

1 **The incidence of delirium in an acute geriatric community hospital: an observational cohort**
2 **feasibility study.**

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51 **Keywords:** delirium, older adults, feasibility study, hospitalization, community hospital.

52 **Abstract**

53 **Objectives** Delirium in hospitalised older adults is associated with negative health outcomes.
54 Admission to an alternative care setting may lower the incidence of delirium. The Acute Geriatric
55 Community Hospital (AGCH) was recently opened in the Netherlands and uses a multi-component
56 non-pharmacological intervention strategy to prevent delirium. The objective of this study was to
57 describe the incidence of delirium at the AGCH and compare this incidence to existing rates from
58 literature. If a possible effect on delirium is seen in this comparison this would support conducting a
59 larger prospectively controlled study on delirium in this new care setting.

60 **Design** Prospective cohort feasibility study; exploratory meta-analysis of proportions.

61 **Setting and Participants** The AGCH is an acute geriatric unit in a skilled nursing facility for patients
62 aged >65 years with acute medical conditions.

63 **Methods** Delirium assessment using the Confusion Assessment Method (CAM) upon admission and
64 on day one, two and three or until delirium had resolved. Patients' charts were reviewed if CAM was
65 missing. In an linear mixed-effects model, the delirium incidence rate in AGCH was compared to
66 pooled delirium incidence rates from six studies found in a high-quality review.

67 **Results** 214 patients from the AGCH (mean age 81.9 years, 47% male, 12% with a history of
68 dementia) were included in the analysis. Delirium developed in 8% (18/214) (95% confidence
69 interval [CI] 5-13%) of patients during AGCH admission compared to 16% (95% CI 12-21%) in
70 hospitals. Admission to the AGCH was associated with a decreased delirium incidence rate compared
71 to the hospital control group (OR[odds ratio]= 0.49, 95% CI 0.24-0.98, p-value=0.044).

72 **Conclusions and implications** The delirium incidence in the AGCH was low compared to those
73 incidences found in general hospitals in literature. Based on these findings a controlled observational
74 or randomized study measuring delirium in this care setting is recommended.

75 **Introduction**

76 A common complication of hospitalization in older adults is the development of delirium, an acute
77 disturbance in attention and cognitive functions.¹ The etiology of delirium is considered
78 multifactorial.² Delirium is associated with negative health outcomes, including functional and
79 cognitive decline, institutionalization, and mortality.^{3,4} The prevalence and incidence of delirium
80 varies between settings and populations, with new-onset delirium during hospitalization ranging
81 from 10% to 56%.⁵

82 An alternative to conventional hospitalization is admission to an acute geriatric unit outside
83 of a general hospital. This unit may be better adapted to the needs of older adults.⁶ In the
84 Netherlands, the Acute Geriatric Community Hospital (AGCH) was introduced in 2018.⁷ This
85 geriatrician-led unit located in a skilled nursing facility integrates specialized medical treatment with
86 geriatric nursing care. This is the first unit of its kind in the Netherlands but other examples exist
87 internationally.⁸ At the AGCH a non-pharmacological multi-component delirium prevention strategy
88 has been implemented, consisting of encouraging early mobilization, preventing overstimulation
89 (single rooms, noise reduction), management of delirium-inducing drugs and improving orientation
90 through e.g. family involvement.^{6,7} It is unknown what the effect of this intervention is on the
91 incidence of delirium in this new care setting.⁷ A feasibility study can help to determine if a large
92 effectiveness study regarding delirium incidence at the AGCH should be conducted.⁹

93 We hypothesize that the non-pharmacological interventions at the AGCH reduce the
94 incidence of delirium compared to usual care. The objective of this feasibility study was therefore to
95 determine the incidence of delirium and compare this incidence to those incidences found in
96 literature from general hospitals. This should help determine if an effect from this intervention in
97 this new care setting is to be expected; and therefore determine if a larger prospectively controlled
98 or randomized study on the incidence of delirium in the AGCH is advisable.

99 As secondary aims, we determined the duration of delirium and we quantified the use of
100 pharmacological delirium treatment. The duration of delirium is relevant as it can also be shortened
101 by a multi-component non-pharmacological intervention.¹⁰ Moreover, it is clinically relevant to know
102 if patients (with or without delirium) were prescribed antipsychotics and/or benzodiazepines for the
103 pharmacological treatment or prevention of delirium, as this is not recommended for the prevention
104 of delirium.¹¹⁻¹³

105

106 **Methods**

107 *Design and setting*

108 Data from a prospective cohort study were used. The study protocol was published
109 elsewhere.⁷ Data collection started in February 2019 and was ceased in March 2020 during the
110 COVID-19 pandemic.

