## **Appendix K-Forest Plots**

### Diagnosis

# Diagnosis and accuracy of diagnostic test

Figure 6.1: forest plot of DSM-III-R diagnostic test with DSM-IV as a reference standard in a hospital setting

Study	TP	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Cole 2003 Whole_either	168	0	45	109	0.79 [0.73, 0.84]	1.00 [0.97, 1.00]	-	•
Cole 2003_whole_bothcrite	89	79	20	134	0.82 [0.73, 0.88]	0.63 [0.56, 0.69]	-	-
Cole2003_whole_clouding	89	79	21	133	0.81 [0.72, 0.88]	0.63 [0.56, 0.69]		
							0 02 04 06 08 1	0 02 04 06 08 1

Figure 6.2: forest plot of DSM-III diagnostic test with DSM-III-R as a reference standard in a hospital setting

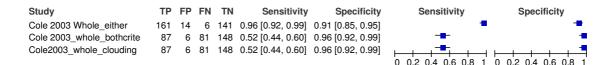


Figure 6.3: forest plot of ICD-10 diagnostic test with DSM-III-R as a reference standard in a hospital setting

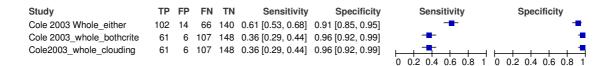


Figure 6.4: forest plot of DSM-III-R compared with DSM-IV in a hospital settingsubgroup analyses

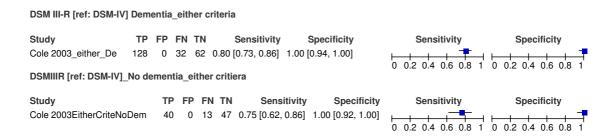


Figure 6.5: forest plot of DSM-III-R compared with DSM-III-R in a hospital setting - subgroup analyses

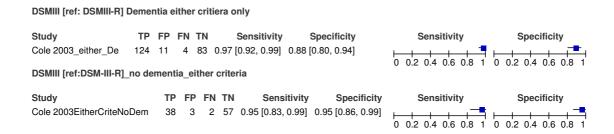


Figure 6.6: forest plot of ICD-10 compared with DSM-III-R in a hospital settingsubgroup analyses

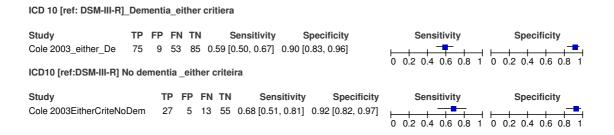


Figure 6.7: forest plot of index tests compared with DSM-IV in a hospital setting

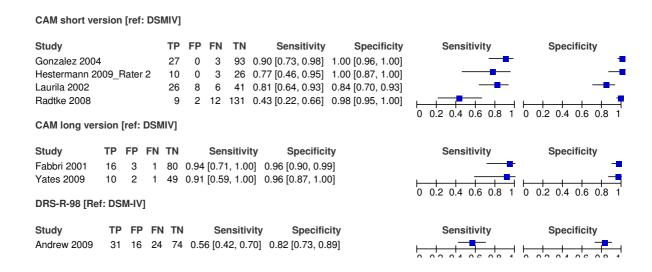


Figure 6.8: forest plot of DRS-R-98 compared with DSM-IV in a hospital settingsubgroup analysis



Figure 6.9: forest plot of CAM compared with ICD-10 in a hospital setting- subgroup analysis



Figure 6.10: forest plot of index test compared with DSM-III-R

#### CAM short version [ref: DSM III-R] TP FP FN TN Study Sensitivity Specificity Sensitivity Specificity 17 17 4 43 0.81 [0.58, 0.95] 0.72 [0.59, 0.83] Laurila 2002 Pompei 1995 28 28 33 338 0.46 [0.33, 0.59] 0.92 [0.89, 0.95] 0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1 CAM long version [ref: DSM-III-R] Study TP FP FN TN Sensitivity Specificity Sensitivity Specificity Cole 2003 Dementia more than 6 smptoms 125 24 3 75 0.98 [0.93, 1.00] 0.76 [0.66, 0.84] Cole 2003 No dementia; more than 6 symptoms 38 10 2 50 0.95 [0.83, 0.99] 0.83 [0.71, 0.92] 0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 CAM [type of version unclear] [ref: DSM-III-R] TP FP FN TN Specificity Sensitivity Sensitivity Specificity Rolfson 1999b\_nurseassess 1 0 7 22 0.13 [0.00, 0.53] 1.00 [0.85, 1.00] Rolfson 1999b\_physician 15 0 0 26 1.00 [0.78, 1.00] 1.00 [0.87, 1.00] MMSE [ref: DSM-III-R] Sensitivity Study TP FP FN TN Sensitivity Specificity **Specificity** 8 9 15 39 0.35 [0.16, 0.57] 0.81 [0.67, 0.91] Rolfson 1999b



0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8

Figure 6.11: forest plot of number of symptoms in index test compared with DSMIII-R as the reference standard in a hospital setting

#### CAM [number of symptoms] [ref: DSMIII-R] patients with dementia

Study				TP	FP	FN	TN		Sens	sitivity	Spe	cificity		Sei	nsitiv	ity			Speci	ificity	
Cole 2003 Dementia >2				128	67	0	27	1.0	0 [0.97	, 1.00]	0.29 [0.20	0, 0.39]					•	-	•		
Cole 2003 Dementia >3				128	52	0	47	1.0	0 [0.97	, 1.00]	0.47 [0.37	7, 0.58]					•		-	-	
Cole 2003 Dementia >4				128	49	0	50	1.0	0 [0.97	, 1.00]	0.51 [0.40	0, 0.61]					•		-	-	
Cole 2003 Dementia >5				128	39	0	60	1.0	0 [0.97	, 1.00]	0.61 [0.50	0, 0.70]					•			-	
Cole 2003 Dementia more than 6	smp	tom	S	125	24	3	75	0.9	8 [0.93	, 1.00]	0.76 [0.66	6, 0.84]	<del>   </del>	2 0	4 0	6 0.8	- <b>1</b>	0 0	2 0.4	0.6.0	8 1
CAM [number of symptoms] [ref	: DSN	IIII-R	] no	dem	entia	<u>a</u>										0.0			2 0.1	0.0 0	
Study	TP	FP	FN	TN		Se	nsiti	ivity	9	Specifi	icity			Sei	nsitiv	ity			Speci	ificity	
Cole 2003 No dementia >2	40	28	0	32	1.0	0 [0.9	91, 1	.00]	0.53 [	0.40, 0	0.66]						-		-	_	
Cole 2003 No dementia >3	40	24	0	36	1.0	0 [0.9	91, 1	.00]	0.60 [	0.47, 0	).72]						-		-	-	
Cole 2003 No dementia >4	40	21	0	39	1.0	0 [0.9	91, 1	.00]	0.65 [	0.52, 0	).77]						-			-	
Cole 2003 No dementia >5	40	17	0	43	1.0	0 [0.9	91, 1	.00]	0.72 [	0.59, 0	).83]						-			-	-
Cole 2003 No dementia>6sy	38	10	2	50	0.9	5 [0.8	B3, 0	.99]	0.83 [	0.71, 0	).92]		<del></del>		<del>   </del>		٠,	-			_

NB: > indicates 'more	tha	ın';	'&g	ıt2'	would indicat	te 'more than 2	2 symptoms'	
DI- dementia								
Study	TP	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Cole 2003 Dementia >2	116	66	12	28	0.91 [0.84, 0.95]	0.30 [0.21, 0.40]	-	-
Cole 2003 Dementia >3	99	40	29	54	0.77 [0.69, 0.84]	0.57 [0.47, 0.68]	-	-
Cole 2003 Dementia >4	78	14	50	80	0.61 [0.52, 0.69]	0.85 [0.76, 0.92]	0 0.2 0.4 0.6 0.8 1	0 02 04 06 08 1
DI- no dementia							0 0.2 0.1 0.0 0.0 1	0.2 0.1 0.0 0.0 1
Study	TI	P FI	P FN	I I	I Sensitivity	y Specificity	Sensitivity	Specificity
Cole 2003 No dementia >2	3	3 2	2 7	7 38	0.82 [0.67, 0.93	0.63 [0.50, 0.75]	-	-
Cole 2003 No dementia >3	2	4 1	1 16	6 49	0.60 [0.43, 0.75	0.82 [0.70, 0.90]		-
Cole 2003 No dementia >4	1	7	5 23	3 55	5 0.42 [0.27, 0.59	] 0.92 [0.82, 0.97]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1

Figure 6.12: ROC plot of effects of varying threshold for CAM and DI compared with DSM-III-R

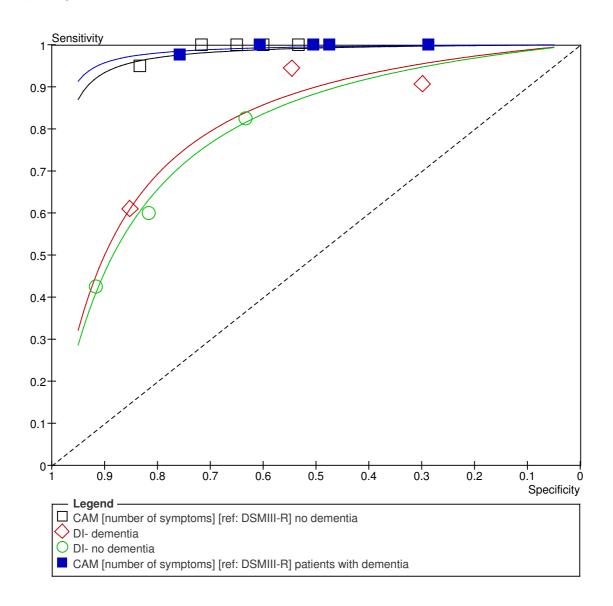


Figure 6.13: forest plot of index tests with DSM-III as the reference standard in a hospital setting

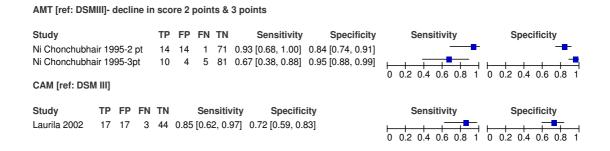


Figure 6.14: forest plot of index test compared with consensus diagnosis as the reference standard in a hospital setting

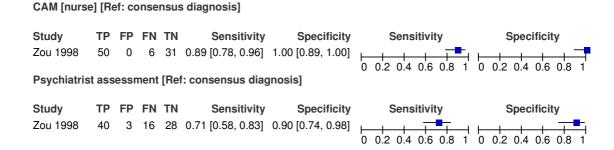


Figure 6.15: forest plot of index test compared with CAM (short version) and clinical interview as the reference standard



