

# The Prudent Prescriber

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### An Update: e-cigarettes

The CDC sprung some really good news on us recently. **Smoking rates among adults in the USA have fallen to 15%.** In the same week, the British added e-cigarettes to their stop smoking arsenal, the FDA promised new regulations for these same e-cigarettes and the American public health community was locked in a debate regarding the role of e-cigarettes.

#### Limitations of evidence

As you peruse this newsletter, keep the following skeptical analysis in mind, "The research field on e-cigarettes is characterized by: severe methodological problems, severe conflicts of interest, relatively few and often small studies, inconsistencies and contradictions in results, and a lack of long term follow-up." C. Pisinger BMC MED 2014; 12:226.

#### Epidemiology of smoking

As smoking prevalence rates have declined in the traditional markets of North America and Western Europe, the tobacco industry has refocused its promotional efforts onto the less developed and emerging nations in Africa, Asia, the Middle East, the former Soviet Union and Latin America. If current patterns continue, tobacco use will kill approximately 10 million people *every year* throughout the world by 2020; 70% of these deaths will occur in less developed and emerging nations.

Pharm Reps  $\neq$  Rational Prescribing  
(PR)  (RP)

Antibiotics do  
**NOT**

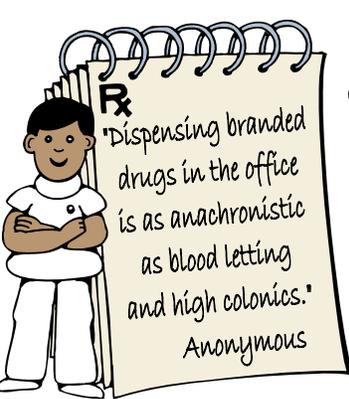


help  
acute bronchitis

**$\beta$ -blockers in  
post-MI  
save  
lives**



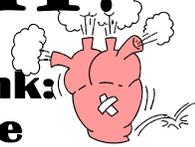
Pill splitters save  
BIG



## CHE?

Think:

- Ace
- Aldactone
- B-blocker
- Dig
- Diuretic



Avoid these expensive  
"me-too" drugs:

- Intermezzo
- Vimovo
- Livalo
- Pristiq
- Viibryd
- Edarbi
- Daliresp



Treat patients  
> 60 years to 150/90



**NOW AVAILABLE**  
ON THE  
**GENERIC MARQUEE**

Frova	→	frovatriptan
Voltaren gel	→	diclofenac Na 1% gel
Crestor	→	rosuvastatin
Nuvigil	→	armodafinil
Jalyn	→	dutasteride/tamsulosin
Ortho Tri-Cyclen Lo	→	Tri-Lo-Marzia,
Tri-Lo-Sprintec,	&	others

## E-cigarettes

### Anatomy and function

- ◆ The user activates the atomizer either by inhaling or by pressing a button, depending on the device. The atomizer heats and aerosolizes the liquid, creating a vapor that emulates, but is not tobacco smoke.
- ◆ The process simulates the experience of smoking a conventional cigarette, but no combustion occurs.
- ◆ The term "vaping" is used to distinguish the process from smoking a conventional cigarette.



### E-liquid components

Nicotine content can vary from none to 36mg/ml or higher (some up to 100mg/ml). Common nicotine concentrations are 6mg/ml, 12mg/ml, 18mg/ml and 24mg/ml. The level of nicotine measured by chemical analysis often has been found to be inconsistent with the manufacturer's product labeling.

Propylene glycol/glycerol/ethylene glycol are added to prevent drying out of the e-cig liquids and to create "smoke."

Flavoring increases the attractiveness of e-cigs to youths. Some 6000 flavors are available including candy, fruit soda and alcohol flavors.

Other compounds such as metals (lead, tin, nickel and chromium), nitrosamines, and volatile organic and phenolic compounds have been found in e-cig liquids and vapors.

### 1st Generation e-cigarettes



### 2nd Generation e-cigarettes



### 3rd Generation e-cigarettes



1<sup>st</sup> generation: mimic the size and shape of conventional cigarettes. Some are disposable.

2<sup>nd</sup> generation: larger than conventional cigarettes and are either pen style (medium size) or tank style (large size). They feature stronger rechargeable batteries that may have a switch or electronic circuits that allow users to regulate the frequency and length of puffs.

