



Top 10 Self Learning Articles

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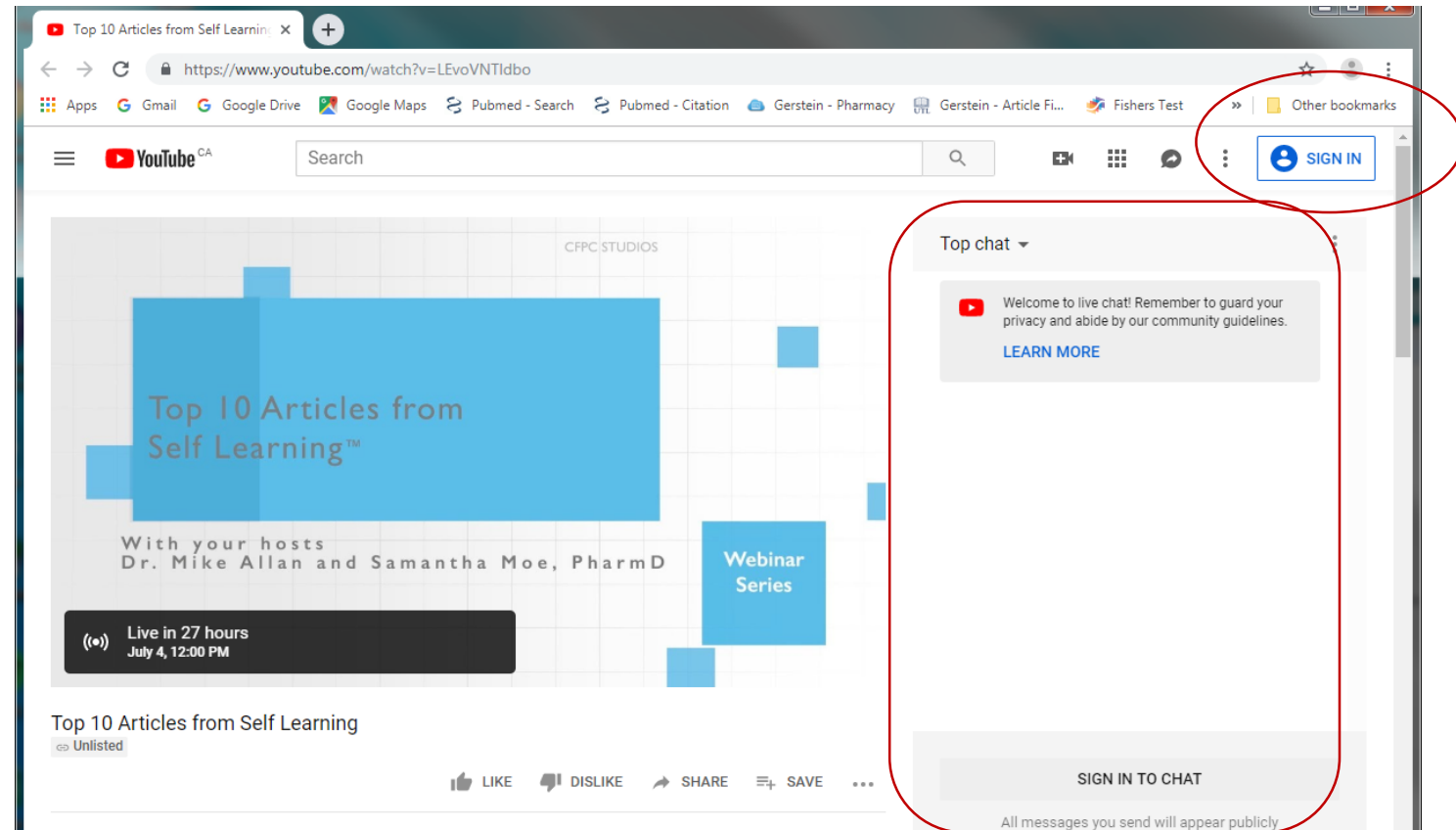
Logistics

