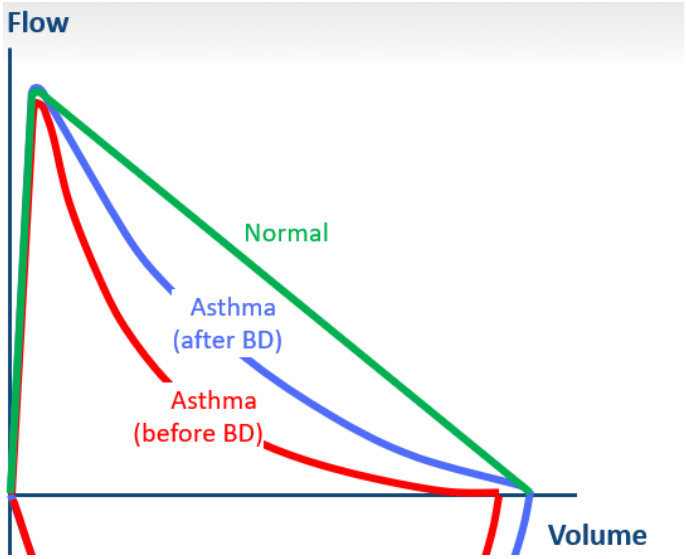
Allergy Potpourri



When poll is active, respond at **pollev.com/tomgerstner243**

Text **TOMGERSTNER243** to **37607** once to join

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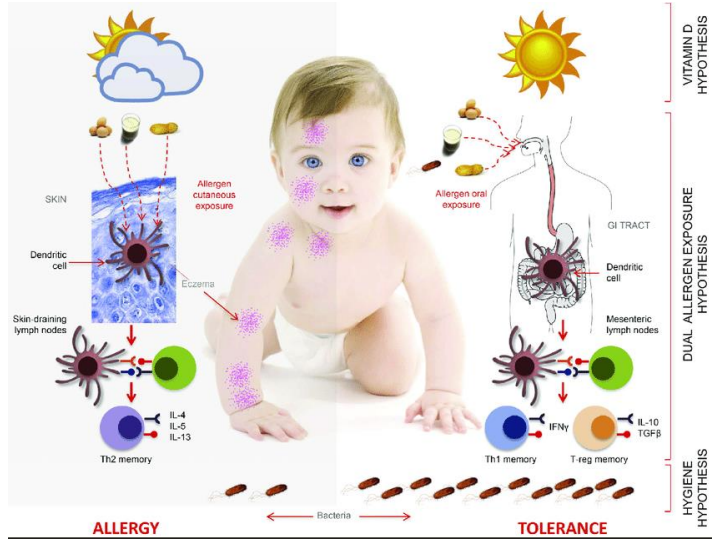

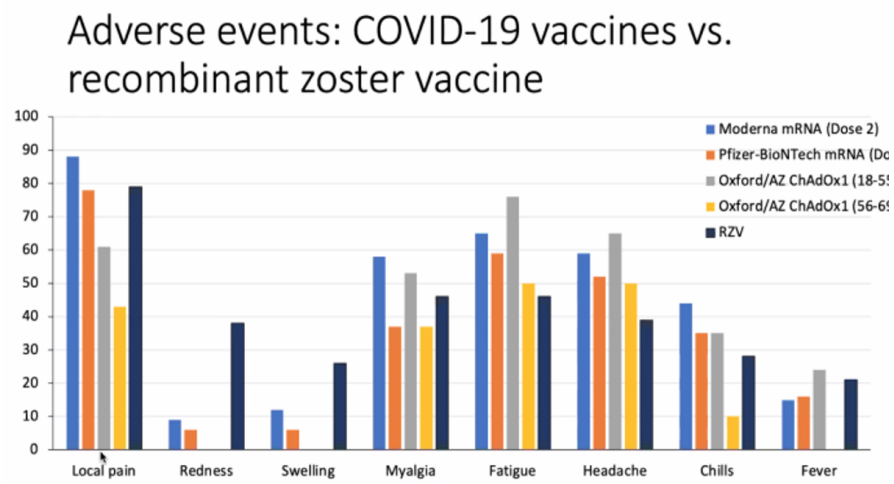

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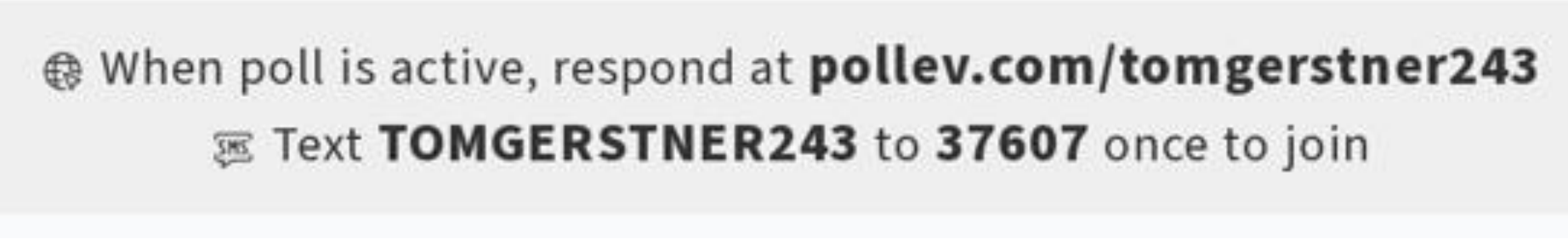
Text **TOMGERSTNER243** to **37607** once to join

An Allergy “Potpourri” of new developments…

- Know the evidence and implement the latest recommendations for optimizing management of mild asthma?
- Should I worry about my asthmatics who contract COVID-19?
- When should one be concerned about COVID vaccine allergic reactions and who needs referral?
- What can be done to prevent development of food allergy in high-risk infants(what is “high risk”?)?
- In our food allergic patients…autoinjector and avoidance, is that it? What more can be done?

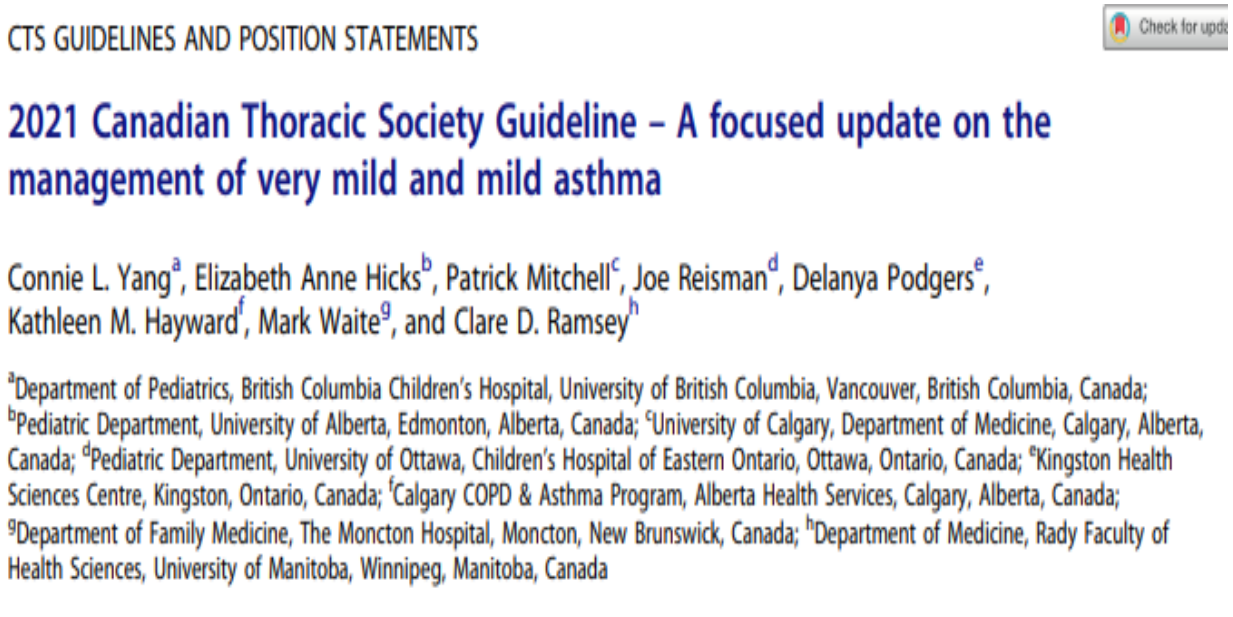


New approach to treatment of mild asthma

- Latest GINA guidelines and Canadian Thoracic Society guidelines for management of mild asthma

<u>Key points:</u>

- Assess control AND patient risk at each visit to determine need for controller therapy
- B2-agonist alone is almost completely eliminated



CTS GUIDELINES AND POSITION STATEMENTS

Check for updates

2021 Canadian Thoracic Society Guideline – A focused update on the management of very mild and mild asthma

Connie L. Yang[a], Elizabeth Anne Hicks[b], Patrick Mitchell[c], Joe Reisman[d], Delanya Podgers[e], Kathleen M. Hayward[f], Mark Waite[g], and Clare D. Ramsey[h]

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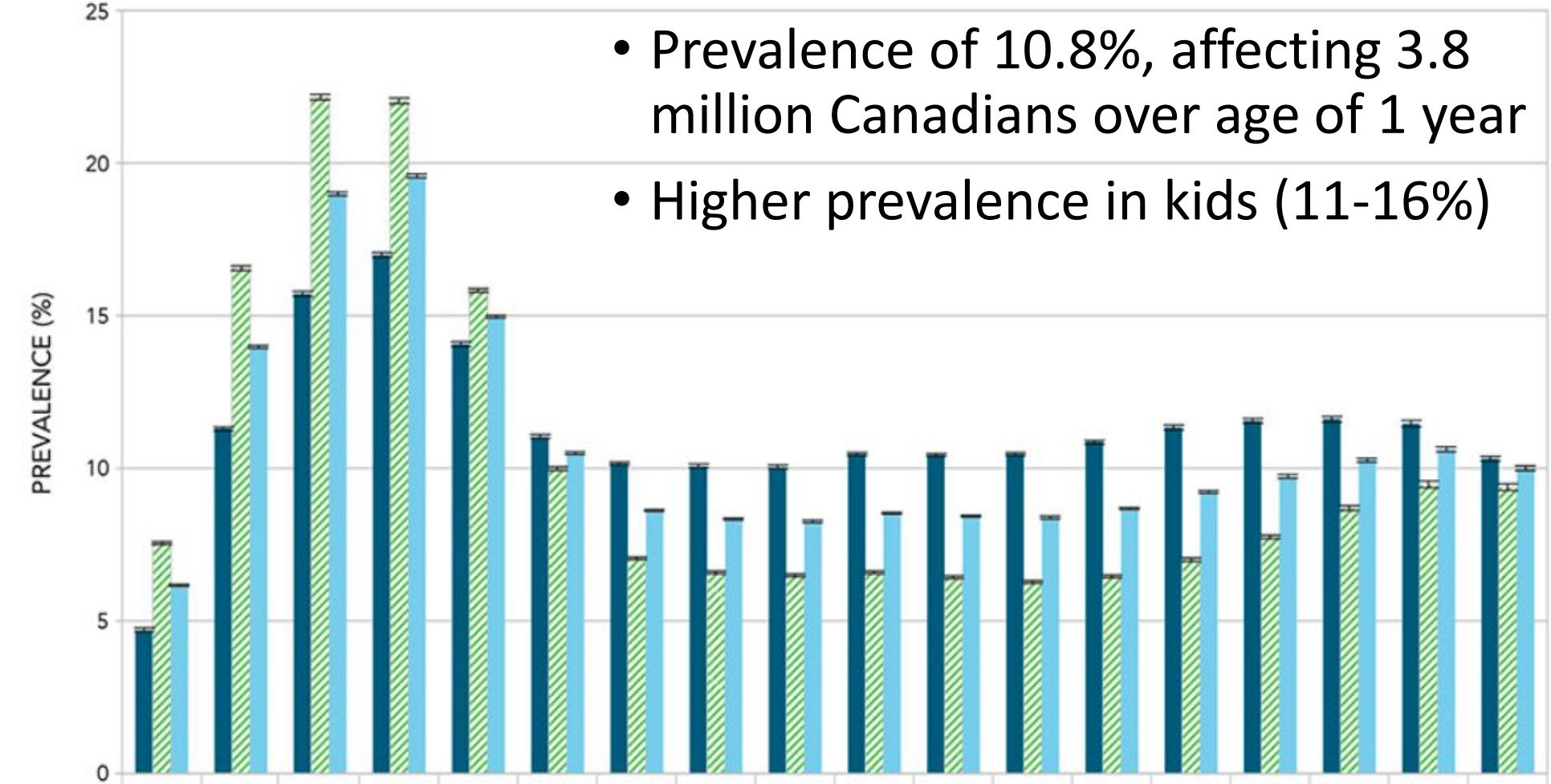
What is the prevalence of asthma in Canada?

3-5%, depending on the age group	**A**
6-8% overall, up to 10% in children	**B**
10-11% overall, up to 11-16% in children	**C**
20-25% overall, gradually decreasing prevalence with age	**D**
None of the above	**E**

Figure 1.1 Prevalence of diagnosed asthma among Canadians aged one year and older, by age group and sex, Canada, 2011-2012



	1–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
Females	4.7	11.3	15.7	17.0	14.1	11.1	10.2	10.1	10.0	10.5	10.4	10.5	10.9	11.4	11.6	11.6	11.5	10.3
Males	7.6	16.6	22.2	22.1	15.8	10.0	7.1	6.6	6.5	6.6	6.4	6.3	6.5	7.0	7.8	8.7	9.5	9.4
Total	6.2	14.0	19.0	19.6	15.0	10.5	8.6	8.3	8.3	8.5	8.4	8.4	8.7	9.2	9.7	10.3	10.6	10.0

AGE GROUP (YEARS)

- Prevalence of 10.8%, affecting 3.8 million Canadians over age of 1 year
- Higher prevalence in kids (11-16%)

Public Health Agency of Canada, using Canadian Chronic Disease Surveillance System data files contributed by provinces and territories.

What is asthma?

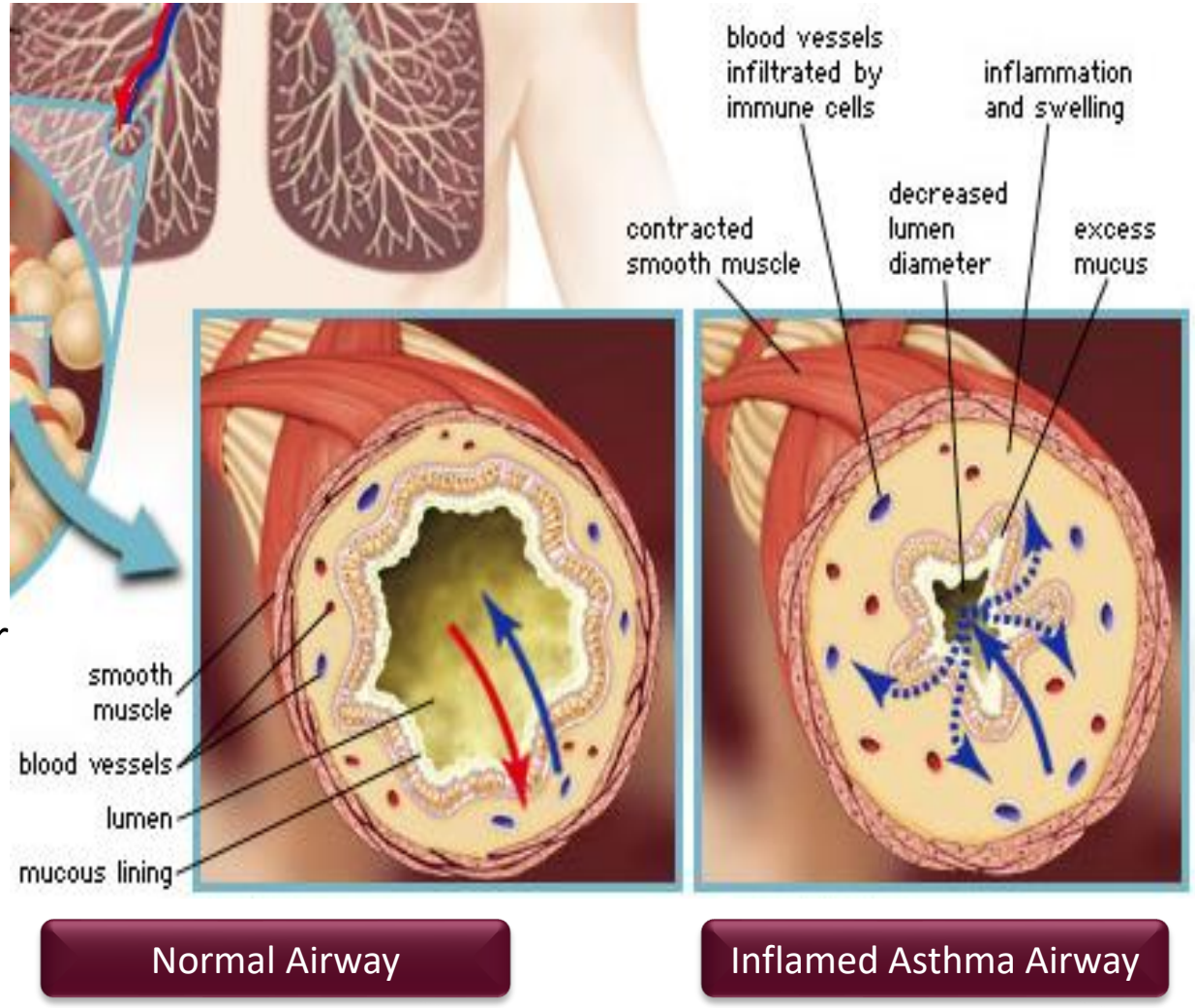
- Characterized by chronic airway inflammation
- Multiple phenotypes

<u>Defining features:</u>

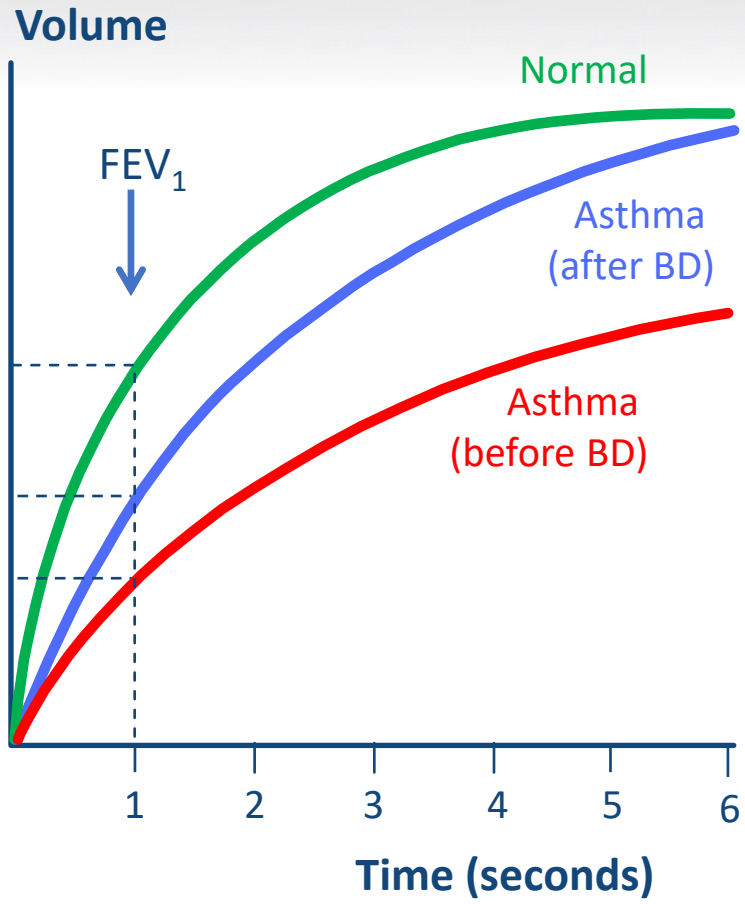
1. Wheeze, breathlessness and cough that vary over time and in intensity
   - Often occur at night and exercise, laughter, cold air
   - Symptoms worsen with viral infections

2. Variable airflow obstruction
   - Low FEV1, or low FEV1/FVC (<0.9 in kids, <0.75 adults)
   - 12% improvement in FEV1 post bronchodilator (or after weeks of Inhaled corticosteroid)
   - Daily diurnal PEF variability is >10% (>13% in kids)

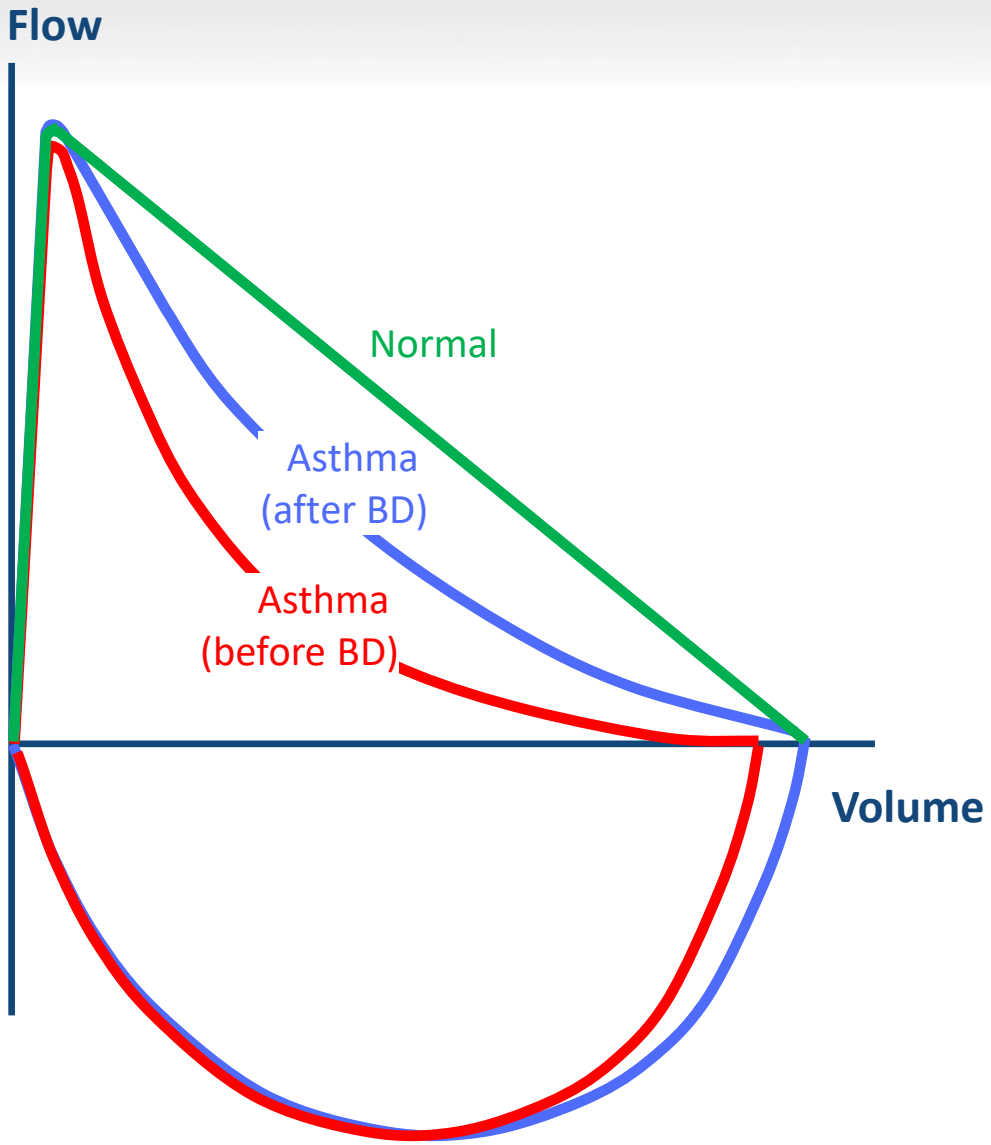
3. Increased airways reactivity (hyperresponsiveness, or “twitchy airways”)



