Two new asthma guidelines:

What is still true and how to make sense of the discordance

DATE: July, 2021 PRESENTED BY: Williams, Craig; Clinical Professor, williacr@ohsu.edu

Conflicts of Interest: None

Key Objectives:

- Revisit a couple aspects of asthma that continue to be true
- Consider the discordance of recent guideline updates which no longer completely agree

First, a little context….

Asthma: National Asthma Education and Prevention Program (NAEPP) Expert Panel 3 Asthma Guidelines; 2007

NIH Report:
Guidelines for the Diagnosis and Management of Asthma
Summary report available online: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.Htm
(Original in 1997, updated in 2002 and 2007, 2020)

COPD: Global Initiative for Chronic Obstructive Lung Disease (GOLD)

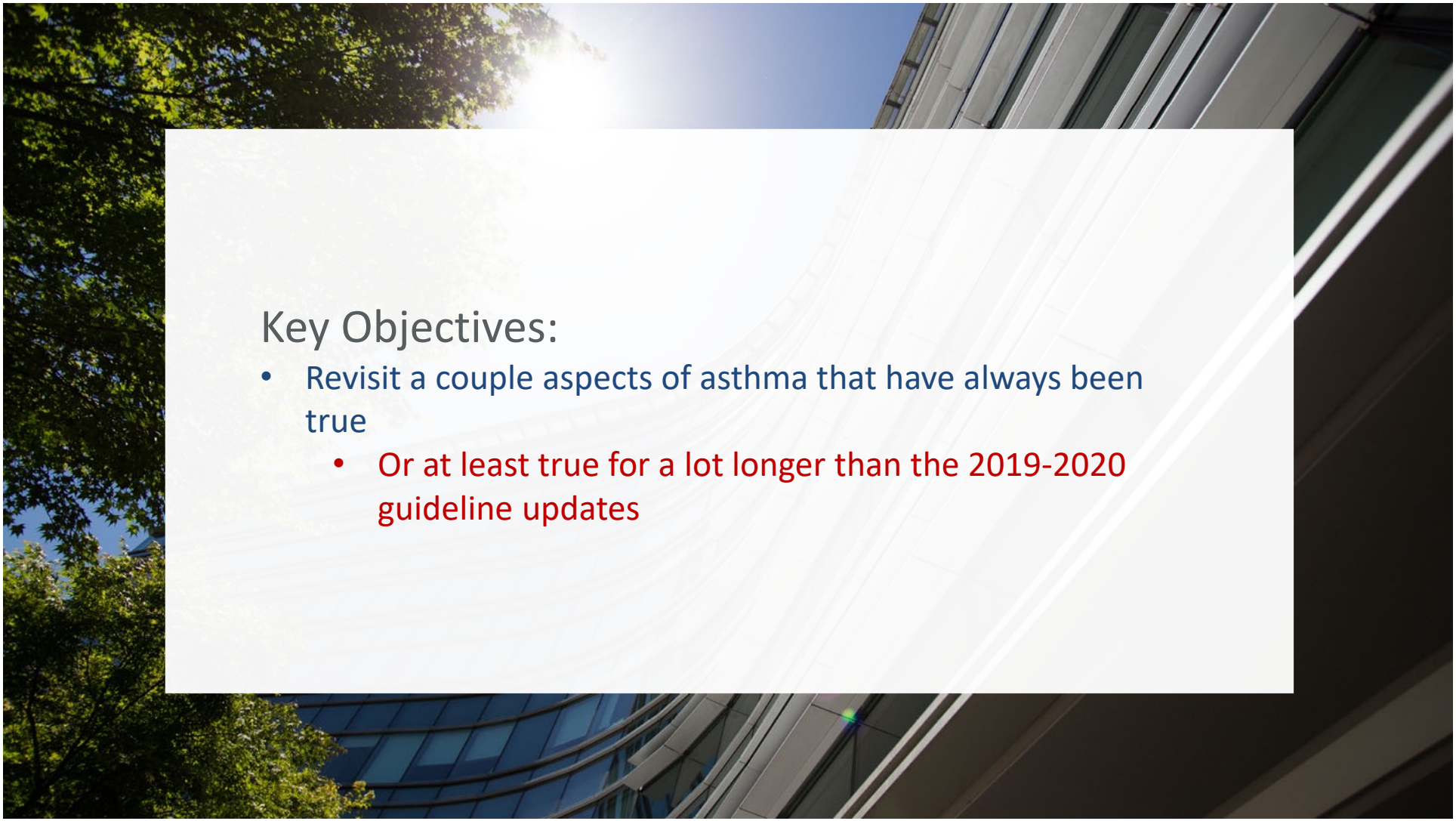
WHO and NHLBI institute. 2001, 2003, 2007,2011, 2014, 2015, 2016, 2017, 2018, 2019, 2020…

www.goldcopd.com

GINA 2019: Global INitiative for Asthma; concept behind GINA was to be a bit more nimble like the GOLD guidelines