A recording of this webinar and copy of slides - see CFPC clinical webinars website

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The screenshot shows a YouTube video player interface. The video title is "Top 10 Articles from Self Learning" and it is part of a "Webinar Series" by "CFPC STUDIOS". The video is hosted by "Dr. Mike Allan and Samantha Moe, PharmD" and is scheduled to go live in 27 hours on July 4, 12:00 PM. The video is currently unlisted. The interface includes a search bar, a "SIGN IN" button, and a "Top chat" overlay. The chat overlay contains a welcome message: "Welcome to live chat! Remember to guard your privacy and abide by our community guidelines." with a "LEARN MORE" link. At the bottom of the chat overlay, there is a "SIGN IN TO CHAT" button and a note: "All messages you send will appear publicly." The browser's address bar shows the URL "https://www.youtube.com/watch?v=LEvoVNTIdbo".

Conflict of Interest

Faculty: Mike Allan

Salary: College of Family Physicians of Canada, University of Alberta, Billing Income

Relationships with financial sponsors:

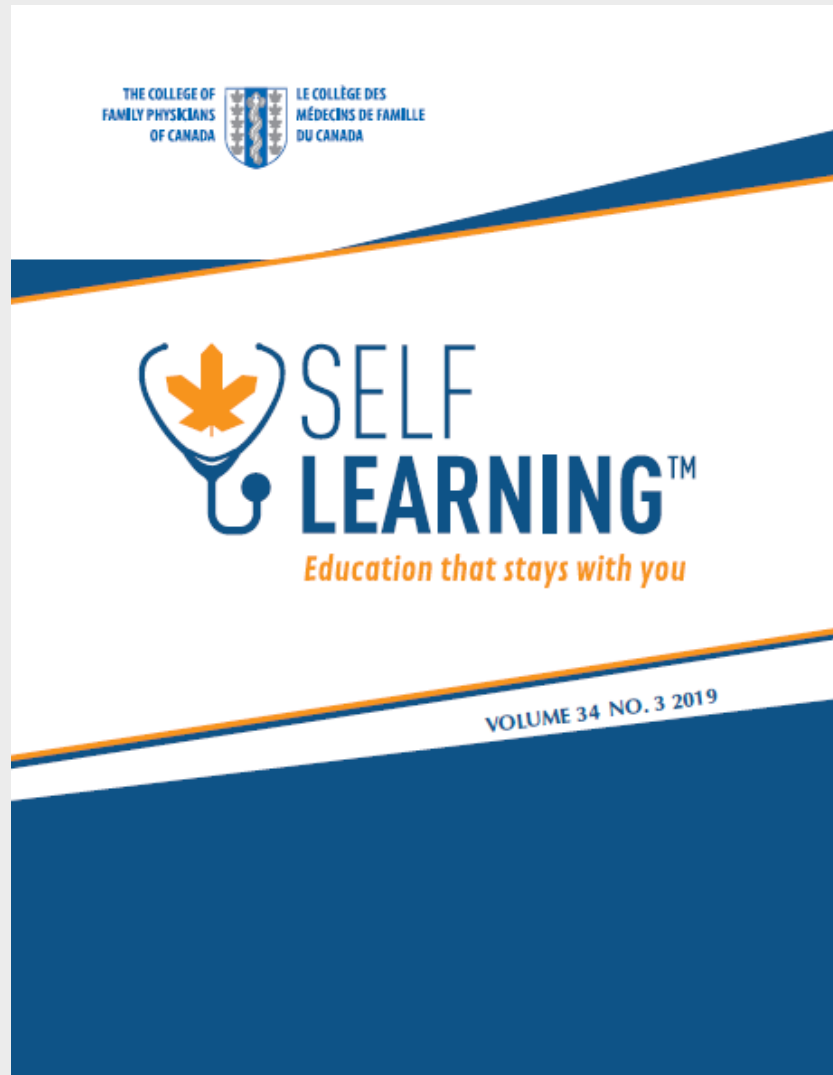
- Grants/Research Support: CIHR, PRIHS, Alberta Health, Alberta College of Family Physicians, Toward Optimized Practice, etc.
- Speaker's Bureau/Honoraria: Varying Provincial Chapters of CFP, University Departments of CPD, Others.
- Consulting Fees, Patents, Other: NA

