

Bijlage 5 Evidence tabellen en Grade profielen

Wat zijn de (on)gunstige effecten van medicamenteuze behandelingen (haloperidol en rivastigmine) bij patiënten in de palliatieve fase en een delier doormaken?

P: Patiënten in de palliatieve fase die een delier doormaken
I: Haloperidol
C: Geen behandeling, gebruikelijke zorg, placebo of een andere interventie
O: Delirante symptomen en agitatie score (>24 uur, tussen 24 en 48 uur en >48 uur), aantal bijwerkingen (waaronder extrapiramidale effecten), gebruik van reddingsmedicatie (zoals midazolam), cognitieve status, functionele status, kwaliteit van leven, kwaliteit van sterven of overleving.

P: Patiënten in de palliatieve fase die een delier doormaken
I: Rivastigmine
C: Geen behandeling, gebruikelijke zorg, placebo of een andere interventie
O: Delirante symptomen en agitatie score (>24 uur, tussen 24 en 48 uur en >48 uur), aantal bijwerkingen (waaronder extrapiramidale effecten), gebruik van reddingsmedicatie (zoals midazolam), cognitieve status, functionele status, kwaliteit van leven, kwaliteit van sterven of overleving.

In- en exclusiecriteria

De literatuur is systematisch geselecteerd op basis van vooraf gestelde criteria. Deze criteria luiden als volgt:

- Gerandomiseerde trials (RCT's), quasi gerandomiseerde trials en gecontroleerde trials (CCT's).
- Systematische reviews waarin RCT's, quasi gerandomiseerde trials of CCT's zijn geïncludeerd, waarvan de primaire onderzoeken aan de selectiecriteria voldoen zoals gesteld voor de literatuuranalyse.
- Palliatieve patiënten met een (gediagnosticeerd) delier.
- De interventie bestaat uit haloperidol of rivastigmine (onafhankelijke van de dosering of de wijze van toediening).
- De controle interventie bestaat geen behandeling, gebruikelijke zorg, placebo of een andere interventie.
- De uitkomstenmaten zijn gerapporteerd.
- De effectmaten met significantie of variantie zijn gerapporteerd.

Literatuur is geëxcludeerd wanneer er geen kwalitatieve data werd gepresenteerd of wanneer het een narratieve review betrof.

Database: Ovid MEDLINE(R) ALL <1946 to March 29, 2021>
Search Strategy:

- 1 "richtlijn delier".ti. (0)
- 2 Delirium/ (9858)
- 3 (delirium? or delirious).tw,kw. (1442)
- 4 Psychomotor Agitation/ (5272)
- 5 agitat*.tw,kw. (20902)
- 6 (distress or distressed).tw,kw. (124715)
- 7 restless*.tw,kw. (9202)
- 8 ((disturbed or disordered or abnormal* or change*) adj2 (attention or cognition or cognitive or consciousness or perception)).tw. (16053)
- 9 "acute brain syndrome".tw. (43)
- 10 "acute cerebral insufficiency".tw. (14)
- 11 "acute confusion".tw. (379)
- 12 "acute confusional state".tw. (398)
- 13 Cognitive Dysfunction/ (20972)
- 14 (cognitive adj2 (dysfunction or decline)).tw. (39330)
- 15 (mental* adj2 deterioration).tw. (1423)
- 16 Consciousness Disorders/ (3002)
- 17 (diminish* adj2 consciousness).tw. (60)
- 18 Brain Diseases/ (54852)
- 19 encephalopathy.tw. (46849)
- 20 (fail* adj2 cognit*).tw. (944)
- 21 Neurocognitive Disorders/ (9355)
- 22 organic mental disorder.tw. (186)
- 23 "acute organic psychosyndrome*".tw. (7)
- 24 "acute psycho-organic syndrome*".tw. (6)
- 25 "exogenous psychosis".tw. (35)
- 26 clouded state.tw. (2)
- 27 (Cloud* adj2 conscious*).tw. (244)
- 28 Brain Diseases, Metabolic/ (2051)
- 29 (metabolic adj2 encephalopathy).tw. (532)
- 30 (disturbance adj2 brain function).tw. (31)
- 31 toxic psychosis.tw. (158)
- 32 toxic confusion.tw. (6)
- 33 or/2-32 (338766)
- 34 exp Alprazolam/ (1788)
- 35 Alprazolam.tw,kw. (2399)
- 36 Amisulpride.tw,kw. (1160)
- 37 Amobarbital/ (2565)
- 38 Amobarbital.tw,kw. (1171)
- 39 Aripiprazole/ (2485)
- 40 Aripiprazole.tw,kw. (4184)
- 41 Benperidol/ (799)
- 42 Benperidol.tw,kw. (140)
- 43 Bromazepam/ (354)
- 44 Bromazepam.tw,kw. (512)
- 45 Clorazepate Dipotassium/ (324)
- 46 Chlorazepate.tw,kw. (117)
- 47 Chlordiazepam.tw,kw. (20)
- 48 Chlordiazepoxide/ (3886)
- 49 Chlordiazepoxide.tw,kw. (3250)
- 50 Chlorpromazine/ (17284)
- 51 Chlorpromazine.tw,kw. (13613)
- 52 Cytidine Diphosphate Choline/ (918)
- 53 Citicoline.tw,kw. (455)
- 54 Clobazam.tw,kw. (990)
- 55 Clonazepam/ (2580)
- 56 Clonidine/ (13296)

