Agents Intervening against Delirium in Intensive Care Unit (AID-ICU):

An international inception cohort study

Protocol Synopsis

Title	Agents Intervening against Delirium in Intensive Care Unit (AID-ICU): An international inception cohort study
Objectives	To describe current use of haloperidol and other pharmacological agents for delirium in critically ill patients admitted to ICU in Denmark, Norway, Sweden, Finland, Netherland, Switzerland, Germany, United Kingdom, Italy, Belgium, Canada, Brazil, Spain and France.
Study Design	An inception **Cohort study**
Outcomes	*Primary outcome measure:* Number of patients with delirium intervened with haloperidol. *Secondary outcome measures:* Number of patients with delirium intervened with antipsychotics other than haloperidol, number of patients with delirium, mortality at 90 days after ICU admission, days alive without coma- and delirium and days alive without mechanically ventilation. In a sub-group of patients included in Denmark cognitive impairment at 6 months will be evaluated.
Study Duration	14-day inception period (Marts 1st to May 30th 2016); patients will be followed for the duration of admission in ICU with final follow-up at 90 days (6 month at selected sites).
Number of subjects	N=1000
Population	Acutely ill patients aged 18 years or older admitted to one of the participating ICUs in the inception period.

Contents

1. Investigators and Facilities

1.1 Study Location

Coordinating administrative centre: Centre for Research in Intensive Care – CRIC

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1.2 Study Management
The Management Committee will manage and coordinate the study centrally. A local research team consisting of a Principal Investigator and a study coordinator will manage and coordinate the study locally. The Principal Investigator has the responsibility for data collection and maintenance of study documentation on site.

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1.8 Funding and resources

The AID-ICU research program is funded by Innovation Fond Denmark, the Dept. of Intensive Care Unit, Rigshospitalet and the participating ICUs.

The study is not supported by the industry.

2. Introduction and background

2.1 Background information

The American Clinical Practice Guideline for Adult Intensive Care Unit (ICU) patients in 2002 recommended haloperidol as the therapeutic agent for delirium in critically ill patients, with the requirement of monitoring side effects such as prolongation of QT intervals and arrhythmias[1]. However, in the 2013 update of the guidelines this recommendation was changed; haloperidol was no longer recommended for delirium in critically ill patients due to lack of evidence of effect. The same guideline suggests that atypical antipsychotics and continuous IV infusion of dexmedetomidine rather than benzodiazepines is suggested to reduce the duration of delirium in ICU patients with delirium even though these interventions also have low level of evidence. Presently, there are no pharmacologic agents with solid evidence of effect for the treatment of delirium in ICU patients[2].

Delirium is a complex acute or sub-acute organic mental syndrome characterized by altered level of consciousness, comprehensive cognitive impairment, disorientation, perceptual disturbances, attention impairment, reduced or activated motor activity, disturbed sleep patterns and fluctuating motor and mental performances[3]. Observed incidence rates of delirium in ICU patients range from 16% to 89%[4]. According to The American Society of Critical Care Medicine the most valid and reliable monitoring tools for routine assessment of delirium is the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and Intensive Care Delirium Screening Checklist (ICDSC)[2].

The risk factors for delirium can be divided into two groups: *non-correctable factors* such as previous delirious episodes, age, dementia, smoking, alcohol and other drug abuse and potentially *correctable factors* such as several categories of medication, acute severe illness, lack of sleep, uneasy environment, and co-morbidities[2,5].

Delirium in mechanically ventilated patients is associated with increased 6-month mortality rates, more days on the ventilator and longer stay in ICU and hospital[6–8]. A meta-analysis assessing clinical outcomes in critically ill patients indicated that delirium was associated with more complications including Acute Respiratory Distress Syndrome (ARDS), nosocomial pneumonia, cardiopulmonary oedema, re-intubation, self-extubation, removal of catheter, and cardiac arrhythmia [9]. After discharge from ICU, patients with delirium report more long-term cognitive impairment, which may last up to 12 months[10,11].

In a survey from 2011 in USA, haloperidol was reported to be the most widely used neuroleptic agent for delirium in ICU patients, although prolonged QT intervals were observed[12].

Non-pharmacological interventions such as early mobilization have in a randomized clinical trial been suggested to decrease delirium and increase the number of ventilator-free days [13].
In spite of the lack of evidence for haloperidol, widespread use for delirium is likely. Because of the potentially serious adverse reactions, large randomised trials assessing the overall benefit and harm of haloperidol for delirium in ICU are needed. Such trials may be complex to perform and we need more knowledge on the current use of haloperidol in the ICU setting to better design such trials.

2.2 Study Objectives
2.2.1 Aim
To describe and explore current use of haloperidol and other pharmacological interventions for delirium in critically ill patients admitted to ICUs in selected countries[1].

2.2.2 Research Question
Which pharmacologic agents are used for delirium in ICU in 2015 and how are they administered?

2.2.3 Hypothesis
Haloperidol is still widely used and remains the first choice pharmacological intervention for delirium in ICU.