Faculty: Samantha Moe

Salary: College of Family Physicians of Canada

Relationship with financial sponsors:

- Grants/research support: NA
- Speaker's Bureau/Honoraria: NA
- Consulting fees, Patents, Others: NA



- Subscribers complete 6 issues per year
- Available in English and French
- Each issue has ~ 40 questions; eligible for up to 5 certified Mainpro+ credits
- Questions:
 - Developed by 12 regional groups of family physicians
 - Reviewed/approved by the Self Learning Committee
 - “How will this information impact my practice?”
- Availability: Online access or hard copy books



Q8 Blood Pressure Targets in the Elderly

In ambulatory adults aged 75 or older, treating to a systolic blood pressure target of less than 120 mm Hg (versus 140 mm Hg) results in *each* of the following *except*:

- 1. Reduction of all-cause mortality rate
- 2. More injurious falls
- 3. Reduction of cardiovascular mortality rate
- 4. A greater likelihood of reduction in estimated glomerular filtration rate from baseline

Educational Point In the United States, 75% of persons over age 75 have hypertension. Cardiovascular disease complications are a leading cause of disability, morbidity, and mortality in this population. Current guidelines provide inconsistent recommendations about the optimal systolic blood pressure (SBP) treatment target in geriatric populations. Whether treatment targets should consider factors such as frailty or functional status is also unknown. The Systolic Blood Pressure Intervention Trial (SPRINT) recently reported that participants assigned to an intensive SBP treatment target of less than 120 mm Hg vs the standard SBP treatment goal of less than 140 mm Hg had a 25% lower relative risk of major cardiovascular events and death and a 27% lower relative risk of death from any cause. This trial was specifically funded to enhance recruitment of a prespecified subgroup of adults aged 75 or older, and the study protocol also included measures of functional status and frailty.

Study participants were required to be at increased risk for cardiovascular disease (based on a history of clinical or subclinical cardiovascular disease, chronic kidney disease [CKD], a 10-year Framingham general cardiovascular

For each issue:

- Readers answer a true/false, multiple-choice, or short answer questions
- “Educational points” drawn from peer-reviewed journal articles
- Impact assessment (Mainpro+) questions:
 - One is: “Which two questions from this issue will have the greatest impact on your practice”?

Learning Objectives

By the end of this activity, participants will be able to:

1. Identify the 10 articles family physicians picked as the most impactful from the Self Learning Program
2. Describe and interpret the findings in each article to identify practical key take away messages
3. Learn how Self Learning articles fit with existing literature for final application into practice

Is cannabis use associated with an increased risk of schizophrenia?

Article: Review article.

Self Learning Quote: If cannabis used ≥ 50 times then 6x more likely to develop schizophrenia (over 15 years) than never users.

12 cohort studies: For 1 to 35 years & 591 to 50,053 patients. All positive odds ratio and 9 of 12 statistically significant.

Best (largest) study - (1.7 million patient years)

- Adjusted odds ratio was 1.8 (~doubling of baseline risk)
- Absolute risks of schizophrenia (unadjusted):
 - For never users = 0.7%
 - For ever users = 1.5%
 - For users >50 times = 4.2% (yep: 4.2% is 6 times 0.7%)

Is cannabis use associated with an increased risk of schizophrenia?

Other Articles:

- Systematic Review of cohorts: Any use - Adjusted OR 1.41 (1.20–1.65)
 - Regular Use OR = 2.09 (1.54–2.84).¹
- Another Systematic Review: similar (Unadjusted OR 3.90 (2.84 - 5.34)) for higher users²
- If past psychosis: Continued cannabis use predicts higher relapse rates & longer hospital admissions.³

Caveats: observational & adjustment reduced effect⁴ (but still significant)

Bottom-Line: Cannabis use is associated with an increased risk of schizophrenia. Over ~30 years, never users have a 0.7% chance, compared to 4.2% for regular users.