Figure 6.16: forest plot CAM (lay person) compared with CAM (geriatrician) - subgroup analyses

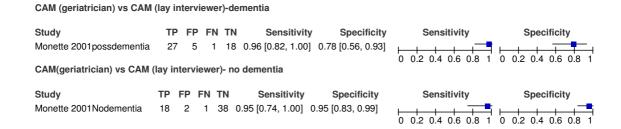
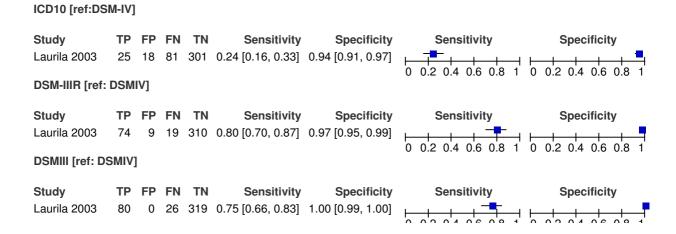


Figure 6.17: forest plot of CAM-ICU index test with DSM-IV as reference standard in an ICU setting

Study	TP	FP	FN	TN	Sensitivity	Specificity	Sensitivity	Specificity
Ely 2001-assessor 2	74	0	6	12	0.93 [0.84, 0.97]	1.00 [0.74, 1.00]	-	
Ely 2001b- assessor 2								
Lin 2004	20	2	2	78	0.91 [0.71, 0.99]	0.97 [0.91, 1.00]		0 0.2 0.4 0.6 0.8 1
							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 6.18: forest plot of ICD-10, DSM-III-R and DSM-III compared with DSM-IV; mixed setting (hospital and long-term care)



# Risk factors for delirium: nonpharmacological

Figure 7.1: hospital unit as a risk factor for an increased severity of delirium

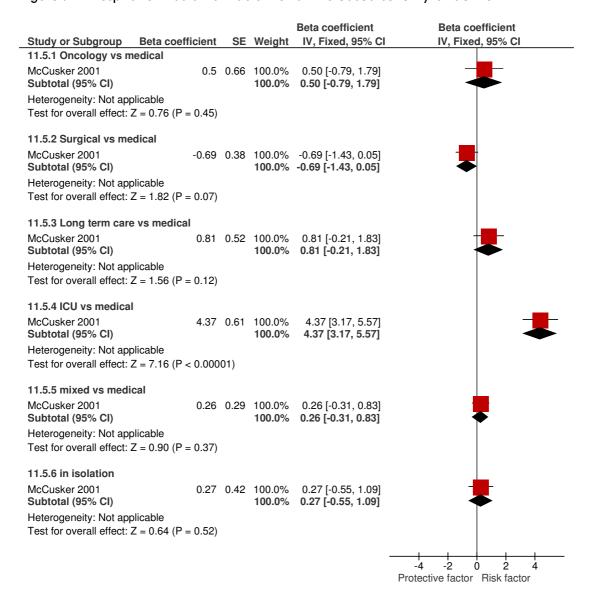


Figure 7.2: age as a risk factor: incidence of delirium

			<b>Odds Ratio</b>	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
2.5.1 Age as continuous var	iable			
Andersson 2001 (Hazard R)	0.09531	0.025648	1.10 [1.05, 1.16]	+
Leung 2007	0.076961	0.037862	1.08 [1.00, 1.16]	<del>  1 -</del>
Rudolph 2007	0.09531	0.024314	1.10 [1.05, 1.15]	+
Santos 2004	0.09531	0.041837	1.10 [1.01, 1.19]	<del>                                     </del>
Sheng 2006	0.09531	0.046511	1.10 [1.00, 1.20]	<del>                                     </del>
				0.5 0.7 1 1.5 2
				protective factor risk factor

Figure 7.3a: age as a risk factor: incidence of delirium

			Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
2.6.2 Over 65 vs under 65				
Bohner 2003	1.108563	0.476525	3.03 [1.19, 7.71]	<del></del>
Caeiro 2004	0.875469	0.448433	2.40 [1.00, 5.78]	<del></del>
Kazmierski 2006	1.386294	0.493964	4.00 [1.52, 10.53]	<del>-   -</del>
2.6.3 Over 70 vs under 50				_
Bucerius 2004	4.545455	0.185188	94.20 [65.53, 135.42]	
2.6.4 Over 70 vs 50-59				
	0.044470	0 110715	10.04[15.04.00.00]	+
Bucerius 2004	2.941176	0.118715	18.94 [15.01, 23.90]	•
2.6.5 over 70 vs 60-69				
Bucerius 2004	1 666667	0.068435	5.29 [4.63, 6.05]	+
Baccinas 2004	1.000007	0.000+00	0.20 [4.00, 0.00]	_
2.6.6 Over 70 vs under 60				
Hofste 1997	1.252763	0.457081	3.50 [1.43, 8.57]	<del></del>
			. , .	
2.6.7 Over 80 vs under 80				
Goldenberg 2006	1.629241	0.865756	5.10 [0.93, 27.83]	<del>                                     </del>
Levkoff 1992 community	1.68639895	0.41687	5.40 [2.39, 12.22]	<del></del>
Levkoff 1992 institution	-0.1392621	0.690829	0.87 [0.22, 3.37]	<del></del>
Ranhoff 2006	0.262364	0.303465	1.30 [0.72, 2.36]	++-
Schor 1992	1.6524974	0.353647	5.22 [2.61, 10.44]	—
				0.01 0.1 1 10 100
				protective factor risk factor
				•

Figure 7.3b: age: incidence of delirium excluding studies with a low quality rating

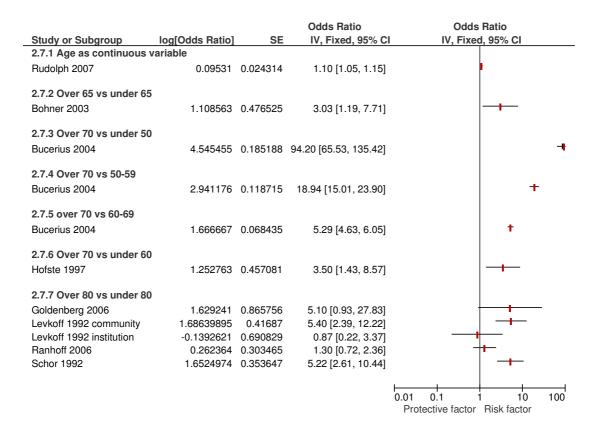


Figure 7.4: age as a risk factor: duration of delirium

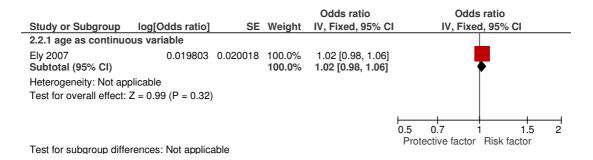


Figure 7.5: patient characteristics as risk factors: severity of delirium

Study or Subgroup Beta coeff	icient	SF	Weight	Beta coefficient IV, Fixed, 95% CI	Beta coefficient IV, Fixed, 95% CI
11.1.1 Delirium Index score at bas			worgine	11,1100,00700	11,11,100,0075
McCusker 2001 Subtotal (95% CI)	0.54	0.03	100.0% <b>100.0</b> %	0.54 [0.48, 0.60] <b>0.54 [0.48, 0.60]</b>	<b>—</b>
Heterogeneity: Not applicable					
Test for overall effect: Z = 18.00 (P	< 0.00	001)			
44.4.0.4					
11.1.2 Age	0.00	0.00	400.00/	0.001.004.0071	_
McCusker 2001 Subtotal (95% CI)	0.03	0.02	100.0% 100.0%	0.03 [-0.01, 0.07] <b>0.03 [-0.01, 0.07</b> ]	<del>-</del>
Heterogeneity: Not applicable					
Test for overall effect: Z = 1.50 (P =	0.13)				
`	,				
11.1.3 Charlson comorbidity inde	x sco	re			<u></u>
McCusker 2001	0.09	0.06	100.0%	0.09 [-0.03, 0.21]	
Subtotal (95% CI)			100.0%	0.09 [-0.03, 0.21]	•
Heterogeneity: Not applicable	0.40\				
Test for overall effect: Z = 1.50 (P =	: 0.13)				
11.1.4 dementia					_
McCusker 2001	1.13	0.28	100.0%	1.13 [0.58, 1.68]	
Subtotal (95% CI)			100.0%	1.13 [0.58, 1.68]	
Heterogeneity: Not applicable	. 0 000	4١			
Test for overall effect: Z = 4.04 (P <	0.000	1)			
11.1.5 prevalent delirium (versus	incide	ent)			_
McCusker 2001	0.39	0.35	100.0%	0.39 [-0.30, 1.08]	
Subtotal (95% CI)			100.0%	0.39 [-0.30, 1.08]	
Heterogeneity: Not applicable	0.07\				
Test for overall effect: Z = 1.11 (P =	0.27)				
11.1.6 Visual/hearing impairment					<u></u>
McCusker 2001	0	0.32	100.0%	0.00 [-0.63, 0.63]	
Subtotal (95% CI)			100.0%	0.00 [-0.63, 0.63]	
Heterogeneity: Not applicable					
Test for overall effect: Z = 0.00 (P =	1.00)				
					-2 -1 0 1 2
					Protective factor Risk factor

Figure 7.6a: cognitive impairment and/or dementia as a risk factor: incidence of delirium

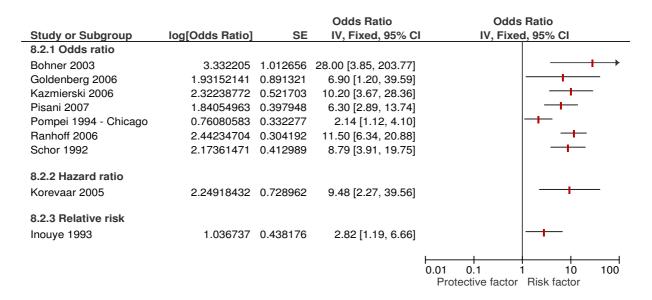


Figure 7.6b: cognitive impairment and/or dementia: incidence of delirium excluding studies with a low quality rating, and also Ranhoff (2006)

