



Just Breathe and Reset: Rethinking Community-Acquired Pneumonia, Asthma, and Smoking Cessation

**GMCCP Winter/Spring Educational Session
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There is no CAP to Your Knowledge: A Review of the Community Acquired Pneumonia Guidelines

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Disclosures

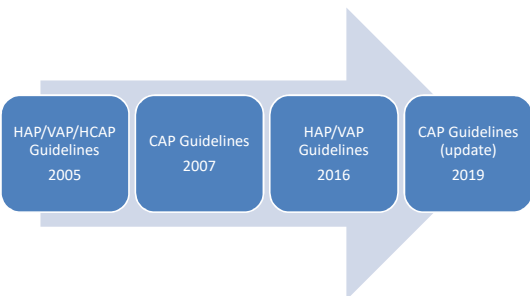

- I have no conflicts of interest to disclose




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Objectives

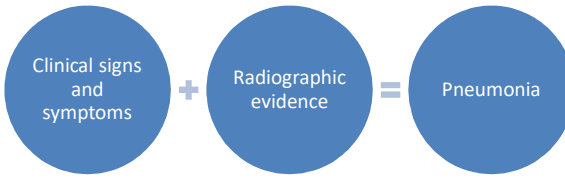
- Identify updates to the IDSA/ATS Community Acquired Pneumonia (CAP) guidelines that impact clinical practice in both inpatient and outpatient settings
- Select an optimal antibiotic regimen for treatment of CAP in various clinical scenarios




HAP: Hospital acquired pneumonia
VAP: Ventilator associated pneumonia
HCAP: Healthcare associated pneumonia



CAP Diagnosis




Mandell LA. Clin Infect Dis. 2007;44:827-72.



CAP Microbiology


- Bacterial pathogens
 - *Streptococcus pneumoniae*
 - *Haemophilus influenzae*
 - *Staphylococcus aureus*
 - *Mycoplasma pneumoniae*
 - *Legionella spp.*
 - *Chlamydia pneumoniae*
- Multi-drug resistant Gram-negative bacteria (including *Pseudomonas aeruginosa*)
- Viral pathogens
 - Rhinovirus
 - Human metapneumovirus
 - Influenza
 - Respiratory syncytial virus
 - COVID-19
- Emerging threats
 - Methicillin-resistant *Staphylococcus aureus* (MRSA)



Mellay JP. Am J Respir Crit Care. 2019; 200(7): e45-e67.

Diagnostic Tests


- Blood and respiratory cultures
 - Not routinely recommend in the outpatient setting
 - Recommended for antibiotic optimization in the inpatient setting
- *Legionella* and Pneumococcal urinary antigen testing
- Influenza molecular testing (NAAT)
- Serum procalcitonin



Mellay JP. Am J Respir Crit Care. 2019; 200(7): e45-e67.


Serum Procalcitonin

- NOT recommended to differentiate viral vs. bacterial etiology amongst patients with confirmed CAP based on diagnostic criteria
 - Sensitivity has been reported to be 38 to 91%
 - Self WH et al. reported that a procalcitonin cutoff of 0.1 ng/mL had a sensitivity of 80.9% to identify bacterial pathogens
 - “No procalcitonin threshold perfectly discriminated between viral and bacterial pathogens.”



Mellay JP. Am J Respir Crit Care. 2019; 200(7): e45-e67. Self WH. Clin Infect Dis. 2017; 65(2): 188-195.


EMPIRIC ANTIBIOTIC SELECTION



Outpatient Setting

<p>No comorbidities or risk factors for MDROs</p> <ul style="list-style-type: none"> Amoxicillin 1 g three times daily Doxycycline 100 mg twice daily Alternative: Azithromycin 500 mg on day 1 then 250 mg daily* <p><small>*only if pneumococcal resistance to macrolides is <20%</small></p>	<p>Presence of comorbidities</p> <ul style="list-style-type: none"> Amoxicillin/clavulanate OR 2nd or 3rd generation cephalosporin + Azithromycin OR doxycycline Moxifloxacin, levofloxacin, or gemifloxacin
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Comorbidities: chronic heart failure, lung, liver, or renal disease, diabetes, alcoholism, malignancy or asplenia



Mellay JP. Am J Respir Crit Care. 2019; 200(7): e45-e67.

Supporting Evidence

- Evidence is lacking
- Sixteen randomized control trials evaluated
 - No clear difference in clinically significant outcomes amongst different antibiotic groups
- Macrolide monotherapy no longer recommend first-line
 - Studies showing treatment failure due to antibiotic resistance
 - *Streptococcus pneumoniae* resistance to macrolides is reported to be >30% in the US




Mellay JP. Am J Respir Crit Care. 2019; 200(7): e45-e67.

Knowledge Application

What antibiotic regimen would you select for the following patients diagnosed with community acquire pneumonia being treated in the outpatient setting?

- WG who is a 76 year old female with PMH including dementia, HTN, and hypothyroidism and no known medication allergies/intolerances.
- JR who is a 33 year pregnant female with no PMH and no known medication allergies/intolerances.
- MJ who is an 82 year old male with PMH including COPD, CHF, DM2, and Afib who has no known medication allergies/intolerances. He is currently taking dofetilide and his most recent EKG had a QTc of 495.
- AP who is an 45 year old male with PMH including alcoholic cirrhosis who reports an anaphylaxis reaction to amoxicillin 3 years ago.



Inpatient Setting

Non-severe CAP with no risk factors for MRSA or *P. aeruginosa*

Ampicillin/sulbactam, cefotaxime, ceftriaxone, or ceftaroline
+
Azithromycin or clarithromycin*


Levofloxacin or moxifloxacin

*can use doxycycline in place of azithromycin

Severe CAP with no risk factors for MRSA or *P. aeruginosa*

Ampicillin/sulbactam, cefotaxime, ceftriaxone, or ceftaroline
+
Azithromycin or clarithromycin

Ampicillin/sulbactam, cefotaxime, ceftriaxone, or ceftaroline
+
Levofloxacin or moxifloxacin




Mellay JP. Am J Respir Crit Care. 2019; 200(7):e45-e67.

