Legemiddelbehandling hos eldre innlagt for psykisk lidelse

Notat
Litteratursøk med sortering
September 2009

kunnskapssenteret

Bakgrunn: Nasjonalt kunnskapssenter for helsetjenesten fikk januar 2008 i oppdrag fra Diakonhjemmet sykehus å gjøre litteratursøk med sortering over emnet: Legemiddelbehandling hos eldre innlagt for psykisk lidelse. Hovedfokus skulle være på bivirkninger av legemidler hos denne gruppen. **Metode:** Vi utarbeidet i samarbeide med bestiller en søkestrategi på bakgrunn av forhåndsde-finerte kriterier fra bestillers prosjektbeskrivelse. Faste kriterier var eldre (≥60 år) pasienter innlagt på psykiatrisk avdeling. Dette ble koblet til ulike legemidler og ulike utfall. Deretter ble det utført systematiske søk i følgende databaser: Embase, Medline, PsycInfo og The Cochrane Library. Søkene ble utført i mai 2009. Søket var begrenset fra og med 1980. Det var ingen begrensninger med hensyn på studiedesign eller språk. **Resultat:** Søket resulterte i 2156 unike referanser som ble gjennomgått på sammendragsnivå. Av disse ble 47 publikasjoner vurdert som relevante i henhold til oppdraget.

(fortsetter på baksiden)

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September 2009

kunnskapssenteret

(fortsettelsen fra forsiden) Publikasjonene ble kategorisert i to kategorier, hvor katogori 1 tilfredsstilte alle inklusjonskriteriene og katogori 2 tilfredsstilte alle med unntak av at det ikke kom frem fra sammendraget eller tittelen at pasientene var innlagte på psykiatrisk avdeling.

Tittel	Legemiddelbehandling hos eldre innlagt for psykisk lidelse
Institusjon	Nasjonalt kunnskapssenter for helsetjenesten
Ansvarlig	John-Arne Røttingen *direktør*
Forfattere	Pike, Eva, *forsker (prosjektleder)* Harboe, Ingrid, *forskningsbibliotekar* Ringerike, Tove, *forsker* Marianne Klemp, *forskningsleder*
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Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Senteret er formelt et forvaltningsorgan under Helsedirektoratet, uten myndighetsfunksjoner. Kunnskapssenteret kan ikke instrueres i faglige spørsmål.

Nasjonalt kunnskapssenter for helsetjenesten
Oslo, 15. 09.2009

1-side oppsummering

Dette prosjektet ble gjort på oppdrag fra avd. sjef/overlege Bernhard Lorentzen, alderspsykiatrisk avdeling, Diakonhjemmet Sykehus. Det var bedt om hjelp til litteratursøk med sortering i forbindelse med prosjektet: Legemiddelbehandling hos eldre innlagt for psykisk lidelse. Hovedfokus skulle være på bivirkninger av legemidler hos denne gruppen.

Vi utarbeidet i samarbeide med bestiller en søkestrategi på bakgrunn av forhåndsdefinerte kriterier fra bestillers prosjektbeskrivelse. Faste kriterier var eldre (≥60 år) pasienter innlagt på psykiatrisk avdeling. Dette ble koblet til ulike legemidler og ulike utfall. Deretter ble det utført systematiske søk i følgende databaser: Embase, Medline, PsycInfo og The Cochrane Library. Søkene ble utført i mai 2009. Søket var begrenset fra og med 1980. Det var ingen begrensninger med hensyn på studiedesign eller språk.

Søket resulterte i 2156 unike referanser som ble gjennomgått på sammendragsnivå. Av disse ble 47 publikasjoner vurdert som relevante i henhold til oppdraget.

Publikasjonene ble kategorisert i to kategorier, hvor den første kategori tilfredsstilte alle inklusjonskriteriene og den andre tilfredsstilte alle med unntak av at det ikke kom frem fra sammendraget eller tittelen at pasientene var innlagte på psykiatrisk avdeling.

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Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk januar 2008 i oppdrag fra Diakonhjemmet sykehus å identifisere litteratur om emnet: Legemiddelbehandling hos eldre innlagt for psykisk lidelse. Hovedfokus skulle være på bivirkninger av legemidler hos denne gruppen. Nasjonalt kunnskapssenter for helsetjenesten har svart på denne oppgaven ved å gjøre et litteratursøk med sortering.

Dette arbeidet er utført av en intern arbeidsgruppe ved Nasjonalt kunnskapssenter for helsetjenesten:

- Prosjektleder: Forsker Eva Pike
- Prosjektmedarbeider: Forskningsbibliotekar Ingrid Harboe
- Prosjektmedarbeider: Forsker Tove Ringerike
- Prosjektansvarlig: Forskningsleder Marianne Klemp

Gro Jamtvedt	Marianne Klemp	Eva Pike
Avdelingsdirektør	*Forskningsleder*	*Forsker, prosjektleder*

Problemstilling

Dette oppdraget kom fra avd. sjef/overlege Bernhard Lorentzen, alderspsykiatrisk avdeling, Diakonhjemmet Sykehus. Vi ble bedt om hjelp til å søke etter og sortere litteratur i forbindelse med prosjektet: Legemiddelbehandling hos eldre innlagt for psykisk lidelse. Hovedfokus skulle være på bivirkninger av legemidler hos denne gruppen.

Arbeidet skulle resultere i en referanseliste over relevante litteratur og en sortering av denne.

Innledning

Diakonhjemmet sykehus under ledelse av avd. sjef/overlege Bernhard Lorentzen, alderspsykiatrisk avdeling utfører et prosjekt med tittelen: Legemiddelbehandling hos eldre innlagt for psykisk lidelse - en naturalistisk studie av legemiddelrelaterte forhold.

Målet med bestillers prosjekt er å få mer kunnskap om legemiddelbehandling av eldre som legges inn for psykisk lidelse, samt å dokumentere enkelte spesifikke legemiddelrelaterte forhold hos eldre. De ønsker å fokusere på:

- Hvordan endres pasientenes symptombelastning under sykehusoppholdet, og hvilken betydning synes legemiddelbehandlingen å ha for endring i symptomer, funn og kognitiv funksjon?
- Pasientenes etterlevelse av foreskrevet medisinering.
- Identifisere faktorer som er av betydning for forholdet mellom dose og serumkonsentrasjon.
- Kartlegging av legemiddelbivirkninger.

I henhold til bestillers prosjektbeskrivelse vil legemiddelbivirkninger bidra til den totale symptombelastningen hos en stor andel av pasientene.

Til dette prosjektet er Nasjonalt kunnskapssenter for helsetjenesten bedt om å hjelpe til med å søke frem samt sortere relevant litteratur.

Bakgrunnen for søkeordene er basert på prosjektplanen og diskusjon med bestiller.

Metode

Vi har gjort et litteratursøk med sortering. Dette betyr at arbeidets sluttprodukt er en liste over relevante, identifiserte titler med sammendrag, samt en sortering av disse.

LITTERATURSØK

Vi la bestillingen til grunn ved utarbeiding av søkestrategien og søkte etter publisert litteratur som oppfylte våre inklusjonskriterier for populasjon og intervensjon.

Vi søkte systematisk etter litteratur i følgende databaser mai 2009:

- EMBASE 1980 to 2009 week 20
- MEDLINE (In-process & Other Non-Indexed Citations and Ovid medline 1950 to present)
- PsycINFO 1967 to May week 3 2009
- The Cochrane Library

Det ble ikke brukt filter for studiedesign, men søket ble avgrenset til publikasjoner f.o.m. 1980. Emneord og tekstord i litteratursøket ble satt sammen av en bibliotekar etter diskusjon med prosjektleder. Søkestrategien fra Embase er gjengitt i vedlegg 1. Tilsvarende søkestrategier ble laget for søk i de andre litteraturdatabasene.

Vi utførte også håndsøk etter relevant litteratur hos andre organisasjoner som lager systematiske oversikter og medisinske metodevurderinger. Rapporter fra slike organisasjoner blir ikke alltid indeksert i Medline. Håndsøk ble gjort i National Institute for Health and Clinical Excellence (NICE), Danish Centre for Evaluation and Health Technology Assessment (DACEHTA), Finnish Office for Health Technology Assessment (Finohta) og Statens beredning för medicinsk utvärdering (SBU).

INKLUSJONSKRITERIER

Populasjon
Eldre (>60 år), inneliggende på alderspsykiatrisk avdeling

Intervensjoner:
Behandling med enten benzodiazepiner, antikolinergika, antidepressiva eller antipsykotika eller polyfarmasi

Utfall
Kognitiv funksjon, delirium, tretthet, søvnforstyrrelse, ekstrapyramidale symptomer, munntørrhet, kvalme, nedsatt matlyst, forstoppelse, hypotensjon, svimmelhet, hjertesvikt, ødem, rytmeforstyrrelser, hyponatremi, kreatinin, transaminase, prolaktin, CYP-enzym, depresjon og serumkonsentrasjon av psykofarmaka, compliance, kjønnsforskjell, bivirkninger (UKU), klinisk bedring (CGI), EKG, dagliglivets aktiviteter (ADL), symptombelastning

Studiedesign
Ingen begrensninger

Publikasjonsår: 1980 – 2009

Språk
Ingen begrensninger

UTVELGELSE OG SORTERING

To forskere (TR og EP) gikk gjennom alle titler og sammendrag for å vurdere relevans i henhold til inklusjonskriteriene. Vurderingene ble gjort uavhengig av hverandre og sammenlignet i etterkant. Der det var uenighet om vurderingene, ble inklusjon eller eksklusjon avgjort ved konsensus.

Utvelgelse av litteratur ble kun gjort basert på tittel og sammendrag. Det ble ikke bestilt fulltekst av artiklene – dette gjelder også håndsøk.

Publikasjonene presenteres med referanser og sammendrag kopiert fra databasene hvor de ble identifisert. Vi sorterte de utvalgte publikasjonene i to kategorier:

- Kategori 1: Tilfredstilte alle inklusjonskriteriene
- Kategori 2: Tilfredstilte alle inklusjonskriteriene, bortsett fra at det ikke kom frem fra tittel eller sammendrag hvorvidt pasientene var innlagt på psykiatrisk avdeling.

Etter ønske fra bestiller inndeles kategori 2 i to undergrupper:

2a: Publikasjonene som omhandler kun ett legemiddel eller en legemiddelgruppe (hvor de enkelte legemidlene ikke var spesifiserte).

2b: Publikasjonene som omhandler to eller flere legemidler.

Resultat

RESULTAT FRA SØKET

Søket identifiserte 2156 unike referanser (2553 før dublettkontroll).

Vi vurderte 47 publikasjoner som relevante. Disse sorterte vi i to kategorier:

- Kategori 1: Tilfredstilte alle inklusjonskriteriene
- Kategori 2: Tilfredstilte alle inklusjonskriteriene, bortsett fra at det ikke kom frem fra tittel eller sammendrag hvorvidt pasientene var innlagt på psykiatrisk avdeling.

I tillegg ble det funnet en systematisk oversikt i SBU (Rapportnr:193, 2009): Äldres läkemedelsanvänding-hur kan den förbättras? En systematisk litteraturoversikt.