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- 57 Clonidine.tw,kw. (14862)
- 58 Clozapine/ (8432)
- 59 Clozapine.tw,kw. (12022)
- 60 Desmethylalprazolam.tw,kw. (0)
- 61 Dextroamphetamine/ (6941)
- 62 Dextroamphetamine.tw,kw. (684)
- 63 Dexmedetomidine/ (3924)
- 64 Dexmedetomidine.tw,kw. (6482)
- 65 Diazepam/ (17729)
- 66 Diazepam.tw,kw. (20060)
- 67 Diclazepam.tw. (26)
- 68 Donepezil.tw,kw. (3755)
- 69 Droperidol/ (1987)
- 70 Droperidol.tw,kw. (2094)
- 71 Estazolam/ (108)
- 72 Estazolam.tw,kw. (240)
- 73 Flumazenil/ (3455)
- 74 Flumazenil.tw,kw. (3245)
- 75 Flumazepil.tw,kw. (28)
- 76 Flunitrazepam/ (2663)
- 77 Flunitrazepam.tw,kw. (3159)
- 78 Flupenthixol/ (914)
- 79 Flupenthixol.tw,kw. (906)
- 80 Fluphenazine/ (2411)
- 81 Fluphenazine.tw,kw. (2240)
- 82 Flurazepam/ (781)
- 83 Flurazepam.tw,kw. (952)
- 84 Gabapentin.tw,kw. (6510)
- 85 Galantamine/ (1574)
- 86 Galantamine.tw,kw. (1593)
- 87 Halazepam.tw,kw. (55)
- 88 Haloperidol/ (15754)
- 89 Haloperidol.tw,kw. (18438)
- 90 lloperidone.tw,kw. (212)
- 91 Ketazolam.tw,kw. (37)
- 92 Methotrimeprazine/ (795)
- 93 Methotrimeprazine.tw,kw. (206)
- 94 Levomepromazine/ (795)
- 95 Levomepromazine.tw,kw. (506)
- 96 Lorazepam/ (2917)
- 97 Lorazepam.tw,kw. (3876)
- 98 Lormetazepam.tw,kw. (251)
- 99 L-Trptophan.tw,kw. (1)
- 100 Melatonin/ (20253)
- 101 Melatonin.tw,kw. (25726)
- 102 Mesoridazine/ (128)
- 103 Mesoridazine.tw,kw. (180)
- 104 Methotrimeprazine/ (795)
- 105 Methotrimeprazine.tw,kw. (206)
- 106 Methylphenidate/ (7264)
- 107 Methylphenidate.tw,kw. (7371)
- 108 Midazolam/ (9004)
- 109 Midazolam.tw,kw. (13513)
- 110 Modafinil.tw,kw. (1704)
- 111 Nitrazepam/ (776)
- 112 Nitrazepam.tw,kw. (1004)
- 113 Nitrous Oxide/ (14476)
- 114 Nitrous Oxide.tw,kw. (16464)
- 115 Olanzapine/ (5716)
- 116 Olanzapine.tw,kw. (8700)

- 117 Orap.tw. (37)
- 118 Oxazepam/ (1293)
- 119 Oxazepam.tw,kw. (1513)
- 120 Paliperidone Palmitate/ (873)
- 121 Paliperidone.tw,kw. (1244)
- 122 Periciazine.tw,kw. (11)
- 123 Pericyazine.tw,kw. (33)
- 124 Perphenazine/ (1576)
- 125 Perphenazine.tw,kw. (1337)
- 126 Phenobarbital/ (18022)
- 127 Phenobarbital.tw,kw. (17041)
- 128 Phenobarbitone.tw,kw. (2229)
- 129 Phenobarb.tw,kw. (7)
- 130 Pimozide/ (1716)
- 131 Pimozide.tw,kw. (2090)
- 132 Pipotiazine.tw,kw. (63)
- 133 Prazepam/ (119)
- 134 Prazepam.tw,kw. (195)
- 135 Pregabalin/ (2083)
- 136 Pregabalin.tw,kw. (3669)
- 137 Prochlorperazine/ (1071)
- 138 Prochlorperazine.tw,kw. (992)
- 139 Promazine/ (1100)
- 140 Promazine.tw,kw. (863)
- 141 Promethazine/ (3022)
- 142 Promethazine.tw,kw. (2497)
- 143 Propofol/ (15122)
- 144 Propofol.tw,kw. (21434)
- 145 Quetiapine.tw,kw. (4860)
- 146 Ramelteon.tw,kw. (376)
- 147 Remifentanil.tw,kw. (5115)
- 148 Risperidone/ (6324)
- 149 Risperidone.tw,kw. (9245)
- 150 Rivastigmine/ (1138)
- 151 Rivastigmine.tw,kw. (1778)
- 152 Serentil.tw,kw. (14)
- 153 Sertindole.tw,kw. (454)
- 154 Sevoflurane.tw,kw. (9259)
- 155 Sufentanil/ (1897)
- 156 Sufentanil.tw,kw. (2827)
- 157 Sulpiride/ (3961)
- 158 Sulpiride.tw,kw. (4873)
- 159 Tacrine/ (1750)
- 160 Tacrine.tw,kw. (1828)
- 161 Temazepam/ (671)
- 162 Temazepam.tw,kw. (938)
- 163 Thiopental/ (6851)
- 164 Thiopental.tw,kw. (4874)
- 165 Thioridazine/ (2375)
- 166 Thioridazine.tw,kw. (2302)
- 167 Trazadone.tw,kw. (38)
- 168 Triazolam/ (1236)
- 169 Triazolam.tw,kw. (1561)
- 170 Trifluoperazine/ (3588)
- 171 Trifluoperazine.tw,kw. (3918)
- 172 Triflupromazine/ (353)
- 173 Triflupromazine.tw,kw. (271)
- 174 Valproic Acid/ (12804)
- 175 Valproic Acid.tw,kw. (8838)
- 176 Ziprasidone.tw,kw. (1898)