Supporting Evidence

- Decision to NOT include beta-lactam monotherapy as a treatment option

Garin N et al.	Multicenter, non-inferiority, randomized trial	Beta-lactam + macrolide (BLM) vs. beta-lactam monotherapy (BL)	Patients not meeting criteria for clinical stability at day 7	BL 41.2% vs. BLM 33.6%; did NOT meet non-inferiority criteria
Wei N et al.	Systematic review and meta-analysis	Prospective and retrospective studies comparing BLM vs. BL	Mortality	BLM vs. BL mortality (OR 0.67, 95% CI 0.61-0.73, P<0.001)
Horita N et al.	Systematic review and meta-analysis	Randomized controlled trials and observational studies comparing BLM vs. BL	All-cause mortality	BLM vs. BL all cause mortality (OR 0.8, 95% CI 0.69-0.92, p=0.002)




Garin N. JAMA Intern Med. 2014; 174(2):218-24. DOI: 10.1001/2013.2184.
Wei N. J Antimicrob Chemother. 2014; 68: 2441-2446. DOI: 10.1093/acq/kqk214.
Horita N. Respirology. 2015; 20: 1319-1326. DOI: 10.1111/resp.12500.

Inpatient Setting

Presence of risk factors for MRSA and *P. aeruginosa*

MRSA: vancomycin or linezolid


***P. aeruginosa*:** piperacillin/tazobactam, cefepime, ceftazidime, aztreonam, meropenem, imipenem



Mellay JP. Am J Respir Crit Care. 2019; 200(7):e45-e67.

Determining Risk Factors


- No longer recommended to use classification of healthcare-associated pneumonia
- Recommend to identify "locally validated risk factors"
- Risk factors identified in literature
 - Previous isolation of the multi-drug resistant organism in the past year
 - Recent hospitalization and receipt of parenteral antibiotics in the last 90 days



Mellay JP. Am J Respir Crit Care. 2019; 200(7):e45-e67.

Antibiotic De-escalation

- Tailor antibiotic therapy to identified pathogens
- MRSA nasal PCR
 - Dangerfield et al. reported sensitivity of 88.0% and specificity of 90.1% resulting in negative predictive value (NPV) of 99.2%
 - Parente et al. performed a meta-analysis and determined a pooled sensitivity and specificity of 85% and 92.1% and NPV 98.1% for CAP/HCAP
- Antibiotic de-escalation with negative culture data at 48 hours
- Parenteral to oral transition



Mellay JP. Am J Respir Crit Care. 2019; 200(7):e45-e67.
Dangerfield R. Antimicrob Agents Chemother. 2014; 58(2):519-524. DOI: 10.1128/AAC.1211-13.
Parente RM. Clin Infect Dis. 2018; 67(1):1-7.

Aspiration Pneumonia

- Adding anaerobic coverage is not routinely recommend
 - Exception: patients with lung abscess or empyema
- Aspiration of gastric contents results in aspiration pneumonitis
 - Resolution of symptoms within 24-48 hours without need for antibiotics
- Anaerobic organisms have not been identified as a major etiology of pneumonia resulting from acute aspiration events



Mellay JP. Am J Respir Crit Care Med. 2019; 200(7):e45-e47.
Eisold DA. Am J Respir Crit Care Med. 2020;191:2650-2654.

Duration of Therapy

- Continue antibiotic therapy for a minimum of 5 days and until clinical stability is achieved
- Clinical stability:
 - Resolution of vital sign abnormalities (heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature)
 - Ability to eat
 - Normal mentation
- Duration of 7 days is recommended for presumed or confirmed MRSA or *P. aeruginosa* pneumonia



Mellay JP. Am J Respir Crit Care Med. 2019; 200(7):e45-e47.

Supporting Evidence

Less is More

Study design	Multicenter, noninferiority randomized clinical trial
Patient population	Adult hospitalized patients diagnosed with CAP <ul style="list-style-type: none"> • Exclusions: immunocompromised, MRSA or <i>P. aeruginosa</i> pneumonia, hospitalization in the past 14 days, extrapulmonary infection
Intervention	Randomized to an intervention and control group: <ul style="list-style-type: none"> • Intervention: duration of therapy based on guidance from Infectious Diseases Society of America/American Thoracic Society guidelines • Control: duration of therapy determined by physicians
Outcomes	Clinical success at day 10: Control 48.6% vs intervention 56.3% (p= 0.18) Clinical success at day 30: Control 88.6% vs intervention 91.9% (p= 0.33) Mean CAP-related symptoms score at day 5: Control 24.7 vs. intervention 27.2 (p=0.10)
Conclusion	The IDSA/ATS guidance on duration of therapy for CAP is appropriate and can be safely implemented into practice.



Uranga A. JAMA Intern Med. 2016;176(10):1257-1265.

Summary

	Cultures	Procalcitonin	HCAP Definition	Outpatient Treatment
2007 Guidelines	Respiratory and blood cultures recommended mainly for severe CAP	Procalcitonin not addressed	Accepted to be used per IDSA HAP/VAP/HCAP guidelines	Macrolide monotherapy recommended
2019 Guidelines	Respiratory and blood cultures also recommended in patients empirically treated for MRSA or <i>P. aeruginosa</i>	Procalcitonin not recommended to be used to determine whether or not antibiotics should be initiated	Recommended to be abandoned	Macrolide monotherapy no longer recommended first line



Mellay JP. Am J Respir Crit Care Med. 2019; 200(7):e45-e47.