				Odds Ratio	Odds I	Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI	IV, Fixed	, 95% CI
8.2.1 Odds ratio						
Bohner 2003	3.332205	1.012656	6.8%	28.00 [3.85, 203.77]		<del></del>
Goldenberg 2006	1.93152141	0.891321	8.7%	6.90 [1.20, 39.59]	-	•
Kazmierski 2006	2.32238772	0.521703	0.0%	10.20 [3.67, 28.36]		
Pisani 2007	1.84054963	0.397948	43.8%	6.30 [2.89, 13.74]		<del></del>
Pompei 1994 - Chicago	0.76080583	0.332277	0.0%	2.14 [1.12, 4.10]		
Ranhoff 2006	2.44234704	0.304192	0.0%	11.50 [6.34, 20.88]		
Schor 1992	2.17361471	0.412989	40.7%	8.79 [3.91, 19.75]		<b>—</b>
						•
•						
8.2.2 Hazard ratio						
Korevaar 2005 Subtotal (95% CI)	2.24918432	0.728962	0.0%	9.48 [2.27, 39.56] Not estimable		
Heterogeneity: Not applica	able					
Test for overall effect: Not						
	• •					
8.2.3 Relative risk						
Inouye 1993 Subtotal (95% CI)	1.036737	0.438176	0.0%	2.82 [1.19, 6.66] <b>Not estimable</b>		
Heterogeneity: Not applica	able					
Test for overall effect: Not						
	• •					
					0.01 0.1 1	10 100
					0.01 0.1 1 Protective factor	10 100
					Frolective factor	nisk iacioi

Figure 7.7: cognitive impairment and/or dementia as a risk factor: persistent delirium



Figure 7.8: impaired vision as a risk factor: incidence of delirium

			Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
3.2.1 Odds ratio				
Ranhoff 2006	0.530628 0.2	264309	1.70 [1.01, 2.85]	<del>                                     </del>
Schor 1992	0.44468582 0.2	291598	1.56 [0.88, 2.76]	+-
3.2.2 Hazard ratio				
Andersson 2001 (Hazard R)	1.508512 0.3	350821	4.52 [2.27, 8.99]	<del></del>
3.2.3 Relative risk				
Inouye 1993	1.25561604 0.5	569239	3.51 [1.15, 10.71]	<del></del>
				0.1 0.2 0.5 1 2 5 10  Protective factor Risk factor

Figure 7.9: impaired vision as a risk factor: persistent delirium

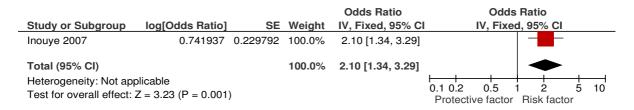


Figure 7.10: polypharmacy: incidence of delirium

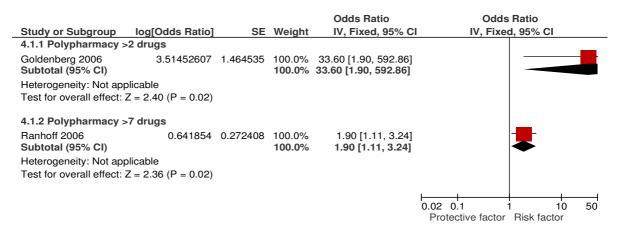


Figure 7.11: dehydration as a risk factor: incidence of delirium

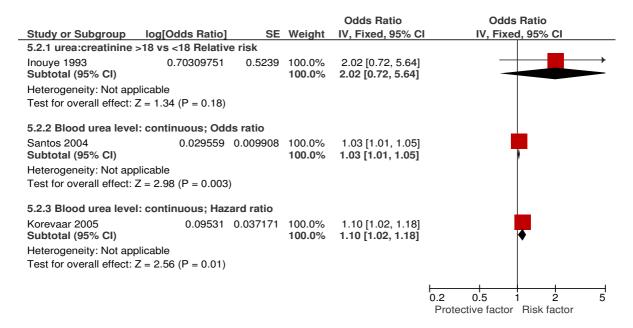


Figure 7.12: illness severity as a risk factor: incidence of delirium

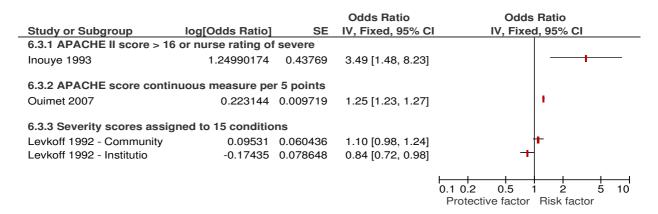


Figure 7.13: illness severity as a risk factor: duration of delirium

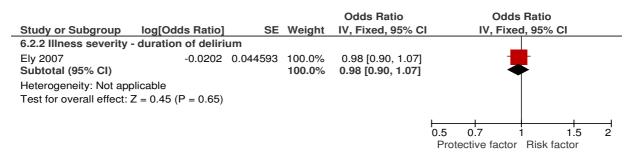


Figure 7.14: comorbidity as a risk factor: incidence of delirium

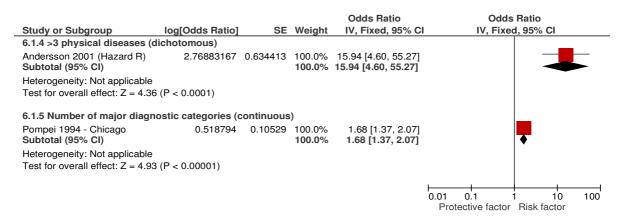


Figure 7.15: comorbidity as a risk factor: persistent delirium

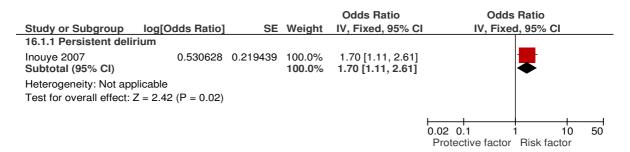


Figure 7.16: sex (male) as a risk factor: incidence of delirium

		Odds Ratio	Odds Ratio
log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
-0.91629	0.338487	0.40 [0.21, 0.78]	<del></del>
0.307485	0.385459	1.36 [0.64, 2.89]	<del>-  -</del>
0.33647224	0.422438	1.40 [0.61, 3.20]	<del>- </del>
1.58923521	0.575982	4.90 [1.58, 15.15]	<del>-   -</del>
0.87546874	0.357898	2.40 [1.19, 4.84]	<del></del>
			0.01 0.1 1 10 100  Protective factor Risk factor
	-0.91629 0.307485 0.33647224 1.58923521	-0.91629 0.338487 0.307485 0.385459 0.33647224 0.422438	log[Odds Ratio]         SE         IV, Fixed, 95% CI           -0.91629         0.338487         0.40 [0.21, 0.78]           0.307485         0.385459         1.36 [0.64, 2.89]           0.33647224         0.422438         1.40 [0.61, 3.20]           1.58923521         0.575982         4.90 [1.58, 15.15]

Figure 7.17: electrolyte disturbance as a risk factor: incidence of delirium

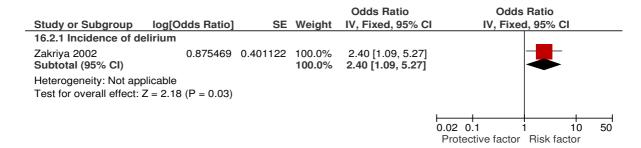


Figure 7.18: depression as a risk factor: incidence of delirium

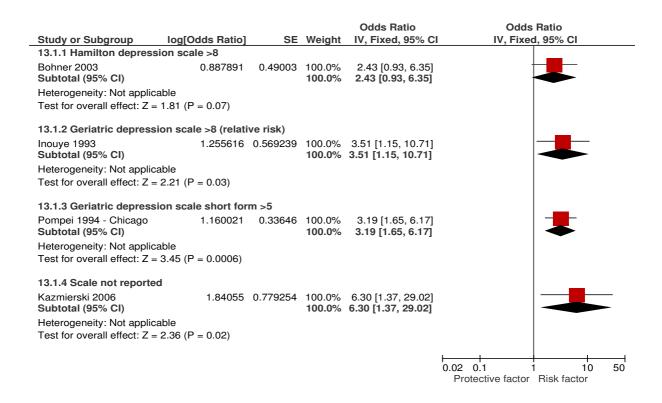


Figure 7.19: infection as a risk factor: incidence of delirium

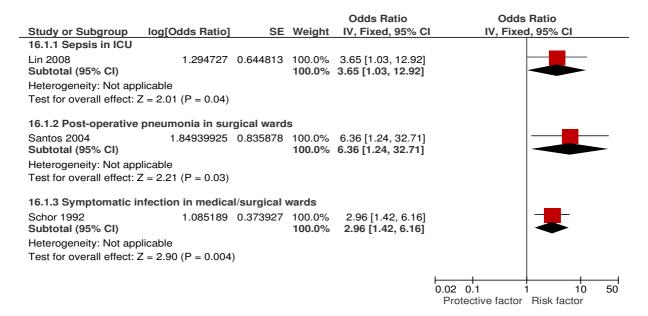


Figure 7.20: infection as a risk factor: duration of delirium

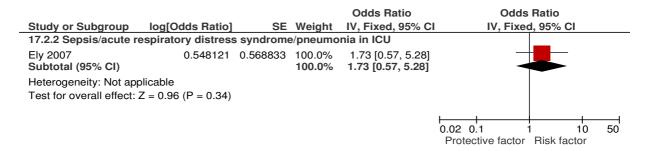


Figure 7.21: fracture on admission as a risk factor

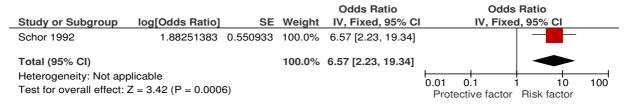


Figure 7.22: environmental risk factors: severity of delirium

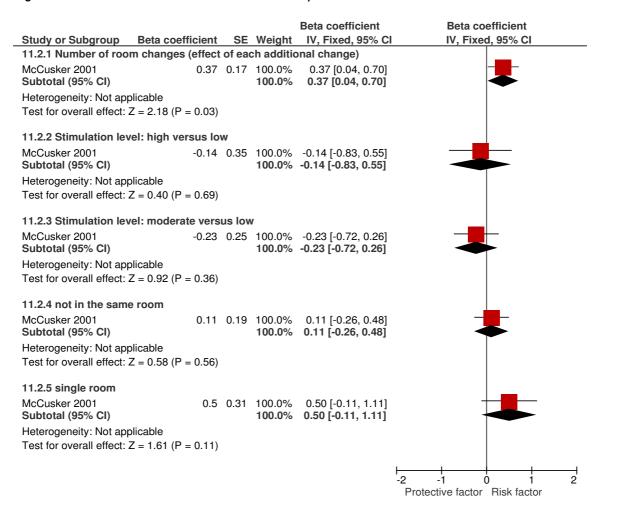
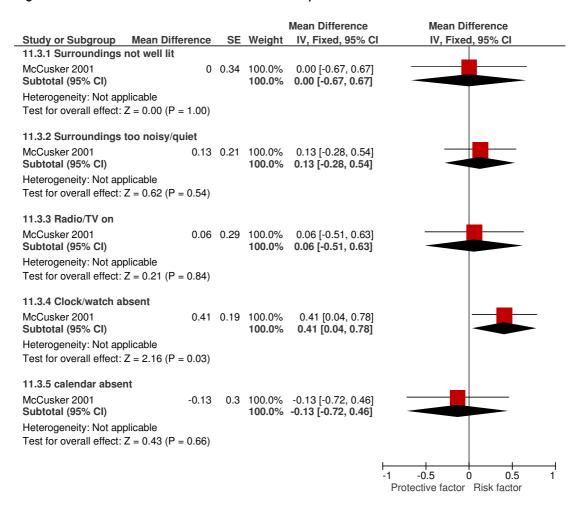