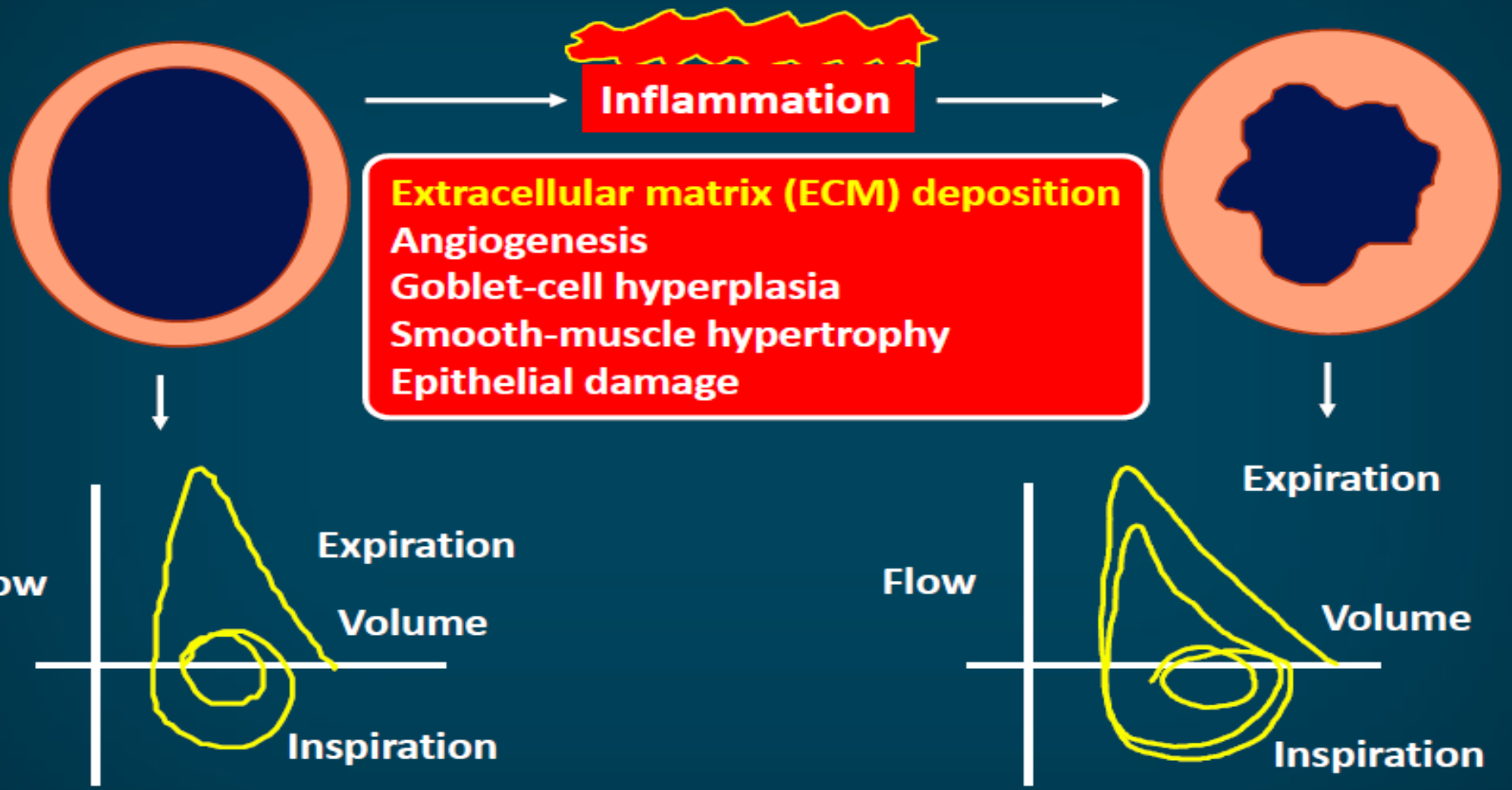
Typical spirometric tracings



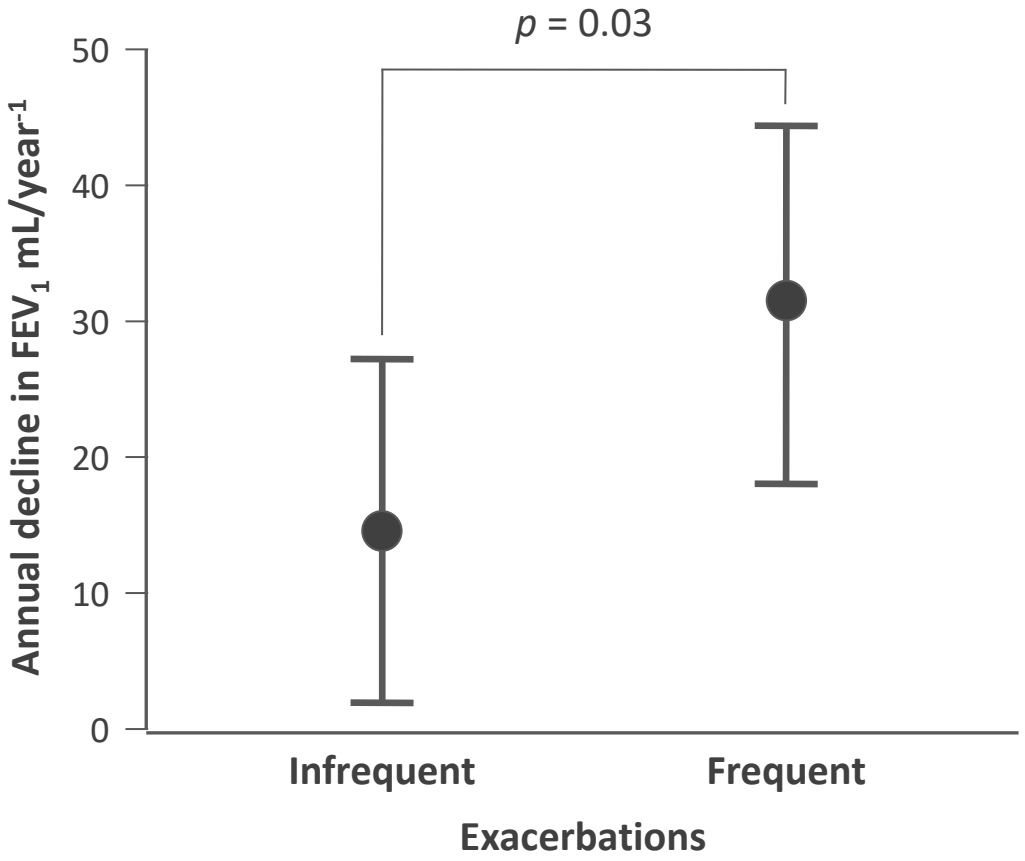
Note: Each FEV_1 represents the highest of three reproducible measurements



Airway Remodeling



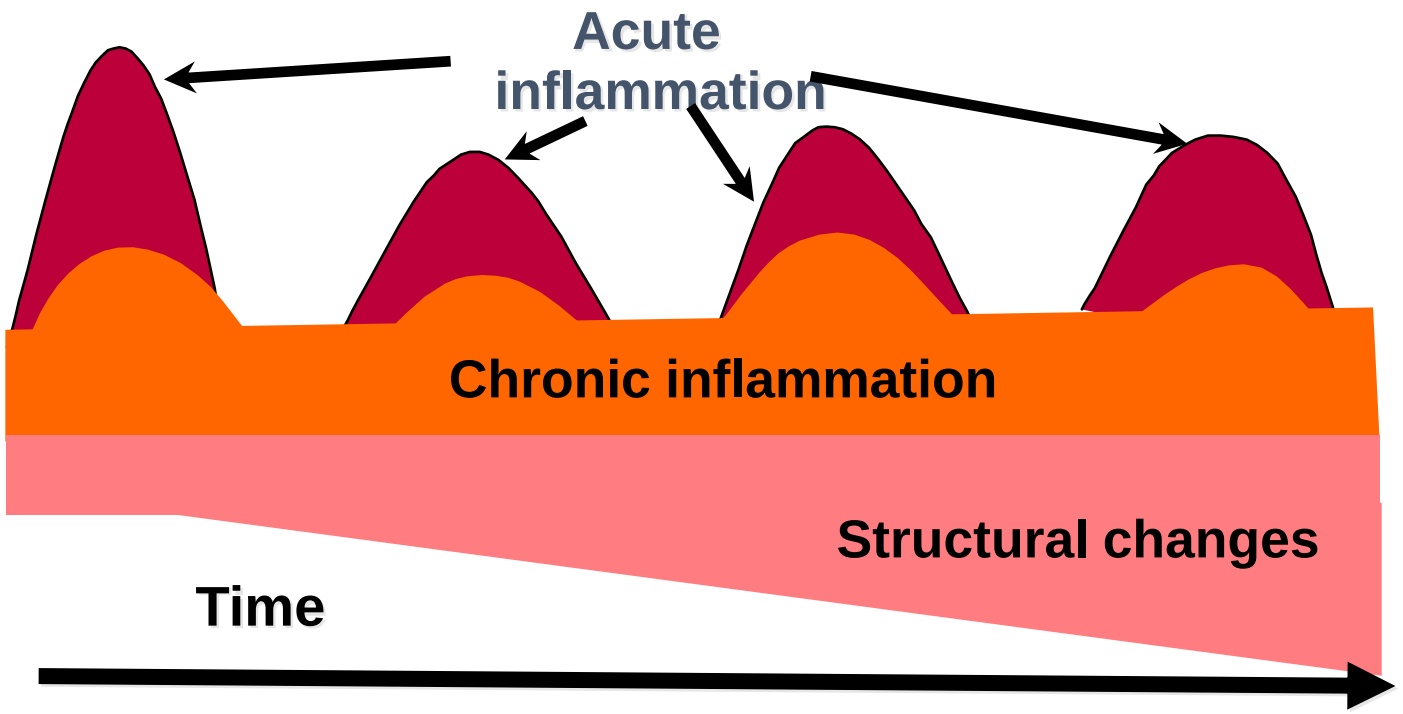
Frequent Asthma Exacerbations are Associated with Excess Decline in Lung Function



Exacerbations are bad for lung function

Bai TR, et al. Eur Respir J 2007; 30(3):452-6.

Effects of recurrent acute exacerbations on chronic airway changes.



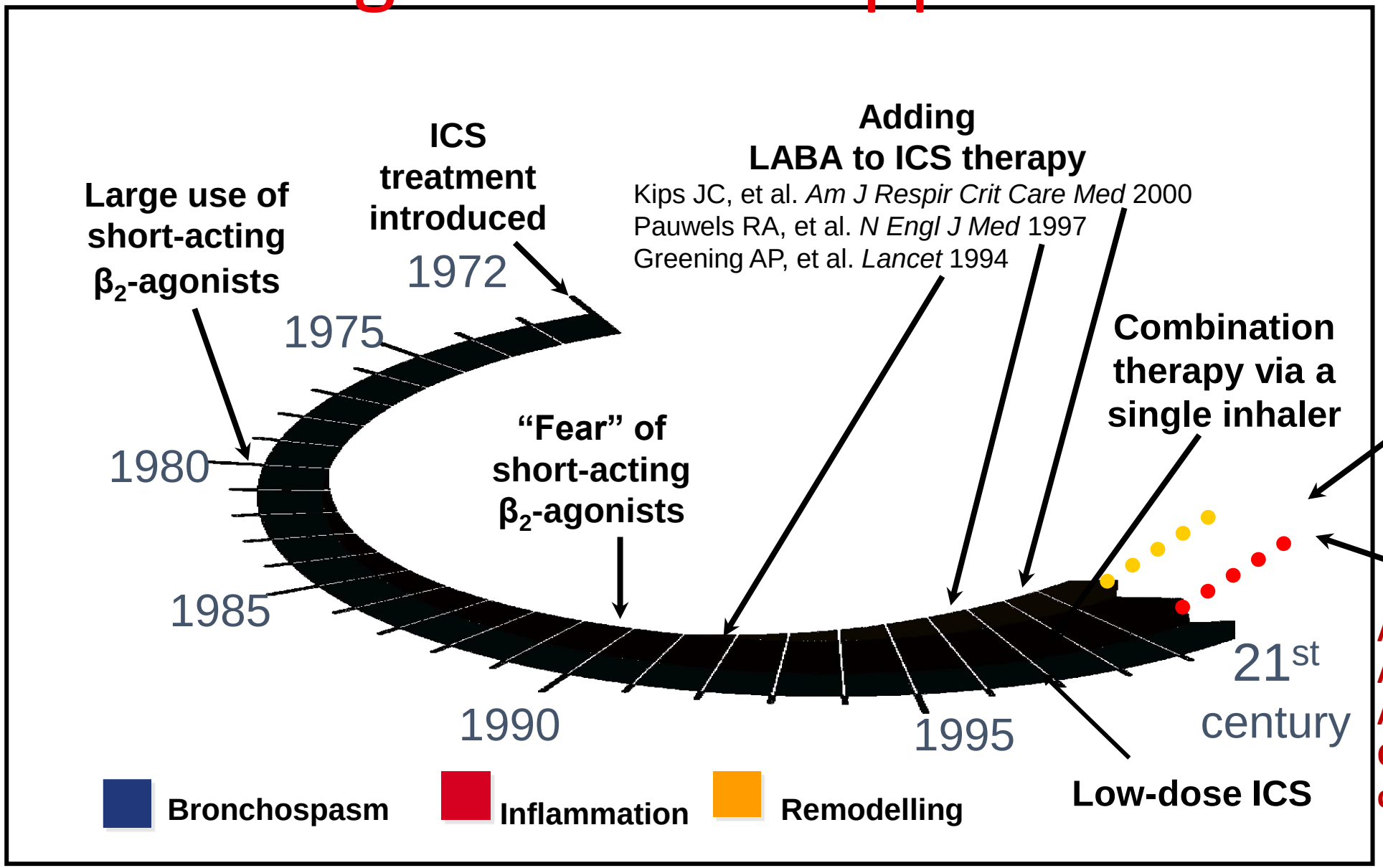
Management of Asthma as a Chronic Disease:

2 components:

1.Achieving Current Control
(symptoms and function)

2.Minimizing Future Risk (exacerbations, loss of lung function, med side effects)

Evolving treatment approaches



Case: Matthew, age 19

- Reports cough, wheeze and difficulty breathing around cats, and has prolonged coughing for 2-3 weeks after some colds
- He sometimes gets winded faster than his peers when playing hockey and other sports. Coughs at night maybe once per week.
- He has a salbutamol inhaler for which he uses 2-3x/week for symptoms

Based on the info given, is Matthew's asthma controlled?

Yes	**A**
No	**B**
Unsure	**C**

NEW

Change to criteria for well-controlled asthma

Characteristic	Frequency or value
Daytime symptoms	≤ 2 days/week
Nighttime symptoms	< 1 night/week and mild
Physical activity	Normal
Exacerbations	Mild and infrequent*
Absence from work or school due to asthma	None
Need for a reliever (SABA or bud/form)†	≤ 2 doses per week
FEV_1 or PEF	≥ 90% of personal best
PEF diurnal variation	< 10-15%#
Sputum eosinophils	< 2-3%●

A patient who meets all of the above criteria would be considered to have well-controlled asthma

* A mild exacerbation is an increase in asthma symptoms from baseline that does not require systemic steroids, an ED visit, or a hospitalization. "Infrequent" is not specifically defined, since the frequency of mild exacerbations that patients consider an impairment to quality of life varies. If the patient feels that the frequency of mild exacerbations is impairing their quality of life, then their asthma should be considered poorly-controlled. If a patient is having frequent mild exacerbations, they should be assessed to determine if at baseline, they have poorly-controlled asthma.

† There are no established criteria for control when using bud/form as a reliever, however, use of a reliever often indicates that a patient is having symptoms and is a criterion that can be objectively assessed.

\# Diurnal variation is calculated as the highest peak expiratory flow (PEF) minus the lowest divided by the highest peak flow multiplied by 100, for morning and night (determined over a two-week period).

● Consider in adults ≥ 18 years of age with uncontrolled moderate to severe asthma who are assessed in specialist centres.

More stringent GINA guidelines for control

GINA assessment of symptom control

A. Symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well-controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice a week?	Yes☐ No☐	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• Reliever needed for symptoms* more than twice a week?	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

How do you define asthma severity and asthma control? What is the difference?

- CONTROL:
  - refers to the extent to which symptoms of asthma have been reduced or removed by treatment
- SEVERITY
  - determined by ***the intensity of treatment*** needed to maintain asthma control.

- Therefore, mild asthma is asthma that can be controlled with reliever alone or low dose ICS.
- Severe asthma is asthma that requires more intense treatment (ie high dose inhaled corticosteroids-LABA +/-biologics

Is Matthew’s asthma well controlled?

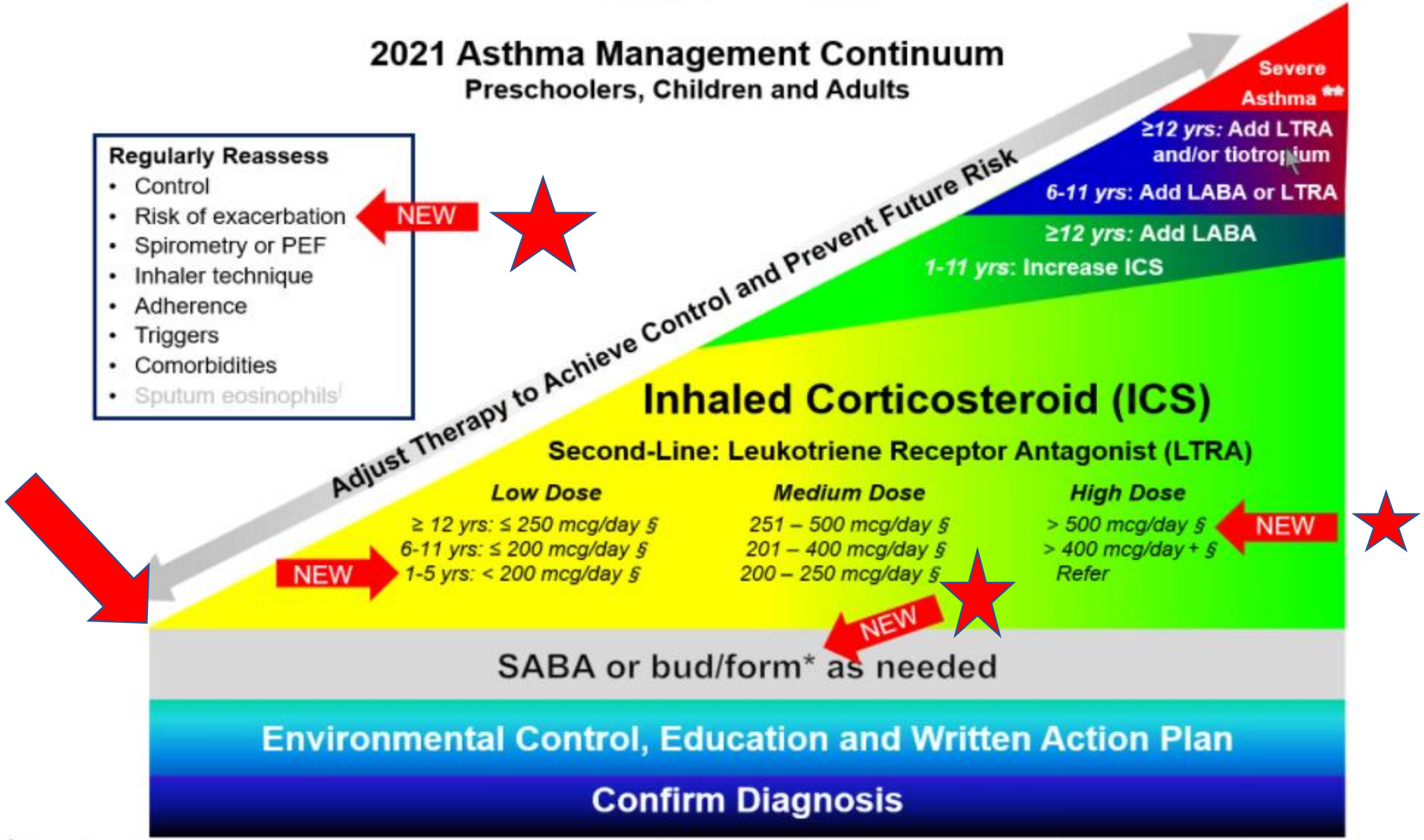
- No- salbutamol more than 2x/ week, waking up at night, and exercise impact.

What are Matthew's treatment options?

Continue with SABA as needed	**A**
SABA plus add on low dose ICS	**B**
ICS-LABA as needed (formoterol, as in Symbicort)	**C**
Use an ICS dose every time SABA is needed	**D**
All of the above	**E**

2021 Asthma Management Continuum

Preschoolers, Children and Adults



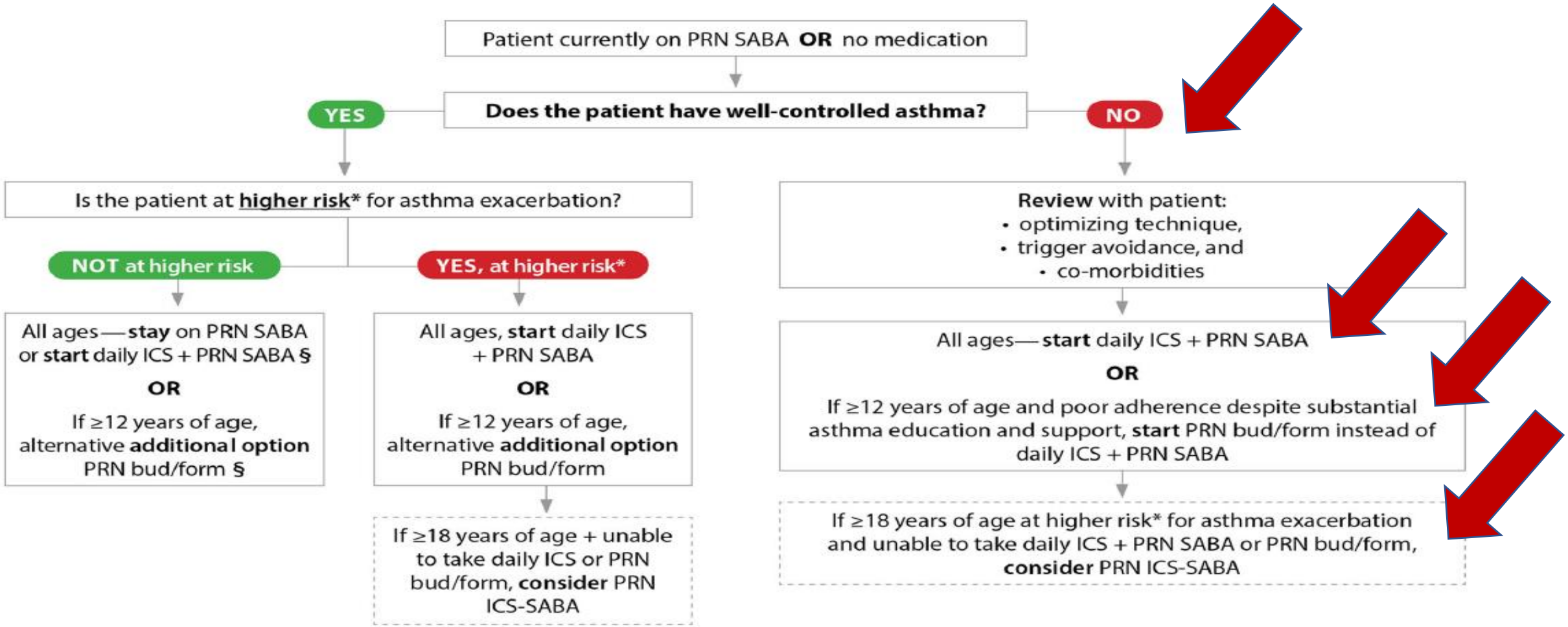
* Or an alternative ICS/form preparation if another is approved for use as a reliever in the future. Bud/form is approved as a reliever for ≥12 years of age and should only be used as a reliever in individuals using it as monotherapy or in conjunction with bud/form maintenance therapy

§ HFA Fluticasone propionate or equivalent

\+ Not approved for use in Canada

∫ In adults, 18 years old and over with moderate to severe asthma assessed in specialist centres

** For severe asthma refer to GTS 2017 Recognition and management of Severe Asthma Position Statement



***Higher risk if a patient had any of the following:**

1) any history of a previous severe asthma exacerbation requiring:
   - systemic steroids,
   - ED visit, or
   - hospitalization
2) poorly-controlled asthma as per CTS criteria
3) overuse of short-acting beta-agonist (defined as use of more than two inhalers of SABA in a year)
4) current smoker

§ Based on patient preference—the decision to switch from PRN SABA to daily ICS + PRN SABA or PRN bud/form is for those that want better asthma control and to decrease their risk of exacerbation

Dash boxes represent harm reduction strategy

What are Matthew's treatment options ("Step 1 therapy")

1. Continue with SABA as needed
2. SABA plus add on low dose ICS
3. ICS-LABA (formoterol, as in Symbicort) as needed
4. Use ICS dose with every salbutamol requirement

Case: Emily, a 16 year old girl

- In the past 6 months, she has needed salbutamol a few times during colds, which last about a week
- History of intermittent wheeze/cough with intense exercise especially in cold air
- No nocturnal symptoms
- Needs salbutamol maybe once every week or 2, most often after basketball games at school

Based on the info given, is Emily's asthma controlled?

Yes

No

Unsure

What are Emily's treatment options?

SABA as needed/pre-exercise

SABA plus low dose regular ICS

ICS-LABA (Symbicort) as needed

Add an ICS dose with every SABA requirement

Unsure

1. History of hospitalization in the past year/ICU ever
2. Smoking
3. History of using >1 salbutamol MDI/6 months
4. Poor adherence to controller therapies (includes poor technique with devices.
5. Presence of co-morbidity (GERD, or sinus disease)
6. Obesity
7. Allergen exposure (e.g. pets)
8. Low lung function (FEV1 <70%)
9. Depression, low SES
10. Eosinophilia

CTS 2021

Table 4. Risk factors associated with severe asthma exacerbations

(This table is adapted from SIGN 158 - British guideline on the management of asthma by kind permission of the Scottish Intercollegiate Guidelines Network).[22]

≥12 years of age	6-11 years of age	<6 years of age
Greatly increased risk (Odds Ratio (OR) > 2.5*)		
History of previous severe exacerbation	• History of previous severe exacerbation • Poorly-controlled asthma • FEV_1 <60% predicted	History of previous severe exacerbation
Moderate increased risk (OR 1.5-2.5*)		
• Poorly-controlled asthma • Excessive SABA use (>2 inhalers/year[48]) • Current smoker**	• Excessive SABA use (>2 inhalers/year) • Comorbid atopic/allergic disease • Low socioeconomic status • Vitamin D deficiency (<30 nmol/L) • FEV_1 60–80% predicted	
Slightly increased risk (OR 1.1-1.5*)		
• Older age (especially >55 years of age) • Female • FEV_1 < 70% predicted • Obesity • Previous smoker** • Depression	• Exposure to environmental tobacco smoke** • Younger age • Obesity • Low parental education	• Comorbid atopic/allergic disease • Raised blood eosinophils (>300/μL) • Younger age • Low socioeconomic status • Male gender • Underweight

* OR reported represent the OR found in the majority of studies examining the risk factor.[22,47]

** Studies have examined the risk of tobacco smoking; however, vaping and smoking of other substances should also be considered risk factors.[49,50]

NEW

Assessing risk of exacerbations in addition to asthma control

- When deciding on optimal treatment, in addition to evaluating asthma control, risk of asthma exacerbation should be assessed.
- A higher risk for an exacerbation is defined by any of the following criteria:

History of a previous severe asthma exacerbation (requiring any of: systemic steroids; ED visit; or hospitalization)
Poorly-controlled asthma as per CTS criteria
Overuse of SABA (defined as use of more than 2 inhalers of SABA in a year[1]); or
Current smoker

Risk factors chosen based on: OR >1.5, certainty of the effect of the risk factor, ease of use in clinical practice

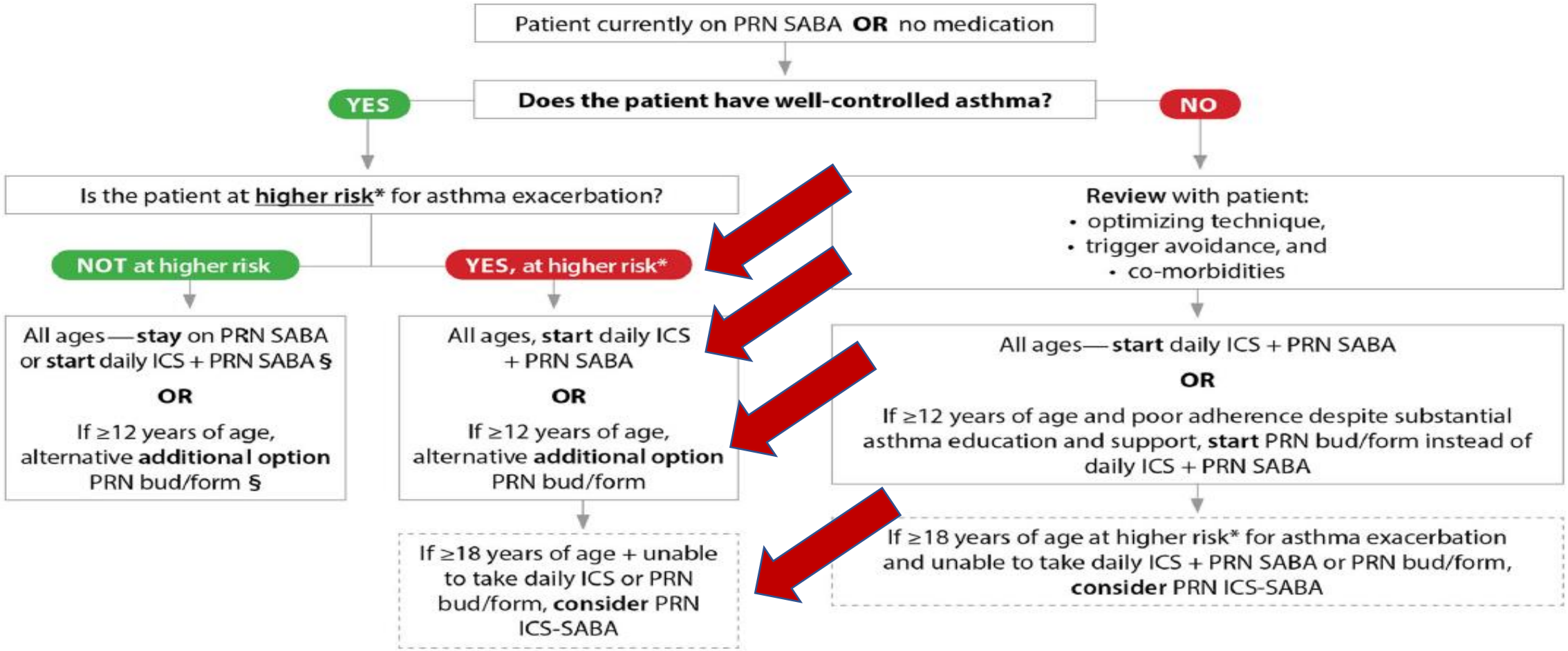
Case: Emily age 16

- Frequent smoker (marijuana)
- In the ED 8 months ago for an asthma flare, no history of admissions including ICU admissions
- Known to have poor adherence to treatment in the past
- Salbutamol MDI's usually last a year
- BMI = 32

Therefore, although symptoms are controlled (e.g. Ventolin <once per week), Emily has identifiable core risk factors- smoking, recent ED visit, with additional risk factors of poor adherence, elevated BMI

Emily, treatment options?