Proton pump inhibitors have been associated with a number of long-term adverse events including:

Vitamin B12 Deficiency

C difficile infection

Fractures

Dementia

All of the above

Vitamin B12 deficiency and C
difficile infections only

Is chronic use of PPIs associated with vitamin B12 deficiency, fracture, dementia, or C.difficile infections?

Article: Review article of PPI associated adverse events.

Self Learning Quote: 4 main areas reported. Chronic PPI associated with:

- **B12 Deficiency:** risk HR 1.83 (1.36-2.46). ? lowering pH, thus decreasing B12 absorption
- **Fractures risk:** NNH ~2,672 hip and 337 vertebral fractures, (using baseline risk without PPIs).
- **New dementia:** possible increased risk, adjusted HR 1.38 (1.04–1.83).
- **C. difficile:** increased incidence has a RR of 1.69 (1.40–1.97),
 - Highest risk = hospitalized on antibiotics, NNH 50 at 14 days
 - Recurrence of C. difficile also increased, HR 1.5 (1.1–2.0).
- 50% of chronic PPI use maybe unnecessary.

Is chronic use of PPIs associated with vitamin B12 deficiency, fracture, dementia, or C.difficile infections?

Other Articles:

- **B12 Def:** Newer systematic review adds little (similar studies)¹
 - Absolute Risk (from cohort): Needing B12 treatment, 4.6% baseline but 11% on PPIs.²
- **Fractures:** Risk was ~16% baseline and ~22% for PPI users over ~6 years.³
 - Another study (of hip fracture) also found increase risk.⁴
- **Dementia:** 3 of 4 studies found PPI associated with higher risk (two were ~1.4).⁵
- **C diff:** 2 new meta-analysis, both finding very similar things.^{6,7}
 - C diff incidence OR ~2.^{6,7} Odds ratio ~1.7 for recurrence.⁶
 - Many studies during outbreaks: rates of 38% without PPI and 52% with.⁶
 - Estimation of risk after 14 days in hospital = 1.7% without versus 3.3% with PPI.⁷
 - All ages at risk^{6,7} – peds, adults <65 and adults ≥65.

1) J Pharm Pract 2017; 30(6): 639-42.

2) J Clin Epi 2001; 54: 531-4.

3) J Bone Metab 2018;25(3):141-51

4) Rheumatology International 2018; 38:1999-2014.

5) J Gastroenterol Hepatol. 2017;32(8):1426-35.

6) J Gastroenterol 2018; 53:84-94.

7) World J Gastroenterol 2017; 23(35): 6500-15.

Is chronic use of PPIs associated with vitamin B12 deficiency, fracture, dementia, or C. difficile infections?

Caveats: All data is observational, at high risk of confounding.

Bottom-Line: There is relatively consistent evidence of potential increased of prolonged PPI use associated with B12 deficiency, fracture risk, dementia and C difficile infection. All the evidence is based on observational studies, leaving these associations at high risk of bias. Regardless though, these potential risks exists and the prolonged use of PPI in patients needs to be re-evaluated and PPI use stopped where feasible.

Does lowering or discontinuing PPIs cause an increase in GERD symptoms compared to continuing the PPI?

Article: Clinical Guideline

Self Learning Quote: Five studies - abrupt discontinuation and on demand PPI use vs continuous PPI use.

- Symptom relapse RR 1.71 (1.31-2.21), NNH 14
- Patient dissatisfaction with discontinuation RR 1.82 (1.26-2.56), NNH 14 vs continuous PPI use.
- Weekly pill burden reduced by ~4 pills

Other Articles:

- Open label RCT: Patients who completed 8-week course of PPI therapy.
 - Esomeprazole 40mg as needed vs esomeprazole 20mg OD for 12 weeks.³
- Results: patients symptoms and satisfaction not significantly different. Patients consumed less tablets/day on average.
- Limitation: Not double blinded and patients consumed same average mg of esomeprazole/day.

