Delirium

Bjørn Erik Neerland
Overlege/forsker
Geriatrisk avdeling OUS
Oslo Delirium Research Group

Legevaktskonferansen

Fredrikstad 14 september 2023

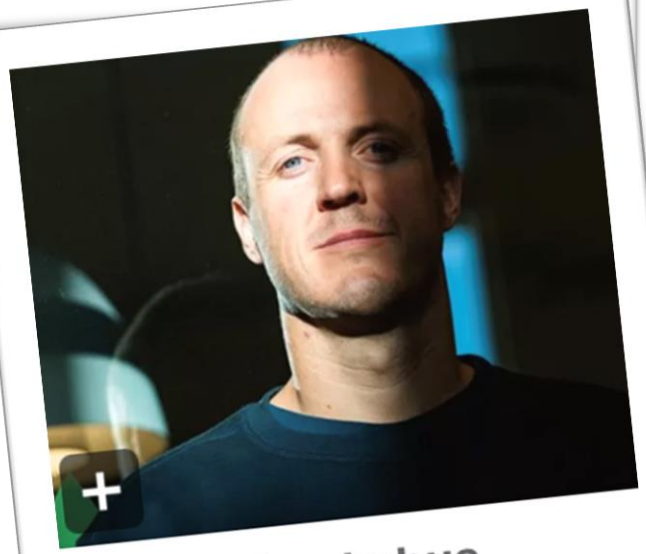
«Jeg har alltid innbilt meg at en slik tilstand ville vært helt kaos. Men det var ikke kaos. Jeg var ikke et øyeblikk i tvil om at dette var virkeligheten.»

«Lønner det seg for meg å svare?»

«Et av budskapene til fagfolk er at jeg fikk med meg mye mer enn de trodde»

Telia N 4G 12:16 30 %

VG Logg inn



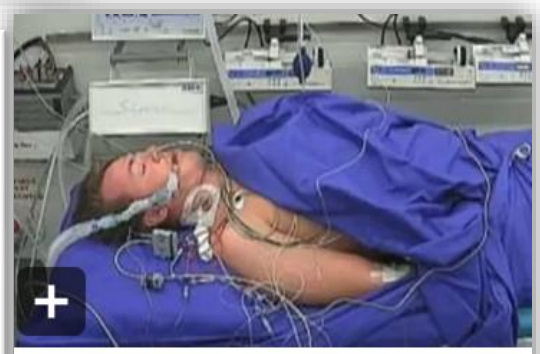
1 av 5 på sykehus rammes:

Stian (33) fikk delirium

Han ble overført til Ullevål sykehus hvor han lå i et trykkammer som en del av behandlingen.

Da kom den verste opplevelsen med delirium.

– Jeg var inne i en spillkonsoll, som var veldig fancy, men jeg satt fast inne i den, og kom meg ingen vei. Jeg prøvde å spille spill for å løse gåten, men klarte aldri å runde det. I tillegg var jeg i Asia på et luksushotell, hvor jeg fikk strikkepinner gjennom kroppen, og ble spiddet. Og det bare fortsatte og fortsatte.



1 av 5 på sykehus rammes:

Stian (33) fikk delirium

i går, 15:13

Jeg har selv opplevd to døgn med delirium under sykehusopphold for en omfattende infeksjon. Mine deliriumvarianter var fargerike og i grunnen godartede, men frakoblet den eksisterende virkelighet. To snille og hvitkledte sykepleiere var i min daværende verden utstyrt med englevinger; en klar hyllest til sykehusvesenet!

↑ 1 ↓ 0 Logg inn for å svare

Nasjonal deliriumkonferanse

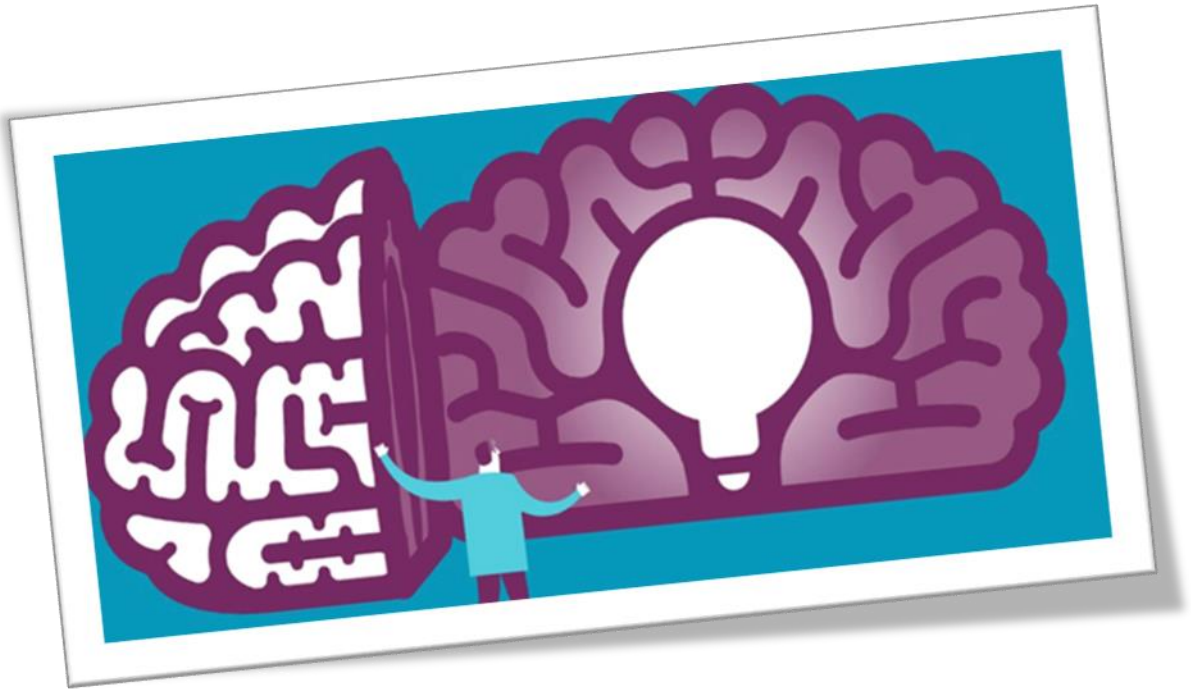
- Pasienterfaringer
- Opplæringsmateriell
- 4AT
- Medisinbruk, behandlingsplaner
- Interaktive sesjoner
- Video og e-læring
- Erfaringer fra ulike avdelinger

Neste mulighet
18 oktober 2024!

bjonee@ous-hf.no

Hva vil jeg snakke om?

- Hva er delirium
  - Akutt endring i bevissthet og oppmerksomhet
- Hvem får delirium?
- Hvor vanlig er delirium?
- Forebygging – tidlig oppdagelse - behandling



HVA ER DELIRIUM?

Delirium - diagnosen

- Delirium er en akutt forstyrrelse i **oppmerksomhet** og **bevissthet/klarhet**

- Tenderer til å **fluktuere**
- Påvirkning av **kognisjon**

- Delirium er per definisjon forårsaket av en **underliggende medisinsk tilstand**, forgiftning, abstinens eller en kombinasjon av flere årsaker

Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (AmericanPsychiatricAssociation, 2013)

Delirium - motoriske subtyper

- Hyperaktiv - «agitert»
  - Økt og ukontrollert motorisk aktivitet
  - Rastløs, vandrende
- Hypoaktiv – «stille»
  - Reduserte og langsomme motoriske funksjoner
  - Nedsatt reaksjonsevne
  - Mindre og tregere tale
- Blandet

Meagher 2008, 2014

Delirium vs demens

RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Regional cerebral hypometabolism on 18F-FDG PET/CT scan in delirium is independent of acute illness and dementia

Anita Nitchingham[1,2] | Jarett Vanz-Brian Pereira[2] | Eva A. Wegner[2,3] | Vincent Oxenham[4,5] | Jacqueline Close[1,2,6] | Gideon A. Caplan[1,2]

3	Cognition	**Kognisjon**
2	Attention	**Oppmerksomhet**
	Awareness	**«Klarhet»**
	Alertness	
1	Arousal	**Døsig-våken-agitert**

DELIRIUM

DEMENS

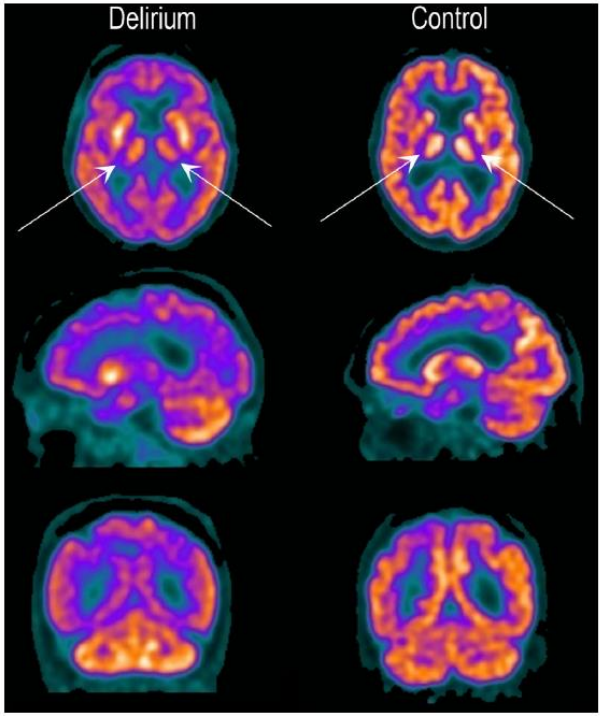


FIGURE 2 ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) images. FDG-PET during delirium compared to control. Top: axial; middle: sagittal; bottom: coronal slices. The delirium scan is an 89-year-old female with delirium but no dementia with acute gastroenteritis. The control scan is a cognitively intact 80-year-old male with pneumonia and acute kidney injury. Darker colors indicate lower metabolism. There is relative hypometabolism in the thalamus bilaterally (arrows) and also throughout the cerebral cortex in the delirious patient compared to cognitively intact control. During

Neerland, Krogseth, Wyller. *Hvordan beskrive delirium?* Tidsskriftet 2018

4AT

Screening for delirium og kognitiv svikt

[1] ÅRVÅKENHET (forholder seg normalt til omgivelsene)

Pasienten virker tydelig døsig (dvs. vanskelig å vekke og/ eller er åpenbart søvnig ved undersøkelsen) eller motorisk urolig/hyperaktiv. Observer pasienten. Hvis pasienten sover, forsøk å vekke pasienten med vanlig stemme eller ved varsom berøring på skulderen. Be pasienten oppgi navn og adresse til hjelp med vurderingen.

Normal (helt årvåken, ikke urolig ved undersøkelse)	**0**
Lett søvnig < 10 sekunder etter oppvåkning, deretter normal	**0**
Tydelig unormal(t)	**4**

[2] AMT4 (Forkortet mental vurdering)

Alder, fødselsdato, sted (navnet på sykehuset eller bygning), årstall

Ingen feil	**0**
1 feil	**1**
2 feil eller flere/ikke testbar	**2**

[3] OPPMERKSOMHET

Spør pasienten: "Kan du i baklengs rekkefølge nevne for meg årets måneder, begynn med desember»
Å hjelpe pasienten med et innledende spørsmål «hva er måneden før desember?» er tillatt

Rekkefølgen av årets måneder baklengs	Oppgir 7 måneder eller flere korrekt	**0**
	Begynner, men klarer <7 måneder/ avslår å begynne	**1**
	Ikke testbar (er uvel, døsig, uoppmerksom)	**2**

[4] AKUTT ENDRING ELLER FLUKTUASJON I TILSTAND

Holdepunkter for betydelige endringer eller fluktuasjoner knyttet til: årvåkenhet, kognisjon, annen mental funksjon
(F.eks. paranoide symptomer, hallusinasjoner) oppstått i løpet av de siste to uker og fremdeles tilstede de siste 24 timer

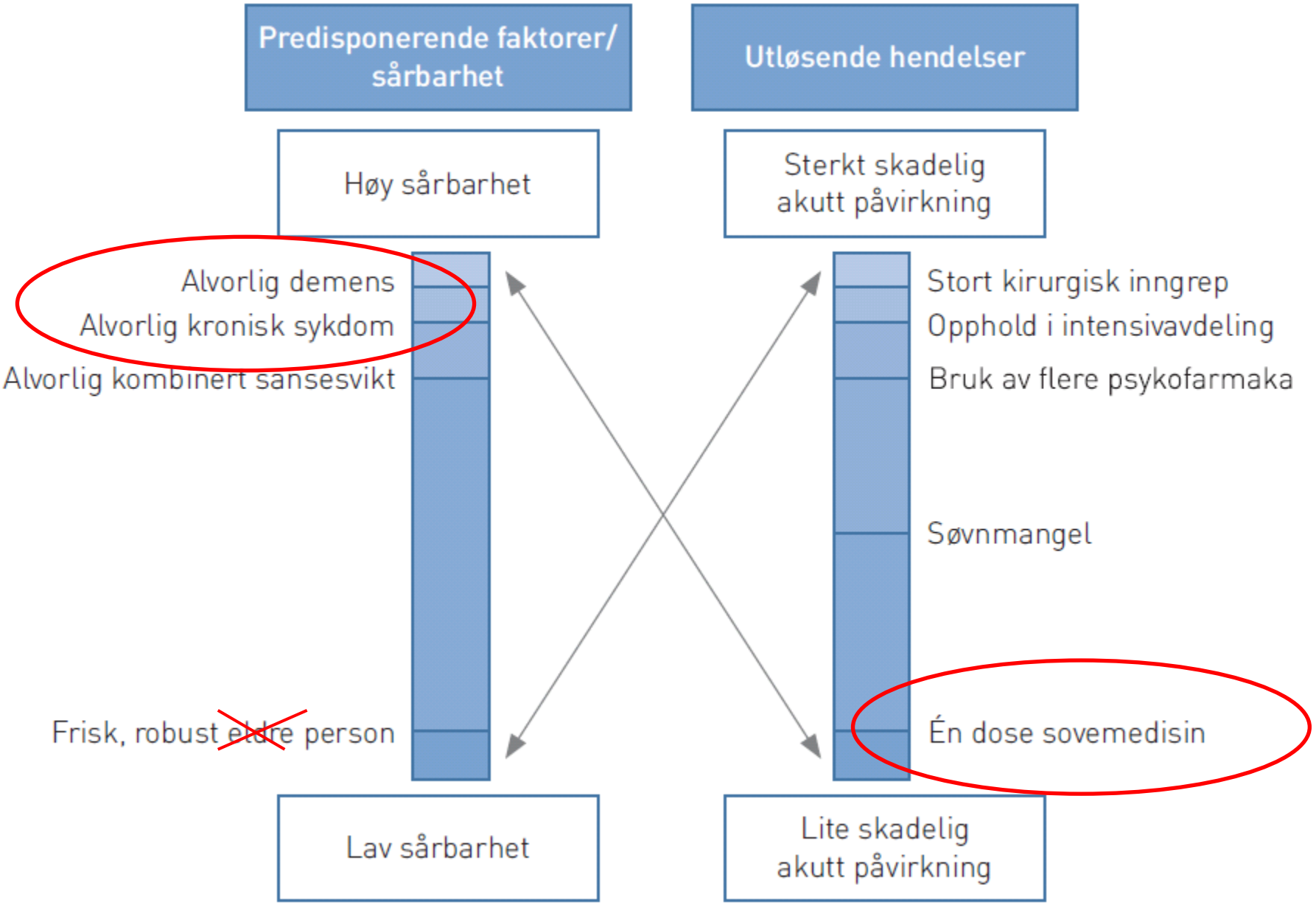
Nei	**0**
Ja	**4**

www.the4at.com

≥4: mulig delirium og eller kognitiv svikt
1-3: mulig kognitiv svikt
0: delirium eller alvorlig kognitiv svikt usannsynlig (men fremdeles mulig delirium hvis informasjon under punkt [4] er ufullstendig)

4AT SKÅR ☐

HVEM FÅR DELIRIUM?