Notable update in “What’s New”:

‘SABA only’ for prn intermittent no longer recommended



Key Objectives:

- Revisit a couple aspects of asthma that have always been true
  - Or at least true for a lot longer than the 2019-2020 guideline updates

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 9, 2009 VOL. 360 NO. 15

Efficacy of Esomeprazole for Treatment of Poorly Controlled Asthma

APPENDIX

The members of the research group for the trial were as follows: **Baylor College of Medicine, Houston** — N.A. Hanania (principal investigator), M. Sockrider (coprincipal investigator), L. Giraldo (principal clinic coordinator), R. Valdez, E. Flores (coordinators); **Columbia University–New York University Consortium, New York** — J. Reibman (principal investigator), E. DiMango, L. Rogers (coprincipal investigators), C. Cammarata, K. Carapetyan (clinic coordinators at New York University), J. Sormillon, E. Simpson (clinic coordinators at Columbia University); **Duke University Medical Center, Durham, NC** — L. Williams (principal investigator), J. Sundy (coprincipal investigator), G. Dudek (principal clinic coordinator), R. Newton, A. Dugdale (coordinators); **Emory University School of Medicine, Atlanta** — W.G. Teague (principal investigator), A. Fitzpatrick, S. Khatri (coprincipal investigators), R. Patel (principal clinic coordinator), J. Peabody, E. Hunter, D. Whitlock (coordinators); **Illinois Consortium, Chicago** — L. Smith (principal investigator), J. Moy, E. Naureckas, C.S. Olopade (coprincipal investigators), J. Hixon (principal clinic coordinator), A. Brees, G. Rivera, S. Sietsema, V. Zagaja (coordinators); **Indiana University, Asthma Clinical Research Center, Indianapolis** — M. Busk (principal investigator), C. Williams (coprincipal investigator), P. Puntenney (principal clinic coordinator), N. Busk (coordinator); **University of Pennsylvania, Philadelphia** — F. Leone (principal investigator), M. Hayes-Hampton (principal clinic coordinator); **Louisiana State University Health Sciences Center,**

CONCLUSIONS

Despite a high prevalence of asymptomatic gastroesophageal reflux among patients with poorly controlled asthma, treatment with proton-pump inhibitors does not improve asthma control. Asymptomatic gastroesophageal reflux is not a likely cause of poorly controlled asthma. (ClinicalTrials.gov number, NCT00069823.)

(coprincipal investigator), S. Erwin (principal clinic coordinator), A. Kelley, D. Laken (coordinators); **University of Miami at Miami–University of South Florida, Tampa** — A. Wanner (principal investigator, Miami), R. Lockey (principal investigator, Tampa), E. Mendes (principal clinic coordinator for University of Miami), S. McCullough (principal clinic coordinator for University of South Florida), B. Fimbel, M. Grandstaff (coordinators); **University of Minnesota, Minneapolis** — M.N. Blumenthal (principal investigator), G. Brottman, J. Hagen (coprincipal investigators), A. Decker, D. Lascewski, S. Kelleher (principal clinic coordinators), K. Bachman, C. Quintard, C. Sherry (coordinators); **University of Missouri–Kansas City School of Medicine, Kansas City** — G. Salzman (principal investigator), D.

Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma

Full Report 2007

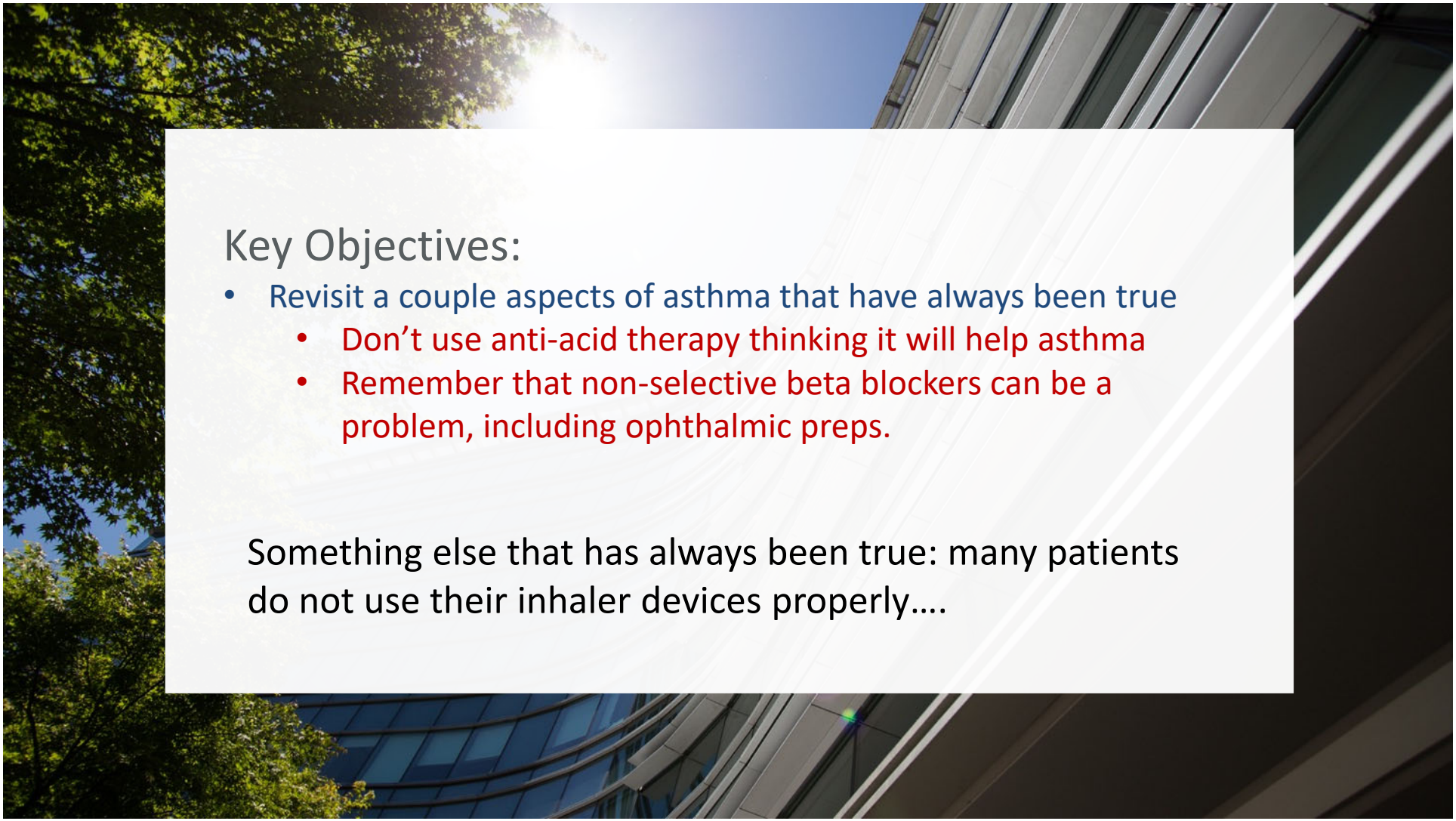
The 2007 National Asthma Education Prevention Program (NAEPP) guidelines were too old to address our 2009 study and the 2020 targeted update did not address anti-acid therapy for asthma

So the NIH asthma guidelines still don't mention the futility of anti-acid therapy for asthma control but….anti-acid therapies do not improve asthma control

Another pharmacy pearl……Beta blockers. Carvedilol has been generic for a few years now and is a popular non-selective (β1 and β2) beta blocker

Beta-Blockers

The Expert Panel recommends that clinicians advise asthma patients to avoid nonselective beta-blockers, including those in ophthalmological preparations (Evidence B). Nonselective beta-blockers can cause asthma symptoms (Odeh et al. 1991; Schoene et al. 1984), although cardioselective beta-blockers, such as betaxolol, may be tolerated (Dunn et al. 1986). A recent systematic review, primarily of single dose or short-term studies in younger subjects, indicates that patients who have mild to moderate airway obstruction can tolerate cardioselective beta-blockers; therefore, if needed for managing cardiovascular disorders, these agents may be administered after careful evaluation (Salpeter et al. 2002).