3. Study Design
3.1 Type of study
A multicentre 14-day inception cohort study investigating the pharmacological intervention practices of delirium in acutely ill ICU patients (estimated 50 ICUs in 8 countries). The 14-day study period can be selected by sites from Marts 1st to May 30th 2016.

4. Method
4.1 Number of subjects
We expect to include 1000 acutely ill patients admitted to the participating ICUs.

4.2 Expected duration of study
We will include patients in a 14-day inception period and perform final follow-up at 90 days after ICU admission. A subgroup of conveniently sampled patients will be cognitively assessed at 6 months after ICU admission.

4.3 Primary and secondary outcome measures
4.3.1 Primary
Number of ICU patients with delirium intervened with haloperidol (N05AD01)
(Definition: Patients receiving one or more doses of haloperidol and are described as delirious. Delirium defined as below in secondary outcome 2).

4.3.2 Secondary
1. Number of ICU patients with delirium intervened with other antipsychotics than haloperidol
(Definition: Patients receiving one or more doses of 2nd generation anti-psychotics[2] including olanzapin (N05AH03), rivastigmin (N06DA03), risperidon (N05AX08) and quetiapine (N05AH04),

[1] Denmark, Norway, Sweden, Finland, Netherland, Switzerland, Germany, United Kingdom, Belgium, Spain, Italy, Canada, Brazil and France

AND described as delirious (see definition in secondary outcome 2. Number of patient with delirium)

2. Number of patients with delirium
(Definitions: ICU documented CAM-ICU positive or ICDSC ≥ 4 points (0-8 points) or DOS >3 points (0-13/day points) or Nu-DESC ≥ 2 (0-15 points), ICD-10 code (DF05, DF050, DF05), or agitated and/or non-cooperative and/or eyes open wide with no contact (Glasgow Coma Score (GCS) > 7 or Reaction Level Scale (RLS) < 4) or restrained to the bed).

3. Mortality at 90 days
(Definition: Death within 90 days of ICU admission)

4. Days alive in ICU without coma and/or delirium
(Definition Coma: Number of calendar days the patient is alive without coma in the period from ICU admission to discharge. Coma defined as RASS (Richmond Agitation Sedation Score) score -3 to -5, Ramsey sedation score 4 to 6, MASS (Motor Activity assessment Scale)1 to 0, GCS < 8 or RLS > 3).
Delirium Definition: Number of calendar days the patient is alive without delirium in the period from ICU admission to discharge. Delirium defined as above in secondary outcome 2. All assessments in a 24 hour period need to be negative for a patient to be assessed delirium-free).

5. Days alive without mechanical ventilation and days alive out of hospital (ICU) in a 90-day period
(Definition: Patient treated with mechanical ventilation either endotracheal intubated or tracheostomy, on controlled or spontaneous mode or patient treated with continuous non-invasive ventilation (NIV) for more than 1 hour. Number of days without a ventilator is registered every 24 hours; every new day at 6 AM is registered as one day. If a patient is re-intubated/or started NIV within 24 hours it will be registered as a full day of mechanical ventilation.
Definition: Number of days alive after discharge from the hospital (ICU), the day of discharge do not count, but from the next day at 6 AM).

6. Rate of cognitive impairment at 6 months after ICU discharge (only in Denmark)
(Definition: Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)[14] *is a comprehensive and validated neuro-psychometric battery for the evaluation of global cognition, including individual domains of immediate and delayed memory, attention, visuospatial construction, and language. RBANS scale ranging from 40 to 160, with lower scores indicating worse performance. With a population age-adjusted mean [±SD] of 100±15 (a scale ranging from 40 to 160, with lower scores indicating worse performance))*[11].

5. Recruitment

Potential patients will be identified and recruited in participating ICUs by the local investigators.

5.1 Eligibility

5.1.1 Inclusion Criteria

All adult (age ≥18 years) patients admitted acutely to one of the participating ICUs during the 14-day inception period.

[2] amisulprid (N05AL05), aripiprazol (N05AX12), asenapin (N05AH05), clozapin (N05AH02), lurasidon (N05AE05), olanzapin (N05AH03), paliperidon (N05AX13), quetiapin (N05AH04), risperidon (N05AX08), sertindol (N05AE03), ziprasidon (N05AE04).

5.1.2 Exclusion Criteria

- Pre-diagnosed mental illness of schizophrenia and/or psychosis and/or major depression (ICD 10; F20-29; F30, F31, F32, F33)
- Terminal status (i.e., expected to survive < 24 hr. and/or withdrawal of life-support)
- Pre-diagnosed neurodegenerative disorders Dementia and Parkinson (ICD 10; F02-04)
- Mental illness recurring institutionalization or acquired or congenital mental retardation
- Patients with congenital or acquired brain damage, i.e.; stroke in the past 2 weeks, transient cerebral ischemic in the past 2 weeks, subarachnoid haemorrhage, cerebral cancer, meningitis, encephalopathies, ongoing seizures and suspected anoxic brain injury or traumatic brain injury
- Patients admitted with hepatic coma, drug overdose or suicide attempt (within the past 6 months necessitating hospitalization)
- Blind and/or deaf

5.2 Readmission to an ICU

When included patients in the 14-day inception period are discharged from the ICU and, are readmitted during the same hospital admission, to an ICU that participates in AID-ICU registration will be continued. If the included patient is discharged from the hospital and readmitted at another ICU at another hospital he/she will not have data registered from that ICU.