111 Patients seen at the emergency department (ED) of the Amsterdam University Medical
112 Centers in Amsterdam were assessed by an on-call geriatrician. Patients admitted to the AGCH were
113 65 years or older, presenting with an acute medical problem requiring hospitalization and one or
114 more geriatric conditions, such as a fall, functional impairment or polypharmacy.¹⁴ Patients who did
115 not require hospitalization, but needed short-term residential care in a skilled nursing facility, were
116 excluded from admission to the AGCH. See the study protocol⁷ and appendix 1 for complete
117 admission eligibility criteria.

118 *Ethical considerations*

119 The local Ethics Committee of the the Amsterdam UMC, location AMC waived the obligation
120 for the study to undergo formal ethical approval as described under Dutch law. We included patients
121 who, or whose legal representative, could provide written informed consent. The study was
122 registered in the Dutch Trial Registry, trial registration number NL7896.

123 *Control population from literature*

124 We did not recruit a control group during the study period and we did not have delirium
125 measurements available in a historical control group.⁷ To determine if a larger prospectively
126 controlled study would be advisable we compared the incidence of delirium at the AGCH to existing
127 literature. We searched for sources of aggregated data on the incidence rate of delirium in medical
128 or geriatric (non-surgical) inpatients with a mean age of about 80 years (search strategy and
129 excluded studies- appendix 2 and 3). We selected six studies from a review by Inouye et al. as a
130 control group.⁵

131

132 *Measurement of incident delirium*

133 Incident delirium, the number of new cases of delirium during admission, was the study
134 outcome.¹⁵ No sample size was calculated. Patients were excluded from our analysis if delirium was
135 present at the ED. The diagnosis of delirium was made by the geriatrician or geriatric nurse specialist
136 by clinical assessment and using the Confusion Assessment Method (CAM).¹⁶ The CAM was filled out
137 upon presentation to the ED and during the first three days of admission or until delirium had
138 resolved. Nurses screened for signs of possible delirium, three times a day, during the first three
139 days of admission using the Delirium Observation Screening Scale (DOSS).¹⁷ Patients were assessed
140 by the same clinician for several consecutive days to recognize changes in mental status. On the
141 weekend an on-call geriatrician assessed delirium status if delirium was clinically suspected. The
142 DOSS and nursing chart covering the previous 24 hours were also considered in the delirium
143 assessment. If there was a possible delirium after day three of admission, CAM assessments were
144 continued until delirium had resolved.

145 *Duration of delirium*

146 The duration of delirium was counted from the day the diagnosis was made until the CAM
147 was permanently negative and/or the treating physician stated the delirium had resolved. In
148 patients with an unresolved delirium at the time of discharge, we defined the first day of delirium
149 until discharge as the duration of delirium.

150 *Use of antipsychotics and/or benzodiazepines*

151 The administration of haloperidol, other antipsychotics, and benzodiazepines was collected
152 from patients' charts. We also checked if patients categorized as not delirious had received
153 antipsychotics. This was 1) a check to see if no patient with a delirium diagnosis was missed and 2) a
154 measure to quantify the use of antipsychotics and/or benzodiazepines as a preventive measure for
155 delirium, although this is not recommended.¹¹⁻¹³

156 *Statistical analysis*

157 Descriptive statistics, chi-square, t-test, and Mann-Whitney U test were used to compare
158 patients with and without delirium upon admission. To compare incidence rates from literature we
159 pooled studies in a meta-analysis of proportions, using a random-effects model.¹⁸ We tested if the
160 difference in delirium incidence was statistically significant by creating a logistic mixed-effects meta-
161 regression model with the location of the study (hospital versus AGCH) as a moderator.¹⁹ We did not
162 perform meta-regression of other covariates because the number of included studies was limited
163 (<10).¹⁸ All analyses were performed using SPSS version 26.00 (IBM SPSS Statistics, IBM Corporation,
164 Armonk, NY) and R version 3.6.1. We used the metaphor (Viechtbauer, 2010) and meta (Schwarzer
165 et al., 2015) packages in R.