Figure 7.23: environmental risk factors: severity of delirium



NB scale -1 to +1

Figure 7.24: environmental risk factors: severity of delirium

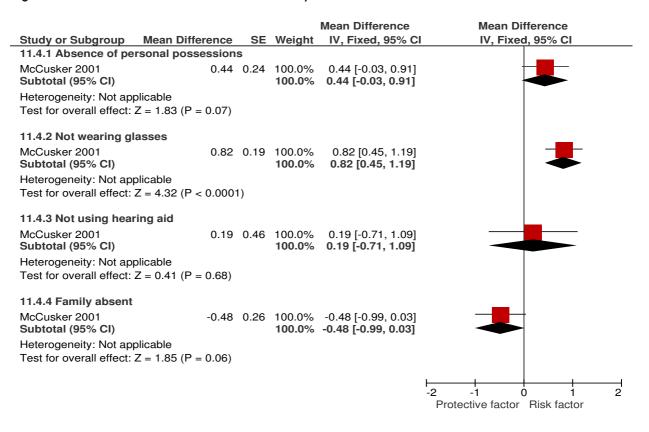


Figure 7.25: cardiac surgery risk factors: incidence of delirium

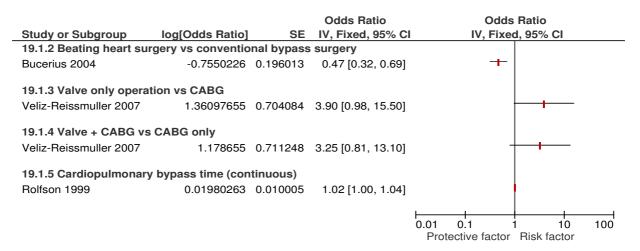


Figure 7.26: type of surgery a risk factor: incidence of delirium

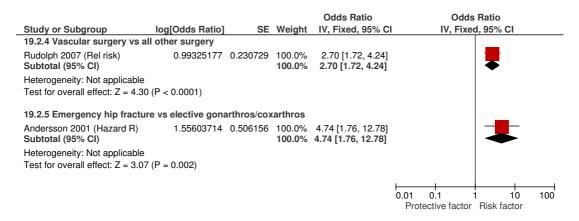


Figure 7.27: iatrogenic intervention as a risk factor: incidence of delirium

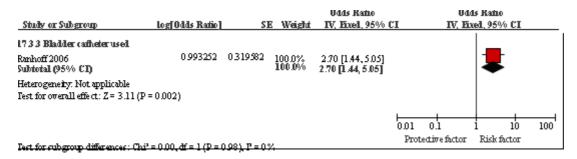


Figure 7.28: physical restraint during delirium: persistent delirium

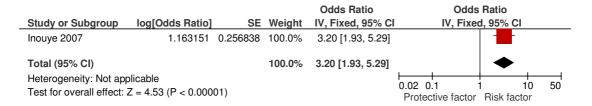
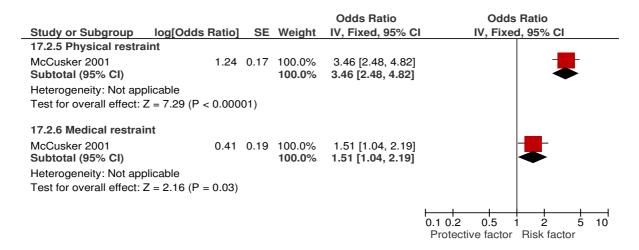


Figure 7.29: physical and medical restraint as a risk factor for the severity of delirium



# Risk factors for delirium: pharmacological agents

Figure 8.1: Midazolam as a risk factor for development of delirium

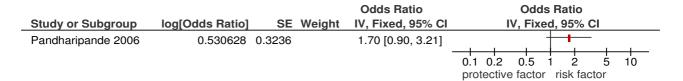


Figure 8.2: lorazepam as a risk factor for development of delirium

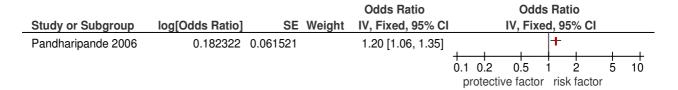


Figure 8.3: benzodiazepines as a risk factor for delirium

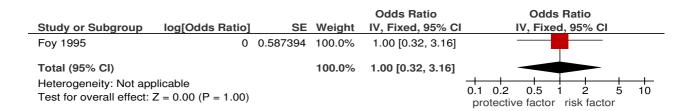
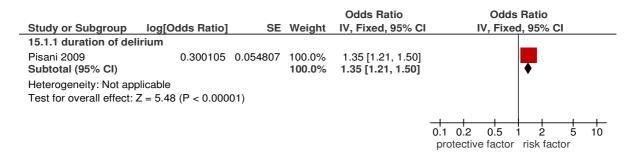


Figure 8.4: Haloperidol as a risk factor for duration of delirium



NB: Scale 0.1 to 10

Figure 8.5: antihistamines with anticholinergic activity

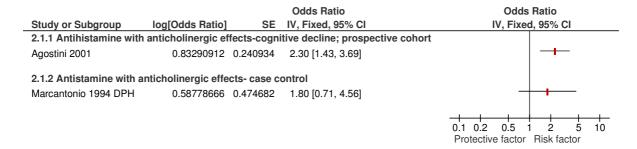


Figure 8.6: exposure to H2 blockers on the incidence of delirium

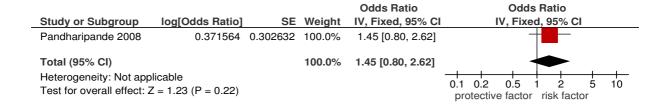
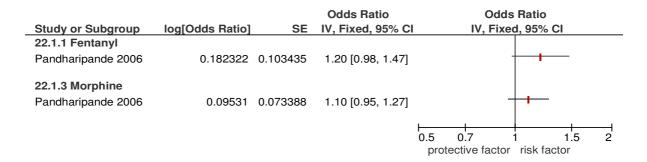


Figure 8.7a: effect of individual opioids on delirium



NB: Scale 0.5 to 2

Figure 8.7b: effect of individual opioids on delirium

			Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
22.2.2 Meperidine				
Morrison 2003RR	0.875469 0	.316764	2.40 [1.29, 4.47]	<del></del>
22.2.4 Oxycodone				
Marcantonio 1994	-0.35667495 0	.427035	0.70 [0.30, 1.62]	<del></del>
				0.1 0.2 0.5 1 2 5 10 protective factor risk factor

Figure 8.8: effect of opioids on the incidence of delirium

				Risk Ratio			Ris	k Ra	atio		
Study or Subgroup	log[Risk Ratio]	SE	Weight	IV, Fixed, 95% CI			IV, Fix	ed,	95% C		
Morrison 03 10-30mg vs 30	0.336472	0.434885		1.40 [0.60, 3.28]			_	+	1		
Morrison 2003 <10mgvs30mg	1.686399	0.41687		5.40 [2.39, 12.22]					_	_	
					0.1	0.2	0.5	+		<del></del>	10
							e facto	or F	Risk fac	tor	.0

Figure 8.9: effect of intrathecal morphine + PCA morphine versus placebo + PCA morphine



Figure 8.10: effect of PCA opioid analgesics versus oral opioids

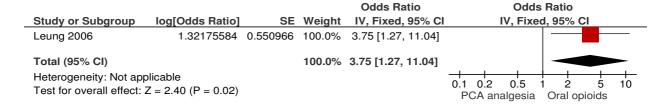


Figure 8.11: effect of general anaesthesia versus regional anaesthesia on delirium

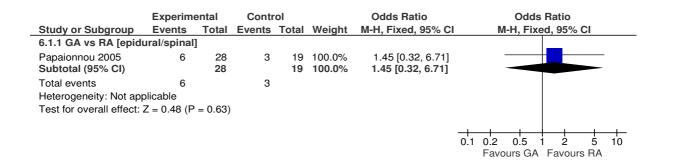
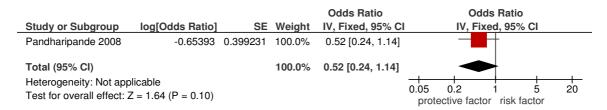


Figure 8.12: effect of N<sub>2</sub>O plus O<sub>2</sub> versus O<sub>2</sub> on delirium

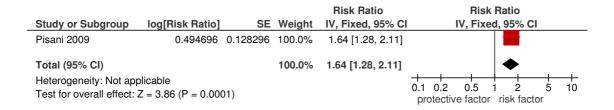


Figure 8.13: effect of anaesthetics on delirium



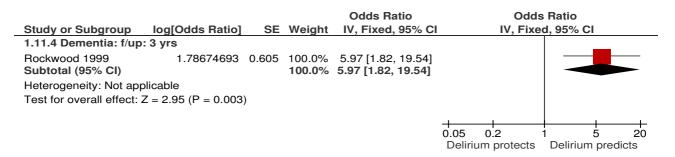
NB: Scale 0.05 to 20

Figure 8.14: effect of benzodiazepines or opioids on the duration of delirium



# Consequences of delirium

Figure 9.1: dementia as a consequence of delirium



NB: Scale 0.05 to 20

Figure 9.2a: new admission to institution as a consequence of delirium

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI
1.2.1 at discharge				
Balas 2009	1.974081	0.671334	7.20 [1.93, 26.84]	
Bourdel-M 2004 [prevalent	1.160021	0.445974	3.19 [1.33, 7.65]	- <del></del>
Bourdel-M2004 [incident]	0.970779	0.591963	2.64 [0.83, 8.42]	+ + -
Inouye 1998	1.09861229	0.379611	3.00 [1.43, 6.31]	<del>-1-</del>
Levkoff 1992	1.98787435	0.526764	7.30 [2.60, 20.50]	
1.2.2 3 months				
Inouye 1998 3 months	1.09861229	0.353647	3.00 [1.50, 6.00]	-1-
1.2.3 6 months				
O'Keeffe 1997	1.02961942	0.394368	2.80 [1.29, 6.07]	-
1.2.4 2 years				
Pitkala 2005	0.89608802	0.358234	2.45 [1.21, 4.94]	1
				0.02 0.1 1 10 50 Delirium protects Delirium predicts

