

2019 articles which may change your practice

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OLTCC 2019



2019 articles which may change your practice

Faculty/Presenter Disclosure

- Faculty: **Christopher Patterson**
- Relationships with financial sponsors:
 - Grants/Research Support:** CIHR, McMaster University
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 - Patents:** Nil
 - Other:** Hamilton Health Sciences, Niagara Health System
- **Potential for conflict(s) of interest:**
 - Dr. Patterson has no real or potential conflict(s) of interest relevant to this presentation

2019 articles

Objectives

- Examine new evidence on the care of frail older adults in Long Term Care
- Recognize the relevance of the research to one's Long Term Care practice
- Identify effective, targeted interventions from each article that could change one's practice

To prepare, I perused contents of JAMDA, Age and Ageing, J Am Geriatr Society, Ann Intern Med, CMAJ and personal alert services

2019 articles

- Would CBD help my mother's dementia?
- He hasn't been the same since his hip replacement...
- Dual antiplatelet drugs: how long after CVE?
- Can we reduce the risk of catheter associated infection?
- Gabapentinoids for LBP: good or bad..
- Trazodone is safe, right?
- Save that leg!
- Latest from Canadian Consensus Conference on Dementia
- Can hearing aids prevent dementia?

Would CBD help dementia?

- Agitation and aggression common in AD

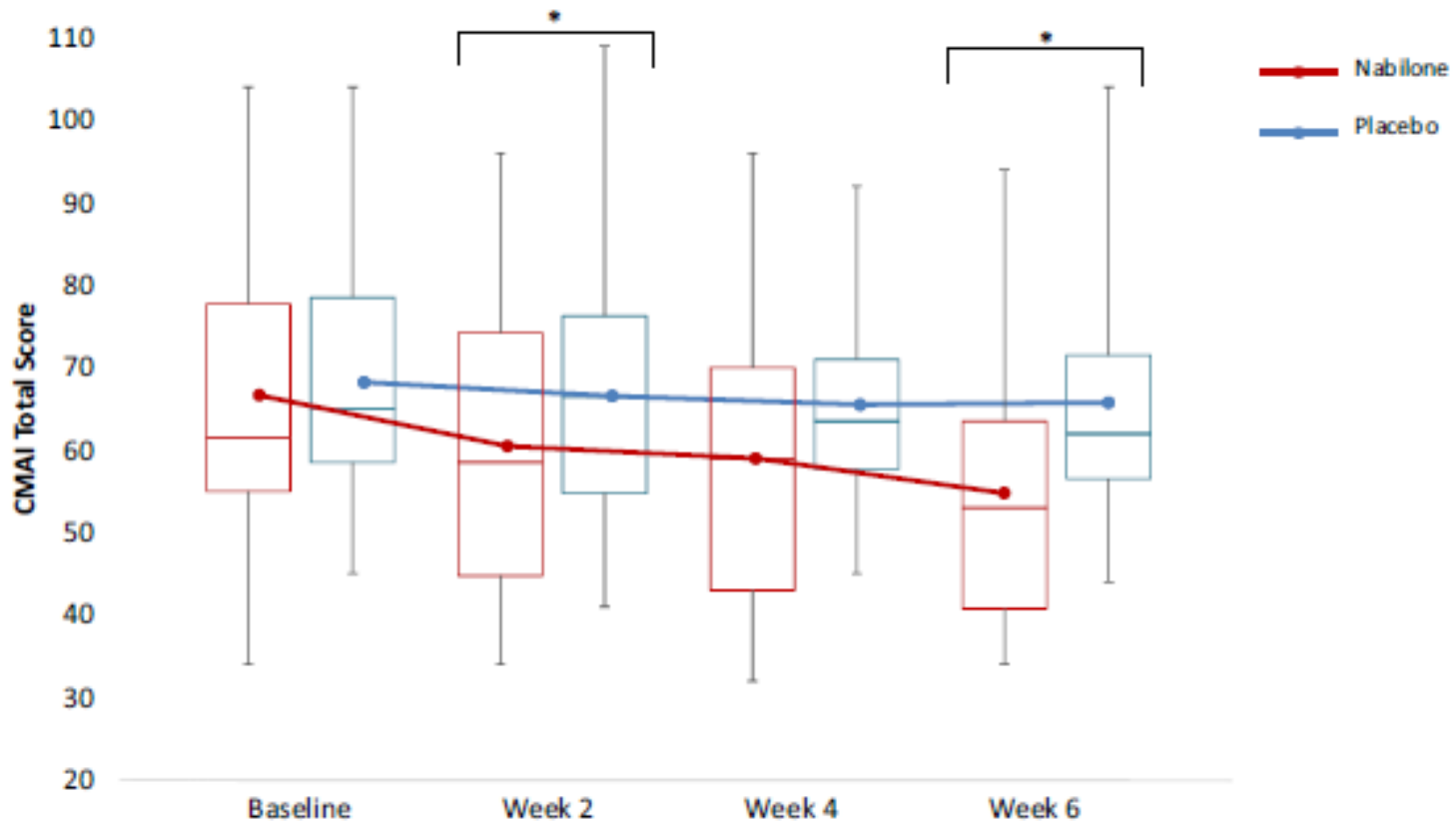
Management

1. non pharmacological
 2. antidepressants
 3. antipsychotics
- Endocannabinoid receptors widespread in CNS
 - Small trials and case reports have suggested that cannabinoids may reduce agitation in AD

Nabilone for agitation in AD

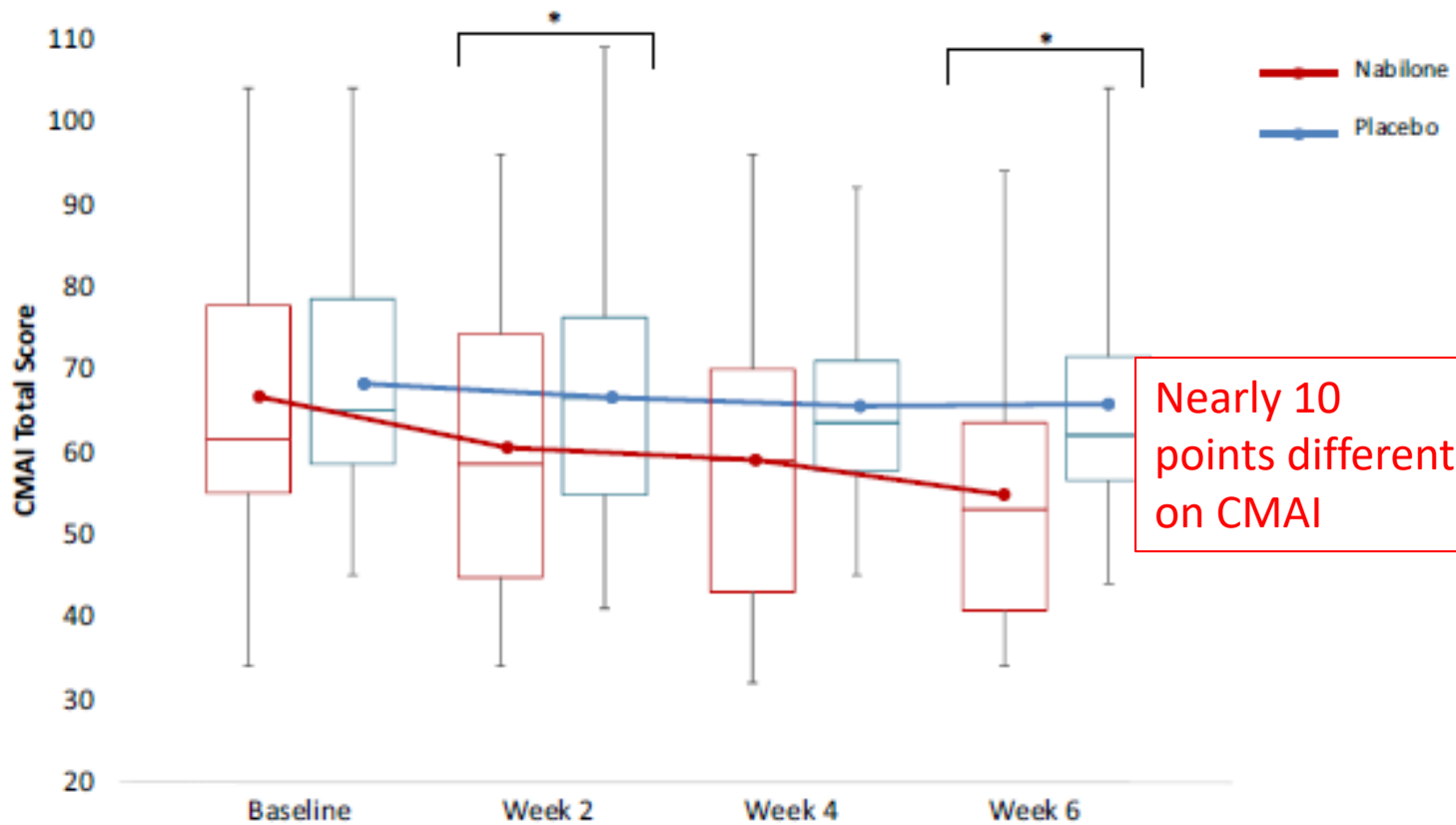
RCT double blind crossover-6 weeks	
Number of participants	39
Age (years)	87 ± 10
Male %	77
Inpatient %	72
Medications %	Cholinesterase inhibitors 53, memantine 29, antidepressant 87, atypical antipsychotic 45
sMMSE score	6.5 ± 6.8
CMAI	67.9 ± 17.6
NPI total	34.3 ± 15.8
NPI agitation/aggression	7.1 ± 3.3

