensive care unit (Watson, 2007; Beecroft *et al.*, 2008; Bourne *et al.*, 2007). Polysomnography was too expensive to implement in a large scale design and the results were often corrupted. Actigraphy and observation by nurses were unreliable to assess the patient's sleep (Beecroft *et al.*, 2008).

The University Hospital of Antwerp sleep laboratory suggested ambulant polysomnography devices, using less electroencephalography leads, to assess the effect of the quality and the quantity of sleep on delirium. The study group managed to filter the obtained signals. Only two patients were included at this time for polysomnography due to problems in obtaining the informed consent for this test on admittance. The first case showed a severe fragmented sleep with absence of slow wave sleep and REM but did not develop delirium. The second case showed many artefacts due to a hyperactive delirium. The results showed a higher absence of sleep and an even higher fragmentation. The use of wires on the head of the delirious patient seemed to evoke agitation in this case. This study failed since not

enough patients could be included within the planned schedule. A new study will include a larger sample where intubated patients will be observed for sleep, ventilation and delirium during several days. Delirium will be diagnosed using the newly validated NEECHAM-ICU compared to the CAM-ICU.

A second study assessed the sleep perception using the Brussels Indices of Sleep Quality (BISQ). The questions of this scale result in a score indicating the subjective sleep perception by the patient. Using this two page questionnaire, patients lost concentration or became too tired to continue the assessment. Therefore, in cooperation with a sleep physician, the assessment was limited to three questions from the BISQ scoring on a four point Likert scale: "1. Did you sleep well? 2. Did you sleep better as expected? 3. Did you sleep better or worse as you do at home?" A score could not be calculated. The three questions were assessed in 84 patients. The incidence of delirium in this population was 18 %. More than 85 % delirious and about 45 % mild confused patients, however, were not able to answer the selected questions compared to about 10 % in non delirious patients ($p<0.001$). The high number of missing data in delirious patients indicated a problem in assessing delirious patients for sleep perception by a questionnaire.

A third study was based on the results of the study in chapter 6 relating the amount of alarms and sound changes during the night to delirium. The quality of sleep in the intensive care unit has been related to environmental sound (Freedman et al., 2001; Freedman et al., 1999; Gabor et al., 2003; Stanchina et al., 2005; Walder et al., 2000). Disturbed sleep has been suggested as a factor in the onset of delirium (Mistraletti et al., 2008). The design of the third study was based on a paper studying healthy subjects in an artificial intensive care environment. In this paper, a study group received earplugs during the night to improve the quality of sleep (Wallace et al., 1999). Based on these observations, we developed a randomized controlled trial aiming to lower the incidence of delirium by reducing the environmental sound changes. Two groups of patients in the intensive care unit are compared for sleep perception, using the three selected questions from the BISQ, and the onset of delirium. The study group are patients sleeping with earplugs; the control group does not receive earplugs. Patients are randomized using a computer program. An interim analysis on 67 patients after 6 months showed results in favour of the patients with the earplugs. Additionally, these patients reported a significant better sleep perception resulting in less delirium. The question remains if this direct relationship is caused by the reduced changing in the sound levels or by the intermediate effect on sleep disturbance. The next analysis in this study will be done on the total population. A penalization for the interim analysis will be the statistical review of the sample size and the significancy level. This trial will be continued until 140 patients are included; the significancy level will be set at 0.0294 (Pocock, 1982).

The study of the effect of sleep on the onset of delirium in the ICU has not been finished within the context of this thesis. Delirious patients were not able to report on the quality of their sleep. The validated tools to assess sleep or sleep perception seem too complicated or too expensive to use in the intensive care unit. Consequently, there is an urgent need to develop cheaper more accessible uncomplicated tools to assess sleep in this specific population. Research might also focus on serum melatonin levels as a marker for sleep deprivation in intensive care patients (Bourne and Mills, 2006).

7.8 Clinical relevance

First of all, this research project caused a Hawthorne effect in the intensive care unit of the participating centres. Before the start of the research, delirium was no issue in any of the included units. No scales were available and patients were not screened for delirium in standard nursing care. During the studies, nurses and physicians became more alert for the syndrome. The implementation of a delirium screening tool, requiring little additional effort, was discussed with the medical and the nursing staff of different hospitals. The NEECHAM was accepted as the standard screening tool in the included intensive care units. Also, the scale is available for nurses and physicians in the electronic patient data management system of the University Hospital. The effect on the observed incidence of delirium was probably small. First, during the study no instruments were implemented to screen for delirium. Second, the different chapters showed high incidences for delirium comparable with international publications. Third, a lower incidence by an augmented attention for the syndrome seems not plausible since neither a treatment nor a preventive action was available to influence the onset of delirium. Also, preventive actions on the reduction of risk factors had not been started yet. After implementing a screening tool for delirium, data can routinely be gathered for further research. There is an urgent need for the validation of the NEECHAM-ICU as a standard nursing instrument to include all intensive care patients.

Delirium was mainly diagnosed shortly after admittance to the intensive care unit. A later onset of the syndrome or a fluctuating course might indicate underlying changes in the current illness. In this context, cognitive impairment is an important marker of physiological changes.

A delirious experience is associated with higher morbidity and mortality in the hospital causing higher healthcare needs. Also, patients with a higher morbidity are more vulnerable for delirium. The triangle between morbidity as a risk factor, morbidity as an outcome and delirium has to be studied thoroughly. Clearly, a vulnerable patient with a higher degree of illness meets a cascade of risk factors. The consequent negative outcome may not be induced by delirium alone. After several months, however, delirious patients still encounter a lower quality of life and a higher mortality after correction for severity of illness. Evidence is growing that brain tissue might be damaged after delirium. An interdisciplinary cognitive program has to focus on the revalidation of delirious patients in order to obtain a more positive long term outcome.

This research project indicated several modifiable risk factors. Studies may be designed to clearly distinct factors from outcome. Prevention programs can be developed to lower the incidence of delirium in the intensive care unit. Each factor, however, calls for a specific approach. First, procedures in the intensive care unit have to be reconsidered towards a positive delirium policy. Unpublished comments by nurses show that the removal of catheters, tubes and drains may be delayed unnecessary once the acute illness of the patient is stabilised. Physical restraints can only be used with high caution and standardised use must be discussed. An open visit policy is advised to stimulate an orientating contact between the patient and his family. In addition, sound reduction can be achieved by the architectural structure of the unit (MacKenzie and Galbrun, 2007). Individual rooms with a high quality sound isolation have to be promoted. Staff members have to be educated to minimize sound changes during the night.

Several risk factors can be eliminated by simple actions, e.g. the use of earplugs during the night as discussed in the randomised clinical trial. Therefore, the identification of modifiable risk factors has to be a main focus in further research.

This research showed the tip of the iceberg of delirium in the intensive care unit. The incidence showed to be high in the Antwerp region. Intensive care nurses and physicians play a key role in an early identification and prevention of the syndrome. This research project identified several modifiable risk factors. Although knowledge on the subject has grown for the past years, several questions remain unanswered. The high incidence of the syndrome might not be tackled for the moment. As long as adequate treatments, preventive actions and revalidation programs are lacking, the patient remains vulnerable for cognitive decline after admittance to the intensive care unit.

7.9 What this thesis adds to the topic

known	added
The CAM-ICU is widely spread and is considered as the gold standard in delirium assessment in the intensive care unit.	The NEECHAM is a valuable tool in non intubated intensive care patients. The instrument is based on standard nursing observations and requires minimal additional interaction with the patient.
Incidences were reported worldwide ranging from 11 to 87 %	The incidences of delirium, ranging from 18 to 50 %, were the first to be reported on a Belgian intensive care population in international publications.
Delirium in the intensive care unit is associated with a higher length of stay in the unit and the hospital, a higher cost, more self-extubation, a higher morbidity and mortality.	The quality of life after three and six months showed to be lower in patients who experienced delirium in the intensive care unit. Mortality was higher within three months after discharge of the intensive care unit for delirious patients.
Risk factors were presented as predisposing and precipitating. Most studied risk factors refer to the acute illness. Factors are often transferred from studies outside the intensive care unit.	Risk factors were studied in the intensive care unit in four domains: patient characteristics, chronic pathology, acute illness and the environment. Several modifiable factors, including sound changes, seem to be related to the onset of delirium.