Does lowering or discontinuing PPIs cause an increase in GERD symptoms compared to continuing the PPI?

Bottom Line:

- CPG recommends PPIs be decreased/stopped/changed to prn in patients with resolution of GI symptoms following 4 weeks of PPI treatment.
- Relapse symptoms and dissatisfaction (NNH 14) may occur when switching to on-demand PPIs.
 - Implementation into practice may be difficult.
- Weekly pill burden could be reduced by about 4 pills.

Is ten days of bismuth quadruple therapy more effective than triple therapy for eradicating *H pylori*?

Article: Randomized, open label trial, 1620 patients with *H pylori* infection or positive ¹³C-urea breath test

Self Learning Quote:

Bismuth based quadruple therapy	Non-bismuth based quadruple therapy	Triple therapy
Bismuth 300mg QID	Amoxicillin 1000mg BID	Amoxicillin 1000mg BID
Tetracycline 500 QID	Clarithromycin 500mg BID	Clarithromycin 500mg BID
Metronidazole 500mg TID	Metronidazole 500mg BID	--
All groups received lansoprazole 30mg BID		
10 days	10 days	14 days

- Age ~53 years
- 49% male
- 25% duodenal ulcer
- 39% gastric ulcer

Is ten days of bismuth quadruple therapy more effective than triple therapy for eradicating *H pylori*?

	Bismuth-based quadruple therapy x 10 d	Non-bismuth based quadruple therapy x 10d	Triple therapy x 14d
Eradication rates	90%	<u>86%</u>	84%
			NNT 15
Discontinuation due to side effects	10%	7%	4%
	Dizziness, headache, nausea, vomiting, dark stool		Diarrhea Taste Distortion
Poor adherence	9%	5%	3%

Is ten days of bismuth quadruple therapy more effective than triple therapy for eradicating *H pylori*?

Context/Other Research

Quadruple therapy is recommended as first line by guidelines¹. This study and others^{2,3}:

- Bismuth-based quadruple therapy (10-14 days) is more effective than 14 days of triple therapy
- Next best option is non-bismuth quadruple therapy x 14 days³

Bottom Line

Bismuth based quadruple therapy is 6% more effective than triple therapy at eradicating *H pylori* but is accompanied by slightly poorer tolerability and adherence rates. Bismuth quadruple therapy x 10 days may be an effective option, but non-bismuth based therapy should be prescribed for 14 days.

1. Fallone CA et al. Gastroenterology 2016; 151:51-69.
2. Uygun A et al. J Dig Dis 2007; 8: 211-15.
3. Songur Y et al. Am J Med Sci 2009; 338: 50-53.
4. Molina-Infante J. Alimen Pharmacol Therap 2015; 41(6): 581-9.

It's a busy clinic day. Mrs. Johnson is an 85 year old patient who needs a BP measurement. You consider doing a reading over her shirt sleeve. BP readings done over a sleeved arm are likely to be:

Higher, compared to bare arm

Lower, compared to bare arm

No different, compared to bare arm

Are blood pressure measurements over clothing equivalent to measurements on a bare arm?

Article: Controlled clinical trial in primary care of 186 patients.¹

- Compared BP in different scenarios: bare arm vs sleeved arm

Self Learning Quote: 61% female, mean 75 y, 64% hypertensive

- Compared with bare arm, BP higher over sleeved arm (4/5mmHg, $p < 0.001$)
- With greater age → more variability in BP
- Authors recommended against measuring BP over clothing

Other research: Controlled trial of 147 long term care residents²

- 76% women, mean age 87, 50% HTN
- Compared to bare arm, wearing shirt + sweater resulted in higher readings (8/9.5mmHg, $p < 0.002$)

1. Ozone S et al. Family Practice 2016; 33 (5): 517-22.

2. Ozone et al. Blood Pressure Monitoring 2018; 23: 9-11.

Are blood pressure measurements over clothing equivalent to measurements on a bare arm?