Knowledge Application

GO is a 77 year old male with past medical history of severe COPD, HTN, DM2, and CAD s/p 2vCABG in 2015. GO has had two hospital admissions over the past 3 months. His most recent admission was 12/15-12/30 and he spent 4 days in the ICU and received cefepime for treatment of pneumonia.

He presents to the hospital on 1/15 with shortness of breath, worsening cough with thick sputum production and fever to 101.3. Patient was brought from his nursing home and his caretakers reported as aspiration event while eating dinner the day before his symptoms started. In the ED he is intubated due to his acute respiratory failure and admitted to the medical ICU. CXR reveals left lower lobe and right middle lobe consolidations concerning for pneumonia. Tracheal aspirate is collected for culture and ceftriaxone, metronidazole, and azithromycin are started for empiric treatment of community acquired pneumonia.



Knowledge Application

Ht 6'3" Wt 95 kg Allergies: none known

Vitals:

BP 86/62 mmHg @ 0100 HR 120 bpm T 101.4 F

BP 92/76 mmHg @ 0600 HR 92 bpm T 99.6 F

BP 98/78 mmHg @ 1000 HR 110 bpm T 98.6 F

Pertinent labs:

ScR 1.4 mg/dL

WBC 16.7 x 10³/L

Infectious work-up:

12/16 sputum cx: 3+ Pseudomonas aeruginosa

1/15 tracheal aspirate cx: pending

1/15 Nasal MRSA NAAT: negative

1/15 atypical NAAT: pending



Knowledge Application

Would you recommend any changes to the patient's empiric antibiotic regimen. If so, what would you recommend?



Knowledge Application

1/18: Patient has been transferred to the medicine unit and the team is preparing him for discharge.

Vitals:

1/18: BP 112/82 mmHg HR 88 bpm T 98.6 F RR 20 rpm

Oxygen saturation 96% on baseline 2L O2 requirement

Pertinent labs:

WBC $8.7 \times 10^3/L$

Infectious work-up:

1/15 tracheal aspirate cx: *Haemophilus influenzae* (beta-lactamase positive)

1/15 Nasal MRSA NAAT: negative

1/15 atypical NAAT: negative for all pathogens



Knowledge Application

What antibiotic regimen would you recommend for discharge?

What duration of antibiotic therapy would you recommend?



NEW ANTIBIOTICS FOR CAP TREATMENT



Lefamulin

- FDA approved for adults with CAP in August 2019
- Spectrum of activity
 - *Streptococcus pneumoniae*
 - *Moraxella catarrhalis*
 - *Haemophilus influenzae*
 - *Staphylococcus aureus* (including MRSA)
 - Atypical bacteria



Lefamulin (Xarelta) for injection [package insert] Prussia, PA: Nabriva Therapeutics US, Inc.; 2019.

Lefamulin

- LEAP-1 study: lefamulin was non-inferior to moxifloxacin +/- linezolid for seven day treatment course for CAP
- LEAP-2 study: lefamulin 5 day course was non-inferior to moxifloxacin 7 day course for treatment of CAP
- Limitations
 - QT prolongation
 - Drug interactions
 - Teratogenicity



Lefamulin (Xarelta) for injection [package insert] Prussia, PA: Nabriva Therapeutics US, Inc.; 2019.
Schwarz, et al. JAMA. 2019; 322(17):1661-1671.
Fitz TM, et al. Clinical Infectious Diseases. 2019; cdoi:10.1093/cid/ciz000:1-12.

Omadacycline

- FDA approved for adults with CAP and skin and soft tissue infections in October 2018
- Broad spectrum of activity
 - Gram-positive bacteria
 - Gram-negative bacteria
 - Anaerobes
 - Atypical bacteria



Omadacycline (Nayra) for injection (package insert). Boston, MA: Paratek Pharmaceuticals, Inc.; 2018.

Omadacycline

- OPTIC study: omadacycline found to be noninferior to moxifloxacin for treatment of CAP
- Limitations
 - Broader than necessary spectrum of activity
 - Mortality rate higher in omadacycline arm in OPTIC study
 - Tetracycline class effects



Omadacycline (Nayra) for injection (package insert). Boston, MA: Paratek Pharmaceuticals, Inc.; 2018. Sims R. N Engl J Med. 2019;380:517-527.

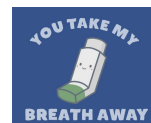
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Updates in the Treatment of Asthma: They'll Take your Breath Away

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Disclosures

- I have no conflicts of interest to disclose



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Learning Objectives

1. Discuss updates to the Stepwise Approach for Managing Asthma, specifically recommendations for use of inhaled corticosteroids and long-acting antimuscarinic antagonists (LAMAs) in the treatment of asthma
2. Describe updated recommendations for indoor allergen mitigation in the management of asthma
3. Summarize changes to the role of subcutaneous and sublingual immunotherapy in the management of allergic asthma




Asthma – What’s New?

- Landmark changes to GINA 2019
 - Controller vs reliever therapy
 - SYGMA, NOVEL-START, and Practical Trials
- NHLBI 2020 Focused Updates (December 2020)
 - Controller vs reliever therapy
 - Allergen mitigation
 - Immunotherapy



GINA 2019 Milestone Changes

- SABA-only treatment for Step 1 no longer recommended
- Symptom-driven or regular low dose ICS-containing controller treatment now recommended
 - Population-level risk reduction strategy
- GINA recommends budesonide or beclomethasone as the inhaled corticosteroid in the ICS-LABA, and formoterol as the long-acting beta agonist
 - Symbicort (budesonide-formoterol)



GINA 2020 Updates

Box 3-5A
Adults & adolescents 12+ years

Personalized asthma management:
Assess, Adjust, Review response


Asthma medication options:
Adjust treatment up and down for individual patient needs

Confirmation of diagnosis if necessary:
Symptom control & modifiable risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient goals