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8 Conclusions

Part 1: Screening for delirium in the intensive care unit

The Neelon and Champagne Confusion Scale is a valuable tool for screening non-intubated conscious intensive care patients for delirium. An early onset delirium was observed after inclusion. A smaller group of patients developed a later onset delirium, probably indicating underlying physiological changes or upraising illness. The incidences for delirium ranged from 18 % to 50 % in the included intensive care units. These results are comparable to internationally reported incidences using different assessment tools. Delirium seems a major issue in the studied Belgian intensive care units.

Part 2: The outcome of intensive care delirium

A long term follow-up design studied patients in the intensive care unit, at three months and at six months. Delirious patients showed a higher mortality in the intensive care unit and after three months. Similarly, delirious patients had lower scores in all domains of the SF-20 quality of life scale.

Part 3: Risk factors for intensive care delirium

A systematic review showed that factors for delirium were understudied in the intensive care unit. Most factors referred to the acute illness. Consequently, a prospective cohort study included factors relating to patient characteristics, chronic pathology, acute illness and the environment. Especially in the two latter domains, several risk factors are suitable for preventive actions.
A prospective design studying the direct effect of sound on the onset of delirium showed a relation between the amount of alarms and the delirium score of a patient. Also, the amount of sound changes from the ambient sound level was related to the onset of delirium.

A standardised screening for delirium is advised in the intensive care unit. Simple preventive actions focusing on modifiable risk factors have to be developed to lower the incidence of delirium in the intensive care unit.

9 Summary Samenvatting

9.1 Summary

Intensive care delirium is the presentation of the general picture of delirium in the specific setting of the intensive care unit with a patient encountering an acute confusional state, knowing a fluctuating course with periods of inattentions, an altered level of consciousness and disorganised thinking. The onset of delirium is induced by a physical cause stimulated by predisposing and precipitating factors. Predisposing factors exist in the patient before admittance to the intensive care unit and relate to personal characteristics and chronic conditions. The precipitating factors challenge the patient's resistance during the stay in the intensive care unit. The higher the baseline vulnerability, the fewer challenging factors are required to push the patient into a delirium. For the typical clinical situation of the intensive care patient, there will always be a high vulnerability because of severe illness or trauma at the time of admittance. These illness and trauma provoke treatment with tubes, drains and psychoactive medication. The illness and the environment may cause disturbance of the circadian rhythm. Consequently, an intensive care patient encounters a cascade of predisposing and precipitating risk factors entering the intensive care unit.
Despite the existence of validated instruments, the syndrome remains unrecognized by nurses and clinicians in three out of four delirious patients. Nurses and clinicians might fail to recognize symptoms because of the lack of appropriate tools and knowledge on the subject. The Neelon and Champagne Confusion Scale (NEECHAM) was developed to assess delirium based on standard nursing observations. The scale was translated and validated for intensive care patients in a Dutch intensive care unit. The necessity to screen patients for intensive care delirium is sustained by a poor outcome for delirium. Yet, the studied outcome was mainly limited to the intensive care unit or the hospital. Few data are available on long term outcome.

This thesis aimed to describe the incidence of intensive care delirium in a Flemish adult population. Consequently, patients were included in a long term follow up study on the outcome of delirium. Additionally, risk factors, including those from the environment, were studied to suggest interventions to lower the incidence of delirium in the intensive care unit.

The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is widely used. A binary result diagnoses delirium. The NEECHAM has a numeric assessment ranging from 30 (normal) to minus 20 (delirium). This scale allows the patients to be classified in four categories: non-delirious, at risk, confused, and delirious. The results of the NEECHAM were compared with the results of the CAM-ICU. The CAM-ICU showed a 19.8 % incidence of delirium. The NEECHAM detected incidence rates of 20.3 % for delirious, 24.4 % for confused, 29.7 % for at risk and 25.6 % for normal patients. The sensitivity of the NEECHAM was 87 % and the specificity was 95 % with the CAM-ICU as golden standard. The positive predictive value and the negative predictive value were 79 % and 97 %, respectively. In non-intubated patients, the NEECHAM scale identified most cases of delirium which were detected by the CAM-ICU. Additional confused patients were identified in the categorical approach of the scale. The NEECHAM scale proved to be a valuable screening tool compared with the CAM-ICU in the early detection of intensive care delirium by nurses.

Delirium in the intensive care unit is known to be associated with worse outcomes. Cognitive impairment, a longer stay in the hospital or in the intensive care unit and a raised mortality have been reported. This research studied the long term outcome after intensive care delirium defined as mortality and quality of life at three and six months after discharge of the intensive care unit. Compared to the non delirious patients, more delirious patients died. All SF-20 quality of life scores showed lower results for the delirious patients compared to the non delirious patients. Evidence is growing that delirium may not be fully reversible in all patients.

Risk factors for delirium in the intensive care unit were studied. First, a systematic review identified four predisposing and 21 precipitating factors, including nine laboratory blood values and seven items relating to the use or the administration of medication in six publications. The APACHE II score and hypertension were the only factors reported twice. This review concluded that risk factors for the development of intensive care delirium were understudied and underreported in literature.
Consequently, a prospective study in four hospitals of the Antwerp area was set up. All consecutive newly admitted adult patients were screened in a multicenter study at one university hospital, two community hospitals and one private hospital. Patients were included when reaching a Glasgow Coma Scale greater than 10. Nurse researchers assessed 523 patients for delirium using the NEECHAM. The overall delirium incidence was 30 %. Risk factors covered four domains: patient characteristics, chronic pathology, acute illness and environmental factors. Odds ratios were calculated using univariate binary logistic regression. Age was not a significant risk factor. Intensive smoking (OR 2.04), daily use of more than three units of alcohol (OR3.23) and living single at home (OR 1.94), however, contributed to the development of delirium. In the domain of chronic pathology a pre-existing cognitive impairment was an important risk factor (OR 2.41). In the domain of factors related to acute illness the use of drains, tubes and catheters, acute illness scores, the use of psychoactive medication, a preceding period of sedation, coma or mechanical ventilation showed significant risk with odds ratios ranging from 1.04 to 13.66. Environmental risk factors were isolation (OR 2.89), the absence of visit (OR 3.73), the absence of visible daylight (OR 2.39), a transfer from another ward (OR 1.98) and the use of physical restraints (OR 33.84). Particularly risk factors related to the acute illness and the environment are suitable for preventive action. Predisposing patient characteristics and chronic pathology make the intensive care patient vulnerable at admittance. A higher degree of illness generates disease or treatment related risk factors. Moreover, the intensive care environment holds precipitating factors for delirium.

Sound in the intensive care unit has been a subject of research for years. Although the impact on sleep has been studied, contradicting results require the study of the direct impact of sound on the patient's outcome. The assessment of sleep remains a problem in the intensive care unit. This study assessed different sound levels and the sound level changes in the intensive care unit and related them to the onset of delirium. Three different approaches in a university and a private hospital assessed sound by counting alarms or using sound level meters. Delirium was assessed using the NEECHAM. All registered sound levels were over the WHO maximum limit of 40 decibels. During the night, the same sound levels were registered, but a lower amount of sound changes was observed than during the day. The median sound level during the night was 44 decibels in the private hospital and 52 decibels in the university hospital. The 27 % audible sound changes during the night in the university hospital were related to the onset of delirium ($p=0.05$). A higher amount of alarms in the private hospital was also related to delirium ($p=0.008$). This research pointed to a possible relation between the amount of alarms and sound changes during the night and the onset of delirium.

Before the start of this research project, delirium was no issue in any of the included intensive care units. During the study, nurses and physicians became more alert for the syndrome. The intensive care staff is now aware of the syndrome and seems motivated for further research. The NEECHAM was accepted as the standard screening tool in the included intensive care units.

This research showed the tip of the iceberg of delirium in the intensive care unit. The incidence showed to be high in the Antwerp region. Intensive care nurses and physicians play a key role in an early identification and prevention of the syndrome. This research project identified several modifiable risk factors. Although knowledge on the subject has grown for the past years, several questions remain unanswered. The high incidence of the syndrome might not be tackled for the moment. As long as adequate treatments, preventive actions and revalidation programs are lacking, the patient remains vulnerable for cognitive decline after admittance to the intensive care unit.