SORTERING AV RELEVANTE PUBLIKASJONER

Kategori 1: Tilfredstilte alle inklusjonskriteriene

Vi fant fem publikasjoner som tilfredstilte kriteriene til kategori 1. Hvordan disse var fordelt på studietype, populasjon, intervensjon og utfall sees av tabell 1.

Tabell 1 - Relevante publikasjoner i kategori 1.

Studie	Studietype	Populasjon	Intervensjon	Utfall
Omura et al 2003	Primærstudie	24 eldre med delirium innlagte på alderspsykiatrisk avdeling	Quetiapin	Effekt, ekstrapyramidale bivirkninger
Heeren et al 1998	Primærstudie	Eldre, deprimerte innlagte på psykiatrisk sykehus, n?	Antidepressiva	Effekt
Orengo et al 1996	Primærstudie	31 eldre innlagte på alders psykiatrisk avdeling	Fluoksetin	Effekt og sikkerhet
Sweet et al 1992	Primærstudie	45 eldre innlagte på psykiatrisk avdeling	Neuroleptika	Tardiv dyskinesi
Yassa et al 1992	Primærstudie	162 eldre innlagte på alderspsykiatrisk avdeling	Neuroleptika	Tardiv dyskinesi

For å se tittel og sammendrag av publikasjonene i kategori 1 se vedlegg 2.

Kategori 2: Tilfredstilte alle inklusjonskriteriene, bortsett fra at det ikke kom frem fra tittel eller sammendrag hvorvidt pasientene var innlagt på psykiatrisk avdeling.

Vi fant 42 publikasjoner som fylte kriteriene til kategori 2. Disse presenteres i tabell 2a og 2b. Tabell 2a lister de publikasjonene som omhandler kun ett legemiddel eller en legemiddelgruppe (hvor de enkelte legemidlene ikke var spesifiserte) og 2 b lister de publikasjonene som omhandler to eller flere legemidler.

Kategori 2a

Tabell 2a - Relevante publikasjoner i kategori 2 som omhandler ett legemiddel eller en legemiddelgruppe

Studie	Studietype	Populasjon	Intervensjon	Utfall
Bose et al 2008	Primærstudie	264 deprimerte eldre	Escitalopram vs placebo	Effekt og tolerabilitet
Draper et al 2008	Oversikt	Deprimerte eldre, n?	Selektive serotonin-reopptakshemmere	Tolerabilitet
Barak et al 2007	Primærstudie	2583 psykiatriske eldre, innlagte	Anti-psykotika	Hjerte og cerebrovaskulær morbiditet og mortalitet
Gorwood et al 2007	Primærstudie	405 deprimerte eldre	Escitalopram	Tid til tilbakefall
Kissing et al 2007	Primærstudie	52 eldre psykotiske pasienter	Risperidon	Sikkerhet, effekt, funksjonell kapasitet, livskvalitet og pasienttilfredshet
Kok et al 2007	Primærstudie og kommentar til en annen studie	81 deprimerte eldre, innlagte	Venlafaksin	Kardiovaskulære endringer
Nelson et al 2005	Meta-analyse av 2 primærstudier	90 deprimerte eldre	Duloksetin vs placebo	Effekt og frafall p.g.a. bivirkninger
Yang et al 2005	Primærstudie	100 psykotiske eldre, innlagte	Quetiapin	Effekt og sikkerhet
Sheikh et al 2004	Primærstudie	752 deprimerte eldre	Sertralin vs placebo	Effekt og sikkerhet
Wee et al 2004	Primærstudie	116 eldre	Selektive serotonin-reopptaks-hemmere	Forekomst av hyponatremi

Barek and Aizenberg 2003	Primærstudie	21 eldre schizofrene, innlagte	Olanzapin	Effekt
Kirkwood et al 2003	Oversikt	Eldre psykotiske pasienter, n?	Antipsykotika	Effekt og bivirkninger
McSwan et al 2003	Enkelt rapporter	2 eldre	Selektive serotoninreopptakshemmere	Hyponatremi
Maxwell et al 2002	Primærstudie	20 innlagte eldre	Risperidon	Kinetikk
Kennedy et al 2001	Oversikt	Eldre, n?	Olanzapin	Sikkerhet
Madhusoodnan et al 2000	Primærstudie	7 psykotiske eldre, innlagte	Quetiapin	Effekt og sikkerhet
Solomons et al 2000	Primærstudie	58 eldre med behandlingsresistent psykose, innlagte	Olanzapin	Effekt og sikkerhet
Barak et al 1999	Oversikt	133 eldre psykiatriske pasienter	Klozapin	Effekt og sikkerhet
Strachan et al 1998	Primærstudie	53 psykotiske eldre, innlagte	Selektive serotoninreopptakshemmere	Hyponatremi
Zarate 1997	Primærstudie	122 psykotiske eldre, innlagte	Risperidon	Effekt og sikkerhet
Peter et al 1996	Primærstudie	Eldre med agitasjon, innlagte	Neuroleptika	Effekt og sikkerhet
Lemke et al 1994	Primærstudie	29 eldre med agitasjon, innlagte	Karbamazepin	Effekt og sikkerhet
Shaw et al 1992	Primærstudie	119 psykiatriske eldre med søvnproblemer, innlagte	Zolpidem vs placebo	Effekt og sikkerhet
Newhouse et al 1988	Primærstudie	9 deprimerte eldre	Skopolamin	Effekt og sikkerhet
Miller, Whitcup 1986	Uklart, mangler abstract	Eldre psykiatriske pasienter, innlagte. n?	Benzodiazepiner	Bruken av benzodiazepiner
Toenniessen et al 1985	Primærstudie	57 eldre psykiatriske pasienter, innlagte	Neuroleptika	Tardiv dyskinesi

For å se tittel og sammendrag av publikasjonene i kategori 2a se vedlegg 2.

Kategori 2b

Tabell 2b - Relevante publikasjoner i kategori 2 som omhandler to eller flere legemidler

Studie	Studietype	Populasjon	Intervensjon	Utfall
Mazeh et al 2007	Primærstudie	30 eldre med resistent depresjon	Venlafaksin vs paroksetin	Remisjonsrate og tolerabilitet
Rossini et al 2005	Primærstudie	93 deprimerte eldre, innlagte	Sertralin vs fluvoksamin	Effekt
Sajatovic et al 2005	Primærstudie	48 eldre med bipolar lidelse, innlagte	Polyfarmasi	Kliniske karakteristika og ressursbruk
Hwang et al 2004	Primærstudie	Deprimerte eldre, innlagte	Venlafaksin vs paroksetin	Effekt og Tolerabilitet
Portella et al 2003	Primærstudie	Eldre deprimerte	Farmakologisk behandling	Kognitiv funksjon
Malur et al 2000	Primærstudie	5 eldre med forverring av mental sykdom, innlagte	Medikasjon utvasking	Effekt
Walters et al 1999	Primærstudie	25 deprimerte eldre	Paroksetin vs nortriptylin	Effekt
Zanalda et al 1999	Primærstudie	40 deprimerte eldre	Trisykliske antidepressiva vs selektive serotoninreopptakshemmere	Kognitiv funksjon
Pabis et al 1996	Oversikts studie	Aggresive eldre	Farmakoterapi	Effekt
Tourigny et al 1996	Primærstudie	47 deprimerte eldre	Fluvoksamin vs desipramin	Effekt og sikkerhet
Wong et al 1995	Oversikts studie	Eldre med medikamentrelatert delirium	Deliriumrelaterte legemidler	Legemidler og delirium
Stewart et al 1992	Enkelt rapporter	3 eldre psykiatriske pasienter, innlagte	Polyfarmasi	Bivirkninger. Metoder for å redusere polyfarmasi.
Cohn et al 1990	Primærstudie	241 deprimerte eldre	Sertralin vs amitriptylin	Effekt og sikkerhet

Viukari et al 1983	Primærstudie	37 psykotiske eldre, innlagte	Flunitrazepam vs nitrazepam	Effekt (søvn) og sikkerhet
Viukari et al 1983	Primærstudie	37 psykotiske eldre, innlagte pasienter	Flunitrazepam vs nitrazepam	Effekt (psyko-motoriske ferdigheter og muskelstyrke) og sikkerhet
Thienhaus et al (årstall ikke oppgitt)	Primærstudie	25 eldre med psykisk lidelse, innlagte	Anti depressiva og/eller neuroleptika	Antikolinerg plasmaaktivi-tet og kognitiv funksjon

For å se tittel og sammendrag av publikasjonene i kategori 2b se vedlegg 2.

Diskusjon

I dette litteratursøket med sortering, er både identifisering av litteratur og sortering basert kun på tittel og sammendrag. Artiklene ble ikke hentet inn fulltekst.

Dette kan ha medført at vi har inkludert titler som vil vise seg ikke å være relevante ved gjennomlesning av fulltekst.

På den annen side kan vi ha utelatt studier som bestiller muligens ville betraktet som relevante fordi de kriterier vi har sortert etter ikke fremgår av tittel eller sammendrag.

Vi har bare inkludert studier som var i henhold til inklusjonskriteriene. Dette betyr for eksempel at titler og sammendrag som omhandler utfall som lipider, foreskrivningsmønstre og blandet alderspopulasjon (hvor ikke resultatene for eldre var rapportert spesifikt) ikke er inkludert. Dette er gjort etter avtale med bestiller. Bestiller får imidlertid i tillegg til dette litteratursøket med sortering også overlevert samtlige treff i søket slik at han om ønskelig kan gå mer detaljert inn i dette.

Det er viktig å være klar over at fremgangsmåten som brukes i søk og sorter har utfordringer knyttet til seg. Manglende innhenting av artiklene i fulltekst umuliggjør en kvalitetsvurdering av studiene.

Vedlegg 1

SØKESTRATEGI

EMBASE 1980 to 2009 Week 21

1 Mental patient/

2 Mental disease/

3 ((mental* or psychiatric) adj2 (disease? or disorder? or patient? or person?)).tw.

4 or/1-3

5 hospital patient/

6 (hospital* or inpatient* or in patient*).tw.

7 5 or 6

8 4 and 7

9 Aged/

10 Geriatrics/

11 (aged or elderly or geriatr*).tw.

12 or/9-11

13 8 and 12

14 benzodiazepine/

15 benzodiazepine derivative/

16 flunitrazepam/

17 nitrazepam/

18 midazolam/

19 zolpidem/

20 zopiclone/

21 (flunitrazepam or nitrazepam or nitra?zepam or midazolam or zolpidem or zopiclon*).tw.

22 diazepam/

23 oxazepam/

24 anticholinergic effect/

25 exp Antidepressant Agent/

26 exp Neuroleptic Agent/

27 Alprazolam/

28 (benzodiazepin* or diazepam* or oxazepam* or alprazolam* or anticholinergic effect? or Antidepressant Agent? or antidepressive agent? or antipsychotic agent? or Neuroleptic Agent?).tw.

29 ((cholinergic or antidepressant or antidepressive or antipsychotic or neuroleptic) adj2 drug?).tw.

