I have no financial disclosures or conflicts of interest to report
Quick Internal Medicine Topics

- Electronic cigarettes
- Aspirin for primary prevention of heart disease in elderly
- CBD oil
- How to get Fido on the plane at MSP
Topic 1: E-cigarettes

1. Are e-cigs safer than cigarettes and do they assist in smoking cessation?
2. What about the kids? Are e-cigs a potentially safer product for adolescents and young adults?

Is there evidence for any of this?
Electronic cigarettes and tobacco

- Adolescents - current use (high school)
  - Any tobacco product: 19.6% (2011 = 24.2%)
  - E-cigarettes: 11.7% (2011 = 1.5%)
  - Cigars: 7.7%
  - Cigarettes: 7.6% (2011 = 15.8%)
  - Smokeless tobacco: 5.5%

- Adults – current use
  - Any tobacco product: 10.2 – 27.7% (CA, WV)
  - Cigarettes: 8.0 - 21.7% (UT, WV)
  - E-cigarette: 1.3 – 4.4% (DE, WY)
Components of an electronic cigarette.

- Mouthpiece
- Heating element (atomiser) heats the “juice” to make vapour
- Cartridge (tank) holds the liquid “juice”
- Microprocessor
- Battery
- Many devices have a switch to activate the heating element
- Some devices have a light-emitting diode on the end to stimulate the glow of a burning cigarette

Source: Jamie Hartmann-Boyce et al. BMJ 2018;360:bmj.j5543
E-cigarettes and safety

What is known:

- E-cig nicotine levels can equal cigarette levels
- Carcinogen and toxin levels are lower

E-cigs are a safer alternative to combustible tobacco

- But long-term evidence is lacking
- Consensus opinion: perhaps only 5% as risky

E-cigs may help people quit, but data are poor

- RCT: 9% quit 6-12 month quite rate vs 4% control


Hartmann-Boyce J et al Electronic Cigarettes for Smoking Cessation, BMJ 2018;360:j5543
Safer for teens?

Major manufacturer website:

“*** was created to be a satisfying alternative to cigarettes. Learn about our mission to improve the lives of the world's one billion adult smokers.”

90% of e-cigs contain flavors that adolescents favor: mango, mint, fruit medley, cappuccino, strawberry

Do they become cigarette smokers?

Answer: 3.5x higher risk of initiating cigarettes (23.2% vs 7.2%)

Tips to tell your patients

• Smoking is deadly, and e-cigs may help you quit
• E-cigarettes are very likely safer than smoking, though we don’t have long-term safety data
• Other smoking cessation techniques (meds, NRT) are known to be safe and effective
• E-cigs should only be used in people who smoke cigarettes as an aid to quitting

• Kids who vape are at higher risk for starting smoking
Topic 2: Aspirin for primary prevention

Should healthy elderly people take aspirin to extend healthy lifespan?
ASPREE study

• ASPREE published NEJM on September 16, 1028
• Largest aspirin primary prevention trial ever done in elderly
• Randomized, double-blind controlled trial
• ~19,000 participants, 34 sites in Australia and US over 5 years
• Funded by US and Australia governments

Anne Murray, MD
US Principal Investigator, ASPREE trial
Hennepin Healthcare / Univ of Minnesota
Table 2. Composite Primary End Point, Including the Components, and Secondary End Points of Death, Dementia, Persistent Physical Disability, and Major Hemorrhage.*

<table>
<thead>
<tr>
<th>End Point</th>
<th>Aspirin (N = 9525)</th>
<th>Placebo (N = 9589)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
</tr>
<tr>
<td>Primary end point†</td>
<td>921</td>
<td>21.5</td>
<td>914</td>
<td>21.2</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>480</td>
<td>11.2</td>
<td>431</td>
<td>10.0</td>
</tr>
<tr>
<td>Dementia</td>
<td>274</td>
<td>6.4</td>
<td>275</td>
<td>6.4</td>
</tr>
<tr>
<td>Persistent physical disability</td>
<td>167</td>
<td>3.9</td>
<td>208</td>
<td>4.8</td>
</tr>
<tr>
<td>Secondary end points‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>558</td>
<td>12.7</td>
<td>494</td>
<td>11.1</td>
</tr>
<tr>
<td>Dementia</td>
<td>283</td>
<td>6.7</td>
<td>292</td>
<td>6.9</td>
</tr>
<tr>
<td>Persistent physical disability</td>
<td>188</td>
<td>4.9</td>
<td>224</td>
<td>5.8</td>
</tr>
<tr>
<td>Major hemorrhagic event</td>
<td>361</td>
<td>8.6</td>
<td>265</td>
<td>6.2</td>
</tr>
<tr>
<td>Clinically significant bleeding</td>
<td>312</td>
<td>7.4</td>
<td>225</td>
<td>5.3</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>49</td>
<td>1.2</td>
<td>40</td>
<td>0.9</td>
</tr>
</tbody>
</table>