9.2 Samenvatting

Delirium bij patiënten op de afdeling voor intensieve zorg wordt intensive care delirium genoemd. Het acute syndroom uit zich door wisselende periodes van verwarring, een gewijzigd bewustzijnsniveau en een gestoord denkpatroon. Delirium kent een organische oorzaak die in de hand gewerkt wordt door voorbestemmende en uitlokkende factoren. Voorbestemmende factoren zijn bepaald in het dagelijkse leven door persoonsgebonden kenmerken en chronische condities. De uitlokkende factoren spelen in op de weerstand van de patiënt tijdens zijn verblijf op de afdeling voor intensieve zorg. Des te kwetsbaarder een patiënt is, des te minder factoren zijn nodig om een delirium uit te lokken. Een patiënt op intensieve zorg heeft steeds een hoge graad van kwetsbaarheid door de ernst van de ziekte of het trauma bij opname. Deze ziekte of trauma resulteert in een behandeling uit waar katheters, tubes en drains veelvuldig gebruikt worden. Bovendien verstoort de pathologie het circadiaan ritme. Bijgevolg wordt een patiënt vanaf zijn opname op de afdeling voor intensieve zorg overweldigd door het samenspel van de voorbestemmende en uitlokkende factoren.

Drie op vier delirante patiënten worden door artsen en verpleegkundigen niet ontdekt. Mogelijk herkennen zij de symptomen niet door een gebrek aan kennis over het syndroom of de afwezigheid van diagnostische instrumenten. De Neelon and Champagne Confusion Scale (NEECHAM) werd ontwikkeld om delirium op te sporen aan de hand van standaard verpleegkundige observaties. De schaal werd in Vlaanderen vertaald en in Nederland gevalideerd voor intensieve zorg patiënten. De nadelige gevolgen voor patiënten die een delirium doormaakten werden vooral op de afdeling voor intensieve zorg of in het ziekenhuis bestudeerd. Er zijn weinig gegevens bekend over de gevolgen op langere termijn. De ernst van de nadelige gevolgen noodzaken het standaard opsporen van het syndroom en de verdere opvolging van patiënten gedurende een langere periode.

Deze thesis beschrijft de incidentie van intensive care delirium in een steekproef van volwassen patiënten op een Vlaamse afdeling voor intensieve zorg. Vervolgens worden patiënten opgenomen in een onderzoek dat langere termijn effecten van delirium bekijkt. Daarna worden mogelijke risicofactoren voor delirium bestudeerd. Hieruit worden interventies voorgesteld om de incidentie te verlagen waarbij vooral aandacht wordt besteed aan factoren uit de omgeving.

De Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) wordt veelvuldig gebruikt. Een binair antwoord op dit instrument diagnosticeert delirium. De NEECHAM kent een numerieke beoordeling. Aan de hand van deze laatste schaal kunnen patiënten ingedeeld worden in vier categorieën: niet delirant, risico op verwardheid, verward en delirant. De resultaten van de NEECHAM en de CAM-ICU werden vergeleken. De CAM-ICU stelde 19.8 % delirium vast. De NEECHAM ontdekte

20.3 % delirium, 24.4 % verwardheid, 29.7 % patiënten met een risico op verwardheid en 25.6 % normale patiënten in een cohorte van niet geïntubeerde patiënten. De sensitiviteit van de NEECHAM was 87 % en de specificiteit was 95 % vergeleken met de CAM-ICU als gouden standaard. De positieve en de negatieve voorspellende waarde waren 79 % en 97 %. De NEECHAM ontdekte de meeste patiënten die door de CAM-ICU als delirant werden aangeduid. Door de categorische benadering kon de schaal bijkomend verwarde patiënten aanduiden. De NEECHAM bleek in vergelijking met de CAM-ICU een waardevolle schaal voor verpleegkundigen te zijn om vroegtijdig delirium te kunnen vaststellen.

De ernstige gevolgen van delirium op de afdeling voor intensieve zorg werden reeds eerder aangetoond. Cognitieve achteruitgang, een verlengd verblijf in het ziekenhuis of op de afdeling voor intensieve zorg, een verhoogde mortaliteit en hogere kosten voor gezondheidszorg werden vermeld. Dit onderzoek bestudeerde de gevolgen op langere termijn, gedefinieerd als mortaliteit en kwaliteit van leven drie en zes maanden na ontslag uit de afdeling voor intensieve zorg. In vergelijking met de niet-delirante patiënten werd een grotere mortaliteit vastgesteld bij de delirante patiënten. Alle SF-20 kwaliteit van leven scores lagen lager voor de delirante patiënten vergeleken met de niet-delirante patiënten. Onderzoek toont aan dat sommige patiënten niet volledig herstellen na een periode van delirium op de afdeling voor intensieve zorg.

Risicofactoren voor intensive care delirium werden bestudeerd. Aan de hand van een systematische literatuurstudie werden vier voorbestemmende en 21 uitlokkende factoren gevonden in zes publicaties. Hieronder waren negen bloedwaarden en zeven factoren die een verband hielden met het toedienen van medicatie. Alleen de APACHE II score en hypertensie werden twee maal vermeld. De literatuurstudie stelde vast dat risicofactoren voor intensive care delirium slechts beperkt gerapporteerd werden. Vervolgens werd een prospectieve cohort studie uitgevoerd in vier ziekenhuizen in de Antwerpse regio. Alle volwassen patiënten die nieuw opgenomen werden op de afdeling voor intensieve zorg werden in het onderzoek opgenomen wanneer ze minimaal 10 scoorden op de Glasgow Coma Schaal. Verpleegkundige onderzoekers observeerden 523 patiënten voor delirium aan de hand van de NEECHAM. De totale incidentie van delirium in de verschillende ziekenhuizen was 30 %. Er werden vier domeinen van risicofactoren bestudeerd: persoonsgebonden eigenschappen, chronische pathologie, acute ziekte en omgeving. Bij de persoonsgebonden factoren was leeftijd geen significante risicofactor. Intensief rookgedrag (OR 2.04), het dagelijks gebruik van meer dan drie eenheden alcohol (OR3.23) en alleenstaand wonen (OR 1.94), droegen wel bij tot de ontwikkeling van delirium. In het domein van de chronische pathologie bleek een cognitieve achteruitgang een belangrijke risicofactor te zijn (OR 2.41). In het domein gerelateerd aan de acute ziekte bleken het gebruik van leidingen, drains en katheters, , het gebruik van psychoactieve medicatie, een voorafgaande periode van beademing, sedatie, coma en een hoge mortaliteitsscore risicofactoren te zijn met odds ratio's tussen 1.04 en 13.66. Omgevingsfactoren die bijdroegen tot de ontwikkeling van delirium waren isolatie (OR 2.89), de afwezigheid van bezoek (OR 3.73), de afwezigheid van daglicht (OR 2.39), een transfer van een andere afdeling (OR 1.98) en het gebruik van middelen om de patiënt in beperkte vrijheid te stellen (OR 33.84). Vooral de risicofactoren gerelateerd aan de acute ziekte en de omgeving blijken geschikt voor de ontwikkeling en toepassing van preventieve maatregelen. Een patiënt is kwetsbaar voor delirium op het moment van opname door de persoonsgebonden eigenschappen en aanwezige chronische pathologie. De ernst van de aandoening waarvoor de patiënt opgenomen wordt genereert verschillende ziekte- of behandelingsgebonden factoren. Bijkomend bevinden er zich binnen de muren van de afdeling voor intensieve zorg nog verschillende factoren die een delirium mee kunnen uitlokken.