1. Continue with SABA as needed
2. SABA plus add on low dose ICS
3. ICS-LABA (Symbicort) as needed
4. Use ICS dose with every salbutamol requirement



***Higher risk if a patient had any of the following:**

1) any history of a previous severe asthma exacerbation requiring:
   - systemic steroids,
   - ED visit, or
   - hospitalization
2) poorly-controlled asthma as per CTS criteria
3) overuse of short-acting beta-agonist (defined as use of more than two inhalers of SABA in a year)
4) current smoker

§ Based on patient preference—the decision to switch from PRN SABA to daily ICS + PRN SABA or PRN bud/form is for those that want better asthma control and to decrease their risk of exacerbation

Dash boxes represent harm reduction strategy

Lucas age 26

- Long history of asthma, previously outgrown eczema and egg allergy during childhood
- Currently requires salbutamol when visiting aunt who has a cat, and a few times in the spring during grass pollen season, when he also uses a nasal corticosteroid
- No night time symptoms, exercise tolerance good
- Overall requires salbutamol maybe once per month, up to once per week during the spring season.

Controlled?

1. Yes
2. No

What next?

Assess Risk….

Lucas: risk assessment

- Non smoker
- No admissions to hosp for asthma since childhood
- Ventolin MDI usually expires before he refills it
- No history of mental illness, obesity
- FEV1 = 89%, FEV1/FVC 0.92
- Atopic

High risk?

1. Yes
2. No

Lucas: Treatment options?

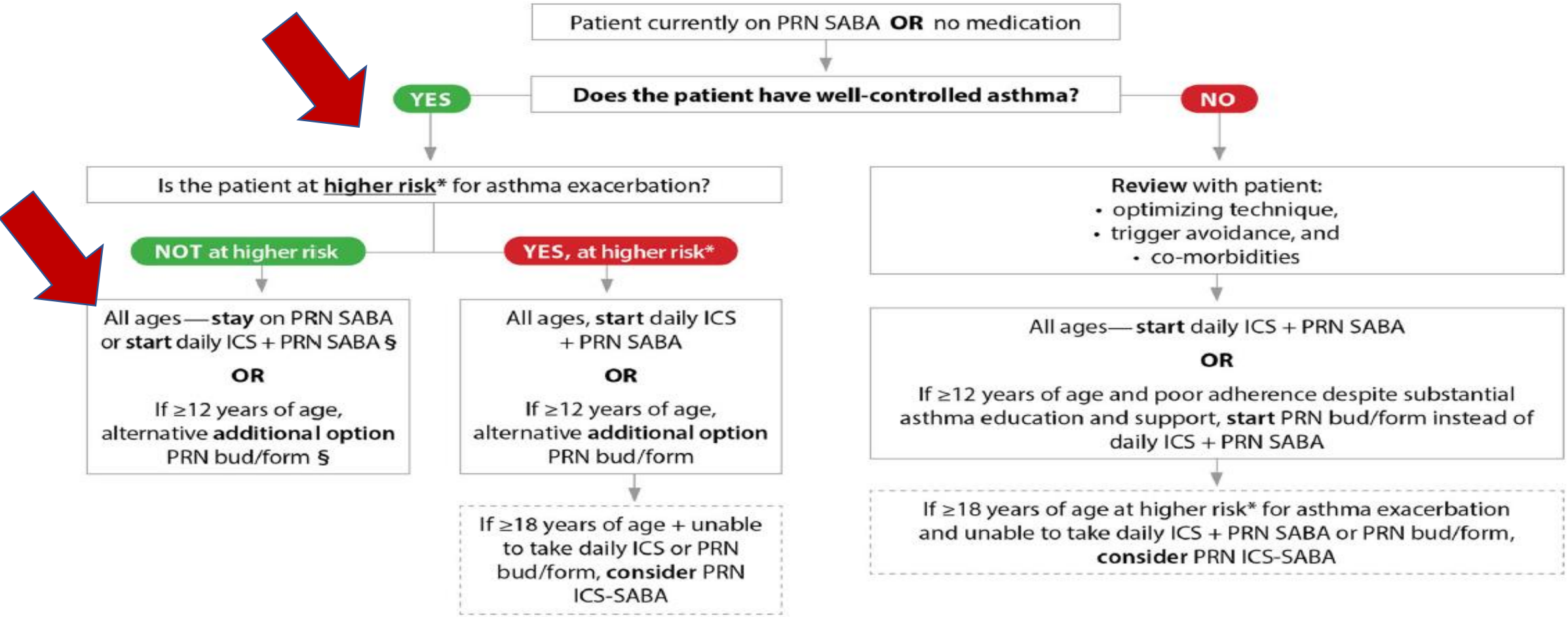
Continue with SABA as needed

SABA plus add on low dose ICS

ICS-LABA (Symbicort) as needed

Use ICS dose with every SABA requirement

All of the above



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   - systemic steroids,
   - ED visit, or
   - hospitalization
2) poorly-controlled asthma as per CTS criteria
3) overuse of short-acting beta-agonist (defined as use of more than two inhalers of SABA in a year)
4) current smoker

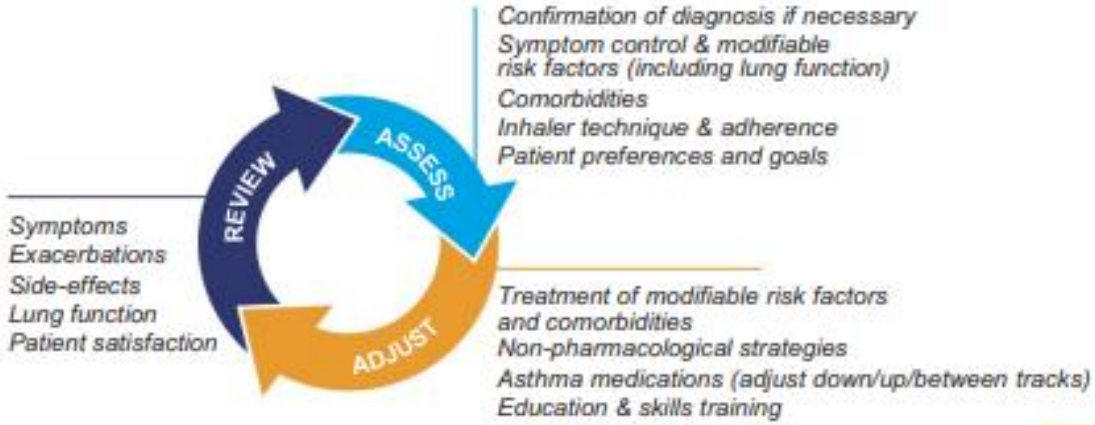
§ Based on patient preference—the decision to switch from PRN SABA to daily ICS + PRN SABA or PRN bud/form is for those that want better asthma control and to decrease their risk of exacerbation

Dash boxes represent harm reduction strategy

Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

Other controller options for either track	*Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT*	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects*

The Biggest Controversy

A Role for SABA Monotherapy?

The Role of SABA Monotherapy

GINA

- Ventolin prn monotherapy is completely gone!!
- Inhaled Budesonide / Formoterol is the recommended anti-inflammatory reliever therapy
- Every patient with asthma gets an inhaled corticosteroid!

Canadian Thoracic Society

- Ventolin prn monotherapy is **almost** gone
- Inhaled Budesonide / Formoterol is the recommended anti-inflammatory reliever therapy
- **Almost** every patient with asthma gets an inhaled corticosteroid!

Why would GINA and CTS move towards eliminating or severely curtailing the use of SABA only?

Pressure from makers of ICS to use more of their products

Patients can be poor perceivers, may not use SABA's often enough to trigger need for controller therapy (even though they should)

SABA's when used alone can make asthma worse

Inhaled SABA has been first-line treatment for asthma for 50 years and experts felt it was time for a change

Asthma exacerbations can occur even in patients only occasionally needing SABA for relief, and these can be prevented by ICS therapy

Why did GINA and CTS extend ICS to Step 1?

- **Patients with apparently mild asthma are still at risk of serious adverse events**
  30–37% of adults with acute asthma exacerbations, 16% of patients with near-fatal asthma, and
  15–20% of adults dying of asthma *had symptoms less than weekly in previous 3 months* (Dusser, Allergy 2007)
- **Regular use of SABA, even for 1–2 weeks, is associated with adverse effects**
  β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response
- **Higher use of SABA is associated with adverse clinical outcomes**
  Dispensing of ≥3 canisters per year (i.e. daily use) is associated with higher risk of severe exacerbations
  Dispensing of ≥12 canisters per year (1 per month) is associated with much higher risk of death

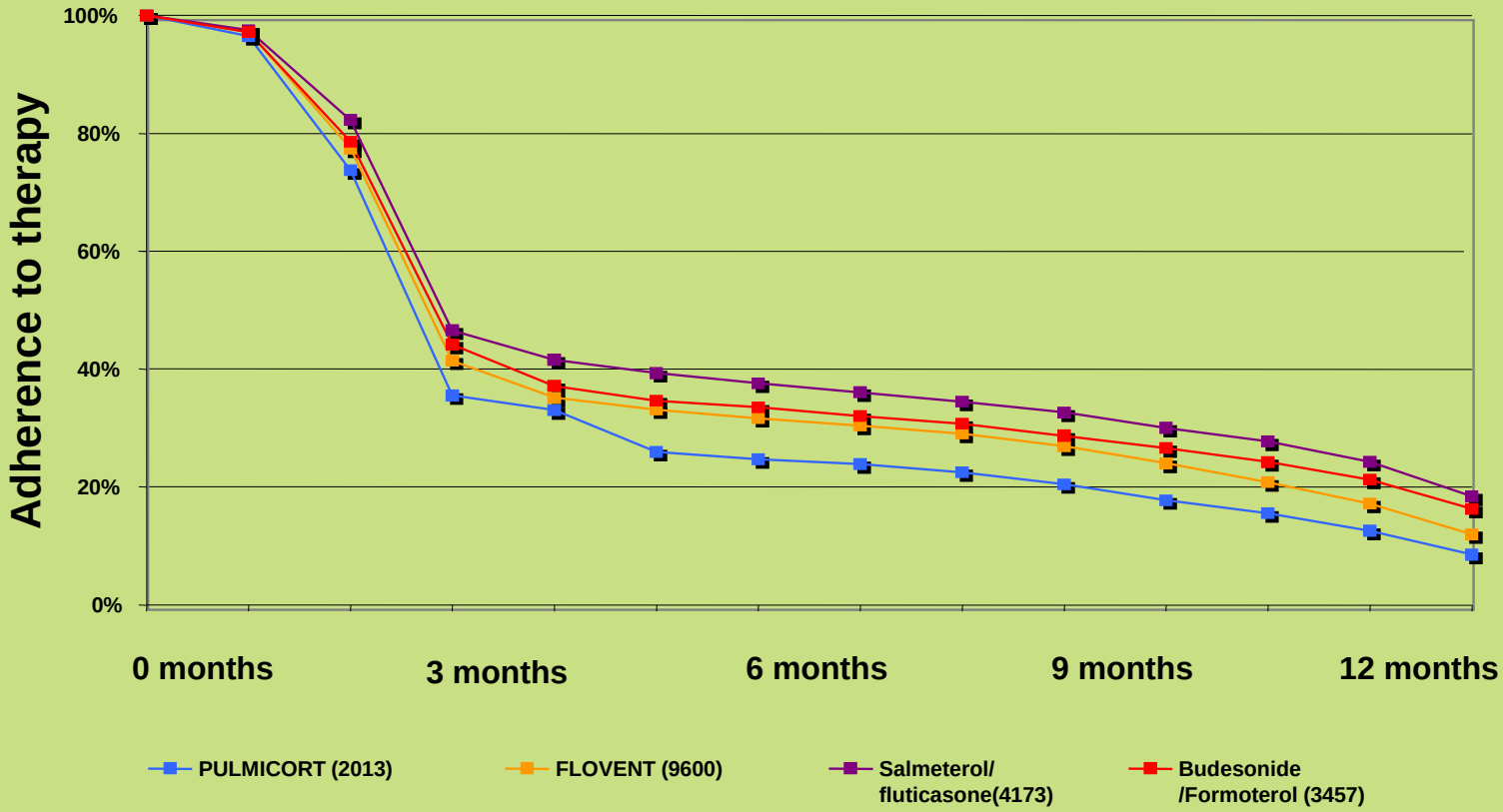
Inhaled corticosteroids are known to reduce this risk reduce the risk of asthma deaths, hospitalization and exacerbations requiring oral corticosteroids

Hancox, Respir Med 2000); Aldridge, AJRCCM 2000
Stanford, AAAI 2012; Nwaru, ERJ 2021
Suissa, AJRCCM 1994; Nwaru, ERJ 2021
Suissa, NEJM 2000 & 2002; Pauwels, Lancet 2003

Why did GINA and CTS extend ICS to Step 1?

- Inhaled SABA has been first-line treatment for asthma for 50 years
  - Dating from an era when asthma was thought to be a disease of bronchoconstriction
- Starting with SABA alone trains the patient to regard it as their primary asthma treatment
  - Goals of treatment are symptom control AND risk reduction, across the entire spectrum of asthma severity

Poor adherence to inhaled asthma (controller) agents that contain steroids



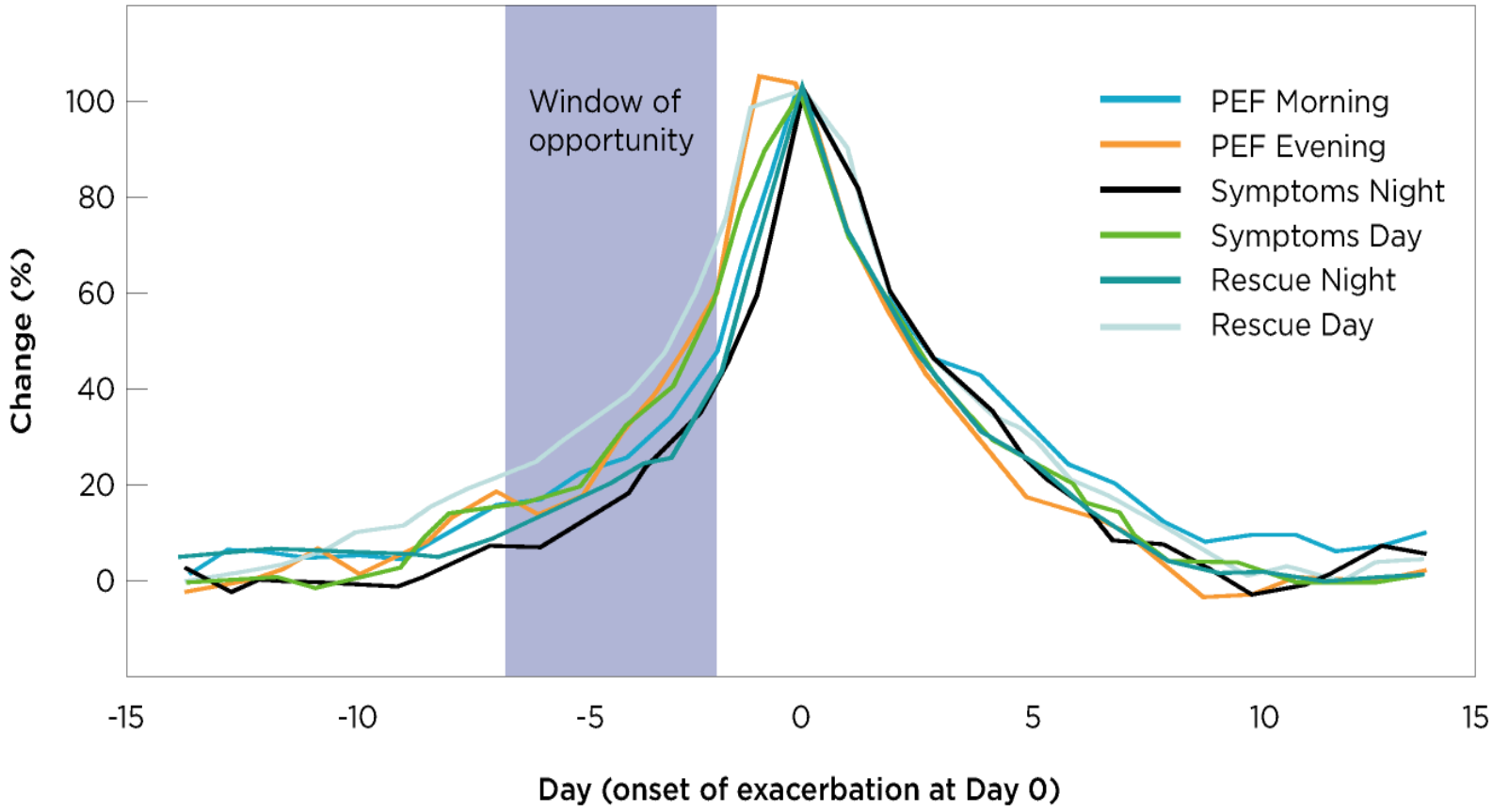
After 3 months, over 50% of patients stopped inhaled maintenance therapy. After a year, adherence decreased to below 20%.

Adapted from Brogan Canadian Private Payer data. March 2005-Feb 2006.

So to summarize rationale for paradigm shift…no more SABA alone

- To reduce the risk of asthma-related exacerbations and death, including in patients with so-called mild asthma
- To provide consistent messaging about the aims of treatment, including prevention of exacerbations across the spectrum of asthma severity
- To avoid establishing a pattern of patient reliance on SABA early in the course of disease

A new paradigm: SMART therapy
"Prelude to an exacerbation"



Tattersfield A. Am J Respir Crit Care Med 1999;160:594

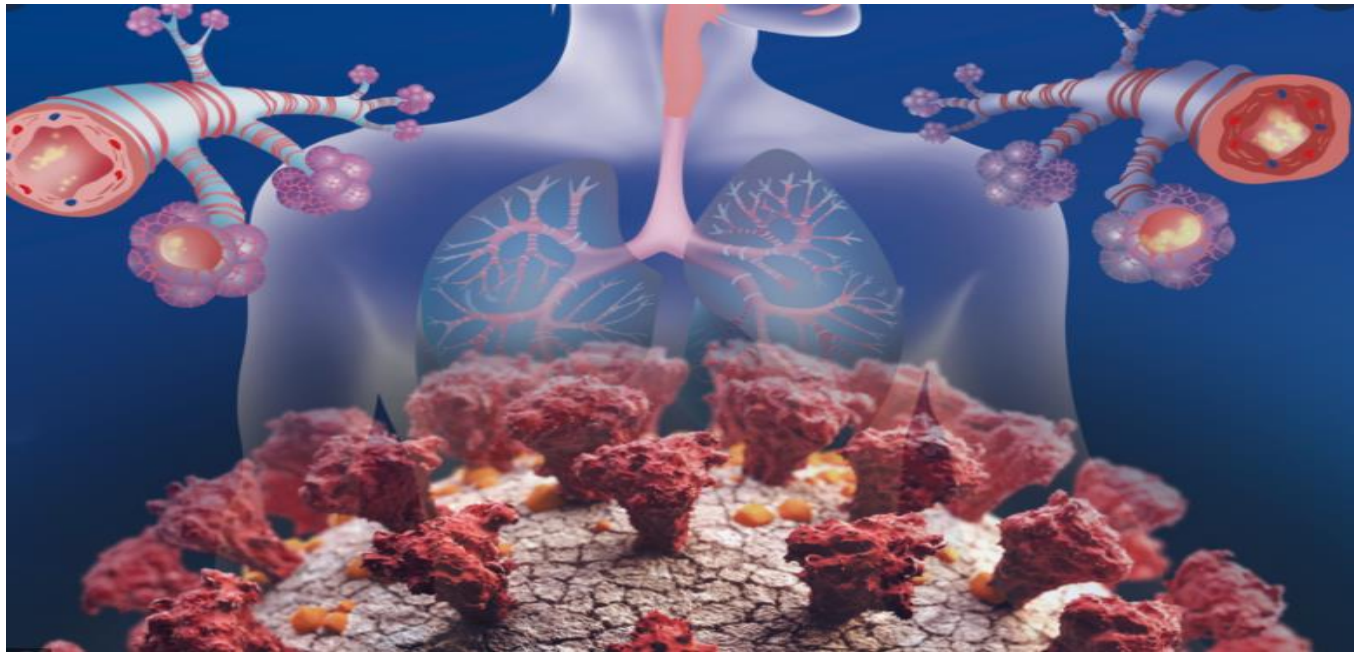
Short-term change (2 weeks) for worsening asthma, evidence for alteration of controller dose?

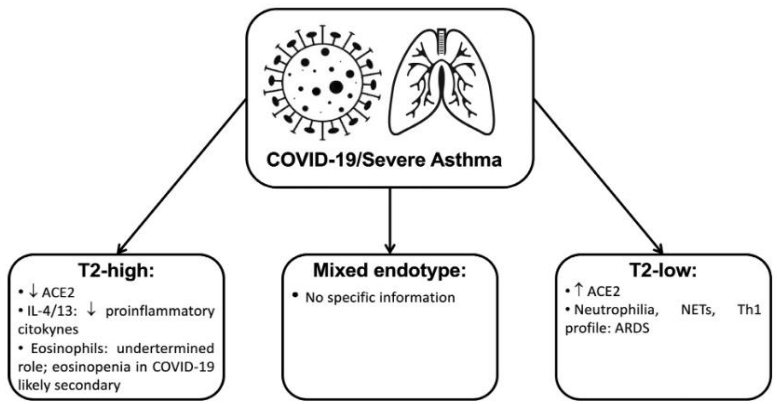
Controller approach:	**Increase to:**
Maintenance ICS (with SABA as needed)	> 12 years, quadruple ICS dose. In children with high adherence, 5x increase in ICS dose not effective
Maintenance and reliever ICS-form (Symbicort)	Continue “SMART”; increase doses as needed for symptoms (auto titrates need for ICS)
Maintenance ICS-formoterol (Symbicort) (with SABA as reliever)	Quadruple maintenance ICS formoterol
Maintenance ICS-LABA (eg Advair, Zenhale) with SABA as reliever	Step up to higher dose formulation (eg from Advair 125 to Advair 250), or add additional ICS separately to quadruple the ICS dose

Conclusions

- Mild asthma can lead to severe outcomes, such as ED visits, hospitalizations and death
- Use of inhaled corticosteroids is the most effective way to improve control and reduce risk in asthmatic patients
- Most (if not all) asthmatics deserve ICS treatment
  - SABA alone is now rarely justified
- Identify measures of CONTROL and then RISK when deciding to treat with controller therapy
  - Know the new control measures and important risk factors to assess (CTS 2021)
- Need to be more aggressive in managing short term worsening symptoms
- Single inhaler maintenance and reliever therapy is effective in titrating need for ICS with severity of symptoms

"I stopped to smell the flowers. Where's my inhaler?"





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Text **TOMGERSTNER243** to **37607** once to join

Which of the following statements surrounding asthma and COVID-19 is true?

Asthma represents an underlying risk factor for the acquisition of COVID-19	**A**
Asthma is an underlying risk factor for severity of COVID-19 illness	**B**
Use of inhaled corticosteroids, especially at the time of a positive PCR test, is a risk factor for more severe COVID-19	**C**
Use of biologics in asthma, due to their immunosuppressive effects, represent a risk factor for COVID-19 severity	**D**
All of the above	**E**
None of the above	**F**

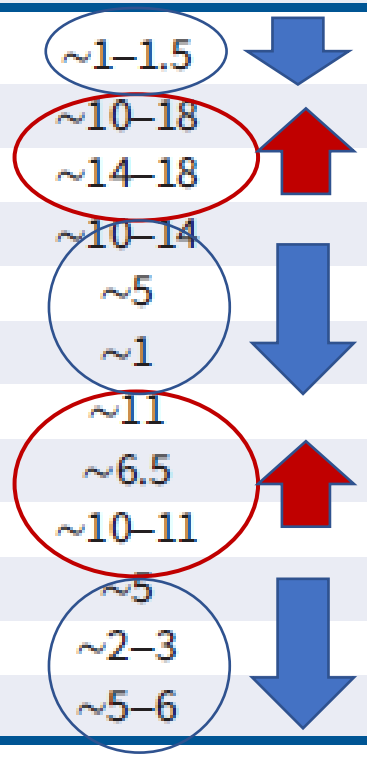
Which of the following statements surrounding asthma and COVID-19 is true?