Nabilone for agitation in AD



Herrmann N et al. Am J Psychiatr 2019; 27(11): 1161

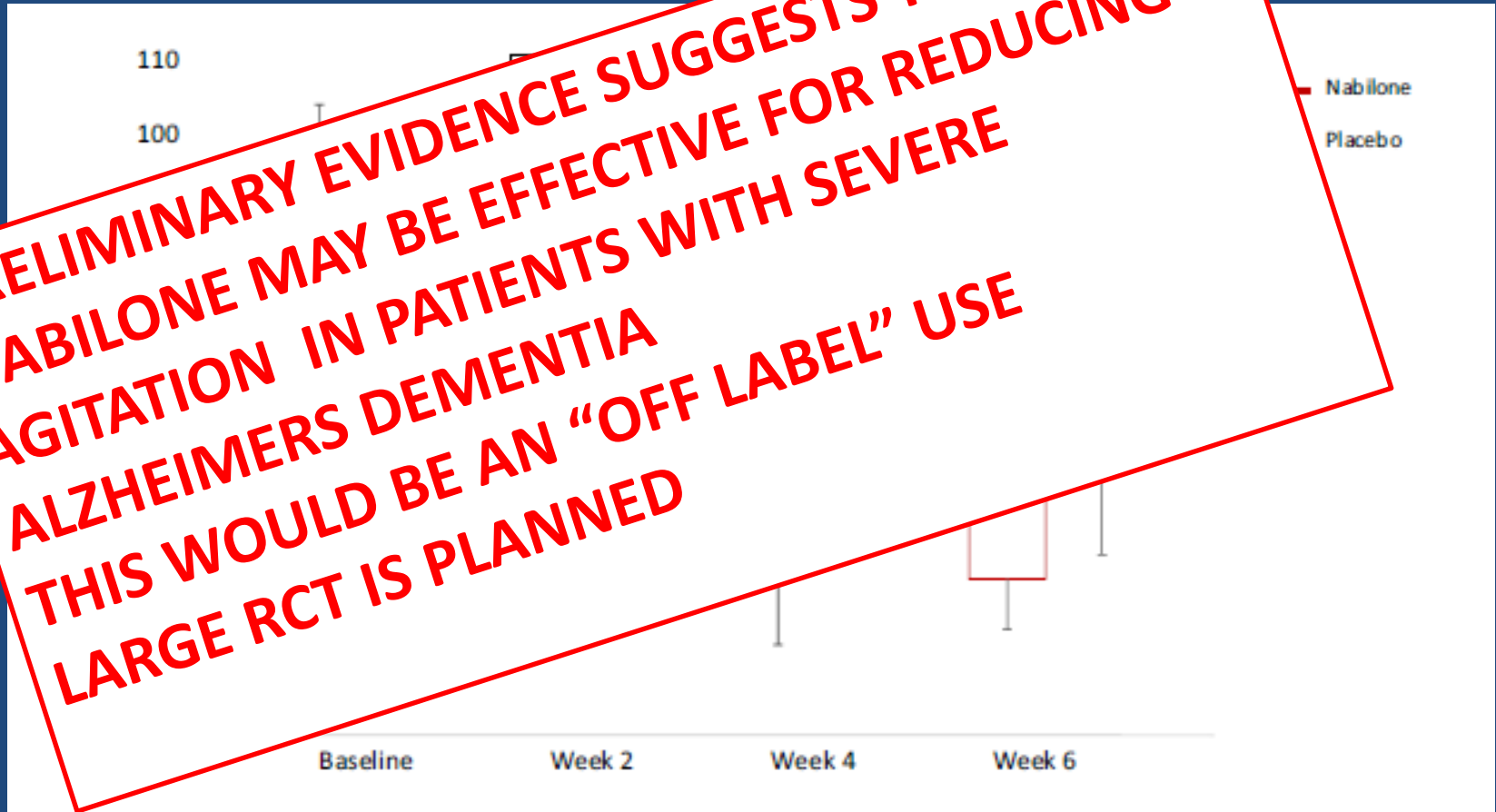
Nabilone for agitation in AD



Herrmann N et al. Am J Psychiatr 2019; 27(11): 1161

Nabilone for agitation in AD

PRELIMINARY EVIDENCE SUGGESTS THAT NABILONE MAY BE EFFECTIVE FOR REDUCING AGITATION IN PATIENTS WITH SEVERE ALZHEIMERS DEMENTIA THIS WOULD BE AN "OFF LABEL" USE LARGE RCT IS PLANNED



Herrmann N et al. Am J Psychiatr 2019; 27(11): 1161

He hasn't been the same since his hip replacement

- In older people, postoperative delirium is very common
- We frequently encounter the “never the same” scenario...
- Estimated risk of diagnosed postoperative stroke 0.14-0.7%¹
- High risk surgery (cardiac, vascular) 2.2-5.2%²

1. Lancet 2019; 6736(19): 31795

2. Wong GY et al Anesthesiology 2000; 92: 425

NeuroVISION

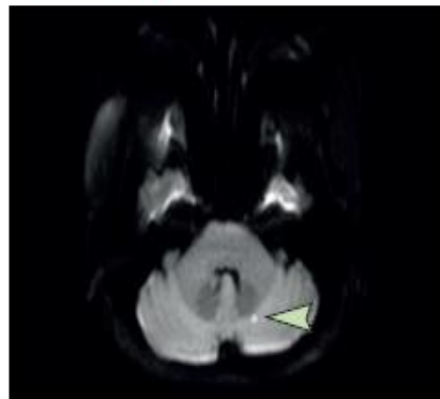
Non cardiac surgery in people over 65 years of age

N (19 sites in 9 countries)	1114
Mean age	73 ± 6
Female %	44
Hypertension %	64
DM %	27
CAD %	15
Stroke %	5
TIA %	4
PVD %	4
Type of surgery %	Ortho 41, uro/gyne 24, general 23

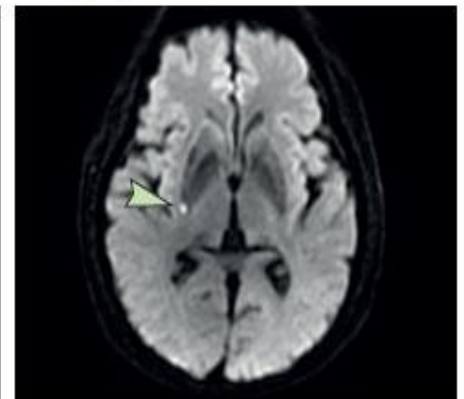
NeuroVISION

Perioperative
covert strokes
7% (95% CI: 1-9)
of people ≥ 65
undergoing non
cardiac surgery