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  - Don't use anti-acid therapy thinking it will help asthma
  - Remember that non-selective beta blockers can be a problem, including ophthalmic preps.

Something else that has always been true: many patients do not use their inhaler devices properly….

One intervention with durable benefits….delivery device teaching

Watch patient using their inhaler

Discuss adherence and barriers to use

- Watch patient use their inhaler(s), check against inhaler checklist. Show correct method, and recheck, up to 3 times. Re-check each visit.
- Have empathic discussion to identify poor adherence, e.g. *"Many patients don't use their inhaler as prescribed. In the last 4 weeks, how many days a week have you taken it?" (0 days, 1, 2, 3 etc)* and/or: *"Do you find it easier to remember your inhaler in the morning or the evening?"* Ask about beliefs, cost of medications, and refill frequency.

NAEPP, pg 128

Spacers always recommended for pMDIs to both increase lung distribution and reduce systemic adverse effects

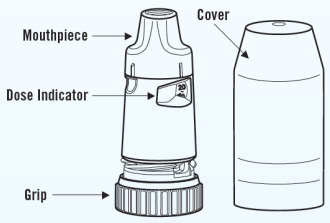
How to Get Started Using Your PULMICORT FLEXHALER® (budesonide inhalation powder, 90 mcg & 180 mcg)

Please read these instructions carefully before you start to take your medicine, and use only as directed by a healthcare professional.

Priming Your PULMICORT FLEXHALER

Before you use a new PULMICORT FLEXHALER for the first time, you must prime it.

Figure 1- Parts of your PULMICORT FLEXHALER



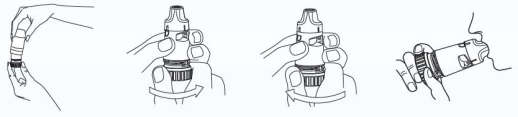


Figure 2 - Load | Figure 3 - Twist | Figure 4 - Click | Figure 5 - Inhale

Loading a Dose

1. Hold your PULMICORT FLEXHALER upright as described above. With your other hand, twist the white cover and lift it off (see Figure 2).
2. Continue to hold your PULMICORT FLEXHALER upright to be sure that the right dose of medicine is loaded.
3. Use your other hand to hold the inhaler in the middle. Do not hold the mouthpiece when you load the inhaler.
4. Twist the brown grip fully in one direction as far as it will go. Twist it fully back again in the other direction as far as it will go (it does not matter which way you turn it first) [see Figure 3].
   - You will hear a "click" during one of the twisting movements (see Figure 4).
   - PULMICORT FLEXHALER will only give one dose at a time, no matter how often you click the brown grip, but the dose indicator will continue to move (advance). This means that if you continue to move the brown grip, it is possible for the indicator to show fewer doses or zero doses even if more doses are left in the inhaler.
   - **Do not shake the inhaler after loading it.**

How To Use Your Metered-Dose Inhaler

Using an inhaler seems simple, but most patients do not use it the right way. When you use your inhaler the wrong way, less medicine gets to your lungs.

For the next few days, read these steps aloud as you do them or ask someone to read them to you. Ask your doctor or nurse to check how well you are using your inhaler.

Use your inhaler in one of the three ways pictured below. A or B are best, but C can be used if you have trouble with A and B. Your doctor may give you other types of inhalers.

