

The Prudent Prescriber

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Pharm Reps ≠ Rational Prescribing

(PR)



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Bedtime better than morning for BP meds?

The Study: These Spanish investigators (European Heart J 2019 Oct 22) identified 19,168 adults, 18 years or older, (all Spanish Caucasians, 55% men, average age 60) who met the criteria for hypertension that required prescription treatment to lower blood pressure. The study participants randomly received assignment to the intervention group (told to take the entire daily dose of one or more prescribed blood pressure lowering medicines at bedtime) or to the control group (told to take the entire daily dose on awakening).

Methods: Clinicians provided care without restriction to choice of the BP pressure lowering medicine approved for once daily dosing (angiotensin receptor blockers, angiotensin converting enzyme inhibitors, calcium channel blockers, beta-blockers and/or diuretics). At inclusion and at every scheduled clinical visit (at least annually) throughout follow-up, ambulatory blood pressure (ABP) monitoring was performed for 48 hours. Individuals masked to treatment group assignment assessed outcomes, including the primary composite outcome of myocardial infarction, coronary revascularization, heart failure, stroke and CVD death. Complete follow-up occurred for more than 99% of participants for a median time of 6.3 years.

Antibiotics do NOT

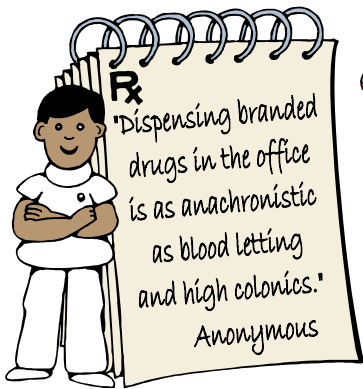


help acute bronchitis

β-blockers in post-MI save lives



Pill splitters save BIG

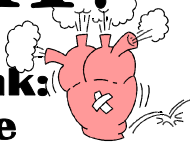


"Dispensing branded drugs in the office is as anachronistic as blood letting and high colonics."
Anonymous



CHE?

Think:
Ace
Aldactone
B-blocker
Dig
Diuretic

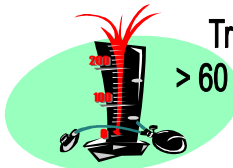


Avoid these expensive "me-too" drugs:

- Mydayis
- Lucemyra
- Xyzal
- Gralise
- Viibryd
- Lexette foam
- Drizalma DR



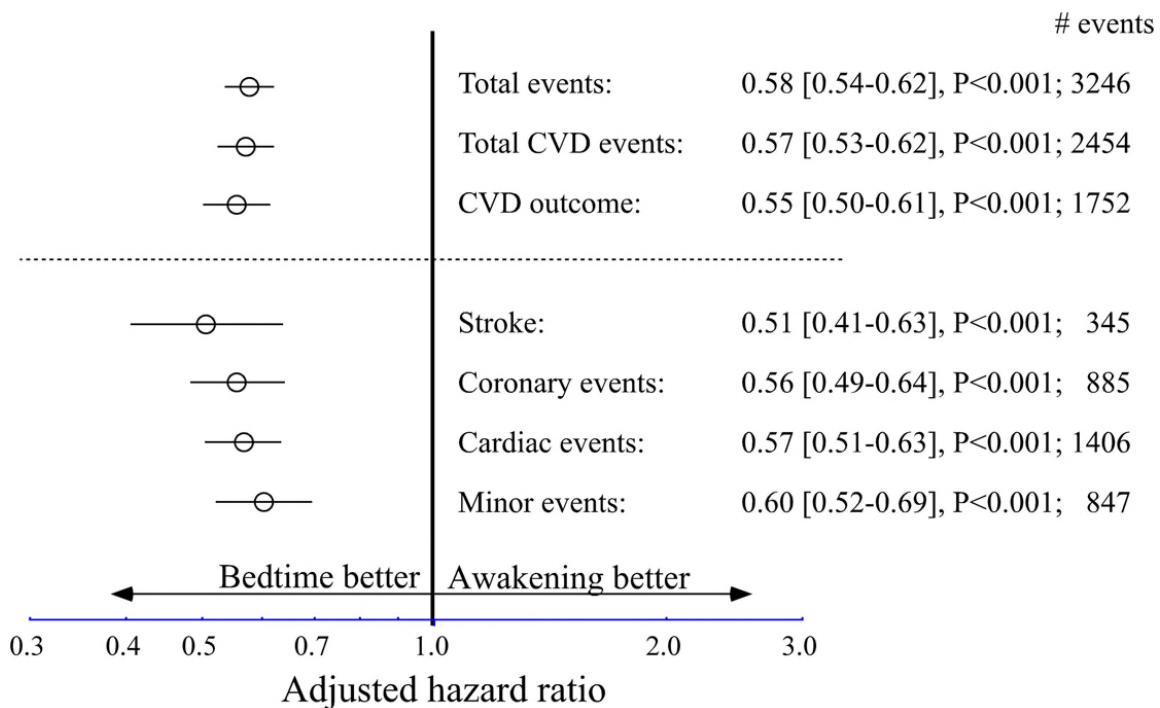
Treat patients > 60 years to 150/90



NOW AVAILABLE
ON THE
GENERIC MARQUEE

Advair → fluticasone/salmeterol
or Wixela Inhub
Eliquis → apixaban
Lyrica → pregablin
Apriso → mesalamine ER capsules
Nuvaring → etonogestrel & EE ring