A Participant with a single acute ischaemic lesion in the left cerebellum



B Participant with a single acute ischaemic lesion in the right putamen



C Participant with multiple acute ischaemic lesions in the right frontal lobe, left parietal lobe, and left occipital lobe

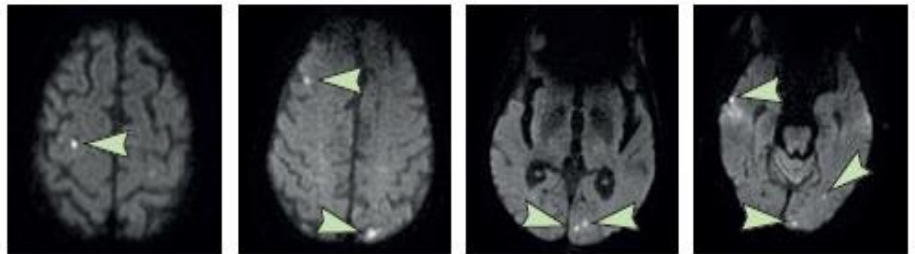
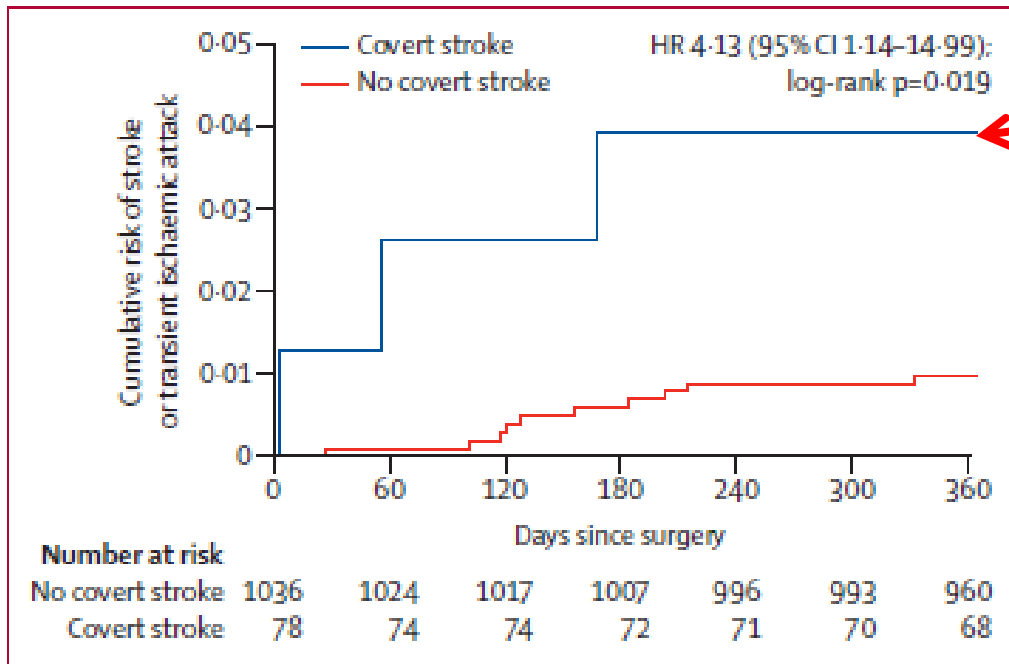


Figure 1: Examples of acute perioperative brain infarcts in study participants
Examples are shown on diffusion-weighted imaging sequences.

NeuroVISION



Stroke and TIA in people who experienced a perioperative covert stroke

Figure 2: Kaplan-Meier estimates of the composite outcome of overt stroke and transient ischaemic attack at 1 year

HR=hazard ratio.

NeuroVISION

	Covert stroke	No covert stroke	Hazard ratio
Delirium in first 3 days%	10	5	2.24 (1.06-4.730)
Stroke at 1 year%	3	1	3.92 (0.82-18.870)
Stroke or TIA at one year%	4	1	4.13 (1.14-14.95)
Cognitive decline at 1 year (≥ 2 points on MoCA)	42	29	1.98 (1.22-3.20)

The NeuroVISION Investigators Lancet 2019; 6736(19): 31795

NeuroVISION

Covert stroke

Delirium in first 2

**For our older patients going for noncardiac surgery
We can estimate a risk of covert stroke < 10%
But a covert stroke:
Doubles the risk of postoperative delirium
Doubles the risk of cognitive decline at one year
Quadruples the risk of Stroke or TIA**

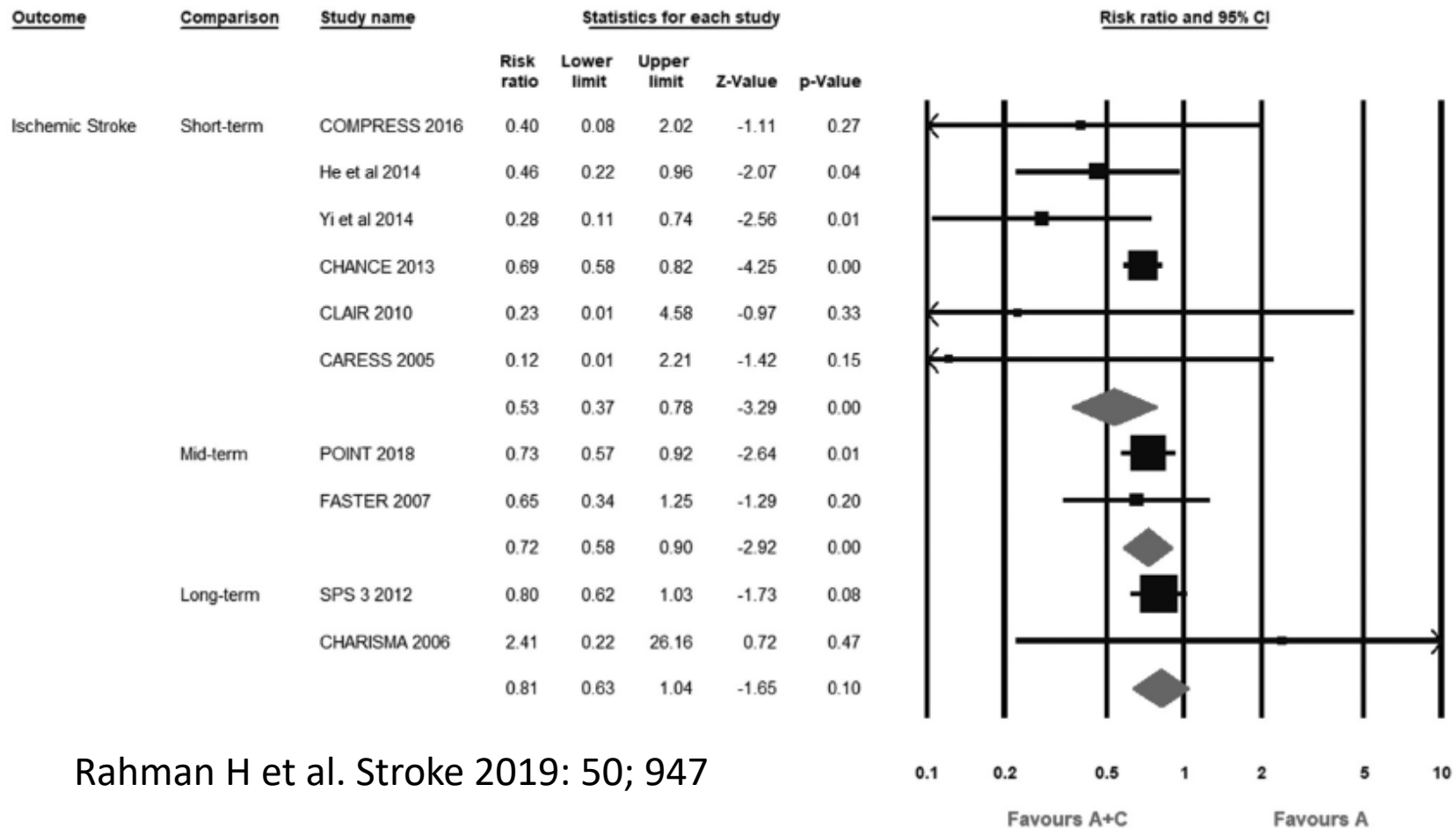
5.20)