177 Zotepine.tw,kw. (276)
 178 Clopenthixol/ (399)
 179 (Zuclopenthixol or Clopenthixol).tw,kw. (460)
 180 Ondansetron/ (3131)
 181 Ondansetron.tw,kw. (4530)
 182 quazepam.tw,kw. (140)
 183 or/34-182 (325076)
 184 33 and 183 (11556)
 185 184 (11556)
 186 limit 185 to yr="2019 -Current" (1427)
 187 "medline filter rct".ti. (0)
 188 controlled-clinical-trial.pt. (94111)
 189 randomized-controlled-trial.pt. (525891)
 190 randomized controlled trial/ (525891)
 191 randomi?ed controlled trial?.tw. (194194)
 192 randomi?ed controlled trial?.kf. (12971)
 193 random-allocation.tw,kf. (1787)
 194 double-blind-method.tw,kf. (504)
 195 single-blind-method.tw,kf. (91)
 196 (random adj8 (selection? or sample?)).kf,tw. (47301)
 197 random*.tw,kf. (1211315)
 198 or/188-197 (1422728)
 199 186 and 198 (388)
 200 humans.sh. (19125540)
 201 199 and 200 (220)
 202 (dutch or english or german or french).la. (29302349)
203 201 and 202 (210)=rcts

Database: Embase <1974 to 2021 March 30>

Search Strategy:

1 "richtlijn delier embase".ti. (0)
 2 *Delirium/ (10468)
 3 (delirum or delirious).tw,kw. (2396)
 4 *restlessness/ (1524)
 5 agitat*.tw,kw. (33029)
 6 (distress or distressed).tw,kw. (179638)
 7 restless*.tw,kw. (15150)
 8 ((disturbed or disordered or abnormal* or change*) adj2 (attention or cognition or cognitive or consciousness or perception)).tw,kw. (23953)
 9 "acute brain syndrome".tw. (53)
 10 "acute cerebral insuEiciency".tw. (0)
 11 "acute confusion".tw. (595)
 12 "acute confusional state".tw. (636)
 13 *Cognitive Defect/ (55690)
 14 (cognitive adj2 (dysfunction or decline)).tw. (61120)
 15 (mental* adj2 deterioration).tw. (1894)
 16 *Consciousness Disorder/ (1997)
 17 (diminish* adj2 consciousness).tw. (82)
 18 *Brain Disease/ (26588)
 19 encephalopathy.tw,kw. (73090)
 20 (fail* adj2 cognit*).tw. (1345)
 21 ""disorders of higher cerebral function"/ (628)
 22 organic mental disorder.tw. (239)
 23 "acute organic psychosyndrome"".tw. (7)
 24 "acute psycho-organic syndrome"".tw. (6)
 25 "exogenous psychosis".tw. (42)
 26 clouded state.tw. (1)
 27 (Cloud* adj2 conscious*).tw. (375)
 28 metabolic encephalopathy/ (1846)