Treatment of modifiable risk factors & comorbidities:
Non-pharmacological strategies
Education & skills training
Asthma medications



STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
<p>PREFERRED CONTROLLER As-needed low dose ICS-formoterol* Low dose ICS taken whenever SABA is taken †</p>	<p>Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol* Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA is taken †</p>	<p>Low dose ICS-LABA Medium dose ICS, or low dose ICS+LTRA ‡</p>	<p>Medium dose ICS-LABA High dose ICS, or low dose ICS+LTRA ‡</p>	<p>High dose ICS-LABA Add low dose add-on therapy, e.g. tiotropium, anti-IgE, anti-IL5/5R, anti-IL4/13R</p>
<p>PREFERRED RELIEVER As-needed short-acting β₂-agonist (SABA)</p>	<p>As-needed low dose ICS-formoterol* As-needed short-acting β₂-agonist (SABA)</p>	<p>As-needed low dose ICS-formoterol †</p>	<p>As-needed low dose ICS-formoterol †</p>	<p>As-needed low dose ICS-formoterol †</p>

* Consider use only with budesonide-formoterol (Symbicort)
† Off-label; separate or combination ICS and SABA inhalers
‡ Consider adding LAMA (LTRA) for asthmatic patients with allergic rhinitis and FEV₁ >70% predicted




Why the Change?

- Over-use of SABA linked with increased risk of death
- Improved QOL and protective effect with ICS therapy
- Low ICS adherence (25-35%)
- Symptom relief vs asymptomatic daily therapy

Why budesonide/formoterol?


- Formoterol widely available with ICS, SABA not
- Formoterol onset of action shorter than salmeterol
 - Formoterol: 1 to 4 minutes
 - Salmeterol: 10 to 30 minutes
- Evidence is based on studies specific to budesonide/formoterol

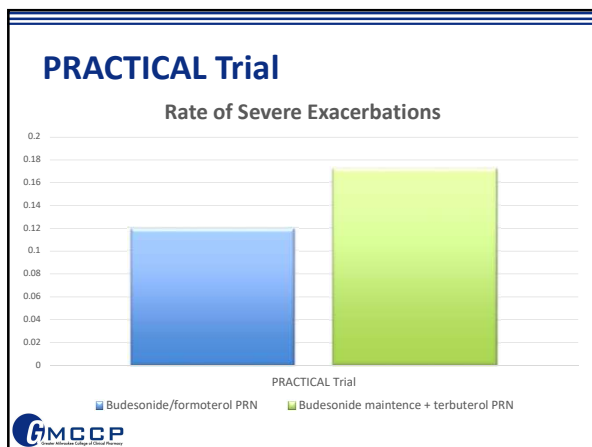
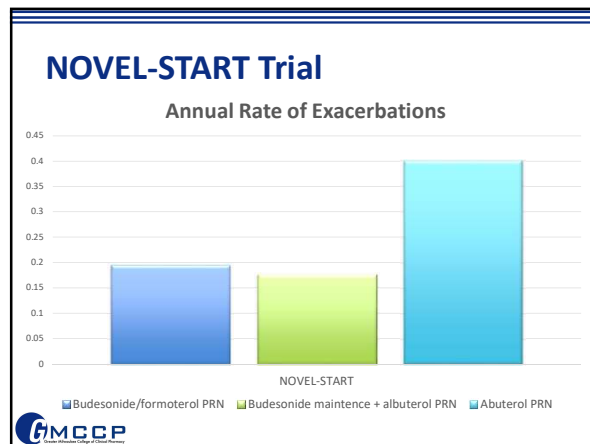
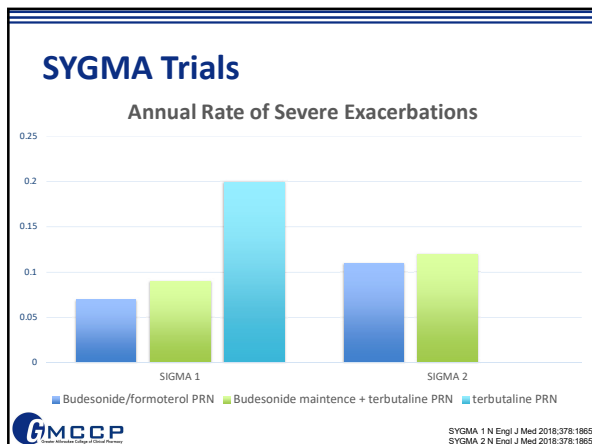


Evidence

SIGMA TRIALS → NOVEL-START TRIAL → Practical Trial

- Good evidence to support daily ICS therapy
- PRN budesonide/formoterol as effective as daily ICS in the prevention of severe exacerbations
- Daily ICS therapy better at symptom control





Major Asthma Updates

Gina 2019/2020 Updates

- PRN ICS/formoterol added as controller for Step 1
 - No previous controller option
 - Only reliever therapy with PRN SABA
- Addition of PRN ICS/formoterol to Step 2
 - Maintains daily low-dose ICS as controller

NHLBI 2020 Focused Updates

- No changes to Step 1 therapy
- Addition of PRN low dose ICS and SABA used concomitantly for Step 2
 - Alternative preferred therapy remains with daily low-dose ICS and PRN SABA
- Daily and PRN ICS/formoterol preferred for Steps 3 and 4

NHL Asthma management guidelines: Focused updates 2020. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2020. Available from: www.giaasthma.org

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines

Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6*
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS/formoterol*	Daily and PRN combination medium-dose ICS/formoterol*	Daily medium-high dose ICS-LABA + LAMA and PRN SABA*	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative	Daily LTRA† and PRN SABA or Cromolyn,† or Nedocromil,† or Theophylline,† and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, or daily LTRA,† and PRN SABA or Daily low-dose ICS + Theophylline,† or Zileuton,† and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA*	Daily medium-high dose ICS + LTRA,† or daily medium-dose ICS + Theophylline,† or daily medium-dose ICS + Zileuton,† and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,† and PRN SABA	

Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals >5 years of age whose asthma is controlled at the initiation, built up, and maintenance phases of immunotherapy.*

Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL13/4/7)*

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

- First check adherence, inhaler technique, environmental factors, 4 and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks
- Step down if possible (if asthma is well controlled for at least 3 consecutive months)
- Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Assess Control

Step-up Preferred Asthma Therapy Ages 12+

Asthma Severity	Step	Preferred Therapy	
Intermittent	1	PRN SABA	
Persistent	Mild	2	Daily low-dose ICS and PRN SABA Or PRN ICS and SABA
	Moderate	3	Daily and PRN low-dose ICS/formoterol (SMART)*
		4	Daily and PRN medium-dose ICS/formoterol (SMART)*
	Severe	5	Daily medium to high-dose ICS/LABA plus LAMA and PRN SABA
		6	Daily high-dose ICS/LABA plus oral systemic corticosteroids and PRN SABA

* Single maintenance and reliever therapy (SMART)

Step up Therapy

- Step 1 (intermittent asthma):
 - No recommended change in PRN SABA therapy
- Step 2 (mild persistent asthma) recommendations:
 - Daily low-dose ICS plus PRN SABA therapy or PRN concomitant ICS and SABA therapy
- Steps 3-4 (moderate persistent asthma):
 - Single maintenance and reliever therapy (SMART) therapy
- Step 5 (severe persistent asthma):
 - Addition of LAMA to ICS/formoterol



SMART Therapy

- Recommended in ages 12 and older with moderate persistent asthma (steps 3 and 4)
- SMART has been reported only with ICS/formoterol
 - Should not be used as reliever in combination with ICS-salmeterol maintenance therapy
- Dosing: 1 to 2 puffs once to twice daily and 1-2 puffs every 4 hours PRN for asthma symptoms
 - Maximum of 12 total puffs/day (54 ug)



PRN ICS/formoterol Concerns

- Potential for increased copays
- Off label use?
- Insurance coverage with 2 different ICS/LABA inhalers? (GINA)
- Expiration dates
 - Symbicort expires 90 days after opening foil package
 - Albuterol typically expires 12 months after opening packaging



Long-Acting Muscarinic Antagonist (LAMA) Recommendations

- ICS/LABA > ICS/LAMA
- Addition of LAMA to ICS/LABA therapy is recommended for step 5 (moderate-severe persistent asthma) in ages 12+
- Use of LAMA in step 6, not addressed in update
- Do not use in patients with or at risk of urinary retention or glaucoma
- Tiotropium is currently the only LAMA FDA approved for use in asthma



NHL Asthma management guidelines. Focused updates 2020.

Application

- 13 year-old presents to the clinic with complaints of cough, wheezing, and chest tightness on and off for the past 3 months
- He has no chronic conditions and takes no daily medications

Assessment	Description
Symptoms:	Patient reports symptoms most days Reports night-time awakenings about once per week
Spirometry:	Demonstrates FEV1/FVC of 81% and a FEV1 that is 72% of predicted
Severity:	Moderate-persistent asthma – Step 3

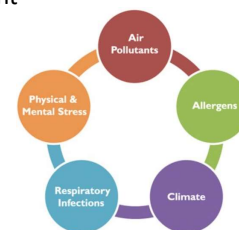
- Based on both GINA 2020 and the updated NHLBI guidelines, what is the preferred therapy?

- Daily and PRN Low dose ICS/formoterol
- Daily and PRN Low dose ICS/LABA
- Daily Low dose ICS and LTRA plus SABA PRN
- Daily Medium dose ICS plus PRN SABA



Allergy Mitigation

- Environmental assessment for exposure to allergens
 - History of symptoms on exposure
 - Evidence of sensitization
 - Allergy skin testing
 - Allergen-specific immunoglobulin E



Cloutier MM, Dixon AE, Krishnan JA, Lemanske RF, Pace W, Schatz M. Managing Asthma in Adolescents and Adults: 2020 Asthma Guidelines Update From the National Asthma Education and Prevention Program. JAMA. 2020;324(20):2004-2017.

Allergy Mitigation

- Recommended only in individuals with exposure and relevant sensitivity or symptoms
- If used, should be allergen specific and include multiple allergen-specific mitigation strategies

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Allergy Mitigation

- Dust mites
 - Recommend impermeable pillow/mattress covers **only** as part of a multicomponent allergen-specific mitigation intervention

Mitigation Strategies	
• Impermeable pillow and mattress covers	• High-energy particulate air (HEPA) filter–equipped vacuum cleaner
• Carpet and curtain removal	• Pest management/cleaning products

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Allergy Mitigation

- Rodents and/or cockroaches
 - Integrated pest management including:
 - Measures to block infestation (eg, filling holes in walls, reducing standing water)
 - Abatement (eg, traps, fumigation)
- Mold
 - HEPA purifiers/air filtration and mold abatement

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Application

A 20-year-old patient presents to the clinic for asthma follow-up. She has recently undergone allergy testing that has confirmed a sensitization to dust mite exposure. According to the updated NHLBI guidelines, which allergen mitigation strategies should be recommended to the patient?