Results: During the 6.3-year median patient follow-up, 1,752 patients experienced the primary CVD outcome. Patients of the bedtime, compared with those of the upon-wakening treatment time regimen, showed a significantly lower hazard ratio after correcting for age, sex, type II diabetes, chronic kidney disease, smoking, HDL cholesterol, sleep systolic blood-pressure mean, and previous CVD event. The hazard ratio of the primary CVD outcome was 0.55 (95% CI 0.50– 0.61). The Number Needed to Treat (NNT) to prevent one CVD outcome was 20.3 (17.4 – 24.3). As noted in the table below, for each of the single outcome components, the before bedtime dosing was superior to the upon-awakening dosing.



Why does it work? Multiple prospective clinical trials document improved normalization of asleep blood pressure when hypertension medications are ingested at bedtime rather than upon awakening [Chronotherapy for hypertension (*Curr Hypertens Rep* 2018 20:97)]. In this study, the main differences in BP control were achievement with bedtime treatment of significantly lower asleep BP mean without loss of awake BP-lowering efficacy. Findings of numerous independent prospective studies and meta-analyses demonstrate that the asleep BP mean determined by ambulatory BP monitoring (ABPM) is a significantly more sensitive prognostic marker of cardiovascular disease risk than either daytime office BP measurements or the ABPM-derived awake or 24 hr BP mean. (*Eur Heart J* 2018 39:4159–4171)

My Take:

- This is the best of several studies demonstrating the benefits of ingesting blood pressure medications at bedtime. The length of follow-up, the lack of dropouts (1%), large "N" and ambulatory BP monitoring speak to its power.
- The authors suggest that having the clinicians pick the anti-hypertensive drugs rather than mandating the hypertensive regimen is a weakness. My feeling, on the contrary, is that this makes this study more applicable to the real world. The other real world part of this study: the participants were type II diabetics (24%), renally impaired (29%) and obese (average BMI 29.7).
- The good news is that the study found no significant difference in adverse effects by giving the medications at bedtime versus upon awakening (~6%). The non-adherence rates were similar in both groups (2.9%).

- This is a reasonable, practical intervention.

ARBs and Zantac Recalls: What do they mean?

- Over the last 18 months, 12 different manufacturers have recalled an angiotensin II receptor blocker (ARB) due to contamination. These include valsartan, irbesartan and losartan. In September 2019, contamination recalls for ranitidine capsules and OTC products began.
- The contamination with each of these meds is primarily with N-nitrosodimethylamine (NDMA), a research chemical in the USA. It was previously used to make rocket fuel, but this practice has been discontinued. It is unintentionally formed during various manufacturing processes.
- NDMA has been shown to be harmful to the liver: high doses over several days and low levels over the long term can cause serious, noncancerous liver disease.
- Put concerns in perspective. The FDA estimated that if 8,000 people took the highest valsartan dose (320mg) containing NDMA from the recalled batches daily for four years, there might be one additional case of cancer over the lifetimes of those 8,000 people.

My Take: Imagine my chagrin (or was it heartburn?) in September to learn about NDMA. I'd spent 18 months getting myself off a PPI and on to "safer" ranitidine. (Yes, "fool for a patient".) For now, I'm sticking with Zantac, recalling that the bacon I consume every Saturday morning is also laced with NDMA.

Immunization Updates

Pprevnar 13: Reconsider giving this vaccine to seniors. Healthy immuno-competent adults 65 and older are protected by the herd immunity extended by immunizing kids with Pprevnar 13. The vaccine is safe in adults, but does not offer much benefit. The Number Needed to Immunize (NNI) to prevent one case of invasive pneumococcal disease per year is over 25,000! At \$190 a dose, that's \$4,750,000 to avoid one case of invasive pneumococcal illness. Healthy seniors should get a single dose of Pneumovax 23. Continue to immunize immune-compromised adults with both Pprevnar 13 and Pneumovax 23.

HPV: The Advisory Committee on Immunization Practices (ACIP) found that two doses of HPV have efficacy equal to the three-dose schedule for 9 to 14 year-olds. In October 2018, the FDA expanded the approved age range for 9vHPV use from 9 through 26 years to 9 through 45 years in women and men.

You may access previous issues at <https://www.rmhp.org/i-am-a-provider/provider-resources/publications-for-providers>.

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