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- 29 (metabolic adj2 encephalopathy).tw. (911)
- 30 (disturbance adj2 brain function).tw. (51)
- 31 toxic psychosis.tw. (155)
- 32 toxic confusion.tw. (8)
- 33 or/2-32 (445999)
- 34 exp Alprazolam/ (19814)
- 35 Alprazolam.tw,kw. (3472)
- 36 Amisulpride.tw,kw. (1885)
- 37 Amobarbital/ (3571)
- 38 Amobarbital.tw,kw. (1090)
- 39 Aripiprazole/ (16227)
- 40 Aripiprazole.tw,kw. (7158)
- 41 Benperidol/ (687)
- 42 Benperidol.tw,kw. (114)
- 43 Bromazepam/ (3564)
- 44 Bromazepam.tw,kw. (848)
- 45 Clorazepate Dipotassium/ (1875)
- 46 Chlorazepate.tw,kw. (142)
- 47 Chlordiazepam.tw,kw. (23)
- 48 Chlordiazepoxide/ (10895)
- 49 Chlordiazepoxide.tw,kw. (3013)
- 50 Chlorpromazine/ (39656)
- 51 Chlorpromazine.tw,kw. (11589)
- 52 Cytidine Diphosphate Choline/ (2188)
- 53 Citicoline.tw,kw. (716)
- 54 Clobazam.tw,kw. (1834)
- 55 Clonazepam/ (26866)
- 56 Clonidine/ (42181)
- 57 Clonidine.tw,kw. (18711)
- 58 Clozapine/ (33595)
- 59 Clozapine.tw,kw. (16823)
- 60 Desmethylalprazolam.tw,kw. (0)
- 61 Dextroamphetamine/ (12578)
- 62 Dextroamphetamine.tw,kw. (844)
- 63 Dexmedetomidine/ (12619)
- 64 Dexmedetomidine.tw,kw. (9180)
- 65 Diazepam/ (72649)
- 66 Diazepam.tw,kw. (25805)
- 67 Diclazepam.tw. (37)
- 68 Donepezil.tw,kw. (5802)
- 69 Droperidol/ (9242)
- 70 Droperidol.tw,kw. (2614)
- 71 Estazolam/ (1354)
- 72 Estazolam.tw,kw. (353)
- 73 Flumazenil/ (8646)
- 74 Flumazenil.tw,kw. (4183)
- 75 Flumazepil.tw,kw. (25)
- 76 Flunitrazepam/ (7956)
- 77 Flunitrazepam.tw,kw. (3728)
- 78 Flupenthixol/ (4939)
- 79 Flupenthixol.tw,kw. (1046)
- 80 Fluphenazine/ (9327)
- 81 Fluphenazine.tw,kw. (2360)
- 82 Flurazepam/ (4902)
- 83 Flurazepam.tw,kw. (1165)
- 84 Gabapentin.tw,kw. (10827)
- 85 Galantamine/ (7635)
- 86 Galantamine.tw,kw. (2469)
- 87 Halazepam.tw,kw. (74)
- 88 Haloperidol/ (58208)

- 89 Haloperidol.tw,kw. (23079)
- 90 Iloperidone.tw,kw. (310)
- 91 Ketazolam.tw,kw. (77)
- 92 Methotrimeprazine/ (5473)
- 93 Methotrimeprazine.tw,kw. (137)
- 94 Levomepromazine/ (5473)
- 95 Levomepromazine.tw,kw. (616)
- 96 Lorazepam/ (27483)
- 97 Lorazepam.tw,kw. (6473)
- 98 Lormetazepam.tw,kw. (363)
- 99 L-Trptophan.tw,kw. (3)
- 100 Melatonin/ (36407)
- 101 Melatonin.tw,kw. (32625)
- 102 Mesoridazine/ (1013)
- 103 Mesoridazine.tw,kw. (155)
- 104 Methotrimeprazine/ (5473)
- 105 Methotrimeprazine.tw,kw. (137)
- 106 Methylphenidate/ (21969)
- 107 Methylphenidate.tw,kw. (10282)
- 108 Midazolam/ (49265)
- 109 Midazolam.tw,kw. (20888)
- 110 Modafinil.tw,kw. (2620)
- 111 Nitrazepam/ (6687)
- 112 Nitrazepam.tw,kw. (1263)
- 113 Nitrous Oxide/ (33881)
- 114 Nitrous Oxide.tw,kw. (18324)
- 115 Olanzapine/ (35236)
- 116 Olanzapine.tw,kw. (13793)
- 117 Orap.tw. (630)
- 118 Oxazepam/ (8275)
- 119 Oxazepam.tw,kw. (1834)
- 120 Paliperidone Palmitate/ (3723)
- 121 Paliperidone.tw,kw. (2490)
- 122 Periciazine.tw,kw. (22)
- 123 Pericyazine.tw,kw. (32)
- 124 Perphenazine/ (6877)
- 125 Perphenazine.tw,kw. (1245)
- 126 Phenobarbital/ (59555)
- 127 Phenobarbital.tw,kw. (20293)
- 128 Phenobarbitone.tw,kw. (2818)
- 129 Phenobarb.tw,kw. (24)
- 130 Pimozide/ (8029)
- 131 Pimozide.tw,kw. (2512)
- 132 Pipotiazine.tw,kw. (100)
- 133 Prazepam/ (1442)
- 134 Prazepam.tw,kw. (294)
- 135 Pregabalin/ (15024)
- 136 Pregabalin.tw,kw. (6521)
- 137 Prochlorperazine/ (5842)
- 138 Prochlorperazine.tw,kw. (1022)
- 139 Promazine/ (2448)
- 140 Promazine.tw,kw. (553)
- 141 Promethazine/ (13265)
- 142 Promethazine.tw,kw. (2727)
- 143 Propofol/ (56864)
- 144 Propofol.tw,kw. (32013)
- 145 Quetiapine.tw,kw. (8646)
- 146 Ramelteon.tw,kw. (566)
- 147 Remifentanil.tw,kw. (7552)
- 148 Risperidone/ (37791)