5.3 Patients transferred between hospitals

Patients transferred from one ICU participating in AID-ICU to another ICU participating in AID-ICU: day from registration will be continued at the receiving hospital and the investigator at the last hospital will complete follow-up.
Patients transferred from an ICU participating in AID-ICU to an ICU not participating in AID-ICU: Collection of data will end at discharge from AID-ICU participating ward except for the time dependent outcome measures.

5.4 Patients eligible for RBANS assessment (only in Denmark)

We will chose a convenience sample of patients who have been admitted to a Danish ICU and who are alive at 6 months with no new diagnosis of mental illness such as schizophrenia and/or psychosis and/or major depression (ICD 10; F20-29; F30, F31, F32, F33), no new neurodegenerative disorders Dementia and Parkinson (ICD 10; F02-04), no stroke in the past 2 weeks before the test, no suspected anoxic brain injury or acute traumatic brain injury, blind and/or deaf after admission or have poor Danish and English skills. The patients for RBANS assessment will be sampled based on pragmatic selection (availability of patient and staff).

5.5 Study completion

When the 14-day inception period and the 90-day (for some sites 6 month) follow-up period has ended.

6. Clinical and laboratory assessments – Methodology

See appendix 1.

6.1 Patient evaluation

<u>Baseline patient characteristics</u>

1. Age on the day of ICU admission (years).

2. Gender (male/female).
3. Simplified Acute Physiology Score II (SAPS II) within the first 24 hours of the ICU admission (0-163 points).
4. Use of dialysis, vasopressors or inotropes (noradrenaline (C01CA03), adrenaline (C01CA24), dobutamine (C01CA07), dopamine (C01CA04), milrinone (C01CE02), levosimendan (C01CX08) vasopressin (H01BA01) or phenylephrine (C01C A06) and/or medical ventilation (y/n).
5. Days admitted in the hospital prior to ICU admission (number of days).
6. Type of admission diagnose (sepsis y/n [15], trauma y/n, surgery 24 hour prior to admission y/n, elective surgery y/n, emergency surgery y/n).
7. Treatment with bencodiazepines (N05BA)(N05CD08) such as Diazepam, Oxazepam, Lorazepam, Bromazepam, Cloxazolam and Midazolam prior to or at admission to ICU.
8. Risk factor status prior to hospital/ICU: treatment with haloperidol (N05AD01) before ICU admission, smoking every day (yes/no), alcohol abuse more than 3 units (1 units defined as 12 g of alcohol) a day (yes/no)).
9. Hearing or vision impairment (y/n).

<u>Daily data collection from admission through last day of follow-up (discharge from ICU or day 90</u>

10. Sedation assessment (the sites will only register the score (a, b or c) they use in clinical practice), as described in patient files, one score equals one positive day with sedative induced coma.
    a. RASS score -3- (-5) (y/n) at any time during the day or
    b. Ramsey sedations score 4-6 points (y/n) at any time during the day or
    c. MASS score 1-0 (y/n) at any time during the day.
11. Coma assessment, as Glasgow Coma Scale (GCS) score without any sedation.
    a. GCS < 8 point (y/n) at any time during the day.
    b. RLS > 3 point (y/n) at any time during the day.
12. Delirium assessment (the sites will only register the score (a, b or c) they use in clinical practice), as described in patient files, one positive score equals one delirium day. (appendix 2)
    a. CAM-ICU (positive /negative/UTA, Unable To Assess).
    b. ICDSC ≥ 4 point (0-8 point).
    c. DOS>3 point (0-13 point).
    d. Nu-DESC ≥ 2 (0- 15 point).
    e. ICD 10 code DF05, DF050, DF058.
13. Subtype description of delirium (hypo, hyper or mixed[16]).
14. Restrained to the bed (y/n).
15. Treatment with continuous vasopressor or inotropes at any time during this day (noradrenaline (C01CA03), adrenaline (C01CA24), dobutamine (C01CA07), dopamine (C01CA04), milrinone (C01CE02), levosimendan (C01CX08), phenylephrine (C01C A06) or vasopressin (H01BA01)).
16. Use of invasive mechanical ventilation (y/n) or use of non-invasive ventilation at any time during this day (y/n).
17. Is the patient sedated at any time during this day (y/n), with continuous infusion of
    a. Propofol (N01AX10).
    b. Midazolam (N05CD08).
    c. Dexmedetomidine (N05CM18) (continues > 18 hours pr./day or continuous > 4 hours between 10 pm – 06 am).
    d. Other.