Predisponerende faktorer/ sårbarhet
Utløsende hendelser
Høy sårbarhet
Sterkt skadelig akutt påvirkning
Alvorlig demens
Alvorlig kronisk sykdom
Alvorlig kombinert sansesvikt
Stort kirurgisk inngrep
Opphold i intensivavdeling
Bruk av flere psykofarmaka
Søvnmangel
Frisk, robust eldre person
Én dose sovemedisin
Lav sårbarhet
Lite skadelig akutt påvirkning

Age and Ageing 2022; **51**: 1–9
https://doi.org/10.1093/ageing/afac051

RESEARCH PAPER

Positive scores on the 4AT delirium assessment tool at hospital admission are linked to mortality, length of stay and home time: two-centre study of 82,770 emergency admissions

Atul Anand[1,†], Michael Cheng[2,†], Temi Ibitoye[3], Alasdair M.J. Maclullich[3,‡], Emma R.L.C. Vardy[4,5,‡]

[1]Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK
[2]Salford Care Organisation, Northern Care Alliance NHS Foundation Trust, Salford, UK
[3]Edinburgh Delirium Research Group, Ageing and Health, Usher Institute, University of Edinburgh, Edinburgh, UK
[4]Salford Care Organisation, Northern Care Alliance NHS Foundation Trust, Stott Lane, Salford, UK
[5]NIHR Applied Research Collaboration Greater Manchester, University of Manchester, Manchester, UK

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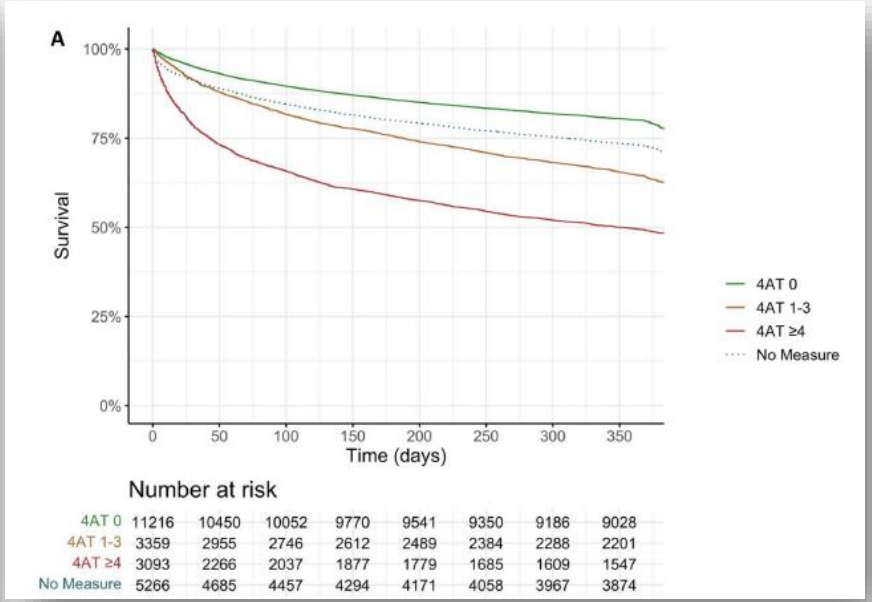
†Shared first authorship ‡Shared senior authorship

Abstract

Background: Studies investigating outcomes of delirium using large-scale routine data are rare. We performed a two-centre study using the 4 'A's Test (4AT) delirium detection tool to analyse relationships between delirium and 30-day mortality, length of stay and home time (days at home in the year following admission).
Methods: The 4AT was performed as part of usual care. Data from emergency admissions in patients ≥65 years in Lothian, UK ($n = 43,946$) and Salford, UK ($n = 38,824$) over a period of ~3 years were analysed using logistic regression models adjusted for age and sex.
Results: 4AT completion rates were 77% in Lothian and 49% in Salford. 4AT scores indicating delirium (≥4/12) were present in 18% of patients in Lothian, and 25% of patients in Salford. Thirty-day mortality with 4AT ≥4 was 5.5-fold greater than the 4AT 0/12 group in Lothian (adjusted odds ratio (aOR) 5.53, 95% confidence interval [CI] 4.99–6.13) and 3.4-fold greater in Salford (aOR 3.39, 95% CI 2.98–3.87). Length of stay was more than double in patients with 4AT scores of 1–3/12 (indicating cognitive impairment) or ≥ 4/12 compared with 4AT 0/12. Median home time at 1 year was reduced by 112 days (Lothian) and 61 days (Salford) in the 4AT ≥4 group ($P < 0.001$).
Conclusions: Scores on the 4AT used at scale in practice are strongly linked with 30-day mortality, length of hospital stay and home time. The findings highlight the need for better understanding of why delirium is linked with poor outcomes and also the need to improve delirium detection and treatment.

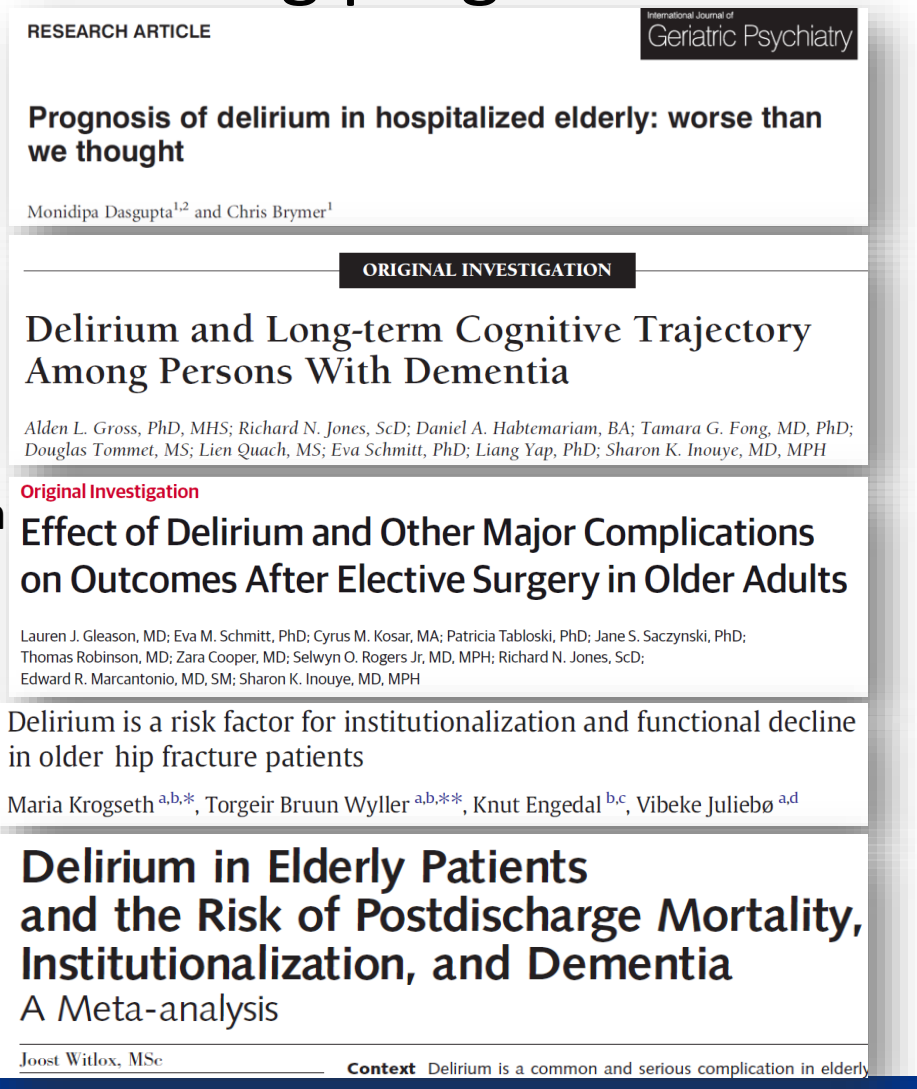
Keywords: delirium, hospitalisation, geriatrics, dementia, 4 'A's Test (4AT), older people, emergency department (ED)



- Rutinedata
- 4AT ≠ 0 : dobbelt så langt sykehusopphold
- 4AT ≥4 vs 0 : 3-5 ganger høyere dødelighet (30 d)

Delirium er forbundet med dårlig prognose

- Vond og skremmende opplevelse
- Fall
- Lengre sykehusopphold
- Tap av funksjon
- Kognitiv forverring
- En vesentlig postoperativ komplikasjon
- Behov for sykehjem
- Død



RESEARCH ARTICLE

International Journal of Geriatric Psychiatry

Prognosis of delirium in hospitalized elderly: worse than we thought

Monidipa Dasgupta[1,2] and Chris Brymer[1]

ORIGINAL INVESTIGATION

Delirium and Long-term Cognitive Trajectory Among Persons With Dementia

Alden L. Gross, PhD, MHS; Richard N. Jones, ScD; Daniel A. Habtemariam, BA; Tamara G. Fong, MD, PhD; Douglas Tommet, MS; Lien Quach, MS; Eva Schmitt, PhD; Liang Yap, PhD; Sharon K. Inouye, MD, MPH

Original Investigation

Effect of Delirium and Other Major Complications on Outcomes After Elective Surgery in Older Adults

Lauren J. Gleason, MD; Eva M. Schmitt, PhD; Cyrus M. Kosar, MA; Patricia Tabloski, PhD; Jane S. Saczynski, PhD; Thomas Robinson, MD; Zara Cooper, MD; Selwyn O. Rogers Jr, MD, MPH; Richard N. Jones, ScD; Edward R. Marcantonio, MD, SM; Sharon K. Inouye, MD, MPH

Delirium is a risk factor for institutionalization and functional decline in older hip fracture patients

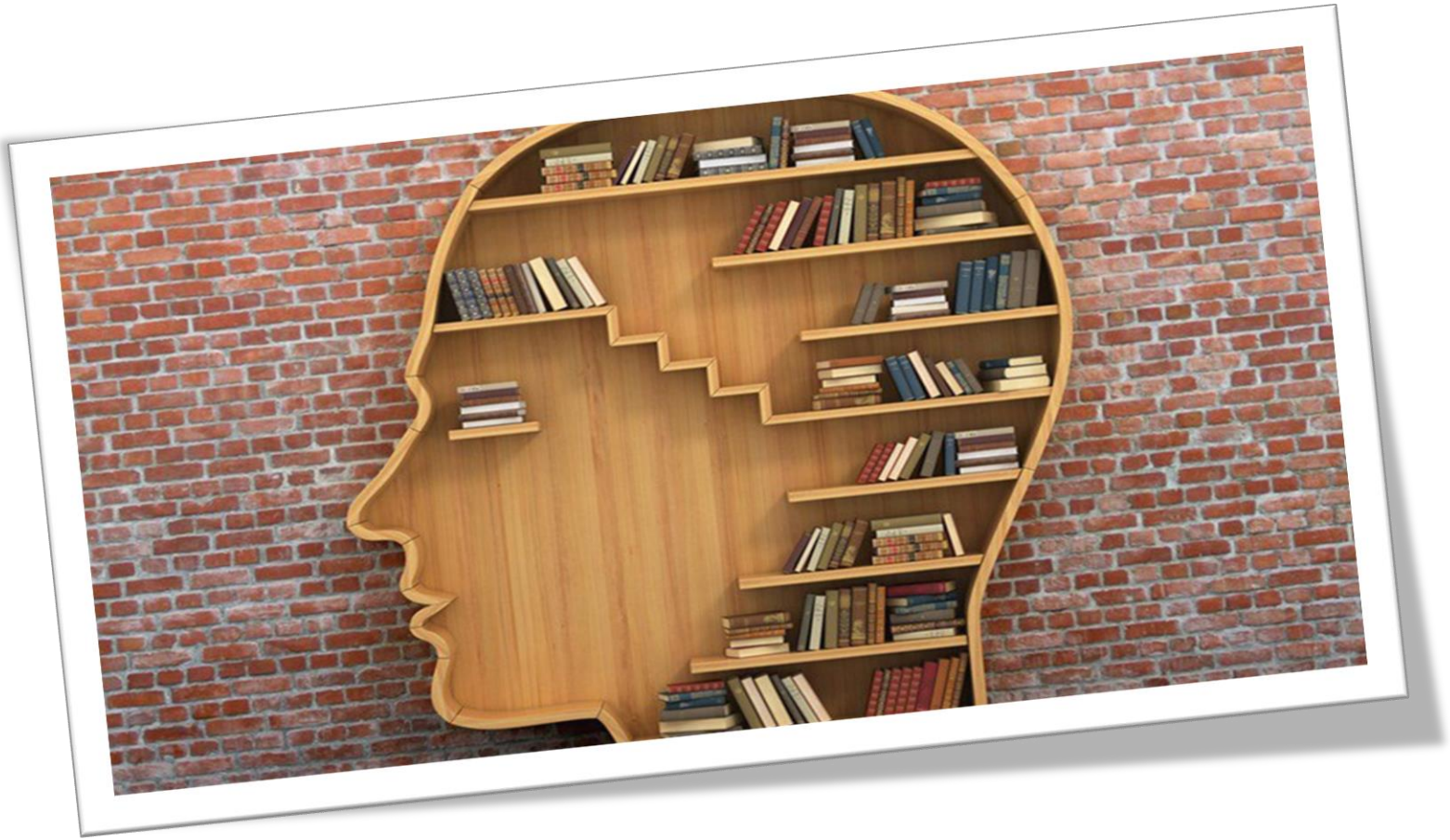
Maria Krogseth [a,b,*], Torgeir Bruun Wyller [a,b,**], Knut Engedal [b,c], Vibeke Juliebø [a,d]

Delirium in Elderly Patients and the Risk of Postdischarge Mortality, Institutionalization, and Dementia

A Meta-analysis

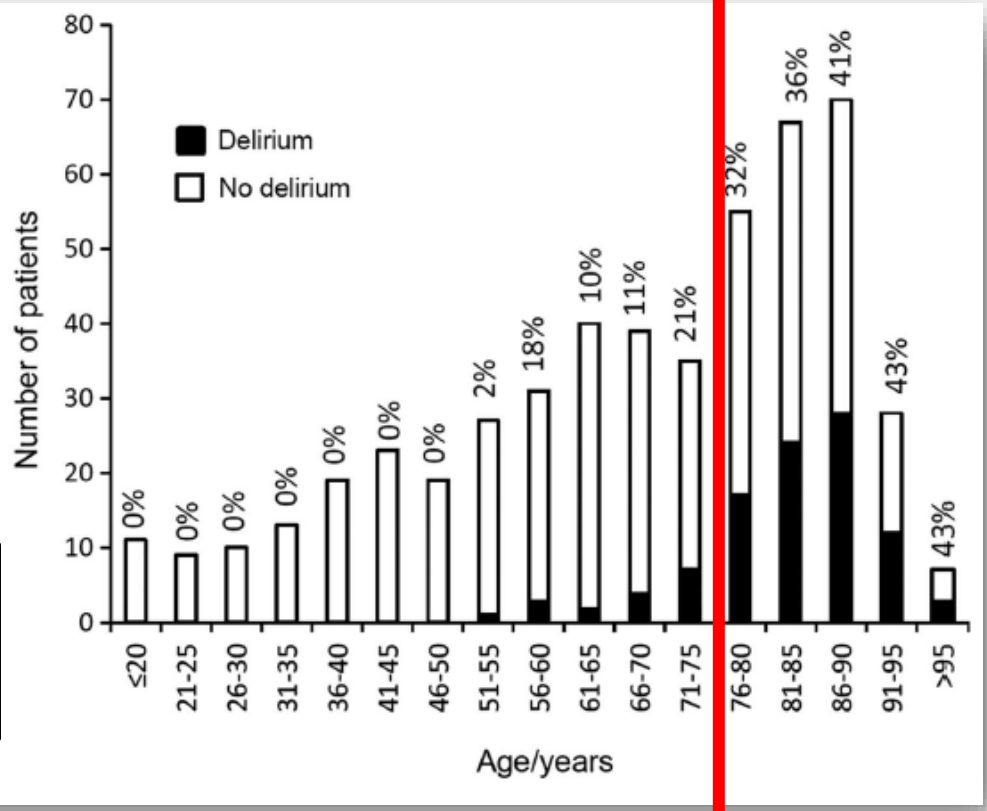
Joost Witlox, MSc

Context Delirium is a common and serious complication in elderly



HVOR VANLIG ER DELIRIUM?

Figure 1 Age-specific rates of delirium in an unselected consecutive cohort of 503 patients admitted to one team in acute general medicine over a 4-month period, showing the proportion with delirium shaded black in each age category.