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167

168

169 **Results**

170 Between January 31, 2019 and March 13, 2020, a total of 466 consecutive patients were admitted to
171 the AGCH (figure 1). Of the 261 patients who participated in the study 47 were excluded because of
172 prevalent delirium or because of missing delirium assessments at the ED. The sample for this study
173 therefore consisted of 214 patients (figure 1). Mean (SD) age was 81.9 (8.1) years, 47.2% was male,
174 12.1% had a diagnosis of dementia, and 47.2% of the patients was frail (table 1). Development of
175 delirium during admission occurred in 18 out of 214 patients, which is an incidence rate of 8.4%
176 (95% CI [confidence interval] 5-13%). The median (IQR [interquartile range]) duration of delirium in
177 the AGCH was 2.5 days (1.0-5.3) (table 1). Mean length of stay (SD) was 9.6 (7.3) days in all patients,
178 9.4 (7.4) days in patients with no delirium and 11.9 (6.4) days in patients with delirium. Median
179 length of stay (IQR) was 7.0 (5.0-11.00) days in patients with no delirium and 10 (7.5-16.8) days in
180 patients with delirium.

181 *Pharmacological treatment for delirium*

182 Eleven out of 18 patients (61.1%) with a diagnosis of delirium were administered medication for the
183 treatment of delirium. Haloperidol was administered most frequently (n=11). The regular
184 prescription of haloperidol was 0.5-2.0mg per dose, typically given once a day, or twice in case of
185 severe delirium, with a maximum of three dosages. Five (5 out of 196, 2.6%) patients without
186 delirium were administered haloperidol, either as prevention due to a high risk of delirium or as
187 treatment for pre-existing symptoms unrelated to delirium (table 1).

188 *Delirium incidence in comparison to reference group from literature*

189 The control group was based on six studies (appendix 4).⁵ In total 1546 study participants with a
190 mean age of 80 years (Appendix 4). None of the studies, except for Friedman et al.²⁰ reported to
191 have implemented multi-component delirium prevention strategies, we therefore assumed usual
192 care was delivered. The pooled delirium incidence rate of these six studies was 16% (95% CI random

193 effects model 12-21%) (Figure 2). The meta-analysis showed a high heterogeneity ($I^2=84\%$). In a
194 separate logistic mixed-effects model comparing general hospitals (reference category) versus the
195 AGCH, we found that admission to the AGCH was associated with a decrease in delirium incidence
196 (OR [odds ratio]= 0.49, 95% CI 0.24-0.98, $p=.044$).

197 *Adherence to CAM evaluations and missing data*

198 In patients with delirium 27.8% of total CAM evaluations and 46.3% of total DOSS scores were
199 missing during the first three days of admission. For patients without delirium 46.9% and 66.7%
200 were missing, respectively. In 15% of all cases all three CAM evaluations were missing. Based on the
201 CAM evaluation and daily delirium assessment by the attending clinician we could ascertain the
202 presence delirium in the first three days of admission in all patients.

203 **Discussion**

204 We measured the effect of a non-pharmacological multi-component delirium prevention strategy at
205 the AGCH and found an incidence rate of delirium of 8.4%. This incidence is lower compared to rates
206 found in hospital medical or geriatric wards found in historical cohorts from literature. This finding is
207 in line with previous literature on multi-component interventions for preventing delirium in
208 hospitalized patients: a 2016 Cochrane review reports moderate quality evidence that multi-
209 component interventions in medical, non-surgical, patients lower delirium incidence.⁶ Moreover, the
210 median duration of delirium of 2.5 days at the AGCH is comparable to the duration that is found in
211 literature on non-pharmacological interventions.²¹ The prescription rate of medication (61.1%) may
212 be lower in the AGCH compared to other studies, which report rates of 74-86%.^{22,23} The Dutch
213 guideline on delirium, and international guidelines alike, recommends to take a cautious approach to
214 the prescription of medication for the treatment of delirium.¹¹⁻¹³ In addition, only a few patients
215 received medication, in this case haloperidol, for the prevention of delirium, meaning that there
216 were not many non- delirious patients receiving haloperidol. This is relevant because,
217 administration of anti-psychotics such as haloperidol could lower delirium incidence rates in high

218 incidence groups.¹¹ Moreover, not all CAM measurement on day 1-3 of admission were complete,
219 but it was possible to ascertain the presence of delirium based on daily clinical delirium assessment.