- 149 Risperidone.tw,kw. (14759)
- 150 Rivastigmine/ (7642)
- 151 Rivastigmine.tw,kw. (2821)
- 152 Serentil.tw,kw. (157)
- 153 Sertindole.tw,kw. (650)
- 154 Sevoflurane.tw,kw. (12635)
- 155 Sufentanil/ (9569)
- 156 Sufentanil.tw,kw. (3876)
- 157 Sulpiride/ (12136)
- 158 Sulpiride.tw,kw. (5640)
- 159 Tacrine/ (5480)
- 160 Tacrine.tw,kw. (2287)
- 161 Temazepam/ (5971)
- 162 Temazepam.tw,kw. (1234)
- 163 Thiopental/ (23213)
- 164 Thiopental.tw,kw. (5415)
- 165 Thioridazine/ (11758)
- 166 Thioridazine.tw,kw. (2283)
- 167 Trazadone.tw,kw. (101)
- 168 Triazolam/ (6102)
- 169 Triazolam.tw,kw. (1984)
- 170 Trifluoperazine/ (9790)
- 171 Trifluoperazine.tw,kw. (3845)
- 172 Triflupromazine/ (1044)
- 173 Triflupromazine.tw,kw. (154)
- 174 Valproic Acid/ (65787)
- 175 Valproic Acid.tw,kw. (13483)
- 176 Ziprasidone.tw,kw. (2907)
- 177 Zotepine.tw,kw. (377)
- 178 Clopenthixol/ (743)
- 179 (Zuclopenthixol or Clopenthixol).tw,kw. (627)
- 180 Ondansetron/ (18571)
- 181 Ondansetron.tw,kw. (6921)
- 182 quazepam.tw,kw. (173)
- 183 or/34-182 (661333)
- 184 (dutch or english or german or french).la. (32777119)
- 185 "rct filter embase".ti. (0)
- 186 randomization/ (90903)
- 187 exp randomized controlled trial/ (656520)
- 188 exp controlled clinical trial/ (845246)
- 189 Major Clinical Study/ (4100113)
- 190 random\$.tw,kw. (1664007)
- 191 double blind procedure/ (183576)
- 192 or/186-191 (5546702)
- 193 33 and 183 and 184 (29682)
- 194 random\$.tw. (1658275)
- 195 factorial\$.tw. (40903)
- 196 crossover\$.tw. (80074)
- 197 cross over\$.tw. (34087)
- 198 cross-over\$.tw. (34087)
- 199 placebo\$.tw. (325510)
- 200 (doubl\$ adj blind\$).tw. (220029)
- 201 (singl\$ adj blind\$).tw. (26848)
- 202 assign\$.tw. (420967)
- 203 allocat\$.tw. (166337)
- 204 volunteer\$.tw. (268562)
- 205 Crossover Procedure/ (66748)
- 206 double-blind procedure.tw. (241)
- 207 Randomized Controlled Trial/ (655541)
- 208 Single Blind Procedure/ (42559)

209 or/194-208 (2482532)
210 (animal/ or nonhuman/) not human/ (5893941)
211 209 not 210 (2202296)
212 33 and 183 and 184 and 211 (5010)
213 212 (5010)
214 limit 213 to yr="2019 -Current" (609)= rcts

Cochrane search

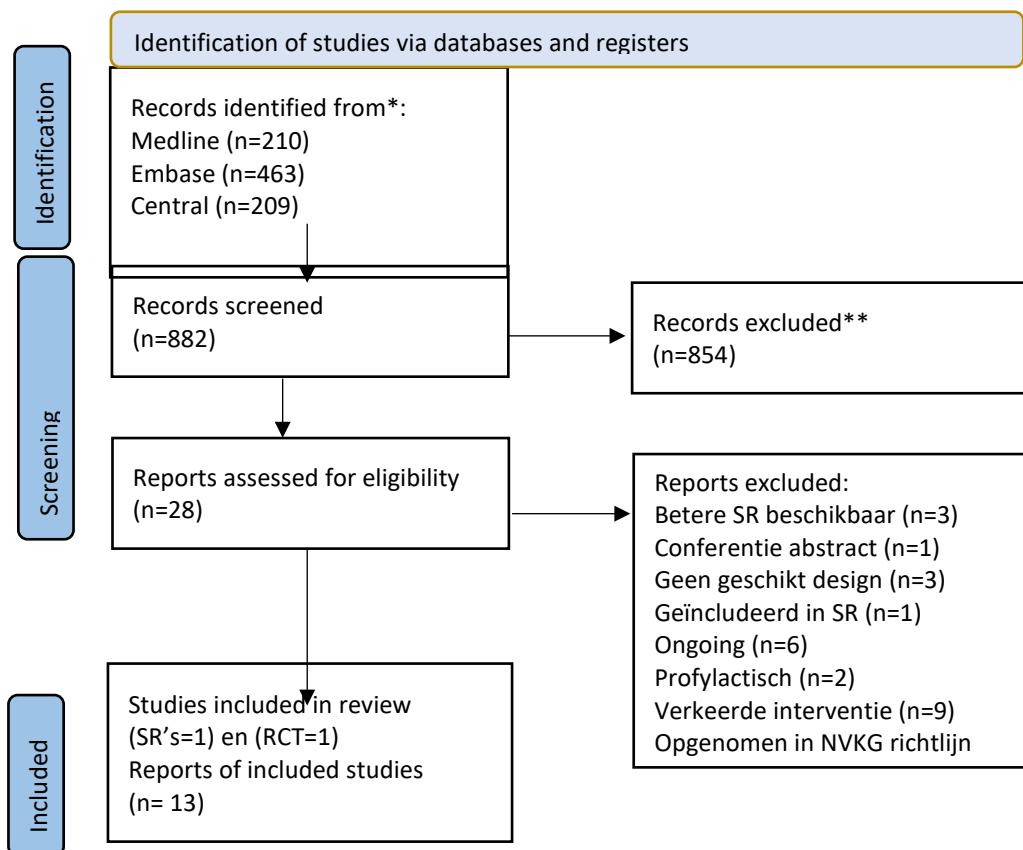
Search Name: P delier met haldol en rivastigmine