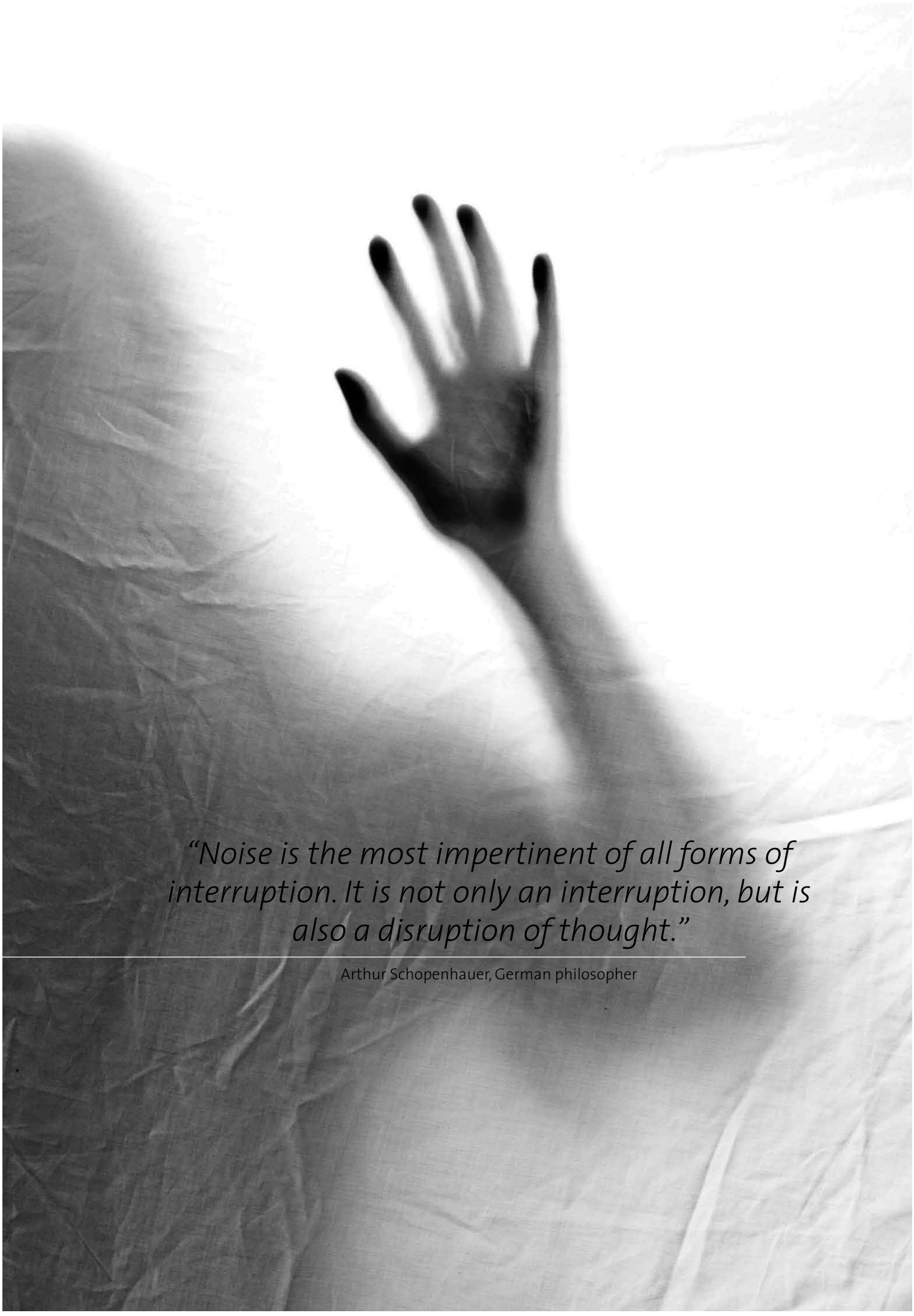
Omgevingsgeluid is reeds gedurende verschillende jaren het voorwerp van wetenschappelijk onderzoek. De invloed op slaap werd onderzocht maar tegenstrijdige resultaten noodzaken het onderzoek van de directe invloed van geluid op de patiënt. De registratie van de kwantiteit en de kwaliteit van slaap bij patiënten op de afdeling voor intensieve zorg blijft een probleem. In deze studie werden verschillende geluidsniveaus en veranderingen in geluidsniveau bestudeerd in relatie tot delirium. Aan de hand van drie verschillende methoden in een universitair en een privaat ziekenhuis werd geluid bestudeerd door auditieve alarmsignalen te tellen of door decibelmeters te gebruiken. Delirium werd geobserveerd aan de hand van de NEECHAM. Alle geluidsniveaus overschreden de WHO limiet van 40 decibel. Gedurende de nacht werden dezelfde geluidsniveaus vastgesteld dan tijdens de dag. Er waren echter minder veranderingen in geluidsniveau. Het gemiddelde geluidsniveau bedroeg 44 decibel in het privaat ziekenhuis en 52 decibel in het universitair ziekenhuis. De door de patiënt waarneembare geluidsveranderingen in het universitair ziekenhuis (27 %) konden in verband gebracht worden met delirium ($p=0.05$). In het privaat ziekenhuis werd een groter aantal alarmen gekoppeld aan het ontstaan van delirium ($p=0.008$). Dit onderzoek toonde een mogelijk verband aan tussen het aantal auditieve alarmen, de veranderingen in geluidsniveau en het ontstaan van delirium.

Vóór de start van dit doctoraal onderzoek was de aandacht voor delirium minimaal in de bestudeerde afdelingen voor intensieve zorg. Tijdens het onderzoek werden artsen en verpleegkundigen waakzamer voor het optreden van het syndroom en groeide de motivatie om aan verder onderzoek deel te nemen. De NEECHAM werd in de deelnemende afdelingen aanvaard als het standaard observatie instrument voor delirium. Aan de hand van dit doctoraal onderzoek werden verschillende risicofactoren vastgesteld. De kennis over het onderwerp is sterk gegroeid gedurende de laatste jaren. Verschillende vragen blijven echter onbeantwoord. Als volgende stap kunnen interventieprogramma's ontwikkeld worden om delirium te voorkomen of de incidentie te doen dalen. Op dit ogenblik lijkt het niet mogelijk om het syndroom te voorkomen. Zolang er onvoldoende basis is om een meer adequate behandeling, preventie of revalidatie te implementeren, blijft de patiënt kwetsbaar voor cognitieve achteruitgang na zijn opname op intensieve zorg.

Delirium

Focusing on intensive care patients

Het syndroom belicht bij patiënten op intensieve zorg



"Noise is the most impertinent of all forms of interruption. It is not only an interruption, but is also a disruption of thought."

Arthur Schopenhauer, German philosopher

10 List of abbreviations

- APACHE — Acute Physiology and Chronic Health Evaluation II score

  A severity of disease classification score for the intensive care unit. The score is calculated once based on 12 routine physiological measurements within the first 24 hours of admittance.
  Knaus W.A., Zimmerman J.E., Wagner D.P., Draper E.A. & Lawrence D. (1985) APACHE II: a severity of disease classification system. *Crit Care Med* 13, 818-829.

- BISQ — Brussels Indices of Sleep Quality

  A questionnaire assessing the patient's perception of the quality of sleep
  The instrument is used in sleep laboratories and sleep research at the Vrije Universiteit Brussel and the University Hospital of Antwerp.
  Van Even P., Cluydts R. (2004) Een psychometrisch onderzoek naar de BISQ (Brussels Indices of Sleep Quality), een nieuwe methode om slaapkwaliteit te kwantificeren., Vrije Universiteit Brussel, Faculteit geneeskunde, unpublished work

- CAM — Confusion Assessment Method

  A delirium assessment tool
  Inouye S.K., Van Dyck C.H., Alessi C.A., Balkin S., Siegal A.P. & Horwitz R.I. (1990) Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 113, 941-948.

- CAM-ICU — Confusion Assessment Method for the Intensive Care Unit

  A delirium assessment tool for intubated patients in the intensive care unit
  The development was based on based on the CAM.
  A detailed description is included in Chapter 12.
  Ely E.W., Inouye S.K., Bernard G.R., Gordon S., Francis J., May L., Truman B., Speroff T., Gautam S., Margolin R., Hart R.P. & Dittus R.S. (2001) Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001, 2703-2710.

- CI — Confidence interval

  A description of an estimated interval based on selected data. The width informs on the certainty of an unknown parameter.

- dB(A) — A-weighted decibels

  A logarithmic measurement of the intensity of sound. The suffix A refers to sound measurements close to the human hearing.

- DSM-IV — Diagnostic and Statistical Manual of Mental Disorders-IV

  A manual published by the American Psychiatric Association categorizing psychiatric diagnoses

- ICD-10 — International Classification of Diseases and Related Health Problems-10

  An international standard diagnostic classification under supervision of the World Health Organization

- ICDSC Intensive Care Delirium Screening Checklist

  A delirium assessment tool for the intensive care unit
  Bergeron N., Dubois M.J., Dumont M., Dial S. & Skrobik Y. (2001) Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med* 27, 859-864.

- ICU Intensive care unit

  A specialized department in the hospital admitting severely ill patients

- NA Not available

- NEECHAM Neelon and Champagne Confusion Scale

  A delirium assessment tool
  A detailed description is included in Chapter 12.
  Milisen K., Foreman M.D., Hendrickx A., Godderis J., Abraham I.L., Broos P.L.O. & De Geest S. (2005) Psychometric properties of the Flemish translation of the NEECHAM Confusion Scale. *BMC Psychiatry* 25, 16.
  Neelon V.J., Champagne M.T., Carlson J.R. & Funk S.G. (1996) The NEECHAM Confusion Scale: Construction, validation, and clinical testing. *Nurs Res* 45, 324-330.