30 (biperidon* or tricyclic antidepressant* or clomipramin* or trimipramin* or amitryptylin* or nortriptylin* or doxepin*).tw.

31 (selective serotonin-reuptake inhibitor* or SSRI or Fluoxetin* or citalopram* or paroxetin* or sertralin* or fluvoksamin* or escitalopram*).tw.

32 (MAO-inhibitor* or MAOI or moclobemid* or mianserin* or mirtazapin* or venlafaxin* or reboxetin* or duloxetin*).tw.

33 (levomepromazin* or perfenazin* or haloperidol* or sertindole* or ziprasidon* or flupentixol* or chlorprotixen* or zuklopentixol* or clozapin* or olanzapin* or quetiapin* or amisulprid* or lithium* or risperidon* or aripiprazol*).tw.

34 Polypharmacy/

35 polypharmacy.tw.

36 or/14-35

37 13 and 36

Vedlegg 2

PUBLIKASJONENE LISTET ETTER DATO

Publikasjonene i kategori 1 listet etter dato (nyeste øverst)

1. Omura K, Amano N. Clinical experience of quetiapine in 24 elderly patients with delirium. Psychogeriatrics 2003;3(2):69-72.
   Ref ID: 1710
   Abstract: Background: A recent study reported that patients with delirium responded well to the administration of atypical antipsychotic agents. In the present study we administered quetiapine to patients with delirium and obtained good results. Methods: This study included 24 patients (10 men, 14 women), referred to the psychiatry department during admission to other hospital departments, who were diagnosed as having delirium according to the diagnostic and statistical manual of mental disorders (4th edition) (DSM-IV) between April 2001 and September 2002. The mean age of the patients was 76.5 years (men 71.0 years; women 80.5 years). An initial dose of quetiapine was established at 25-50 mg/day. Depending on the symptoms, the dose and frequency were increased as required. According to Trzepacz's delirium rating scale (DPS), the treatment response was evaluated prior to the administration of quetiapine and 1, 3, 5 and 7 days after administration began. Results: Prior to the administration of quetiapine, the mean DPS score was 18.1. The mean scores were 12.2, 10.8, 9.7 and 8.9 after 1, 3, 5 and 7 days of quetiapine administration, respectively. These values were significantly lower than the value before administration ($P < 0.001$). Seven days after the administration of quetiapine commenced, the total DPS score was lower than the cutoff point (12) in 20 patients (83.3%). In 18 patients (75.0%), delirium was clinically relieved. Doses ranged from 25 mg/day to 125 mg/day, with a mean dose of 54.7 mg/day. With respect to the administration method, the majority of patients (i.e. 13 patients) received quetiapine once per day (after dinner). Somnolence was observed in three patients as a side-effect of quetiapine administration. However, this side-effect improved after 1-2 days, without decreasing the dose. Conclusions: Quetiapine may be useful for controlling delirium and concerning side-effects and extrapyramidal symptoms were not recorded in the present study. Thus, it is appropriate to trial quetiapine in the treatment of delirium. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

2. Heeren TJ, Derksen P, ten Ham BFVH, van Gent PPJM. Elderly depressed patients in three psychiatric hospitals: Treatment and outcome. Tijdschrift voor Psychiatrie

1998;40(6):323-34.
Ref ID: 816
Abstract: Full recovery rates in naturalistic studies of the treatment of elderly depressives have been invariably lower than in clinical trials. This may he the result of inadequate treatment due to the lack of clear treatment strategy recommendations for the elderly. The present study is a naturalistic prospective study of depressed elderly inpatients in three Dutch psychiatric hospitals. Patients were included when they suffered from any mood disorder according to the DSM-III-R-criteria. Severity of the depression was measured on the Montgomery Asberg Rating Scale (MADRS). Antidepressants were prescribed to more than 90% of the patients. More than half of them only received one treatment. The dose of the antidepressants was in 55% of the cases less than the recommended dose for adults. Full recovery of the depressive episode was achieved in less than half of the patients (33-45%). In the present study a relatively poor outcome of the antidepressant treatment of elderly depressives has been found. A combination of low treatment expectations and fear of vigorous treatment seem to have played an important role

3. Orengo CA, Kunik ME, Molinari V, Workman RH. The use and tolerability of fluoxetine in geropsychiatric inpatients. J Clin Psychiatry 1996;57(1):12-6.
Ref ID: 1392
Abstract: BACKGROUND: The efficacy and tolerability of fluoxetine were examined in 31 patients admitted to a geropsychiatric inpatient unit who were initiated and maintained on a regimen of fluoxetine. METHOD: The Hamilton Rating Scale for Depression, the Brief Psychiatric Rating Scale, the Mini-Mental State Examination, and the Rating Scale for Side Effects were administered at admission and discharge, and scores were compared using paired t tests. Two patients were withdrawn from fluoxetine prior to discharge because of side effects; their data are not included in the analysis. RESULTS: We found significant improvement both in depressive symptoms and in general psychiatric symptoms and nonsignificant improvement in cognitive function. Fluoxetine was well-tolerated, and a significant decrease in the total scores of the Rating Scale for Side Effects was found. Subgroups of older patients (mean age = 75 years), less depressed patients, and demented patients were also examined. In all three groups, we found a statistically significant improvement in depressive symptoms, general psychiatric symptoms, and total side effects. CONCLUSION: Fluoxetine appears to be an effective and well-tolerated antidepressant in elderly inpatients of varying age, levels of depression, and psychiatric diagnoses

4. Sweet RA, Mulsant BH, Rifai AH, Zubenko GS. Dyskinesia and neuroleptic exposure in elderly psychiatric inpatients. J Geriatr Psychiatry Neurol 1992;5(3):156-61.
Ref ID: 958
Abstract: A wide variation in prevalence rates of tardive dyskinesia and spontaneous orofacial dyskinesia has been reported in the elderly. To clarify these discrepancies, we studied 45 patients over the age of 60 years admitted to a short-term psychiatric unit. Standardized criteria for the diagnosis of dyskinesia were used. We found a rate of tardive dyskinesia of only 21% (7/33) in our patients having a history of neuroleptic ex-

posure. We found no cases (0/12) of spontaneous orofacial dyskinesia. There was a significant association between tardive dyskinesia and psychiatric diagnosis, with the highest rate of tardive dyskinesia in those patients with schizophrenic disorders, followed by those with organic disorders and mood disorders, respectively. There was also a significant association between the presence of tardive dyskinesia and radiographic evidence of cortical atrophy, and a trend towards an association with leukoencephalopathy. Our results suggest that published rates of tardive and spontaneous dyskinesia in the elderly may overestimate the prevalence of these disorders, especially among geriatric patients with acute psychiatric presentations

5. Yassa R, Nastase C, Dupont D, Thibeau M. Tardive dyskinesia in elderly psychiatric patients: a 5-year study. Am J Psychiatry 1992;149(9):1206-11.
   Ref ID: 1449
   Abstract: OBJECTIVE: The authors investigated the prevalence of tardive dyskinesia among elderly psychiatric patients who had never received neuroleptic medication before their first hospitalization. METHOD: The study was performed in the geriatric psychiatry unit of a university-affiliated hospital in Canada and involved all first-admission patients admitted from September 1984 through August 1989 who had never taken neuroleptic drugs. In September and October 1989, the patients who were available for follow-up were examined and given ratings on the Abnormal Involuntary Movement Scale to establish the presence or absence of tardive dyskinesia. The patients' records were reviewed for information on age, diagnosis, duration of hospitalization, neuroleptic treatment received after admission, anticholinergic drugs received, and drug-free periods. RESULTS: Of the 162 patients who were available and whose data were analyzed, a total of 99 had been treated with neuroleptics, and 35 (35.4%) of these were found to have tardive dyskinesia. Two of the 35 also had tardive dystonia. Significantly more patients with major depression than patients with primary degenerative dementia or delusional psychosis had tardive dyskinesia. CONCLUSIONS: This study confirms the higher vulnerability of elderly psychiatric patients treated with neuroleptics to the development of tardive dyskinesia. The authors stress that caution is especially necessary when neuroleptics are prescribed for older patients with major affective disorders.

Publikasjonene i kategori 2a listet etter dato (nyeste øverst)

Publikasjonene i katogori 2a listet etter dato (nyeste øverst).

1. Bose A, Li D, Gandhi C. Escitalopram in the acute treatment of depressed patients aged 60 years or older. Am J Geriatr Psychiatry 2008;16(1):14-20.
   Ref ID: 1046
   Abstract: OBJECTIVE: The present study examined the efficacy and tolerability of acute escitalopram treatment in depressed patients aged 60 years or older. METHODS: Patients aged > or =60 years with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition major depressive disorder were randomized to 12 weeks of double-blind, flexible-dose treatment with escitalopram (10-20 mg/day; N = 130) or placebo (N = 134). The prospectively defined primary efficacy end point was change from baseline to week 12 in Montgomery-Asberg Depression Rating Scale (MADRS) total score using the last

observation carried forward approach. RESULTS: A total of 109 (81%) patients in the placebo group and 96 (74%) patients in the escitalopram group completed treatment. Mean age in both groups was approximately 68 years. Mean baseline MADRS scores were 28.4 and 29.4 for the placebo and escitalopram treatment groups, respectively. Escitalopram did not achieve statistical significance compared with placebo in change from baseline on the MADRS (least square mean difference: -1.34; last observation carried forward). Discontinuation rates resulting from adverse events were 6% for placebo and 11% for escitalopram. Treatment-emergent adverse events reported by >10% of patients in the escitalopram group were headache, nausea, diarrhea, and dry mouth. CONCLUSIONS: Escitalopram treatment was not significantly different from placebo treatment on the primary efficacy measure, change from baseline to week 12 in MADRS. In patients aged 60 years or older with major depression, acute escitalopram treatment appeared to be well tolerated

2. Draper B, Berman K. Tolerability of selective serotonin reuptake inhibitors: Issues relevant to the elderly. Drugs Aging 2008;25(6):501-19.
   Ref ID: 72
   Abstract: Selective serotonin reuptake inhibitors (SSRIs) continue to be the first-choice antidepressant treatment for the elderly as they have similar efficacy to other antidepressants but better tolerability. However, recent concerns have emerged regarding a range of adverse effects that are more likely to occur in the elderly. In part this relates to the increased risk of drug interactions. Platelet dysfunction induced by SSRIs with high serotenergic activity is associated with gastrointestinal bleeding in the first month of treatment, although the overall evidence is weak. The risk of falls and fractures in elderly patients taking SSRIs is similar to that reported with use of tricyclic antidepressants. Hyponatraemia due to induction of the syndrome of inappropriate antidiuretic hormone secretion may be life threatening in the elderly but in most cases is asymptomatic and reversible. Extrapyramidal disorders such as parkinsonism and dyskinesias are more common in the elderly but are rare. There is a very low risk of cerebrovascular adverse reactions in patients taking SSRIs. There are inconsistent findings linking SSRIs with suicidal behaviour in late life and with the risk of cancer. Most of the newly identified adverse effects are either relatively uncommon or of debatable significance. Few differences have been identified among the SSRIs that are of clinical significance. However, it is recommended in the elderly that SSRIs should be titrated slowly to recommended therapeutic doses and used cautiously with other agents known to have the potential for drug interactions.