- Use of systemic corticosteroids during COVID-19 illness in asthmatics is associated with more severe outcomes
- Asthma hospitalizations did trend up during the 1st and 2nd waves of COVID-19
- Mainly due to fear of medication side effects, adherence to regular use of inhaled corticosteroids in asthmatics fell during the COVID pandemic
- Recent use of systemic corticosteroids prior to aquiring COVID-19 was associated with more severe outcomes
- All of the above
- None of the above

Asthma and risk of COVID-19

TABLE 1 Estimated asthma prevalence (%) among patients with coronavirus disease 2019 (COVID-19) in comparison with the general population asthma prevalence in various countries [13–27, 38, 46]

Country	National asthma prevalence (%)	Asthma prevalence among SARS-CoV-2 positive patients (%)
China	~1.5–6.5	~1–1.5
USA	~8	~10–18
UK	~12–18	~14–18
Australia	~20	~10–14
Spain	~6–7	~5
Italy	~6	~1
Ireland	~9	~11
Switzerland	~5	~6.5
Germany	~7–8	~10–11
Israel	~7.5–8.5	~5
Mexico	~2.5	~2–3
Brazil	~12.5–13.0	~5–6

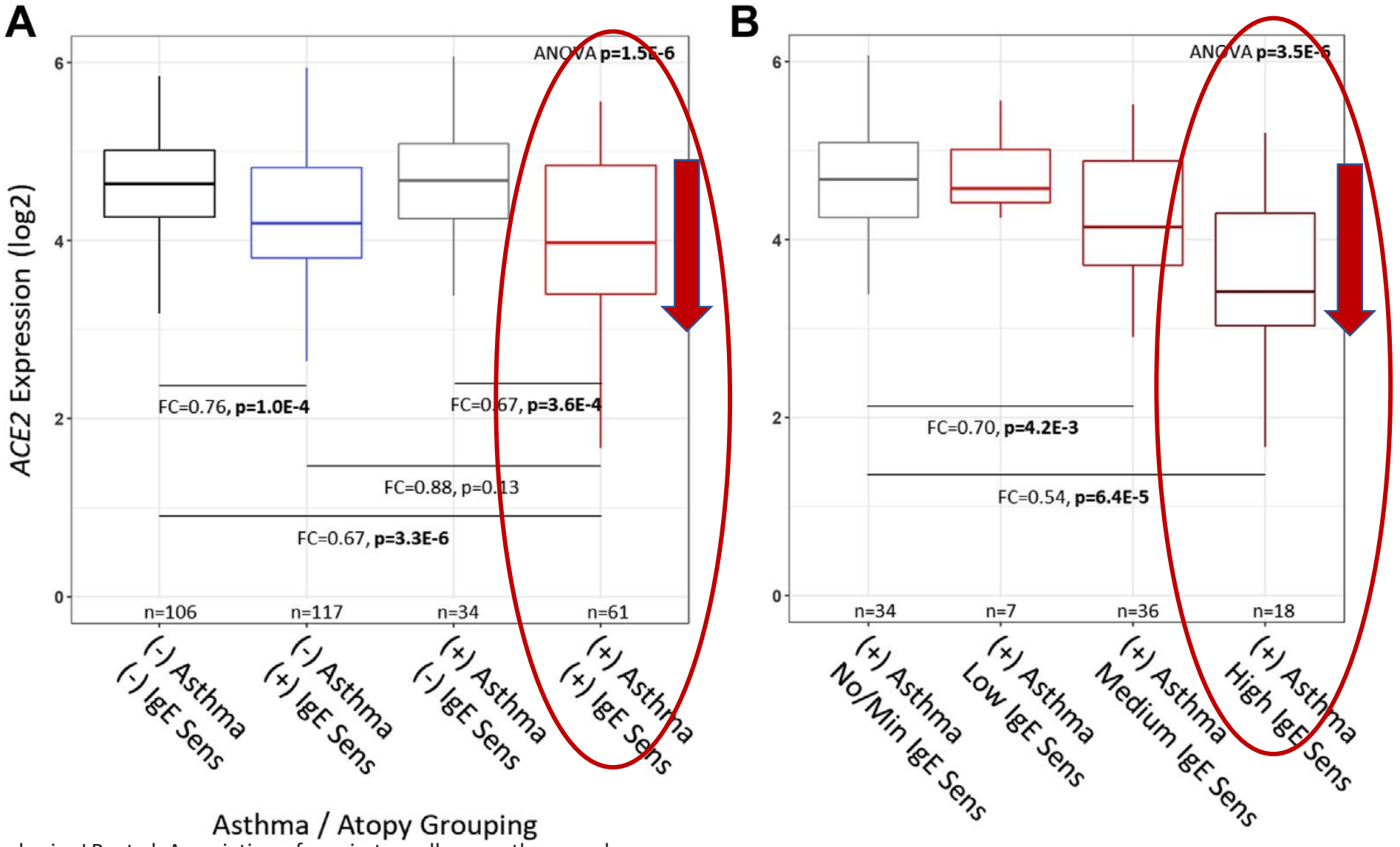


Asthma and COVID-19 severity

- Older age, obesity, CV disease and diabetes….what about asthma?
- Some studies did show asthma was a risk factor, but not after controlling for age and other co-morbidities
  - Based on prevalence data from 150 studies worldwide- no clear evidence of increased risk of COVID-19 diagnosis, hospitalization, severity or mortality in asthma (Terry et al, 2021)
  - Pts with asthma showed a tendency of LOWER death risk compared with patients without asthma (LIU et al,131 studies, systematic review, >400,000pts)
- Severe asthma: Recent data from the Belgian Severe Asthma Registry and the Severe Asthma Network in Italy conclude that in patients with severe asthma, COVID-19 was not an independent risk factor.

Terry PD, Heidel RE, Dhand R. Asthma in adult patients with COVID-19: prevalence and risk of severe disease. Am J Respir Crit Care Med 2021; 203: 893–905.
Liu S, Cao Y, Du T, et al. Prevalence of comorbid asthma and related outcomes in COVID-19: a systematic review and meta-analysis. J Allergy Clin Immunol Pract 2021; 9: 693–701.

ACE2 expression is decreased in nasal epithelium of children with allergic sensitization and allergic asthma (Th2)



Jackson DJ, Busse WW, Bacharier LB, et al. Association of respiratory allergy, asthma, and expression of the SARS-CoV-2 receptor ACE2. J Allergy Clin Immunol 2020

Asthma phenotype and COVID-19

- Th2-high (allergic asthma) vs Th1 asthma types
  - Th2-high gene expression→ reduced ACE2 gene expression, reduction in exaggerated immune response
  - Asthmatics with Th1-high inflammation usually older, comorbidities, may have exaggerated immune response to COVID infections (e.g. cytokine storm)
- Studies show non-allergic asthma (Th1) associated with greater risk of severe clinical outcomes of COVID-19 than those with allergic asthma, supporting the idea that the Th2-low phenotype may be protective

Bradding P, Richardson M, Hinks TSC, et al. ACE2, TMPRSS2, and furin gene expression in the airways of people with asthma-implications for COVID-19. J Allergy Clin Immunol 2020; 146: 208–211.
Yang JM, Koh HY, Moon SY, et al. Allergic disorders and susceptibility to and severity of COVID-19: A nationwide cohort study. J Allergy Clin Immunol 2020; 146: 790–798.

What about asthma medications and COVID-19 risk?

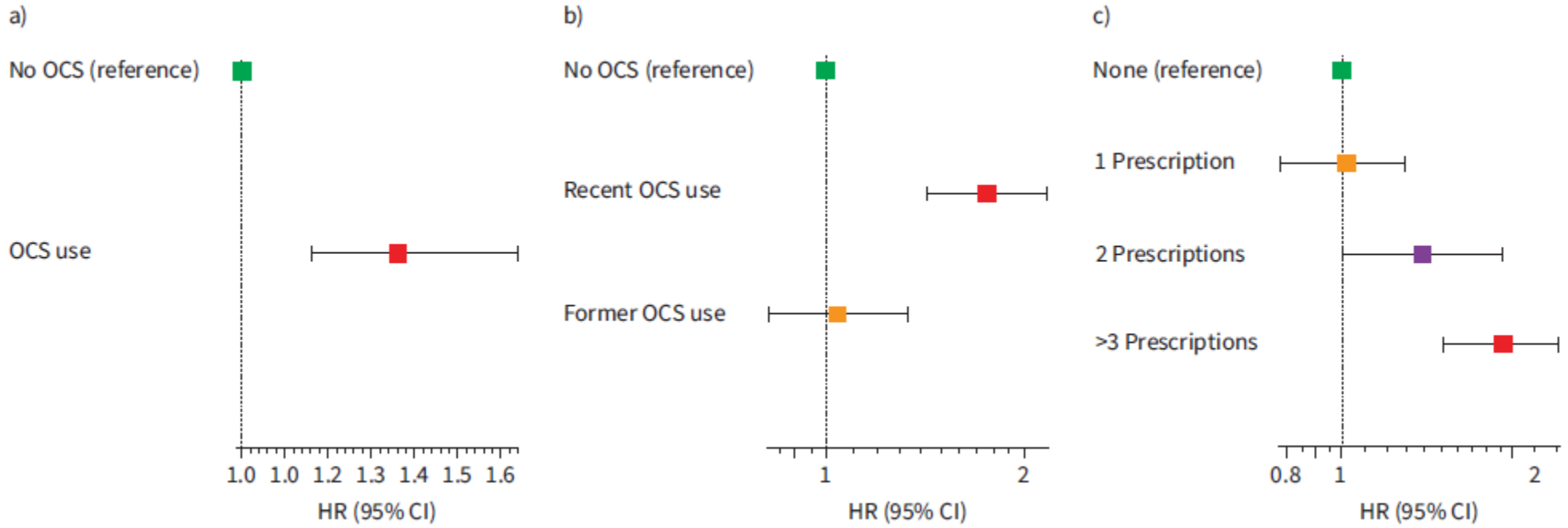
1. Inhaled corticosteroids

- Also associated with reduced expression of ACE2 receptors!
- Use of ICS in patients aged 50 years and older within 2 weeks of admission was associated with decreased mortality.
  - ICS have anti-inflammatory effects in the lungs, reduce expression of ACE-2 in bronchial epithelial cells, and may reduce replication of SARS-CoV-2 in epithelial cells in vitro
  - ? Possible protective effect
- Most studies show no evidence that use of ICS neither increases or decreases infectivity or severity of COVID
  - Some report that compared to asthmatics who required hospitalization for COVID-19, a higher % of nonhospitalized patients used ICS

- Altogether, it seems that ICS are not an independent risk factor for increased SARS-CoV-2 infectivity or COVID-19 severity. ? May be helpful

Lipworth B, Chan R, Kuo CR. Use of inhaled corticosteroids in asthma and coronavirus disease 2019: Keep calm and carry on. Ann Allergy Asthma Immunol 2020; 125: 503–504.
Choi YJ, Park J-Y, Lee HS, et al. Effect of asthma and asthma medication on the prognosis of patients with COVID-19. Eur Respir J 2021; 57:
Solís P, Carreno H. COVID-19 fatality and comorbidity risk factors among confirmed patients in Mexico.medRxiv 2020; preprint [https://doi.org/10.1101/2020.04.21.20074591].
Bloom CI, Drake TM, Docherty AB, et al. Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study. Lancet Respir Med 2021

Oral corticosteroids and outcomes in asthmatic patients with COVID-19



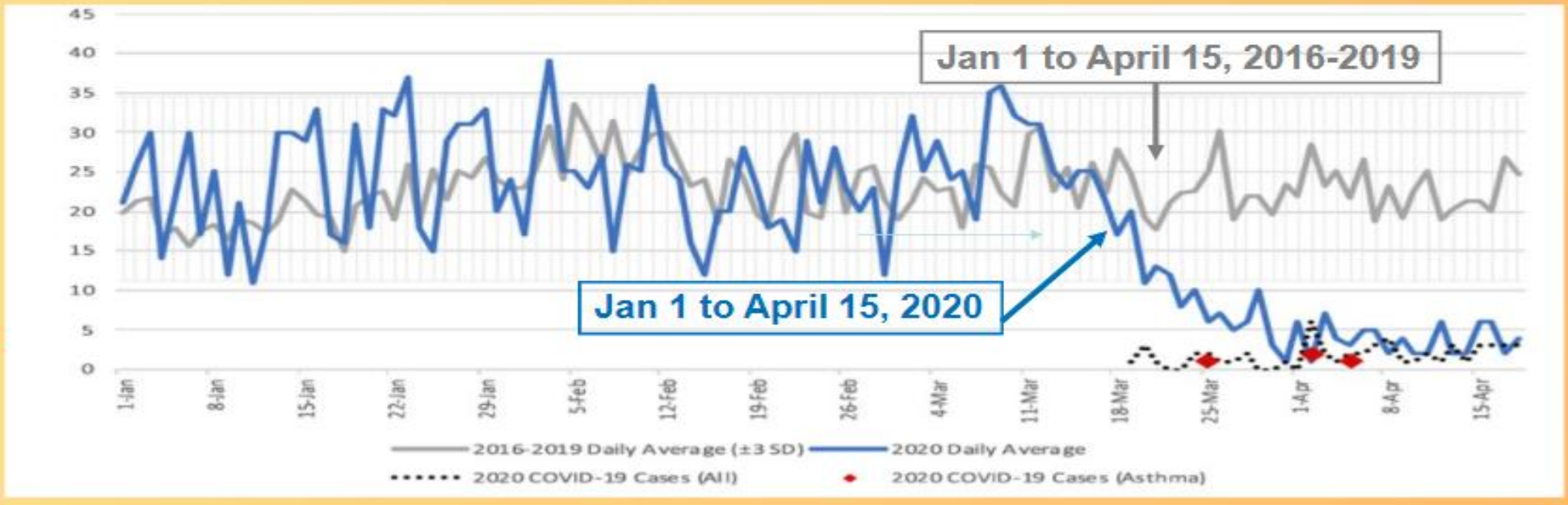
Adir Y, Humbert M, Saliba W. COVID-19 risk and outcomes in adult asthmatics treated with biologics or systemic corticosteroids: nationwide real-world evidence. J Allergy Clin Immunol 2021; 15: S0091-6749(21) 00938-6.

Other (indirect) Effects of COVID-19 on asthma outcomes- Reduction of ER visits

Initial Effects of the COVID-19 Pandemic on Pediatric Asthma Emergency Department Utilization

Design: Retrospective study of ED visits during the 1st 4-months of 2016-2020 from Children's Hospital of Philadelphia (CHOP)

Objective: Determined improvement change in asthma ED visits.



Conclusion: Dramatic decrease in asthma-related ED use was well below historical seasonal variation.

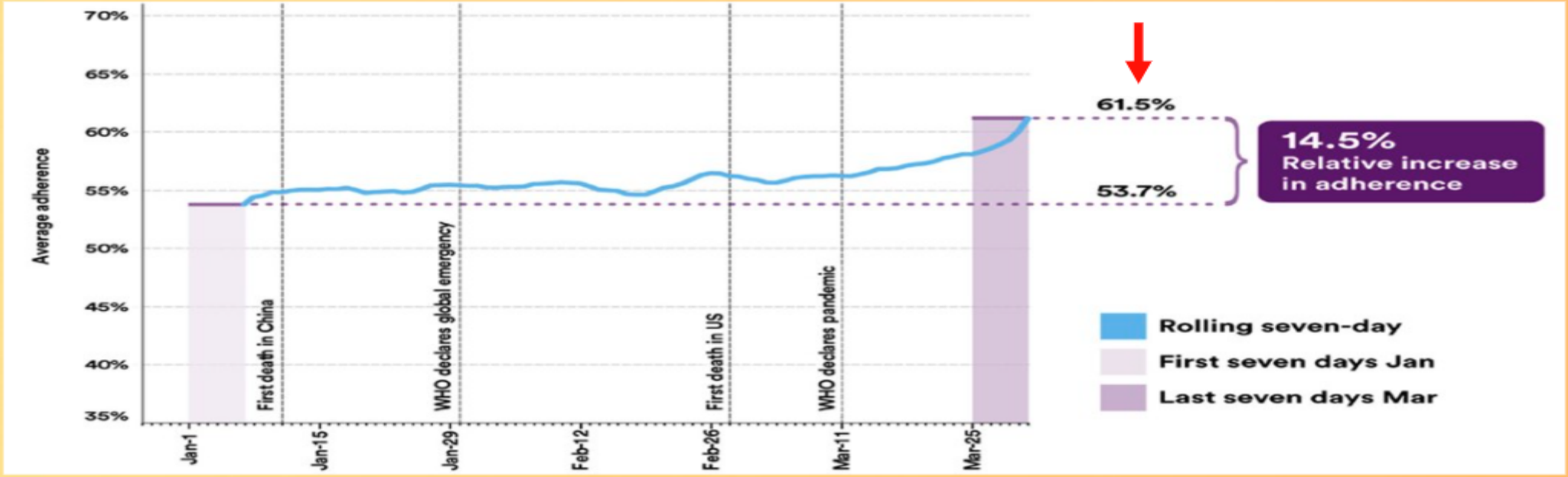
Kenyon, et al. JACI: IP 2020; 2774

Other (indirect) Effects of COVID-19 on asthma outcomes- increased medication adherence

Changes in Medication Adherence among Patients with Asthma and COPD during the COVID-19 Pandemic

Design: Propeller Health digital platform determined adherence to controller inhaler use in 7,578 adult patients (77% asthma, 67% females)

Figure. Mean daily controller adherence in asthma and COPD before and during COVID-19 pandemic.



Conclusion: Increased medication adherence seen during COVID-19.

Kaye, et al. JACI: IP 2020; 8:2384

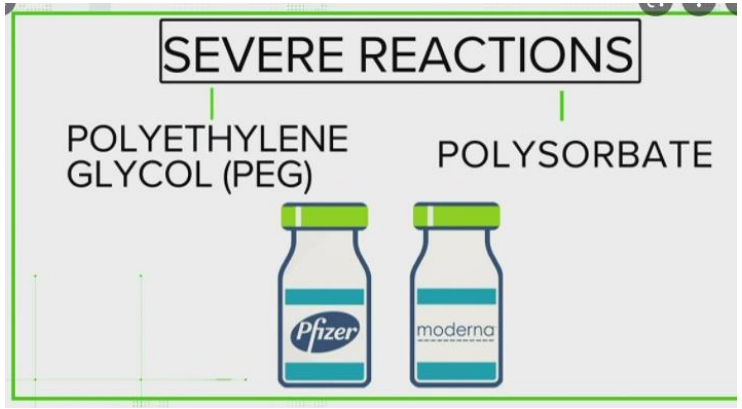
Asthma and COVID-19

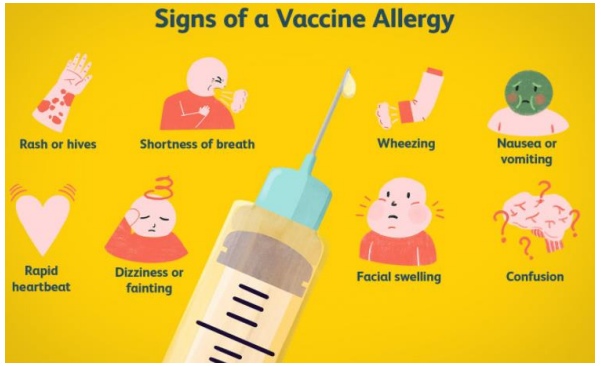
1. Asthma represents an underlying risk factor for the acquisition of COVID-19
2. Asthma is an underlying risk factor for severity of COVID-19 illness
3. Use of inhaled corticosteroids, especially at the time of a positive PCR test, is a risk factor for more severe COVID-19
4. Use of biologics in asthma, due to their immunosuppressive effects, represent a risk factor for COVID-19 severity
5. All of the above
6. None of the above

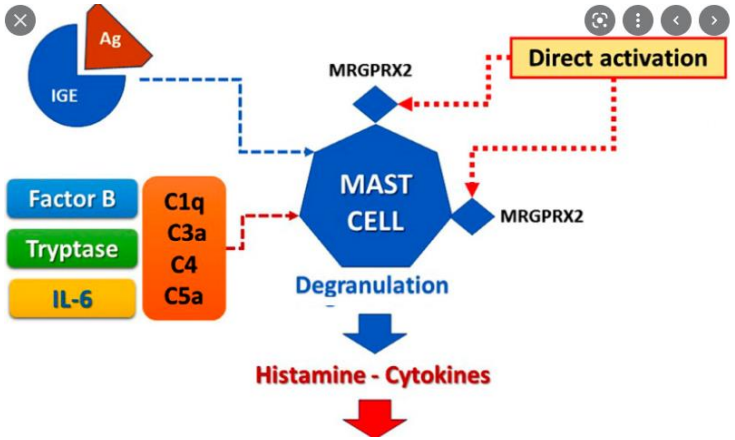
Asthma and COVID-19

1. Use of systemic corticosteroids during COVID-19 illness in asthmatics is associated with more severe outcomes
2. Asthma hospitalizations did trend up during the 1st and 2nd waves of COVID-19
3. Mainly due to fear of medication side effects, adherence to regular use of inhaled corticosteroids in asthmatics fell during the COVID pandemic
4. Recent use of systemic corticosteroids prior to acquiring COVID-19 was associated with more severe outcomes
5. All the above
6. None of the above

Coffee Break







COVID Vaccine Allergy

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Text **TOMGERSTNER243** to **37607** once to join

DEC 2020 Headlines

Global News

HEALTH

U.K. warns people with 'significant' allergies to avoid Pfizer coronavirus vaccine

By **Staff · Reuters**

Posted December 9, 2020 9:23 am EST

The New York Times

The Coronavirus Pandemic › | LIVE Covid-19 Updates

Boston Doctor Reports Serious Allergic Reaction After Getting Moderna's Covid Vaccine

The patient, who has a severe shellfish allergy, recovered quickly with treatment. Until now, reports of severe reactions had been linked to the Pfizer vaccine.

Patient questions about COVID vaccines and risk for allergic reactions…

- I had a severe reaction to a flu shot, can I get the COVID-19 vaccine?
- I have severe food allergies that required epinephrine, can I get the COVID vaccine?
- What is PEG and how am I supposed to know if I'm allergic to it? If I am, can I still get the COVID vaccine?
- I had a reaction after my first dose, the ER nurse/GP/pharmacist/Aunt Sally said not to get the 2nd dose, now what?
- I developed some hives after my first dose, and after my second dose I was covered in hives, can I get my COVID booster dose?

How Frequent are Allergic Reactions to Vaccines?

- Estimated risk of anaphylaxis is 0.65-1.53 per 1 million doses
- Constituents causing IgE reactions:
  - Gelatin
  - Egg
  - Latex
  - Yeast
- A 3 year study population based study in the US Vaccine Safety Datalink
  - Incident rate of anaphylaxis was 1.31 (92% CI, 0.9-1.84) cases per million vaccine doses
  - Trivalent influenza vaccine was a major contributor to the cases
  - No deaths

McNeill MM et al. *J Allergy Clin Immunol* 2018; 141: 463-72.

Kelso JM et al. *J Allergy Clin Immunol*, 2012; 130(1): 25-43.

How Frequent are Allergic Reactions to COVID Vaccines?