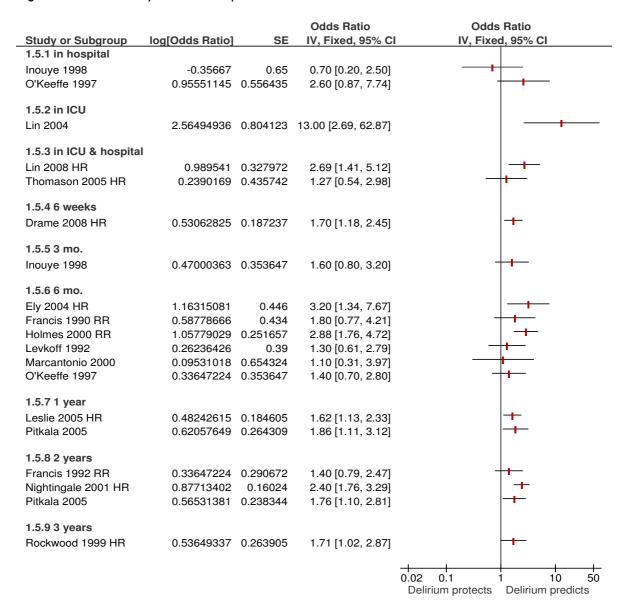
NB: Scale 0.05 to 20

Figure 9.2b: new admission to institution [moderate quality studies]

			Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.3.1 at discharge				
Bourdel-M 2004 [prevalent	1.160021	0.445974	3.19 [1.33, 7.65]	
Bourdel-M2004 [incident]	0.970779	0.591963	2.64 [0.83, 8.42]	+
Inouye 1998	1.09861229	0.379611	3.00 [1.43, 6.31]	
1.3.2 3 months				
Inouye 1998 3 months	1.09861229	0.353647	3.00 [1.50, 6.00]	
1.3.3 6 months				
O'Keeffe 1997	1.02961942	0.394368	2.80 [1.29, 6.07]	<del></del>
1.3.4 2 years				
Pitkala 2005	0.89608802	0.358234	2.45 [1.21, 4.94]	<del></del>
				0.1 0.2 0.5 1 2 5 10  Delirium protects Delirium predicts

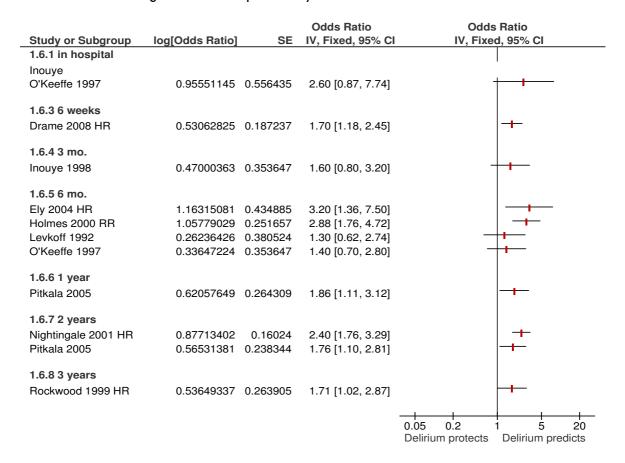
NB: Scale 0.1 to 10

Figure 9.3a: mortality as a consequence of delirium



NB: Scale 0.02 to 50

Figure 9.3b: mortality as a consequence of delirium; high and moderate quality studies and restricting to the UK hospital study



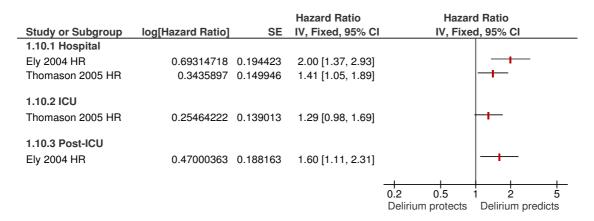
NB: Scale 0.05 to 20

Figure 9.4a: length of stay (discharge from hospital) as a consequence of delirium

			Risk Ratio	Risk Ratio	
Study or Subgroup	log[Risk Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% (	CI
1.15.4 Discharge from	n hospital- 6 mo.				
Holmes 2000 RR	-0.63488	0.129065	0.53 [0.41, 0.68]	+	
				0.1 0.2 0.5 1 2	<del>1 1</del> 5 10
					n protects

NB: Scale 0.1 to 10

Figure 9.4b: length of stay as a consequence of delirium



NB: Scale 0.2 to 5

Figure 9.5: hospital acquired complications as a consequence of delirium

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI			Ratio	
O'Keeffe 1997	0.83290912	0.396	100.0%	2.30 [1.06, 5.00]		,		
Total (95% CI)			100.0%	2.30 [1.06, 5.00]			-	<b>-</b>
Heterogeneity: Not app Test for overall effect: 2					0.2 Deliriun	0.5 protects	1 2 Delirium	5 predicts

NB: Scale 0.2 to 5

Figure 9.6: mortality or new admission to institution as a consequence of delirium

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI
2.1.1 hospital- OR	regional radio		,,	
Inouye 1998	0.741937	0.329333	2.10 [1.10, 4.00]	<del></del>
2.1.2 1 month- OR				
Givens 2008	1.449269	0.535	4.26 [1.49, 12.16]	<del>-   -</del>
Marcantonio 2000	1.098612	0.518602	3.00 [1.09, 8.29]	<del></del>
2.1.3 3 months- OR Inouye 1998	0.955511	0.277777	2.60 [1.51, 4.48]	-
2.1.4 6 months- OR				
Givens 2008	0.774727	0.559	2.17 [0.73, 6.49]	++-
Marcantonio 2000	0.587787	0.545935	1.80 [0.62, 5.25]	<del>                                      </del>
2.1.5 1 year- Delirium at discharg McAvay 2006DischargeVsNev (1)	ge vs Never deliriou 0.97077892		2.64 [1.60, 4.35]	
workly zoodbiodial governov (1)	0.07077002	0.200110	2.01[1.00, 1.00]	
2.1.6 1 year- Resolved vs Never	delirious			
McA 2006 resolve vs never (2)	0.42526774	0.236917	1.53 [0.96, 2.43]	<del>  1                                   </del>
,			[,]	
2.1.7 1 year- Delirium at discharg	ge vs Delirium resol	ved		
McAvay 2006DischargeVsRes (3)	0.54812141	0.322732	1.73 [0.92, 3.26]	<del>  1                                   </del>
2.1.8 2 years- Mortality or residia	na in nursina home			
Pitkala 2005	0	0.362598	2.81 [1.38, 5.72]	<del></del>
				0.05 0.2 1 5 20 Delirium protects Delirium predicts

NB: Scale 0.05 to 20

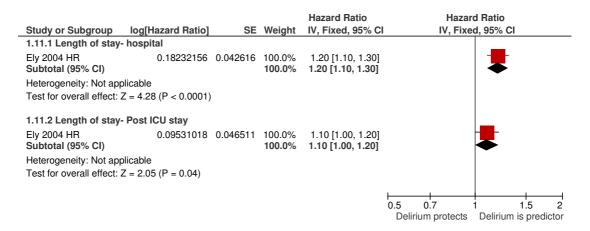
Figure 9.7: mortality as a consequence of increased duration of delirium

				Hazard Ratio	Hazard	d Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% CI	IV, Fixed	d, 95% CI		
Ely 2004 HR	0.09531	0.05	100.0%	1.10 [1.00, 1.21]				
Total (95% CI)			100.0%	1.10 [1.00, 1.21]	_	<b>•</b>		
Heterogeneity: Not app Test for overall effect: 2					 0.7 protects	1 Delirium	1.5 predic	2 cts

NB: Scale 0.5 to 2

<sup>(1)</sup> HR (2) HR (3) HR

Figure 9.8: length of stay as a consequence of increased duration of delirium



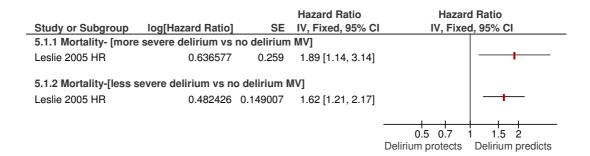
NB: Scale 0.5 to 2

Figure 9.9: mortality or functional decline as a consequence of increased duration of delirium

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
4.1.1 at hospital disc	:harge				<u>_</u>
Andrew 2005 Subtotal (95% CI)	0.09531	0.046511	100.0% <b>100.0</b> %	1.10 [1.00, 1.20] <b>1.10 [1.00, 1.20]</b>	
Heterogeneity: Not ap	pplicable				
Test for overall effect	Z = 2.05 (P = 0.04)	ı			
4.1.2 6 months					
Andrew 2005 Subtotal (95% CI)	0.182322	0.0945	100.0% <b>100.0</b> %	1.20 [1.00, 1.44] <b>1.20 [1.00, 1.44</b> ]	
Heterogeneity: Not as	pplicable				
Test for overall effect	: Z = 1.93 (P = 0.05)	ı			
					0.5 0.7 1 1.5 2
					Delirium protects Delirium predicts

NB: Scale 0.5 to 2

Figure 9.10: mortality (at 1 year) as a consequence of delirium (severity)



NB: Scale 0.5 to 2

Figure 9.11: mortality or new admission to institution (at 1 month and 6 months) as a consequence of delirium severity

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI
3.1.1 1 month Marcantonio 2002	0.641854	0.6862	1.90 [0.50, 7.29]	
3.1.2 6 months Marcantonio 2002	1.481605	0.80134	4.40 [0.91, 21.16]	-
				0.05 0.2 1 5 20 Delirium protects Delirium predicts

NB: Scale 0.05 to 20

## Prevention of delirium: nonpharmacological

HYDRATION FOR THE PREVENTION OF DELIRIUM (LONG-TERM CARE SETTING)

Figure 10.1: acute confusion.

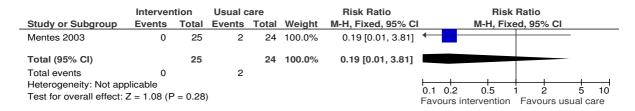
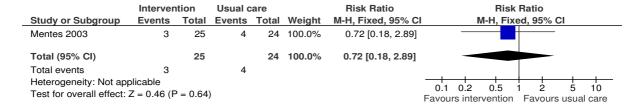


Figure 10.2: hydration-linked events.