18. Pain management with intravenous opioid infusion for more than 2 consecutive hours at any time during this day (y/n).
    a. Remifentanil (N01AH06).
    b. Sufentanil (N01AH03).
    c. Fentanyl (N01AH01).
    d. Morphine (N02AA01).
19. Pharmacologic intervention for delirium (first initial dose will be recorded, then the 24 hour accumulated verified administrated dose. Is treatment prescribed as fixed or per need or both).
    a. Antipsychotics.
        i. Haloperidol (N05AD01) (mg/day) (prophylaxis y/n)(regular dosing mg/day or as needed mg/day).
        ii. Olanzapine (N05AH03) (mg/day) (prophylaxis y/n)(regular dosing mg/day or as needed mg/day).
        iii. Quetiapin (N05AH04) (mg/day) (prophylaxis y/n)(regular dosing mg/day or as needed mg/day).
    b. Anxiolytics.
        i. Benzodiazepine (N05BA) (y/n).
        ii. Rivastigmin (N06DA03) (y/n).
        iii. Other (y/n).
    c. Hypnotics and sleeping pills (y/n) if any of the below.
        i. Zopiclon (N05CF01).
        ii. Zolpidem (N05CF02).
        iii. Triazolam (N05CD05).
        iv. Lormetazepam (N05CD06).
        v. Nitrazepam (N05CD02).
        vi. Chloralhydrate (N05CC01).
        vii. Melatonin (N05CH01).
        viii. Promethazine (R06AD02).
        ix. Other.

Day 90 after ICU admission

20. Vital status (dead/alive) (if relevant, date of death).
21. Discharged from ICU (Y/N and date).
22. Discharge from hospital (Y/N and date).

6 month after ICU admission

23. Cognitive impairment assessment with RBANS (40 to 160 points).

6.2 Unit/department evaluation

24. Type of hospital (< 500 beds/500-1000 beds/ > 1000 beds).
25. Type of ICU (Medical/Surgical/Mixed/Specialised).
26. Number of ICU beds open for admission.
27. Does your ICU have a general guideline/protocol for identifying delirium?
28. Does your ICU have a general guideline/protocol for interventions of delirium?
29. When do you intervene for delirium?
30. Are patient restrained in your ICU (never, sometimes, often)?
31. Average nurse to patient ratio during the day, evenings and nights.

7. Statistical Methods

7.1 Sample size estimation

In a case control study with a simple random sampling, and an estimated treatment prevalence of delirious patients treated with haloperidol in the ICU of 13% (preliminary data at Dept. of Intensive Care 4131, Rigshospitalet, Copenhagen from May 2014), inclusion of at least **1000** patients is required to yield a 95% confidence interval of a rate of haloperidol use of 11%-15%. With expected mortality rate of 30% 1000 patients will yield a 95% confidence interval of 23% - 38% for 90-day mortality. Fifty ICUs are estimated to include this sample of patients within 14 days [17].

7.2 Population to be analysed

All patients who are acutely admitted to one of the study ICUs at any point of the 14-day study period (the 1st day at 00:01 to the last day at 23:59).

7.3 Statistical plan

The number of patients receiving haloperidol (totally and regularly, as needed and mixed dosing) will be presented as frequencies (% with 95% confidence intervals). Numeric data will be given as medians (interquartile range [IQR]). We will compare differences in baseline characteristics using non-parametric tests between patients who receive haloperidol and patients who do not receive haloperidol. To assess risk factors for the use of haloperidol, we will do multivariate analyses including patient characteristics (age, dialysis, shock and mechanical ventilation and delirium in the first 24 h of admission) and ICU characteristic (university hospital, guidelines for identifying and/or treating delirium and average staff-patient ratio). To assess if haloperidol is an independent predictor of 90-day mortality, we will do multivariate analysis including patient characteristics (age, dialysis, shock and mechanical ventilation and delirium in the first 24 h of admission) and time. We will do exploratory analyses on the interaction between delirium and use of haloperidol and the patient-relevant outcomes measure (mortality, days alive without mechanical ventilation and days alive and out for hospital). All statistical tests will be 2-tailed and $p<.05$ considered statistically significant.

8. Data Handling

8.1 Data collection and storing records

An electronic case report form, CRF (eCRF) will be programmed by Copenhagen Trial Unit (OpenClinica). Data will continuously be collected in electronic case report forms (e-CRFs) from source data (patient records and laboratory reports) throughout the whole study. Subsequently, the data from the e-CRFs will be exported as an electronic study database and stored as required by the data protection authorities in each participating country.

8.2 Data management and quality control

The e-CRF will contain an automated logic control system to minimize data entry errors and check for completeness. The local investigators will be responsible for CRF completeness and accuracy against the source data. No data analyses will be done until an accurate database has been assured.

8.3 Study Record Retention

All research data and study related documents will be stored confidentially and securely for 15 years in CRIC. The members of the study Management Committee and CRICs Steering Committee

will have access to the stored data. Upon request, principal investigators will get data from their own unit.

9. Administrative Aspects

9.1 Confidentiality

Subject confidentiality is strictly held in trust by the participating investigators, research staff, and the sponsoring institution. The study protocol, documentation, data and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party, without prior written approval of the study Management Committee.

