



## Top 10 Family Medicine Practice Changers from CFPC Self Learning

Mike Allan, MD  
Samantha Moe, PharmD  
Joey Ton, PharmD

Director, Programs and Practice Support  
Clinical Evidence Expert, KET Program  
Clinical Evidence Expert, KET Program

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### Conflict of Interest Disclosure

Faculty/Presenter: Mike Allan

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

Relationships with financial sponsors:

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- Other: Bedmed, INRange (Publicly Funded Research Studies)



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### Conflict of Interest Disclosure

Presenter: 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

Presenter: Joey Ton

Salary: College of Family Physicians of Canada, Costco

Relationship with financial sponsors:

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



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- 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



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**QB Blood Pressure Targets in the Elderly**

In ambulatory adults aged 75 or older, meeting to a modest blood pressure target of less than 130 mm Hg versus 140 mm Hg results in one of the following ranges:

- 1. Reduction of all cause mortality rate
- 2. More hospital stays
- 3. Reduction of cardiovascular mortality rate
- 4. A greater likelihood of admission to retirement glaucoma filtration case from hospital

**Educational Point** In the United States, 71% of persons over age 75 have hypertension. Cardiovascular disease complications are a leading cause of disability, mortality, and morbidity in this population. Current guidelines provide treatment recommendations about the optimal systolic blood pressure (SBP) treatment target in geriatric populations. Whether treatment targets should consider factors such as falls or functional status is still unknown. The Specific Blood Pressure Assessment 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 160 mm Hg had a 21% 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 younger/racial/ethnic group of adults aged 75 or older and the study protocol also included measures of retention rates and safety.

Study participants were assigned to be an increased risk for cardiovascular disease based on a history of clinical or subclinical cardiovascular disease, chronic kidney disease (CKD), a 10-year Framingham annual 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?"



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**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



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**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 <sup>13</sup>C-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



Liou JM et al. The Lancet 2016; 388: 2355-65.

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**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%	86%	84% NNT 15
Discontinuation due to side effects	10% Dizziness, headache, nausea, vomiting, dark stool	7%	4% Diarrhea Taste Distortion
Poor adherence	9%	5%	3%



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### 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 guidelines<sup>1</sup>. This study and others<sup>2,3</sup>:

- 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 days<sup>3</sup>

**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.

SM

1. Furlong CA et al. *Gastroenterology* 2016; 151:51-59.  
 2. Srinivasan A et al. *J Dig Dis* 2007; 8: 271-76.  
 3. Srinivasan A et al. *Ann Acad Sci* 2010; 118: 30-35.  
 4. Medina-Infante J. *Alimen Pharmacol Therap* 2015; 41(5): 581-9.



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### What does 13 pills per day for 10 days look like?



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### 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 may be unnecessary.

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CMAJ 2016;188(9):657-62

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

MA

1) *J Pharm Pract* 2017; 30(6): 639-42.  
 2) *Clin Epi* 2003; 54: 531-6.  
 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) *Gastroenterol* 2018; 153:94-94.  
 7) *World J Gastroenterol* 2017; 23(35): 6500-15.

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

**Article:** Controlled clinical trial in primary care of 186 patients.<sup>1</sup>

- 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 residents<sup>2</sup>

- 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. Osame S et al. Family Practice. 2016; 38(1):137-22.  
2. Osame S et al. Blood Pressure Monitoring. 2016; 21: 9-11.



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

### Other Studies

Eight controlled trials<sup>1-8</sup> 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. Hollander SP et al. J Gen Intern Med. 2010; 35:221-6.  
2. Kahari E et al. Fam Pract. 2010; 32(2):150-2.  
3. Klotz W et al. Hypertension. 2012; 59:164-51.  
4. Lohr ME et al. Blood Pressure. 2004; 13: 279-82.



5. Shi C et al. JAMA. 2008; 299(12):1489-9.  
6. Pappas M et al. J Clin Hypertens. 2012; 24: 186S-4.  
7. Zhou Y et al. J Hypertens. 2015; 33: 1214-4.  
8. Eder M et al. Dtsch Med Wochenschr. 2008; 133: 1288-92.

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## 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 risk<sup>1</sup>

**Article:** A subgroup of elderly patients (>75 years old) studied in SPRINT trial, follow up 3y<sup>2</sup>

### 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

JT



1. NEJM. 2015 Nov 26;373(22):2103-16.  
2. JAMA. 2016 Jun 28;315(24):2673-82.

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## 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.

THE COLLEGE OF AMERICAN PSYCHIATRISTS  
 JAMA, 2016 Jun 28;315(24):2673-82.  
 Allan GM et al. TFP 2016, Article #37

JT

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## 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%)

World Psychiatry 2016;15:195-204  
 Psychological Medicine (2012), 42, 1321-1338.