3<sup>rd</sup> generation: "personal vaporizers" Allow the user to adjust the resistance in the atomizer to produce higher heating temperatures. Longer lived batteries.



### Hookah pipes

- Originated in Persia and India
- Hookah pipes and Hookah bars are making a resurgence, particularly around college campuses.
- Modern hookah pipe smoking is done by indirectly heating specially made tobacco (often flavored), usually with burning embers or charcoal. The tobacco smoke is then filtered through water or other liquids and then drawn through a rubber hose to a mouth piece where it is inhaled.
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## Health Concerns

- Are hookahs similar to smoking cigarettes? Hookah pipe smokers smoke the water pipe longer (40-45 minutes) than cigarettes (5-10 minutes). Concern that exposure to nicotine and other carcinogens is greater. It is estimated that in a one hour smoking session the hookah smoker inhales 100-200 times the volume of smoke from a single cigarette. (CDC Hookahs, December 17, 2013)
- Hookah pipes are often passed around and shared mouthpieces are used. TB, herpes and hepatitis can be transmitted this way. (American Lung Association: Tobacco Policy Trend Alert, February 2007)

## What's in a name?

- There is concern that epidemiological surveys that have looked at e-cigarette use have not captured use of "hookah pens", "e-hookahs" and "vape pipes". The CDC admits that they asked the wrong questions.
- These devices have been shrewdly marketed to avoid the stigma associated with cigarettes of any kind.
- Sales of e-hookahs have grown exponentially in the last 18 months.
- Public health officials in Northern California convened a student advisory board to discuss how to approach "e-cigs". They said, "What's an e-cig?" She showed them what she meant. They said, "That's a vape pen."

## Prevalence and Patterns of e-cigarette use

- Take these data with a huge grain of salt. These numbers probably underestimate true use.
- In the US, the use of e-cigs by adults has increased from 3.3% in 2010 to 8.5% in 2013. (Nicotine Tob Res 2015; 17:219)
- The 2014 National Health Interview Survey revealed that 12.6% of adults had *ever* used an e-cig. The prevalence of *current* e-cig use was highest in current cigarette smokers (16%) and *former* smokers who had quit in the last year (22%). There was minimal use of e-cigs by *never* smokers (<1%).
- E-cig use in high school students increased from 1.5% in 2011 to 13.4% in 2014. Middle and high school students reported more current use of e-cigs than conventional cigarettes in 2014. (MMRW 2015:64:381)
- E-cigarette users are generally nondaily users. Only 5.3% of *ever* e-cigarette users report daily use. (AM J Prev Med 2013; 44:207)
- Most adult and adolescent regular users of e-cigarettes already smoke conventional cigarettes. (Addiction 2014; 109:1801)

## Adverse effects of e-cigarettes

- Experienced e-cigarette users tend to take longer puffs and use the devices more intensively than novice users. As a consequence they have higher blood nicotine levels that more closely resemble those achieved by smoking conventional cigarettes. With less experienced users, the nicotine delivered by e-cigarettes is consistently lower than nicotine delivered by conventional cigarettes. (Tob Control 2010: 19:98)
- Studies of chronic users of nicotine replacement products do **not** suggest that chronic nicotine exposure increases long term cardiopulmonary or cancer risk.

- E-cigarettes do not expose the user to many of the constituents of cigarette smoke (tars, oxidant gases and CO) that are responsible for many of the tobacco attributable diseases.
- Although it's likely that inhaling e-vapors is less likely to be harmful than inhaling cigarette smoke, the consequences of chronic inhalation of e-cigarette vapors is UNKNOWN!

### **E-cigarette poisoning in kids**

- Since the introduction of e-cigarettes, the number of calls to poison control centers has increased. There was an average of 1 e-cigarette call per month in the US in September 2010. That number increased to 215 calls per month by February 2014.
- Liquid nicotine is available in a variety of fragrances and flavors including bubblegum, chocolate and strawberry.
- No requirement for childproof caps.
- Symptoms of toxicity in kids: nausea, vomiting, diarrhea, salivation, weakness, hypertension and tachycardia. Because liquid nicotine is so concentrated, toxicity can occur with skin contact and absorption. (MMRW 2014; 63: 292-3)
- Just 1mg can cause symptoms in a toddler.
- 6-13mg/kg can be lethal in a child. (Arch Toxicol 2014;88:5-7)

### **Brits urge smokers to use e-cigarettes**

- The Royal College of Physicians in April 2016 summarized the science on e-cigarettes and concluded that their benefits far outweigh their harms.
- "This is the first genuinely new way of helping people stop smoking that has come along in decades. E-cigarettes have the potential to help half or more of all smokers get off cigarettes." John Britton, director of the U.K. Center for Tobacco and Alcohol Studies.
- American public health experts are divided in their response to U.K.'s decision.  
Stanton Glantz (UCSF), "These guys (British) are going off a cliff."

vs.