3. Barak Y, Baruch Y, Mazeh D, Paleacu D, Aizenberg D. Cardiac and cerebrovascular morbidity and mortality associated with antipsychotic medication in elderly psychiatric inpatients. Am J Geriatr Psychiatry 2007;15(4):354-6.
   Ref ID: 1665
   Abstract: Objective: To evaluate the rate of adverse medical outcomes for elderly exposed to antipsychotic treatment. Methods: This was a retrospective evaluation of psychiatric inpatients records. Age, gender, diagnosis, treatment with antipsychotics, and duration of treatment were analyzed. An acute cardiac or cerebrovascular event necessi-

tating transfer to a general hospital or resulting in death was the outcome measure. Results: During 15 years (1990 to 2005), 3,111 elderly were hospitalized. Their mean age was 73.5 6.1 years, 1,220 were male (39%), and 1,891 were female (61%). Most patients (2,583 [83%]) were exposed to antipsychotics, of which 1,402 (54%) were exposed to second-generation antipsychotics (SGAs). Antipsychotic-treated patients did not have a higher rate of adverse medical outcomes compared with patients who had not received antipsychotics. No significant differences were noted between patients exposed to typical antipsychotics or SGAs. Conclusion: Treatment of elderly psychiatric inpatients with antipsychotics did not increase their risk of adverse medical outcomes. Thus, regulating the use of conventional antipsychotics or SGAs for all elderly patients in all indications may be premature. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract).

4. Gorwood P, Weiller E, Lemming O, Katona C. Escitalopram prevents relapse in older patients with major depressive disorder. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2007;15(7):581-93.
   Ref ID: 2154
   Abstract: OBJECTIVE: The present study investigated the efficacy and tolerability of escitalopram in the prevention of relapse of major depressive disorder (MDD) in older patients who had responded to acute treatment with escitalopram. METHOD: A total of 405 patients who were aged 65 years or older with a primary diagnosis of MDD (according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria) and a Montgomery-Asberg Depression Rating Scale (MADRS) total score of 22 or more received 12-week, open-label escitalopram 10 or 20 mg per day treatment. Remitters (MADRS </=12) were randomized to 24-week double-blind treatment with escitalopram or placebo. The primary efficacy parameter was the time to relapse, defined as either an increase in MADRS total score to 22 or more or lack of efficacy as judged by the investigator. RESULTS: Three hundred five patients achieved remission and were randomly assigned to treatment with escitalopram (N = 152) or placebo (N = 153). The primary analysis showed a clear beneficial effect of escitalopram relative to placebo on the time to relapse (log-rank test, chi(2) = 27.6, df = 1, p <0.001). The risk of relapse was 4.4 times higher for placebo- than for escitalopram-treated patients (chi(2) test, chi(2) = 22.9, df = 1, p <0.001). Significantly fewer escitalopram-treated patients relapsed (9%) compared with placebo (33%) (chi(2) test, chi(2) = 27.1, df = 1, p <0.001). Escitalopram was well tolerated with 53 patients (13%) withdrawn as a result of adverse events during the open-label period and three (2%) escitalopram-treated patients and six (4%) placebo-treated patients during double-blind treatment (not significant). The overall withdrawal rate, excluding relapses, was 7.2% for escitalopram and 8.5% for placebo during the double-blind period (not significant). CONCLUSION: Escitalopram was effective in preventing relapse of MDD in older patients and was well tolerated as continuation treatment

5. Kissling W, Glue P, Medori R, Simpson S. Long-term safety and efficacy of long-acting risperidone in elderly psychotic patients. Human Psychopharmacology 2007;22(8):505-13.

Ref ID: 2160

Abstract: This subgroup analysis of the 6-month, open-label Switch to Risperidone Microspheres (StoRMi) trial evaluated long-term safety and efficacy of a direct conversion to risperidone long-acting injectable (RLAI) in 52 elderly patients (> or =65 years) with psychosis stabilized on oral or depot antipsychotic. Study outcomes included adverse events, movement disorder severity, psychiatric symptoms, functional ability, quality of life and patient satisfaction. Change in the Positive and Negative Syndrome Scale at endpoint was the primary efficacy measure. The most common dosage of RLAI used at endpoint was 25 mg every 14 days (60%). The trial was completed by 81% of patients, with six patients discontinuing treatment due to an adverse event. Tolerability was good and most side effects were mild to moderate. Serious adverse events occurred in 11 patients. Two of these (suicidal attempt, n = 1; exacerbation of disease, n = 1) were considered possibly related to RLAI. Conversion to RLAI resulted in significant improvements in movement disorder severity, psychiatric symptoms, functional status and patient satisfaction. Mean PANSS total decreased by 15.8 at endpoint, with 23 patients (46.9%) experiencing a > or =20% improvement. This post-hoc analysis supports that RLAI is well tolerated and safe in elderly patients with psychotic illnesses switched from stable antipsychotic regimens, and suggests possible efficacy, although inferences are limited

6. Kok R, Nolen W, Heeren T. Cardiovascular changes associated with venlafaxine in the treatment of late-life depression. Am J Geriatr Psychiatry 2007;15(8):725.
   Ref ID: 1668
   Abstract: Comments on an article by Johnson et al. (see record 2006-11933-010). Recently we finished a double-blind randomized study with a duration of 12 weeks, in 81 elderly inpatients diagnosed with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition major depression and comrobid physical illness in which we used comparable procedures and definitions to assess cardiovascular changes. Our findings are comparable with the results from Johnson's study. Unfortunately, Johnson et al. do not report how often treatment was necessary for orthostatic hypotension in their patients Other randomized double-blind studies found no significant changes in blood pressure or heart rate with use of venlafaxine either or showed less changes in blood pressure and electrocardiogram intervals compared with dothiepin. We conclude that cardiovascular side effects may be prevalent in patients using venlafaxine, but treatment was not necessary in the vast majority of these patients and that only one patient in Johnson's study and one in our study discontinued venlafaxine as a result of these side effects. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

7. Nelson JC, Wohlreich MM, Mallinckrodt CH, Detke MJ, Watkin JG, Kennedy JS. Duloxetine for the treatment of major depressive disorder in older patients. Am J Geriatr Psychiatry 2005;13(3):227-35.
   Ref ID: 384
   Abstract: Objective: The efficacy and safety of duloxetine, a dual reuptake inhibitor of serotonin (5-HT) and norepinephrine (NE), were evaluated in the treatment of major depressive disorder (MDD) and associated pain symptoms in patients age 55 and older.

Methods: Efficacy data were obtained from patients age [greater-than or equal to]55 who participated in two identical, multicenter, double-blind studies in which patients with MDD were randomized to receive placebo (N = 43) or duloxetine (60 mg/day; N = 47) for 9 weeks. The primary efficacy measure was the mean change in Ham-D-17 total score. Pain symptoms were assessed with visual-analog scales. Safety data for patients age [greater-than or equal to]55 were pooled from six randomized, 8- or 9-week, double-blind studies of duloxetine in which patients with MDD were randomized to receive placebo (N = 90) or duloxetine (40 mg/day-120 mg/day; N = 119). Results: The combined results of these two investigations found that duloxetine was significantly superior to placebo for mean change in Ham-D-17 total score. The estimated probability of remission for duloxetine-treated patients (44.1%) was also significantly higher than that for placebo (16.1%). Reductions in overall pain, back pain, and pain while awake were also significantly greater for duloxetine than placebo. The rate of discontinuation due to adverse events was significantly higher for duloxetine-treated patients (21.0%) than placebo (6.7%). Abnormal elevations in vital signs at endpoint were not significantly different from placebo. Conclusions: In these two investigations, duloxetine 60 mg/day was an efficacious treatment for MDD and also alleviated pain symptoms in depression patients age 55 and older. copyright 2005 American Association for Geriatric Psychiatry

8. Yang CH, Tsai SJ, Hwang JP. The efficacy and safety of quetiapine for treatment of geriatric psychosis. J Psychopharmacol (Oxf) 2005;19(6):661-6.
Ref ID: 1124
Abstract: Quetiapine, an atypical antipsychotic, is effective for psychosis in younger patients, with limited adverse effects reported. This open-label naturalistic study was conducted to assess the 4-week efficacy and safety of quetiapine for treatment of geriatric psychosis. Clinical efficacy was evaluated using the Brief Psychiatric Rating Scale (BPRS) and Clinical Global Impression Improvement (CGI-I) instruments before and after 4 weeks of quetiapine treatment. The sample population consisted of 100 geropsychiatric inpatients with psychosis, with the therapeutic evaluation completed by 91. Eighty-one of these 91 patients (89.0%) experienced mild-to-substantial improvement, as determined from the CGI-I. Further, a mean reduction in BPRS score of 39.5% (from baseline) was also determined. The mean daily dose of quetiapine for the fourth week was 276.1 177.2mg/day (range 50-800). Higher quetiapine dosages were administered for patients with functional psychoses compared to an analogous group with organic mental disorders. The most common adverse effects were somnolence (30.0%), lower-limb weakness (28.0%) and dizziness (27.0%). Body weight and fasting triglyceride were significantly elevated after quetiapine treatment (2.2% and 8.9% from baseline, respectively). Based on the results of this study, it appears that quetiapine is an efficacious and safe treatment for geriatric inpatients with psychosis, however, there is a wide dosing range and optimal dosage is diagnosis-dependent

9. Sheikh JI, Cassidy EL, Doraiswamy PM, Salomon RM, Hornig M, Holland PJ, et al. Efficacy, safety, and tolerability of sertraline in patients with late-life depression and comorbid medical illness. J Am Geriatr Soc 2004;52(1):86-92.
Ref ID: 1210

Abstract: OBJECTIVES: To report on the efficacy, safety, and tolerability of sertraline in the treatment of elderly depres-sed patients with and without comorbid medical illness. SETTING: Multicenter. DESIGN: Randomized, double-blind, placebo-controlled study. PARTICIPANTS: A total of 752 patients aged 60 and older with diagnosis of major depressive disorder according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, diagnosis. MEASUREMENTS: Outcome measures included the 17-item Hamilton Depression Scale (HAMD); the Clinical Global Depression-Severity/Improvement (CGI-S/CGI-I); efficacy and safety/adverse event assessments; Quality of Life, Enjoyment, and Satisfaction Questionnaire; and the Medical Outcomes Study 36-Item Short-Form Health Status Survey. RESULTS: In the overall sample, sertraline was superior to placebo on all three primary outcome measures, HAMD, and overall clinical severity and change (CGI-S/CGI-I). Furthermore, therapeutic response to sertraline was comparable in those with or without medical comorbidity, and there were no treatment-by-comorbidity group interactions. Sertraline was also associated with a faster time to response than placebo in the comorbid group (P<.006). Sertraline-treated patients in the comorbid group had similar adverse events and discontinuations when compared to those in the noncomorbid group. CONCLUSION: Sertraline was efficacious in reducing depressive symptomatology, regardless of the presence of comorbid medical illness. Sertraline was safe and well tolerated by patients with or without medical illness