220 A strength of this feasibility study is the relatively large study sample. Limitations of the study
221 include that the incidence rate of delirium could have been influenced by selection bias as legal
222 representatives of patients could not always be contacted to obtain consent. Moreover, even
223 though we selected a control group from a high-quality review article; this review was not recently
224 published (2014) and the selected studies were conducted in different countries than the
225 Netherlands.⁵ We also did not have insight into all of the baseline characteristics of these studies,
226 which makes it difficult to assess comparability. In addition, we could not definitively ascertain that
227 ‘usual care’ was delivered in each unit or what this was composed of. Finally, we did not collect data
228 on illness severity, which can be associated with delirium.²⁴

229

230 **Conclusion and implications**

231 This feasibility study shows that the incidence rate of delirium in the AGCH may be lower than in
232 general hospitals. Based on this result we would recommend a randomized controlled study or a
233 two-armed observational study using e.g. inversely weighted propensity scores²⁵ to test if
234 admission to the AGCH is effective in reducing the incidence of delirium. Moreover, attention
235 should be given to collecting complete CAM assessments in this ‘real-world’-setting. If in a larger,
236 prospective and controlled study the incidence of delirium at the AGCH is lower than in hospital this
237 would support the implementation of the AGCH model of care elsewhere.

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Figure 1 – Participant flow-chart Acute Geriatric Community Hospital (AGCH) study.