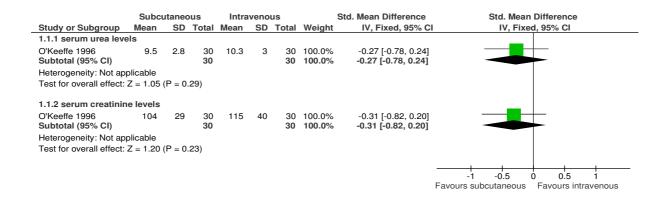
#### HYDRATION FOR THE PREVENTION OF DELIRIUM (HOSPITAL SETTING

Figure 10.3: agitation



NB: Scale 0.2 to 5

Figure 10.4: serum levels



NB: Scale -1 to 1

Figure 10.5: local oedema

	Subcutaneous		Intraver	ous		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% C	CI M-H, Fixed, 95% CI
O'Keeffe 1996	2	30	0	30	100.0%	5.00 [0.25, 99.95]	
Total (95% CI)		30		30	100.0%	5.00 [0.25, 99.95]	
Total events	2		0				
Heterogeneity: Not ap Test for overall effect:					0.01 0.1 1 10 100		
rest for overall effect.					Favours subcutaneous Favours intravenous		

NB: Scale 0.01 to 100

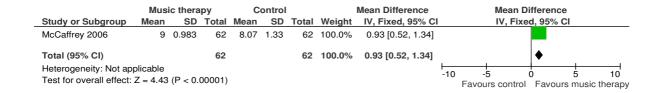
#### MUSIC THERAPY FOR THE PREVENTION OF DELIRIUM (HOSPITAL SETTING)

Figure 10.6: number of patients with delirium

	Music therapy +	SPO	С		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
McCaffrey 2006	2	62	36	62	100.0%	0.06 [0.01, 0.22]		
Total (95% CI)		62		62	100.0%	0.06 [0.01, 0.22]		
Total events	2		36					
Heterogeneity: Not app Test for overall effect:		1)				Far	+ + + + + + + + + + + + + + + + + + +	100

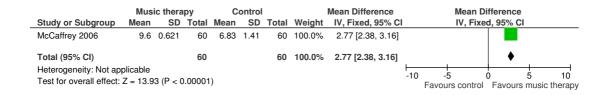
NB: forest plot scale 0.01 to 100

Figure 10.7: patient's readiness to ambulate after undergoing surgery



NB: Scale -10 to 10

Figure 10.8: patient satisfaction



NB: Scale -10 to 10

### **Multicomponent prevention**

Figure 10.9: number of patients with delirium in hospital

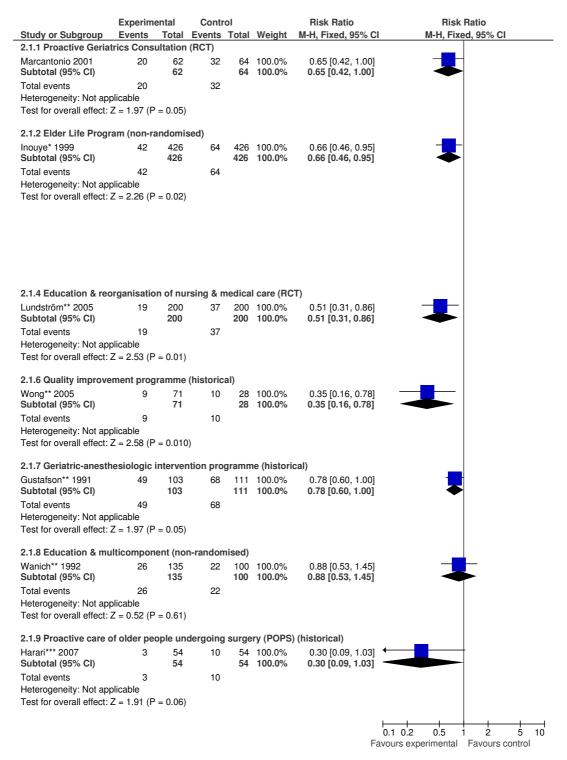


Figure 10.10: number of patients with delirium at 6 months follow-up

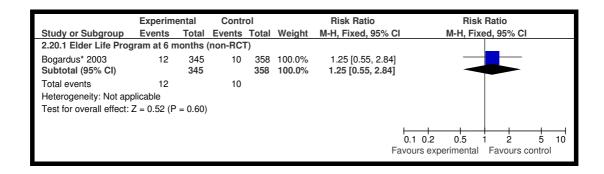


Figure 10.11: mean duration of delirium

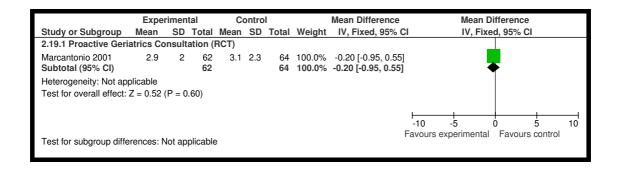


Figure 10.12: number of patients with delirium at 7 or more days

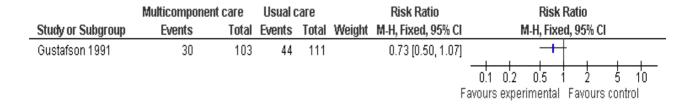


Figure 10.13: severity scores

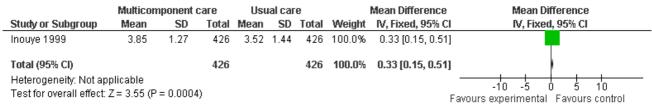


Figure 10.14: length of hospital stay

	Exper	imental		Co	ontrol			Mean Difference	Mean Difference		
Study or Subgroup	Mean [days]	SD [days]	Total	Mean [days]	SD [days]	Total	Weight	IV, Fixed, 95% CI [days]	IV, Fixed, 95% CI [days]		
2.2.2 Education progra	mme & reorg	anisation of	nursi	ng & medical o	care (RCT)				_		
Lundström** 2005 Subtotal (95% CI)	9.4	8.2	200 <b>200</b>	13.4	12.3	200 <b>200</b>	100.0% 100.0%	-4.00 [-6.05, -1.95] -4.00 [-6.05, -1.95]			
Heterogeneity: Not applie	cable										
Test for overall effect: Z	= 3.83 (P = 0.0	0001)									
2.2.6 Geriatric-anesthe	siologic inter	vention pro	gramm	ne (historical)					_		
Gustafson** 1991 Subtotal (95% CI)	11.6	8.2	103 103	17.4	14		100.0% 100.0%	-5.80 [-8.85, -2.75] <b>-5.80 [-8.85, -2.75</b> ]			
Heterogeneity: Not applie	cable							• / •			
Test for overall effect: Z		0002)									
2.2.7 Education & multi	icomponent (	non-randon	nicod)								
Wanich** 1992	8.5	9.2	135	9.7	9.8	100	100.0%	-1.20 [-3.67, 1.27]			
Subtotal (95% CI)	0.5	3.2	135	3.1	3.0		100.0%	-1.20 [-3.67, 1.27]			
Heterogeneity: Not applie	cable							. , .			
Test for overall effect: Z		34)									
2.2.8 Proactive care of	older people	undergoing	surge	ry (POPS) (his	storical)						
Harari*** 2007	11.5	5.2	54	15.8	13.2	54	100.0%	-4.30 [-8.08, -0.52]	<b>_</b> _		
Subtotal (95% CI)			54			54	100.0%	-4.30 [-8.08, -0.52]			
Heterogeneity: Not applie	cable										
Test for overall effect: Z	= 2.23 (P = 0.0	03)									
									-10 -5 0 5 1		
Test for subgroup differe	ences: Chi² = 5	.91, df = 3 (F	o = 0.1	2), I <sup>2</sup> = 49.2%				Fav	ours experimental Favours control		

Figure 10.15: improvement in cognitive impairment at 5 days or discharge

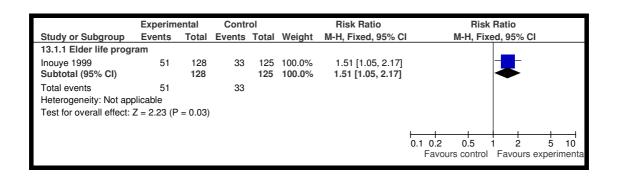
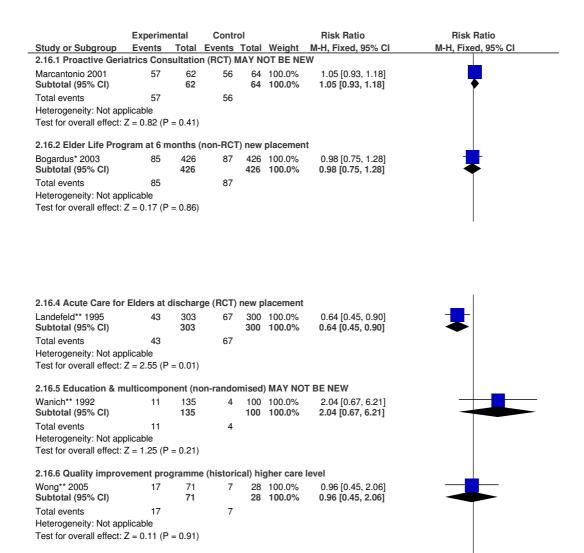


Figure 10.16: number of patients discharged to a new institutional setting



0.1 0.2

0.5 Favours experimental Favours control

Figure 10.17: mortality in hospital

	Experime	ental	Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.3.1 Elder Life Prog	ram (non-ra	andomi	sed)				
Inouye* 1999 Subtotal (95% CI)	6	426 <b>426</b>	7	426 <b>426</b>	100.0% 100.0%	0.86 [0.29, 2.53] <b>0.86 [0.29, 2.53</b> ]	
Total events	6		7				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.28 (P)	= 0.78)					
							į