Av de som hadde delirium:

- 70% ved innleggelse
- 30% utviklet etter innkomst

75+

Delirium in nursing homes

- incidence, predisposing and precipitating factors -

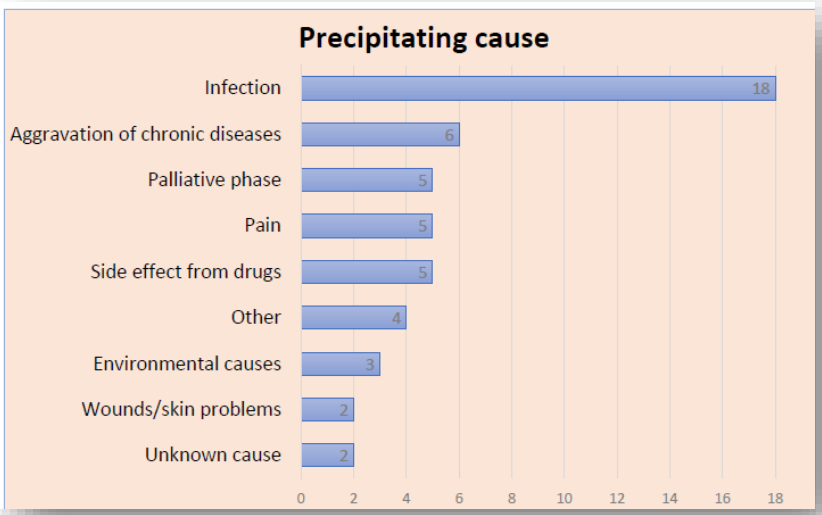
Wenche Helen Skretteberg [1,2], Ingunn Holmefoss Hovland [3], Leiv Sandvik [2], Maria Krogseth [2, 4, 5]

3 sykehjem (fast plass), 145 pasienter
2 måneder

Legekontakt pga akutt sykdom

- Deliriumvurdering (OSLA + CAM)

Resultater:
77 legekontakter (57 pas)
34 av 145 pas **(23%)** fikk delirium



Presentert som poster på European Delirium Association, Edinburgh sept 2019

Delirium, neurofilament light chain, and progressive cognitive impairment: analysis of a prospective Norwegian population-based cohort

Maria Krogseth, Daniel Davis, Thomas Andrew Jackson, Henrik Zetterberg, Leiv Otto Watne, Morten Lindberg, Petronella Chitalu, Alex Tsui, Geir Selbæk, Torgeir Bruun Wyller

- Hjemmeboende med hj spl
  - ➢ n=210, 53% demens
- MoCA/6.mnd
- Deliriumvurdering (DSM-5) ved akutt sykdom eller innleggelse
  - ➢ 89/210 (42%) i løpet av 2 år (2066 vurderinger)

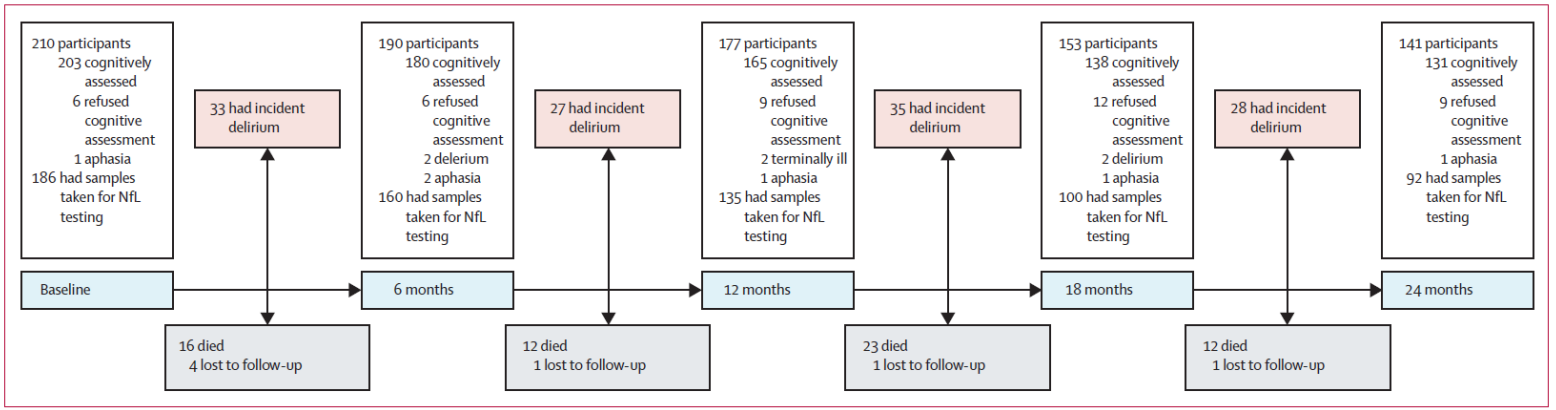


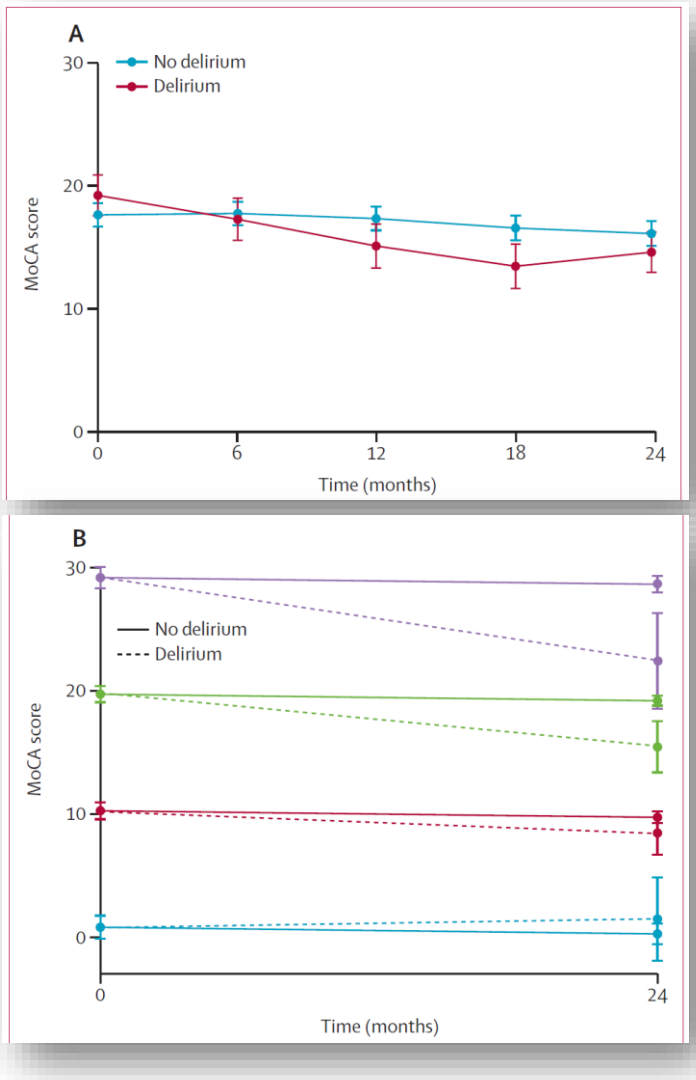
Figure 1: **Flow diagram**
One participant was not assessed at 18 months but remained in the study for the 24-month home visit. NfL=neurofilament light chain.

Delirium, neurofilament light chain, and progressive cognitive impairment: analysis of a prospective Norwegian population-based study

Maria Krogseth, Lancet HL 2023

CASCADE

- Incident delirium was independently associated with a -1.5-point (95% CI -2.9 to -0.1 points) decrease on MoCA at the next 6-month follow-up
- The largest cognitive decline being observed in those with better baseline cognition
- Incident delirium was associated with increased median NfL levels during admission and at follow-up



FORSKNINGSFRONTEN

Farlig forvirring

Delirium bidrar til demens. Bør det satses mer på å bekjempe akutt forvirring?

Scenarioet er helt dagligdags på ethvert norsk sykehus. Bestemor har falt og brukket lårhalsen. Kirurgene har reparert hoften hennes, hun er vekket fra narkosen og får smertestillende, men nå er hun fjern, forvirret og urolig. Hun skjønner ikke hvor hun er, tar feil av folk og snakker usammenhengende. Det er skremmende for familien, men leger og sykepleiere kan berolige med at dette er helt vanlig og forbigående. Tilstanden kalles *delirium* og forekommer hyppig hos eldre og skrøpelige pasienter, typisk utløst av akutte påkjenninger som skade, sykdom eller legemidler.

Etter noen dager kommer bestemor gradvis til seg selv igjen og kan etter hvert reise hjem. Men episoden indikerer en sårbarhet. Det er velkjent at gjennomgått delirium er assosiert med økt risiko for senere demens. Men hva skyldes dette? En hypotese har vært at delirium utløses lettere når hjernen *allerede* er svekket, for eksempel av tidlige forandringer som senere vil føre til Alzheimers sykdom. Men kan det også tenkes at deliriumstilstanden i seg selv skader hjernen?

Spørsmålet er ikke enkelt å besvare. Skal man belyse hele forløpet og mulige årsakssammenhenger, bør man helst begynne å studere forskningsdeltagerne allerede *før* de får delirium. En fersk studie fra Oslo Delirium Research Group har gjort nettopp det. Maria Krogseth og hennes medarbeidere fulgte 210 eldre mottagere av hjemmetjenester i opptil to år. Av disse fikk 42 prosent delirium i løpet av oppfølgingstiden. Resultatene er publisert i *The Lancet Healthy Longevity* og viser tydelig at å gjennomgå delirium gir økt tendens til kognitiv svekkelse etterpå – uavhengig av kognitiv status på forhånd.

Lenge neglisjert

Hvis delirium er både vanlig og skadelig, hvorfor har ikke fenomenet fått mer oppmerksomhet i forskning og pasientbehandling til nå? Leger har verktøy til å diagnostisere og behandle akutt hjertesvikt, nyresvikt eller leversvikt hos alvorlig syke pasienter. Delirium kan forstås som *akutt hjernesvikt*, men til forskjell fra svikt i andre organer ser man ikke avvik i vanlige blodprøver eller billedundersøkelser. Det vi ikke kan måle objektivt, blir lettere neglisjert.

Dette kan være i ferd med å endre seg. I tillegg til å gjøre kognitive tester har det norske forskerteamet også tatt blodprøver og målt nivået av *neurofilament light chain* (NfL) – et stoff som kan indikere pågående skade på hjerneceller. Målingene viste at deltagere som fikk delirium under sykehusinnleggelse, hadde høyere NfL både under innleggelsen og ved oppfølging flere måneder senere. Observasjonen kan tyde på at delirium utløser en skadelig prosess som senere vedvarer og bidrar til å svekke kognisjonen.

De siste tiårene har det vært brukt enorme ressurser på å forstå og forebygge demens, men forholdsvis lite på å forstå og forebygge delirium. Den norske studien er med på å rette oppmerksomheten mot delirium både som et vindu inn til grunnleggende innsikt om demens og som et mulig angrepspunkt for demensforebygging i daglig praksis. Med systematisk forebygging ville kanskje bestemor kunne komme seg gjennom lårhalsbrudd og operasjon uten å bli forvirret? Hvor stor kan folkehelsegevinsten av slike tiltak bli? Tiden synes nå moden for studier som ikke bare reduserer forvirring i fagfeltet, men som tester effekten av målrettede tiltak mot delirium hos den enkelte pasient. ■

HVA:
Forvirring ved akutt sykdom er skadelig for hjernen.

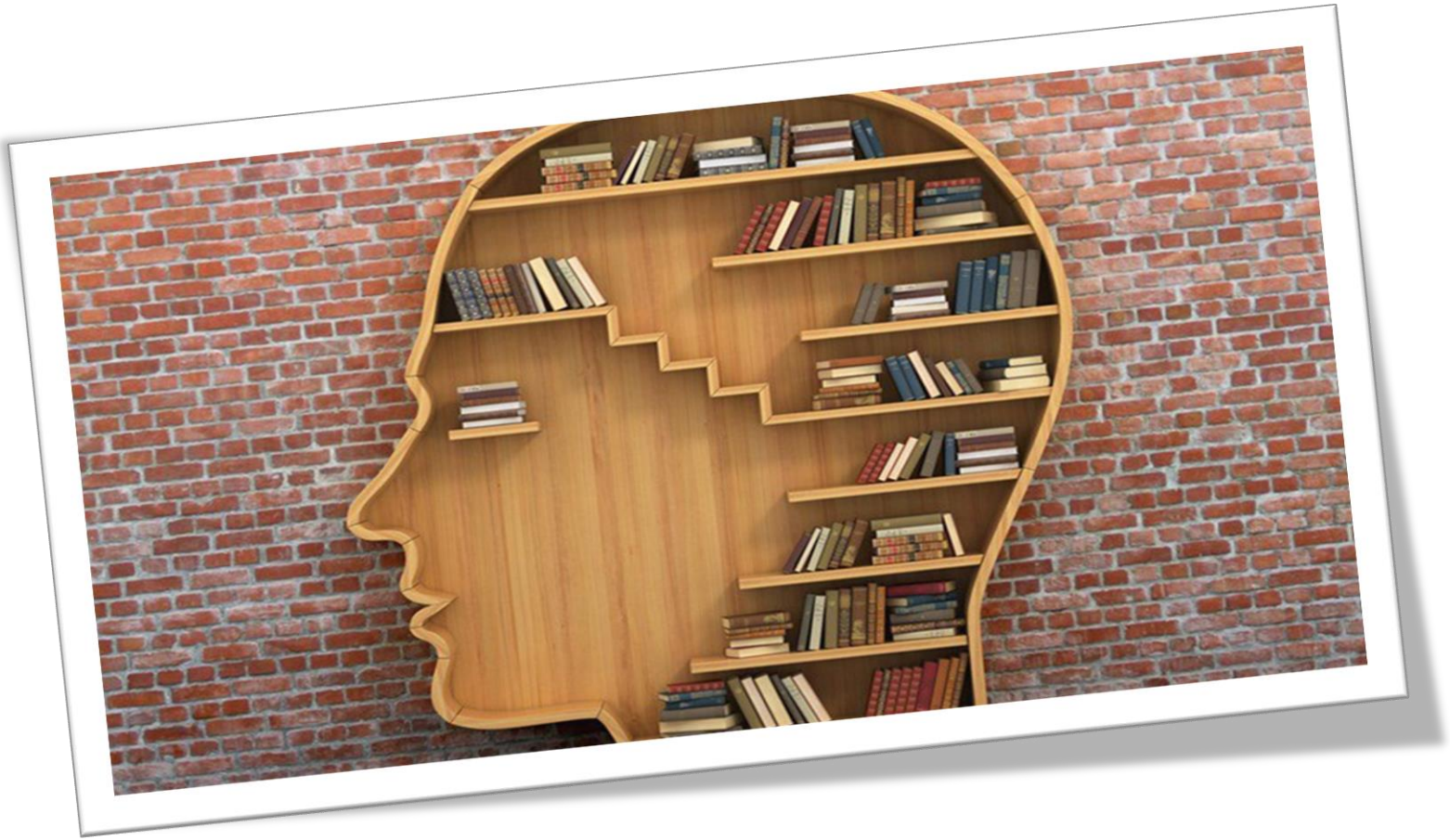
HVEM:
Norske forskere fra Oslo Delirium Research Group.

BETYDNING:
Stiller spørsmål ved håndteringen av en hyppig tilstand i norsk sykehushverdag.

Morgenbladets forskningsskribenter er Ida Roland Birkvad (samfunnsforskning og politisk historie), Carl Henrik Knutsen (statsvitenskap), Andreas Moxnes (økonomi), Lasse Pihlstrøm (medisin), Inga Strümke (teknologi), Vigdis Vandvik (klima og naturtap) og Ylva Østby Berger (psykologi).

Den omtalte forskningsstudien utgår fra Oslo universitetssykehus der også skribenten er ansatt. Han har ikke vært involvert i dette arbeidet eller hatt annet direkte samarbeid med den aktuelle forskningsgruppen.