Other Studies

Eight controlled trials¹⁻⁸ previously published:

- No meaningful differences in BP over bare vs sleeved arm (range: -1.7 to +1.0mmHg)
- Most used automated BP cuff, < 2mm clothing thickness

Caveats:

Differences between two newest trials and previous 8: may be differences in ages studied (newest trials: mean age 74-87; other studies: 44-62);

- Most studies included mix of patients with and without hypertension

Bottom Line: Perform blood pressure measurement over a bare arm whenever possible; measurements done over sleeved arm *in elderly patients* may result in higher and more variable readings

1. Holleman DR et al. J Gen Intern Med 1993; 8: 325-6.
2. Kahan E et al. Fam Prac 2003; 20(6):730-2
3. Ki JH et al. Korean J Fam Med 2013; 34: 145-51.
4. Liebl ME et al. Blood Pressure 2004; 13: 279-82.

5. Ma G et al. CMAJ 2008; 178(%): 585-9.
6. Pinar R et al. J Clin Nurs 2010; 19: 1861-4.
7. Thien T et al. BI Press Monitor 2015; 20: 320-4.
8. Eder MJ et al. Dtsch Med Wochenschr 2008; 133: 1288-92.

Does targeting lower blood pressure in older adults have more benefits than harms?

Background: SPRINT is a RCT comparing intensive BP lowering (SBP<120mmHg) versus standard (SBP<140mmHg) among patients with high CV risk¹

Article: A subgroup of elderly patients (>75 years old) studied in SPRINT trial, follow up 3y²

Self Learning Quote:

- N= 2636: mean age 80, 38% female, baseline BP 142/71, Framingham risk 25%, 30% frail
- Patients achieved mean SBP of 123mmHg vs 135mmHg, ~11mmHg difference
- Composite CV events: HR 0.66 (95% CI 0.51, 0.85), NNT 27
- All-cause mortality: HR 0.67 (0.49, 0.91) NNT 41
- Serious adverse events: no difference (48% vs 48%)
- Trend towards an increase in hypotension (HR 1.7, 0.97-3.09), syncope (HR 1.2, 0.76-2.00) and acute kidney injury (HR 1.4, 0.98, 2.04);
 - Patients with no underlying CKD: kidney injury risk greater with intense BP lowering (NNH 90)
 - Injurious falls and orthostatic hypotension: no different between groups

Does targeting lower BP in older adults have more benefits than harms?

Context/Other Studies

- General population: evidence supports BP <140/90, including diabetes and renal disease
- Results of SPRINT can be applied to patients >75 years but trial excludes many:
 - Diabetes, history of stroke, ejection fraction <35% or symptomatic HF, GFR < 20ml/min, BP <110 after 1min standing, diagnosis of dementia, nursing home residents

Bottom Line:

Over 3 years, an intense BP target lead to a reduction in CV events and all-cause mortality in older adults, compared to a standard target. If considered, ensure no exclusions; advise patient of potential harm. Check standing blood pressure prior to initiation and monitor electrolytes, creatinine and vitals.

Sally is a 25 year old healthy patient presenting with a 2-day history of dysuria and urinary frequency. Based on the most recent evidence about diagnosing urinary tract infections, what course of action should be taken?

Perform urine dipstick and treat if positive for nitrites or WBC.

Send urine for culture and treat based on results.

Send urine for culture but initiate immediate treatment with antibiotics.

Initiate immediate treatment with antibiotics (and don't worry about urinalysis or culture).

Does a negative urine culture mean there is no infection?