- Mattress and pillow covers
- HEPA vacuum cleaners
- Integrated pest management, such as acaricides
- Carpet removal, if possible
- All of the above

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Subcutaneous and Sublingual Immunotherapy

- Subcutaneous immunotherapy (SCIT) is recommended as adjunct therapy in patients with all of the following:
 - Individuals aged 5 years or older
 - Mild to moderate persistent asthma (steps 2-4)
 - Symptoms and sensitization to specific allergens
- SCIT should be administered under direct clinician supervision

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Subcutaneous and Sublingual Immunotherapy

- Asthma should be well controlled at the time of initiation, buildup, and maintenance of SCIT
 - Do not administer SCIT in individuals with severe persistent asthma
- Sublingual immunotherapy (SLIT) is not supported by current evidence to treat allergic asthma

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Application



MH is a 23 year-old male with moderate-persistent asthma. He is currently prescribed daily and PRN low-dose ICS/formoterol. He states that he typically uses his inhaler as reliever therapy 1 time per week. However, the patient reports that he experiences worsening symptoms and an increase in PRN inhaler use every September. Allergy testing has confirmed an allergic sensitization to ragweed. The patient has tried intranasal corticosteroids in the past with little impact on inhaler use frequency. He is not currently experiencing symptoms.

True or False? This patient would be an appropriate candidate for subcutaneous immunotherapy (SCIT) as an adjunct asthma treatment.



References

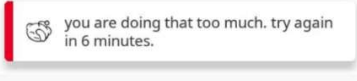
1. GINA 2020: Available at www.ginaasthma.org
2. GINA 2019: A fundamental change in asthma management. *Eur Resp J* 2019;53: 1901046. Editorial explaining rationale for changes to GINA 2019.
3. Inhaled combined budesonide-formoterol as needed in mild asthma (SYGMA 1). *N Engl J Med* 2018;378:1865-1876.
4. As needed budesonide-formoterol versus maintenance budesonide in mild asthma (SYGMA 2). *N Engl J Med* 2018;378:1877-1887.
5. NIH. Asthma management guidelines: Focused updates 2020.
6. Cloutier MM, Dixon AE, Krishnan JA, Lemanske RF, Pace W, Schatz M. Managing Asthma in Adolescents and Adults: 2020 Asthma Guideline Update From the National Asthma Education and Prevention Program. *JAMA* 2020;324(22);2301–2317.



Questions?

Me: I'd sure like to breathe

Asthma Attack:



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Nicotine Addiction: The Beginning of the ENDS

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2/16/2021



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Disclosures

- I have no conflicts of interest to disclose



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Learning Objectives

- Summarize evidence regarding harmful effects of electronic nicotine delivery systems (ENDS) and under-investigated areas that require further research
- Outline the role healthcare providers play for patient safety regarding ENDS



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Abbreviations

- ATS – American Thoracic Society
- ENDS - electronic nicotine delivery systems
- EVALI - E-Cigarette or vaping Associated lung injury
- NRT – Nicotine replacement therapy



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JUUL THE ALTERNATIVE FOR ADULT SMOKERS

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We Believe That

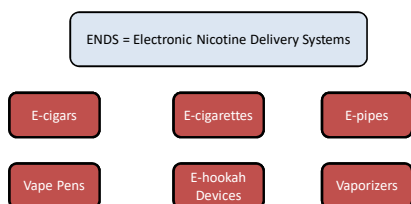
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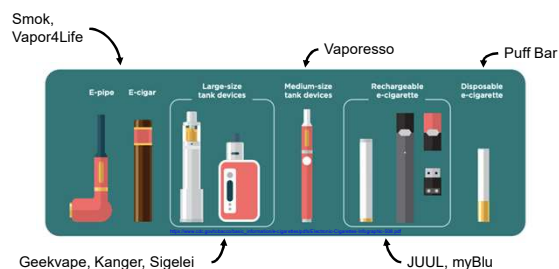
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What are ends?

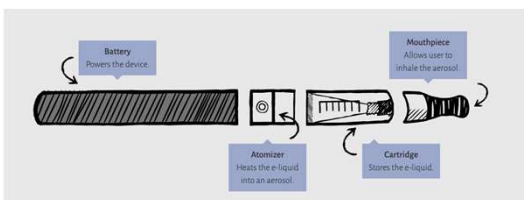


US Food and Drug Administration. "Vaporizers, e-cigarettes, and other electronic nicotine delivery systems." <https://www.fda.gov/tobacco-products/e-cigarettes-other-electronic-nicotine-delivery-systems>

The new look of nicotine



How they work



U.S. Department of Health and Human Services. Know the Risks: E-cigarettes & Young People. <https://www.e-cigarettesurgeongeneral.gov/the-facts.html>

The history

Vaping products first entered the market in 2006

The use of ENDS have drastically increased the last few years

Use has especially increased among teens

- CDC and FDA data found that in 2019 more than 5 million U.S. youth used e-cigarettes in the past 30-days
 - Including 1 in 4 high school students and 1 in 10 middle school students



American Thoracic Society. Vaping associated pulmonary illness. Am J Respir Crit Care Med. 2019;200:13-14. DOI: <https://doi.org/10.1164/rccm.201903-0713RE>; Information on e-cigarettes (E-Cigarettes) and Youth. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/E-Cigarettes-and-Youth-What-PCPs-Need-to-Know-20190327-408.pdf


Trends in adults

2.8% of U.S. adults were current e-cigarette users in 2017

Among Adult E-cigarette users in 2015:

- 29.8% were former cigarette smokers
- 58.8% were current regular cigarette smokers
- 11.4% had never been regular cigarette smokers

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CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/Electronic-Cigarettes-Infographic.pdf



VS



Is vaping better than smoking?

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The short answer

Probably True

- E-cigarettes contain fewer toxins than cigarettes however the aerosol in ENDS is not harmless.
- Additionally, ENDS are still new and long-term health effects are still unknown.

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CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/Electronic-Cigarettes-Infographic-208.pdf
 U.S. Department of Health and Human Services https://www.e-cigarettesurgeonsgeneral.gov/documents/2018_509_Elec_Summ_508.pdf

What is in vaping devices?