Lasse Pihlstrøm
Lege og seniorforsker ved Oslo universitetssykehus, fast spaltist
aktuelt@morgenbladet.no



FOREBYGGING AV DELIRIUM

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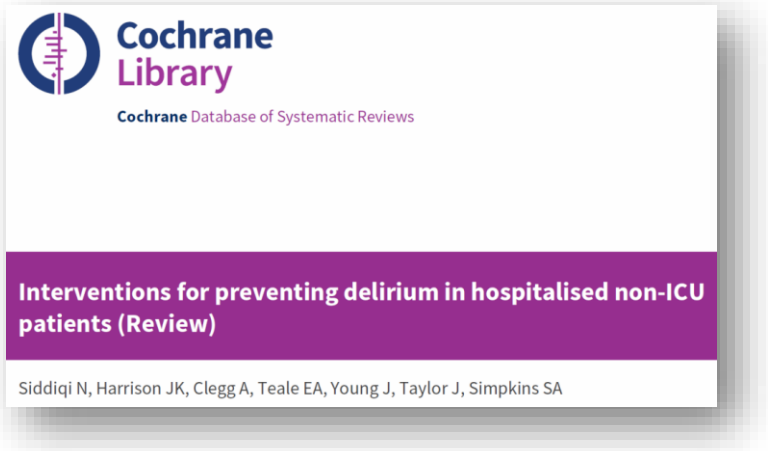
Forebygging av delirium uten medisiner er effektivt

↓ delirium 30-50%

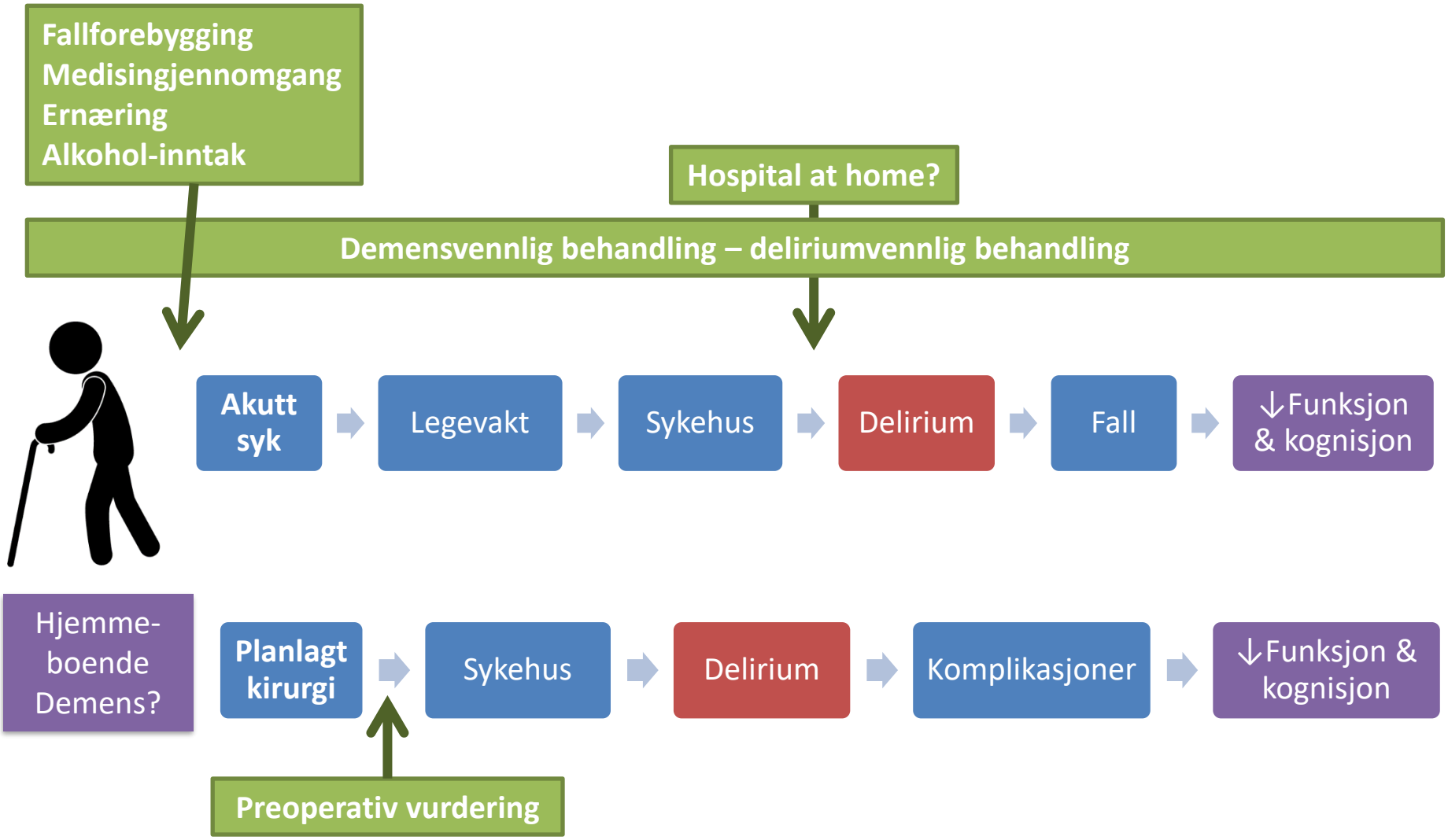
↓ fall 60%

- Intervensjoner for forebygging av delirium **bør implementeres i behandlingsrutinene** for alle pasienter på sykehus



Young, 2010, Hshieh , 2015, Siddiqi , 2016

Et videre perspektiv på forebygging av delirium



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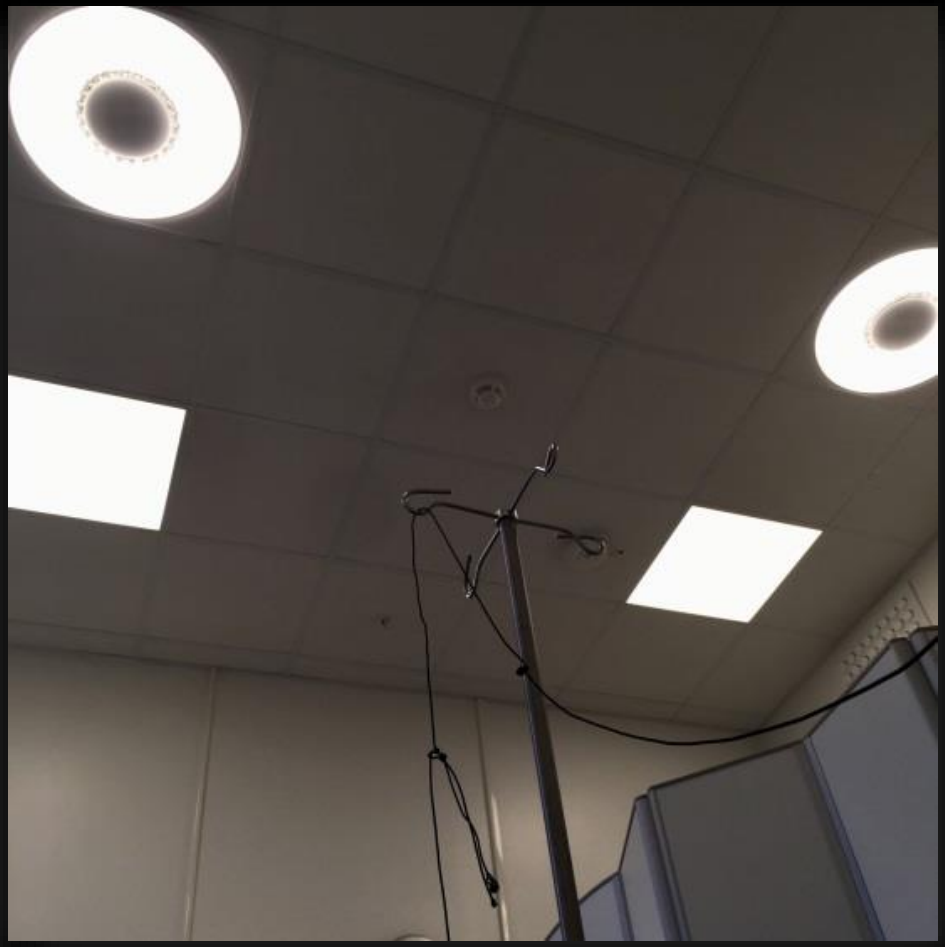
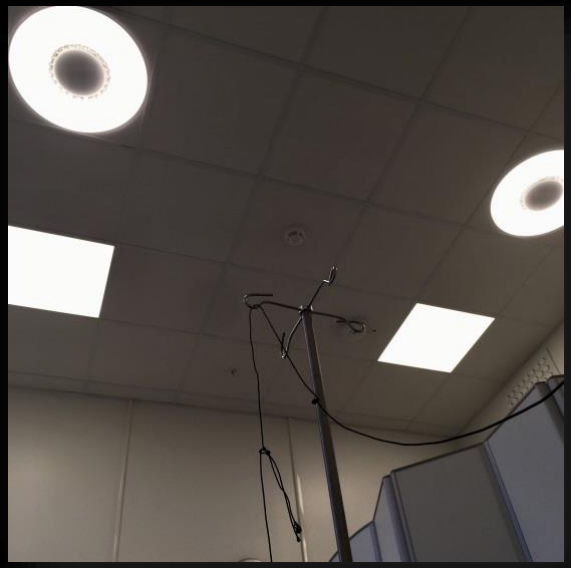


Patient room with a view

Same patient room with another view!



How do we get from here..

…to there?

The solution!

UiO : Institutt for klinisk medisin
Det medisinske fakultet

Husk delirium

Mobilisering

Kognitiv svekkelse/forvirring
Klokke og kalender
Reorientering og tydelig kommunikasjon
Høreapparater og briller

Dårlig mat- og væskeinntak
Oppmuntre å spise og drikke

Smerte
Se etter tegn på smerte, spesielt ved demens
Tilstrekkelig smertelindring

Medisiner
Medikamentgjennomgang

Omgivelser
Holde omgivelsene kjent
Unngå å flytte personen unødvendig

Omsorgspersoner
Velkjent personale
Fastvakt? Familie?

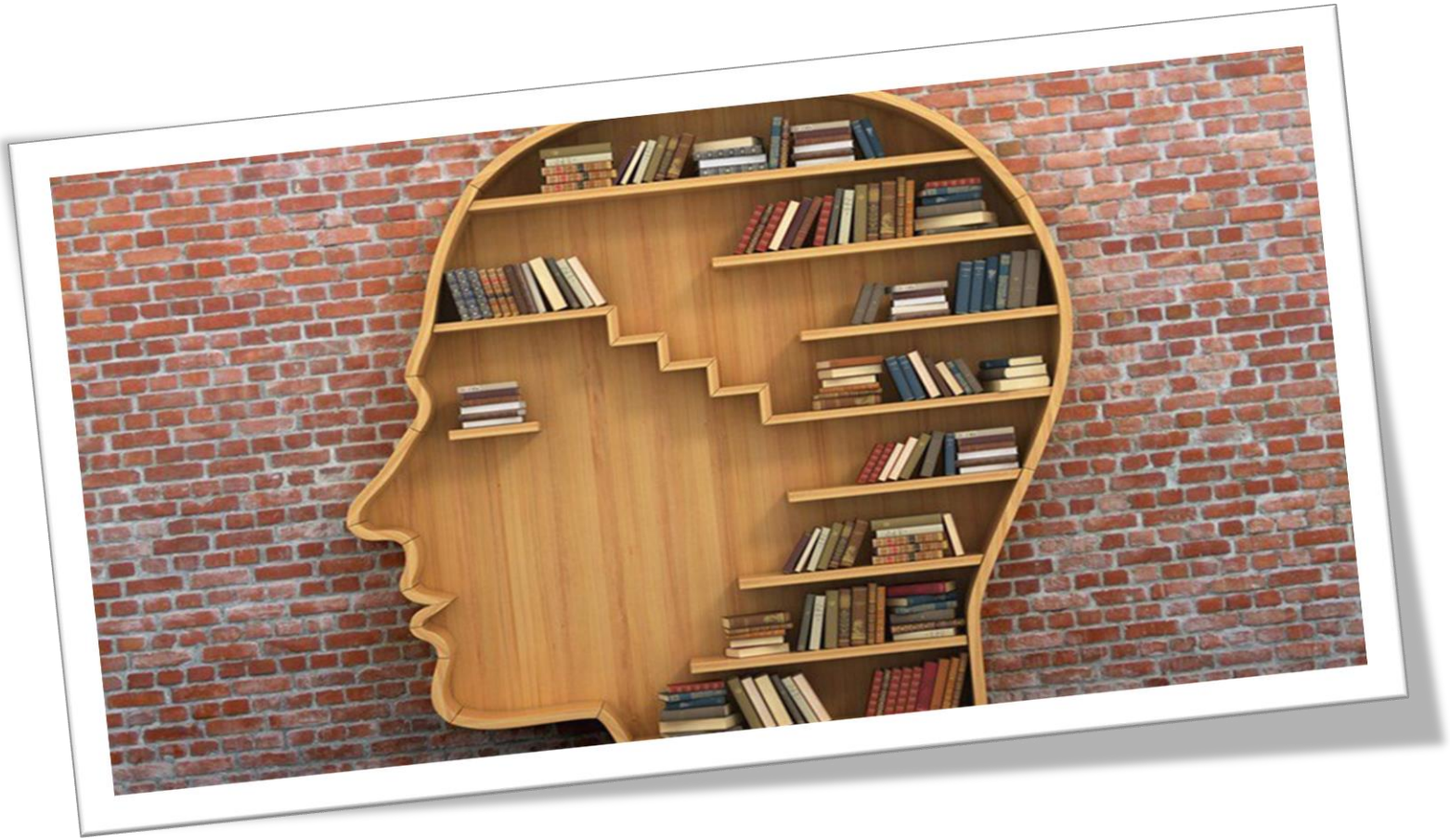
Ubehagelig utstyr
Unngå urinkateter og iv-kanyler hvis mulig

Forstyrret søvn
Unngå å forstyrre søvn. God søvnhygiene

Forstoppelse og urinretensjon
Forhindre/behandle forstoppelse
OBS Urinretensjon!

NICE guidelines, Young 2010
American Geriatrics Society Expert Panel on Postoperative Delirium in Older, Adults, 2015
Fagprosedyre, Helsebiblioteket.no

bjonee@ous-hf.no



TIDLIG OPPDAGELSE AV DELIRIUM

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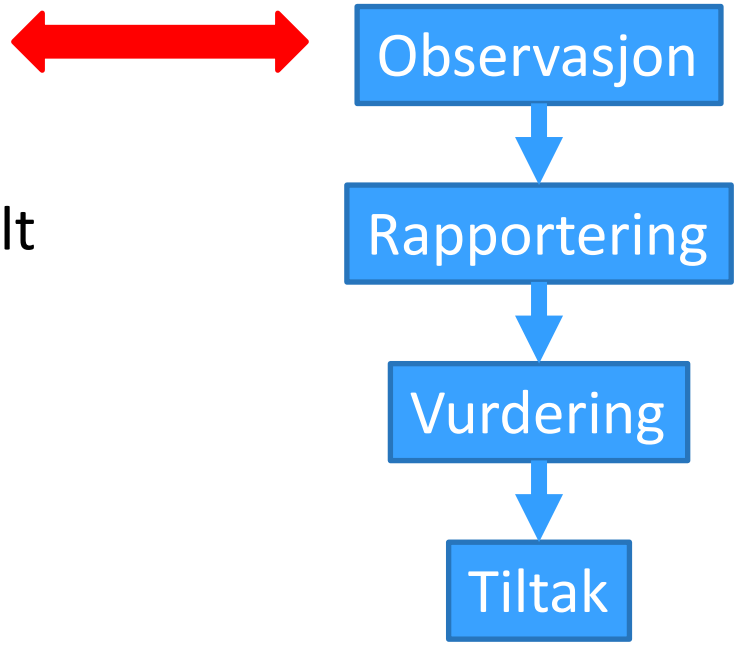
Tidlig oppdagelse av delirium

- **Endring** i funksjon
  - Fysisk
  - Kognitivt/mentalt



Deliriumdiagnostikk utenfor sykehus

Fordeler

Pårørendeinformasjon

Observasjon av pasienten i kjente omgivelser

Kjennskap til pasienten over lang tid

Utfordringer

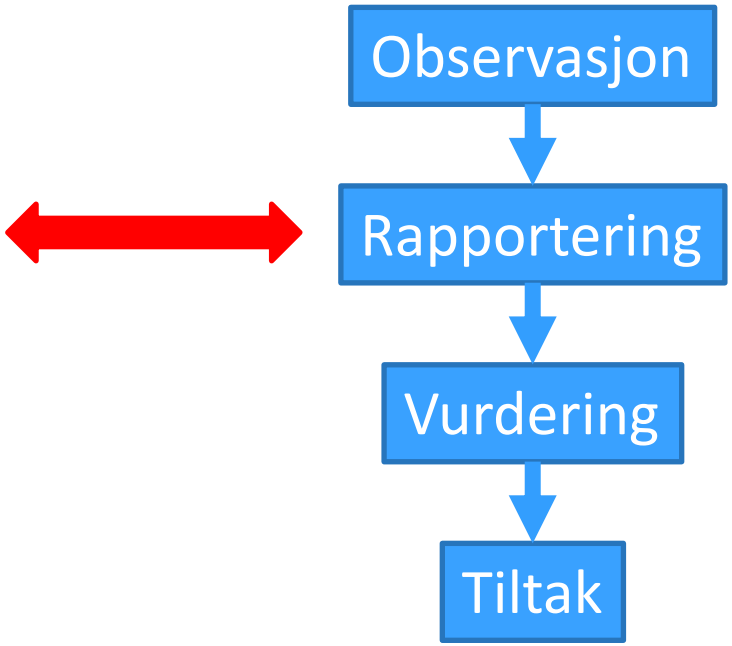
«Øyeblikksbilde», man observerer ikke pas hele vakten

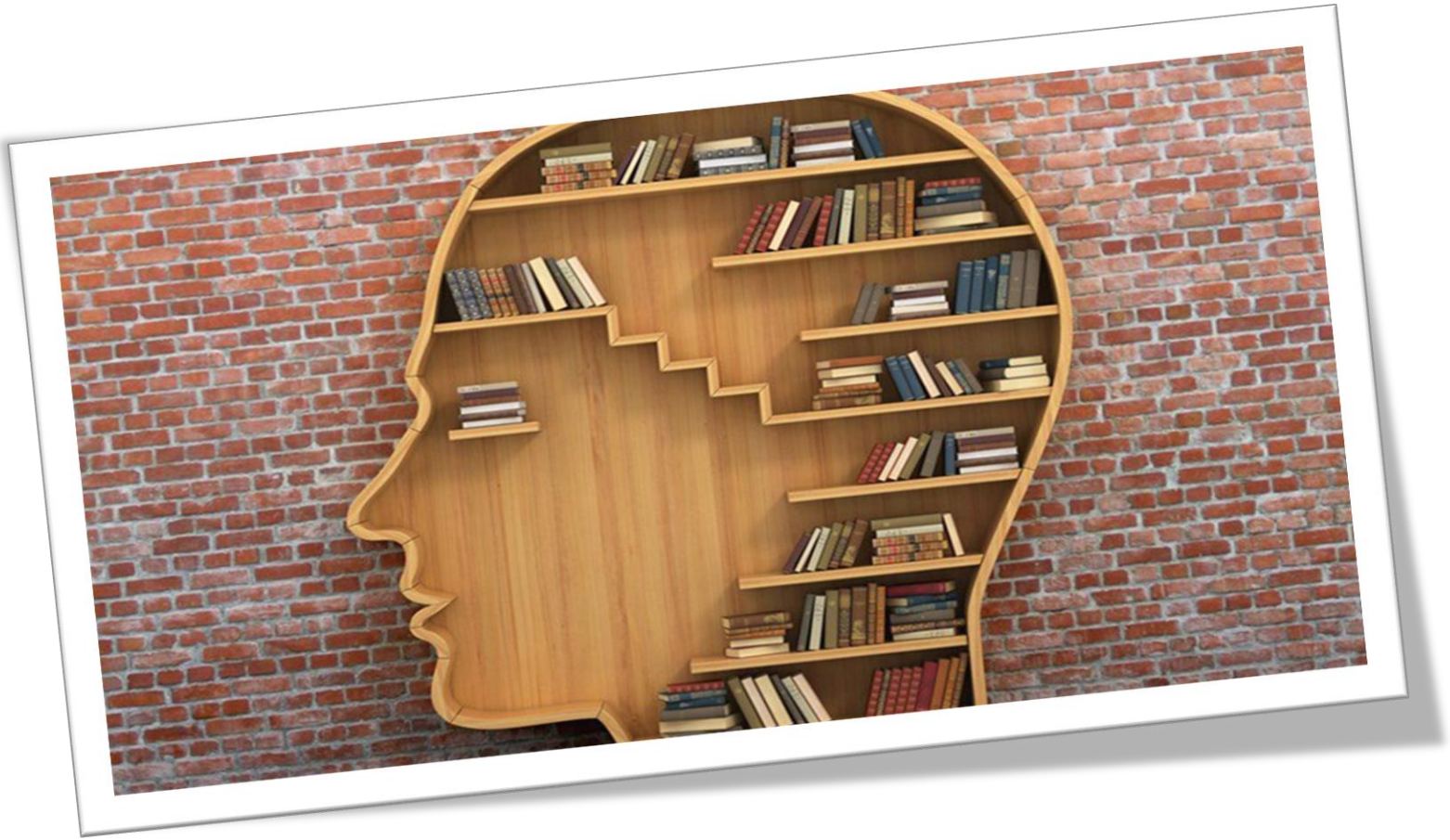
Faglig kompetanse, nok helsefaglige ansatte?