Last Saved: 31/03/2021 12:17:49

Comment: P delier conform cochrane SR 2020

- ID Search
- #1 MESH DESCRIPTOR Delirium
 - #2 ((delirum or delirious)):TI,AB,KW
 - #3 MESH DESCRIPTOR Psychomotor Agitation
 - #4 agit*:TI,AB,KW
 - #5 ((distress or distressed)):TI,AB,KW
 - #6 restless*:TI,AB,KW
 - #7 (((disturbed or disordered or abnormal* or change*) NEAR/2 (attention or cognition or cognitive or consciousness or perception))):TI,AB,KW
 - #8 ("acute brain syndrome"):TI,AB,KW
 - #9 ("acute cerebral insufficiency"):TI,AB,KW
 - #10 ("acute confusion"):TI,AB,KW
 - #11 ("acute confusional state"):TI,AB,KW
 - #12 MESH DESCRIPTOR Cognitive Dysfunction
 - #13 ((cognitive NEAR/2 (dysfunction or decline))):TI,AB,KW
 - #14 ((mental* NEAR/2 deterioration)):TI,AB,KW
 - #15 MESH DESCRIPTOR Consciousness Disorders
 - #16 ((diminish* NEAR/2 consciousness)):TI,AB,KW
 - #17 MESH DESCRIPTOR Brain Diseases
 - #18 encephalopathy:TI,AB,KW
 - #19 ((fail* NEAR/2 cognit*)):TI,AB,KW
 - #20 MESH DESCRIPTOR Neurocognitive Disorders
 - #21 (organic mental disorder):TI,AB,KW
 - #22 (acute NEAR/1 organic NEAR/1 psychosyndrome*):TI,AB,KW
 - #23 ("acute psycho-organic syndrome*"):TI,AB,KW
 - #24 ("exogenous psychosis"):TI,AB,KW
 - #25 (clouded state):TI,AB,KW
 - #26 ((Cloud* NEAR/2 conscious*)):TI,AB,KW
 - #27 MESH DESCRIPTOR Brain Diseases, Metabolic
 - #28 ((metabolic NEAR/2 encephalopathy)):TI,AB,KW
 - #29 ((disturbance NEAR/2 brain function)):TI,AB,KW
 - #30 (toxic psychosis):TI,AB,KW
 - #31 (toxic confusion):TI,AB,KW
 - #32 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31
 - #33 MESH DESCRIPTOR Haloperidol
 - #34 Haloperidol:TI,AB,KW
 - #35 Olanzapine:TI,AB,KW
 - #36 **#32 and (#33 or #34 or #35)**
 - #37 MESH DESCRIPTOR Rivastigmine
 - #38 Rivastigmine:TI,AB,KW
 - #39 **#32 and (#37 or #38)**

Overzicht van geëxcludeerde studies



Karakteristieken van de geïncludeerde studies
Evidence table

Finucane, 2020							
Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
A. Agar 2017 B. Breitbart 1996 C. Hui 2017 D. Lin 2008	Type of study: RCT's Search date: 8 July 2019 Number of included studies: N=4 Country A. Australia B. USA C. USA D. Taiwan Source of funding: Marie Curie, UK Inclusion criteria: - Terminally ill patients (>18 years) with delirium symptoms - Pharmacological interventions in any dose via any route - Reports on outcome of	N total at baseline (n analysed): A. 247 B. 30 C. 58 D. 30 Age in years, mean (SD): A. 74.5 (10.6) risperidone arm, 76.5 (8.2) haloperidol arm, 73.8 (10.7) placebo arm B. 39.2 (8.8) C. Range 30 to 90 D. 61 (16.5) olanzapine arm, 68 (12.1) haloperidol arm Gender: A. 34.4% female B. 23% female C. 46.6% female D. 56.7% female Illness: A. 218 (88%) cancer B. 30 (100%) AIDS	A. Risperidone 1mg/4ml or haloperidol 1mg/4ml every 12 hours for 72 hours, B. Haloperidol 1.4 mg or chlorpromazine 36 mg for 7 days C. Haloperidol 2mg/4 hours plus lorazepam 3mg as rescue medication, single administration D. Olanzapine 5mg/day for 7 days	A. Placebo B. Lorazepam 4.6 mg for 7 days C. Haloperidol 2mg/4 hours plus placebo as rescue medication, single administration D. Haloperidol 5mg/day for 7 days	Length of follow-up: A. 6 months B. 7 days C. 8 hours D. 7 days	Haloperidol vs placebo Delirium symptoms at 24 hours: MD 0.34, 95%CI -0.07;0.75 Delirium symptoms at 48 hours: MD 0.49, 95%CI 0.10;0.88 Agitation: MD -0.14, 95%CI -0.28;-0.00 Extrapyramidal adverse effects: MD 0.79, 95%CI 0.17;1.41 Haloperidol vs risperidone Delirium symptoms at 24 hours: MD -0.42, 95%CI -0.90;0.06 Delirium symptoms at 48 hours: MD -0.36, 95%CI -0.92;0.20 Haloperidol vs olanzapine Delirium symptoms at 24 hours: MD 2.36, 95%CI -0.75;5.47	There were insufficient data to assess GRADE