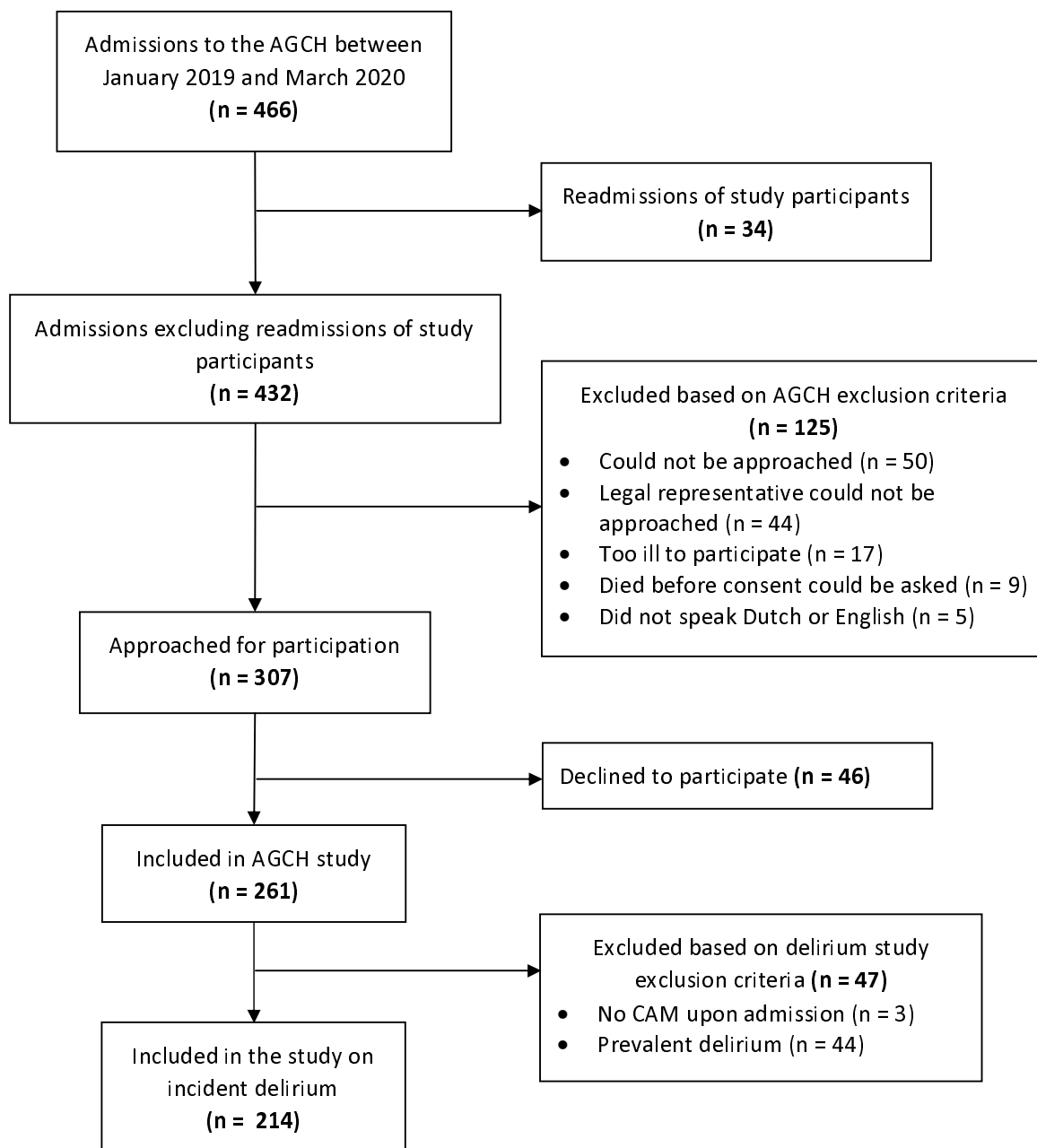


Table 1 – Baseline characteristics of the total study population grouped by patients with and without delirium.

	Total (n = 214)	No delirium (n = 196) 91.6%	Incident delirium (n = 18) 8.4%	p value^a
Age (years), mean (SD)	81.9 (8.1)	81.6 (8.0)	85.2 (8.8)	.08
Male, n (%)	101 (47.2)	93 (47.4)	8 (44.4)	.81
Born in the Netherlands, n (%)	160 (74.8)	146 (74.5)	14 (77.8)	.99
Marital status, n (%)				.58
Married/living together	69 (32.2)	65 (33.2)	4 (22.2)	
Single/Divorced	45 (21.0)	40 (20.4)	5 (27.8)	
Widow(er)	99 (46.3)	90 (45.9)	9 (50.0)	
Living arrangement before admission, n (%)				.80
Independent	174 (81.3)	158 (80.6)	16 (88.9)	
Nursing home	5 (2.3)	5 (2.6)	-	
Senior residence	33 (15.4)	31 (15.8)	2 (11.1)	
Other	2 (0.9)	2 (1.0)	-	
Level of education, n (%)				.44
Primary school	37 (17.3)	32 (16.3)	5 (27.8)	
Elementary technical/domestic science school	45 (21.0)	43 (21.9)	2 (11.1)	
Secondary vocational education	63 (29.4)	58 (29.6)	5 (27.8)	
Higher-level high school/third-level education	49 (22.9)	43 (21.9)	6 (33.3)	
Polypharmacy (≥ 5 medications), n (%)	160 (74.8)	147 (75.0)	13 (72.2)	.80
Primary admission diagnosis, n (%)				.44
Pneumonia	40 (18.7)	38 (19.4)	2 (11.1)	
Urinary tract infection (UTI)	27 (12.6)	25 (12.8)	2 (11.1)	
Other infections (excl. pneumonia/UTI)	21 (9.8)	8 (4.1)	3 (16.7)	
Congestive heart failure	20 (9.3)	18 (9.2)	2 (11.1)	
Neurologic disorders	19 (8.9)	17 (8.7)	2 (11.1)	
COPD exacerbation	15 (7.0)	15 (7.7)	-	
Fall(s)	13 (6.1)	12 (6.1)	1 (5.6)	
Gastrointestinal disease	10 (4.7)	10 (5.1)	-	
Electrolyte disturbance	6 (2.8)	4 (2.0)	2 (11.1)	
Other	43 (20.1)	39 (19.9)	4 (22.2)	
Katz-ADL^b score two weeks before admission, median (IQR)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	2.0 (0.8-3.0)	.054
Katz-ADL^b score upon admission, median (IQR)	2.5 (1.0-4.0)	2.0 (1.0-4.0)	3.5 (0.8-5.3)	.34
Frailty^c, n (%)	101 (47.2)	92 (46.9)	9 (50.0)	.94
Unknown	59 (27.6)	55 (28.1)	4 (22.2)	
MMSE^d score, median (IQR)	25.0 (22.0-28.0)	25.0 (23.0-28.0)	23.0 (20.0-24.8)	.035
- Unknown or not done, n (%)	56 (26.2)	50 (25.5)	6 (33.3)	
History of dementia, n (%)	26 (12.1)	22 (11.2)	4 (22.2)	.17