* The 95% confidence intervals and P values were not adjusted for multiple comparisons.
† The primary end point was the first occurrence of any one of the three components (death from any cause, dementia, or persistent physical disability).
‡ For the secondary end points, all the participants who had an event at any time during the trial are counted. Other secondary end points included fatal and nonfatal cardiovascular disease, fatal and nonfatal cancer, mild cognitive impairment, and depression. Further results regarding the secondary end points of death, cardiovascular disease (including stroke), and major hemorrhage are reported in two accompanying articles in the *Journal.*

Effect of Aspirin on Disability-free Survival in the Healthy Elderly

HennepinHealthcare
ASPREE study

Primary outcome (composite death, dementia or disability)

No benefit with aspirin

8 secondary endpoints

Death from any cause  No benefit
(cancer = ~50%)

Dementia  No benefit

Permanent physical disability  No benefit

CV disease, including stroke  No benefit

Cancer

Mild cognitive impairment

Depression

Major hemorrhage
ASPREE study

For healthy people >70 years old
(> 65 years old for US blacks & Latinos)

• Bottom line: there is no benefit in taking daily aspirin
• Applies to healthy people:
  No significant heart or cerebrovascular disease
  No venous thromboembolic disease
  No dementia
• The risk of major bleeding is 38% higher in ASA patients
  (3.8% vs 2.8%, p<0.001)
• Trial stopped a few months early due to lack of benefit and increased risk
Take home point

Daily low dose aspirin does not prolong disability-free survival in healthy elderly people

Note: Should you tell those already taking ASA to stop? This trial can’t answer that
Read the ASPREE trials

McNeil JJ, et al Effect of Aspirin on Disability-free Survival in the Healthy Elderly, NEJM, September 16, 2018

Topic 3: Cannabidiol (CBD)

Is CBD beneficial for any health condition and is it safe?
Cannabidiol (CBD)

Major substances in cannabis (>100 in total)

**Tetrahydrocannabinol (THC) = Psychoactive**
Many studies have shown benefits for seizures, anorexia, nausea, pain

**Cannabidiol (CBD) = NOT psychoactive = no high**
Lack of research
Was thought to be inactive
CBD: what we know

Regulatory

- DEA moved from Schedule 1 to Schedule 5 September 2018 for specific fixed-dose formulation
- The raw hemp/cannabis is still Schedule 1
- FDA-approved June 2018 for single indication: seizures due to Lennox-Gastaut Syndrome and Dravet Syndrome
- Murky legality (Federal vs state laws)
- May not be called a “dietary” or “nutritional” supplement, it is a drug

Low abuse potential

Even among polydrug users


Schoedel KA et al Abuse potential assessment of cannabidiol (CBD) in recreational polydrug users: A randomized, double-blind, controlled trial. Epilepsy Behav. 2018 Oct 1;88:162-171
CBD uses: what is claimed

- Seizures (strongest evidence)
- Anxiety, esp social anxiety (some evidence)
- Inflammation (some evidence)

The rest of the potential uses do not have strong human studies

- Depression, pain, nausea and vomiting, sleep disorders, acne and other skin conditions, multiple sclerosis, arthritis, fibromyalgia, cancer symptoms . . .
CBD uses: what is not known

- Long-term effects
- Efficacy / benefit in high-quality human trials for any of the claimed conditions
- Where the regulatory environment is going

- The actual CBD content of products on the market (next slide)

Table 1. Label Accuracy by Cannabidiol Extract Type

<table>
<thead>
<tr>
<th>Cannabidiol Extract Products</th>
<th>Oil (n = 40)</th>
<th>Tincture (n = 20)</th>
<th>Vaporization Liquid (n = 24)</th>
<th>Total (N = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Label accuracy, No. of products (%) [95% CI]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accurate*</td>
<td>18 (45.00)</td>
<td>5 (25.00)</td>
<td>2 (12.50)</td>
<td>26 (30.95)</td>
</tr>
<tr>
<td>[30.71-60.17]</td>
<td>[11.19-46.87]</td>
<td>[55.10-88.00]</td>
<td>[4.34-31.00]</td>
<td>[22.08-41.49]</td>
</tr>
<tr>
<td>Under*</td>
<td>10 (25.00)</td>
<td>8 (40.00)</td>
<td>18 (75.00)</td>
<td>36 (42.85)</td>
</tr>
<tr>
<td>[14.19-40.19]</td>
<td>[21.88-61.34]</td>
<td>[55.10-88.00]</td>
<td>[4.34-31.00]</td>
<td>[32.82-53.53]</td>
</tr>
<tr>
<td>Over†</td>
<td>12 (30.00)</td>
<td>7 (35.00)</td>
<td>3 (12.50)</td>
<td>22 (26.19)</td>
</tr>
<tr>
<td>[18.07-45.43]</td>
<td>[18.12-56.71]</td>
<td>[4.34-31.00]</td>
<td>[17.98-36.48]</td>
<td></td>
</tr>
<tr>
<td>Labeled concentration, mg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>56.15 (42.3-98.07)</td>
<td>11.14 (5.60-16.60)</td>
<td>26.15 (12.50-39.74)</td>
<td>36.86 (16.21-57.51)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>22.26 (2.50-800.00)</td>
<td>8.33 (1.33-50.00)</td>
<td>18.33 (2.00-160.00)</td>
<td>15.00 (1.33-800.00)</td>
</tr>
</tbody>
</table>