Article: An observational survey

Self Learning Quote:

- 220 women with Urinary Tract Symptoms (UTI) (dysuria, urinary urgency and/or frequency) versus 86 women without UTI symptoms.
- Bacterial urine culture compared to quantitative PCR.
- Women with UTI symptoms: 81% on urine culture and 96% on qPCR.
- Women without symptoms: 11% on urine culture and 12% on qPCR.
- Majority of cases (68% of samples) found E.Coli.

Does a negative urine culture mean there is no infection?

Other Articles:

- RCT: If UTI symptoms but negative dipstick, 3-days of trimethoprim reduced symptoms.
- RCT: Minimal cost effectiveness differences between immediate antibiotics, delayed antibiotics (by 48 hours) and targeted Abx.

Limitations:

- Quantitative PCR is not used in practice
- Results only applicable to uncomplicated UTIs
- Majority of cases were E.coli, findings limited for non-E.Coli UTIs.

Bottom Line: A negative urine culture does not necessarily mean no infection. Symptoms are a stronger indicator and women can be treated immediately rather than wait for a culture.

Is there a correlation with Mini-Mental State Exam and driving risk in patients with dementia?

Article: Guidance document with review.

Self Learning Quote: Strongly consider driving risk if

- Family members concerned about driving safety.
- TMT-B (Trail Making Test-B): unsafe if ≥ 3 minutes to do or ≥ 3 errors (3 or 3 rule)
- TMT-A (Trail Making test-A): >48 seconds suggest need for driving evaluation.
- Other Features
 - Clock-drawing test predicts performance on a driving simulator.
 - Other tools/criteria: History of MVC or near crashes, MoCA ≤ 18 , intersecting pentagrams.
 - CMA criteria: moderate dementia = trouble with 2 IADLs or 1 basic ADL
 - MMSE does not predict driving risk or motor vehicle crashes
- For TMT-B: Unclear safety if takes 2-3 minutes to do or 2 errors.
 - Likely safe if <2 minutes to do and <2 errors.

Is there a correlation with Mini-Mental State Exam and driving risk in patients with dementia?

Other articles:

- While not perfect,¹ TMT (A & B) can help assessment,^{2,3} with TMT-B likely most helpful.²
- MOCA (cut-point ≤ 18) and clock drawing helpful as well.³
- Other studies point to the importance of family members concerns & past MVC or near MVC.⁴

Caveat: No RCT evidence.⁵ No tests reliable by themselves

Bottom-Line: Several factors (family concerns, past/near MVC, MoCA, clock-drawing, and Trail Making Tests (A & B)) can help discerning drivers at risk (not MSE). None are definitive and referral for performance-based, comprehensive on-road driving evaluation provides the best assessment.

1) Age and Ageing 2013; 42: 577–581.
2) Int Psychogeriatr. 2009; 21(4):637-53.
3) Clin Geriatr Med 2018; 34:107–115.

4) J Am Geriatr Soc 2010; 58:1104–1108.
5) Cochrane Database Syst Rev. 2013; (5):CD006222.

Jane is a 32 year old patient who has a history of migraine headaches. She asks if you have heard of melatonin being effective to prevent migraines. You respond that, based on the best available evidence, melatonin is:

No better than placebo

May be more effective
than placebo

Similar in effectiveness
to amitriptyline

More effective than
amitriptyline

Are patients more likely to get reduced migraine frequency with melatonin or amitriptyline?

Article: Double-blind RCT (n= 178) with one year history migraine (\pm aura)

Self Learning Quote: Melatonin 3mg vs. amitriptyline 25mg vs. placebo x 12 weeks; 75% women, mean age 37

- Melatonin & amitriptyline had fewer migraine days/month (2.7, 2.2 days) than PLB (1.1days), $p < 0.05$;
- Both better than placebo: \downarrow headache intensity (1.3 pt on 10-point scale), analgesic use (\downarrow 1/month), mean attack duration (\downarrow 4-5h)
- More responders ($>50\%$ improvement in headache frequency) with melatonin (54% vs 39% amitriptyline, abs diff 15%, NNT 6 over 12 weeks);

Are patients more likely to get reduced migraine frequency with melatonin or amitriptyline?