10. Wee R, Lim WK. Selective serotonin re-uptake inhibitors (SSRIs) and hyponatraemia in the elderly. Int J Geriatr Psychiatry 2004;19(6):590-1.
    Ref ID: 1701
    Abstract: Selective serotonin re-uptake inhibitors (SSRIs) are a popular choice of antidepressant in the elderly. They lack many of the problems of older antidepressants. However they are not without side effects. SSRIs cause hyponatraemia in psychiatric patients. A retrospective case note audit was undertaken at Bundoora Extended Care Centre (BECC) to assess the incidence of hyponatraemia in a geriatric population. Pharmacy records identified all in-patients who received SSRIs between 1 January 2000 and 31 December 2000. These notes were reviewed and data collected relating to reason for admission, SSRI use and sodium levels. Hyponatraemia was defined as a sodium level below 135mmol/L. 116 patients received SSRIs during 2000. Of 40 patients who were commenced on SSRIs during their admission, seven of the 40 patients (17.5%) became hyponatraemic. Other risk factors for hyponatraemia were also assessed. Of these, only the use of a diuretic was more common in the group who became hyponatraemic. These results suggest that hyponatraemia is more common in the elderly than stated in the product information of SSRIs. The incidence of hyponatraemia in this study is similar to that found in psychiatric populations. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

11. Barak Y, Aizenberg D. Effects of olanzapine on lipid abnormalities in elderly psychotic patients. Drugs Aging 2003;20(12):893-6.
    Ref ID: 1219
    Abstract: INTRODUCTION: Recently concern regarding the cause or worsening of diabetes mellitus by some of the second-generation antipsychotics and their adverse af-

fects on lipid metabolism has caused growing concern amongst physicians and patients. This study aims to assess these effects in elderly patients with schizophrenia. METHODS: In a prospective 6-month follow-up study of elderly inpatients experiencing an acute psychotic exacerbation and exposed to olanzapine for the first time, patients underwent physical and psychiatric assessments including: routine laboratory tests (including serum cholesterol and triglycerides levels), and bodyweight and clinical rating scale measurement. All tests and evaluations were performed at baseline and at the end of study. RESULTS: Twenty-one elderly patients with schizophrenia (15 women and six men) mean age 71.7 +/- 8.2 years were included. All were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders (4th edition) as patients with schizophrenia or schizoaffective disorder. Mean duration of olanzapine treatment was 289 days (SD +/- 139) and the mean olanzapine dosage at the end of the study was 12.9 mg/day. At the end of the study, no significant change from baseline serum lipid levels were found for triglycerides (paired differences = -12.8 [SD +/- 38.5], 95% CI -30.3 to +4.7, t = -1.5, df = 20, p = 0.143) or cholesterol (paired differences = -9.0 [SD +/- 43.5], 95% CI = -28.8 to +10.8, t = -0.95, df = 20, p = 0.355). CONCLUSION: The association between olanzapine exposure and lipid abnormalities may not hold true for older patients. Larger studies with elderly patients are needed to support the present report

12. Kirkwood CK, Givone DM. Advances in pharmacotherapy of psychotic disorders in the elderly. Consultant Pharmacist 2003;18(6):539-50.
    Ref ID: 1004
    Abstract: OBJECTIVE: To evaluate the literature on the pharmacotherapy of psychosis in the elderly. DATA SOURCES: Searches of MEDLINE (1996-April 2002) and the Cochrane Database using the terms psychosis, elderly, geriatric, dementia, Alzheimer's disease, Parkinson's disease, antipsychotics, atypical antipsychotics, clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and haloperidol were performed. An updated search of psychosis, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole occurred in April 2003. STUDY SELECTION: Reviews, case reports, and open-labeled and controlled trials were selected. DATA SYNTHESIS: Psychotic symptoms in the elderly can occur in the context of psychiatric disorders, medical conditions, or as a medication complication. Behavioral problems (e.g., agitation, aggression) can accompany psychosis and may not respond to nonpharmacological strategies. Pharmacological management of psychosis in the elderly with typical antipsychotics (e.g., haloperidol, chlorpromazine) can result in intolerable adverse effects (e.g., sedation, anticholinergic effects, extrapyramidal symptoms, tardive dyskinesia, and orthostatic hypotension). The atypical antipsychotic agents (e.g., risperidone, olanzapine, quetiapine, ziprasidone) and the dopamine-serotonin system stabilizer aripiprazole offer more tolerable adverse effects profiles. Most information supporting the use of the atypical antipsychotics is derived from open-label trials involving patients with dementia or Parkinson's disease; however, data from large randomized, controlled trials is emerging. In general, psychosis in elderly patients responds to low doses of antipsychotics. Patients must be monitored closely for adverse effects, especially in light of the new information associating cere-

brovascular adverse events with risperidone in patients with dementia. Further trials are required to determine if this is a disease- or drug-specific phenomenon. CONCLUSION: Psychosis in elderly patients can be managed with antipsychotic agents. The atypical antipsychotics are effective and offer advantages over typical antipsychotics with regard to a reduced rate of adverse effects

13. McSwan KL, Gontkovsky ST, Splinter MY. Acute changes in mental status secondary to selective serotonin reuptake inhibitor-induced hyponatremia. Rehabilitation Psychology 2003;48(3):202-6.
Ref ID: 545
Abstract: Hyponatremia represents the most common electrolyte abnormality in hospitalized patients and is of particular concern in hospitalized elderly patients. Multiple studies have identified an association between hyponatremia and selective serotonin reuptake inhibitor (SSRI) therapy. The present report provides as illustration 2 elderly patients identified to develop hyponatremia following initiation of SSRI therapy, which subsequently resolved following discontinuation of the medications. These cases demonstrate the unique position of the rehabilitation psychologist in identifying SSRI-induced hyponatremia as one potential mechanism underlying acute changes in mental status. Diagnostic factors and differential causes of hyponatremia are discussed, and alternative medications for addressing depressive symptomatology in cases of SSRI-induced hyponatremia are provided

14. Maxwell RA, Sweet RA, Mulsant BH, Rosen J, Kirshner MA, Kastango KB, et al. Risperidone and 9-hydroxyrisperidone concentrations are not dependent on age or creatinine clearance among elderly subjects. J Geriatr Psychiatry Neurol 2002;15(2):77-81.
Ref ID: 1733
Abstract: Risperidone is extensively metabolized to an active metabolite, 9-hydroxyrisperidone (9-OH),which is dependent on renal clearance. Risperidone and 9-OH clearances are reduced in the elderly when compared to young subjects. The objective of this study was to determine whether among elderly subjects, risperidone and 9-OH clearance would further decline with increasing age and decreasing creatinine clearance (CrCl). Twenty geriatric inpatients were evaluated in a naturalistic setting with regard to total daily risperidone dose and dosing interval. Creatinine clearance as determined using an 8-hour urine collection. Risperidone and 9-OH concentrations were determined by radioimmunoassay. Spearman's correlation coefficients were used to examine the impact of age and CrCl on concentrations of risperidone, 9-OH, their sum, and the quotient of 9-OH/risperidone. Mean age was 76.49 yrs (range 56-91 yrs). Mean CrCl was 55.432.8 mL/min/1.73 m2 (range 17-142 mL/min/1.73 m2). Mean risperidone daily dose was 1.30.7 mg. Steady-state risperidone and 9-OH concentrations were 4.15.3 ng/mL and 9.16.2 ng/mL, respectively. Mean 9-OH/risperidone was 6.26.1. Concentrations of risperidone, 9-OH, their sum, and 9-OH/risperidone were not significantly correlated with age or CrCl. These results were unchanged when concentrations were corrected for total daily risperidone dose. Among elderly subjects, risperidone and 9-OH clearance do not decline with increasing age or declining CrCl. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

15. Kennedy JS, Bymaster FP, Schuh L, Calligaro DO, Nomikos G, Felder CC, et al. A current review of olanzapine's safety in the geriatric patient: From pre-clinical pharmacology to clinical data. Int J Geriatr Psychiatry 2001;16(Suppl,1):1-S61.
Ref ID: 1752
Abstract: Olanzapine (OLZ) is unique among currently available antipsychotic medications in its antagonism of a range of receptor systems including dopamine, norepinephrine, serotonin, acetylcholine, and histamine. OLZ's complexity provides a broad efficacy profile in patients with schizophrenia and acute, pure or mixed mania. Patients experience symptomatic relief of mania, anxiety, hallucinations, delusions, and agitation/aggression and reduced depressive, negative, and some cognitive symptoms. This paper reviews the safety profile of OLZ, focusing on the elderly. Preclinical and clinical studies of OLZ are reviewed, with emphasis on its possible effects on the cholinergic system and the histamine H/1 receptor. Weight change and related metabolic considerations, cardiac and cardiovascular safety, and motor function during treatment with OLZ are also reviewed. In vitro receptor characterization methods, when done using physiologically relevant conditions allow accurate prediction of the relatively low rate of anticholinergic-like adverse events, extrapyramidal symptoms, and cardiovascular adverse events during treatment with OLZ. OLZ is safe in treating adults of any age with schizophrenia and acute bipolar mania, as well as patients with neurodegenerative disorders. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

16. Madhusoodanan S, Brenner R, Alcantra A. Clinical experience with quetiapine in elderly patients with psychotic disorders. J Geriatr Psychiatry Neurol 2000;13(1):28-32.
Ref ID: 1800
Abstract: Quetiapine fumarate is a recently marketed atypical antipsychotic medication proved to be effective in the treatment of schizophrenia and schizoaffective disorder in the younger population. Quetiapine was used to treat seven elderly hospitalized patients aged 61-72 yrs who manifested signs of psychosis related to schizophrenia, schizoaffective disorder, or bipolar disorder. All Ss had been treated previously with conventional antipsychotics or other atypical antipsychotics. Response was assessed by observation of Ss' behavior. Four Ss responded to treatment; three did not respond. Positive symptoms decreased markedly in all four responders. Negative symptoms showed marked decrease in two Ss and moderate decrease in one S. Preexisting extrapyramidal symptoms (EPS) diminished in three Ss. Transient hypotension, dizziness, and somnolence occurred in two Ss. No other side effects were noted. No adverse consequences occurred when lithium, carbamazepine, valproic acid, or venlafaxine was given concurrently. The reduction of positive and negative symptoms of schizophrenia and lack of significant EPS and minimal sedative, hypotensive, and anticholinergic side effects indicate that quetiapine may be a safe and effective medication for the elderly. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