9.1 Ethical consideration

This is a low risk study and consent for participating will be obtained according to the national law.

9.2 Approvals

This protocol and any subsequent modifications will be reviewed and approved by the Ethics committees, National Board of Health and National Data Protection Agencies according to national law.

9.3 Modifications of the protocol

The study will be conducted in compliance with the current version of this protocol. Any change to the protocol document that affects the scientific intent, study design, or results is considered an amendment, and therefore will be written and filed as an amendment to the protocol.

9.4 Financial Disclosure and obligations

All participating researchers are obliged to declare any conflicts of interest or financial interest related to the study.

10. Use of Data and Publications Policy

Upon study completion the main manuscript will be submitted to one of the major clinical journals regardless of the result, and the results will in any case be published at the CRIC home page: *(http://www.CRIC.nu).* The Management Committee holds the primary responsibility for publication of the main results of the study.

The listing of authors will be as follows: M Oxenbøll-Collet will be first author and A. Perner as last author. The national investigators and Management Committee members will be granted with co-authorship by the Management Committee if they fulfil the Vancouver definitions for authorship. All investigators will appear as collaborators. The members of the AID-ICU research group and other people who contribute considerably will be investigators and appear in an appendix to the main paper. The funding sources will have no influence on data handling or analyses or writing of the manuscript.

Sub-studies are encouraged and a protocol (CRIC templet) has to be submitted to the Management Committee for approval prior to the release of data.

11. References

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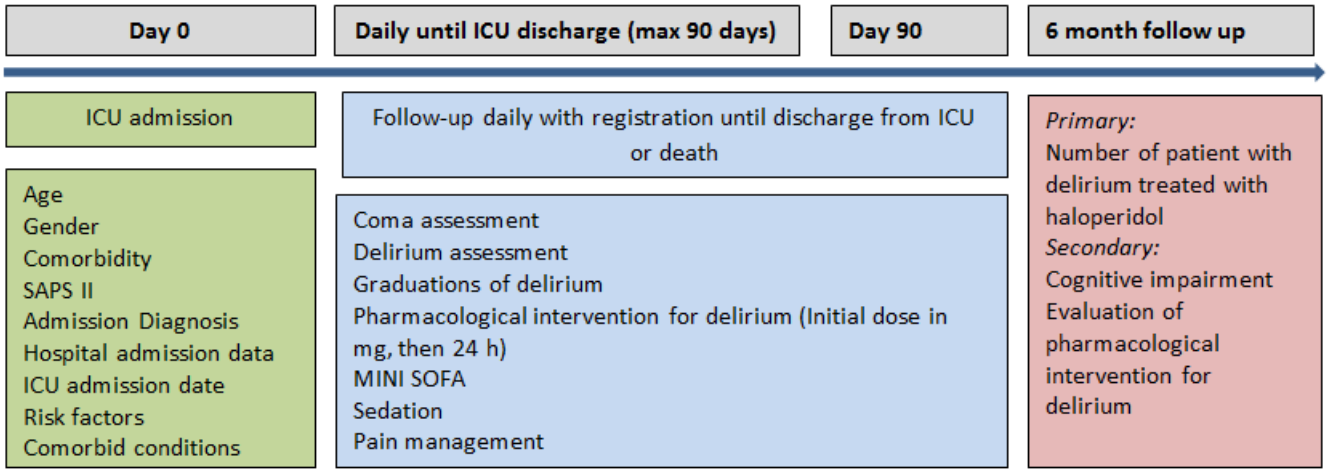
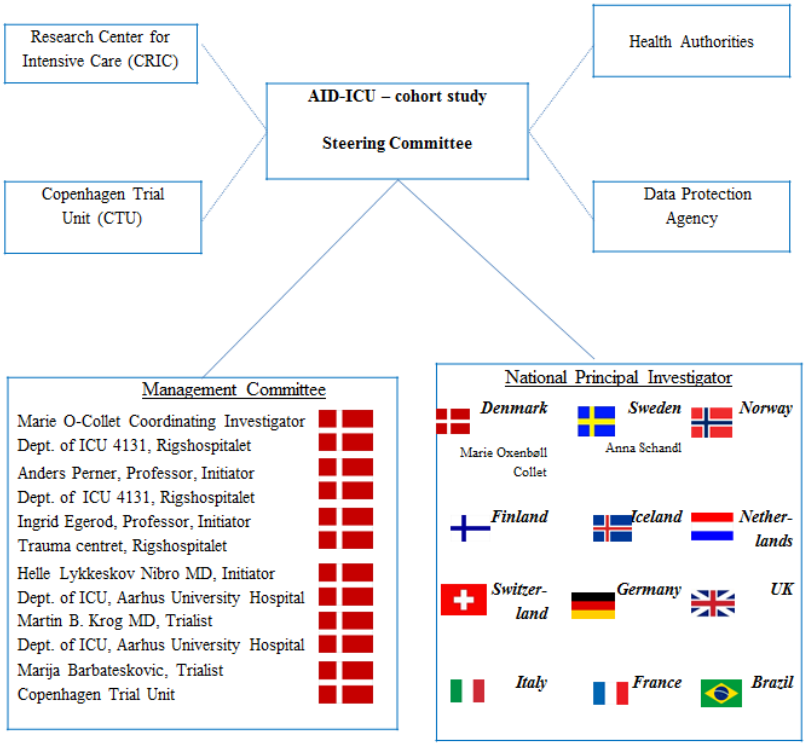
Appendix 1