Other Research

- Melatonin systematic review (7 studies, mixed designs)¹: placebo-controlled and comparator trials - conflicting results;
- RCT in pediatrics²: amitriptyline superior to melatonin for several outcomes including monthly frequency, severity, duration, # analgesics used

Bottom Line

Effectiveness of melatonin versus placebo or amitriptyline is inconsistent. While reasonable to try melatonin for migraine prevention, amitriptyline has consistently shown to be better than placebo with NNT 8 for headache severity and frequency.³

Which complementary health products are effective for the common cold?

Article: Review article¹

Self Learning Quote: 4 main areas reported.

- **Probiotics:** decrease occurrence of URTI (RR 0.62 (0.46-0.76)), perhaps shortened illness duration by ~2d (adults) but low quality evidence² ; well tolerated
 - *Other studies:* have shown similar results^{3,4}
- **Zinc lozenges or syrup:** shortens illness by ~1d, but does not change severity⁵
 - SE: taste disturbance, nausea; loss of smell with nasal formulation (long-lasting)
 - *Other recent meta-analyses:* within 24h of onset of cold, zinc \geq 75mg daily decreases duration of illness^{6,7}; no effect on severity of colds;⁶
- Inconsistencies seen across studies for both probiotics and zinc

1. US Department of Health and Human Services, NIH. Flu and Colds. www.nccih.nih.gov
2. Hao Q et al. Cochrane Database Syst Rev. 2015 (2): CD006895.pub3.
3. Amaral MA et al. Pediatr Pulmonol 2017; 52: 833-43.
4. Wang Y et al. Medicine 2016; 95:31.

5. Singh M et al. Cochrane Review 2013; Issue 6. Art. No.: CD001364.
6. Science M et al. CMAJ 2012; DOI: 10.1503/cmaj.111990.
7. Hemila H et al. BMC Fam Practice 2015; 16: 24.

Which complementary health products are effective for the common cold?

Honey: small studies in children suggest superiority over placebo for reducing cough¹

- *2018 updated review*² – after 3 days of therapy, honey associated with faster onset of relief (~3/4 day) compared with placebo and,
 - On 7-point scale: ↓ frequency (1 point) and severity (0.8 points), improves child & parent's sleep (1 point)
- Up to 3 days of treatment sufficient
- SE: gastrointestinal symptoms (12% vs 11% placebo, NNH 100)
- Data based on small number of trials, with small sample sizes

Saline: May have symptomatic benefit for common cold;

- Most recent meta-analysis³: n=5, small trials; most suggest no difference compared to placebo
- One larger trial: reduction in nasal secretion score, nasal breathing score⁴ of ~ 0.3 on 4-point scales, small improvement and minimal clinical significance
 - Considerations: nasal discomfort and/or irritation; avoid tap water

1. Oduwole O et al. Cochrane Review 2014; Issue 12, Art. No.: CD 007094.

2. Oduwole O et al. Cochrane Review 2018; Issue 4, Art. No.: CD007094.

3. King D et al. Cochrane Database Syst Rev. 2015; (4): CD0006821.

4. Slapak et al. Arch Otolaryng 2008; 134(1): 67-74.

Which complementary health products treat and prevent the common cold?

Bottom Line:

For the treatment of common cold, probiotics and zinc may shorten the course of illness. Honey may have a small effect to relieve cough. Saline rinses may have a small to effect on nasal symptoms in some patients.

However, several limitations with data including few trials, small numbers of patients studied & inconsistent results across studies.

For the prevention of common cold, probiotics may decrease the incidence of common cold.

No evidence to support supplemental vitamin C, American ginseng, echinacea, and garlic for the treatment or prevention of the common cold.

Final Comments

Each question in the Self Learning Program is based on single article

Our review showed that in two of the top 10, minor qualification was needed

- Melatonin for headaches
- BP measurement over clothes

But for the other 8 articles, Self Learning was fully supported by related literature.

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