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## Is cannabis use associated with an increased risk of schizophrenia?

### Other Articles:

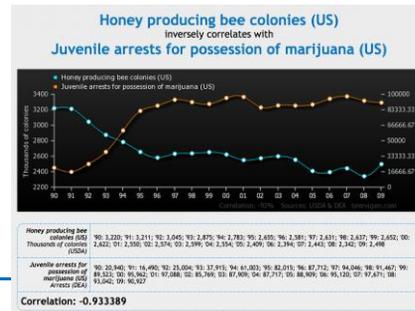
- Systematic Review of cohorts: Any use - Adjusted OR 1.41 (1.20-1.65)
  - Regular Use OR = 2.09 (1.54-2.84).<sup>1</sup>
- Another Systematic Review: similar (Unadjusted OR 3.90 (2.84 - 5.34)) for higher users<sup>2</sup>
- If past psychosis: Continued cannabis use predicts higher relapse rates & longer hospital admissions.<sup>3</sup>

**Caveats:** observational & adjustment reduced effect<sup>4</sup> (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.

THE COLLEGE OF AMERICAN PSYCHIATRISTS  
 JAMA, 2007; 297: 319-28.  
 Schizophrenia Bull 2016; 42(10): 1262-9.  
 Lancet Psychiatry 2016;3: 215-25.  
 Br J Psych 2008; 193: 357-63.

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## Which complementary health products are effective for the common cold?

**Article:** Review article<sup>1</sup>

**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 evidence<sup>2</sup>; well tolerated
  - *Other studies:* have shown similar results<sup>3,4</sup>
- **Zinc lozenges or syrup:** shortens illness by ~1d, but does not change severity<sup>5</sup>
  - 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<sup>6,7</sup>; no effect on severity of colds<sup>6</sup>
- Inconsistencies seen across studies for both probiotics and zinc

1. US Department of Health and Human Services, NIH, Flu and Colds. <https://www.cdc.gov/flu/>

2. Reed C et al. Cochrane Database Syst Rev. 2015 (2): CD009895.pub3.

3. Aronoff SA 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 8, Art. No.: CD001368.

6. Scumfild et al. CMAJ 2012; DOI: 10.1503/cmaj.111990.

7. Heredia H et al. BMC Fam Practise 2015; 16: 24.

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## Which complementary health products are effective for the common cold?

**Honey:** small studies in children suggest superiority over placebo for reducing cough<sup>1</sup>

- 2018 updated review<sup>2</sup> – after 3 days of therapy, honey associated with faster onset of relief (~3/4 day) compared with placebo and,
  - On 7-point scale: 1 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-analysis<sup>3</sup>: n=5, small trials; most suggest no difference compared to placebo
- One larger trial: reduction in nasal secretion score, nasal breathing score<sup>4</sup> of ~ 0.3 on 4-point scales, small improvement and minimal clinical significance
  - Considerations: nasal discomfort and/or irritation; avoid tap water

1. O'Connell D et al. Cochrane Review 2014, Issue 12, Art. No.: CD 007294.

2. O'Connell D et al. Cochrane Review 2018, Issue 4, Art. No.: CD007064.

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

4. Sipek et al. Arch Otolaryngol 2008; 134(1): 67-74.



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## 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 no 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.



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## 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.



Clin Microbiol Infect. 2017 Sep;23(9):647-652.

JT

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## 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.

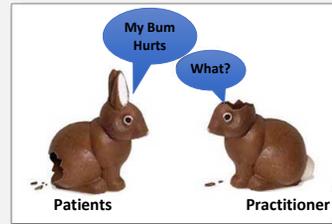
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BMJ. 2010 Feb 5;340:c346.  
BMJ. 2005 Jul 16;331(7509):143.

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## Crazy as it sounds, sometimes listening to the patient can help.



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## 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  $\geq 3$  minutes to do or  $\geq 3$  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  $\leq 18$ , 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.

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Can Fam Physician 2017; 63:27-31.

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

**Other articles:**

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

**Caveat:** No RCT evidence.<sup>5</sup> 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.

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1) Age and Ageing 2013; 42: 577-581.  
2) Int Psychogeriatr. 2009; 21(6):637-53.  
3) Clin Geriatr Med 2016; 34:107-115.



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

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## 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, NNT 6 over 12 weeks);

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Goncalves AL et al. J Neurol Neurosurg Psychiatry 2016; 87: 1127-32.



1. Long R et al. Medicine 2019; 98: 3.  
2. Khatun R et al. Iran J Child Neurol 2018; 12(1): 47-54.  
3. Alban et al. TIF 2015; #51.

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

### Other Research

- Melatonin systematic review (7 studies, mixed designs)<sup>1</sup>: placebo-controlled and comparator trials - conflicting results;
- RCT in pediatrics<sup>2</sup>: 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.<sup>3</sup>

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## 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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