Timeline and study diagram



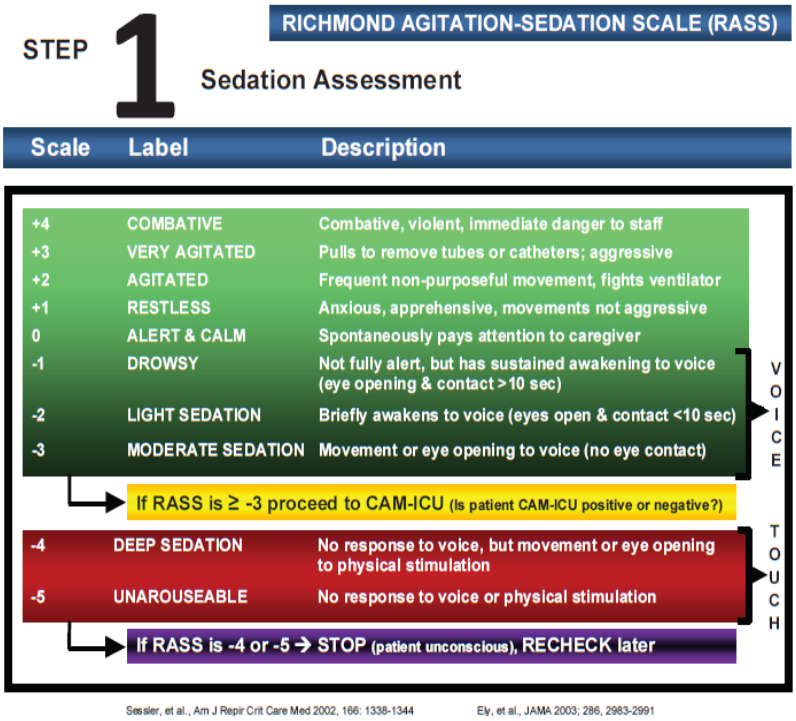
Appendix 2

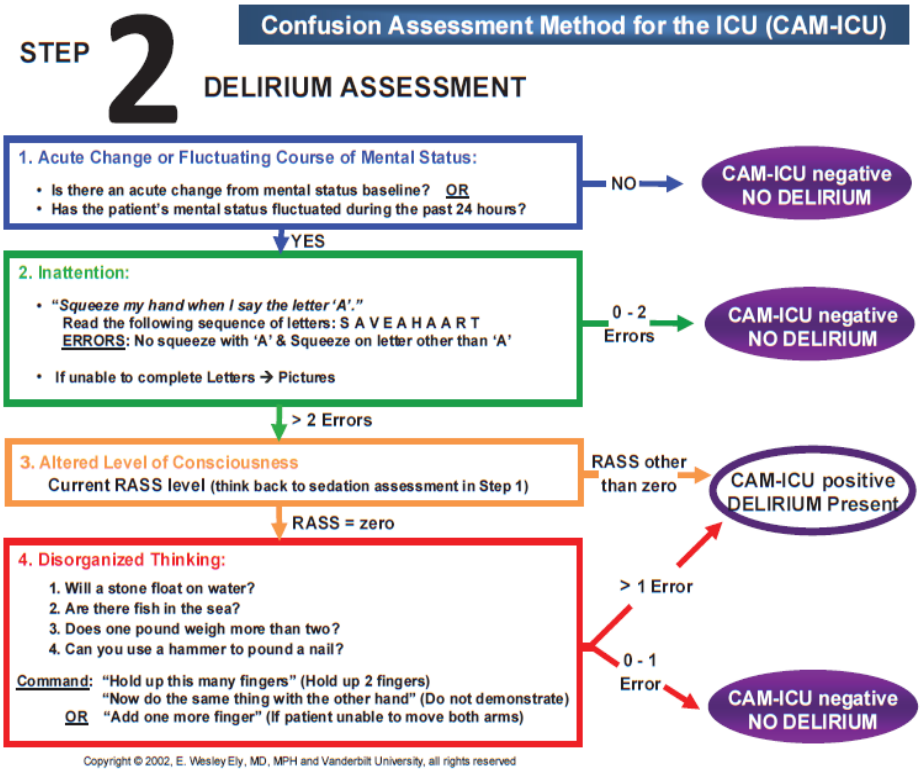
Diagram for principal country investigators



Appendix 3

Assessment tools for detecting of delirium in ICU patients.