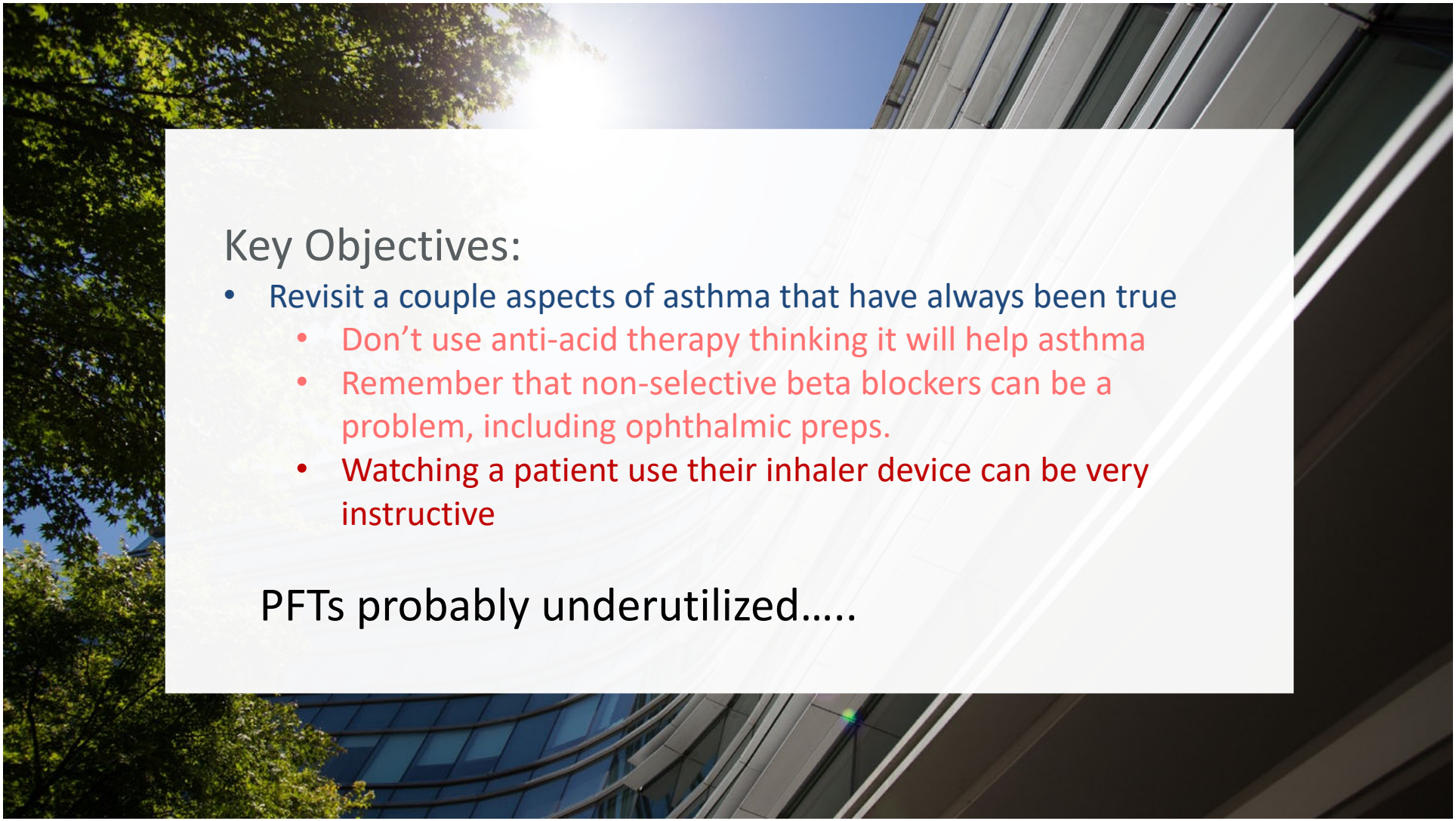
Steps for Using Your Inhaler

Getting ready	1. Take off the cap and shake the inhaler. 2. Breathe out all the way. 3. Hold your inhaler the way your doctor said (A, B, or C below).
Breathe in slowly	4. As you start breathing in slowly through your mouth, press down on the inhaler one time. (If you use a holding chamber, first press down on the inhaler. Within 5 seconds, begin to breathe in slowly.) 5. Keep breathing in slowly, as deeply as you can.
Hold your breath	6. Hold your breath as you count to 10 slowly, if you can. 7. For inhaled quick-relief medicine (beta$_2$-agonists), wait about 15–30 seconds between puffs. There is no need to wait between puffs for other medicines.