- With COVID-19 vaccination
  - VAERS age 6-17: 35 per 9.8 million (3.5 cases per million)
  - VAERS adults US: 1.7 per million
  - Canadian: ~3.6 cases per million
  - No fatalities, no long-term morbidity

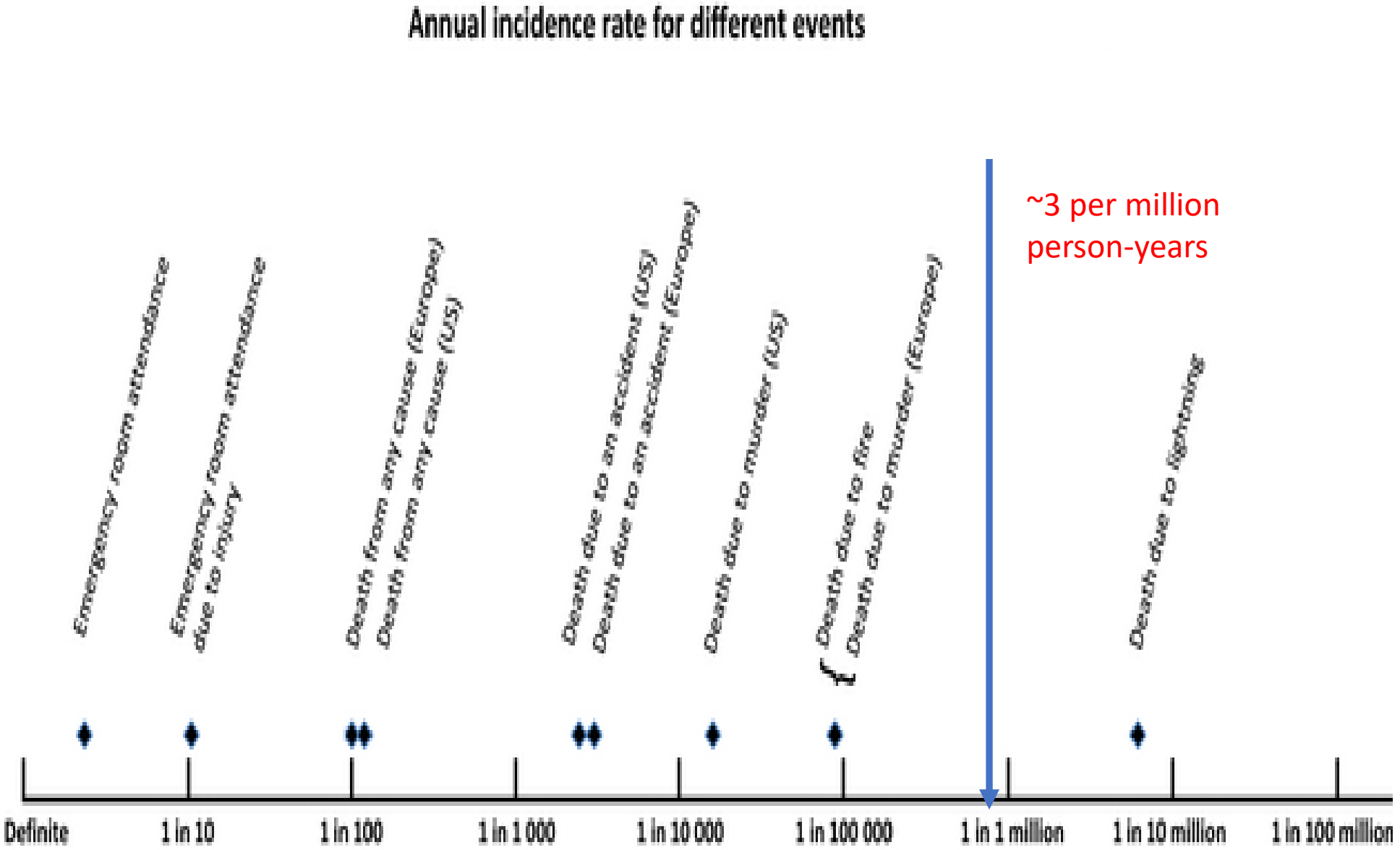
Greenhawt, JACI IP 2021 June

Klein et al, Surveillance for adverse events after COVID-19 mRNA vaccination, JAMA, SEP 2021

Public Health Agency of Canada, www.canada.ca/en/public-health.html

- Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and meta-analysis

T. Umasunthar, J. O. Warner et al, Clin Exp Allergy 2013



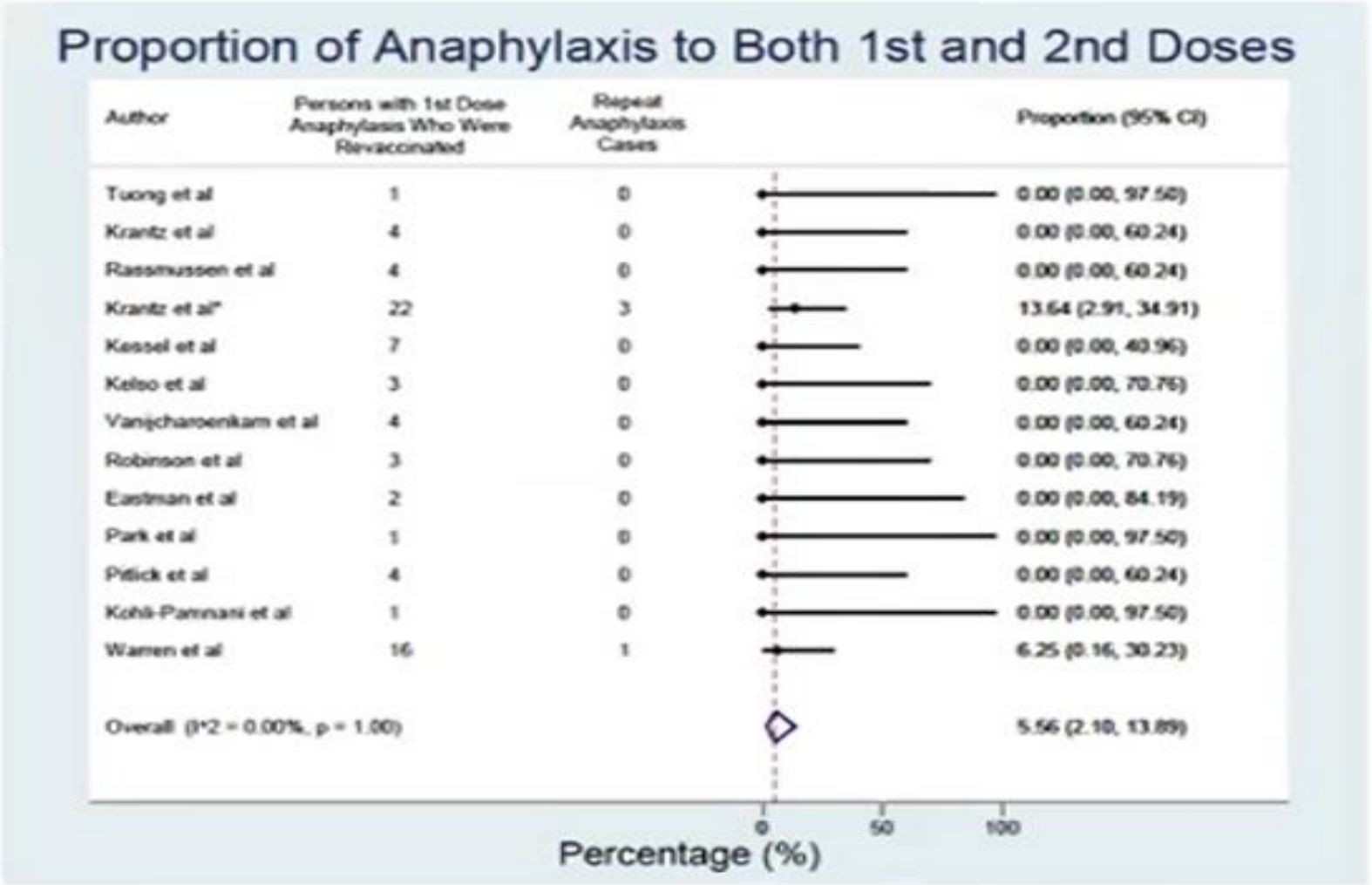
Who is at risk for COVID anaphylaxis?

- Patients with allergy to aeroallergens, venom, food, latex, RCM, drug chronic urticaria, 30 minutes observation
  - No serious allergic reactions in 7668 patients
  - Considered low risk
- Patients with prior anaphylaxis to vaccine or drug, multiple drug allergies, mast cell disorders, Ref by GPs concerned about serious allergic risk: underwent 2 hours observation
  - Identified 429 patients
  - 96% had no immediate symptoms, 6 with mild allergic symptoms resolved with antihistamine, 3 had non life-threatening anaphylaxis

Shavit et al, Prevalence of allergic reactions after Pfizer-BioNTech COVID-19 vaccination among adults with high allergy risk, JAMA AUG 2021

Risk of Severe Reaction if Re-Vaccinated

-Systematic review and meta-analysis of allergic reactions associated with 2nd dose among those having initial reactions
-22 publications identified from 5500 citations, inclusive of 1337 re-vaccinations including 72 with 1st dose anaphylaxis



Repeat Anaphylaxis with 2nd dose: 5.5%

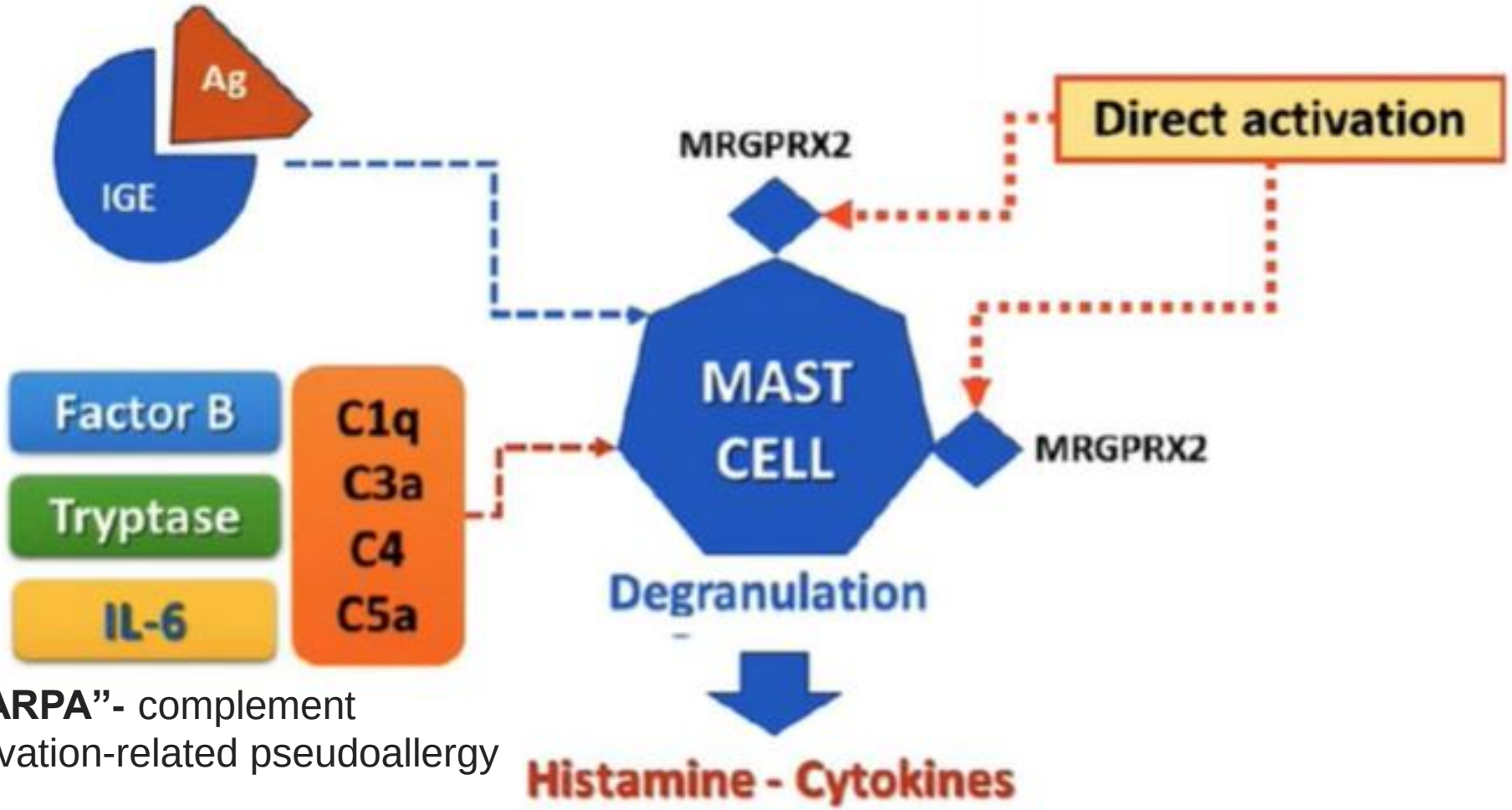
Greenhawt et al, JACI IP 2021

Anaphylaxis to first dose of COVID vaccines: Don't give up on the 2nd dose!

- 2 Allergy clinics (Nashville and Denmark) found 0.06% rate of immediate type allergic reactions to Pfizer in HC workers- 47 patients in total
  - 39 mild reactions, 8 anaphylaxis
  - Of the 8, 5 had tryptase level sent-→ negative
  - 8/8 tested negative for PEG allergy
  - 8/8 tolerated single dose injection of vaccine with no or mild symptoms
- Lack of tryptase elevation, negative PEG testing, observed tolerance of 2nd dose do NOT support an IgE mediated mechanism

Krantz M, et al. Allergy, Sept 2021

Vaccine induced allergic reactions



“CARPA”- complement activation-related pseudoallergy

Kounis, NG et al, Allergic reactions to current available COVID 19 vaccinations: Pathophysiology, causality and therapeutic considerations, Vaccines 2021

What is the risk posed by excipients?

A. The Pfizer-BioNTech COVID-19 Vaccine Excipients-Ingredients
1. mRNA, nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2and constitutes the active ingredient
2. Electrolytes potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodiumphosphate dihydrate,
3. Lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), [(polyethyleneglycol [PEG])-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mgcholesterol)
4. polyethyleneglycol
5. Sugar (sucrose)
6. Saline (Sodium Chloride) acting as adiluent, added to the vaccine forinjection
B. The Moderna COVID-19 Vaccine Excipients-Ingredients
1. Messenger ribonucleic acid (mRNA) as an active ingredient
2. Acetic acid
3. Lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC])
4. polyethylene glycol
5. Sodium acetate
6. Sugar (sucrose)
7. Tromethamine (treat or prevent acidosis)
8. Tromethamine hydrochloride

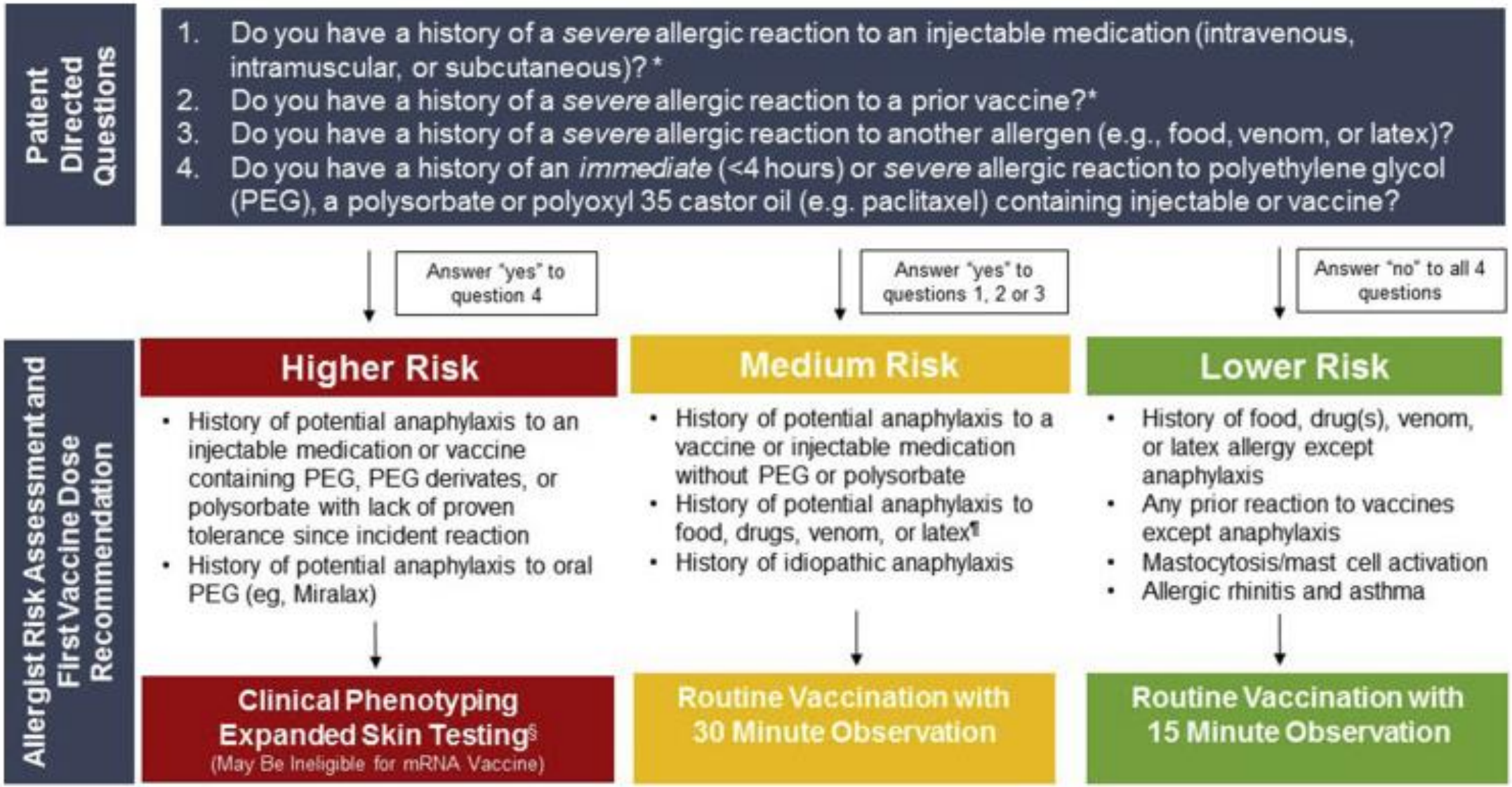
- No common ingredients with any other vaccines
- Allergic reactions to PEG are rare, only case reports
- Risk of reaction to an excipient in the vaccine is low, no causative agent has been confirmed, and a non-IgE mediated mechanism is increasingly likely.

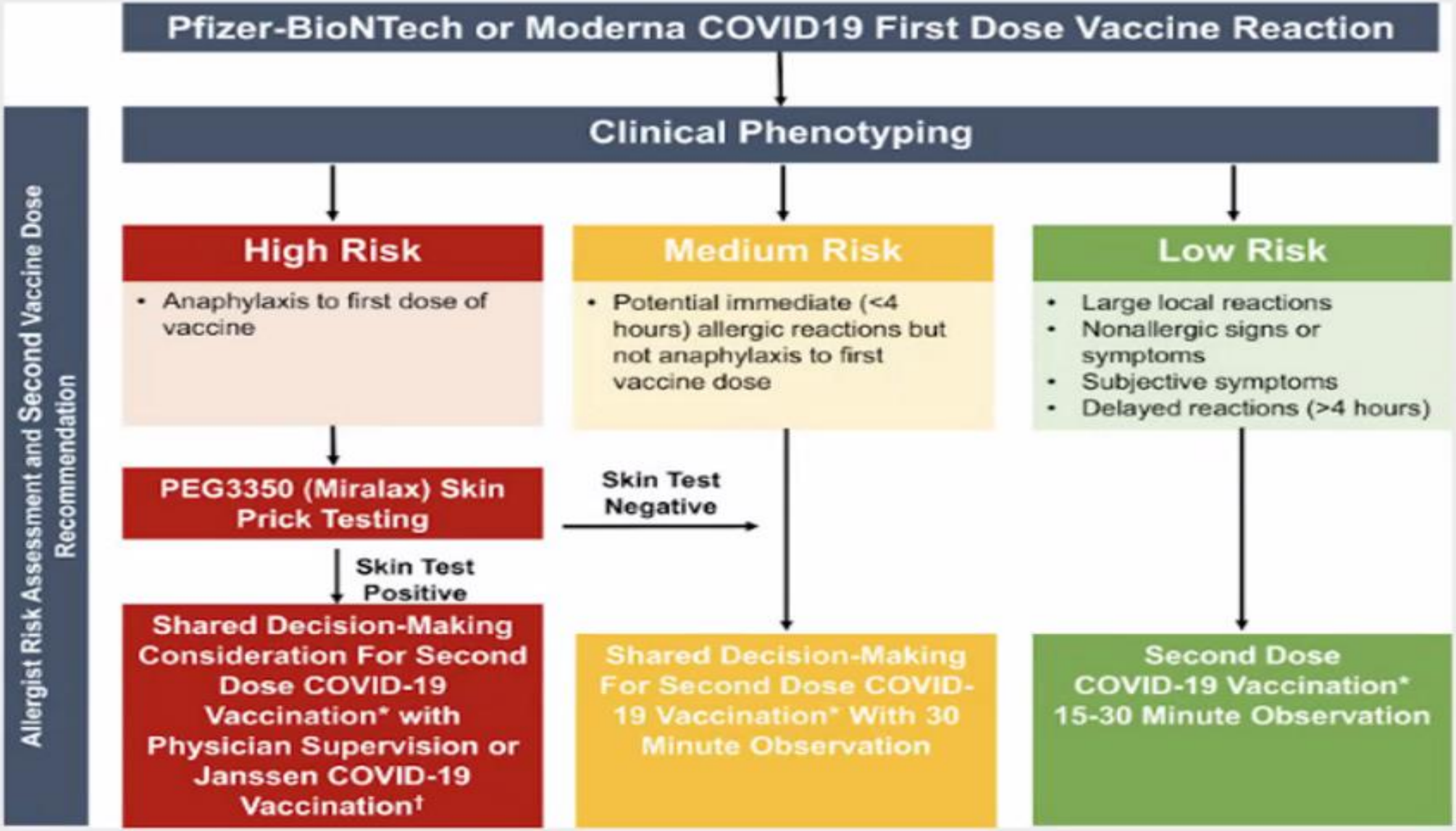
Kounis, NG et al, Allergic reactions to current available COVID 19 vaccinations: Pathophysiology, causality and therapeutic considerations, Vaccines 2021

Wolfson, et al, First-Dose mRNA COVID-19 Vaccine Allergic Reactions: Limited role for excipient skin testing, JACI Pract SEP 2021

CSACI and NACI Recommendations:

- Assessment by an allergist is NOT required for those with unrelated allergies (foods, drugs, venom, environmental)
- Assessment by an allergist is warranted in any individual with suspected allergy to COVID-19 vaccine or its components
- Options for these individuals include
  - Graded vaccine administration if suspected/confirmed allergy to vaccine/component (with or without testing)
  - Selection of alternative vaccine
  - Deferral of the 2nd (or 3rd) vaccine dose


Patient Directed Questions
1. Do you have a history of a *severe* allergic reaction to an injectable medication (intravenous, intramuscular, or subcutaneous)? *
2. Do you have a history of a *severe* allergic reaction to a prior vaccine?*
3. Do you have a history of a *severe* allergic reaction to another allergen (e.g., food, venom, or latex)?
4. Do you have a history of an *immediate* (<4 hours) or *severe* allergic reaction to polyethylene glycol (PEG), a polysorbate or polyoxyl 35 castor oil (e.g. paclitaxel) containing injectable or vaccine?
Answer "yes" to question 4
Answer "yes" to questions 1, 2 or 3
Answer "no" to all 4 questions
Allergist Risk Assessment and First Vaccine Dose Recommendation
Higher Risk
• History of potential anaphylaxis to an injectable medication or vaccine containing PEG, PEG derivates, or polysorbate with lack of proven tolerance since incident reaction
• History of potential anaphylaxis to oral PEG (eg, Miralax)
Clinical Phenotyping Expanded Skin Testing§
(May Be Ineligible for mRNA Vaccine)
Medium Risk
• History of potential anaphylaxis to a vaccine or injectable medication without PEG or polysorbate
• History of potential anaphylaxis to food, drugs, venom, or latex¶
• History of idiopathic anaphylaxis
Routine Vaccination with 30 Minute Observation
Lower Risk
• History of food, drug(s), venom, or latex allergy except anaphylaxis
• Any prior reaction to vaccines except anaphylaxis
• Mastocytosis/mast cell activation
• Allergic rhinitis and asthma
Routine Vaccination with 15 Minute Observation



First-Dose mRNA COVID-19 Vaccine Allergic Reactions: Limited Role for Excipient Skin Testing -JACI in practice Banerji et al June 2021

Take home messages

- True anaphylaxis to COVID-19 vaccines is extremely rare
- Anaphylaxis to COVID-19 vaccines is likely not IgE mediated
- Anxiety/immunization stress related response common
- Patients with history of immediate systemic allergic reaction to vaccine should have an allergist assessment- most will be able to proceed with further vaccination

Where to refer patients for COVID vaccine allergy assessemnt

Manitoba
Health and Seniors Care
Population and Public Health
4th Floor; 300 Carlton Street
Winnipeg MB R3B 3M9
Email: vaccines@gov.mb.ca

Manitoba
Santé et Soins aux personnes âgées
Population et santé publique
4e étage; 300, rue Carlton
Winnipeg MB R3B 3M9
Email : vaccines@gov.mb.ca

July 20, 2021

COVID-19 Vaccine: UPDATE - Allergy Assessment and Referral Update

If a patient you have seen has had an allergic reaction to a COVID-19 vaccine, it is recommended to request a referral for allergy assessment for guidance on future doses of the vaccine by faxing a referral to the appropriate allergy clinic, according to age, to either:

The Allergy Clinic of Health Sciences Center at (204) 940-2223, **OR**
The Pediatric Allergy Department of Children's Hospital at 204-787-5040.

Please include the following information in the referral request:

- Brand of COVID-19 vaccine
- 1st or 2nd dose
- Details of the reaction

Manitoba COVID-19 Vaccine: Clinical Practice Guidelines for Immunizers and Health Care Providers has been updated online at https://manitoba.ca/covid19/vaccine/healthcare-professionals.html.

Report adverse events following (AEFI) immunization, as per www.gov.mb.ca/health/publichealth/cdc/div/aefi.html#rrp. In accordance with Section 59 of The Public Health Act, health care providers are to report a reportable AEFI within seven days of becoming aware of the AEFI. Furthermore, health care providers should report a serious AEFI within one business day, which can be by telephone, followed by the complete written report within 72 hours.

Thank you for your assistance in arranging assessment of these patients.

Sincerely,

Richard Baydack, PhD
Director
Communicable Disease Control

Tim Hilderman, MD FRCPC
Medical Lead, Vaccines
Communicable Disease Control

The Allergy Clinic of Health Sciences Center at (204) 940-2223, **OR**
The Pediatric Allergy Department of Children's Hospital at 204-787-5040.

Please include the following information in the referral request:

- Brand of COVID-19 vaccine
- 1st or 2nd dose
- Details of the reaction

A Peanut a Day Keeps the Allergist Away

When poll is active, respond at **pollev.com/tomgerstner243**

Text **TOMGERSTNER243** to **37607** once to join

Food allergy- objectives

- Know the recent trends in prevalence of food allergy
- Know the evidence of what can be done to help prevent food allergy, and make recommendations to your families
- Food allergy treatment- beyond avoidance and the autoinjector
  - Be aware of new treatment options now available and identify which patients may be most suitable

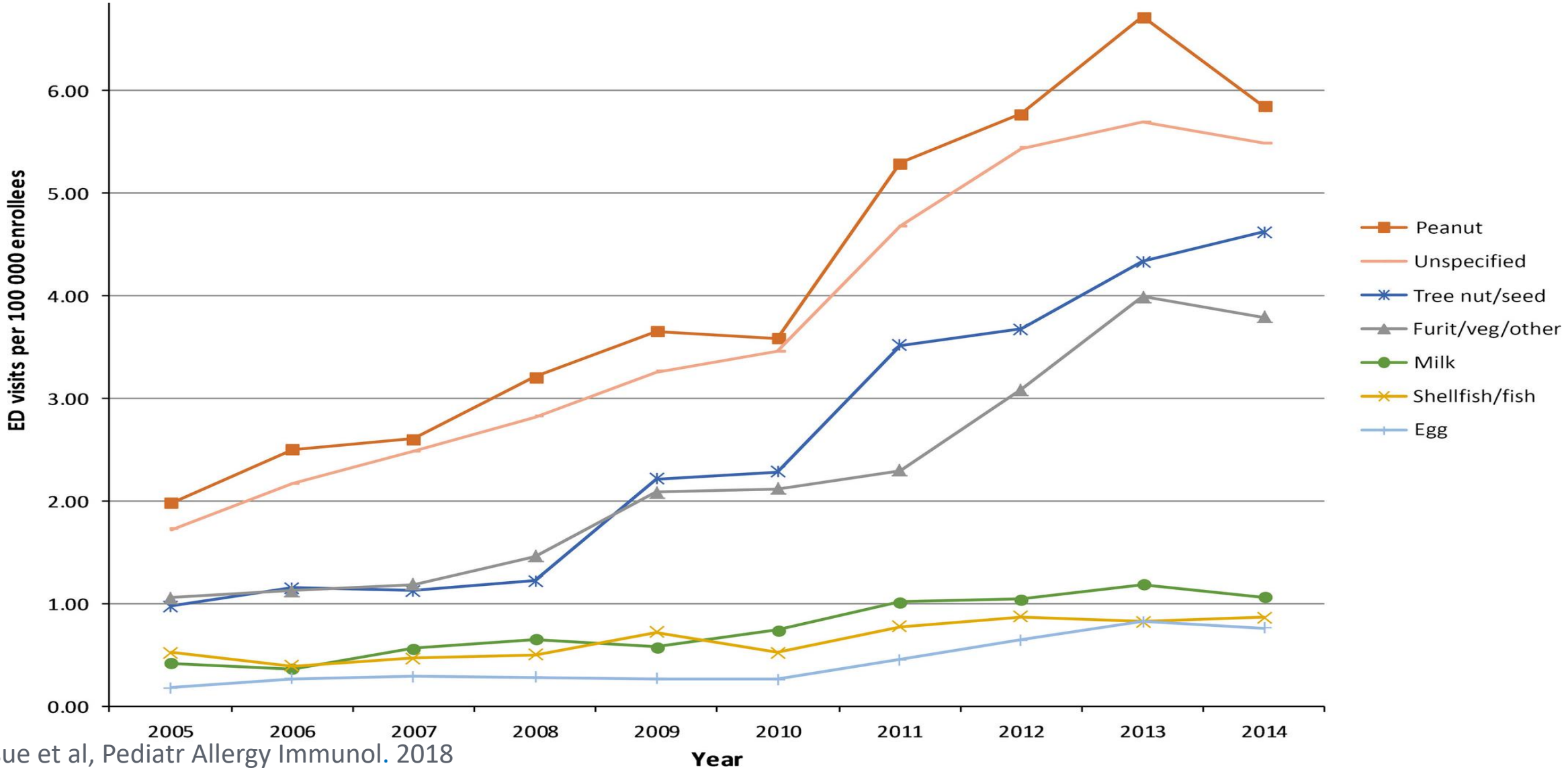
A 3-year-old presents with a reaction following consumption of peanut butter. While helping to prepare for his birthday party, he suddenly developed facial, then generalized hives, and difficulty breathing. Treated in the ER and now parents are in your office.