Dual antiplatelet therapy after thrombotic CVE

- ASA reduces risk of recurrent CVA and TIA if started soon after event
 - ASA plus clopidogrel further reduces risk of recurrent CVE
 - Dual antiplatelet therapy increases risk of bleeding
- SO....
- What is the optimal balance of benefit and risk?
 - SER and meta analysis of 10 RCTS, comparing short, medium and long term DAPT on benefits and risks

ASA plus clopidogrel in CVE

Benefits: reduced recurrent CVE

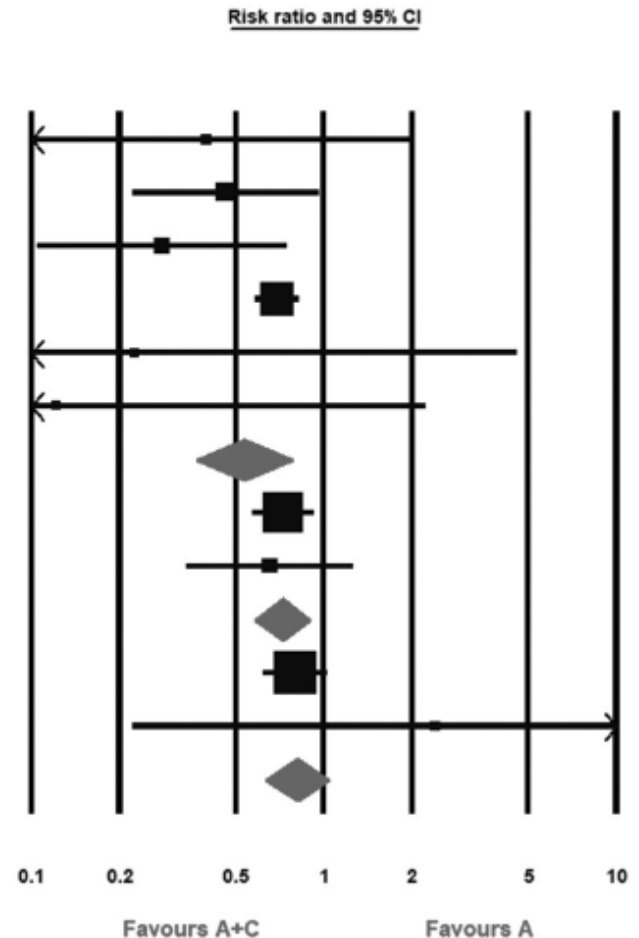


Rahman H et al. Stroke 2019; 50; 947

ASA plus clopidogrel in CVE

Benefits: reduced recurrent CVE

Outcome	Comparison	Study name	Statistics for each study				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Ischemic Stroke	Short-term	COMPRESS 2016	0.40	0.08	2.02	-1.11	0.27
		He et al 2014	0.46	0.22	0.96	-2.07	0.04
		Yi et al 2014	0.28	0.11	0.74	-2.56	0.01
		CHANCE 2013	0.69	0.58	0.82	-4.25	0.00

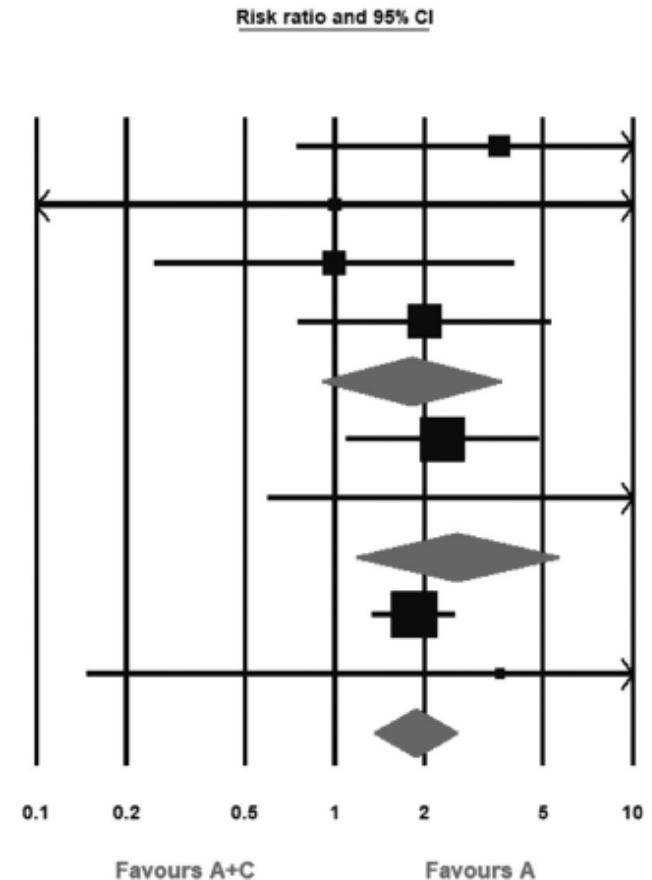


	RR	95% CI	p
1 month	0.53	0.37-0.78	0.00
3 months	0.72	0.58-0.90	0.00
28-42 months	0.81	0.63-1.04	0.10

ASA plus clopidogrel in CVE

Risks: increased bleeding

Outcome	Comparison	Study name	Statistics for each study				
			Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Major Bleeding	Short-term	COMPRESS 2016	3.58	0.75	17.00	1.61	0.11
		Yi et al 2014	1.01	0.06	16.02	0.00	1.00
		CHANCE 2013	1.00	0.25	4.00	0.00	1.00
		POINT 2018 (0-30)	2.01	0.76	5.36	1.40	0.16
			1.82	0.91	3.62	1.70	0.09
	Mid-term	POINT 2018	2.32	1.10	4.86	2.22	0.03
		FASTER 2007	10.78	0.60	193.62	1.61	0.11
	Long-term		2.58	1.19	5.60	2.40	0.02
		SPS 3 2012	1.86	1.35	2.55	3.84	0.00
		CHARISMA 2006	3.61	0.15	87.54	0.79	0.43
		1.87	1.36	2.56	3.90	0.00	