Cognitive impairment^e, n (%)	88 (41.1)	76 (38.8)	12 (66.7)	.022
Charlson comorbidity index score^f, median (IQR)	3.0 (1.0-4.0)	2.5 (1.0-4.0)	3.0 (1.0-4.0)	.99
History of delirium/confusion during sickness, n (%)	55 (25.7)	48 (24.5)	7 (38.9)	.23
Duration of delirium, in median days (IQR)				
NA= not applicable	NA	NA	2.5 (1.0-5.3)	
Pharmacological treatment for delirium, n				
NA= not applicable	NA	NA	11	
- Haloperidol	16	5	11	
- Other antipsychotics	NA	NA	1	
- Benzodiazepines	NA	NA	4	

^a Incident delirium compared to no delirium

^b Katz Index score range 0-6, with a higher score indicating more dependence in activities of daily living (ADL) ²⁶

^c Based on Fried criteria for frailty range 0-5 with a score of 3 and higher indicating presence of physical frailty ²⁷

^d Mini Mental State Exam score ranging 0-30, MMSE score ≤ 23 indicating cognitive impairment ²⁸

^e All patients with a diagnosis of dementia, a MMSE score ≤ 23 , or, in case of missing MMSE score, subjective cognitive problems

^f Range of 0-31, with a higher score indicating more or more severe comorbidity ²⁹

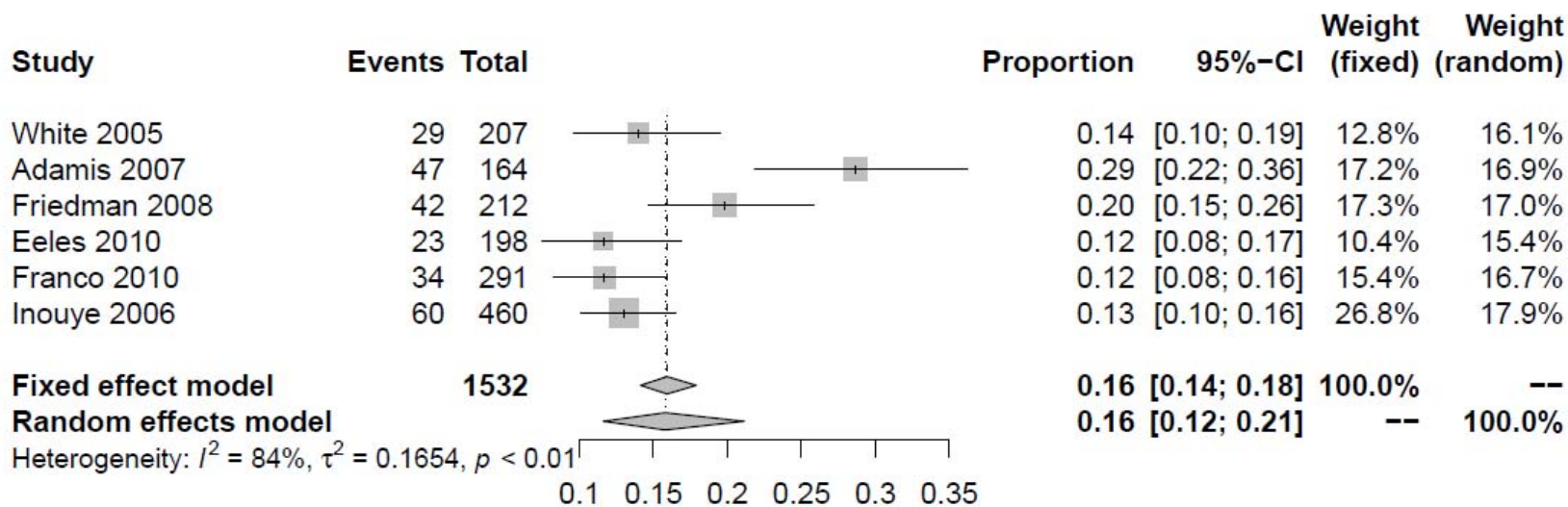


Figure 2 – Meta-analysis of proportions of delirium incidences in older hospitalized medical patients found in literature ⁵. The pooled incidence rate of these six studies was 16% (95% CI [confidence interval]random effects model 12-21%).