- Parent: “Doc, It seems like there’s so much more food allergy now than when I was a kid…is this true”?

Parent: "Doc, It seems like there's so much more food allergy now than when I was a kid…is this true"?

Yes, food allergies have become much more common these days	**A**
No, people just think now that all their symptoms must somehow be related to a food allergy	**B**
Both A and B are correct	**C**

National trends in emergency department visits and hospitalizations for food-induced anaphylaxis in US children



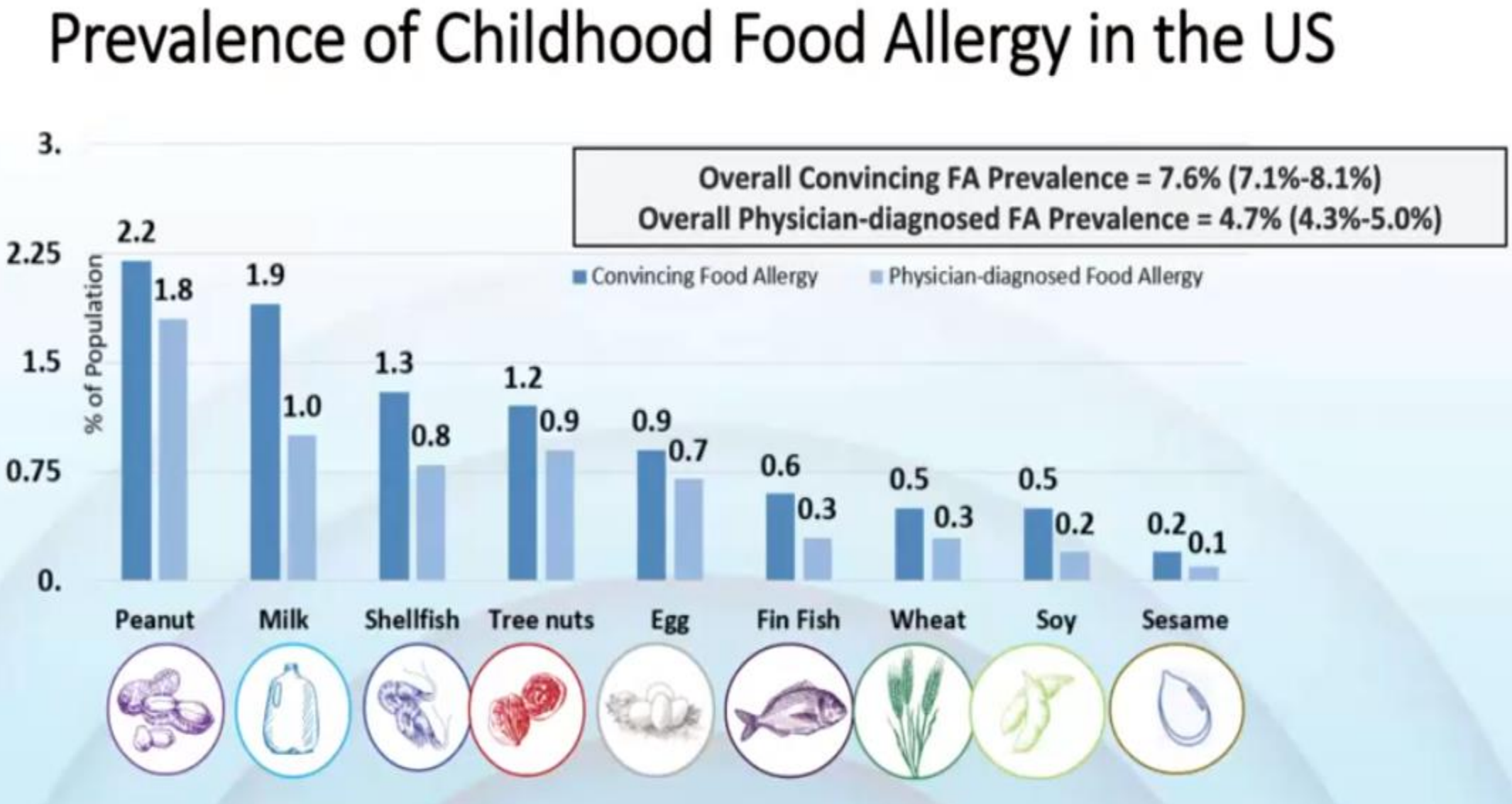
Motosue et al, Pediatr Allergy Immunol. 2018

The scope of the problem…

- 8% of U.S. Children have a food allergy

Prevalence, severity, and distribution of childhood food allergy in the US. Gupta, Pediatrics, 2011

The common culprits…



Gupta RS, Warren CM, Smith BM, Blumenstock JA, Jiang J, Davis MM, Nadeau KC. The Public Health Impact of Parent-Reported Childhood Food Allergies in the United States. Pediatrics 2018-1235

Parent (jumping ahead a bit here, but hey, you're flexible!):

Wow! So, my son is in good company it seems… What are the chances that he may outgrow his allergy?

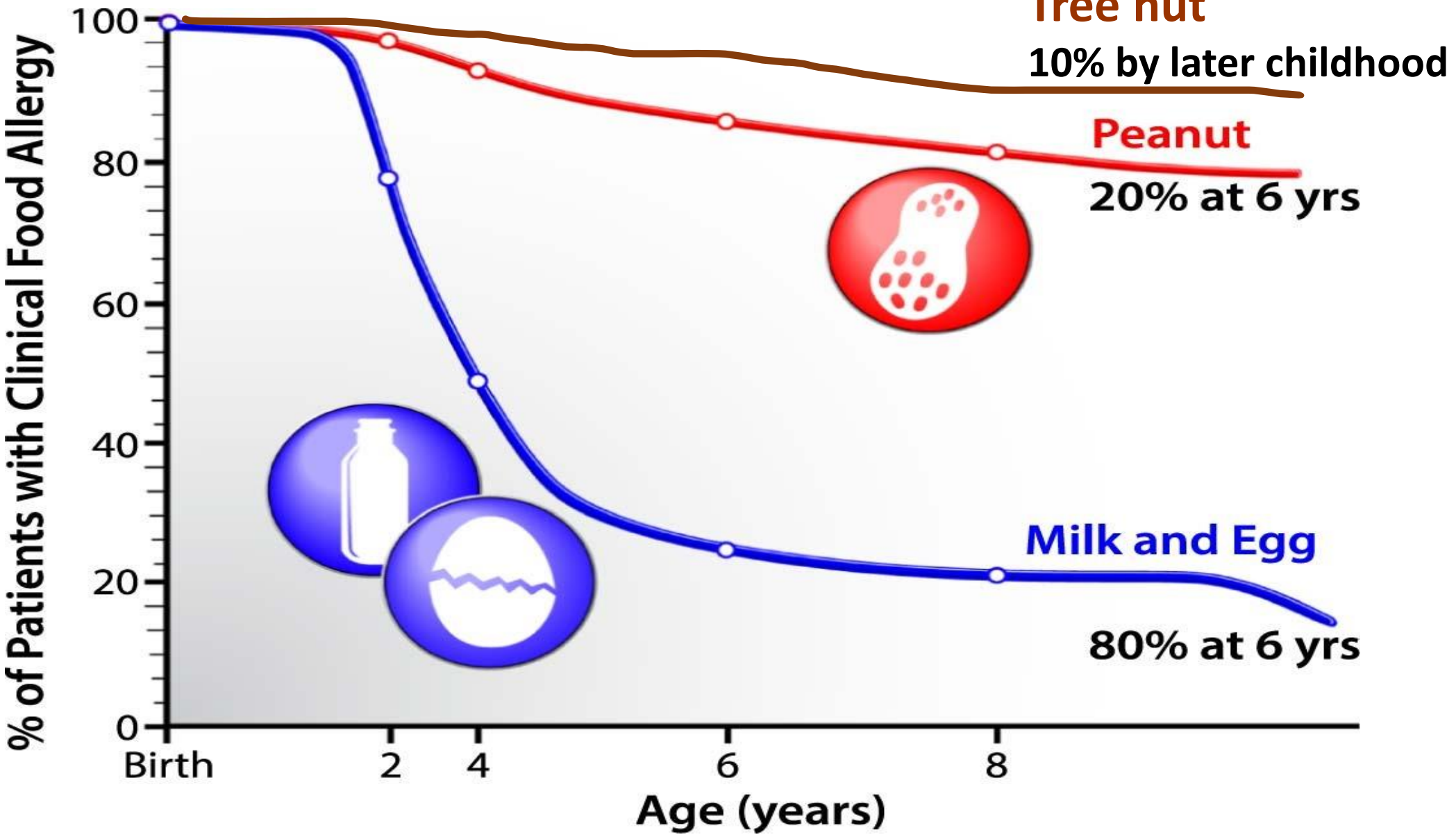
Wow! So, my son is in good company it seems…What are the chances that he may outgrow his allergy?

Sorry, kids do not outgrow peanut or nut allergies

Slight chance, maybe about 10-20%

Typically, 60-70% will outgrow this by school age

Most kids eventually will, so hang in there!



Annals of Allergy, Asthma & Immunology 2018 120245-253DOI: (10.1016/j.anai.2018.01.027)

Parent (pondering some more, and quite “tickled” that you have put so much effort into your answers!)

“OK, Doc, so back to what you were saying earlier, why this increase in food allergy… What are we doing differently?”

(and btw, your waiting room is filling up!)

OK Doc, so why this increase in food allergy?

You're kidding, right?

Must be related to our immune system somehow…

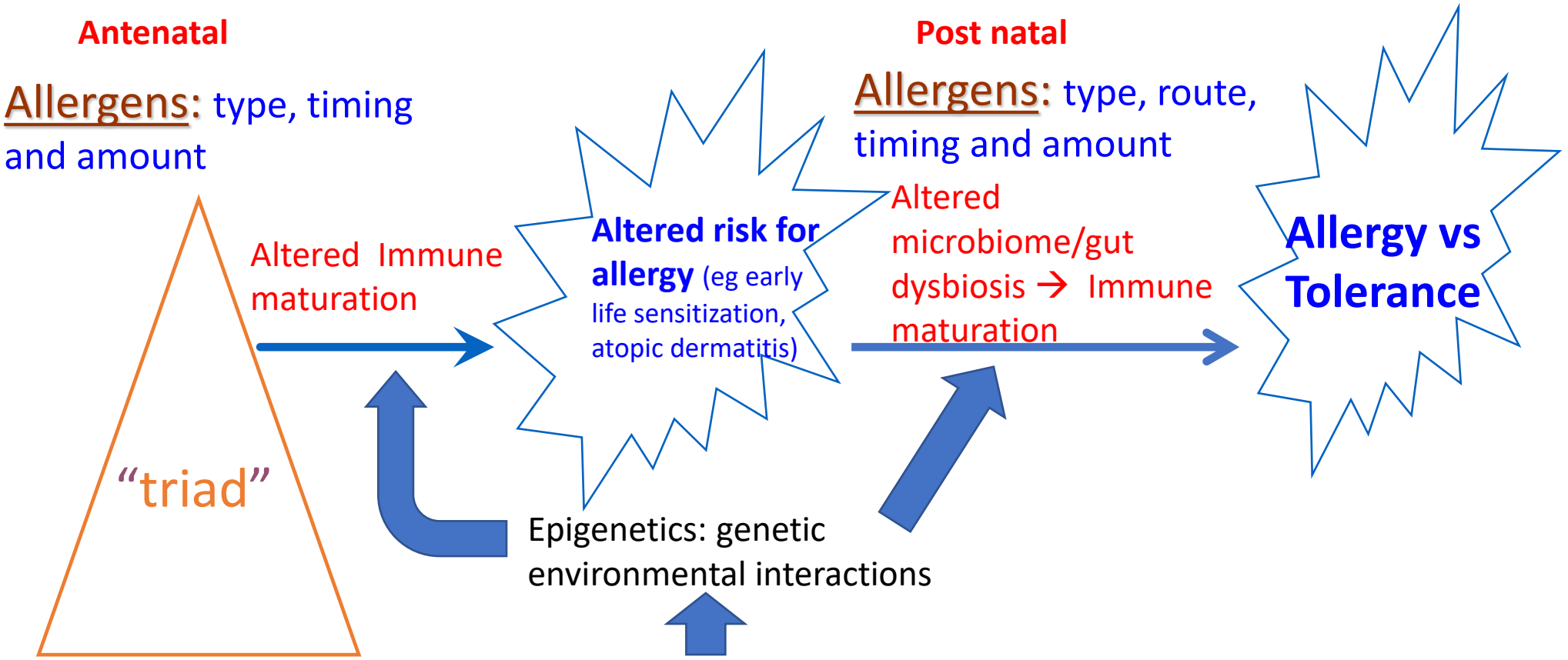
Must be related to our modern western lifestyle

Part of the answer may be found in your kid's poop!

None of the above

All of the above

Food allergy development…



Heredity Atopic genes, fhx

Environmental Adjuvants: early farm/pet exposure, ETS, diesel, maternal/infant nutrition, improved sanitation, c-section delivery, BF, older sibs, daycare, URI's, decreased infections, use of probiotics, vit D, use of antacids

Parent then head bobs from having dozed off during your answer…but then suddenly pivots to ask the dreaded “unscheduled sibling question”…

- Doc, but what about my 4-month-old? She has eczema and I’m worried about her…is there anything I can do?

Doc, but what about my 4-month-old? She has eczema and I'm worried about her...is there anything I can do?

Nope, not really, what will be, will be, the stage is already set

Yes, I'd like you to buy a one-way ticket to a farm in the Swiss Alps!

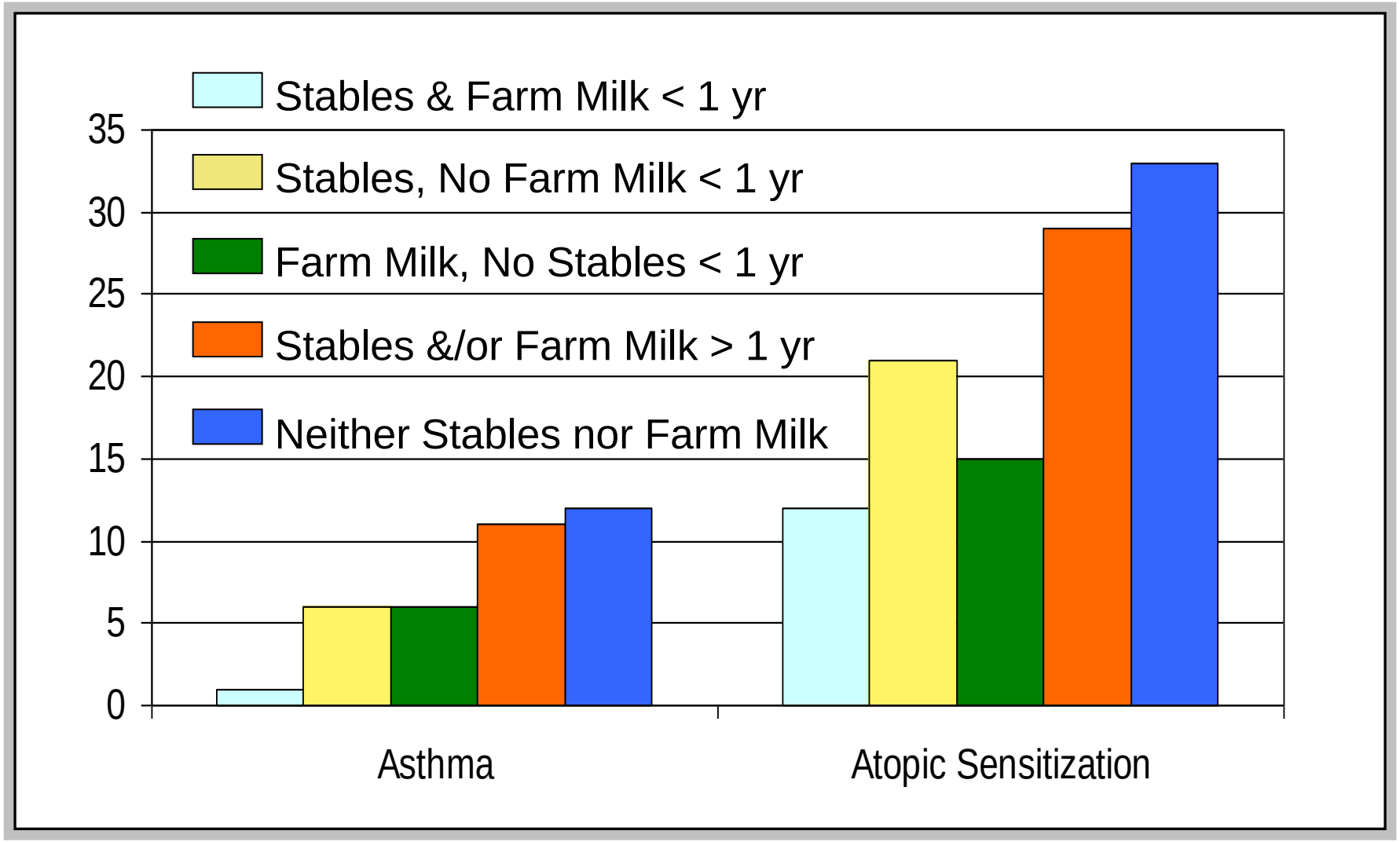
Yes, please make sure your youngster avoids peanuts (and fish) until age 3 or even 4.

Yes, leave now and stop off on your way home to buy some peanut butter or Bamba treats to give her ASAP!

Just make sure her eczema is well controlled, and moisturize, moisturize, moisturize!

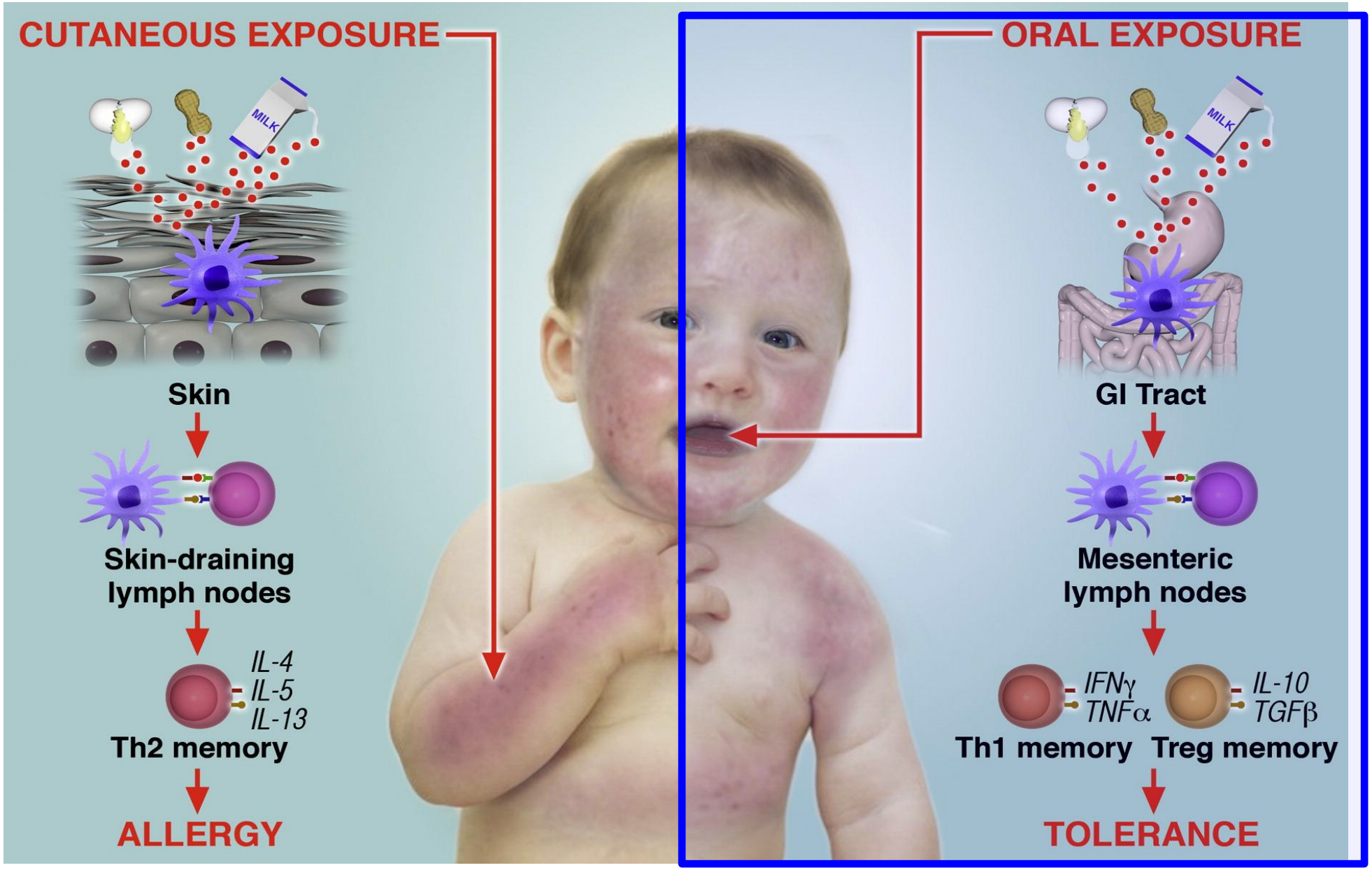
Let's get serious about allergy prevention

Hygiene Hypothesis: Farm life and unpasteurized milk



Riedler J, et al. Lancet 2001;358:1129-33

"Dual-allergen exposure hypothesis"



Lack G: Epidem risks for food allergy JACI 2008

Food allergy prevention: interventional study

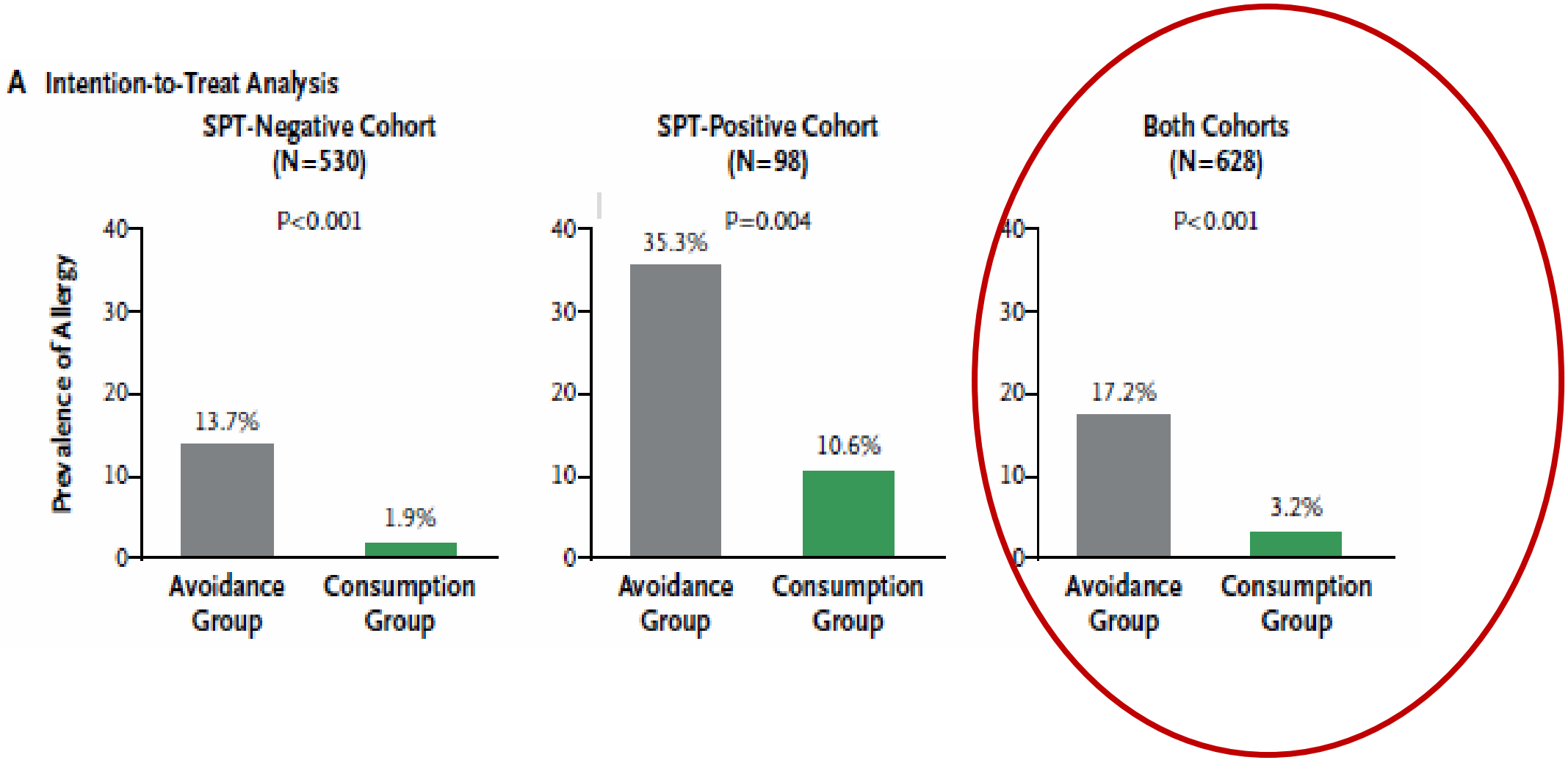
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 26, 2015 VOL. 372 NO. 9

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A., Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

Prevalence of Peanut Allergy Lower in Peanut Consumption Groups



Early introduction of other foods may also prevent allergy

- The most data is for egg allergy
  - Best results from heated egg product/boiled egg vs egg powder
- Accumulating data for other foods
  - Early CM exposure (sustained) also leads to reduced allergy
  - Some data for wheat, fish as well
- Early introduction of other allergenic foods is likely helpful to prevent food allergy.