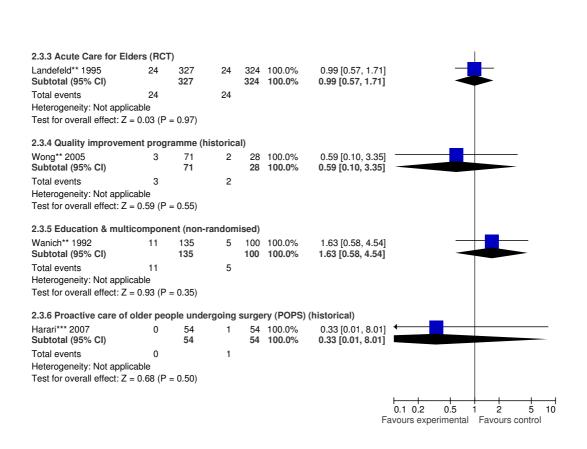


Figure 10.18: mortality at up to 6 months follow up

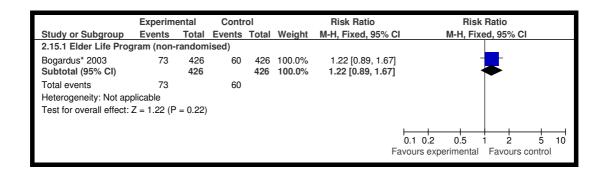


Figure 10.19: number of patients with an improvement in ADL

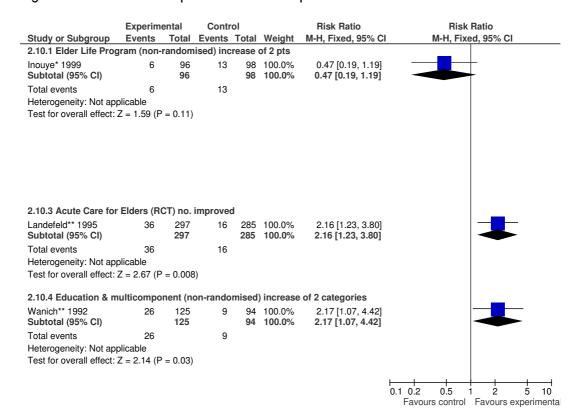


Figure 10.20: adjusted ADL score

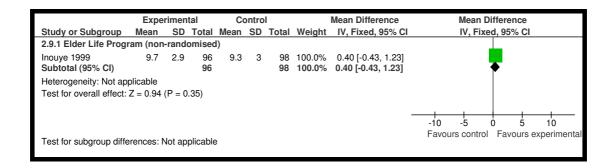


Figure 10.21: number of patients with severe falls



Figure 10.22: urinary tract infections

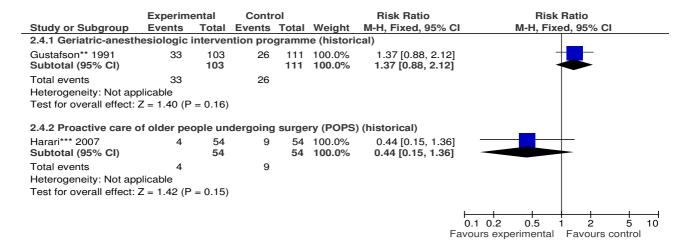
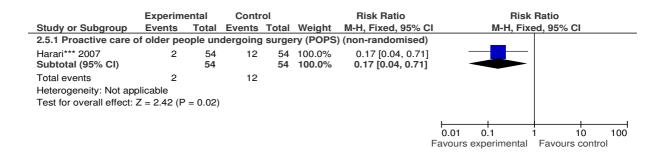


Figure 10.23: wound infections



NB scale 0.01 to 100

Figure 10.24: pressure ulcers

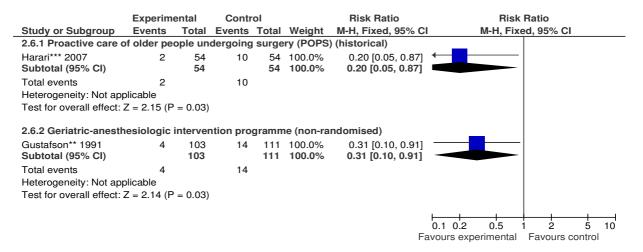


Figure 10.25: early vision correction at reassessment (day 5 or at discharge if earlier)

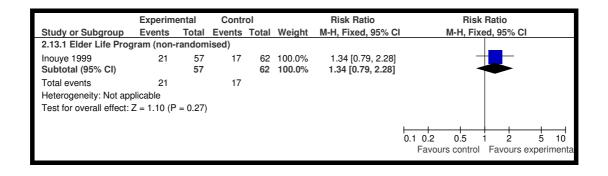


Figure 10.26: whisper test

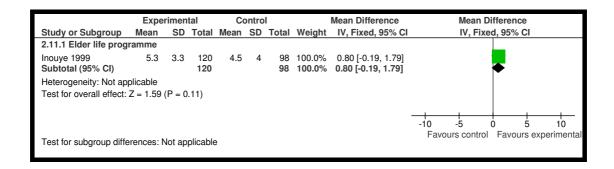


Figure 10.27: whisper test – number of patients with improvement by one point

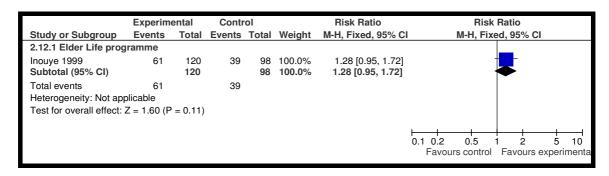


Figure 10.28: number of patients with improvement in dehydration

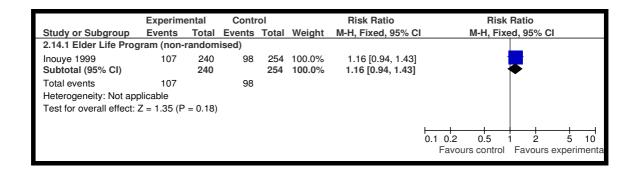
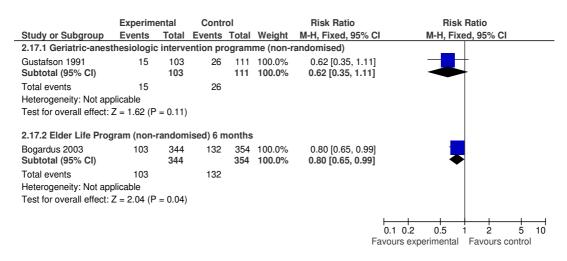


Figure 10.29: number of patients with dehydration



Figure 10.30: urinary incontinence



## Prevention of delirium: pharmacological

Acetylcholinesterase inhibitor versus placebo

Figure 11.1: number of patients with delirium

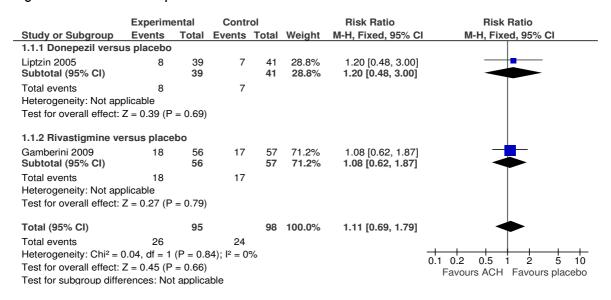


Figure 11.2: duration of delirium

	Donepezil			Placebo				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	IV, Fixed, 95% CI
Liptzin 2005	1	0.001	39	1.3	1.21	41	100.0%	-0.30 [-0.67, 0.07]	<del></del>
Total (95% CI) Heterogeneity: Not app	aliaabla		39			41	100.0%	-0.30 [-0.67, 0.07]	
Test for overall effect:		(P = 0.1	1)						-1 -0.5 0 0.5 1 Favours donepezil Favours control

Figure 11.3: length of hospital stay

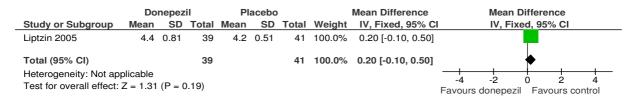


Figure 11.4: discharge to rehabilitation facility

	Donep	ezil	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	<b>Events</b>	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Liptzin 2005	28	39	34	41	100.0%	0.87 [0.68, 1.10]	-
Total (95% CI)		39		41	100.0%	0.87 [0.68, 1.10]	•
Total events	28		34				
Heterogeneity: Not app	olicable						0102 05 1 2 5 10
Test for overall effect:	Z = 1.17 (1	P = 0.2	4)				0.1 0.2 0.5 1 2 5 10 Favours donepezil Favours control

#### Typical antipsychotics versus placebo

Figure 11.5: number of patients with postoperative delirium

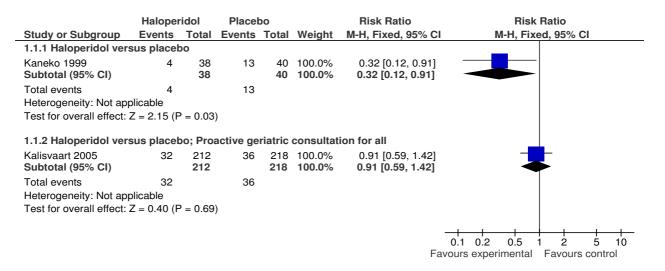


Figure 11.6: severity of delirium scores

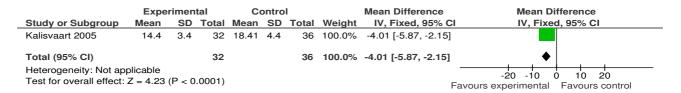


Figure 11.7: duration of delirium

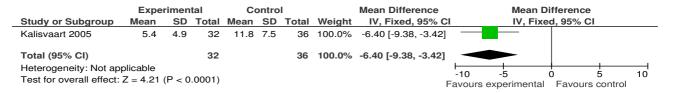
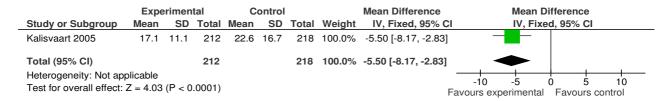


Figure 11.8: length of hospital stay



NB: Scale -10 to 10

Figure 11.9: number of patients with adverse events

	Halopei	ridol	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Kaneko 1999	1	38	0	40	100.0%	3.15 [0.13, 75.12]	
Total (95% CI)		38		40	100.0%	3.15 [0.13, 75.12]	
Total events	1		0				
Heterogeneity: Not ap	oplicable						01 02 05 1 2 5 10
Test for overall effect	Z = 0.71 (	P = 0.4	8)				Favours experimental Favours control

#### Atypical antipsychotics versus placebo

Figure 11.10: number of patients with delirium

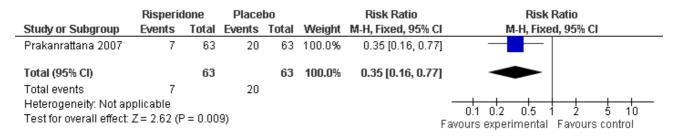


Figure 11.11: length of ICU stay

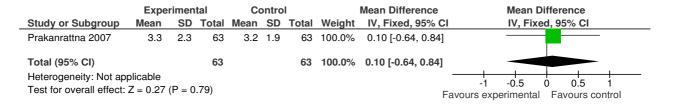
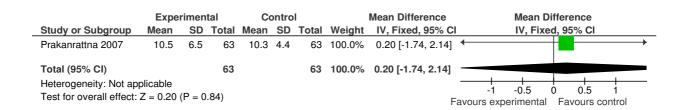


Figure 11.12: length of hospital stay



## Pharmacological Prevention in long-term care

#### Acetylcholinesterase inhibitor versus placebo

Figure 11.13: incidence of delirium

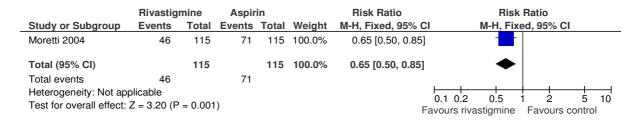


Figure 11.14a: duration of delirium (all patients)