- OR Odds Ratio

  A measure of effect size between two data values

- RR Relative risk ratio

  The probability of an event in the exposed group versus the non exposed group

- SAPI Score of activities and pathologies in intensive care

  A severity of disease classification system for the intensive care unit
  Hanique G., Bossaert L., Roger France F.H., Working group SAPI Belgian Society of Intensive Care and Emergency Medicine (SIZ). (1980) Score of Activities and Pathologies in Intensive care (SAPI). Research financed by the Ministry of Public Health and the SIZ. 102 pages

- SAPS II New Simplified Acute Physiology Score

  A severity of disease classification system for the intensive care unit
  Le Gall J.R., Lemeshow S., Saulnier F. (1993) A New Simplified Acute Physiology Score (SAPS II) Based on a European/North American Multicenter Study. *JAMA:* 270, 2957-2963.

- SD Standard deviation

  A measure of the distribution of the data. The SD shows how the data are spread around the mean.

- SF-20 Medical Outcomes Study Short-Form General Health Survey

  A tool assessing the quality of life in six domains
  A detailed description is included in Chapter 12.
  Kempen G.I.J.M., Brilman E.I., Heyink J.W. & Ormel J. (1995) *Het meten van de algemene gezondheidstoestand met de MOS Short-Form General Health Survey (SF-20)*. Rijksuniversiteit Groningen, Noordelijk Centrum voor Gezondheidsvraagstukken, Groningen.

- SOFA Sequential Organ Function Assessment

  A severity of disease classification system in the intensive care unit
  The SOFA is based on respiratory, cardiovascular, hepatic, coagulation, renal and neurological scores.
  Vincent, JL., de Mendonca, A., Cantraine, F., Moreno, R., Takala, J., Suter, P., Sprung, C., Colardyn, F., Blecher, S. (1998) Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. *Intesiv Care Med:* 26, 1793-1800

- SPSS Statistical Package for the Social Sciences

  Analytical software
  Manufacturer: SPSS Inc. Headquarters, 233 S. Wacker Drive, 11th floor, Chicago, Illinois 60606, USA

- TISS 28 Simplified Therapeutic Intervention Scoring System 28

  A daily score measuring activities and interventions for an intensive care patient
  Moreno R. & Morais P. (1997) Validation of the simplified therapeutic intervention scoring system on an independent database. *Intensive Care Med* 23, 640-644.
  Reis Miranda D., de Rijk A. & Schaufeli W. (1996) Simplified Therapeutic Intervention Scoring System: The TISS-28 items--Results from a multicenter study. *Crit Care Med* 24, 64-73.

- WHO World Health Organization

  The directing and coordinating authority for health within the United Nations system (www.who.int)

11 List of Figures and tables

12 Appendix: description of the most important assessment tools

12.1 Delirium assessment tools

Bron: www.delirant.info

12.1.1 The Neelon and Champagne Confusion Scale

Originele schaal: (Neelon et al., 1992;Neelon et al., 1996)
Vertaling en validatie: (Immers et al., 2005;Milisen et al., 2005)

12.1.1.1 Toelichting

NEECHAM Confusion Scale: Vul deze schaal in op basis van observaties tijdens de zorg aan de patiënt en de routine verpleegkundige gegevensverzameling. Scoor (=omcirkel) het item (vb. AANDACHT, VERWERKING VAN OPDRACHTEN,....) waarvan de beschrijving het meest overeenkomt met de respons of het gedrag van de patiënt tijdens de zorg. Scoor altijd het laagst geobserveerde gedrag. Voor het correct scoren van de NEECHAM dient met altijd rekening te houden met culturele verschillen en fysische handicaps (zicht, gehoor, motoriek,....) die de respons kunnen beïnvloeden niet ieder gedrag beschreven per score dient bij de patiënt aanwezig te zijn, echter het gedrag moet wel representatief zijn voor de beschrijving. LEES EERST ALLE SCORINGSMOGELIJKHEDEN PER ITEM ALVORENS EEN DEFINITIEE SCORE TOE TE KENNEN.

12.1.1.2 Niveau 1 – VERWERKING VAN INFORMATIE

AANDACHT: (aandacht – alertheid – respons)
4 Volledige aandacht / alertheid: reageert onmiddellijk en adequaat op aanspreking of aanraking doormiddel van oogcontact of door het naar je toe draaien met het hoofd: volledig bewust van omgeving, normale aandacht voor gebeurtenissen uit de omgeving.
3 Kortstondige of te hoge aandacht / alertheid: kortstondige aandacht voor aanspreking, aanraking, of gebeurtenissen uit de omgeving of reageert overdreven alert, is vlug afgeleid door gebeurtenissen / voorwerpen uit de omgeving.
2 Wisselende of inadequate aandacht / alertheid: reageert langzaam, herhaaldelijk aanspreken of aanraken is nodig om aandacht te verkrijgen of te behouden; is in staat voorwerpen / stimuli te herkennen, doch kan in slaap vallen tussen de stimuli door.
1 Verstoorde aandacht / alertheid: opent ogen bij lawaai of aanraking, kan er angstig uitzien, onmogelijk om contact te behouden of te herkennen, of vertoont terughoudendheid / defensief gedrag.
0 Verminderde waakzaamheid / respons: ogen kunnen zowel open als gesloten zijn; slechts minimale reactie na herhaaldelijk stimuleren, reageert niet op contact.

VERWERKING VAN OPDRACHTEN: (herkenning – interpretatie – uitvoering)
5 In staat een complexe opdracht uit te voeren: "Bel de verpleegkundige". (Kan de bel zelf vinden, het voorwerp herkennen en bellen).
4 Vertraagde uitvoering van een complexe opdracht: heeft aansporing of herhaalde aanwijzingen nodig om een complexe opdracht te volgen of uit te voeren. Voert een complexe opdracht op een trage manier of met overdreven veel concentratie uit.

3 In staat een eenvoudige opdracht uit te voeren: “Hef uw hand omhoog, hef uw voet omhoog, mevrouw / meneer .....”. (geef slechts 1 opdracht tegelijkertijd).
2 Niet in staat een gegeven opdracht uit te voeren: Voert opdracht pas uit na stimulering door aanraking of visuele aanmoedigingen – drinkt slechts van een glas / beker wanneer het bij de mond gehouden wordt. Contact en geruststelling van verpleegkundige of het vasthouden van de handen heeft een kalmerende invloed.
1 Niet in staat een visueel ondersteunende opdracht uit te voeren: reageert met verbijsterde of angstige gelaatsuitdrukking en / of terughoudende, afwerende reactie op stimuli, hyper/ hypoactief gedrag; reageert niet als verpleegkundige de hand lichtjes vastgrijpt.
0 Hypoactief, lethargisch: minimale psychomotorische respons op omgevingsstimuli.

ORIËNTATIE: (oriëntatie, korte termijn geheugen, gedachten- en gespreksinhoud)
5 Georiënteerd naar tijd, plaats en persoon: gedachtegang inhoud van gesprekken of vragen zijn relevant, adequaat. Korte termijn geheugen is intact.
4 Georiënteerd naar plaats en persoon: minimale geheugenstoornissen, inhoud en antwoorden op vragen zijn over het algemeen adequaat; herhaald zichzelf, vereist stimulering tot het voortzetten van het contact. Werkt over het algemeen mee.
3 Inconsistente oriëntatie: georiënteerd naar zichzelf en familie, maar oriëntatie naar tijd en plaats kan verstoord zijn. Gebruikt visuele geheugensteuntjes om zich te oriënteren Gedachten- en geheugenstoornissen komen vaak voor, kan hallucinaties en illusies vertonen. Passieve medewerking op gerichte vraag.
2 Gedesoriënteerd en geheugenstoornissen: georiënteerd naar zichzelf en familie. Vraagt de noodzaak af de verpleegkundige handelingen of weigert er aan mee te werken. Gesprekken / gedachtegang inhoudelijk verstoord. Illusies en hallucinaties komen vaak voor.
1 Gedesoriënteerd, verstoorde herkenning: inconsistentie in het herkennen van vertrouwde personen, familie, vertrouwde voorwerpen. Abnormaal taalgebruik.
0 Verminderde reactie op stimuli: minimale respons op verbale stimuli.
Totaal score van niveau 1:

12.1.1.3 Niveau 2 – GEDRAG

HET VOORKOMEN
2 Heeft een goede houding, voorkomen, hygiëne netjes gekleed, goede persoonlijke hygiëne proper. Normale houding in bed / stoel.
1 Verstoring van houding of voorkomen: enige wanorde in kledij / bed of persoonlijk voorkomen, of enig verlies van controle in houding, positie.
0 Houding en voorkomen abnormaal: wanorde, slechte hygiëne onmogelijk om een juiste houding in bed te behouden.