A. Hold inhaler 1 to 2 inches in front of your mouth (about the width of two fingers).

B. Use a spacer/holding chamber. These come in many shapes and can be useful to any patient.

C. Put the inhaler in your mouth. Do not use for steroids.



Key Objectives:

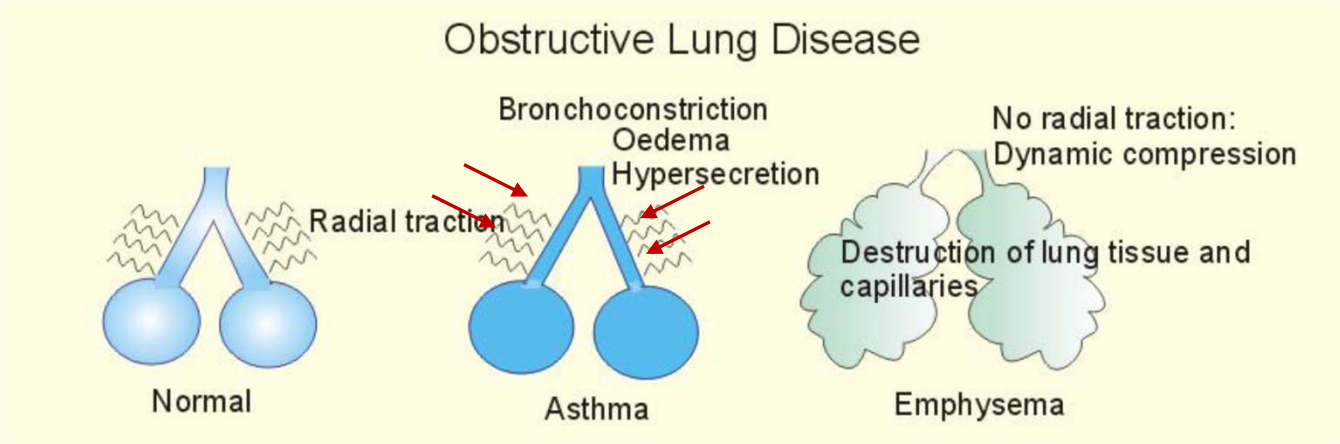
- Revisit a couple aspects of asthma that have always been true
  - Don't use anti-acid therapy thinking it will help asthma
  - Remember that non-selective beta blockers can be a problem, including ophthalmic preps.
  - Watching a patient use their inhaler device can be very instructive

PFTs probably underutilized…..

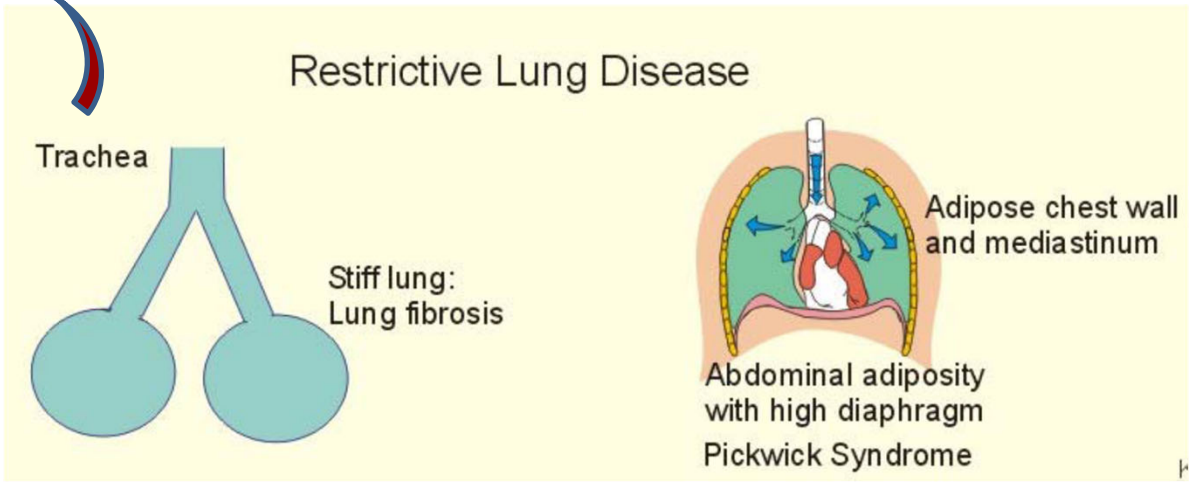
Even though we are all comfortable making a clinical diagnosis of asthma, I'm still a fan of PFTs in many patients, especially if the diagnosis is not a clinical slam dunk (patient is a little older, no real obvious history of triggers and/or no seasonality to their disease)