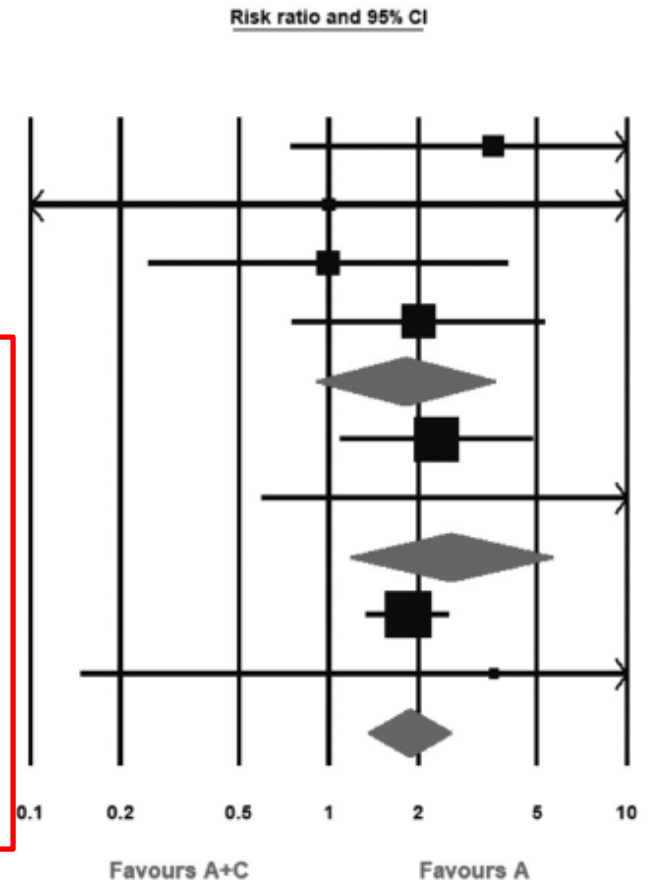


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ASA plus clopidogrel in CVE

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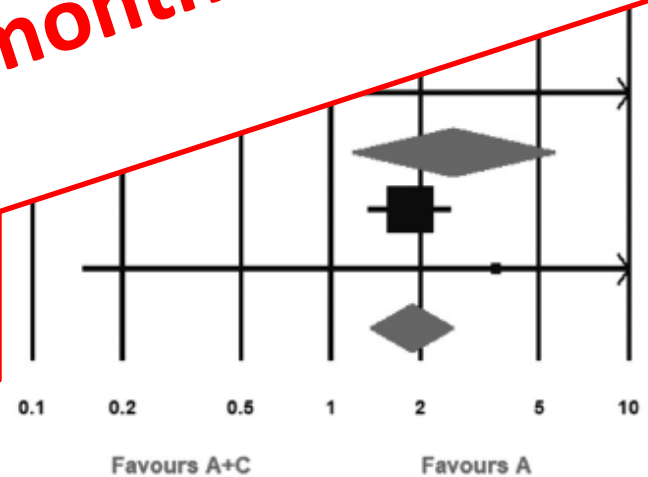
Risk of bleeding	RR	95% CI	p
1 month	1.82	0.91-3.62	0.16
3 months	2.58	2.58-5.60	0.02
28-42 months	1.87	1.36-2.56	0.00

ASA plus clopidogrel in CVE

Risks: increased bleeding

Outcome	Comparison	Study name	Statistics for each study		
			Risk ratio	Lower limit	Upper limit
Major Bleeding	Short-term	COMPRESS 2016	3.58		
		Yi et al 2014			

For optimal reduction CVE and least risk of bleeding complications ASA + clopidogrel for 1 month only



Rahman H Stroke 2019: 50; 947

Can we reduce the risk of catheter associated infections?

“Good quality evidence from one network meta-analysis and one systematic review suggested that there was no statistically significant difference between various topical cleansing agents, ranging from soap and water to chlorhexidine, used prior to urinary catheter insertion in the rate of catheter-associated urinary tract infections”.

Clark M, Wright M-D. Antisepsis for urinary catheter insertion: a review of clinical effectiveness and guidelines. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2019 Jan

Can we reduce the risk of catheter associated infections?

- 3 hospitals in Australia N=1642
- Men and women, not in/out or suprapubic
- Stepped wedge design (control → intervention)
- Control period: meatal cleansing with normal saline
- 2889 catheter days: 13 UTIs, 29 asymptomatic bact.
- Intervention period with chlorhexidine 0.1%
- 2338 catheter days: 4 UTIs, 16 asymptomatic bact.

Can we reduce the risk of catheter associated infections?

Per 100 catheter days	Saline 0.9%	Chlorhexidine 1%	RR	95%
UTI	0.45	0.17	0.26	0.08-0.86
Asymptomatic bacteria	1.0	0.68	0.06	0.01-0.32

Caveats:

- Not a randomized controlled trial, not blinded
- Urine sent for culture when infection suspected (rigorous criteria)
- Urine cultures not sent at prespecified times

Can we reduce the risk of catheter associated infections?

Per 100 catheter days	Saline 0.9%	0.1% chlorhexidine
UTI	0.45	0.35
Asymptomatic bacteria	0.45	0.35

DESPITE FLAWED METHODOLOGY & POTENTIAL ENVIRONMENTAL ISSUES RESULTS OF THIS TRIAL SUGGEST THAT MEATAL CLEANSING MAY REDUCE RISK OF CATHETER ASSOCIATED INFECTIONS

- No difference in catheter associated infections
- Urine culture positive in 10% of catheterized patients
- (approx 10% of catheterized patients)
- Urine culture positive at prespecified times

Gabapentinoids for LBP

- Low back pain is extremely common 90%, most common cause of disability
- 5-10% sciatica: gabapentinoids valuable in neuropathic pain (e.g. diabetic neuropathy)
- Treatment with gabapentinoids included in national guidelines for low back pain (e.g. Institute of Health Economics Alberta)

Gabapentinoids for LBP

- Only one RCT showed benefit in short term pain: gabapentin 3600 mg daily
- Small trial 23 participants received active treatment, 20 received placebo¹
- Recent SER and meta analysis
- 9 randomized controlled trials
- 859 participants
- Gabapentin (GP) and pregabalin (PG)

Gabapentinoids for LBP

SER and Meta analysis of 9 RCTs N = 859

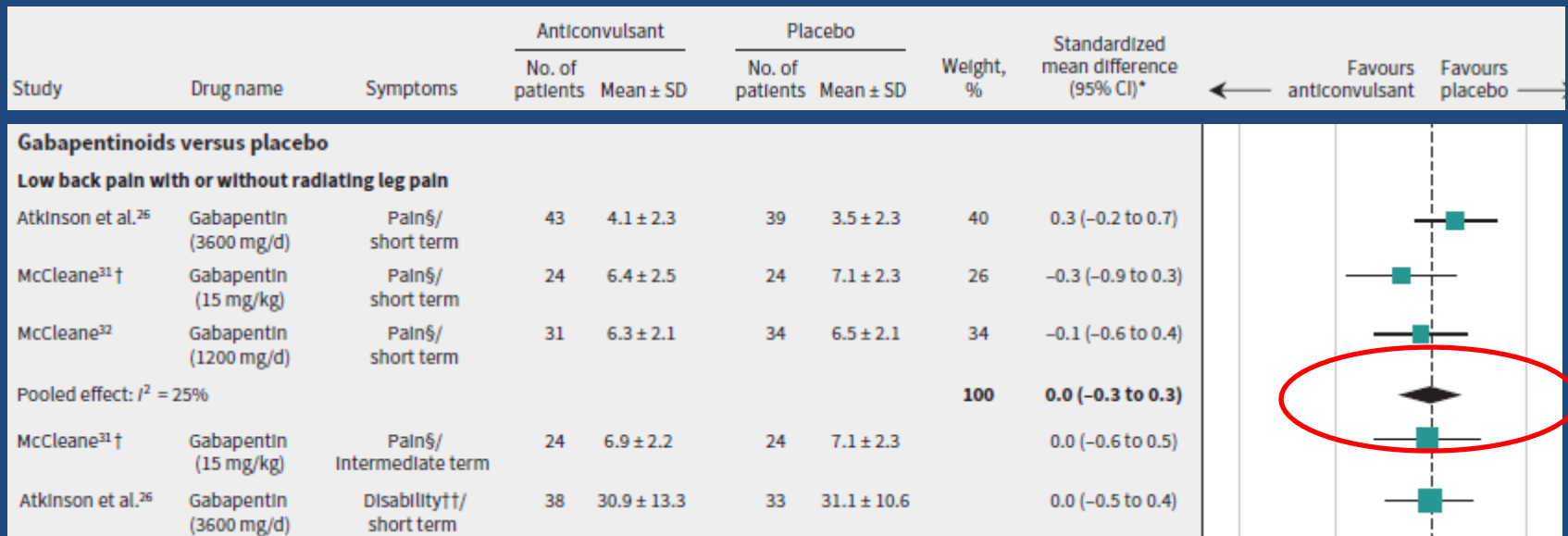
GP in LBP ± radiation to legs short term pain

Study	Drug name	Symptoms	Anticonvulsant		Placebo		Weight, %	Standardized mean difference (95% CI)*	← Favours anticonvulsant	Favours placebo →
			No. of patients	Mean ± SD	No. of patients	Mean ± SD				
Gabapentinoids versus placebo										
Low back pain with or without radiating leg pain										
Atkinson et al. ²⁶	Gabapentin (3600 mg/d)	Pain§/ short term	43	4.1 ± 2.3	39	3.5 ± 2.3	40	0.3 (-0.2 to 0.7)		
McCleane ³¹ †	Gabapentin (15 mg/kg)	Pain§/ short term	24	6.4 ± 2.5	24	7.1 ± 2.3	26	-0.3 (-0.9 to 0.3)		
McCleane ³²	Gabapentin (1200 mg/d)	Pain§/ short term	31	6.3 ± 2.1	34	6.5 ± 2.1	34	-0.1 (-0.6 to 0.4)		
Pooled effect: I ² = 25%							100	0.0 (-0.3 to 0.3)		
McCleane ³¹ †	Gabapentin (15 mg/kg)	Pain§/ Intermediate term	24	6.9 ± 2.2	24	7.1 ± 2.3		0.0 (-0.6 to 0.5)		
Atkinson et al. ²⁶	Gabapentin (3600 mg/d)	Disability††/ short term	38	30.9 ± 13.3	33	31.1 ± 10.6		0.0 (-0.5 to 0.4)		