- Nicotine
- Diacetyl
- Plant oils
- Coconut oil
- Vitamin E acetate
- Petroleum Distillates
- Medium chain triglycerides
- Diluent Terpenes
- Heavy metals


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CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/Electronic-Cigarettes-Infographic.pdf
 CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/e-cigarettes-what-are-they.pdf

Ingredients of concern

<p>Nicotine</p> <ul style="list-style-type: none"> Highly addictive Toxic to a developing fetus Can impact brain development of teens and young adults 	<p>Heavy Metals</p> <ul style="list-style-type: none"> Include tin, lead, cobalt, nickel and cadmium Lead and cadmium have been known to cause respiratory distress
<p>Diacetyl</p> <ul style="list-style-type: none"> Flavoring agent used to a butter-like taste Has been previously linked to severe lung disease by OSHA 	<p>Vitamin E Acetate</p> <ul style="list-style-type: none"> Often used as a thickening agent Does not usually cause harm when taken orally or used topically but per past studies suggest it may impair normal lung functioning when inhaled

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CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/Electronic-Cigarettes-Infographic.pdf
 CDC https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdf/e-cigarettes-what-are-they.pdf
 US Occupational Safety and Health Administration <https://www.osha.gov/TC-16/flavoringlung/> diacetyl.html
 Williams M. *Environ Health Perspect*. 2010;118:156-166

Nicotine




1 JUUL pod contains as much nicotine as 20 cigarettes

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Truth Initiative <https://truthinitiative.org/research-reports/2018/07/19/e-cigarettes-produce-few-much-nicotine.pdf>

Knowledge Check 1

Which ingredient of concern in ENDS is generally safe orally or topically, but may impair normal lung functioning when inhaled?

- Coal tar
- Heavy metals
- Medium chain triglycerides
- Vitamin E acetate



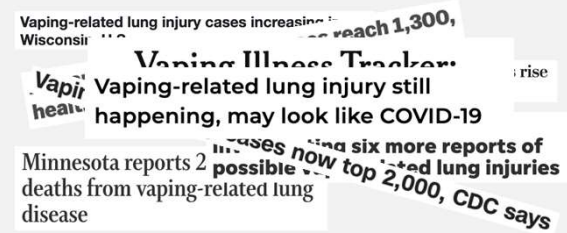

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E-Cigarette or Vaping Associated Lung Injury (EVALI)




Before covid-19 there was a different respiratory threat sweeping news headlines

What is EVALI?

- Lung injury associated with ENDS usage
- First reported to the CDC in August of 2019
- As of February 18th, 2020, among the 50 states, District of Columbia (D.C.), Puerto Rico and the U.S. Virgin Islands there have been 2,807 reported hospitalizations due to EVALI including 68 deaths




CDC https://www.cdc.gov/od/oc/ohrt/evali_information/evali_information_lung_disease.html
 FDA https://www.fda.gov/oc/ohrt/evali_information/evali_information_lung_disease.html
 National TL Update: Safety guidance for health care providers evaluating and caring for patients with suspected EVALI or vaping product use associated lung injury - United States, November 2019. MMWR Morbidity and Mortality Weekly Report 2019; 68(48):1081-1086. <https://www.cdc.gov/mmwr/volumes/68/wrap/pdf/w6804a1.pdf>

What does it look like?

Symptoms are not only respiratory

- Respiratory: shortness of breath, cough, chest pain
- Gastrointestinal: nausea, vomiting, diarrhea
- Constitutional: fever, headache

Can develop in days to weeks



American Thoracic Society. Vaping associated pulmonary illness. Am J Respir Crit Care Med. 2019;200:13-14.


What is causing it?

No one ingredient has been identified universally among patient samples

Both the FDA and CDC are investigating possible causative agents

Most samples collected by the FDA from EVALI patients contain THC

- While THC products correlate more to lung-injury further investigation is needed to determine the relationship between EVALI and THC
- The major concern with THC products are the additives – cooling agents, flavoring agents, nicotine salts, and herbal blends



CDC https://www.cdc.gov/od/oc/ohrt/evali_information/evali_information_lung_disease.html
 FDA https://www.fda.gov/oc/ohrt/evali_information/evali_information_lung_disease.html
 National TL Update: Safety guidance for health care providers evaluating and caring for patients with suspected EVALI or vaping product use associated lung injury - United States, November 2019. MMWR Morbidity and Mortality Weekly Report 2019; 68(48):1081-1086. <https://www.cdc.gov/mmwr/volumes/68/wrap/pdf/w6804a1.pdf>

How do we Manage it?

Diagnosis: Focused on ruling out other causes

- Rule out influenza or CAP
- Gather patient history of ENDS use
- Current lack of biological markers to recognize EVALI

Treatment: Symptomatic supportive therapies

- Inpatient therapy should be considered if a patient has and O₂ saturation <95%, has respiratory distress or comorbidities that compromise pulmonary reserve
- Prophylactic treatment for CAP can be considered until ruled out
- Once other causes are ruled out, a short course of corticosteroids can be considered
- Other supportive respiratory therapies such as oxygen, inhaled bronchodilators and antimuscarinics, and intubation may be needed depending on severity of symptoms

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Gulfport, Mississippi

Jafariati TC. CDC MMWR Morb Mortal Wkly Rep. 2019;68(43):1181-1186
Evans ME. CDC MMWR Morb Mortal Wkly Rep. 2020;69(15):1189-1194

GENERAL TREATMENT FLOWCHART

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Gulfport, Mississippi

CDC https://www.cdc.gov/ebac/ebac_informatics/vapeinfo/outpatient-EVALI-15w-2019.pdf

Treatment flowchart continued

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CDC https://www.cdc.gov/ebac/ebac_informatics/vapeinfo/outpatient-EVALI-15w-2019.pdf

Knowledge Check 2

For the treatment of EVALI, in addition to discontinuing ENDS use which medication may improve patient status and is to be used with caution due to risk of infection?