Varierende kunnskap og interesse for delirium blant fastleger og legevakt

Tidlig oppdagelse av delirium

- Dokumenteres strukturert
- Fastlege / lege kontaktes
- Vurdere innleggelse
- Starte tiltak mot antatt utløsende årsak
- Samarbeid med pårørende





BEHANDLING AV DELIRIUM

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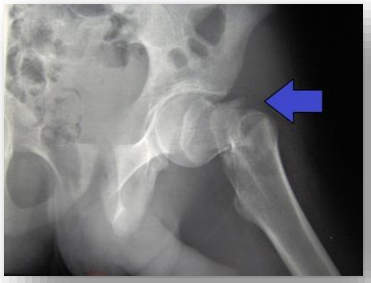
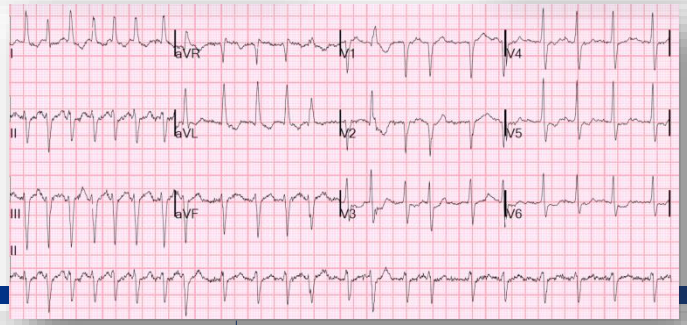
Grunnleggende behandling av delirium

- Påvise og behandle utløsende årsaker
  - Årsakene ligger som oftest utenfor hjernen
  - Ofte mer enn én etiologisk faktor tilstede
- Optimalisere komorbide tilstander og fysiologi
- Håndtere atferdsforstyrrelser og "distress"
- Forebygge komplikasjoner





Videre tiltak avhenger av **avklart** vs **uavklart** årsak

Pas kommer hjem etter sykehusopphold med delirium, f eks

- Smerter
- Nye medisiner

Aktuelle tiltak:

- Justering av medikamenter
- Involvering av fastlege
- Hyppigere besøk av hj.sykepl
- «kognitiv tilrettelegging» og aktivitet
- Ro, trygghet, søvn
- Basal ADL
- Informasjon og involvering av familie

Nyoppstått delirium i hjemmet

- Potensielt alvorlige tilstander

Aktuelle tiltak:

- Kontakte lege
- Innleggelse for diagnostikk og behandling
- Innleggelsesrapport med opplysninger om habitualtilstand og sykdomsutvikling

Fortløpende vurdering av effekt av tiltak

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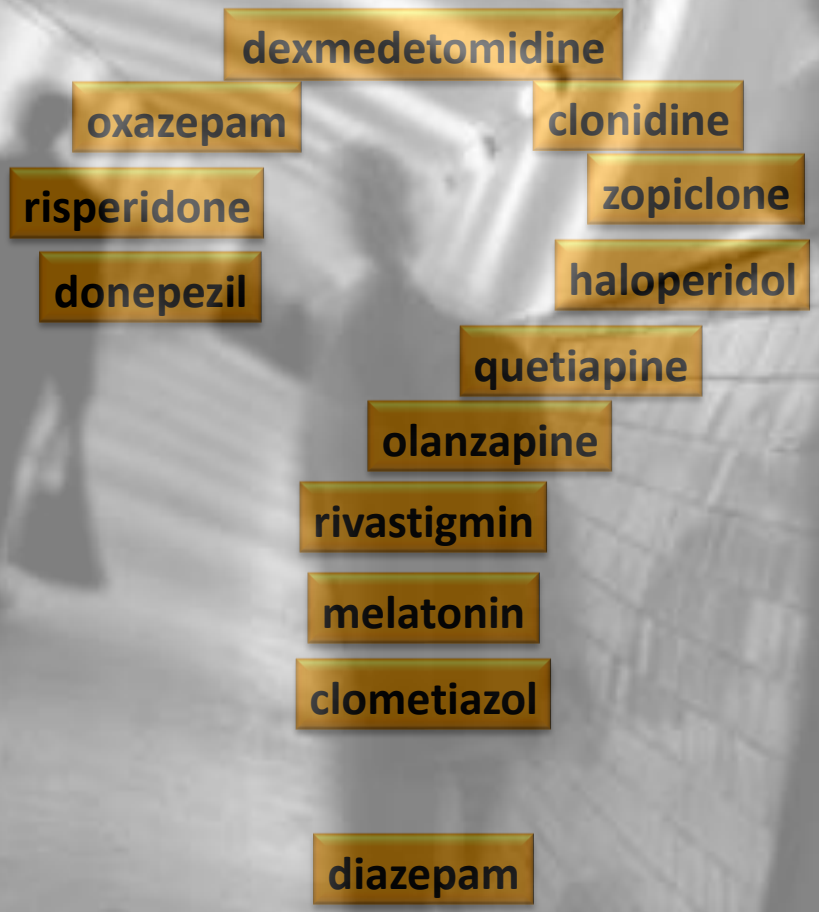
Skal vi bruke medikamenter til å forebygge eller behandle delirium?



Randomised trials for treatment of delirium

Study	Drug	N	Population
Breitbart (1996)	haloperidol vs. chlorpromazine vs lorazepam	30	AIDS
Han (2004)	haloperidol vs. risperidone	28	Mixed medical/surgical
Skrobik (2004)	haloperidol vs. olanzapine	73	Medical/ surgical ICU
Lee (2005)	amisulpride vs. quetiapine	40	Mixed medical/surgical
Hu (2006)	olanzapine vs. haloperidol vs. control	175	"senile delirium"
Raede (2009)	haloperidol vs dexmedetomedine	20	Medical/surgical ICU
Devlin et al. (2010)	quetiapine vs. placebo	36	Medical/surgical ICU
Tahir et al. (2010)	quetiapine vs. placebo	42	Mixed medical/surgical
Girard et al. (2010)	haloperidol vs. ziprasidone vs. placebo	103	Medical/surgical ICU
Kim et al. (2010)	risperidone vs. olanzapine	32	Mixed medical/surgical/cancer
van Eijk et al. (2010)	rivastigmine vs. placebo	109	Medical/surgical CU
Overshott et al. (2010)	rivastigmine vs. placebo	15	Medical wards
Grover et al. (2011)	haloperidol vs. olanzapine vs. risperidone	74	Mixed medical/surgical
Maneeton (2013)	quetiapine vs haloperidol	52	Mixed medical/surgical
Page (2013)	haloperidol vs placebo	141	Medical/surgical ICU
Reade (2016)	Dexmedetomedine vs placebo	74	Medical/surgical ICU
Hui (2017)	Lorazepam + haloperidole vs haloperidole + placeboe	93	Palliative care
Agar (2017)	Risperdone vs Haloperidole vs Placeboe	247	Palliative care
Girard (2018)	haloperidol vs ziprasidone vs placebo	566	Medical/surgical ICU

Randomised trials for treatment of delirium

Study	Drug	N	Population
Neerland/Hov (2019)	Clonidine vs. placebo	20	Mixed medical > 65 y
Andersen-Ranberg	Haldol vs placebo	1000	ICU

Annals of Internal Medicine REVIEW

Antipsychotics for Preventing Delirium in Hospitalized Adults

A Systematic Review

Esther S. Oh, MD, PhD; Dale M. Needham, MD, PhD; Roozbeh Nikooie, MD; Lisa M. Wilson, ScM; Allen Zhang, BS; Karen A. Robinson, PhD*; and Karin J. Neufeld, MD, MPH*

3 September 2019
2 Systematic Reviews
+
Editorial by Marcantonio

Annals of Internal Medicine REVIEW

Antipsychotics for Treating Delirium in Hospitalized Adults

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Prevention: *No difference* in delirium incidence or duration, LOS, or mortality
Treatment: *No difference* in sedation status, delirium duration, LOS or mortality
Potentially harmful effects tended to occur more frequently

Annals of Internal Medicine EDITORIAL

Old Habits Die Hard: Antipsychotics for Treatment of Delirium

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Haloperidol for the Treatment of Delirium in ICU Patients

N.C. Andersen-Ranberg, L.M. Poulsen, A. Perner, J. Wetterslev, S. Estrup, J. Hästbacka, M. Morgan, G. Citerio, J. Caballero, T. Lange, M.-B.N. Kjær, B.H. Ebdrup, J. Engstrøm, M.H. Olsen, M. Oxenbøll Collet, C.B. Mortensen, S.-O. Weber, A.S. Andreasen, M.H. Bestle, B. Uslu, H. Scharling Pedersen, L. Gramstrup Nielsen, H.C. Toft Boesen, J.V. Jensen, L. Nebrich, K. La Cour, J. Laigaard, C. Haurum, M.W. Olesen, C. Overgaard-Steensen, B. Westergaard, B.A. Brand, G. Kingo Vesterlund, P. Thornberg Kyhnauv, V.S. Mikkelsen, S. Hyttel-Sørensen, I. de Haas, S.R. Aagaard, L.O. Nielsen, A.S. Eriksen, B.S. Rasmussen, H. Brix, T. Hildebrandt, M. Schønemann-Lund, H. Fjeldsøe-Nielsen, A.-M. Kuivalainen, and O. Mathiesen, for the AID-ICU Trial Group*

ABSTRACT

BACKGROUND

Haloperidol is frequently used to treat delirium in patients in the intensive care unit (ICU), but evidence of its effect is limited.

METHODS

In this multicenter, blinded, placebo-controlled trial, we randomly assigned adult patients with delirium who had been admitted to the ICU for an acute condition to receive intravenous haloperidol (2.5 mg 3 times daily plus 2.5 mg as needed up to a total maximum daily dose of 20 mg) or placebo. Haloperidol or placebo was administered in the ICU for as long as delirium continued and as needed for recurrences. The primary outcome was the number of days alive and out of the hospital at 90 days after randomization.

RESULTS

A total of 1000 patients underwent randomization; 510 were assigned to the haloperidol group and 490 to the placebo group. Among these patients, 987 (98.7%) were included in the final analyses (501 in the haloperidol group and 486 in the placebo group). Primary outcome data were available for 963 patients (97.6%). At 90 days, the mean number of days alive and out of the hospital was 35.8 (95% confidence interval [CI], 32.9 to 38.6) in the haloperidol group and 32.9 (95% CI, 29.9 to 35.8) in the placebo group, with an adjusted mean difference of 2.9 days (95% CI, −1.2 to 7.0) (P=0.22). Mortality at 90 days was 36.3% in the haloperidol group and 43.3% in the placebo group (adjusted absolute difference, −6.9 percentage points [95% CI, −13.0 to −0.6]). Serious adverse reactions occurred in 11 patients in the haloperidol group and in 9 patients in the placebo group.

CONCLUSIONS

Among patients in the ICU with delirium, treatment with haloperidol did not lead to a significantly greater number of days alive and out of the hospital at 90 days than placebo. (Funded by Innovation Fund Denmark and others; AID-ICU ClinicalTrials.gov number, NCT03392376; EudraCT number, 2017-003829-15.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Andersen-Ranberg can be contacted at ncan@regionsjaelland.dk or at the Department of Anesthesiology and Intensive Care, Zealand University Hospital, Køge, DK-4600 Køge, Denmark.

*A full list of the investigators in the AID-ICU trial group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on October 26, 2022, at NEJM.org.

DOI: 10.1056/NEJMoa2211868

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- N = 1000 med delirium (45 % hyperaktive)
- Haloperidol 2.5 mg x 3 iv, max 20mg/d
- Primært endepunkt: Dager i live og utenfor sykehus/90 dager
  - ikke signifikant forskjell
- Sekundært endepunkt: Mortalitet/90 dager
  - Haldol 36.6%
  - Placebo 43.3%
  - Forskjellen -6.9 (95% -13 til -0.6)

JAMA Internal Medicine | Original Investigation

Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care

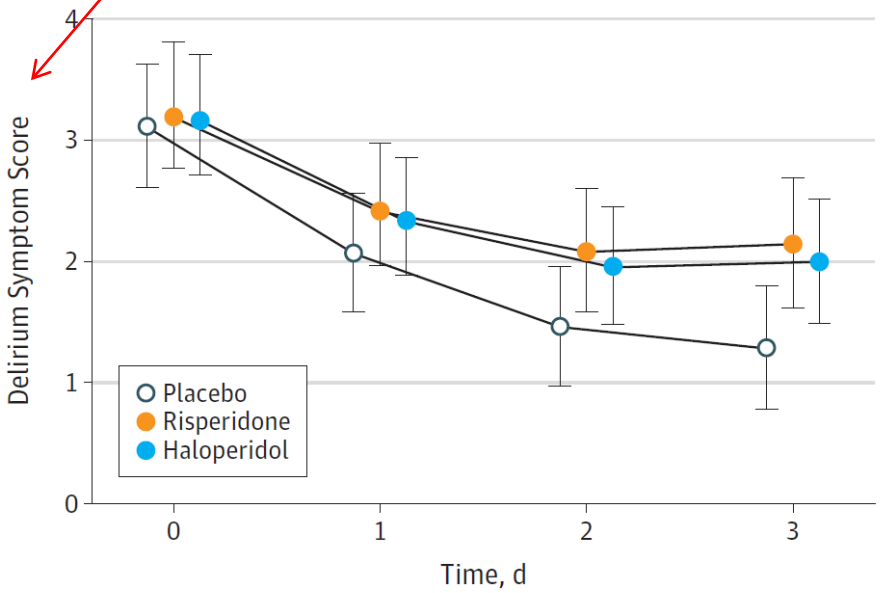
A Randomized Clinical Trial

Meera R. Agar, PhD; Peter G. Lawlor, MB; Stephen Quinn, PhD; Brian Draper, MD; Gideon A. Caplan, MBBS; Debra Rowett, BPharm; Christine Sanderson, MPH; Janet Hardy, MD; Brian Le, MBBS; Simon Eckermann, PhD; Nicola McCaffrey, PhD; Linda Devilee, MBus; Belinda Fazekas, BN; Mark Hill, PhD; David C Currow, PhD

NuDESC
Atferd (0-2)
Kommunikasjon (0-2)
Persepsjon (0-2)

- Palliativ beh, forventet levetid >1u
  - 75 år (80% > 65år)
  - IQCODE median 4
- Risperidone (82) eller haloperidol (81) vs placebo (84)
  - 0.5mg + 0.5mgx2, maks 4mg/d
  - Halvert dose over 65 år
- **Mindre symptomer og mindre alvorlig delirium i placebogruppen**
  - P=0.02 (risperidon) og 0.009 (haloperidol)
- Høyere dødelighet med antipsykotika (HR 1.5, p=0.01)

Figure 2. Secondary Multivariable Mixed-Model Analysis of Delirium



No. at risk				
Placebo	84	63	59	55
Risperidone	82	58	49	39
Haloperidol	81	64	55	51

Når skal vi bruke medisiner ved delirium?