17. Solomons K, Geiger O. Olanzapine use in the elderly: a retrospective analysis. Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie 2000;45(2):151-5.
Ref ID: 1312
Abstract: OBJECTIVE: To evaluate the efficacy and safety of olanzapine in a hospital-

ized geriatric population that had previously failed to respond to, or tolerate, numerous trials with other antipsychotic medications. METHOD: A retrospective chart analysis was conducted on 58 elderly patients with psychotic symptoms who were given a trial on olanzapine. Data was collected regarding patients' psychiatric diagnoses, duration of illness, duration of hospitalization, prior response to psychotropic therapies, concomitant psychotropic agents, side effects, and clinically determined changes over time. RESULTS: Results indicated that 60.3% of this refractory group of patients improved on olanzapine. Side effects were reported for 38% of the patients, with delirium, extrapyramidal symptoms (EPS), and drowsiness or lethargy being the most common. CONCLUSIONS: The reported level of improvement in this group of refractory elderly psychotic patients indicates that olanzapine can make an important contribution to the mental health of elderly patients with similar characteristics

18. Barak Y, Wittenberg N, Naor S, Kutzuk D, Weizman A. Clozapine in elderly psychiatric patients: tolerability, safety, and efficacy. Compr Psychiatry 1999;40(4):320-5.
Ref ID: 1319
Abstract: Psychotic disorders in the elderly are frequent, of multiple etiologies, and little researched. With the advent of "atypical" neuroleptics, their role in treating elderly psychiatric patients needs to be investigated. Clozapine is widely used; however, its use is common in the elderly whose psychosis is a feature of neurological morbidity (Parkinson's disease, dementia, etc.), making it difficult to ascertain the safety, tolerability, and efficacy in psychiatric disorders in late life. The aim of the present review is to evaluate clozapine's effect in elderly psychiatric patients with no neurological comorbidity. A computerized literature search (MedLine 1966 to 1997) revealed 133 patients fulfilling said criteria. Fifteen patients had side effects and/or adverse events during treatment; nine of these were receiving a dosage greater than 100 mg clozapine daily. In 19 patients, treatment was discontinued, three due to noncompliance and 16 due to side effects. In seven patients, leukopenia/agranulocytosis was reported. The majority of side effects (27 of 34) and treatment discontinuations were within the first 90 days of treatment. Although efficacy is difficult to compare across studies because of differing methods of evaluation, the great majority of patients showed moderate to marked improvement of psychotic features. The reported effectiveness in patients able to continue treatment for extended periods is significant. Thus, clozapine at a relatively low mean dose (134 mg daily) seems to be safe, tolerated, and effective in elderly psychiatric patients. Agranulocytosis is more frequent than in younger adults and should be monitored carefully

19. Strachan J, Shepherd J. Hyponatraemia associated with the use of selective serotonin re-uptake inhibitors. Aust N Z J Psychiatry 1998;32(2):295-8.
Ref ID: 1860
Abstract: Examined the frequency and severity of hyponatraemia in a psychogeriatric inpatient population taking selective serotonin reuptake inhibitors (SSRIs). Casenotes for 1 yr were reviewed, and 53 patients (aged 60-87 yrs) with 55 admissions were identified. 18 were treated with fluoxetine and 37 with paroxetine. Data on serum sodium levels, concomitant medications and comorbid medical conditions were collected. Five (28%) of the patients on fluoxetine and 8 (22%) on paroxetine were, or became, hyponatraemic.

The SSRI was discontinued in 2 symptomatic patients. Serum sodium returned to normal in 9 patients maintained on the SSRI. Two patients maintained on an SSRI remained hyponatraemic but asymptomatic. The authors conclude that hyponatraemia may be a relatively common early asymptomatic side effect of SSRIs, especially in older women. Serum sodium should be measured before commencing an SSRI and monitored during the first mo. Any patient who exhibits symptoms of hyponatraemia, or whose depression apparently worsens, while on an SSRI must have their serum sodium measured. Discontinuation of the SSRI may be avoidable if serum sodium levels can be closely monitored. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

20. Zarate CAJ, Baldessarini RJ, Siegel AJ, Nakamura A, McDonald J, Muir-Hutchinson LA, et al. Risperidone in the elderly: a pharmacoepidemiologic study. J Clin Psychiatry 1997;58(7):311-7.
    Ref ID: 1363
    Abstract: BACKGROUND: The possibly limited adverse effects of risperidone encourage interest in its use in geriatric patients. METHOD: Medical records of 122 hospitalized psychogeriatric patients (> or = 65 years old) newly treated with risperidone were reviewed and scored for indications, doses, and effects of this novel neuroleptic. RESULTS: Subjects (83 women, 39 men), mean +/- SD age = 76.5 +/- 6.8 years (range, 65-95), were given risperidone for agitation or psychosis associated with dementia (53%), a major mood disorder (29%), or other disorders (18%). Most (77%) were also medically ill and received other psychotropic (76%) or cardiovascular agents (70%). Daily doses of risperidone averaged 1.6 +/- 1.1 mg (range, 0.25-8.0) (0.025 mg/kg body wt.); 78% received 2.0 mg. Risperidone appeared to be effective in 85% of cases, but 18% were discontinued due to intolerability (11%) or inefficacy (7%). Adverse events occurred in 32% of the patients (36% of those discontinued). These adverse events included hypotension (29%) or symptomatic orthostasis (10%), cardiac arrest (1.6%) with fatality (0.8%), and extrapyramidal effects (11%) or delirium (1.6%). Benefits were associated with younger age and male gender, but not risperidone dose. Adverse effects were associated with cardiovascular disease and its treatment, cotreatment with an SRI antidepressant or valproate, and relatively rapid dose increases. CONCLUSION: Risperidone appeared to be effective and may be safe for many elderly psychiatric patients with comorbid medical conditions provided that doses are low and increased slowly. Particular caution is advised in the presence of cardiovascular disease or cotreatment with other psychotropic agents

21. Peter R, Brigitta B, Gabor G, Eva C. Application of neuroleptic drugs in gerontopsychiatric patients with diseases characterized with agitation as a prominent symptom. [Hungarian]. Psychiatria Hungarica 1996;11(4):424-32.
    Ref ID: 1893
    Abstract: Within a retrospective study, the treatment of agitation in a hospitalized geriatric psychiatric population were analyzed. The prevalence of agitated behavior was rather high (32.5%). Distribution of psychiatric disorders accompanied by this symptom showed that it occurred predominantly with dementias but could also worsen both affective and anxiety disorders. According to the treatment, no strict benzodiazepines are preferred.

Low potential and/or atypical neuroleptics were more efficious in peroral while high potential molecules (in lower doses) in parenteral depot administration. The most significant side effects were also listed. Emphasizing the importance of agitation in compliance of the patients during their chronic care, an estimation was made to evaluate the therapeutic efficacy of the applied treatment considering also the social status of the patient. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

22. Lemke MR, Stuhlmann W. Carbamazepine treatment of agitated behavior in gerontopsychiatric inpatients. Psychiatr Prax 1994;21(4):147-50.
Ref ID: 920
Abstract: Symptomatic behavioral disturbances including agitation, motor restlessness, outbursts and hostility remain a major problem in clinical management of gerontopsychiatric patients. Termination of home care and subsequent hospitalisation is caused largely by behavior disturbances and not cognitive deficits. Clinical efficacy of neuroleptic treatment seems to be modest and is limited by unwanted side effects. Carbamazepine shows psychotropic effects and seems to improve limbic pathology including aggression and poor impulse control in various psychiatric disorders. Treatment with carbamazepine was evaluated in an open study design in 29 gerontopsychiatric inpatients. Carbamazepine was efficient in treating agitated behavior disturbances in dementia and other disorders. Adverse effects of the drug showed up only in a small percentage of the patients and were reversible after discontinuation of the drug. The results suggest that carbamazepine may be effective in treating agitated behavior in gerontopsychiatric patients with different disorders. It may represent a sensible alternative or complementation to other therapeutic interventions

23. Shaw SH, Curson H, Coquelin JP. A double-blind, comparative study of zolpidem and placebo in the treatment of insomnia in elderly psychiatric in-patients. J Int Med Res 1992;20(2):150-61.
Ref ID: 2728
Abstract: The efficacy and tolerability of the imidazopyridine hypnotic, zolpidem, were investigated in 119 elderly psychiatric in-patients complaining of insomnia in a double-blind, parallel-group, placebo-controlled trial. After a 7-day placebo washout period, patients were randomized to receive 10 or 20 mg/day zolpidem, or placebo for 21 days; thereafter, all patients received placebo for 7 days. Sleep was assessed by patient observation on days 0, 1, 7, 14, 21, 22 and 28. Compared with placebo, 20 mg/day zolpidem significantly improved total duration of sleep between day 0 and day 21, and this was maintained at day 28. After 10 or 20 mg/day zolpidem, there was also a trend towards improvement in all other sleep parameters, which remained above baseline at day 28. Zolpidem was well tolerated with no withdrawal symptoms during the second 7-day placebo treatment period. Daytime drowsiness was reported in three patients receiving 20 mg/day zolpidem and in one receiving 10 mg/day zolpidem, but there was no significant increase in daytime drowsiness between days 0 and 21. Ataxia occurred in two, one and one patient, respectively, treated with 20 mg/day zolpidem, 10 mg/day zolpidem and placebo. The incidences of other adverse events or effects on clinical and laboratory parameters were minimal and similar in all three treatment groups. It is concluded that,

in elderly psychiatric patients, 10 mg/day zolpidem can be used to treat insomnia and can be safely added to concomitant psychotropic treatment without inducing daytime drowsiness

24. Newhouse PA, Sunderland T, Tariot PN, Weingartner H, Thompson K, Mellow AM, et al. The effects of acute scopolamine in geriatric depression. Arch Gen Psychiatry 1988;45(10):906-12.
Ref ID: 2574
Abstract: In an intensive multidrug, multidose study, nine elderly depressed patients were administered 0.1, 0.25, and 0.5 mg of scopolamine hydrobromide, 1 mg of oral lorazepam, and placebo in a double-blind investigation aimed at assessing the status of the central cholinergic nervous system in geriatric depression. Significant cognitive and behavioral effects of scopolamine were observed only at the high dose (0.5 mg), while lower doses and lorazepam showed no significant differences from placebo. Cognitive deficits caused by scopolamine were in the areas of new learning, access to semantic memory, vigilance, and continuous performance. Behavioral effects consisted of activation, restlessness, and anxiety, but there was no significant effect on depressed mood. These results suggest that elderly depressed patients with mild to moderate cognitive impairment seem to be more similar to previously studied elderly controls rather than to patients with Alzheimer's disease in their reaction to short-term cholinergic blockade, and suggest that the cognitive and mood changes often seen in geriatric depression may involve factors other than disturbed muscarinic cholinergic mechanisms

25. Miller F, Whitcup S. Benzodiazepine use in psychiatrically hospitalized elderly patients. J Clin Psychopharmacol 1986;6(6):384-5.
Ref ID: 1519

26. Toenniessen LM, Casey DE, McFarland BH. Tardive dyskinesia in the aged. Arch Gen Psychiatry 1985;42(3):278-84.
Ref ID: 1536
Abstract: Although tardive dyskinesia (TD) is recognized to result from neuroleptic drug exposure, data conflict about the importance of the quantity of that exposure in producing TD. The relationship between duration of neuroleptic treatment (one to 301 months) and TD was studied in 57 elderly psychiatric inpatients. Examinations for TD and parkinsonism were quantified on the Abnormal Involuntary Movement Scale (AIMS) and on a parkinsonism severity scale. Prevalence of presumed TD was 49% and of parkinsonism 51%. Prevalence of TD increased with longer treatment, but parkinsonism was independent of treatment duration. Linear multiple regression analysis showed that the AIMS score was correlated positively with treatment duration and negatively with parkinsonism. Logistic multiple regression analysis verified these relationships and was more successful at predicting TD. The length of neuroleptic treatment necessary to produce TD was calculated from the logistic model at 10.8 months (95% confidence interval, zero to 25.6 months). These analyses showed the greatest rise in risk of TD occurred within the first two years of drug therapy.