Deviation of labeled content from tested value, mg/mL:

<table>
<thead>
<tr>
<th>Cannabidiol Extract Products</th>
<th>Oil (n = 40)</th>
<th>Tincture (n = 20)</th>
<th>Vaporization Liquid (n = 24)</th>
<th>Total (N = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (95% CI) [% of deviation]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannabidiol</td>
<td>10.34 (4.95-15.74)</td>
<td>3.94 (2.74-5.14)</td>
<td>11.52 (8.10-14.94)</td>
<td>9.16 (4.96-13.36)</td>
</tr>
<tr>
<td>[29.01]</td>
<td>[220.62]</td>
<td>[1098.70]</td>
<td>[380.26]</td>
<td></td>
</tr>
<tr>
<td>Median (range) [% of deviation]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannabidiol</td>
<td>2.76 (0.13-144.73)</td>
<td>1.48 (0.01-22.30)</td>
<td>4.62 (0.14-66.07)</td>
<td>3.17 (0.10-144.73)</td>
</tr>
<tr>
<td>[12.11]</td>
<td>[19.12]</td>
<td>[67.34]</td>
<td>[20.42]</td>
<td></td>
</tr>
</tbody>
</table>

Note: * Cannabidiol content tested within 10% of labeled value.
† Cannabidiol content exceeded labeled value by more than 10%.
* Cannabidiol content tested more than 10% below labeled value.

Table 2. Observed Cannabinoid Concentration of 84 Tested Extract Products Sold Online

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>Average Observed Concentration Across Tests, mg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabidiol*</td>
<td>30.96 (80.86)</td>
</tr>
<tr>
<td>Cannabidiolic acid</td>
<td>1.35 (6.74)</td>
</tr>
<tr>
<td>Cannabigerol</td>
<td>0.08 (0.55)</td>
</tr>
<tr>
<td>Cannabinol</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Δ-9-Tetrahydrocannabinol</td>
<td>0.45 (1.18)</td>
</tr>
<tr>
<td>Δ-9-tetrahydrocannabinolic acid</td>
<td>0 (0-0)</td>
</tr>
</tbody>
</table>

* The mean labeled concentration for cannabidiol was 36.86 mg/mL (SD, 96.56) and the median was 15.00 mg/mL (range, 1.33-800.0).
CBD oil shows promise treating a variety of conditions, but data for efficacy and long-term safety is lacking.

Few adverse effects and low abuse potential are encouraging.

Marketing and manufacturing of CBD products is unregulated and potentially of concern for our patients.
Topic 4: Getting Fido on the plane at MSP

What are emotional support animals (ESA) and what is the clinician’s role in authorizing air travel for ESAs?

Photo: Megan Peabody via Instagram hamlet_the_beach_hog. Used by permission.
Animals in mental health

Animal-assisted therapy

Accepted as having benefit in clinical & institutional settings.
Ex: Dog-assisted therapy reduces symptoms of depression in institutionalized elderly

Service-animals, mostly dogs and miniature horses

“. . . service animal includes individually trained animals that do work or perform tasks for the benefit of individuals with disabilities, including psychiatric, cognitive, and mental disabilities.”
(ada.gov)

By Pete Markham from Loretto, USA (Big and Little) [CC BY-SA 2.0 (https://creativecommons.org/licenses/by-sa/2.0)], via Wikimedia Commons for public use.
Emotional support animals

Potentially competing interests:

- Legitimate ESA needs
  - Bunny for child with autism
  - Variety of animals for anxious flyers

- Pet-handling fees
  (MSP-LAX for 40# pig = $456)

- Comfort and safety of other travelers

Photo: dexterthepeacock via JetSetTV
Here’s what you need to do . . .

Emotional Support/ Psychiatric Service Animal Request
Medical/Mental Health Professional Form

Please fill out and return the following through a service request at delta.com/mytrips. It must be completed by medical or mental health professional and submitted no less than 48 hours prior to first flight on a customer’s itinerary.

### Customer Full Name or SkyMiles number:

<table>
<thead>
<tr>
<th>I am a licensed medical/mental health professional treating the customer’s mental or emotional disability. (Mark check box to confirm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I certify that the customer has a mental health related disability listed in the Diagnostic and Statistical Manual of Mental Disorders and is under my care. (Mark check box to confirm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
</tr>
</tbody>
</table>

Source: Delta Airlines via delta.com
And if that fails . . . just get this guy to do it
Thank you!

David.Hilden@hcmmed.org