- Hvis pasienten er svært plaget
- Hvis nødvendig for pasientsikkerhet
  - Til fare for seg selv eller andre
- Hvis nødvendig for å gjennomføre nødvendig diagnostikk eller behandling
- Aktuelle lover
  - Helsepersonelloven §7 Øyeblikkelig hjelp
  - Pasientrettighetsloven Kap 4A

- Kortvarig bruk, lav dose antipsykotika
- Benzodiazepiner v/ alkohol- eller bzd-abstinens eller mye angst
- Alltid en avveining
- Alltid *i tillegg til* ikke-farmakologiske tiltak

Medikament	Dosering			
	Esther Oh, **JAMA** 2017	Fagprosedyre, **norskgeriatri.no**	Metodebok OUS **Ullevål (oppdatert 2022)**	**Scottish** Delirium Association
Haloperidol = Haldol	0.25- 0.5 mg Kan gjentas hvert 30.min, maks 3-5 mg/24t	0.5-1 mg p.o./i.m Lavere dosering for de skrøpeligste	0.5 – 1 mg p.o eller i.m. max 2 mg /døgn. Til eldre og pasienter med demens kan 0.25 - 0.5 mg være tilstrekkelig første døgn.	0.5 - 1mg po, max 2mg/24t 0.5 mg IM, max 2mg/24
Olanzapine = Zyprexa	2.5 - 5 mg x 2	5-10 mg vesp p.o./i.m		
Risperidone = Risperdal	0.5 - 1 mg x 2		0.25 - 1 mg x 2 p.o.	
Quetiapine = Seroquel	12.5 – 25 mg x 2	50-100 mg / døgn p.o	Kan vurderes hos pas m/ LBD/Mb Park. 25–100 mg/d fordelt på to doser	
Dersom antipsykotika er kontraindisert (parkinsonisme, LBD) - alternativer				
Lorazepam = Temesta				0.5-1mg po, max 2mg/24t
Midazolam				2.5 mg IM max 7.5mg/24t
Heminevrin		300-600 mg vesp	(300 - 600 mg vesp)	
Melatonin/ ramelteon	3-5 /8mg ves	?		

[eHåndbok - Utredning og behandling av delirium (akutt forvirring) (ous-hf.no)]

Oppsummering

- Eldre personer med akutt sykdom har høy risiko for delirium
  - Men også yngre, alvorlig syke
- Må ha kunnskap og rutiner
  - Hjemmetjenesten
  - Fastlege/legevakt
  - Pårørende
- Delirium med uavklart årsak trenger diagnostisk avklaring (som regel innleggelse)

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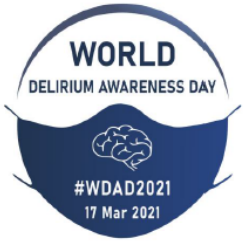
En liten oppfordring til slutt

- Nyhetsbrev og informasjon om delirium:

  bjonee@ous-hf.no

- Faggruppe for delirium, Norsk forening for geriatri

«Verdens deliriumdag» #WDAD2021



17 mars 2021

17 mars markeres #WDAD2021 over hele verden. Hensikten er å øke oppmerksomheten og kunnskapen om delirium. Vi ønsker at dagen markeres på alle landets sykehus og flere aktiviteter er allerede planlagt. Bli med og gjør delirium synlig!

Forslag til hva *du* kan gjøre for å markere #WDAD2021

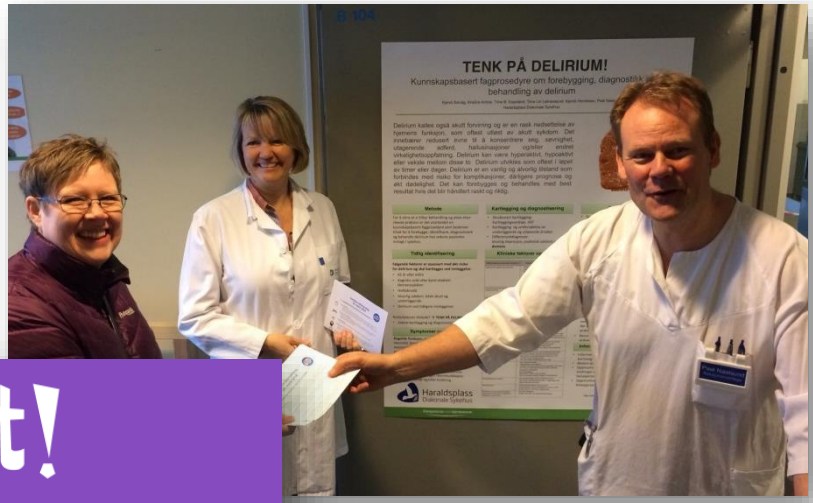
- Ha fokus på delirium på avdelingen. Bruk 4AT på dagens visitt. Lag en plansje om delirium-forebyggende tiltak.
- Spre informasjon om delirium
- Bruk sosiale medier til å dele informasjon om delirium
- Lag stand, heng opp plakater, lag poster eller veggavis
- Trykk opp og spre informasjon i kantina, ved hovedinngangen eller på poliklinikken
- Spre laminerte versjoner av f eks screeningverktøyet «4AT» eller nøkkelinformasjon om delirium
- Hold undervisning om delirium på morgenmøtet eller i lunsjen, eller for en annen avdeling
- Lag quiz (med premier!) - enten på papir eller digitalt – bruk lunsjen!
- Lag et oppslag på sykehusets intranett
- Lag et kvalitetsforbedringsprosjekt med fokus på delirium
- Intervju en pasientrepresentant
- Skriv kronikk i avisen eller et innlegg i Dagens medisin, Tidsskriftet, Sykepleien, Fastlegenytt
- Fortell dine ledere om delirium
- Engasjer politikere

SoMe Facebook Twitter Instagram #WDAD2021

Bruk #WDAD2021 på Twitter til å vise hva du finner på. Merk innlegget med #WDAD2021
Følg @iDelirium_Aware og se på nettsiden www.idelirium.org
Bruk sosiale medier, evt send bilder og informasjon som kan spres til bjorn.erik@neerland.net

Faggruppe for delirium, Norsk forening for geriatri

#WDAD – aktiviteter i Norge



Takk for meg!

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BMJ Open

Alpha-2-adrenergic receptor agonists for the prevention of delirium and cognitive decline after open heart surgery (ALPHA2PREVENT): protocol for a multicentre randomised controlled trial

Bjørn Erik Neerland ,[1] Rolf Busund,[2,3] Rune Haaverstad,[4,5] Jorunn L Helbostad,[6] Svein Aslak Landsverk,[7] Ieva Martinaityte,[3,8] Hilde Margrethe Norum,[7,9] Johan Ræder,[7,10] Geir Selbaek ,[1,10,11] Melanie R Simpson,[12] Elisabeth Skaar,[4] Nils Kristian Skjærvold,[13,14] Eva Skovlund,[12] Arjen JC Slooter,[15,16] Øyvind Sverre Svendsen,[17,18] Theis Tønnessen,[10,19] Alexander Wahba,[13,20] Henrik Zetterberg,[21,22,23,24] Torgeir Bruun Wyller[1,10]

To cite: Neerland BE, Busund R, Haaverstad R, *et al*. Alpha-2-adrenergic receptor agonists for the prevention of delirium and cognitive decline after open heart surgery (ALPHA2PREVENT): protocol for a multicentre randomised controlled trial. *BMJ Open* 2022;**12**:e057460. doi:10.1136/bmjopen-2021-057460

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-057460).

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For numbered affiliations see end of article.

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ABSTRACT

Introduction Postoperative delirium is common in older cardiac surgery patients and associated with negative short-term and long-term outcomes. The alpha-2-adrenergic receptor agonist dexmedetomidine shows promise as prophylaxis and treatment for delirium in intensive care units (ICU) and postoperative settings. Clonidine has similar pharmacological properties and can be administered both parenterally and orally. We aim to study whether repurposing of clonidine can represent a novel treatment option for delirium, and the possible effects of dexmedetomidine and clonidine on long-term cognitive trajectories, motor activity patterns and biomarkers of neuronal injury, and whether these effects are associated with frailty status.

Methods and analysis This five-centre, double-blind randomised controlled trial will include 900 cardiac surgery patients aged 70+ years. Participants will be randomised 1:1:1 to dexmedetomidine or clonidine or placebo. The study drug will be given as a continuous intravenous infusion from the start of cardiopulmonary bypass, at a rate of 0.4 µg/kg/hour. The infusion rate will be decreased to 0.2 µg/kg/hour postoperatively and be continued until discharge from the ICU or 24 hours postoperatively, whichever happens first.
Primary end point is the 7-day cumulative incidence of postoperative delirium (Diagnostic and Statistical Manual of Mental Disorders, fifth edition). Secondary end points include the composite end point of coma, delirium or death, in addition to delirium severity and motor activity patterns, levels of circulating biomarkers of neuronal injury, cognitive function and frailty status 1 and 6 months after surgery.

Ethics and dissemination This trial is approved by the Regional Committee for Ethics in Medical Research in Norway (South-East Norway) and by the Norwegian Medicines Agency. Dissemination plans include publication in peer-reviewed medical journals and presentation at scientific meetings.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This multicentre trial will provide evidence for prophylactic efficacy of dexmedetomidine and clonidine in reducing the incidence of postoperative delirium as well as decline in cognitive function 1 and 6 months postoperatively in older cardiac surgical patients.
- ⇒ Inclusion of preoperative frailty assessments will provide evidence for frailty as a predictive marker of treatment effect.
- ⇒ The analysis of biomarkers will provide insights into the neural mechanisms in postoperative delirium and long-term cognitive dysfunction.
- ⇒ The analysis of activity by accelerometers will provide insight into motor activity patterns in subtypes of delirium.
- ⇒ The dose of the active drugs may potentially be too low or the duration of treatment too short in order to show effects.

Trial registration number NCT05029050.

BACKGROUND

Delirium represents an acute change in awareness, attention and cognition, precipitated by an acute illness, trauma, intoxication or surgery.[1 2] Common additional features are agitation, hallucinations and poor compliance with medical treatment and care.

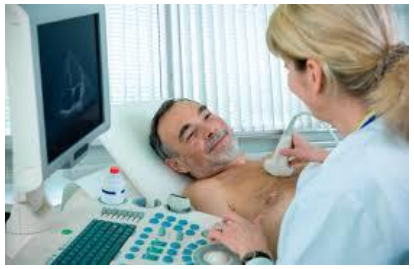
Delirium appears in all parts of the healthcare service, including intensive care units (ICUs) and postoperative settings, regular hospital wards, nursing homes, home nursing services and palliative departments. In a recent meta-analysis, Greaves *et al* found a

ALPHA2PREVENT
Alpha 2 adrenergic receptor agonists for the prevention of delirium and cognitive decline after open heart surgery: randomised controlled trial

OSLO DELIRIUM RESEARCH GROUP

ALPHA2PREVENT

Alpha 2 adrenergic receptor agonists for the prevention of delirium and cognitive decline after open heart surgery: randomised controlled trial



70 år +

Åpen hjertekirurgi

N=900 Oslo, Bergen, TrH, Tromsø

1:1:1 Deksmedetomidin : Klonidin : Placebo

Utredning

Samtykke
Inklusjon
Kognitiv testing
Frailty-vurdering

Kirurgi

Studiemedisin
- Under operasjon
- I inntil 24 timer po

Postoperativt

Daglige vurderinger
av delirium

1 og 6 mnd

Kognitiv testing
Frailty-vurdering

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Takk for meg!

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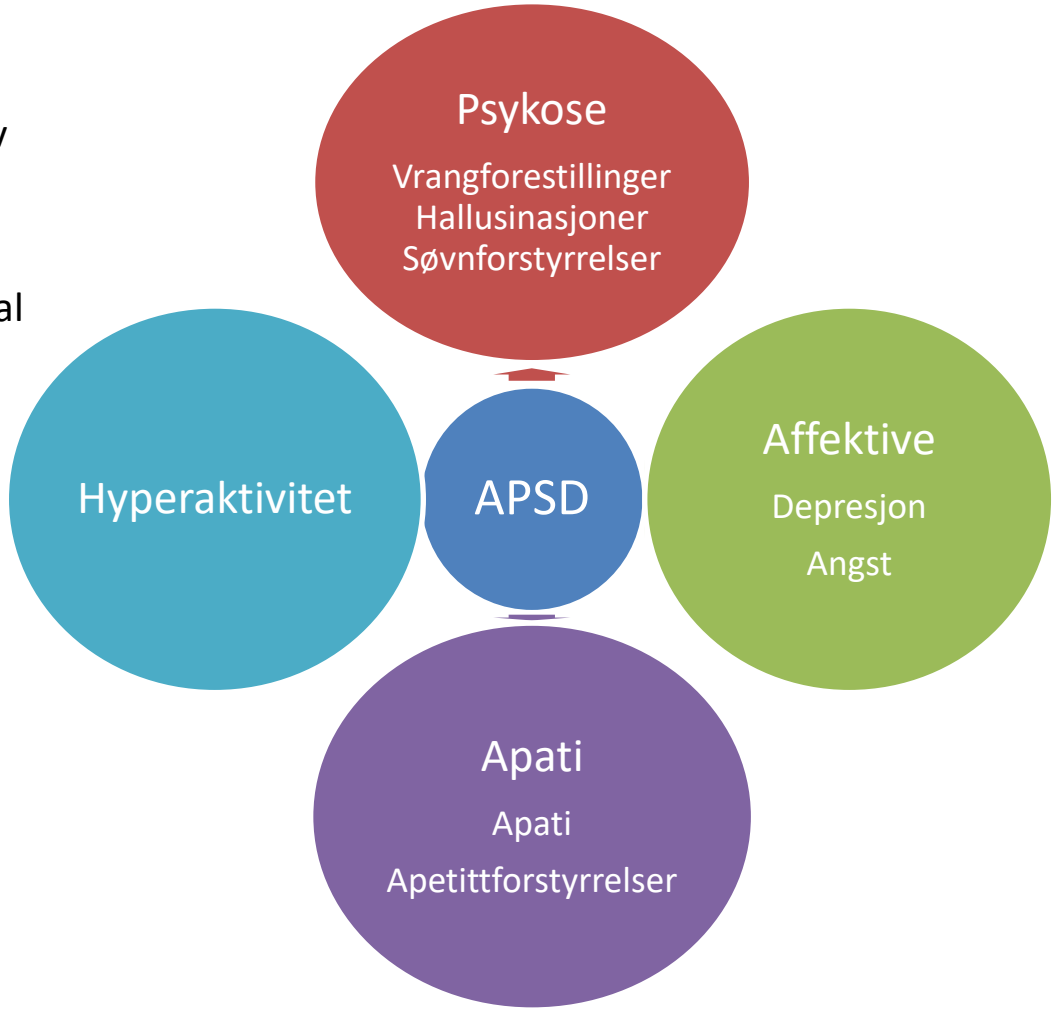
Atferds og psykiatriske symptomer ved demens (APSD)
Nevropsykiatriske symptomer ved demens

- Vanlig og øker med alvorlighetsgraden av demens
- Behandlingen bør være psykologisk, sosial og miljøbehandling
- Hospitaliserte pasienter med demens vil ofte presentere APSD (75%)

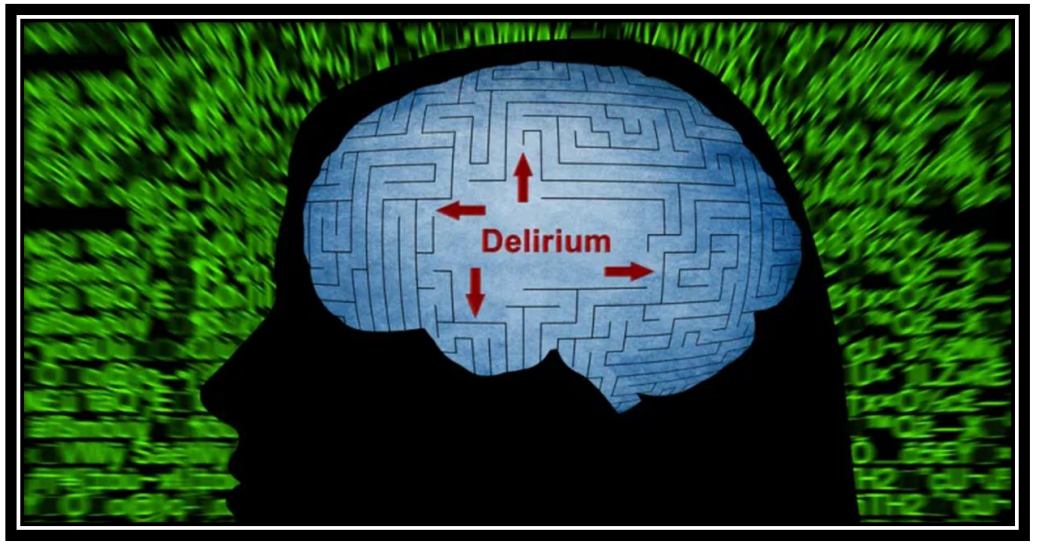


Livingston, 2017
Selbæk, 2013
Sampson, 2014
Abengana, 2017
Landreville, 2013

bjonee@ous-hf.no

Delirium er en vanlig tilstand

- **10-20%** av alle akutte medisinske innleggelser
  - Pendlebury, 2015
  - Marcantonio, 2017
- Høyest forekomst blant de eldste og de mest alvorlig syke
  - Vasilevskis, 2012
  - Inouye, 2014
- Hos **50%** av pas med hoftebrudd
  - Juliebø, 2009
- Intensivpasienter med mekanisk ventilasjon **60-70%**
  - Pandharipande, 2013
- Pas med demens: **50%** utvikler delirium ved akuttinnleggelse
  - Gross, 2012



AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

Clinical Care Standards

FACT SHEET for clinicians

Delirium

Clinical Care Standard

The goal of the *Delirium Clinical Care Standard* is to improve the prevention of delirium in patients at risk and the early diagnosis and treatment of patients with delirium, in order to reduce its incidence, severity and duration.