Timing of introduction of allergenic solids for infants at high-risk CPS Practice point, 2020

- There is emerging evidence that early food introduction, between 4 to 6 months of age, may have a role in preventing food allergy, particularly for egg and peanut, in high-risk infants (severe eczema, first degree relative with allergy).
- For infants at high risk for allergic disease, it is now recommended that commonly allergenic solids be introduced at around 6 months of age, but not before 4 months of age, and guided by the infant's developmental readiness for food.
- Continued breastfeeding should be encouraged and supported because of its many health benefits.

Urban dictionary definition:

“Door knob” Question-

“Those are the dreaded words that doctors hear as they place their hands on the doorknob to leave the examination room, at what they think is the end of the patient encounter.”

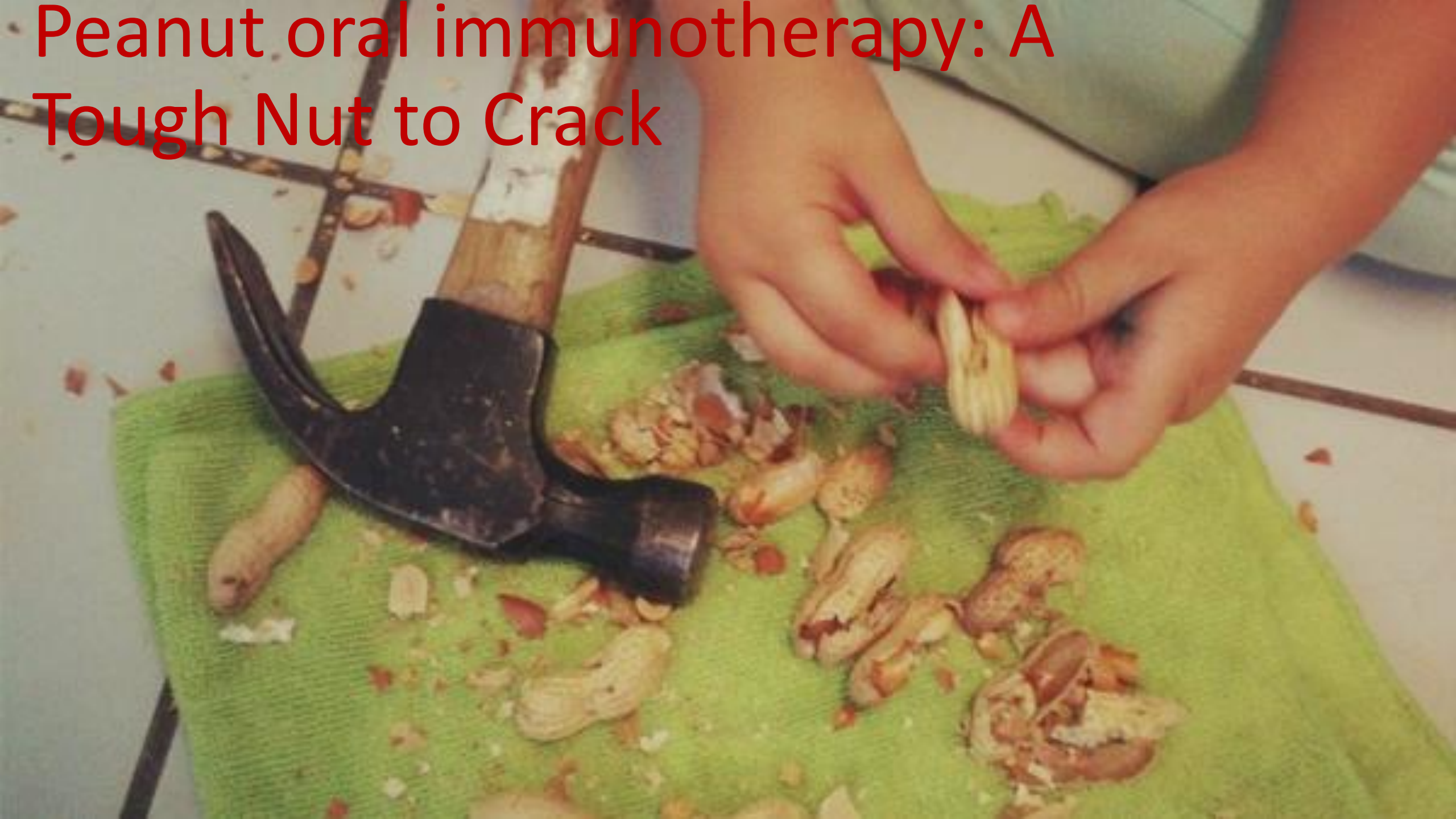
Parent: “ (Just as you reach for the…)

“Hey Doc, I heard that some kids are getting treated by exposure to small amounts of peanut to cure their allergy, do you think that could work for my son?”

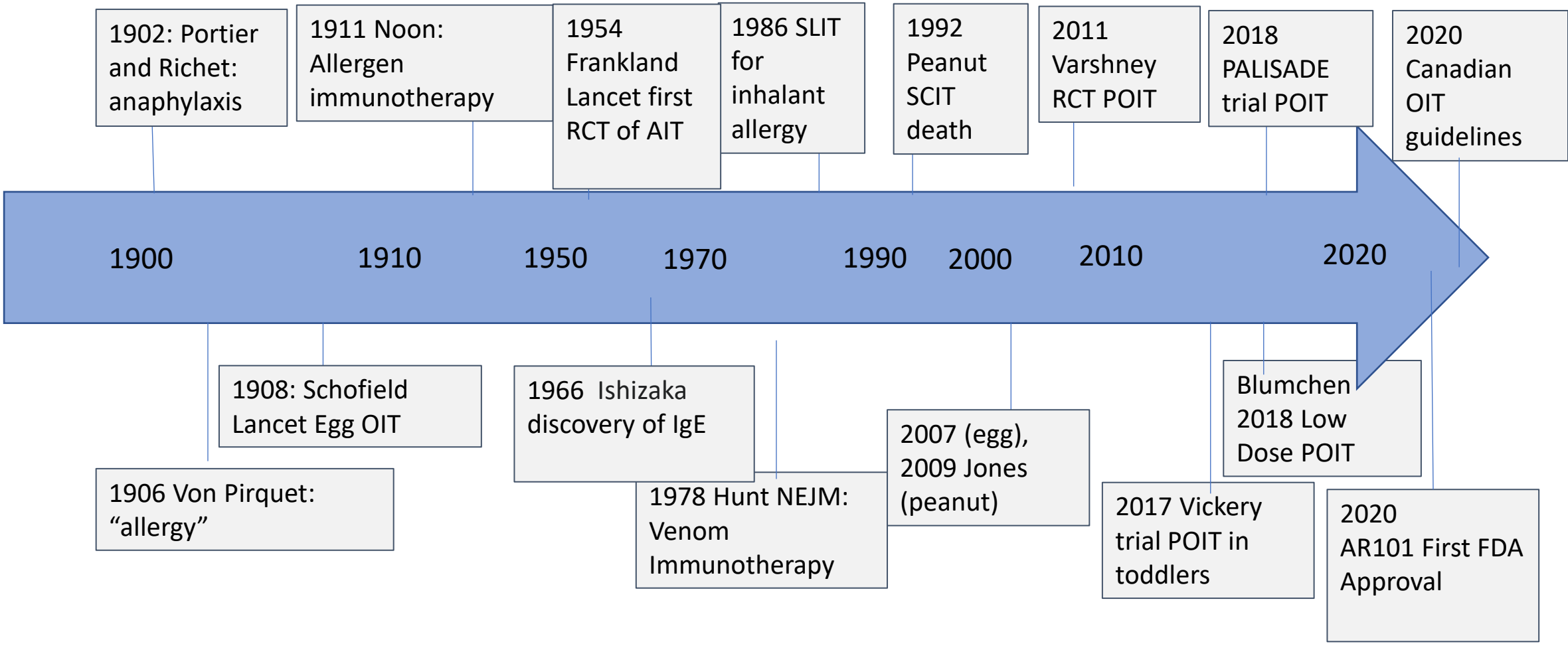
I heard that some kids are getting treated by exposure to small amounts of peanut to cure their allergy, do you think that could work for my son?

Let go of the door knob, have a seat, and say "OK, let's chat some more…"	**A**
Where did you hear such nonsense?	**B**
Its too risky, you'd better stay away from that!	**C**
Oh, you are referring to oral immunotherapy? Let's set up another appointment and chat…	**D**
We don't know, its still early days, we'll see that the research shows…	**E**

Peanut oral immunotherapy: A Tough Nut to Crack

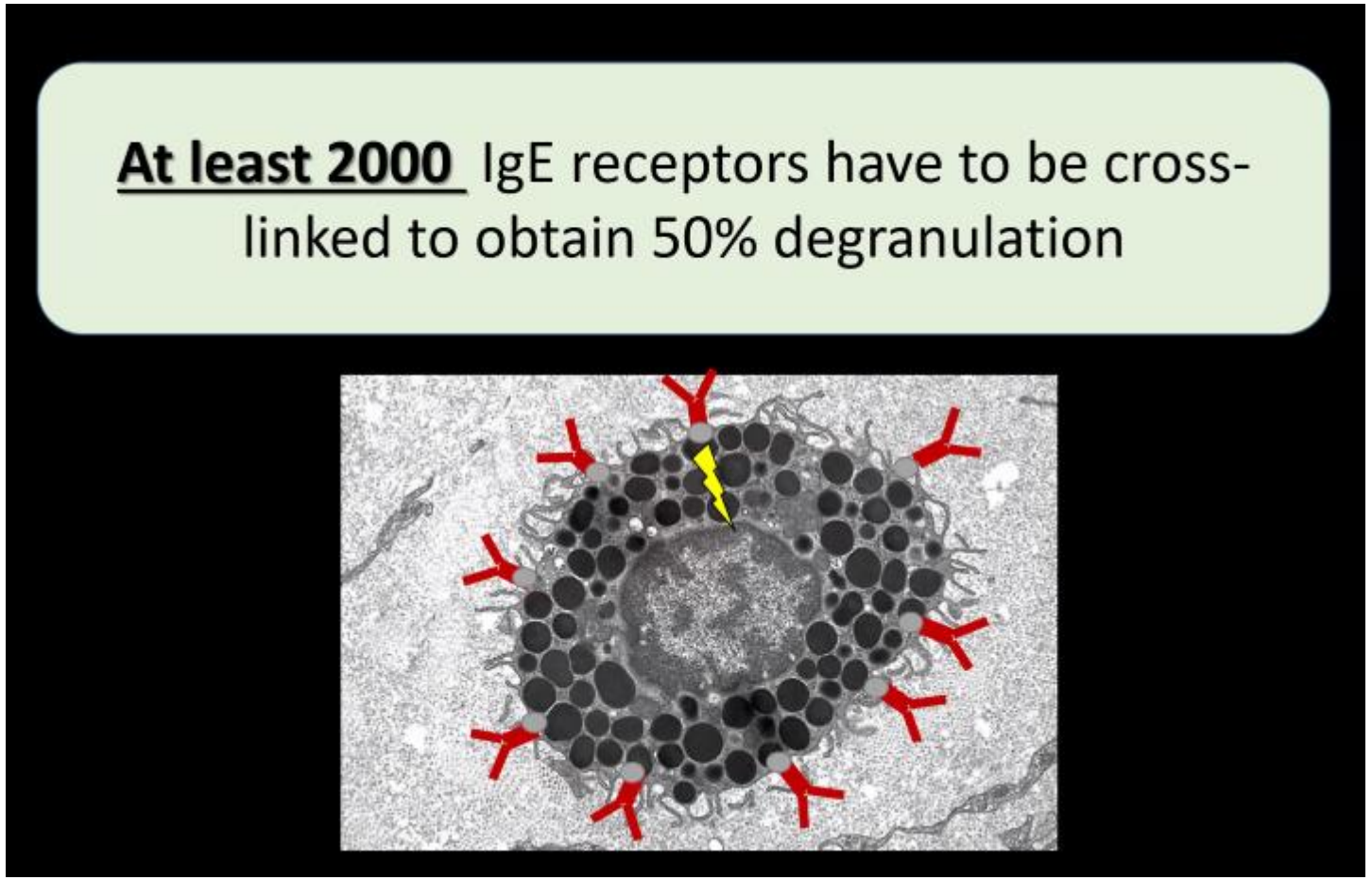


Some Key Events in the History of Oral Immunotherapy



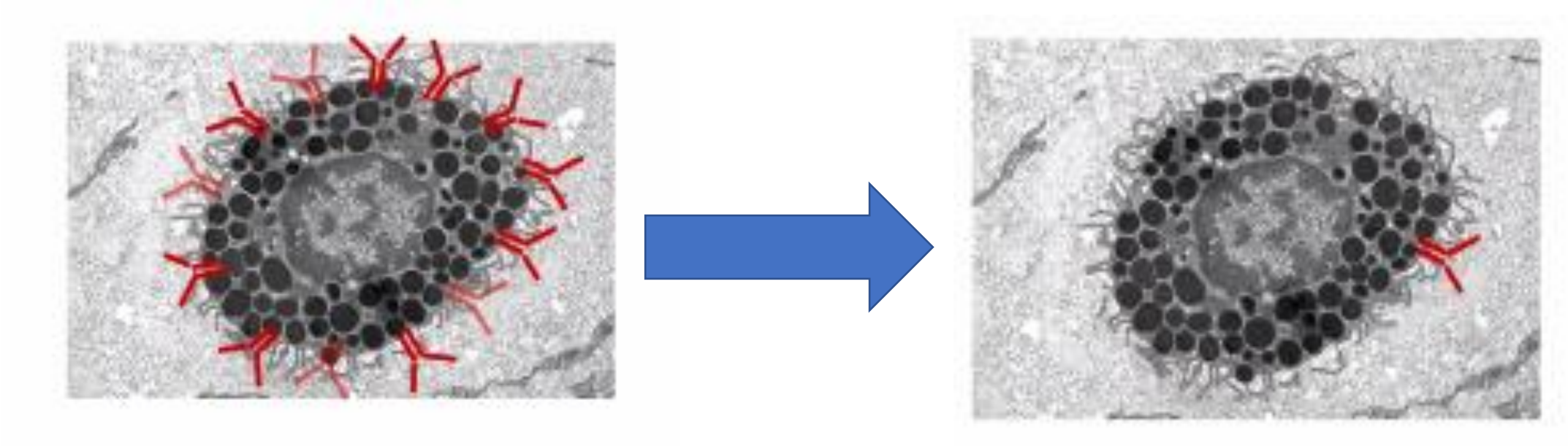
How does OIT work?

1. Disarms mast cells- short term (desensitization)
2. Re-educates the immune response- potential long term effect



How does OIT work-desensitization?

-give a small amount of protein allergen below the threshold
-consumes sIgE, receptors replaced by other IgE we don't care about



How does OIT work?

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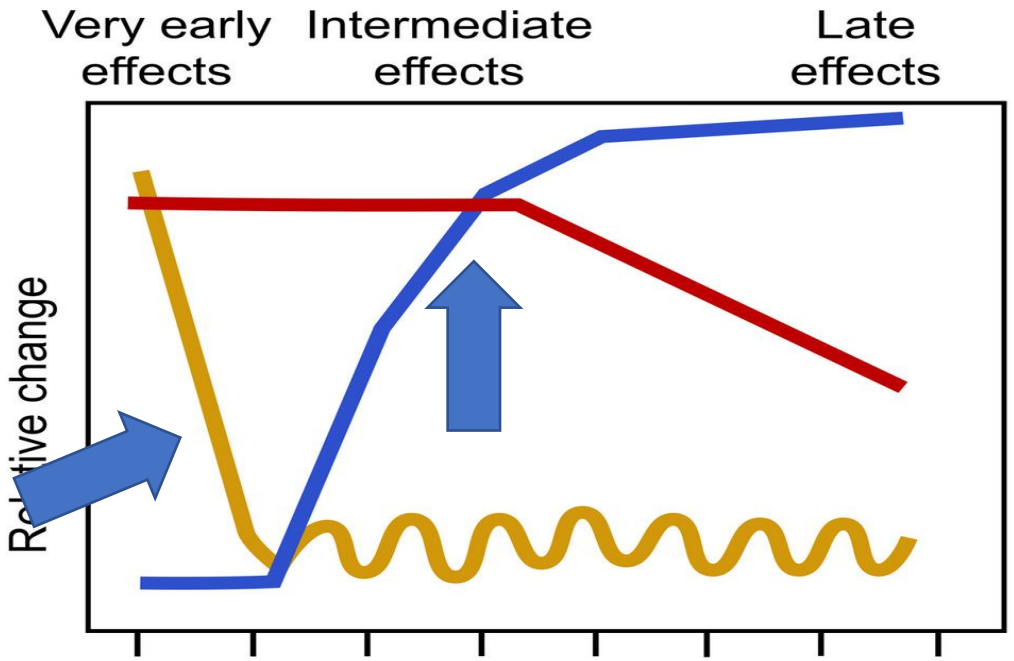
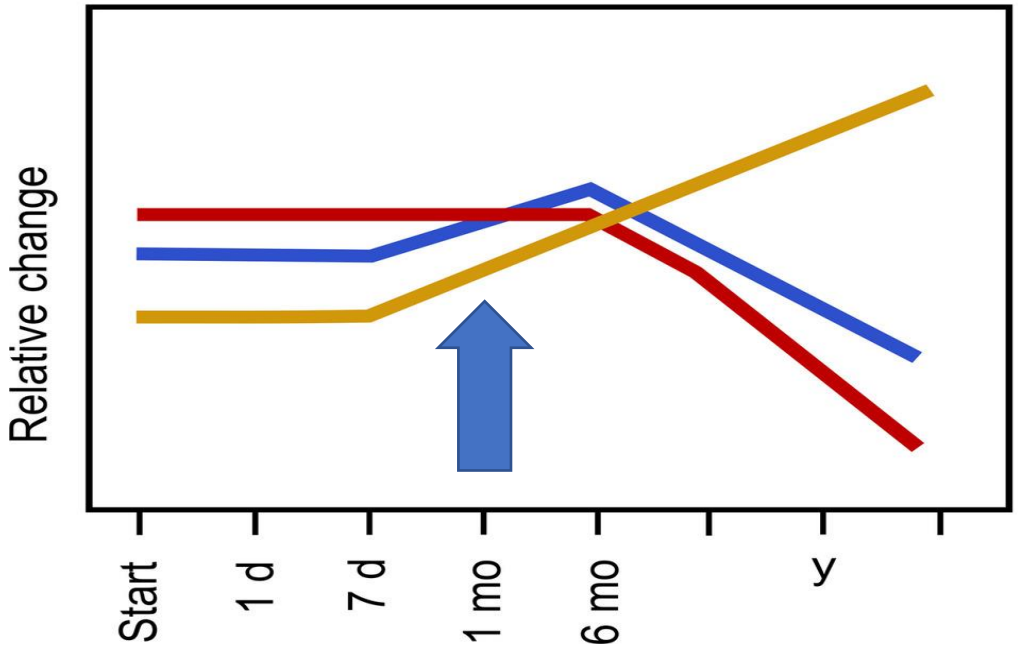


- Very early basophil tolerance, early decrease in mast cell and basophil activity for systemic anaphylaxis
- Induction of Treg and Breg cells
  Suppression of Th2-Th1 cells
- Late decrease in tissue mast cells and eosinophils and release of their mediators
  Decrease in skin late-phase response

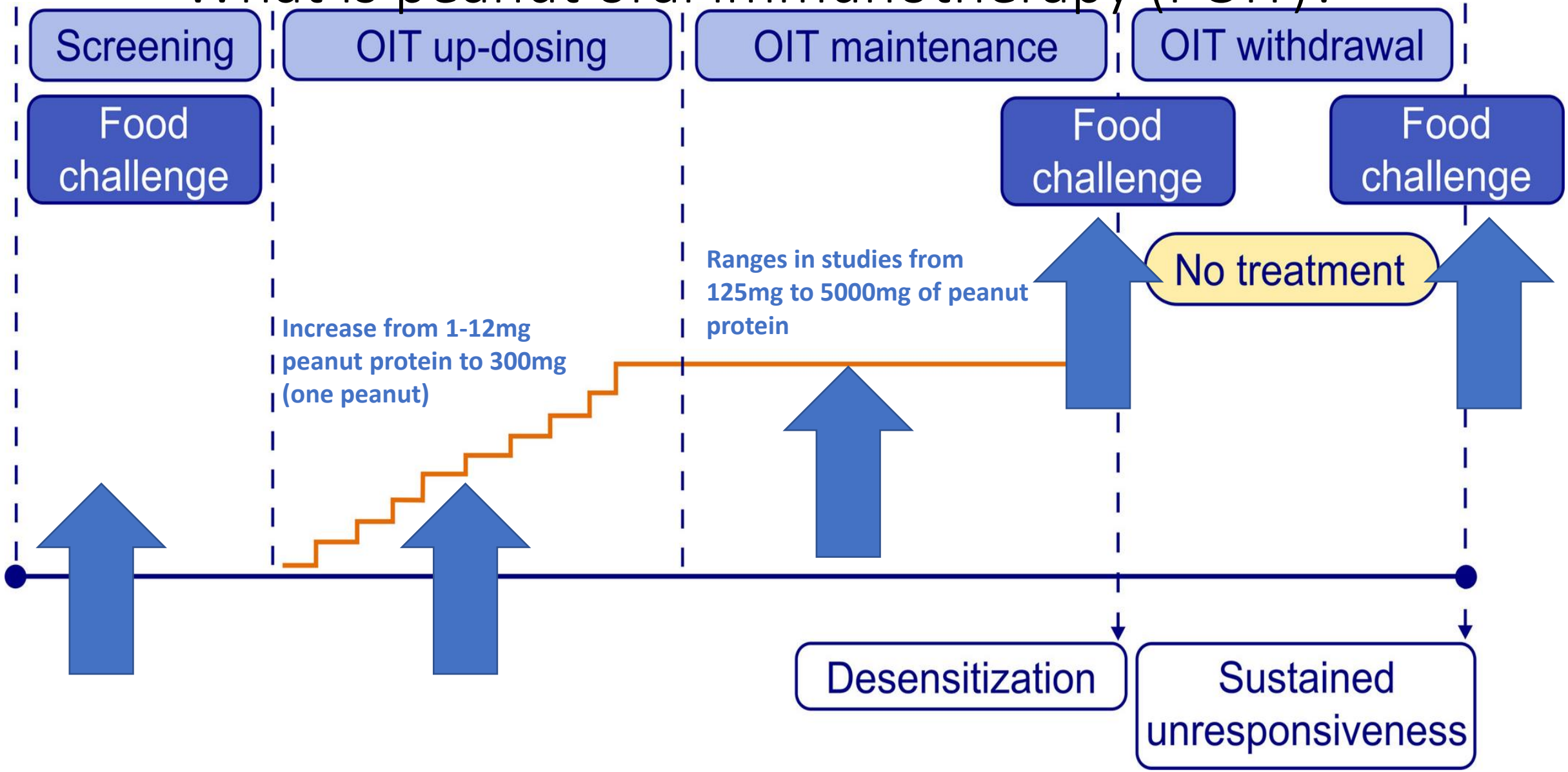


- Late decrease in type I skin test reactivity
- Early increase in specific IgE
  followed by a late decrease in specific IgE
- Increase in specific IgG4

Present study findings in SLIT:
- IgG2 (4 mo)
- IgG4 (4 mo)
- Treg

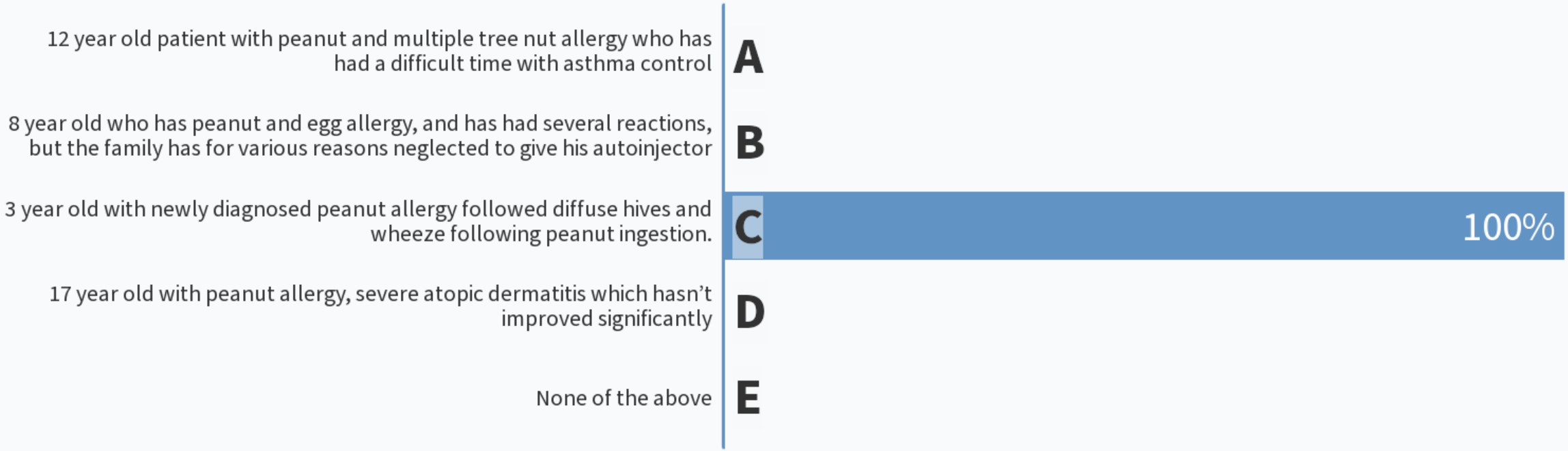
Allergy, Volume: 75, Issue: 5, Pages: 1017-1018, First published: 23 November 2019, DOI: (10.1111/all.14126)

What is peanut oral immunotherapy (POIT)?