MOTORIEK
4 Normaal motorisch gedrag: normale bewegingen, coördinatie en activiteit, kan rustig uitrusten in bed. Normaal bewegen van de handen.
3 Vertraagd of versneld (hyperactief) psychomotorisch gedrag: overdreven rustig of weinig spontane beweging (handen / armen voor de borst gekruist of langs het lichaam) of hyperactief (op en neer, ‘springerig’), beven van handen kan voorkomen.
2 Verstoorde motorische bewegingen: rusteloze of snelle bewegingen. Abnormale handbewegingen, (plukken aan lakens, ...). Kan hulp nodig hebben bij doelgerichte handelingen.

1 Abnormaal / storend gedrag: trekken aan sondes, infusen drains, over bedhekken kruipen, vaak doelloos handelen.
0 Verminderde motoriek: weinig bewegen tenzij gestimuleerd, afwerende bewegingen.

VERBAAL
4 Kan op een normale manier spreken: in staat een gesprek te voeren, kan een gesprek beginnen en onderhouden. Tweegesprek over één en hetzelfde (evt. eenvoudig) thema is mogelijk, normale toon.
3 Beperkte spraakmogelijkheden: respons op verbale stimuli is kort en bondig. Spreekt nog duidelijk en verstaanbaar maar beperkt, toon kan abnormaal zijn, tempo kan vertraagd zijn.
2 Spreekt abnormaal: spreekt soms tegen zichzelf of spreekt wartaal. Geen eigenlijk tweegesprek mogelijk (alleenspraak / incoherent).
1 Stoornissen in spraak / geluid: veranderd geluid / toon. Murmelt onverstaanbaar, schreeuwt, vloekt of is abnormaal stil.
0 Abnormale geluiden: kreunen of andere storende geluiden. Geen gesproken taal meer.
Totaal score van niveau 2:

12.1.1.4 Niveau 3 – FYSIOLOGISCHE TOESTAND

FYSIOLOGISCHE PARAMETERS
Opgemeten waarden: Normaal waarden:
..... Temperatuur 36 – 37 graden C
..... Systolische bloeddruk 100 – 160 mm hg
..... Diastolische bloeddruk 50 – 90 mm hg
..... Pols 60 – 100 p/min.
regelmatig / onregelmatig omcirkel er één
..... Ademhaling 14 – 22 p/min. (tel 1 volle minuut)
..... O_2 saturatie 93 of hoger

VITALE FUNCTIES
Toelichting
Tel abnormale systolische bloeddruk en / of diastolische bloeddruk als 1 waarde. Tel abnormale en / of onregelmatige polsslag als 1 waarde. Tel apnoe en / of abnormale ademhaling als 1 waarde. Tel abnormale temperatuur als 1 waarde.
2 Bloeddruk, pols, temperatuur en ademhaling binnen de normale grenzen en pols is regelmatig.
1 Eén van volgende waarden (bloeddruk, pols, temperatuur en ademhaling) is abnormaal.
0 Twee of meer van de volgende waarden (bloeddruk, pols, temperatuur en ademhaling) is abnormaal.

ZUURSTOF SATURATIE
2 O_2 saturatie binnen normale grenzen (93 of hoger)
1 O_2 saturatie 90 tot en met 92 of krijgt zuurstof toegediend
0 O_2 saturatie 89 of lager

URINE CONTINENTIE
2 Continent (behoudt controle over de blaas).
1 Incontinent voor urine in de laatste 24 uur of heeft een condoom catheter.
0 Is nu incontinent of heeft een urine verblijfscatheter of intermittent cathateriseren of heeft anurie.
Totaal score van niveau 3:

12.1.1.5 TOTAALSCORE

Score niveau 1 (0 – 14)
Score niveau 2 (0 – 10)
Score niveau 3 (0 – 6)
Totaalscore
0 – 19: ernstig tot gemiddeld acuut verward
20 – 24: mild of beginnend acuut verward
25 – 26: niet acuut verward, maar een verhoogd risico om verward te raken
27 – 30: niet acuut verward, functioneert normaal

12.2 The Confusion Assessment Method for the Intensive Care Unit

Originele schaal: (Ely et al., 2001a;Ely et al., 2001c;Ely et al., 2001b)
Vertaling: R. Vreeswijk, J.F.M. de Jonghe , C.J. Kalisvaart, Medisch Centrum Alkmaar, Nederland
Validatie: (Vreeswijk et al., 2009)

12.2.1 Beschrijving van de schaal

1. Acuut begin en fluctuerend beloop Afwezig Aanwezig

a. Zijn er aanwijzingen voor een acute verandering in het psychisch/cognitief functioneren vergeleken met hoe het was in het begin?
Of
b. Fluctueerde het gedrag gedurende de afgelopen 24 uur, d.w.z. was het aanwezig en verdween het later, nam het toe of af in ernst, zoals gemeten met een observatieschaal voor sedatie (bijv. RASS), GCS, of een vorige delier beoordeling?

2. Verminderde aandacht Afwezig Aanwezig
Kost het patiënt moeite de aandacht vast te houden. *Dit wordt aangegeven met een score < 8 van het auditieve of visuele onderdeel van de Attention Screening Examination (ASE).*

De Attention Screening Examination (ASE)
Gehoor en visueel
A. Auditieve (letter) ASE
Aanwijzing: Zeg tegen de patiënt, "Ik ga een reeks van 10 letters opnoemen. Wanneer U de letter A hoort knijpt U in mijn hand". Lees de volgende reeks letters voor zonder nadrukkelijk te articuleren (houdt met het volume rekening met de geluiden op de ICU) en met een snelheid van 1 letter per seconde.
S A H E V A A R A T
Score: Een respons wordt fout gerekend indien patiënt niet knijpt bij de letter "A" of wel knijpt bij een andere letter dan "A" .

B. Visuele (plaatjes) ASE

*** * Neem de Plaatjes Pakketten (A en B) * ***

Stap 1: 5 plaatjes.

Aanwijzing: Zeg tegen de patiënt, "Mevrouw of Meneer ....., Ik laat U nu plaatjes zien van enkele gewone voorwerpen. Kijk goed en probeer elk plaatje te onthouden omdat ik ga vragen welke plaatjes U heeft gezien". Laat dan de plaatjes uit pakket A of B zien, alterneer de sets A en B bij herhaalde metingen. Toon de eerste 5 plaatjes gedurende 3 seconde per plaatje.

Stap 2: 10 plaatjes.

Aanwijzing: Zeg tegen de patiënt, "Nu laat ik U nog enkele plaatjes zien. Sommige heeft U al eens gezien andere zijn nieuw. Kunt U mij laten weten of U ze eerder hebt gezien of niet door ja (doe voor) of nee (doe voor) te schudden met uw hoofd". Toon vervolgens de 10 plaatjes (5 nieuwe en 5 oude) gedurende 3 seconden per plaatje. (Stap 2 van de plaatjes die U hebt gebruikt in stap 1, dus pakket A of pakket B).

Score: Deze test wordt gescoord aan de hand van het aantal goede ja en nee antwoorden dat wordt gegeven in stap 2 (een maximum van 10 antwoorden). Om de zichtbaarheid van de plaatjes voor oudere mensen te verbeteren worden zij op gelig/lichtbruin gekleurd papier afgedrukt en gelamineerd met een matte laag.

Opmerking: indien patiënt een bril heeft zorg er dan voor dat hij/zij hem draagt bij de visuele ASE.

3. Ongeorganiseerd denken **Afwezig** **Aanwezig**

Zijn er aanwijzingen voor gedesorganiseerd of incoherent denken *zoals blijkt uit 2 of meer foute antwoorden op de 4 vragen en/of niet opvolgen van de opdrachten.*

Vragen (wissel set A en set B af):

Set A Set B

1. Blijft een steen drijven in water? 1. Blijft een blad drijven in water?
2. Zijn er vissen in de zee? 2. Zijn er olifanten in de zee?
3. Weegt 1 pond meer dan 2 ponden? 3. Wegen 2 ponden meer dan 1 pond?
4. Kun je met een hamer een spijker inslaan? 4. Kun je met een hamer hout snijden?