	<p>interest (delirium symptoms, agitation, adverse effects)</p> <p>Exclusion criteria: None</p>	<p>C. 58 (100%) cancer D. 30 (100%) cancer</p>				<p>Delirium symptoms at 48 hours: MD 1.90, 95%CI -1.50;5.30</p> <p>Risperidone vs placebo Delirium symptoms at 24 hours: MD 0.76, 95%CI 0.30;1.22 Delirium symptoms at 48 hours: MD 0.85, 95%CI 0.32;1.38 Agitation: MD -0.05, 95%CI -0.19;0.09 Extrapyramidal adverse effects: MD 0.73, 95%CI 0.09;1.37</p> <p>Lorazepam plus haloperidol vs placebo plus haloperidol Delirium symptoms at 24 hours: MD 2.10, 95%CI -1.00;5.20 Agitation: MD 1.90, 95%CI 0.90;2.80 Adverse events: RR 0.70, 95%CI -0.19;2.63</p> <p>Haloperidol vs chlorpromazine Delirium symptoms at 48 hours: MD 0.37, 95%CI -4.58;5.32</p>	
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Barbateskovic, 2019							
Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
<p>A. Atalan, 2013 B. Bakri, 2015 C. Bakri, 2015 D. Breitbart, 1996 E. Breitbart, 1996 F. Girard, 2018 G. Girard, 2018</p>	<p>Type of study: RCT's Search date: 5 March 2019 Number of included studies: N=8 Country: Not reported</p>	<p>N total at baseline (n analysed): A. 53 B. 48 C. 48 D. 19 E. 11 F. 280 G. 286 H. 24 I. 29 J. 73 K. 80</p>	<p>A. 5 mg haloperidol IM every hour until the adequate sedation and target RASS scores (between -1 and + 1) were achieved B. 5 mg haloperidol twice daily (infusion) Rescue haloperidol was used C. 5 mg haloperidol twice daily (infusion). Rescue haloperidol was used D. Haloperidol (oral or IM) dose according to delirium</p>	<p>A. 5 mg morphine IM every hour until the adequate sedation and target RASS scores (between -1 and + 1) were achieved B. 1 µg/kg dexmedetomidine or (infusion). Rescue haloperidol was used C. 4 mg ondansetron twice daily (infusion). Rescue haloperidol was used D. Mean chlorpromazine dose the first 24 hours was</p>	<p>Length of follow-up: A. max 10 days B. 3 days C. 3 days D. max 6 days E. max 6 days F. max 14 days G. max 14 days H. 7 days I. Until liberation from mechanical ventilation or</p>		<p>*RCT identified by the search strategy for this guideline and added tot the body of evidence of the SR</p>

<p>H. Han, 2004 I. ORIC-I, 2017 J. Skrobic, 2004 K. Tagrakis, 2012 L. Van der Vorst, 2020*</p>	<p>Source of funding: No funding</p> <p>Inclusion criteria: RCTs with critically ill patients with delirium at trial enrolment at any clinical setting where patients are at high risk of dying or with potential life-threatening health problems and who are admitted to a high-dependency facility in the hospital, and trials on acutely operated patients and elective cardiac surgical patients. Only trials comparing haloperidol with placebo, any other pharmacological agent, or combinations of (non-) pharmacological interventions (single or</p>	<p>L. 98</p> <p>Age in years, mean (SD): Not reported</p> <p>Setting: A. Patients with hyperactive delirium after cardiac surgery admitted to ICU B. Post-operative trauma patients with delirium admitted to ICU C. Post-operative trauma patients with delirium admitted to ICU D. AIDS patients with delirium admitted to a high dependency AIDS unit E. AIDS patients with delirium admitted to a high dependency AIDS unit F. Patients with delirium admitted to ICU G. Patients with delirium admitted to ICU</p>	<p>symptoms. Mean haloperidol dose the first 24 hours was 2.8 mg. Average maintenance dose was 1.4 mg. E. Haloperidol (oral or IM) dose according to delirium symptoms. Mean haloperidol dose the first 24 hours was 2.8 mg. Average maintenance dose was 1.4 mg. F. IV haloperidol. Mean daily doses of haloperidol administered were 11.0 mg; Rescue haloperidol was used G. IV haloperidol. Mean daily doses of haloperidol administered were 11.0 mg; Rescue haloperidol was used H. Oral flexible dose haloperidol. Mean dose of haloperidol was 1.71 mg I. 5 mg IV haloperidol every 12 hours J. Enteral or oral haloperidol. Initially 2.5-5 mg every 8 hours (patients over 60 received a lower initial dose haloperidol 0.5-1 mg); Rescue haloperidol was used K. 5 mg IV haloperidol L. Haloperidol (age-adjusted, titratable doses)</p>	<p>50 mg. Average maintenance dose was 36 mg E. Mean lorazepam dose the first 24 hours was 3 mg. Average maintenance dose was 4.6 mg. F. Placebo Rescue haloperidol was used G. IV ziprasidone. Mean daily doses of ziprasidone administered were 20.0 mg; Rescue haloperidol was used H. Oral flexible dose risperidone. Mean dose of risperidone 1.02 I. Placebo J. Enteral or oral olanzapine. Initially 5 mg daily (patients over 60 received a lower initial dose olanzapine 2.5 mg); Rescue haloperidol was used K. 8 mg IV ondansetron L. Olanzapine (age-adjusted, titratable doses)</p>	<p>28 days, whichever came first J. 5 days K. unclear L. max 7 days</p>		
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	<p>bundle) were included.</p> <p>Exclusion criteria: - haloperidol administered in both groups per protocol or administered as a combination therapy with another pharmacological agent</p>	<p>H. Patients with delirium admitted to ICU**</p> <p>I. Mechanically ventilated patients with delirium</p> <p>J. Patients with delirium admitted to a medical-surgical ICU</p> <p>K. Patients with delirium after on-pump cardiac surgery</p> <p>L. Patients with advanced cancer and delirium</p>					
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Risk of bias profile