Gabapentinoids for LBP

SER and Meta analysis of 9 RCTs N = 859

GP in LBP ± radiation to legs short term pain



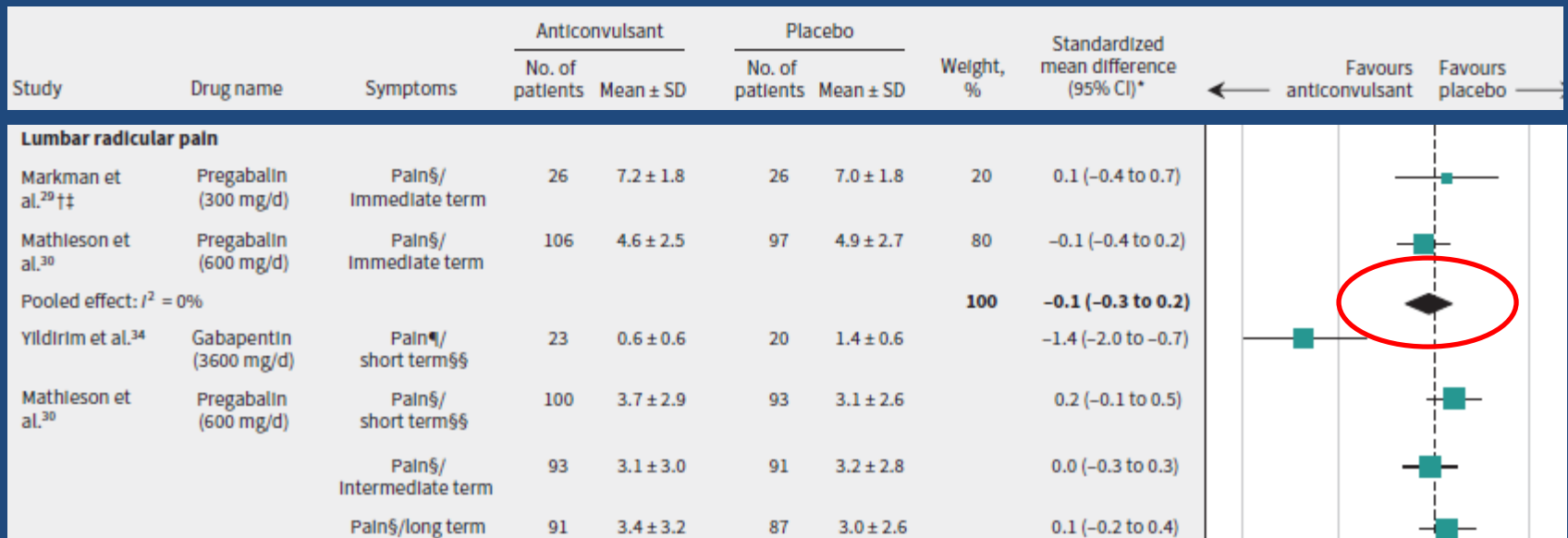
Gabapentinoids for LBP

GP or PG in LBP radiating to legs:
short, medium and long term pain

Study	Drug name	Symptoms	Anticonvulsant		Placebo		Weight, %	Standardized mean difference (95% CI)*	← Favours anticonvulsant	Favours placebo →	
			No. of patients	Mean ± SD	No. of patients	Mean ± SD					
Lumbar radicular pain											
Markman et al. ²⁹ ††	Pregabalin (300 mg/d)	Pain§/ Immediate term	26	7.2 ± 1.8	26	7.0 ± 1.8	20	0.1 (-0.4 to 0.7)			
Mathleson et al. ³⁰	Pregabalin (600 mg/d)	Pain§/ Immediate term	106	4.6 ± 2.5	97	4.9 ± 2.7	80	-0.1 (-0.4 to 0.2)			
Pooled effect: $I^2 = 0\%$								100	-0.1 (-0.3 to 0.2)		
Yildirim et al. ³⁴	Gabapentin (3600 mg/d)	Pain¶/ short term§§	23	0.6 ± 0.6	20	1.4 ± 0.6		-1.4 (-2.0 to -0.7)			
Mathleson et al. ³⁰	Pregabalin (600 mg/d)	Pain§/ short term§§	100	3.7 ± 2.9	93	3.1 ± 2.6		0.2 (-0.1 to 0.5)			
		Pain§/ Intermediate term	93	3.1 ± 3.0	91	3.2 ± 2.8		0.0 (-0.3 to 0.3)			
		Pain§/ long term	91	3.4 ± 3.2	87	3.0 ± 2.6		0.1 (-0.2 to 0.4)			

Gabapentinoids for LBP

GP or PG in LBP radiating to legs:
short, medium and long term pain



Gabapentinoids for LBP

Pregabalin and disability

Study	Drug name	Symptoms	Anticonvulsant		Placebo		Weight, %	Standardized mean difference (95% CI)*	Favours	
			No. of patients	Mean ± SD	No. of patients	Mean ± SD			anticonvulsant	placebo
Markman et al. ^{29†‡}	Pregabalin (300 mg/d)	Disability††/ Immediate term	26	37.8 ± 14.1	26	36.5 ± 14.1	21	0.1 (-0.5 to 0.6)		
Mathleson et al. ³⁰	Pregabalin (600 mg/d)	Disability††/ Immediate term	101	11.7 ± 6.0	96	12.5 ± 6.3	79	-0.1 (-0.4 to 0.1)		
Pooled effect: I ² = 0%							100	-0.1 (-0.3 to 0.2)		
Mathleson et al. ³⁰	Pregabalin (600 mg/d)	Disability††/ short term	93	9.1 ± 7.4	89	8.5 ± 7.1		0.1 (-0.2 to 0.4)		
		Disability††/ Intermediate term	85	7.4 ± 7.4	87	8.8 ± 7.5		-0.2 (-0.5 to 0.1)		
		Disability††/ long term	83	8.2 ± 7.6	79	7.4 ± 7.2		0.1 (-0.2 to 0.4)		

Enke O et al. CMAJ; 190: E786

Gabapentinoids for LBP

Pregabalin and disability

Study	Drug name	Symptoms	Anticonvulsant		Placebo		Weight, %	Standardized mean difference (95% CI)*	← Favours anticonvulsant	Favours placebo →
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		Disability††/ Intermediate term	85	7.4 ± 7.4	87	8.8 ± 7.5		-0.2 (-0.5 to 0.1)		
		Disability††/ long term	83	8.2 ± 7.6	79	7.4 ± 7.2		0.1 (-0.2 to 0.4)		

Enke O et al. CMAJ; 190: E786

Gabapentinoids for LBP

- Adverse effects of gabapentin and pregabalin
- Renally excreted, $t_{1/2}$ greatly increased in renal impairment (and thus many older people)
- Edema common up to 8% GP, 12% PG
- Somnolence up to 20% GP, 35% PG
- Both on Beers list (use with caution or not at all)

Gabapentinoids for LBP

- Adverse effects of gabapentin and pregabalin
- Renally excreted, t_{1/2} greatly increased in renal impairment

- Edema common

- ...

- ...

FOR LOW BACK PAIN WITH OR WITHOUT RADIATION TO LEGS GABAPENTIN AND PREGABALIN ARE NOT ASSOCIATED WITH IMPROVEMENT IN PAIN OR DISABILITY

Trazodone, safe right?

- With the (appropriate) trend to prescribing fewer antipsychotic drugs to older people, especially in long term care...
- Trazodone is being prescribed more frequently
- Is low dose trazodone safer than low dose antipsychotics?

Trazodone, safe right?