Publikasjonene i kategori 2a listet etter dato (nyeste øverst)

1. Mazeh D, Shahal B, Aviv A, Zemishlani H, Barak Y. A randomized, single-blind, comparison of venlafaxine with paroxetine in elderly patients suffering from resistant depression. Int Clin Psychopharmacol 2007;22(6):371-5.
   Ref ID: 2129
   Abstract: It is estimated that up to 45% of patients with depression do not have an adequate response to a first trial of antidepressant therapy with even higher reported rates for the elderly patients. To compare the efficacy and the tolerability of venlafaxine vs. paroxetine in elderly patients suffering from resistant major depression, who did not respond to at least two previous adequate trials of antidepressants. Patients entered an 8-week single-blind study. Patients were rated using the Clinical Global Impression Scale, Hamilton Rating Scale for Depression, and the Geriatric Depression Scale. Assessments were performed at baseline and on days 7, 14, 21, 28, 42 and 56. Side effects were recorded in a systemic manner. Thirty patients were included in the study, (17 women, 13 men; mean age=75.9 years, range: 68-83) and all had completed the 6-week trial. Mean dose of venlafaxine used was 165 mg/day (SD=73.8; range 75-300 mg). Mean dose of paroxetine used was 26 mg/day (SD=15.04; range 10-60 mg). Nine patients treated with venlafaxine (60%) and five patients treated with paroxetine (33%) remitted after 8 weeks of treatment. Four patients treated with venlafaxine and eight patients treated with paroxetine failed to respond. Significant improvement in Hamilton Rating Scale for Depression scores between baseline and endpoint were observed in both groups of patients. The mean Hamilton Rating Scale for Depression change for paroxetine was -12.5 and for venlafaxine -19.1 ($P<0.05$). The mean Geriatric Depression Scale change for paroxetine was -3.2 and for venlafaxine -6.0 ($P<0.3$). The mean Clinical Global Impression Scale change was -2.3 for paroxetine and -3.5 for venlafaxine ($P<0.05$). Venlafaxine was significantly superior to paroxetine on Clinical Global Impression Scale and Hamilton Rating Scale for Depression measures. Side effects were transient and did not differ between treatment groups. Elderly depressed patients resistant to previous treatments had responded to a trial of paroxetine or venlafaxine. Remission rates were higher for venlafaxine and tolerability was acceptable for both compounds

2. Rossini D, Serretti A, Franchini L, Mandelli L, Smeraldi E, De Ronchi D, et al. Sertraline versus fluvoxamine in the treatment of elderly patients with major depression: a double-blind, randomized trial. J Clin Psychopharmacol 2005;25(5):471-5.
   Ref ID: 1130
   Abstract: BACKGROUND: Major depression is a common psychiatric disorder in the elderly population. The efficacy of tricyclic antidepressants is well established, and selective serotonin reuptake inhibitors appear to have a similar effectiveness along with advantages in terms of tolerability and safety. Given the lack of literature data regarding fluvoxamine in the treatment of depressed elderly patients, the aim of the present study was to compare its efficacy and tolerability with those of sertraline in a sample of elderly patients. METHODS: Under double-blind conditions, 93 hospitalized patients older than 59 years, who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

criteria for a major depressive episode, were randomly assigned to receive sertraline (150 mg daily) or fluvoxamine (200 mg daily) for 7 weeks. The clinical response was defined as a reduction on the Hamilton Rating Scale for Depression score to 8 or below. RESULTS: At study completion, the response rates were 55.6% (25/45) and 71.8% (28/39) for sertraline and fluvoxamine, respectively. No significant difference in final response rates was found between the 2 treatment groups (P = 0.12). A repeated-measures analysis of variance on Hamilton Rating Scale for Depression scores revealed a significantly different decrease of depressive symptoms between the 2 treatment groups, favoring fluvoxamine (P = 0.007). The overall safety profile of sertraline and fluvoxamine was favorable with no differences between the 2 drugs. CONCLUSION: The results of this double-blind trial show that sertraline and fluvoxamine may be effective compounds in the treatment of elderly depression with the latter showing some advantage in terms of speed of response. These findings warrant further replication in placebo-controlled studies

3. Sajatovic M, Bingham R, Campbell EA, Fletcher DF. Bipolar Disorder in Older Adult Inpatients. J Nerv Ment Dis 2005;193(6):417-9.
   Ref ID: 1694
   Abstract: The literature on bipolar disorder in older adults is very limited, in spite of the fact that the elderly are a growing population in the United States. This retrospective record review study evaluated clinical characteristics and hospital-based resource use patterns among 48 older adults with bipolar disorder, and compared groups with early-onset (EOS) versus late-onset (LOS) bipolar disorder. The mean age of the group was 67.3 years, with no difference in age between EOS and LOS categories. Late onset illness was identified in 29.2% of the group (N = 14). Compared with individuals with EOS, individuals with LOS were 2.8 times more likely to be female. Both groups had extensive medical comorbidity (mean of 3.7 comorbid medical conditions), substantial hospital usage (mean length of stay, 14.8 days) and polypharmacy usage. Bipolar disorder with onset after age 50 is not uncommon among older adults hospitalized on a geropsychiatric unit. Clinical characteristics may differ between individuals with early-onset and late-onset bipolar illness, and resource utilization may be extensive in both groups. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

4. Hwang JP, Yang CH, Tsai SJ. Comparison study of venlafaxine and paroxetine for the treatment of depression in elderly Chinese inpatients. Int J Geriatr Psychiatry 2004;19(2):189-90.
   Ref ID: 1706
   Abstract: Venlafaxine is a new antidepressant with a unique pharmacological profile that differs from currently available selective serotonin reuptake inhibitor (SSRI) antidepressants (Holliday and Benfield, 1995). Recent meta-analysis of 20 studies suggests that venlafaxine is more effective than the SSRIs (Smith et al, 2002). These comparative studies were all conducted using western adult sample populations. We elected, therefore, to conduct a study for the comparison of venlafaxine and paroxetine in Chinese elderly depressed patients. Adverse effects are a major concern in the treatment of geriatric patients. No significant difference was demonstrated for a ay adverse effect com-

paring the two treatment groups, with the characteristic adverse effects usually mild for both drugs. Our result suggested that both venlafaxine and paroxetine treatments were equally efficacious and were well tolerated by our sample of Chinese geropsychiatric depressed inpatients. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

5. Portella MJ, Marcos T, Rami L, Navarro V, Gasto C, Salamero M. Residual cognitive impairment in late-life depression after a 12-month period follow-up. Int J Geriatr Psychiatry 2003;18(7):571-6.
   Ref ID: 1229
   Abstract: OBJECTIVES: This study investigated cognitive impairment in late-life depression in a follow-up design. The main objective was to assess the most important cognitive domains implicated in late-life depression, in patients who underwent pharmacological treatment, in the acute phase and twelve months after. METHODS: Neuropsychological and clinical data were used from the baseline of patients and controls, to determine the cognitive impairment in the acute phase. Patients repeated the neuropsychological assessment at twelve months. RESULTS: There were significant differences between patients and controls at baseline. But in the patients there was no change over twelve months. There were no differences between remitted and non-remitted patients on neuropsychological scores. CONCLUSIONS: The cognitive impairment seen in the elderly depressed patients seems to be a trait characteristic of this mental disease, even when the depressive episode has remitted. Copyright 2003 John Wiley & Sons, Ltd

6. Malur C, Fink M, Francis A. Can delirium relieve psychosis? Compr Psychiatry 2000;41(6):450-3.
   Ref ID: 718
   Abstract: A delirium presages a poor prognosis in hospitalized patients, but an incidental delirium is a feature of some psychiatric treatments. We report five cases in which delirium preceded the relief of affective and psychotic symptoms of a major mental illness. The experience stimulated a review of the literature on delirium in psychiatric treatments. Five inpatients (aged 53 to 69 years) with an exacerbation of chronic mental iUness developed deliria from medications (n = 4) and electrolyte disturbance (n = 1). The deliria were managed with medication washout or correction of electrolyte imbalance. The progress of the patients was noted clinically and summarized. The clinical signs of delirium such as confusion, disorganized speech, sleep-wake cycle changes, and hallucinations persisted for 24 to 72 hours. As the delirium cleared, psychotic and affective symptoms improved or resolved. The improvements persisted for I to 5 months, with low doses of medications in two of the cases. A delirium may precede clinical improvement in affective and psychotic symptoms. Historically, some treatments for mental illness induce an incidental delirium (e.g., electroconvulsive therapy [ECT] and insulin coma). Why a delirium should presage a beneficial effect on psychosis is unclear, but the emergence of delirium may herald a beneficial pathophysiology. Copyright (C) 2000 by W.B. Saunders Company

7. Walters G, Reynolds CF, Mulsant BH, Pollock BG. Continuation and maintenance pharmacotherapy in geriatric depression: an open-trial comparison of paroxetine and nortriptyline in patients older than 70 years. The Journal of clinical psychiatry 1999;60 Suppl 20:21-5.
Ref ID: 2421
Abstract: We present preliminary data on the efficacy of paroxetine, as compared with nortriptyline, in preventing or delaying relapse and recurrence of major depression in elderly patients. Following double-blind, acute-phase pharmacotherapy, 25 patients (mean age = 72.5 years) began open-trial continuation treatment with paroxetine (mean dose = 24.5 mg/day), and 15 patients (mean age = 77.5 years) received nortriptyline (mean dose = 51.3 mg/day; mean blood level = 85.5 ng/mL). Over an 18-month period, paroxetine and nortriptyline have shown comparable efficacy in preventing or delaying relapse and recurrence, with 80% to 90% of patients remaining well. These data suggest that paroxetine holds promise for long-term maintenance treatment in patients in their 70s and older with depression; however, further controlled evaluation is necessary

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Ref ID: 780
Abstract: Objectives. The aim of our study was to assess cognitive performance in 40 elderly depressed patients during maintenance treatment in relation to clinical outcome. Methods. The neuropsychological evaluation was performed with the Mini Mental State Examination, two subtests of the Wechsler Adult Intelligence Scale and the Trail Making Test, part A and part B. At the end of the continuation treatment, all the patients were maintained on treatment with tricyclic antidepressants (TCAs) or new antidepressants (selective serotonin reuptake inhibitors or venlafaxine). Results. During maintenance treatment, a higher proportion of cognitive impairment was found in patients that did not recover (57%) than in those that recovered (36%). TCA treatment resulted in a higher percentage of cognitive impairment than new antidepressant treatment both in recovered and not recovered patients. In conclusion we suggest that new antidepressants may be the best choice in treatment of elderly depressed patients