STEP 2
Confusion Assessment Method for the ICU (CAM-ICU)
DELIRIUM ASSESSMENT
1. Acute Change or Fluctuating Course of Mental Status:
• Is there an acute change from mental status baseline? OR
• Has the patient's mental status fluctuated during the past 24 hours?
NO
CAM-ICU negative NO DELIRIUM
YES
2. Inattention:
• "Squeeze my hand when I say the letter 'A'."
Read the following sequence of letters: S A V E A H A A R T
ERRORS: No squeeze with 'A' & Squeeze on letter other than 'A'
• If unable to complete Letters → Pictures
0 - 2 Errors
CAM-ICU negative NO DELIRIUM
> 2 Errors
3. Altered Level of Consciousness
Current RASS level (think back to sedation assessment in Step 1)
RASS other than zero
CAM-ICU positive DELIRIUM Present
RASS = zero
4. Disorganized Thinking:
1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two?
4. Can you use a hammer to pound a nail?
Command: "Hold up this many fingers" (Hold up 2 fingers)
"Now do the same thing with the other hand" (Do not demonstrate)
OR "Add one more finger" (If patient unable to move both arms)
> 1 Error
0 - 1 Error
CAM-ICU negative NO DELIRIUM
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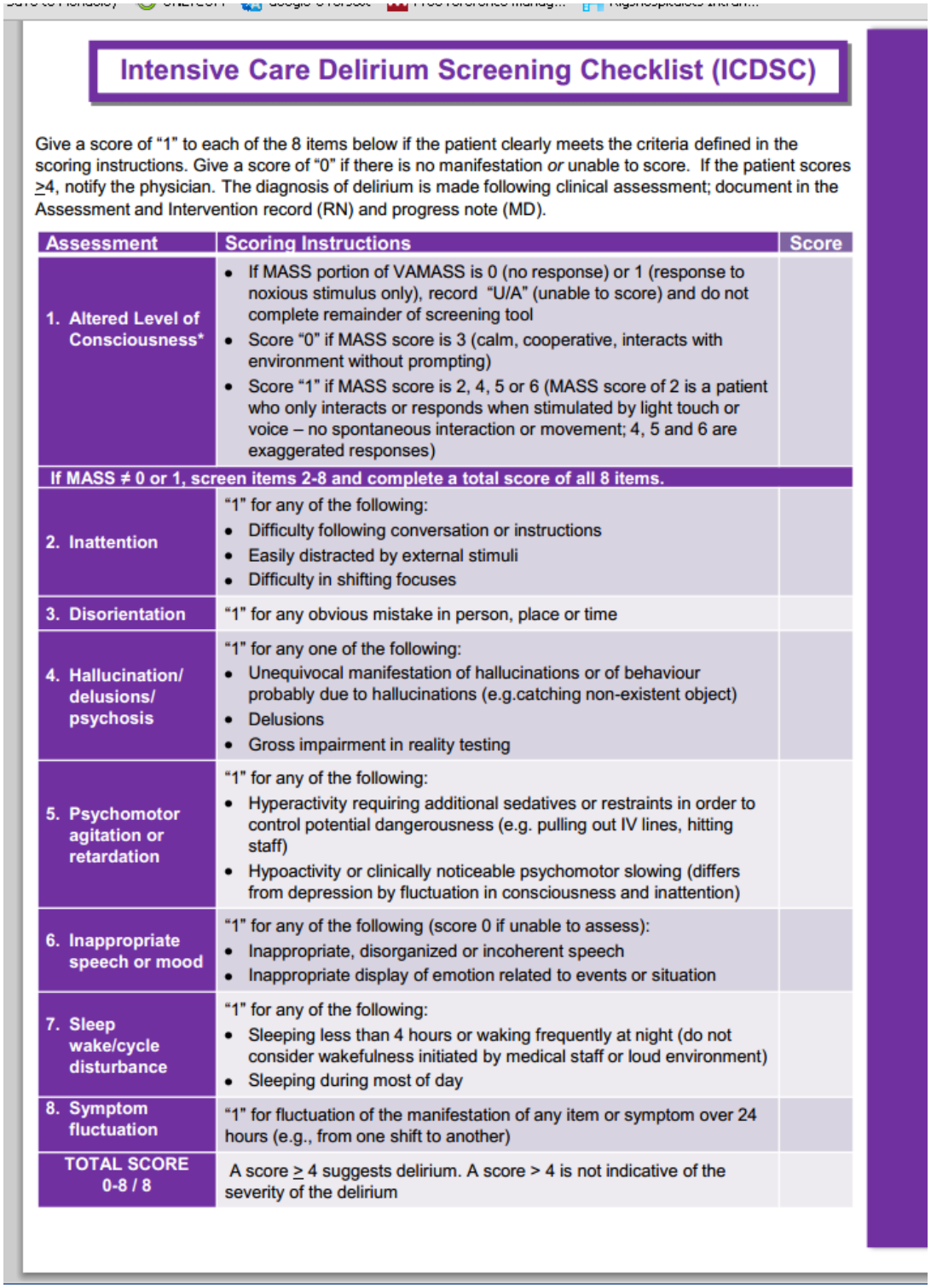

Intensive Care Delirium Screening Checklist (ICDSC)

Give a score of "1" to each of the 8 items below if the patient clearly meets the criteria defined in the scoring instructions. Give a score of "0" if there is no manifestation *or* unable to score. If the patient scores ≥4, notify the physician. The diagnosis of delirium is made following clinical assessment; document in the Assessment and Intervention record (RN) and progress note (MD).