- Source information collected from linked health administration at ICES including Inter RAI data
- Long Term Care residents, Ontario aged ≥ 66 yrs
- December 1st 2009 to December 31st 2015
- 6588 prescribed trazodone
- 2875 quetiapine, olanzapine or risperidone
- Primary outcome: composite of fall or major osteoporotic fracture within 90 days of prescription

Trazodone, safe right?

Events per 100 person years

Outcome	Trazodone	Atypical antipsychotics	Risk difference 95% CI
Falls or major OP fracture	23	25	-0.5 (-1.5 to +0.5)
Falls	22	24	-0.3 (-1.4 to +0.7)
Major OP fracture	8	7	0.1 (-0.5 to +0.7)
Hip fracture	5	5	-0.06 (-0.5 to +0.4)
All cause mortality	60	77	-4.3 (-6.0 to -2.6)

Trazodone, safe right?

Events per 100 person years

Outcome	Trazodone	Atypical antipsychotics
Falls or major OP fracture	23	
Falls		
Major OP fracture		+0.5 to +0.7)
Hip fracture		-0.06 (-0.5 to +0.4)
All cause mortality		-4.3 (-6.0 to -2.6)

**Compared with atypical antipsychotics, trazodone has similar risks for falls and fractures
But lower risk for all cause mortality**

Save that leg!

- **COMPASS** study, a large multicentre RCT of patients with CAD and PAD. This study concerns PAD

Comparing 3 regimens:

- ASA alone plus rivaroxaban placebo
- ASA plus rivaroxaban 2.5 mg bid
- Rivaroxaban plus ASA placebo

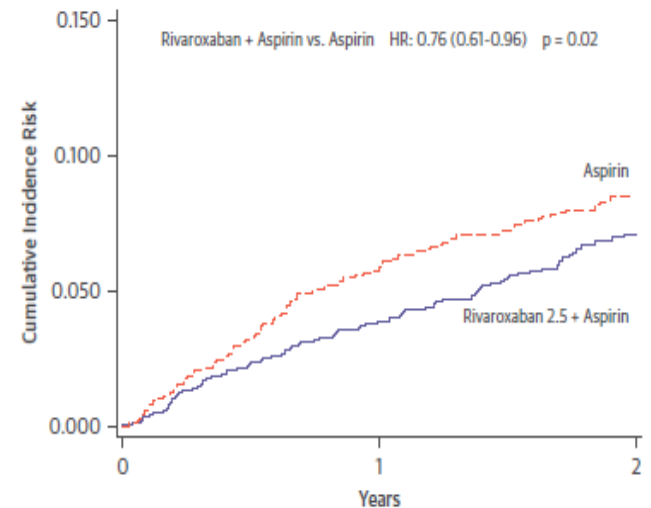
Outcomes:

- Major Adverse Cardiovascular Events (MACE)-cardiac death, MI, stroke
- Major Adverse Limb Events (MALE)-acute or chronic ischemia, angioplasty ± stent, surgery or amputation

Save that leg!

- **COMPASS study**
- N=6,391
- Mean age 67 ± 8.5
- HTN 79%
- CAD 65%
- Smoker 75%
- DM 45%
- Previous vascular surgery or angioplasty 32%

FIGURE 2 Peripheral Artery Outcomes in Trial Participants Treated With Rivaroxaban and Aspirin Compared With Aspirin Alone

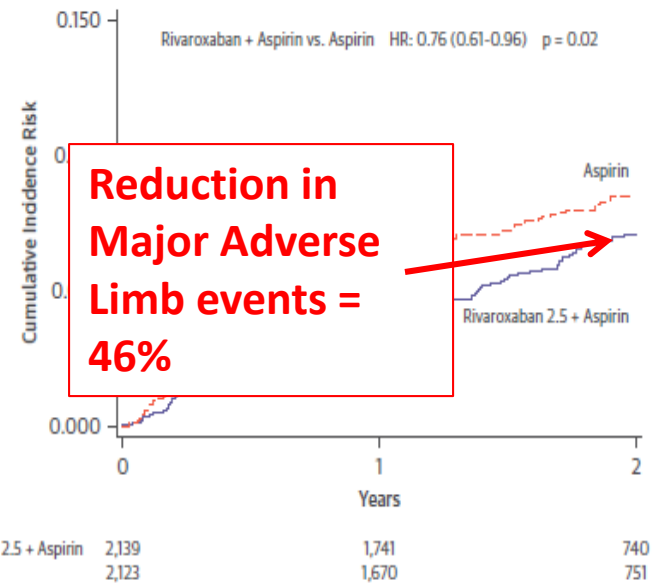


The cumulative incidence risk of total peripheral artery outcomes in patients according to randomized treatment group. Patients who received the rivaroxaban and aspirin combination had a significantly lower incidence of all types of peripheral artery outcomes. HR = hazard ratio.

Save that leg!

- **COMPASS study**
- N=6,391
- Mean age 67 ± 8.5
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FIGURE 2 Peripheral Artery Outcomes in Trial Participants Treated With Rivaroxaban and Aspirin Compared With Aspirin Alone



The cumulative incidence risk of total peripheral artery outcomes in patients according to randomized treatment group. Patients who received the rivaroxaban and aspirin combination had a significantly lower incidence of all types of peripheral artery outcomes. HR = hazard ratio.

Save that leg!

COMPASS Study

ASA vs ASA plus rivaroxaban 2.5 mg bid

Outcome	HR	95% CI
Major Adverse Limb Event (MALE)	0.57	0.37 - 0.88
Total vascular amputation	0.42	0.21 - 0.85
Major vascular amputation	0.33	0.12 - 0.92
Major bleeding	1.61	1.09 – 2.36

Anand S J Am Coll Cardiol 2018; 71(20):230

Save that leg!

COMPASS Study

ASA vs ASA plus rivaroxaban

Major	
Total	
Major	
Major b	

**In people with significant peripheral arterial disease
ASA plus low dose rivaroxaban
reduces risk of Major Adverse Limb
Events by 45%
Low dose rivaroxaban not yet available
in Canada.**

2.36

2018; 71(20):230

5th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia

Deprescription of anti dementia drugs

- After 12 months of use if there has been clinically meaningful worsening of dementia as reflected in changes in cognition, functioning, or global assessment over the past 6 months in the absence of other medical conditions
- If there has been no meaningful benefit (improvement, stabilization, decreased rate of decline)
- Severe/end stage dementia
- Intolerable side effects

5th CCC on the Diagnosis and Treatment of Dementia

Deprescription of anti dementia drugs (2)

- Poor adherence which precludes safe ongoing use
- CHEI should not be discontinued in individuals who have clinically meaningful psychotic symptoms, agitation or aggression, unless these symptoms appear to have worsened by initiation or increase in the dose of CHEI

5th CC on the Diagnosis and Treatment of Dementia

- Individuals who have had a clinically meaningful reduction in neuropsychiatric symptoms (e.g. psychosis) with cognitive enhancers should continue to be treated with cognitive enhancers even if they are not cognitively and functionally improved.
- Cholinesterase inhibitors and memantine should be depressed in individuals with mild cognitive impairment.