9. Pabis DJ, Stanislav SW. Pharmacotherapy of aggressive behavior. Ann Pharmacother 1996;30(3):278-87.
Ref ID: 1381
Abstract: OBJECTIVE: To review the definition, clinical characteristics, prevalence, etiology, neurochemistry, and pharmacologic treatment of aggressive behavior, and provide recommendations regarding the use of specific pharmacologic agents for treating aggressive behavior. DATA SOURCES: Data from the scientific literature were analyzed, interpreted, and summarized. An English-language MEDLINE search yielded clinical trials, case reports, letters, and review articles addressing the etiology and pharmacotherapy of aggression. STUDY SELECTION: Because few well-controlled studies are available in aggression research, all literature addressing the pharmacologic treatment of aggressive behavior, as well as the neurochemistry and psychobiology of aggressive be-

havior, was reviewed. DATA EXTRACTION: The literature was reviewed on the basis of the particular pharmacotherapy and the specific population used. A separate review of the treatment of aggressive behavior in the elderly was included. DATA SYNTHESIS: The literature was assessed for applicability to clinical practice and usefulness to the general clinician. Recommendations were made from the primary literature in conjunction with trends in clinical practice. Pharmacotherapy is a primary mainstay of treatment for aggressive patients. In individuals for whom behavioral intervention alone is unsuccessful, drug therapy should be initiated along with continued nonpharmacologic intervention. Short-acting benzodiazepines and high-potency antipsychotic agents are effective in treating acute aggression on a short-term or as needed basis. Agents such as lithium, beta adrenergic blockers, carbamazepine, valproic acid, buspirone, trazodone, serotonin reuptake inhibitors, and clozapine may be useful in the chronic management of aggressive behavior. Every attempt should be made to streamline drug therapy in patients with chronic aggression and comorbid psychiatric disorders. CONCLUSIONS: On the basis of available research and extensive clinical experience, lithium or propranolol should be considered as first-line antiaggressive agents in patients without comorbid psychiatric disorders. A minimum trial period for assessing drug efficacy should last at least 6-8 weeks at maximum tolerated dosages. Patients responding to pharmacotherapy should be reevaluated every 3-6 months, and periodic medication tapers and/or drug-free periods should be attempted. [References: 106]

10. Tourigny RM, Nair N, Vincent P. Fluvoxamine versus desipramine in elderly patients with major depression: A double-blind comparison CONFERENCE ABSTRACT. 9th European College of Neuropsychopharmacology Congress Amsterdam, The Netherlands 21st 25th September, 1996 1996;
    Ref ID: 2481
    Abstract: Depression is one of the most common psychiatric disorders, especially among the elderly. However, drug treatment is often complicated in this patient population by high rates of coexisting illnesses and concomitant medications, as well as changes in pharmacokinetic parameters, which can result in an increased incidence of adverse events. The selective serotonin reuptake inhibitor fluvoxamine has a good safety profile (Wagner et al, 1994) and may therefore prove particularly suitable for elderly patients. The aim of this double-blind, randomised, multicentre, parallel-group study was to compare the efficacy and safety of fluvoxamine with the tricyclic antidepressant desipramine in elderly patients (at least 60 years old) with DSM-III-R major depression. Following a one-week single-blind placebo run-in period, patients were randomised to receive fluvoxamine or desipramine for 10 weeks. Each drug was given at a daily dose of up to 150 mg, titrated up as necessary during the first 5 weeks of treatment. Mean dose after titration: 135 mg/day for fluvoxamine and 121 mg/day for desipramine. The primary efficacy variable was the total score on the Hamilton Depression Scale (HAM-D). Twenty two patients (mean age 67.9 years; range 60–) received fluvoxamine and 25 (mean age 68.7 years; range 60–) received desipramine. Both groups showed a clinically significant improvement throughout the study. The mean total HAM-D score fell from 24.1 at baseline to 4.0 at Week 10 with fluvoxamine and from 24.3 to 8.7 with desip-

ramine; this difference at Week 10 was statistically significant ($p < 0.05$). There were no other statistically significant differences between the groups on the HAM-D. However, the following secondary efficacy variables also showed some evidence of a superior effect of fluvoxamine towards the end of the study: Montgomery-Asberg Depression Rating Scale, Geriatric Depression Scale, Clinical Global Impressions Scale, and the Brief Symptom Inventory. Adverse events were reported more frequently with desipramine than with fluvoxamine. The most common adverse events with desipramine were dry mouth (83%), dizziness (57%), constipation (44%), headache (39%) and hypotension (35%), whilst fluvoxamine was most commonly associated with headache (36%) and nausea (36%). Only two adverse events (one in each group) were considered serious. A similar percentage of patients in both groups withdrew as a result of adverse events. Fluvoxamine had no effect on vital signs or laboratory parameters; one patient treated with desipramine had significantly elevated hepatic enzymes. The results indicate that fluvoxamine, at a dose of up to 150 mg/day, is at least as effective as desipramine for the treatment of major depression in elderly patients. However, fluvoxamine is better tolerated than desipramine in this patient population. Reference: Wagner, W., Zaborny, B. A. and Gray, T. E. (1994) Fluvoxamine. A review of its safety profile in world-wide studies. International Clinical Psychopharmacology 9, 222–

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    Ref ID: 905
    Abstract: Delirium is one of the most common mental disorders encountered in elderly hospitalized patients, and may be associated with increased morbidity, mortality, length of stay, and patient care costs. This review discusses the causes of delirium, especially those medications associated with acute confusional states in the elderly. The appropriate management of delirium is also reviewed. Although it is a potentially serious problem, delirium is reversible and management should be directed at removing the underlying cause. Therefore, pharmacists need to be cognizant of those medications which contribute to delirium. If drug therapy is required to manage agitation associated with delirium, high-potency neuroleptics and/or shorter acting benzodiazepines are preferred agents

12. Stewart RB, Yedinak KC, Ware MR. Polypharmacy in psychiatry: three case studies and methods for prevention. Ann Pharmacother 1992;26(4):529-33.
    Ref ID: 1457
    Abstract: OBJECTIVE: To illustrate problems of overprescribing in the elderly and to make practical suggestions for prevention of polypharmacy. DESIGN: Three cases of polypharmacy in psychiatric patients admitted to the hospital between January and March 1990 are described. Intervention to correct drug-related problems in these patients is described and methods of preventing polypharmacy are discussed. SETTING: Inpatient psychiatry service in a tertiary-care center. PATIENTS: Elderly psychiatry patients (n = 3) taking an excessive number of medications. This polypharmacy was believed to contribute to decreased cognitive and/or physical function. INTERVENTIONS: Medication regimens were reviewed by the physician and pharmacist. Those considered

unnecessary or believed to be adversely affecting the patient were discontinued. RESULTS: All patients were discharged on a reduced number of medications, with improvement in cognitive and/or physical function. CONCLUSIONS: Polypharmacy contributes to an increased incidence of adverse reactions in the elderly. Implementation of practical methods for reducing polypharmacy can lead to a reduction in the number of drug-related adverse effects and improved care of the elderly patient

13. Cohn CK, Shrivastava R, Mendels J, Cohn JB, Fabre LF, Claghorn JL, et al. Double-blind, multicenter comparison of sertraline and amitriptyline in elderly depressed patients. The Journal of clinical psychiatry 1990;51 Suppl B:28-33.
Ref ID: 2565
Abstract: Two hundred forty-one elderly depressed patients entered the 8-week, double-blind phase of this parallel-group, multicenter study; 161 patients were randomized to receive sertraline (50-200 mg/day) and 80 were randomized to receive amitriptyline (50-150 mg/day). Among evaluable patients, there were no statistically significant differences between treatments in any of the primary efficacy variables: change in total Hamilton Rating Scale for Depression (HAM-D) score (17 items), percentage change in HAM-D score, change in HAM-D Item 1, change in Clinical Global Impressions (CGI) Severity score, change in the Depression Factor of the 56-item Hopkins Symptom Checklist, and the CGI Improvement score at the last visit. Similar results were obtained using data from all patients (intention-to-treat analysis), except that amitriptyline was superior in HAM-D Total score (p = .044). The two drugs produced a similar degree of response: on the basis of the HAM-D criterion, 69.4% of sertraline patients and 62.5% of amitriptyline patients responded, and, on the basis of CGI criterion, 79.5% of sertraline and 73.4% of amitriptyline patients responded. Twenty-eight percent of the sertraline patients withdrew from the study because of a treatment-related side effect and 2.5% (4) because of a laboratory abnormality. In comparison, 35% of the amitriptyline patients withdrew because of treatment-related side effects. Sertraline was associated with a statistically lower frequency of somnolence, dry mouth, constipation, ataxia, and pain and a higher frequency of nausea, anorexia, diarrhea/loose stools, and insomnia; thus, anticholinergic effects were less common and gastrointestinal effects were more common with sertraline than with amitriptyline.(ABSTRACT TRUNCATED AT 250 WORDS)

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Ref ID: 1547
Abstract: The efficacy and clinical effects of flunitrazepam (1 mg) and nitrazepam (5 mg) as somnifacients were studied in 37 psychogeriatric inpatients. Each drug was administered in a double-blind manner to randomized groups of patients for 14 nights. Compared with placebo, both benzodiazepines proved to be effective in inducing and maintaining sleep. Although both drugs were well tolerated, insomnia resulted when each was withdrawn

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Abstract: The effect of 1 mg of flunitrazepam and 5 mg of nitrazepam on psychomotor skills and muscle strength were investigated in 37 psychogeriatric inpatients (mean age 74 yrs). Drugs were administered in a randomized double-blind order, for 14 nights each. Neither benzodiazepine produced consistent impairment of performance in memory tasks, tapping speed, muscle strength and coordination. About half of the Ss performed better on the drugs than on the subsequent placebo. This offers some support to the notion that sleep has a beneficial restorative function and an inverted U-shaped relationship exists between anxiety and performance. If dosed properly, these benzodiazepines are safe and well tolerated in the elderly. (13 ref) (PsycINFO Database Record (c) 2008 APA, all rights reserved)

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    Abstract: Studied the relationship between anticholinergic plasma activity and cognitive function in elderly psychiatric inpatients who had no symptoms of dementia and who were undergoing psychopharmacotherapy with antidepressives and/or neuroleptics. Human subjects: 25 male and female American old adults (mean age 63 yrs) (mixed psychiatric diagnoses). Anticholinergic plasma activity and cognitive function were assessed shortly after the Ss were hospitalized and again 7 days after achievement of a steady state with the appropriate medication. Correlations between anticholinergic values and the Ss' performances on measures of memory, concentration, and overall functional capacity were analyzed. Tests used: The Mini-Mental State by M. F. Folstein et al (1975), the Global Deterioration Scale by B. Reisberg et al (1982), and the Digit Retention Span by H. Buschke and P. A. Fuld (1974). (English & Russian abstracts) (PsycINFO Database Record (c) 2008 APA, all rights reserved)