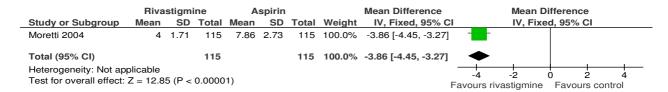


Figure 11.14b: duration of delirium assuming mean is across those with delirium

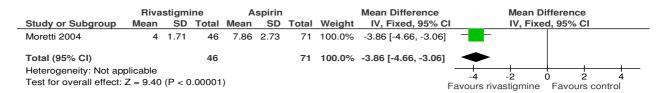


Figure 11.15: cognitive impairment (Clinical Dementia Rating change scores)

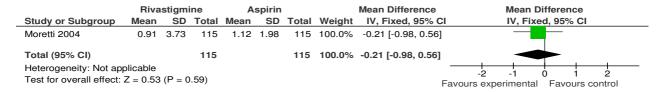


Figure 11.16a: BEHAVE-AD scale change scores

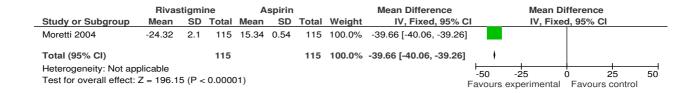
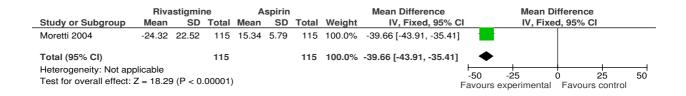


Figure 11.16b: BEHAVE-AD overall change scores



# Treatment of delirium: non-pharmacological (hospital setting)

#### **Multicomponent intervention**

Figure 12.1: number of patients with complete response.

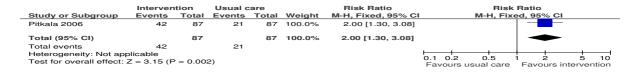


Figure 12.2: cognitive impairment

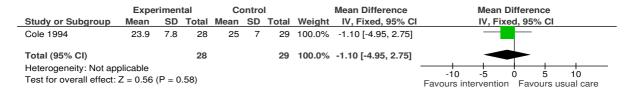


Figure 12.3: length of stay

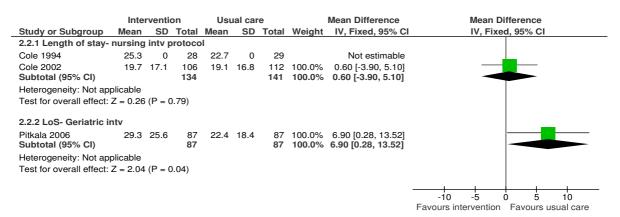


Figure 12.4: discharge to higher dependency or to new long-term care (RCTs)

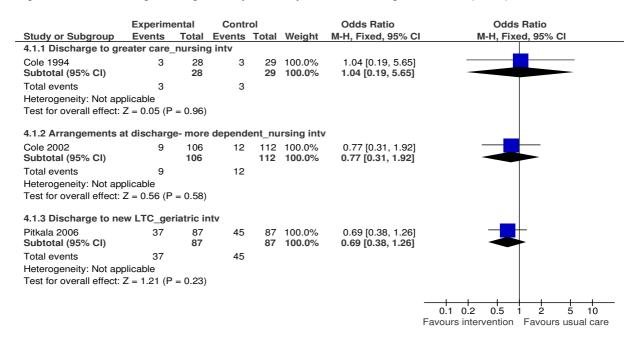
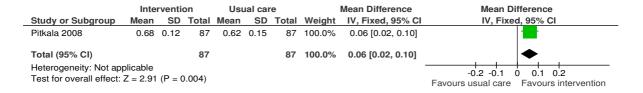


Figure 12.5: number of days in new long-term care (non RCT)

	Expe	rimen	tal	Co	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Rahkonen 2001	441	366	51	535	308	51	100.0%	-94.00 [-225.28, 37.28]	-
Total (95% CI)			51			51	100.0%	-94.00 [-225.28, 37.28]	•
Heterogeneity: Not ap Test for overall effect			1.16)						-1000 -500 0 500 1000 Favours intervention Favours usual care

NB: Scale -1000 to 1000

Figure 12.6: improvement in HRQoL



NB: Scale -0.2 to 0.2

Figure 12.7: mortality (RCTs only)

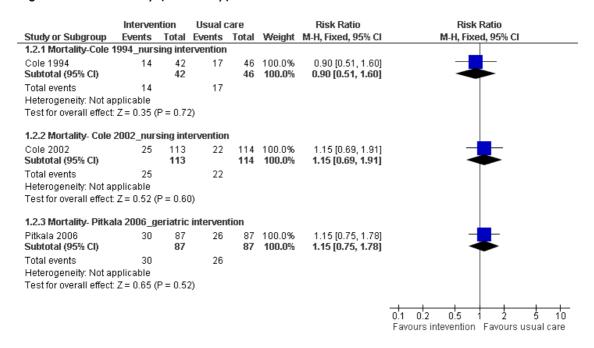


Figure 12.8: mortality (non-RCT)

	Interver	Usual	are		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Rahkonen 2001	20	51	23	51	100.0%	0.87 [0.55, 1.37]	-
Total (95% CI)		51		51	100.0%	0.87 [0.55, 1.37]	•
Total events	20		23				
Heterogeneity: Not ap Test for overall effect:		P = 0.55	)				0.1 0.2 0.5 1 2 5 10  Favours intervention Favours usual care

## Treatment of delirium: pharmacological

#### Typical antipsychotics versus placebo

Figure 13.1: complete response

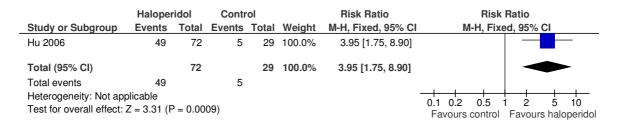
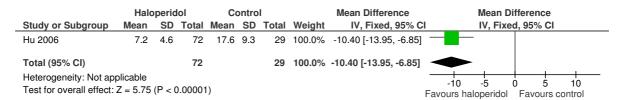


Figure 13.2: severity of delirium

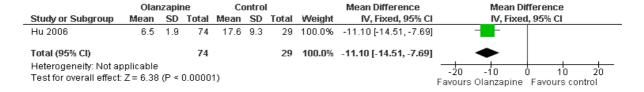


#### Atypical antipsychotics versus placebo

Figure 13.3: complete response



Figure 13.4: severity of delirium



NB: Scale -20 to 20

#### Atypical antipsychotics 1 versus atypical antipsychotics 2

Figure 13.5: duration of delirium

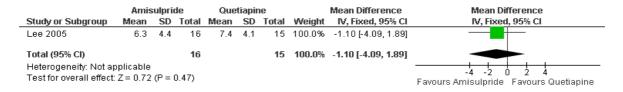


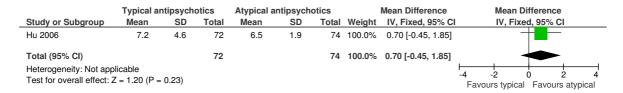
Figure 13.6: severity of delirium

	Amisulpride Quetiapine			ie		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Lee 2005	3.5	1.4	16	3.5	2.6	15	100.0%	0.00 [-1.48, 1.48]	-
Total (95% CI)			16			15	100.0%	0.00 [-1.48, 1.48]	<b>*</b>
Heterogeneity: Not ap Test for overall effect:			1.00)						-10 -5 0 5 10 Favours Amisulpride Favours Quetiapine

Figure 13.7: complete response

	Typical antipsyc	hotics	Atypical antipsy	chotics		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI
7.1.1 Symptoms allev	iated CGI-GI						
Hu 2006	49	72	47	74	68.9%	1.07 [0.85, 1.35]	#
Subtotal (95% CI)		72		74	68.9%	1.07 [0.85, 1.35]	<b>*</b>
Total events	49		47				
Heterogeneity: Not app	plicable						
Test for overall effect:	Z = 0.58 (P = 0.56)						
7.1.2 number who did	d not receive rescu	ie medica	ation				
Skrobik 2004	22	45	17	28	31.1%	0.81 [0.53, 1.23]	<del></del>
Subtotal (95% CI)		45		28	31.1%	0.81 [0.53, 1.23]	•
Total events	22		17				
Heterogeneity: Not app	plicable						
Test for overall effect:	Z = 1.01 (P = 0.31)						
Total (95% CI)		117		102	100.0%	0.99 [0.80, 1.21]	•
Total events	71		64				
Heterogeneity: Chi <sup>2</sup> =	1.36, df = 1 (P = 0.2	(4); I <sup>2</sup> = 27	<b>"</b> %				
Test for overall effect:	,	•					0.1 0.2 0.5 1 2 5 10
	, ,						Favours atypical Favours typical

Figure 13.8: severity of delirium



NB: Scale -4 to 4

Figure 13.9 Adverse events

	Experimental		Conti	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Skrobik 2004	6	45	0	28	100.0%	8.20 [0.48, 140.09]	
Total (95% CI)		45		28	100.0%	8.20 [0.48, 140.09]	
Total events	6		0				
Heterogeneity: Not ap	plicable						0.01 0.1 1 10 100
Test for overall effect:	r = 0.15					0.01 0.1 1 10 100 Favours typical	

### **Adverse effects**

Figure 14.1: antipsychotics as a risk factor for stroke

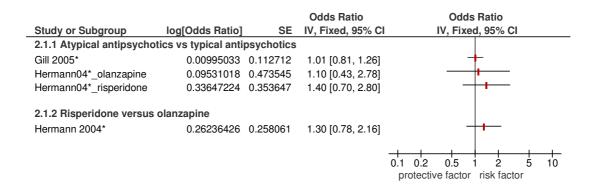


Figure 14.2: antipsychotics as a risk factor for stroke

			Risk Ratio	Risk Ratio
Study or Subgroup	log[Risk Ratio]	SE	IV, Fixed, 95% CI	IV, Fixed, 95% CI
23.1.1 All antipsychotics versus no treatment				
Douglas 2008	0.54812141	0.039779	1.73 [1.60, 1.87]	t
23.1.2 Typical antipsychotics versus no treatment				
Douglas 2008	0.2472853	0.043753	1.28 [1.18, 1.40]	t
23.1.3 Atypical antipsychotics versus no treatment				
Douglas 2008	0.84156719	0.148796	2.32 [1.73, 3.11]	+
				0.1 0.2 0.5 1 2 5 10
				protective factor risk factor