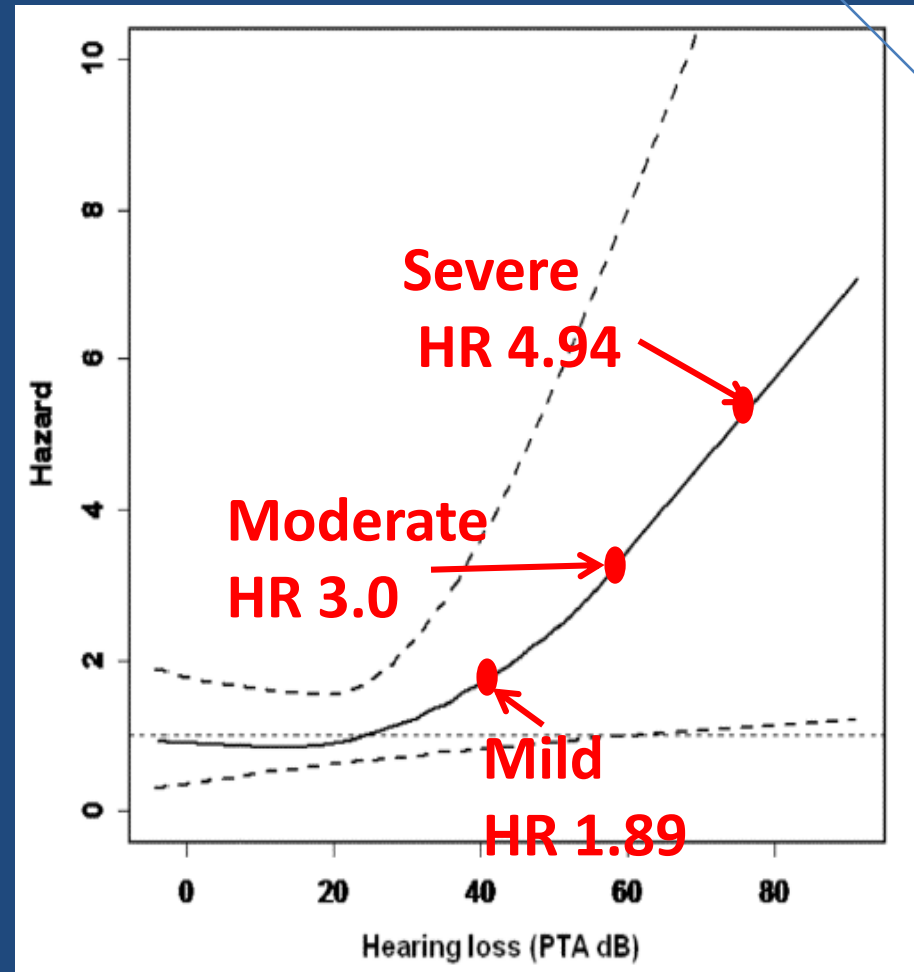
**LOOK OUT FOR CCCDTD5
RECOMMENDATIONS
TO BE PUBLISHED BY END
OF 2019**

Can hearing aids prevent dementia?

Hearing loss is a risk factor for dementia
11.9 years later (BLSA)

No long term RCTs
of hearing aids

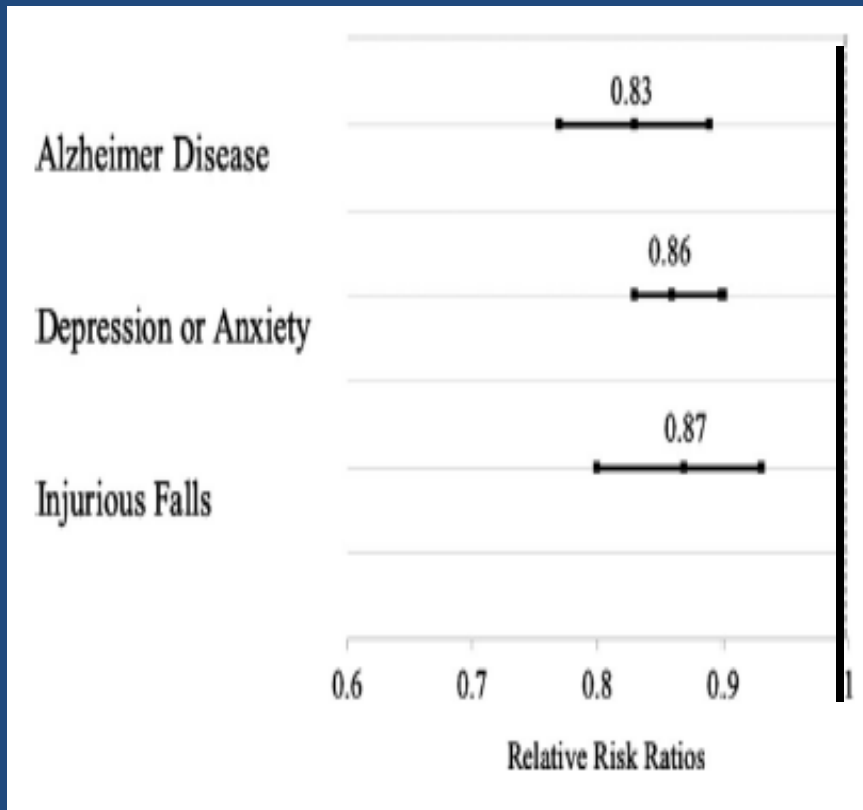
Short term trials
demonstrate cognitive
improvement



Use of hearing aids delay diagnosis

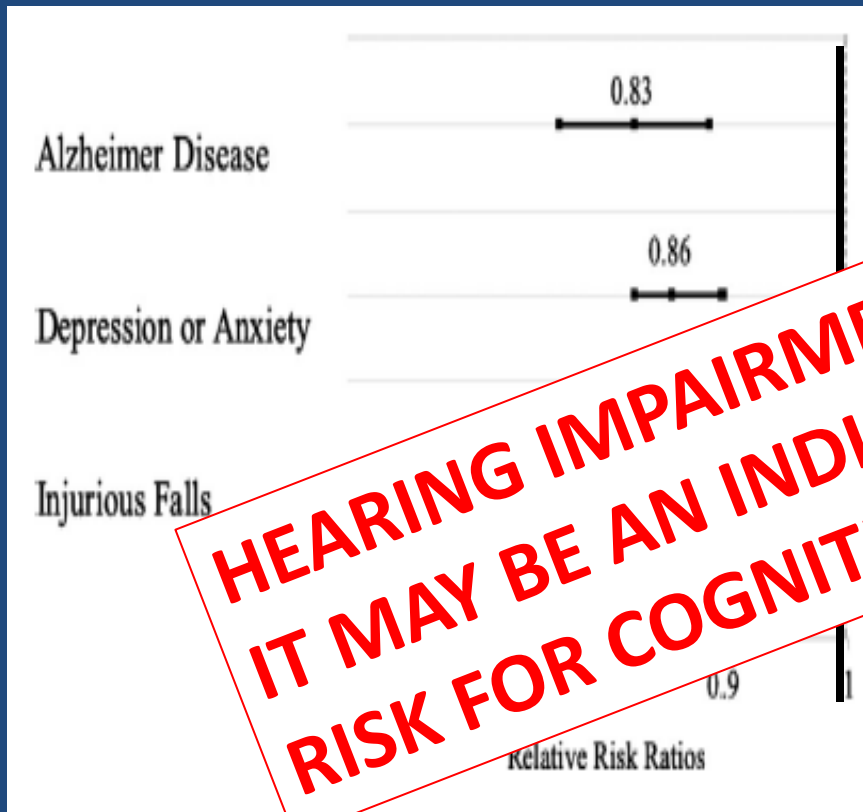
- National Longitudinal claims data (US)
- Based on national private insurance database
- age 66 with no dementia, depression or injurious falls at baseline (2008-2013)
- 14,862 hearing aid users, 100,000 non users
- Follow up 3 years reduced risk of being diagnosed with dementia or Alzheimer's disease, depression anxiety, injurious falls

Use of hearing aids delay diagnosis



- Hazard ratios for each condition
- Association does not imply causation
- Adds to evidence that hearing is related to conditions
- RCT is need to determine benefit
- Refer

Use of hearing aids delay diagnosis



**HEARING IMPAIRMENT IS NOT BENIGN
IT MAY BE AN INDICATION OF FUTURE
RISK FOR COGNITIVE IMPAIRMENT**

- Hazard ratios for each condition
- A hearing impairment is related to conditions
- RCT is need to determine benefit
- Refer

Did I address...

- Would CBD help my mother's dementia? **Maybe**
- He hasn't been the same since his hip replacement... **7%**
- Dual antiplatelet drugs: how long after CVE? **< 1 month**
- Can we reduce the risk of catheter associated infection?
Chlorhexidine 1% for cleansing, perhaps
- Gabapentinoids for LBP: good or bad.. **Mostly not helpful**
- Trazodone is safe, right? **Same falls and fractures, mortality↓**
- Save that leg! **ASA + low dose rivaroxaban in PAD**
- Latest from Canadian Consensus Conference on Dementia
When to deprescribe Cholinesterase inhibitors
- Can hearing aids prevent dementia? **May delay diagnosis..**

2019 articles

**Please remember to
complete your evaluations.**

**Evaluations can be found on
the Mobile App.**

Thank you.