Assessment	Scoring Instructions	Score
1. Altered Level of Consciousness*	• If MASS portion of VAMASS is 0 (no response) or 1 (response to noxious stimulus only), record "U/A" (unable to score) and do not complete remainder of screening tool • Score "0" if MASS score is 3 (calm, cooperative, interacts with environment without prompting) • Score "1" if MASS score is 2, 4, 5 or 6 (MASS score of 2 is a patient who only interacts or responds when stimulated by light touch or voice – no spontaneous interaction or movement; 4, 5 and 6 are exaggerated responses)	
If MASS ≠ 0 or 1, screen items 2-8 and complete a total score of all 8 items.		
2. Inattention	"1" for any of the following: • Difficulty following conversation or instructions • Easily distracted by external stimuli • Difficulty in shifting focuses	
3. Disorientation	"1" for any obvious mistake in person, place or time	
4. Hallucination/ delusions/ psychosis	"1" for any one of the following: • Unequivocal manifestation of hallucinations or of behaviour probably due to hallucinations (e.g.catching non-existent object) • Delusions • Gross impairment in reality testing	
5. Psychomotor agitation or retardation	"1" for any of the following: • Hyperactivity requiring additional sedatives or restraints in order to control potential dangerousness (e.g. pulling out IV lines, hitting staff) • Hypoactivity or clinically noticeable psychomotor slowing (differs from depression by fluctuation in consciousness and inattention)	
6. Inappropriate speech or mood	"1" for any of the following (score 0 if unable to assess): • Inappropriate, disorganized or incoherent speech • Inappropriate display of emotion related to events or situation	
7. Sleep wake/cycle disturbance	"1" for any of the following: • Sleeping less than 4 hours or waking frequently at night (do not consider wakefulness initiated by medical staff or loud environment) • Sleeping during most of day	
8. Symptom fluctuation	"1" for fluctuation of the manifestation of any item or symptom over 24 hours (e.g., from one shift to another)	
TOTAL SCORE 0-8 / 8	A score ≥ 4 suggests delirium. A score > 4 is not indicative of the severity of the delirium	

Delirium Observation Screening (Dos) Scale (version 0 - 1)

Date:
Patient Name:

	OBSERVATION The patient	Day shift			Evening shift			Night shift			TOTAL SCORE TODAY (0 - 39)
		never	sometimes - always	unable	never	sometimes - always	unable	never	sometimes - always	unable	
1	Dozes off during conversation or activities	0	1	-	0	1	-	0	1	-	
2	Is easily distracted by stimuli from the environment	0	1	-	0	1	-	0	1	-	
3	Maintains attention to conversation or action	1	0	-	1	0	-	1	0	-	
4	Does not finish question or answer	0	1	-	0	1	-	0	1	-	
5	Gives answers that do not fit the question	0	1	-	0	1	-	0	1	-	
6	Reacts slowly to instructions	0	1	-	0	1	-	0	1	-	
7	Thinks they are somewhere else	0	1	-	0	1	-	0	1	-	
8	Knows which part of the day it is	1	0	-	1	0	-	1	0	-	
9	Remembers recent events	1	0	-	1	0	-	1	0	-	
10	Is picking, disorderly, restless	0	1	-	0	1	-	0	1	-	
11	Pulls IV tubing, feeding tubes, catheters etc.	0	1	-	0	1	-	0	1	-	
12	Is easily or suddenly emotional	0	1	-	0	1	-	0	1	-	
13	Sees/hears things which are not there	0	1	-	0	1	-	0	1	-	
TOTAL SCORE PER SHIFT (0 - 13)											
DOS SCALE FINAL SCORE = TOTAL SCORE TODAY / 3											

⇓

DOS SCALE Final Score	< 3	Not delirious
	≥ 3	Probably delirious

Table 1. The Glasgow Coma Scale
And The Glasgow Outcome Scale.

Glasgow Coma Scale	
Eye opening	
Spontaneous	4
To speech	3
To pain	2
No response	1
Verbal response	
Alert and oriented	5
Disoriented	4
Speaking but nonsensical	3
Moans	2
No response	1
Motor response	
Follows commands	6
Localizes pain	5
Withdraws to pain	4
Decorticate flexion	3
Decerebrate extension	2
No response	1
Grading of TBI:*	
Mild†	13-15
Moderate	9-12
Severe	3-8

* A single GCS score is neither diagnostic of TBI nor predictive of outcome.
† Because of the 10% or greater incidence of craniotomy in these patients, many authorities now consider a GCS of 13 to represent moderate brain injury.

Glasgow Outcome Score		
D	=	Dead
PVS	=	Persistent vegetative state
SD	=	Severe disability
MD	=	Moderate disability
GR	=	Good recovery