Warner (Univ Michigan School of Public Health), " The British are saying, Let's see how we can help the main smokers today, who by the way, are largely poor and less educated, and let's not focus so much on kids, who may or may not be sickened by this 40 years down the line."

### **What is the role of e-cigarettes in smoking cessation?**

- There are few randomized controlled studies that have evaluated e-cigarettes for smoking cessation.
- In 657 smokers wanting to quit, Bullen et al (Lancet 2013; 382:1692) found that at six months of follow-up, verified smoking cessation was similar in e-cigarette group with nicotine (7.3%), nicotine free e-cigarettes (4.1%) and nicotine patch (5.8%).
- A subsequent trial of 300 smokers not intending to quit compared two strengths of e-cigarettes and a placebo, no nicotine e-cigarette and found no differences in quit rates. (PLoS One 2013; 8:e66317)
- A 2016 meta-analysis (35 observational studies and 2 RCTs) calculated a 0.72 hazard ratio for smoking cessation among e-cigarette users, suggesting users of e-cigarettes were less likely to quit smoking than non-users of e-cigarettes. (Lancet Respir Med 2016 Jan13. pii: S2213-2600 (15)00521-4)

## Cost of e-cigarettes and real cigarettes

- E-cigarette starter kits with device, battery and several cartridges sell for \$12 – \$150.
- A pack of 5 cartridges (each cartridge equal to one pack of cigarettes) costs up to \$20. (online stores)
- At the Corner Stores in Grand Junction, VUSE brand, 10 different flavors, 2 cartridges go for \$4.99.
- “Real” cigarettes going for \$5-\$6 per pack at Safeway. Carton of Marlboros \$58.80.
- Bottom line: e-cigarette prices are about 1/2 to 2/3 of those of conventional cigarettes.

## Regulation of e-cigarettes

- Regulation of e-cig use is evolving.
- Manufacturers of e-cigs often market e-cigarettes as devices you can vape anywhere, but some jurisdictions have limited their use. As of January 2016, eight states and 475 municipalities have banned the use of e-cigarettes in areas where cigarette smoking is also completely banned. And an additional 16 states and 318 municipalities banned e-cigarette use in other venues.
- Australia, Israel, Brazil, Uruguay, Singapore and Mexico have banned e-cigs altogether.
- FDA will review all new tobacco products, starting August 8, 2016, that will:
  - ◆ Help prevent misleading claims by tobacco product manufacturers and placing health warnings on product packages and advertising.
  - ◆ Evaluate the ingredients of tobacco products and how they are made.
  - ◆ Will not allow “in person” or online sales to persons under age 18. Requiring a photo id.
- The regulation falls far short of what the AAP and the ACP had asked for: childproof caps on e-liquids, no flavors, increased taxes, and raising sales age to 21.

## My Take:

- ◆ The British decision to pay for e-cigarettes for smoking cessation is out of character with their usual tight upper lipped stance to underwrite only interventions that pass comparative effectiveness testing with flying colors. John Britton’s (U.K. Center for Tobacco) assertion that, “e-cigarettes have the potential to help half or more of all smokers get off cigarettes” has no evidence base that I can discover.
- ◆ Although a majority of U.S. e-cigarette users perceive e-cigarettes to be a tool to quit conventional cigarettes or reduce their risk of tobacco related disease, (Am J Prev Med 2013; 44: 207), there are no established protocols for using these devices.
- ◆ What “vaping” and hookahs portend for our teenagers is totally unknown. It has not helped that we didn’t ask the right questions.
- ◆ For now, it seems prudent to stick with smoking cessation techniques that are evidence-based. (See July 2016 Prudent Prescriber)

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