Finucane, 2020		
Item	Yes, partial Yes or no	Explanation
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes	It is an update of an earlier version
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Partial yes	Rationale not clearly stated
4. Did the review authors use a comprehensive literature search strategy?	Yes	
5. Did the review authors perform study selection in duplicate?	Yes	
6. Did the review authors perform data extraction in duplicate?	Partial yes	Data extraction was checked by second author, but agreement is not mentioned
7. Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	
8. Did the review authors describe the included studies in adequate detail?	Yes	
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes	
10. Did the review authors report on the sources of funding for the studies included in the review?	Yes	
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	N.A.	
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	N.A.	
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes	
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	N.A.	
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	N.A.	

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	Conflicts are reported
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Barbateskovic, 2019		
Item	Yes, partial yes or no	Explanation
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Yes	The SR was registered in PROSPERO (CRD42017081133)
3. Did the review authors explain their selection of the study designs for inclusion in the review?	No	Rationale not clearly stated
4. Did the review authors use a comprehensive literature search strategy?	Yes	7 databases, ongoing trial registers and screening reference lists
5. Did the review authors perform study selection in duplicate?	Yes	
6. Did the review authors perform data extraction in duplicate?	Partial yes	Data extraction was checked by second author, but agreement is not mentioned
7. Did the review authors provide a list of excluded studies and justify the exclusions?	Partial	The reasons for exclusion were reported in the PRISMA flow-chart
8. Did the review authors describe the included studies in adequate detail?	Yes	
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes	
10. Did the review authors report on the sources of funding for the studies included in the review?	Yes	No funding was received
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes	
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Partial	The subgroup analysis excluding trials at overall high risk of bias could not be performed as no trial was overall low risk of bias.
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes	
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	N.A.	There was no significant heterogeneity observed ($I^2=0\%$ and 27%)
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	N.A.	

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	Conflicts are reported
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Van der Vorst, 2020	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of patient and personell (performance bias)	Blinding of outcome assessor (detection bias)	Follow-up and ITT or per protocol analysis (attrition bias)	Selective reporting	Other bias
	Low risk Sequentially numbered, opaque, sealed envelopes provided by an independent third party	Low risk Enclosing assignments in sequentially numbered, opaque, sealed envelopes provided by an independent third party	High risk Patients and medical staff were not blinded.	Low risk Outcome assessor was blinded.	Low risk Analyzes followed an ITT principle.	Low risk Registered outcomes were reported in publication (NCT01539733).	Low risk No other sources of bias were found.

GRADE profiel

Author, publication year: Finucane, 2020

Vergelijking	Uitkomst	GRADE	Toelichting
Haloperidol vs placebo	Symptomen van delier na 24 uur	Laag	Bewijskracht verlaagd vanwege onduidelijk risico op bias vanwege sample size en ongevalideerde uitkomstmaat
	Symptomen van delier na 48 uur	Laag	Bewijskracht verlaagd vanwege onduidelijk risico op bias vanwege sample size en ongevalideerde uitkomstmaat
	Agitatie	Laag	Bewijskracht verlaagd vanwege onduidelijk risico op bias vanwege sample size en onnauwkeurigheid
	Extrapiramidale bijwerkingen	Redelijk	Bewijskracht verlaagd vanwege onduidelijk risico op bias vanwege sample size
Haloperidol vs risperidone	Symptomen van delier na 24 uur	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
	Symptomen van delier na 48 uur	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
Haloperidol vs olanzapine	Symptomen van delier na 24 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
	Symptomen van delier na 48 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
Risperidone vs placebo	Symptomen van delier na 24 uur	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
	Symptomen van delier na 48 uur	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
	Agitatie	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
	Extrapiramidale bijwerkingen	Laag	Bewijskracht verlaagd vanwege hoog risico op bias
Lorazepam plus haloperidol vs placebo plus haloperidol	Symptomen van delier na 24 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
	Agitatie	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
	Bijwerkingen	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
Haloperidol vs chlorpromazine	Symptomen van delier na 48 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
	Bijwerkingen	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
Haloperidol vs lorazepam	Symptomen van delier na 48 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid

	Bijwerkingen	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
Lorazepam vs chlorpromazine	Symptomen van delier na 48 uur	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid
	Bijwerkingen	Zeer laag	Bewijskracht verlaagd vanwege kleine sample size met hoge onnauwkeurigheid