1 Early identification of risk

A patient with any key risk factor for delirium is identified on presentation and a validated tool is used to screen for cognitive impairment, or obtain a current score if they have known cognitive impairment. Before any planned admission, the risk of delirium is assessed and discussed with the patient, to enable an informed decision about the benefits and risks.

2 Interventions to prevent delirium

A patient at risk of delirium is offered a set of interventions to prevent delirium and is regularly monitored for changes in behaviour, cognition and physical condition. Appropriate interventions are determined before a planned admission or on admission to hospital, in discussion with the patient and their family or carer.

3 Patient-centred information and support

A patient at risk of delirium and their family or carer are encouraged to be active participants in care. If a patient is at significant risk or has, delirium, they and their family or carer are provided with information about delirium and its prevention in a way that they can understand. When delirium occurs, they receive support to cope with the experience and its effects.

4 Assessing and diagnosing delirium

A patient with cognitive impairment on presentation to hospital, or who has an acute change in behaviour or cognitive function during a hospital stay, is promptly assessed using a validated tool by a clinician trained to assess delirium. The patient and their family or carer are asked about any recent changes in the patient's behaviour or thinking.

A diagnosis of delirium is determined and documented by a clinician working within their scope of practice.

5 Identifying and treating underlying causes

A patient with delirium is offered a set of interventions to treat the causes of delirium, based on a comprehensive assessment that includes relevant multidisciplinary consultation.

AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

Clinical Care Standards

6 Preventing complications of care

A patient with delirium receives care to prevent functional decline, dehydration, malnutrition, falls and pressure injuries, based on their risk.

7 Avoiding use of antipsychotic medicines

Antipsychotic medicines are not recommended to treat delirium. Behavioural and psychological symptoms in a patient with delirium are managed using non-drug strategies.

8 Transition from hospital care

Before a patient with persistent or resolved delirium leaves hospital, an individualised comprehensive care plan is developed collaboratively with the patient and their family or carer. The plan describes the patient's post-discharge care needs and includes strategies to help reduce the risk of delirium and related complications, a summary of changes in medicines and any other ongoing treatment. This plan is provided to the patient and their family or carer before discharge, and to their general practitioner and other regular clinicians within 48 hours of discharge.

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2021

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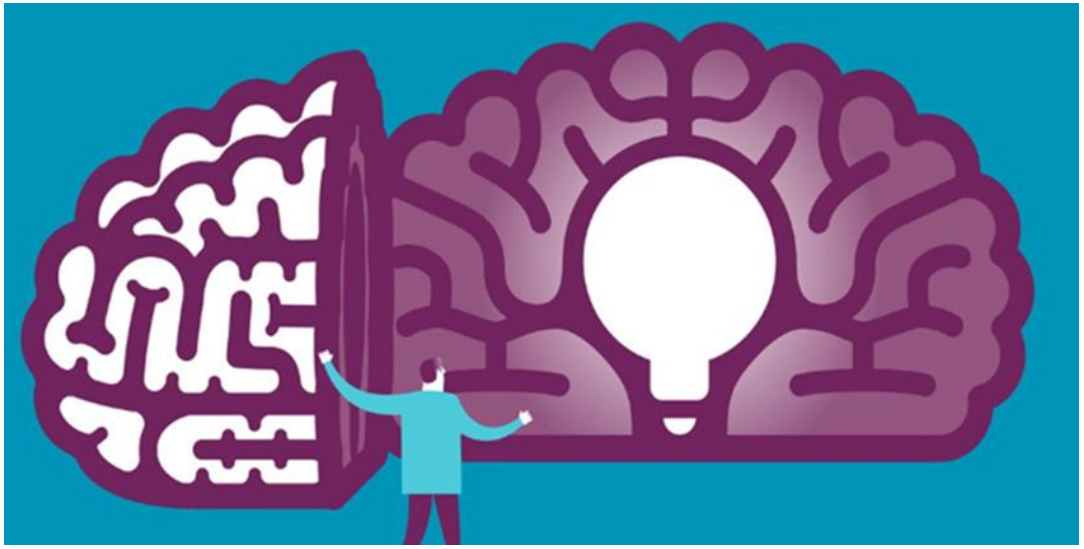
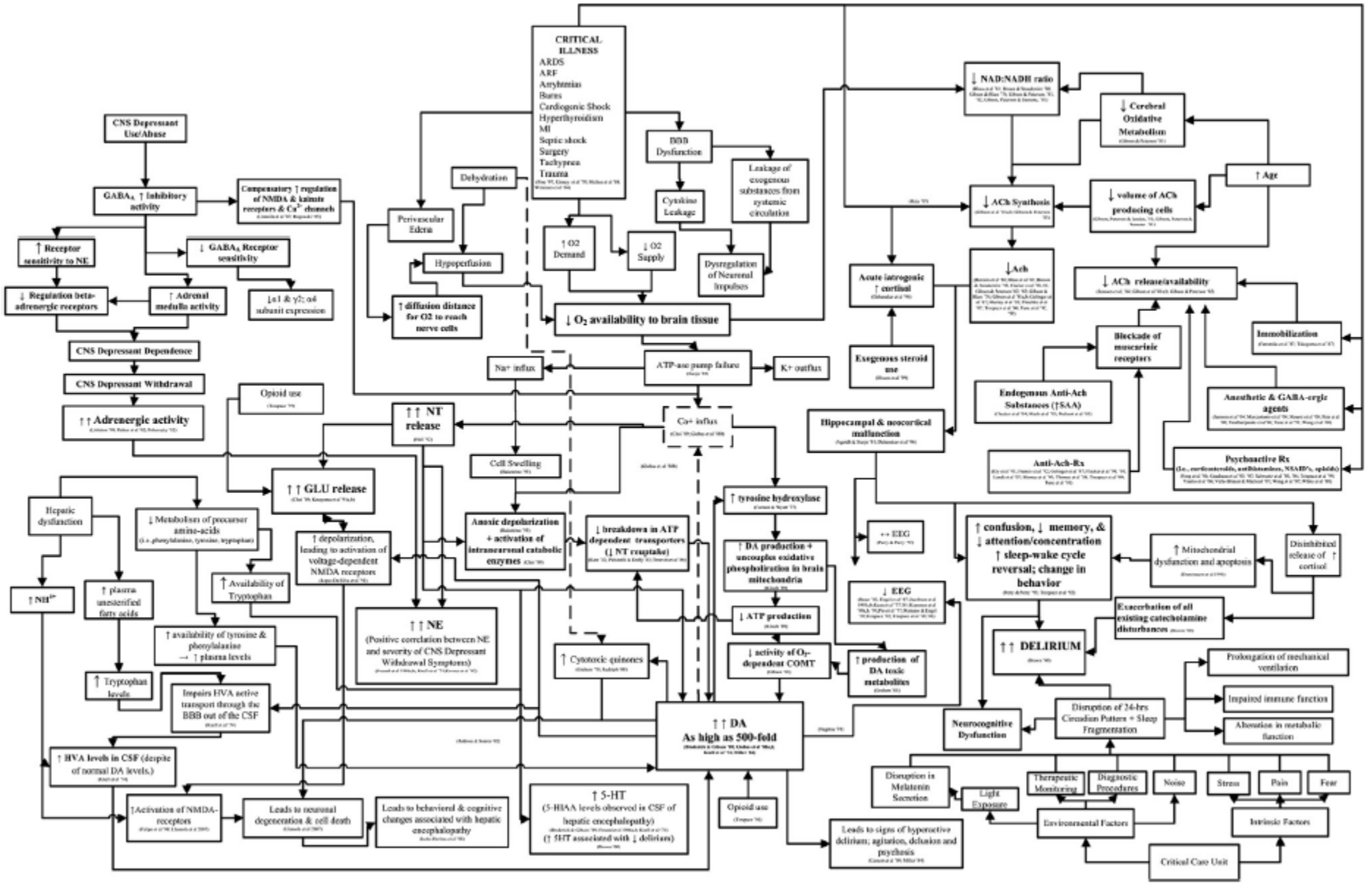


HVA SKJER I HJERNEN VED DELIRIUM? (OG HVORDAN FINNE UT AV DET?)



Oslo University Hospital

Maldonado, Am J Geriatr Psychiatry 2013

PRIMER

Check for updates

Delirium

Jo Ellen Wilson[1,2]✉, Matthew F. Mart[1,3], Colm Cunningham[4], Yahya Shehabi[5,6], Timothy D. Girard[1,7], Alasdair M. J. MacLullich[8], Arjen J. C. Slooter[9] and E. Wesley Ely[1,3,10,11]

Abstract | Delirium, a syndrome characterized by an acute change in attention, awareness and cognition, is caused by a medical condition that cannot be better explained by a pre-existing neurocognitive disorder. Multiple predisposing factors (for example, pre-existing cognitive impairment) and precipitating factors (for example, urinary tract infection) for delirium have been described, with most patients having both types. Because multiple factors are implicated in the aetiology of delirium, there are likely several neurobiological processes that contribute to delirium pathogenesis, including neuroinflammation, brain vascular dysfunction, altered brain metabolism, neurotransmitter imbalance and impaired neuronal network connectivity. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) is the most commonly used diagnostic system upon which a reference standard diagnosis is made, although many other delirium screening tools have been developed given the impracticality of using the DSM-5 in many settings. Pharmacological treatments for delirium (such as antipsychotic drugs) are not effective, reflecting substantial gaps in our understanding of its pathophysiology. Currently, the best management strategies are multidomain interventions that focus on treating precipitating conditions, medication review, managing distress, mitigating complications and maintaining engagement to environmental issues. The effective implementation of delirium detection, treatment and prevention strategies remains a major challenge for health-care organizations globally.

The term 'delirium' is derived from the Latin word *delirare*, meaning 'to go out of the furrow', that is, to deviate from a straight line, to be deranged[1]. Delirium is a severe neuropsychiatric syndrome characterized by the acute onset of deficits in attention and other aspects of cognition. Patients often have altered arousal, from reduced responsiveness at a near-coma level to hypervigilance and severe agitation. They may also experience highly distressing symptoms of psychosis, including delusions and hallucinations, and altered mood. The features of delirium tend to fluctuate in presence and severity. Delirium is associated with considerable distress in patients and caregivers[2].

Delirium is triggered by multiple potential causes, including acute medical illness, drug use or withdrawal, trauma, or surgery. Most causes originate outside of the brain, but delirium with primary neurological causes, such as stroke, is also recognized. Delirium is variable in duration, with most episodes lasting a few days but with episodes persisting for weeks or months in up to 20% of individuals[3–5]. The term 'subsyndromal delirium' has been used to describe patients who have some delirium features but do not fulfil all criteria for a delirium diagnosis[6,7].

Historically, various terms have been used to refer to an acute, global disturbance in mental functioning occurring in the context of medical illness, including encephalopathy, acute brain failure, acute confusional state and organic brain syndrome. The lack of consistent terminology has negatively affected research, with an almost complete segregation of the literature on delirium from that on encephalopathy[8] despite the manifest overlap in the clinical features of the two syndromes. In addition, clinical communication and coding are adversely affected, with a lack of formal labelling of delirium leading to massive under-representation in hospital discharge data[9]. These issues prompted a consensus statement on nomenclature from an interdisciplinary group, which has been endorsed by ten major professional societies and might help to remove some obstacles to research and clinical care in these interrelated states[8]. The statement advocates using only two terms: delirium and acute encephalopathy. Delirium is defined as the clinical state characterized by a combination of features defined by standard diagnostic systems, such as the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5)[4]. Acute encephalopathy is not a clinical syndrome; rather, it is defined as a rapidly developing (usually within hours to a few days), diffuse pathobiological process that might manifest as delirium or, in cases of severely decreased levels of consciousness, as coma.

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https://doi.org/10.1038/s41572-020-00223-4

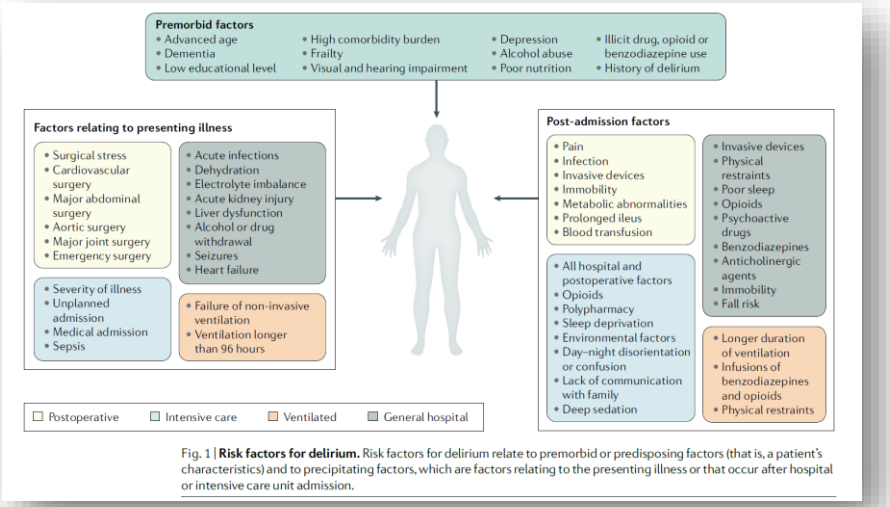


Fig. 1 | **Risk factors for delirium.** Risk factors for delirium relate to premorbid or predisposing factors (that is, a patient's characteristics) and to precipitating factors, which are factors relating to the presenting illness or that occur after hospital or intensive care unit admission.

- Generell og grundig oversiktsartikkel
- «State of the art»

"Over the past few decades, great progress has been made in understanding the epidemiology of delirium (…), and in the development of various clinical screening tools to detect delirium across medical and surgical settings.
(…), our understanding of the prevention, treatment and clinical effects of delirium (that is, morbidities and mortality) has improved."

- Utfordring: implementering

Hvordan studere patofysiologi?