Opdrachten:

1. Vindt U dat U niet helder kunt denken?
2. Steekt U eens zoveel vingers op. (Onderzoeker houdt 2 vingers op)
3. Doe nu hetzelfde met de andere hand. (Onderzoeker laat nu niet twee vingers zien)

4. Veranderd bewustzijnsniveau **Afwezig** **Aanwezig**

Is het bewustzijnsniveau van de patiënt anders dan alert bijv. waakzaam, lethargisch, of stuporeus? (bijvoorbeeld RASS uitslag wijkt af van "0" op het moment van beoordeling)

- **Alert** - Uit zichzelf, zich volledig bewust van de omgeving en reageert hier passend op
- **Waakzaam** - Hyperalert
- **Lethargisch** - Slaperig maar makkelijk wekbaar, niet bewust van sommige aspecten van de omgeving, reageert niet uit zichzelf op de interviewer; maar wordt zich bewust van zijn omgeving en reageert hier passend op bij geringe aansporing.
- **Stuporeus** - Blijft onvoldoende bewust van zijn omgeving, zelfs na sterke prikkeling; is alleen wekbaar door krachtige en herhaalde prikkeling en zo gauw deze prikkeling vermindert valt de stuporeuze patiënt terug in een staat van niet reageren.

Totaal CAM-ICU (kenmerk 1 én 2 en ofwel 3 of 4) **Ja** **Nee**

12.2.2 Samenhang tussen sedatie en deliermonitoring. Een tweetraps benadering van onderzoek naar bewustzijn

Stap 1: Vaststelling van de mate van sedatie De Richmond Agitatie en Sedatie schaal: de RASS*

Score Begrip Beschrijving

+4 strijdlustig oppositioneel/vijandig, gewelddadig, direct gevaar voor personeel
+3 erg geagiteerd trekt aan of verwijderd katheter(s) of tube(s); agressief
+2 geagiteerd regelmatig niet doelgerichte bewegingen, afwerende reacties
+1 onrustig angstig maar bewegelijkheid is niet agressief krachtig.
0 alert en kalm
-1 slaperig niet volledig alert maar is in staat wakker te blijven (ogen open/oogcontact) bij stemgeluid (> 10 seconde) verbale
-2 lichte sedatie kort wakker met oogcontact bij stemgeluid (< 10 seconde) stimulatie
-3 matige sedatie beweging of ogen open bij stemgeluid (geen oogcontact)
-4 diepe sedatie geen reactie op stemgeluid, maar wel beweging en ogen open bij lichamelijke prikkeling lichamelijke
-5 niet wekbaar geen reactie op stemgeluid of lichamelijke prikkeling stimulatie

Als RASS score –4 of –5 is dan **stoppen** en patiënt op een later tijdstip **hertesten**.
Als RASS boven de –4 (-3 tot +4) ligt dan **stap 2 toepassen**.

Stap 2: Vaststelling delier

Kenmerk 1: Acute verandering van mentale toestand of fluctuerend verloop.
EN
Kenmerk 2: Aandachtsstoornis
EN
Kenmerk 3: Ongeorganiseerd denken *OF* **kenmerk 4**: Veranderd bewustzijnsniveau = **DELIER**

CAM-ICU Onderdelen Aanwezig/afwezig

Kenmerk 1: Acuut ontstaan en fluctuerend verloop

De patiënt zijn RASS is nu 0, maar was –1,-3 en +2 in de laatste 24 uur **Aanwezig**
De patiënt zijn RASS was –2 in de laatste 24 uur maar familie geeft aan dat dit niet zijn baseline was voor de opname **Aanwezig**

2: Verminderde aandacht

De patiënt zijn score is 7 bij de ASE plaatjes en 5 bij de ASE letters **Aanwezig**
De patiënt is in staat om 10 correcte antwoorden te geven op zowel de ASE plaatjes als letters **Afwezig**
De patiënt is in staat te communiceren door het knijpen in de onderzoeker zijn hand maar is niet in staat de ASE te beantwoorden **Aanwezig**

Kenmerk 3: Gedesorganiseerd denken

De patiënt beantwoord de helft van de vragen correct **Aanwezig**
De patiënt beantwoord alle vragen correct en is in staat het aantal opgestoken vingers van de interviewer aan te geven **Afwezig**

Kenmerk 4: Veranderd bewustzijnsniveau

De patiënt heeft regelmatig ongecontroleerde bewegingen
en toont weerstand tegen de beademing **Aanwezig**

De patiënt zijn cognitie fluctueert en heeft verschillende RASS scores in de afgelopen 24 uur,
maar is nu alert en kalm (RASS=0) **Afwezig**

12.3 Medical Outcomes Study Short-Form General Health Survey

Originele vragenlijst: RAND Health Insurance Study Questionnaire (Stewart et al. 1988)
Vertaling en validatie: Dutch Medical Outcomes Study Short-Form General Health Survey (SF - 20) (Kempen et al. 1995)

12.3.1 Toelichting bij de SF-20

De Medical Outcomes Study Short Form General Health Survey (SF-20) bevat 20 vragen. Het is een multi-dimensioneel instrument om de algemene gezondheidstoestand van een persoon te meten (fysiek, mentaal en sociaal). Er worden zes dimensies onderscheiden: lichamelijk functioneren (zes items), rolvervulling (twee items), sociaal functioneren (één item), psychische gezondheid (5 items), ervaren gezondheid (5 items) en lichamelijke pijn (één item). Per dimensie wordt een schaalscore berekend. De eindscores worden getransformeerd naar een 100-puntenschaal. Het is niet gebruikelijk om een totaalscore te berekenen met de SF-20.

12.3.2 Nederlandse versie van de SF-20

Hieronder volgt een vraag over uw gezondheid. Wilt U het antwoord dat het best bij U past aankruisen?
Hoe is in het algemeen uw gezondheid?

- ○ uitstekend
- ○ erg goed
- ○ goed
- ○ redelijk
- ○ slecht

De volgende vragen gaan over eventuele beperkingen ten gevolge van uw gezondheid. Heeft uw gezondheidstoestand U de afgelopen periode beperkt in één van de volgende activiteiten? Zo ja, hoe lang al?Wilt u het hokje van het antwoord dat het beste bij uw past aankruisen?

	Ja, al langer dan 3 maanden beperkt	Ja korter dan 3 maanden beperkt	Nee ik ben niet beperkt
Bent u beperkt in zeer inspannende activiteiten zoals optillen van zware voorwerpen, hardlopen, of deelname aan inspannende sporten?			
Bent u beperkt in wat minder inspannende activiteiten zoals een tafel verplaatsen, boodschappen dragen?			
Bent u beperkt in een heuvel oplopen of enkele trappen lopen?			
Bent u beperkt in buigen, tillen, of bukken?			
Bent u beperkt in een blokje omlopen.			
Bent u beperkt in eten, aankleden, douchen of een bad nemen of naar het toilet gaan?			

Hieronder volgen een aantal vragen over uw gezondheid. Wilt u het antwoord dat het best bij uw past aankruisen?

Heeft u de afgelopen 4 weken lichamelijke pijn gehad?

- ○ geen pijn
- ○ zeer lichte pijn
- ○ lichte pijn
- ○ matige pijn
- ○ hevige pijn

Kunt u vanwege uw gezondheid uw werk of huishoudelijke karweitjes niet doen?

- ○ ja, dat kan ik al langer dan 3 maanden niet
- ○ ja, dat kan ik korter dan 3 maanden niet
- ○ nee, ik ben niet beperkt

Heeft u vanwege uw gezondheid bepaalde werkzaamheden niet kunnen doen (bedoeld wordt een bepaald onderdeel of een bepaalde hoeveelheid van het werk of de huishouding)?

- ○ ja, dat kan ik al langer dan 3 maanden niet
- ○ ja, dat kan ik korter dan 3 maanden niet
- ○ nee, ik ben niet beperkt

Hoe vaak heeft uw gezondheid u de afgelopen maand beperkt in uw sociale activiteiten (zoals op bezoek gaan bij vrienden of naaste familie)?

- ○ altijd
- ○ heel vaak
- ○ redelijk vaak
- ○ soms
- ○ bijna nooit
- ○ nooit

De volgende vragen gaan over hoe U zich de afgelopen maand heeft gevoeld. Wilt u weer het hokje dat het meest op U van toepassing is aankruisen.

	altijd	heel vaak	redelijk vaak	soms	bijna nooit	nooit
Hoe vaak bent u in de afgelopen maand erg nerveus geweest?						
Hoe vaak heeft u zich de afgelopen maand kalm en rustig gevoeld?						
Hoe vaak heeft u zich de afgelopen maand neerslachtig en somber gevoeld?						
Hoe vaak heeft u zich de afgelopen maand gelukkig gevoeld?						
Hoe vaak heeft u zich de afgelopen maand zo somber gevoeld dat niets U kon opvrolijken?						