Allergy, Volume: 75, Issue: 6, Pages: 1316-1326, First published: 16 November 2019, DOI: (10.1111/all.14116)

Who would be the best candidate for food oral immunotherapy…



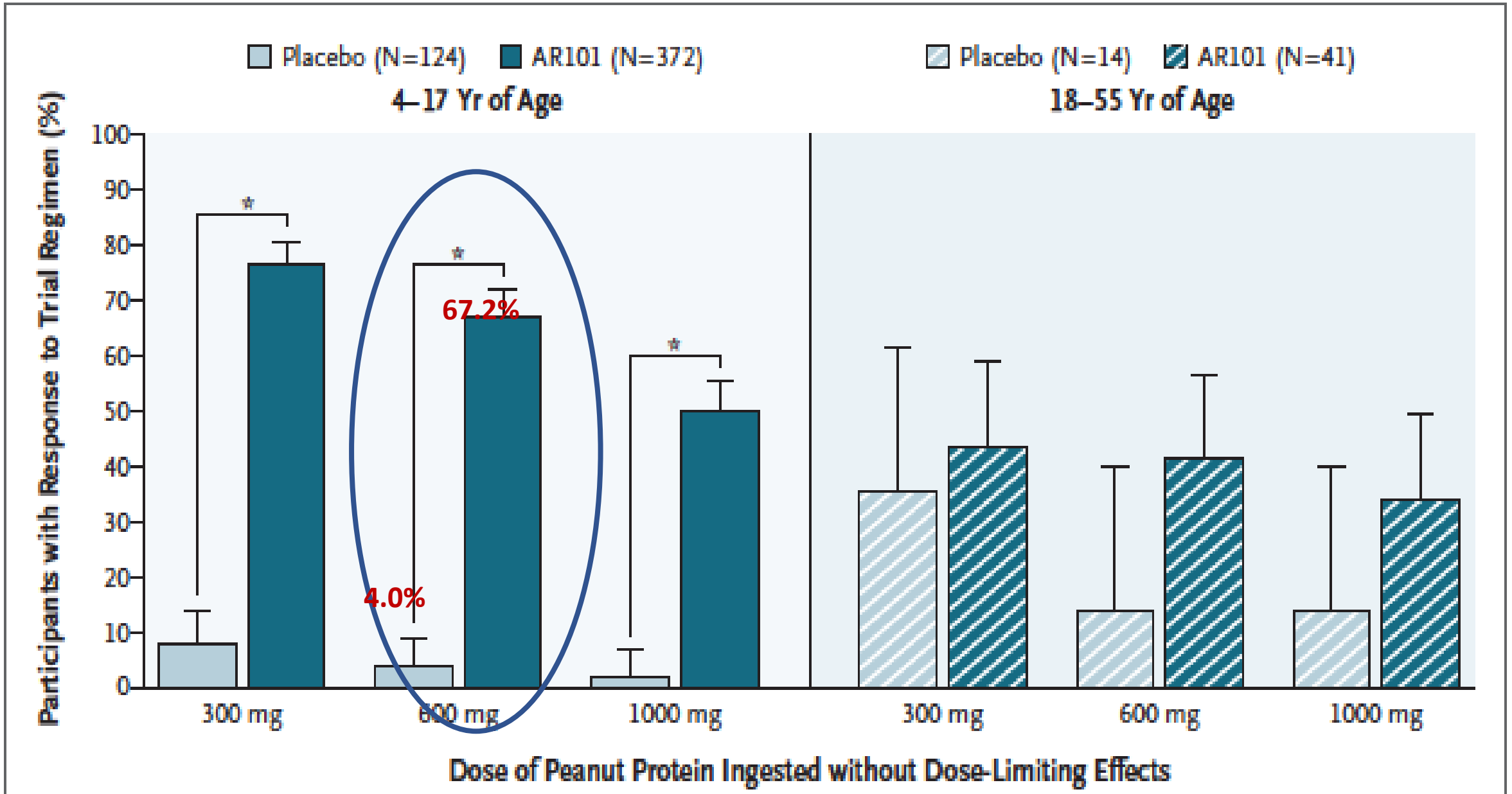
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 22, 2018 VOL. 379 NO. 21

AR101 Oral Immunotherapy for Peanut Allergy

The PALISADE Group of Clinical Investigators*

Results: PALISADE Trial



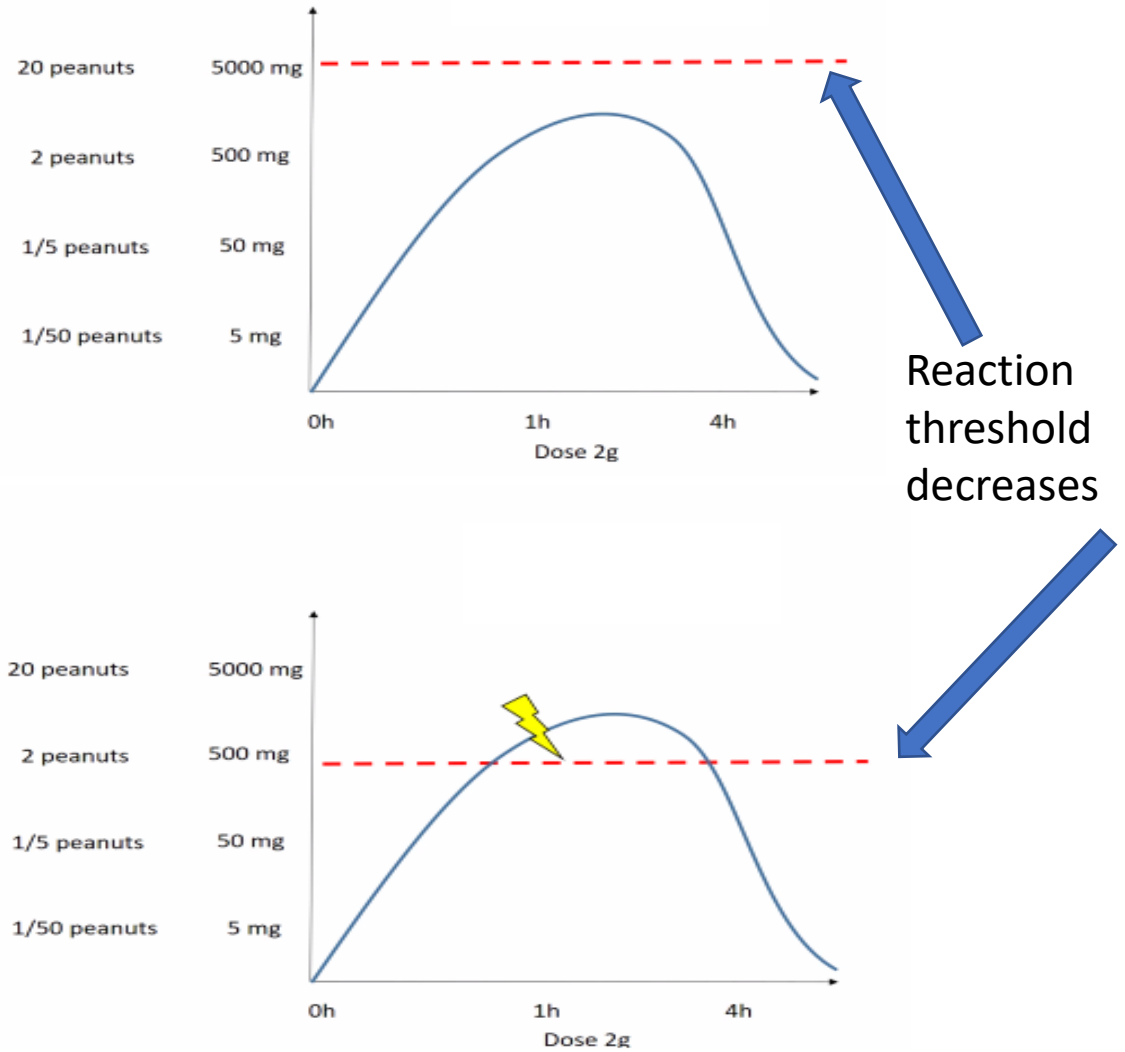
PACE systematic review/meta-analysis

Chu DK et al. Lancet. 2019

Ages and Safety	**PACE**
Number of subjects	1041
Median age	8.7 (IQR 5.9-11.2) years
TREATED GROUPS	
Anaphylaxis risk	16.5% (108/653)
Epinephrine use	11.8%
PLACEBO/AVOIDANCE GROUPS	
Anaphylaxis risk	2.7% (8/297)
Epinephrine use	3.7%

Common cofactors which may be associated with allergic reaction/more serious allergic reactions include

1. Exercise
2. Illness (fever, flu like symptoms)
3. Fatigue
4. Use of NSAID's
5. Alcohol consumption
6. Active asthma
7. Menses
8. Hot showers



Real life risk of reactions in PA children vs POIT treatment

Avoidance

- Children diagnosed < age 4 with PA with initial non-life-threatening reactions, 44% had at least one potentially life-threatening reaction during follow-up [1]
- 10% annual rate of accidental reactions, with 1%-2% requiring epinephrine or emergency department visits [2]
- **3-year follow-up m age 11.5y: 41% accidental exposure reactions (29% severe), or 9.8% annual risk of reactions[5]**

POIT treatment

- Risk 7.6%-11.8% epinephrine requirement [3,4]
- Risk 16.5% of anaphylaxis[3]
- Once reached long term phase of maintenance, risk of significant AE requiring epinephrine 3.2% [4]

1 Vander Leek, T. K., Liu, A. H., Stefanski, K., Blacker, B. & Bock, S. A. The natural history of peanut allergy in young children and its association with serum peanut-specific IgE. J Pediatr (2000).
2 Mansfield LE. Oral immunotherapy for peanut allergy in clinical practice is
ready. Allergy Asthma Proc. 2013
3 Chu DK, Wood RA, French S, et al. Oral immunotherapy for peanut allergy (PACE): a systematic review and meta-analysis of efficacy and safety. Lancet. 2019
4. Adverse events associated with peanut oral immunotherapy in children - a systematic review and meta-analysis LE Grzeskowiak B Tao Sci Rep.2020 Jan
5 From the Netherlands: Kansen HM et al. J Allergy Clin Immunol, Feb 2020 (Similar data from Healthnuts (Australia) and US)

PALISADE has taught use, YET AGAIN, that kids are not just “little adults”…

Could it be too that toddlers are not just “little kids”?

Data show more higher rates of desensitization and remission with far less frequent and severe adverse effects

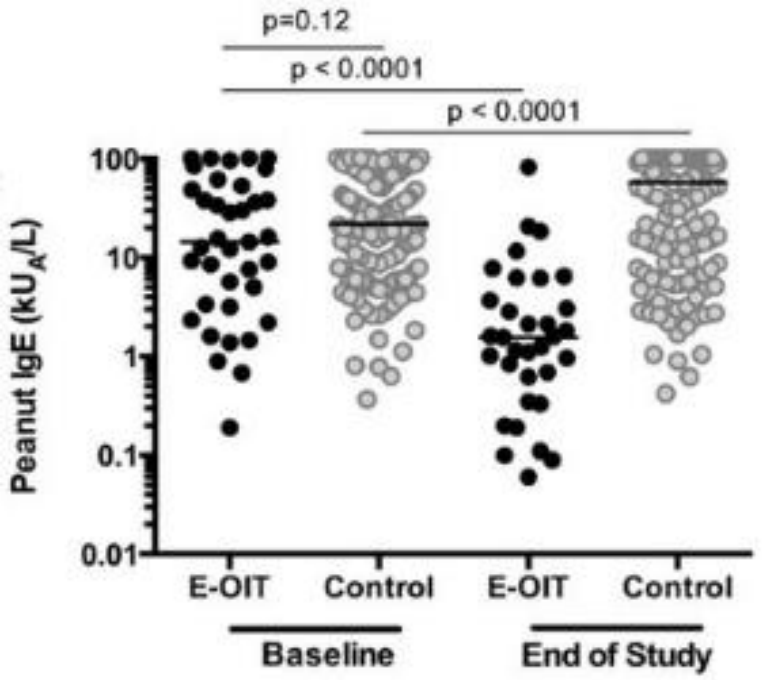
Vickery BP et al. *J Allergy Clin Immunol*. 2017

Food, drug, insect sting allergy, and anaphylaxis

Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective

Brian P. Vickery, MD,[a] Jelena P. Berglund, PhD,[b] Caitlin M. Burk, BA,[a] Jason P. Fine, PhD,[a] Edwin H. Kim, MD, MHS,[a] Jung In Kim, MS,[a] Corinne A. Keet, MD, PhD,[c] Michael Kulis, PhD,[a] Kelly G. Orgel, BS,[a] Rishu Guo, MD, PhD,[a] Pamela H. Steele, CPNP,[a] Yamini V. Virkud, MD, MPH,[d] Ping Ye, PhD,[a] Benjamin L. Wright, MD,[e] Robert A. Wood, MD,[c] and A. Wesley Burks, MD[a] *Chapel Hill and Durham, NC, Baltimore, Md, Boston, Mass, and Scottsdale, Ariz*

- N 37 children, **age 9 to 36 months** randomized to
  - 300 mg vs 3000mg of peanut protein per day; 154 age match controls for m= 29 mos
- Outcomes:
  - 30/37 passed exit challenge 5g peanut protein (81% DS, ITT)
  - 4 weeks of peanut avoidance:
  - **29/37 (78% ITT)) remained unreactive to challenge (SU) and were instructed to consume peanut ad lib**



Vickery, 2017: Safety

- 95% of all participants affected by AE's; 0.8% per dose
- 85% were mild, 15 % moderate, none severe
  - Overall, more reactions in high dose group
- 2 withdrawals due GI complains, one diagnosed EoE
- Epi was only given once in the treatment group
  - High dose group, while at home
- No deaths or hospitalization

Vickery BP et al. *J Allergy Clin Immunol*. 2017;139(1):173-181.

Canadian Preschool Peanut oral immunotherapy (CPP-OIT)

Peanut OIT in Preschoolers: results

243/270 (90%) reached maintenance

67.8% reaction rate*

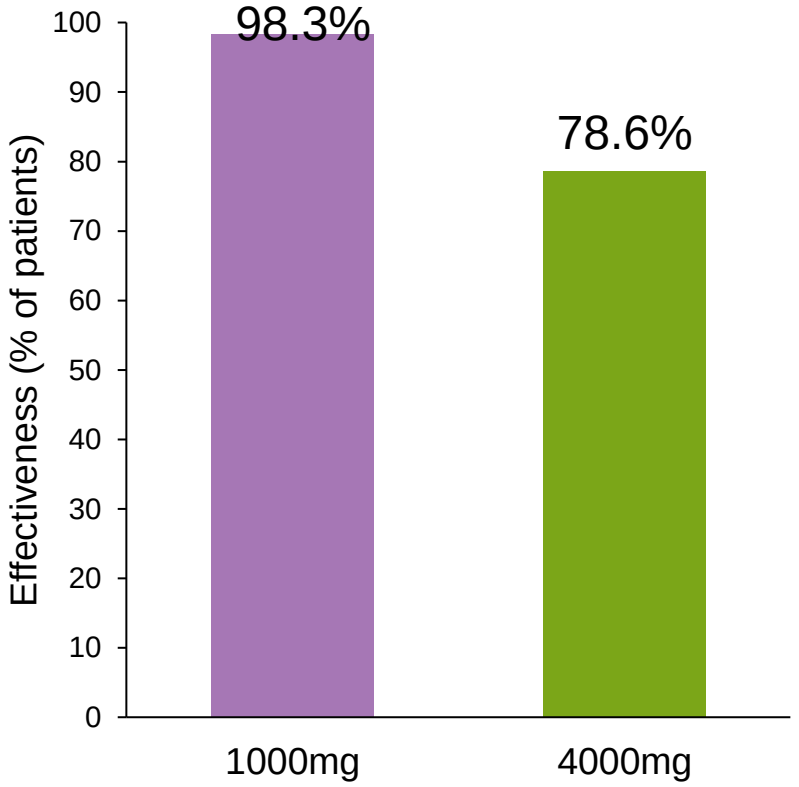
36.3 % grade 1 mild
31.1 % grade 2 moderate
0.4% grade 4 (1pt) severe
4.1% epinephrine
1 pt EoE

27 dropped out

First Real-World Effectiveness Analysis of Preschool Peanut Oral Immunotherapy: JACI IP (2021)

Lianne Soller, PhD,[1,2] Elissa M. Abrams, MD,[2,3,4] Stuart Carr, MD,[5] Sandeep Kapur, MD,[7,8] Gregory A. Rex, MD, [7,8] Sara Leo, MD,[2,9] Mary McHenry, MD, [7,8] Timothy K. Vander Leek, MD,[5,6] Joanne Yeung, MD,[2,10] Victoria E. Cook, MD, [2,11] Tiffany Wong, MD, [1,2] Kyla J. Hildebrand, MD,[1,2] Raymond Mak, MD,[2] Thomas V. Gerstner, MD, [3,4] Scott B. Cameron, MD, PhD [2,11]* Edmond S. Chan, MD.[1,2]*
*co senior-authors

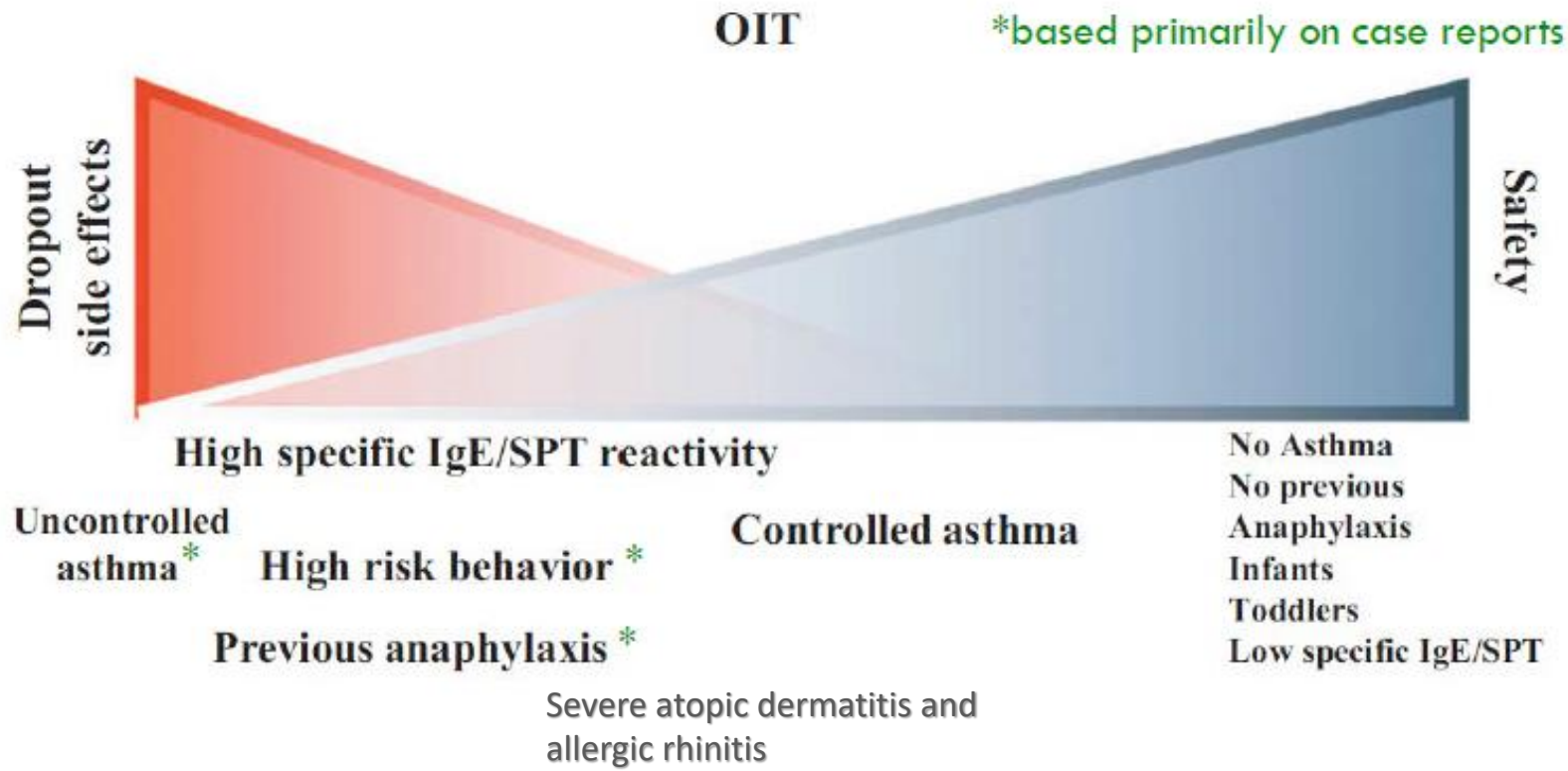
- **Objective:** To determine effectiveness of preschool P-OIT after one year of maintenance.
- 117 patients that successfully completed 1 year of P-OIT and subsequently underwent a cumulative 4000mg follow-up OFC:
  - *115 (98.3%) tolerated cumulative ≥1000mg.*
  - 92 (78.6%) tolerate full oral challenge of 4g
- **Conclusion:** Our data demonstrate real-world preschool P-OIT is effective after 1 year of maintenance for those who received a follow-up OFC. For those who reacted, their threshold increased *sufficiently to protect against accidental exposures*.



Effectiveness of Peanut oral immunotherapy. A: Percent of patients (out of 117) tolerating (cumulative) at least 1000mg protein (98.3%), and 4000mg (78.6%) at follow-up OFC.

POIT Safety and Effectiveness Summary

Age	**Preschool and CPP-OIT**	**Older children to adults**
Approximate age	<1yo to 5yo	6 years and older
Severe reaction/anaphylaxis risk	0 – 0.4%	~14.2 – 16.5%
Epinephrine use	2.7 – 4.1%	8.2 – 14%
Effectiveness	~80-90% tolerated 4-5g protein after 12-29 months of maintenance **78% sustained unresponsiveness***	67.2% tolerated 1043mg protein after 6 months of maintenance. <50% and declining



Can We Predict Response to OIT? Still early days.

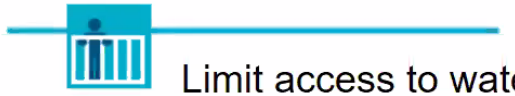
Your patient!

- 3-year-old boy, previous anaphylaxis to a peanut butter sandwich, no other known allergies
- Family undergoes education and review of epinephrine precautions
- Parents want to know what the chances are that he will outgrow his allergy
- Parents hear: “80% chance my child will have peanut allergy for life”
- Parents distraught, anxious about exposures in other foods, especially outside the home.
- Parents want to know if anything can be done?

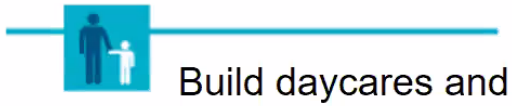
Empowering the patient and family to reduce anxiety and achieve a sense of control can be achieved different ways for different patients

Water safety/drowning prevention

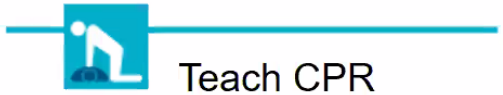
Food allergy/ anaphylaxis prevention



Limit access to water

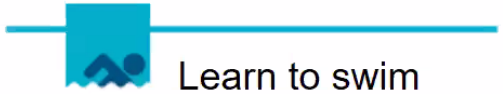


Build daycares and schools away from water



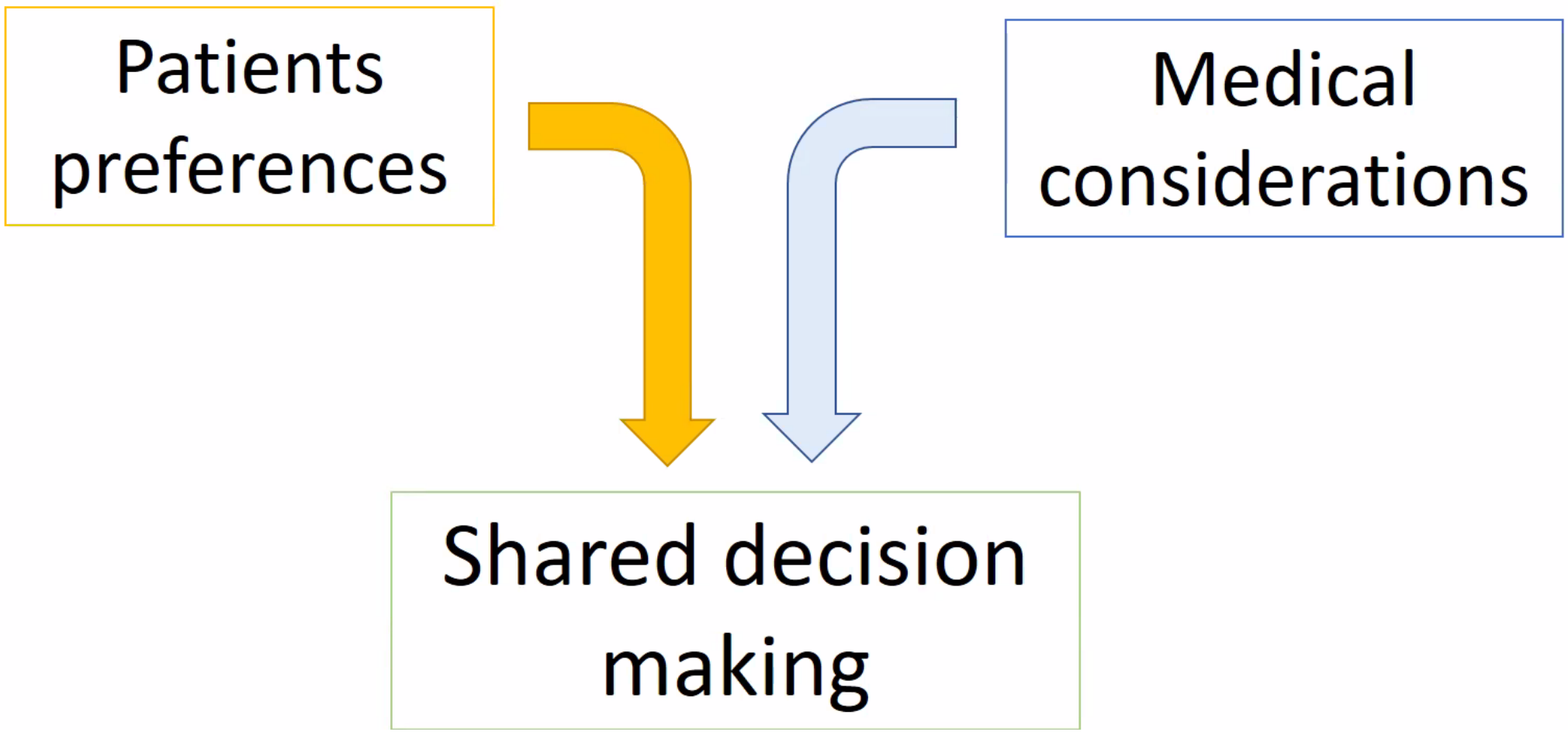
Teach CPR

National regulations



Learn to swim

Is OIT a good option for my patient?



Key Messages

OIT in all children can achieve high rates of **desensitization** and clinically meaningful improved protection from accidental peanut exposure

OIT and promote **remission** in toddlers and preschoolers

Patients more likely to experiences reactions if they undergo OIT, mainly during updose period, and in a controlled environment. Benefit of treatment also comes from improvement of quality of life

OIT has known risks and tradeoffs, and is not right for all patients