- Neuroimaging
- EEG
- Dyrestudier
- Biomarkører

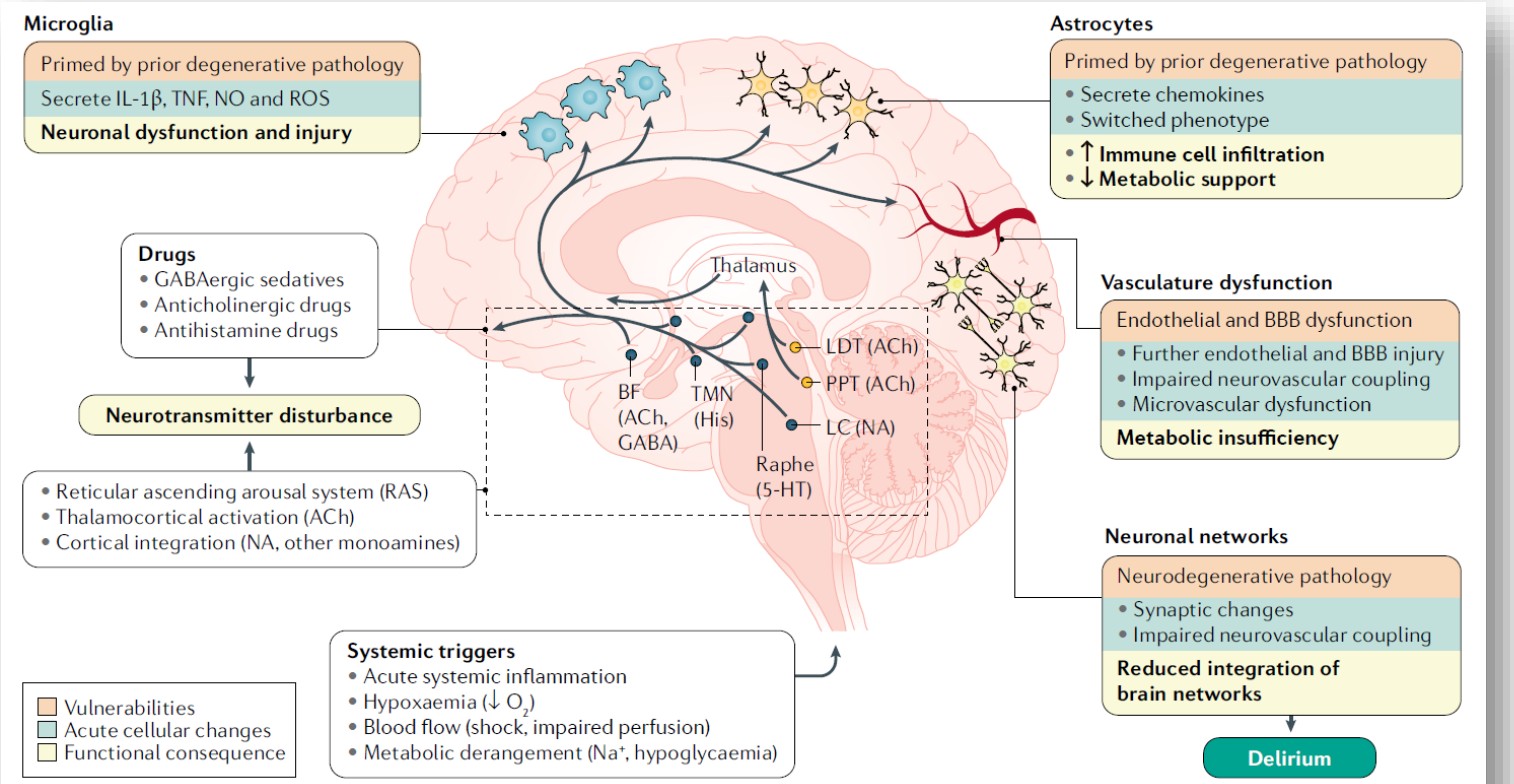


Fig. 4 | **Major mechanisms in delirium pathophysiology.** Major perturbations leading to delirium during acute illness include robust acute mediators can directly affect neuronal function but also act directly on astrocytes. Astrocytes can also be primed during chronic brain pathology,

Delirium

Jo Ellen Wilson[1,2]✉, Matthew F. Mart[1,3], Colm Cunningham[4], Yahya Shehabi[5,6], Timothy D. Girard[1,7], Alasdair M. J. MacLullich[8], Arjen J. C. Slooter[9] and E. Wesley Ely[1,3,10,11]

CSF* from hip fracture patients

Hip - Fracture

Hospital Admission

Serum Samples

Spinal Anesthesia
CSF-samples
Surgery

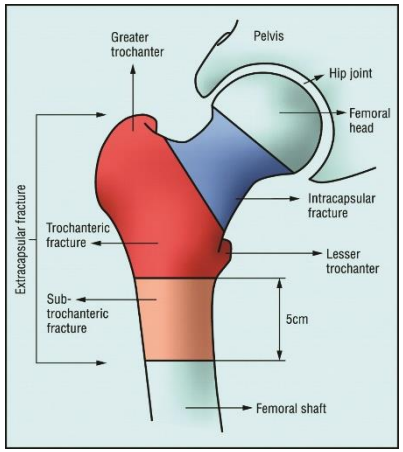
Prefracture Cognitive Impairment

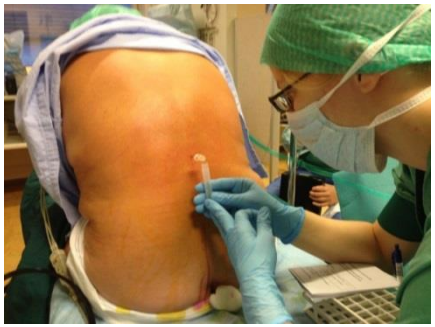
Preoperative Delirium Assessment

Postoperative Delirium Assessment

Preoperative Delirium

Incident [a] Delirium



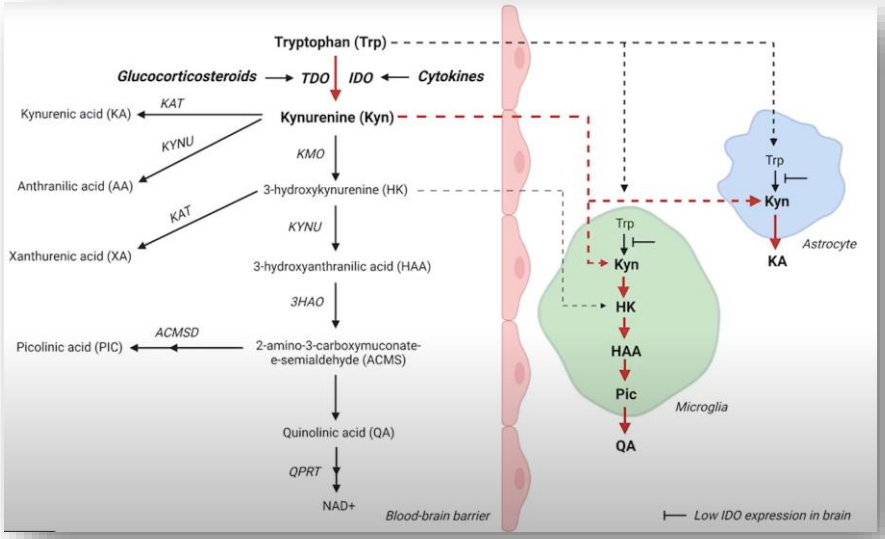


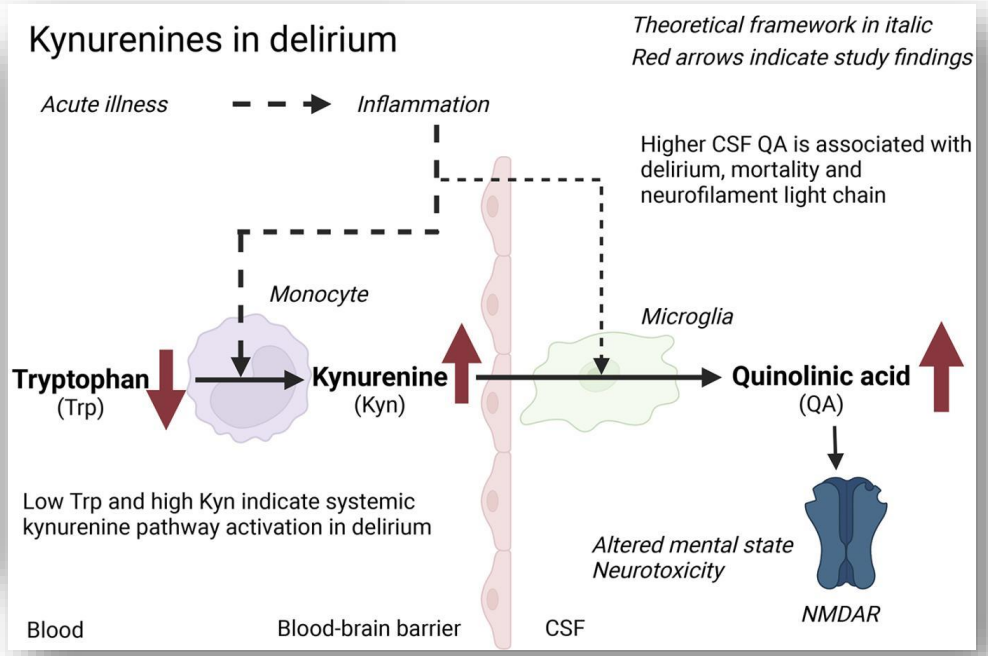
***CSF = cerebrospinal fluid**

The Journal of Clinical Investigation CLINICAL MEDICINE

Cerebrospinal fluid quinolinic acid is strongly associated with delirium and mortality in hip-fracture patients

Leiv Otto Watne,[1,2,3] Christian Thomas Pollmann,[4] Bjørn Erik Neerland,[1] Else Quist-Paulsen,[5] Nathalie Bodd Halaas,[1] Ane-Victoria Idland,[1,6] Bjørnar Hassel,[7] Kristi Henjum,[1,8] Anne-Brita Knapskog,[9] Frede Frihagen,[8,10] Johan Raeder,[8,11] Aasmund Godø,[12] Per Magne Ueland,[13] Adrian McCann,[13] Wender Figved,[8,14] Geir Selbæk,[8,9,15] Henrik Zetterberg,[16,17,18,19,20] Evandro F. Fang,[21,22] Marius Myrstad,[23] and Lasse M. Giil[24,25]





CONCLUSION. Our data identified how systemic inflammation, neurotoxicity, and delirium are strongly linked via the KP and should inform future delirium prevention and treatment clinical trials that target enzymes of the KP.

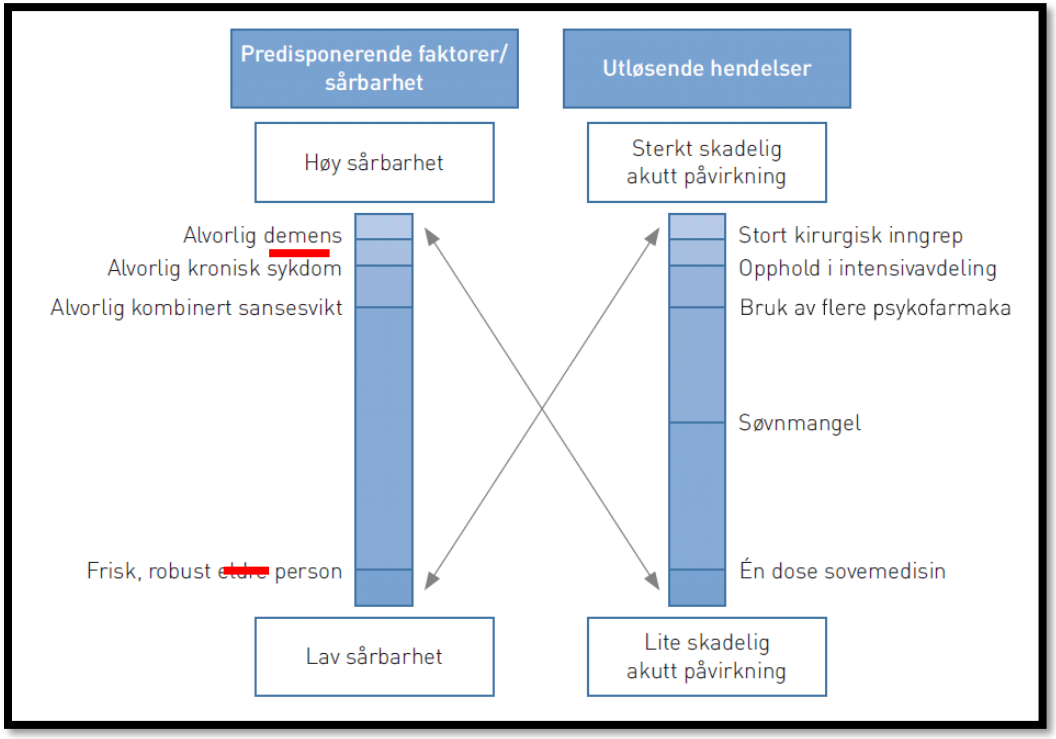
DELIRIUM

… og risiko for kognitiv svikt og demens

Bjørn Erik Neerland
Overlege/postdok, geriatrisk avdeling OUS
Oslo Delirium Research Group

OSLO DELIRIUM RESEARCH GROUP

- Gir delirium økt risiko for kognitiv svikt/demens?
- Hvordan kan man finne det ut?



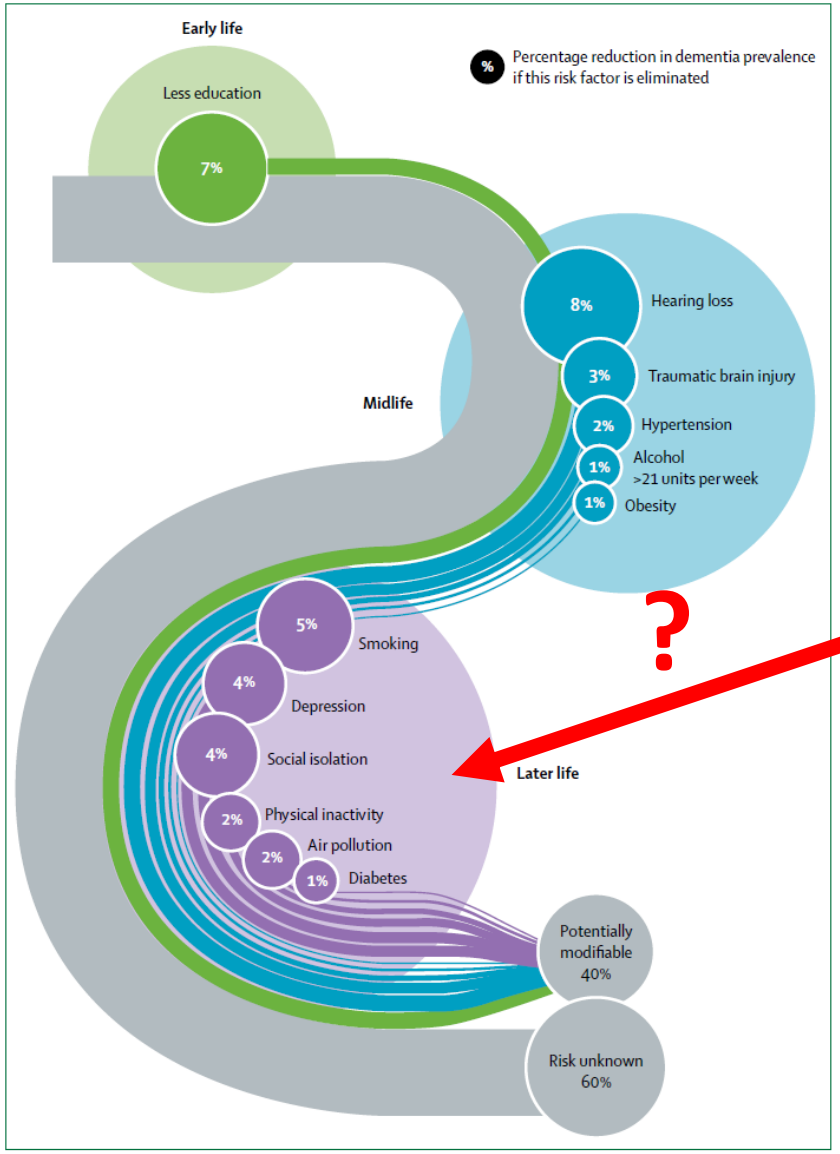


Figure 7: Population attributable fraction of potentially modifiable risk factors for dementia

Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission

Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

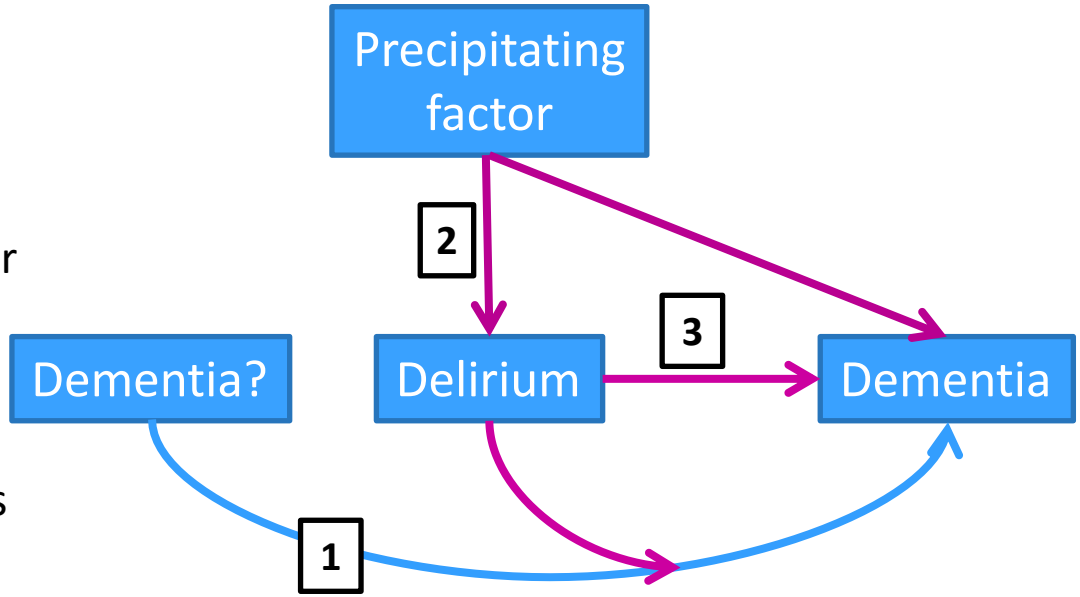
*Given the risk of dementia in people who develop **delirium**, its prevention, and possibly advances in its management, might offer a means for dementia prevention*

Potential mechanisms for how delirium could lead to dementia

1. Delirium unmasks unrecognised or preclinical dementia
   - Dementia pathology responsible for further decline

2. Common shared precipitating factor
   - Sepsis, surgery, drugs

3. Delirium independently contributes to dementia
   - Pathophysiology unknown



Inspired by Fong 2015