Tot slot volgen nog een paar uitspraken over uw gezondheid.

	absoluut waar	groten-deels waar	ben er niet zeker van	groten-deels niet waar	beslist Niet waar
Ik ben een beetje ziek.					
Ik ben zo gezond als ieder ander die ik ken.					
Mijn gezondheid is uitstekend.					
Ik voel me de laatste tijd slecht.					

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13 Acknowledgements

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I would like to thank the University of Antwerp for starting the adventure of a master program for nurses. The organization of this education stimulated academic nurses to start a doctoral program. After the successful accreditation, the dean and the staff of the faculty of medicine created opportunities for the future. The academic environment was often a peaceful, well equipped place to work on the research project.

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With a little help from my friends, I succeeded in surviving and keeping the unhealthy balance of doctoral research and life at a reasonable level. They often wondered what I was doing and why it had to take several years. Some of them where more fanatic in their support, but it would be incorrect to limit this acknowledgement to a few persons. *Mens sana in corpore sano* became true after several games of korfball, diving experiences or a limited skiing holiday. Thanks.

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Curriculum Vitae

Bart Van Rompaey werd geboren op 23 maart 1963 in Deurne (Antwerpen).

Na het middelbaar onderwijs behaalde Bart in 1985 het diploma gegradueerde ziekenhuisverpleegkunde aan het Hoger Instituut voor Verpleegkunde, Stuivenberg in Antwerpen. Daarna behaalde hij achtereenvolgens in 1989 een licentiaat in de biomedische wetenschappen, richting gezondheidszorg (ziekenhuis- en medisch-sociale wetenschappen) en in 1991 het diploma geaggregeerde voor het hoger secundair onderwijs in de biomedische wetenschappen aan de Vrije Universiteit Brussel.

De professionele carrière nam een start in het Algemeen Ziekenhuis Middelheim in Antwerpen op het operatiekwartier en de afdeling voor medisch intensieve zorgen. Later werd Bart daar lid van de werkgroep kwaliteitszorg en verantwoordelijke verpleegkundige van de afdeling voor postanaesthetische zorgen. In 1994 werd de overstap naar het verpleegkundig onderwijs gemaakt. Aanvankelijk in het Hoger Instituut voor Verpleegkunde, daarna gedurende enkele jaren in het Stedelijk Instituut voor Technisch Onderwijs nr. 7 om uiteindelijk een engagement aan te gaan met de Artesis Hogeschool Antwerpen. In deze verschillende instellingen werden naast het onderwijzen van studenten verpleegkunde steeds meer organisatorische en beleidstaken opgenomen. Hiervoor werden de rollen van stagecoördinator, leerplancoördinator, eindwerkcoördinator, coördinator voortgezette opleidingen, campuscoördinator en opleidingscoördinator op verschillende momenten opgenomen. Van bij de ontwikkeling van de master in de verpleegkunde en vroedkunde aan de Universiteit Antwerpen was hij betrokken bij de opbouw en de uitvoering van het programma, de invulling van de leerlijn wetenschappelijk onderzoek en verschillende organisatorische aspecten.

In het recente verleden werd Bart opgenomen in het Utrechtse Rho Chi Chapter van The Honour Society of Nursing, Sigma Theta Tau International. Hij is tevens lid van de Federale Raad voor de Kwaliteit van de Verpleegkundige Activiteit.

1 Wetenschappelijke communicatie relevant voor de thesis

1.1 Artikels in tijdschriften

- Van Rompaey B., Elseviers M., Schuurmans M., Shortridge-Bagett L., Truijen S. & Bossaert L. (2009) Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care* 13, 3, R77.
- Van Rompaey B., Schuurmans M., Shortridge-Bagett L., Truijen S., Elseviers M. & Bossaert L. (2009) Long term outcome after delirium in the intensive care unit. *J Clin Nurs* Published Online: Sep 4 2009 6:17AM, DOI: 10.1111/j.1365-2702.2009.02933.x
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- Van Rompaey B., Schuurmans M., Shortridge-Bagett L., Truijen S. & Bossaert L. (2008) Risk factors for intensive care delirium: a systematic review. *Intensive Crit Care Nurs* 24, 98-107.

1.2 Abstracts

- 13e International Nursing Research Conference, Allicante, 11-13th November 2009
  Van Rompaey, B., Fromont, V., Jorens, P., The use of earplugs during the night to prevent delirium in intensive care patients
- 29e International Symposium on Intensive Care and Emergency Medicine, Brussel, 24-27 maart 2009
  Van Rompaey, B., Elseviers, M., Bossaert, L., Risk factors for intensive care delirium
  Published in *Critical Care* 13, Suppl 1, 410
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  Staes, K.; Van Rompaey, B., Elseviers, M., Bossaert, L, Bepalen van de beïnvloedende extrinsieke en omgevingsfactoren voor een intensive care delirium (winnaar van de VVIZV-award 2008)
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  De Bakker, L., Van Rompaey, B., Elseviers, M., Bossaert, L., De invloed van verpleegkundige handelingen op gestoorde slaap en intensive care delirium
- 25ste jaarcongres Vlaamse vereniging Intensieve Zorgen Verpleegkundigen, mijn IZ eenheid, Gent, 23 november 2007
  Schakman, E., Van Rompaey, B., Elseviers, M., Bossaert, L., Verpleegkundige werklast en delirium op Intensieve Zorg
- 27e International Symposium on Intensive Care and Emergency Medicine, Brussel 27-30 maart, 2007
  Van Rompaey, B., Bossaert, L., Schuurmans, M., L. Shortridge-Bagett, L., Truijen, S., A comparison of the confusion assessment method for the intensive care unit and the NEECHAM confusion scale in intensive care delirium assessment
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1.3 Bijdrage in in boeken

- Van Rompaey, B. (2006). Intensief verward: het delirium op intensieve zorg. In International Center for Reproductive Health (Ed.), Binnenste buiten, intensief bekeken, jaarboek 2006 Vlaamse Vereniging Intensieve Zorgen Vepleegkundigen (pp. 47-57). Gent Belgium. ISBN 9078128135

1.4 Mondelinge presentaties (invited speaker)

- Euroneuro 2008, Maastricht, "Risk factors for critical care delirium"
- Universitair Ziekenhuis Antwerpen research club, 28 februari 2007, "Het delirium op intensieve zorg"
- Vlaamse Vereniging Intensieve Zorgen Verpleegkundigen, symposium, 24 november 2006, Internationaal Congrescentrum Gent "Intensief verward"
- Universiteit Antwerpen, symposium "Onderzoek en praktijk in dialoog", 9 november 2006, onderwerp: "Verward en toch niet dement"

1.5 Andere

- reviewer voor Critical Care
- reviewer voor Intensive and Critical Care Nuring
- beoordelaar van publicaties voor McMaster University Online Rating of Evidence (MORE)

2 Andere wetenschappelijke communicatie

2.1 Abstracts

- 25th Anniversary International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Rhode Island, August 16-19, 2009
  Elseviers, M., Van Rompaey, B., Patients's knowledge about their chronic medication
- UFS' International Research & Development Conference: Knowledge in Nursing, Aarhus, Augustus 22-24, 2007
  Bosmans, J., Mistiaen, W., Van Rompaey, B., Outcome of team learning for nursing skills in a skills laboratory
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  Timmermans O., Biot I., Van Rompaey B., "Organizational Readiness for Evidence Based Education in Bachelor in Nursing Schools
- 22th International Conference of Pharmacoepidemiology, Quebec, Augustus 17-22, 2007
  Elseviers, M., Vander Stichele, R.H., Van Rompaey, B., Characteristics of medication use of frail elderly living at home
- 22th International Conference of Pharmacoepidemiology, Quebec, 17-22 Augustus, 2007
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- Dilles, T., Van Rompaey, B,. (2009). Verpleegkundige handelingen in de geneesmiddelenzorg in rusthuizen. Hoofdstuk in Cahier Ouderenzorg, Kwalitatieve geneesmiddelenzorg, Wolters Kluwer Belgium Mechelen, ISBN 9789046519905, p. 49-56
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Delirium

Focusing on intensive care patients

Het syndroom belicht bij patiënten op intensieve zorg

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