- Tamiflu®
- Prednisone
- Zosyn®
- Albuterol Sulfate

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Vaping for smoking cessation

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Gulfport, Mississippi

Convincing Comments

"Whether nicotine vapes or CBD vapes, they both have an edge over the patch or chewing gum. Those OTC methods simply don't scratch the itch." - Vaping360

"Puff Bar bases its company on three main values: simplicity, value and - most importantly - what we believe is a better alternative to smoking traditional cigarettes." - Puff Bar

"We work to improve the lives of smokers who find it difficult to quit combustible cigarettes, and to design products that allow them to switch over to harm-reduction products." - RELX

"Designed for smokers, by smokers" - JUUL

"After decades of smoking five packs a day, our founder was able to quit smoking and start vaping." - Vapor4Life

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Gulfport, Mississippi

The Data

Carballo RS, Shafer PR, Patel D, Davis KC, McAfee TA. Quit methods used by US adult cigarette smokers, 2014–2016. *Prev Chronic Dis.* 2017;14(e32):e1-e5.

- 35.4% smokers report using e-cigarettes + cigarettes, 24.7% switch to e-cigarettes
- 25.4% using nicotine patch or gum vs 12.2% using varenicline or bupropion for quit attempt

Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy. *N Engl J Med.* 2019;308(7):629-647.

- 886 participants randomized 1:1 to NRT of preference (447) or e-cigarette with individually purchased nicotine e-liquid (439)
- 1 year abstinence: 18.0% e-cigarette arm, 9.9% NRT arm (RR: 1.83, 95% CI: 1.30-2.58)
 - 39.5% e-cigarette arm with continued use at 52-weeks, 4.3% NRT arm
- Major limitations: underdosing of NRT/lack of combination NRT, low quit rates

Clinical Application:

- Mixed benefit
- STRONG risk for addiction
- Safety concerns
- Nicotine dose variability
- Empower patients w/ knowledge

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The PATH Study

Pierce JP, Benmarhnia T, Chen R, et al. Role of e-cigarettes and pharmacotherapy during attempts to quit cigarette smoking: the PATH study 2013-2016. *PLoS One.* 2020;15(9):e1-e16.

Clinical Application:

- Mixed benefit
- STRONG risk for addiction
- Safety concerns
- Nicotine dose variability
- Empower patients w/ knowledge

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2020 ATS Tobacco Treatment Guidelines

Varenicline preferred to ENDS products

- Conditional recommendation with low certainty
- Evidence gathered prior to EVALI & COVID
- Given limited direct comparisons, authors conducted indirect comparison
 - NRT vs Varenicline (11 RCTs) and then NRT vs. ENDS (2 RCTs)

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ENDS for tobacco cessation summary

The FDA has not approved the use of e-cigarettes for smoking cessation

Insufficient research to support the use of e-cigarettes for smoking cessation

The CDC found that many adults who were attempting to quit smoking through e-cigarette use became dual users, using both cigarettes and e-cigarettes.

If patients are adamant about using e-cigarettes for cessation; advise to completely switch from cigarette to e-cigarette and establish a goal for quitting e-cigarettes

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Knowledge Check 3

True or False:

The 2020 American Thoracic Society conditionally recommends varenicline to ENDS for tobacco treatment based on indirect comparison data

a. True
b. False

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The Take-aways

ENDS use is on the rise

ENDS have fewer toxic additives than cigarettes but are still not safe, and long-term effects remain unknown

The only way to avoid EVALI is to avoid ENDS use all together

There is insufficient evidence to support ENDS use in smoking cessation

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Resource Location

FDA: Vaporizers, E-Cigarettes, and other ENDS

- <https://www.fda.gov/tobacco-products/products-ingredients-components/vaporizers-e-cigarettes-and-other-electronic-nicotine-delivery-systems-ends>

CDC: Electronic Cigarettes


- https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm



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Acknowledgements

Isabelle Sviatoslavsky, P4 for putting together an initial version of this presentation adapted for this conference.



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Additional material




Recent Legislation

December 20th, 2019 the federal sale age for all tobacco products was raised from 18 to 21

- This includes e-cigarettes
- Prior to this federal law, 16 states had already raised the minimum sale age
- Hope to reduce the number of younger users and minimize the extent e-cigarette companies target young users

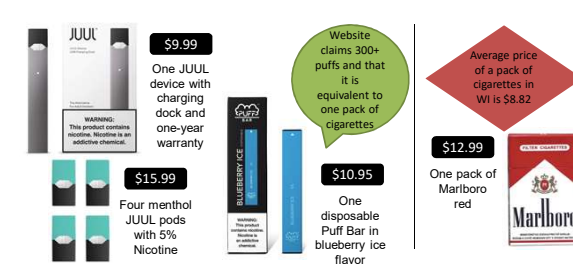
Wisconsin classifies E-cigarettes as a nicotine product

- No other specific additional state legislation
- Updates may be found in Statute - Chapter 134.66 or <https://www.publichealthlawcenter.org/resources/us-e-cigarette-regulations-50-state-review>



Kaplan S. Congress approves raising age to 21 for e-cigarette and tobacco sales. The New York Times. <https://www.nytimes.com/2019/12/19/health/e-cigarette-sale-age-21.html>
American Lung Association. Tobacco 21 laws: raising the minimum sales age for all tobacco products to 21. <https://www.lung.org/bur-initiative/tobacco/cases-and-prevention/tobacco-21-laws.html>

Cost



One JUUL device with charging dock and one-year warranty: **\$9.99**


Four menthol JUUL pods with 5% Nicotine: **\$15.99**

One disposable Puff Bar in blueberry ice flavor: **\$10.95**

One pack of Marlboro red: **\$12.99**

Average price of a pack of cigarettes in WI is \$8.82

Website claims 300+ puffs and that it is equivalent to one pack of cigarettes



Fair Reporters. <https://fairreporters.net/health/series-of-cigarettes-by-stick/>