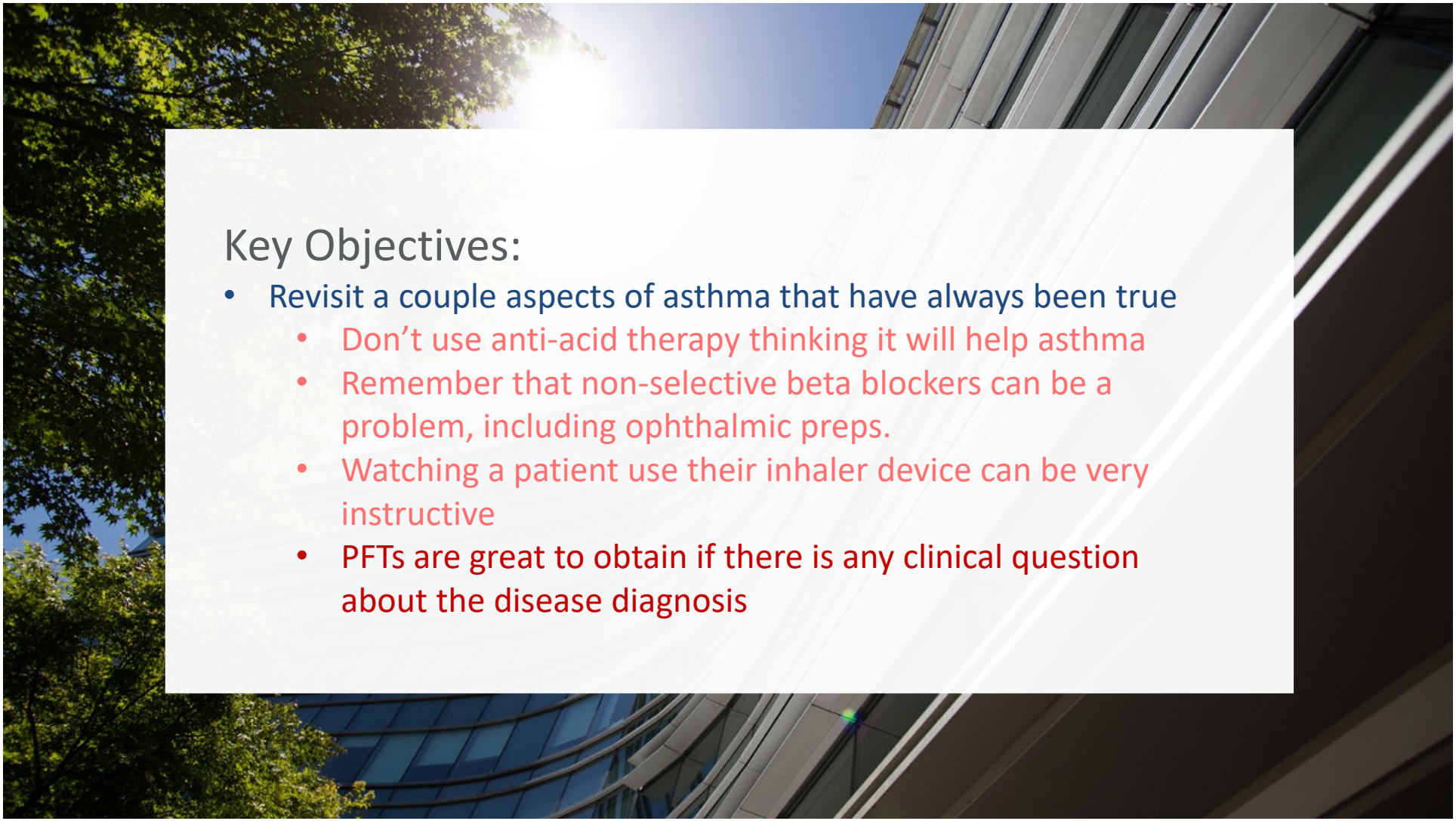
Disease in the airways – an 'obstruction' to the flow of air

About 10% of abnormal PFTs at OHSU are NOT an obstructive pattern



The airways are fine and 'restriction' is to lung expansion vs. bronchial air flow. Amiodarone is classic example of drug-induced restrictive disease





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  - PFTs are great to obtain if there is any clinical question about the disease diagnosis

I’m always reminded when I talk to patients in the hospital with an asthma exacerbation that subjective symptoms are very discordant from objective measures of lung function…

Daily symptoms of asthma do not correlate well with lung volume findings:

clinical investigations

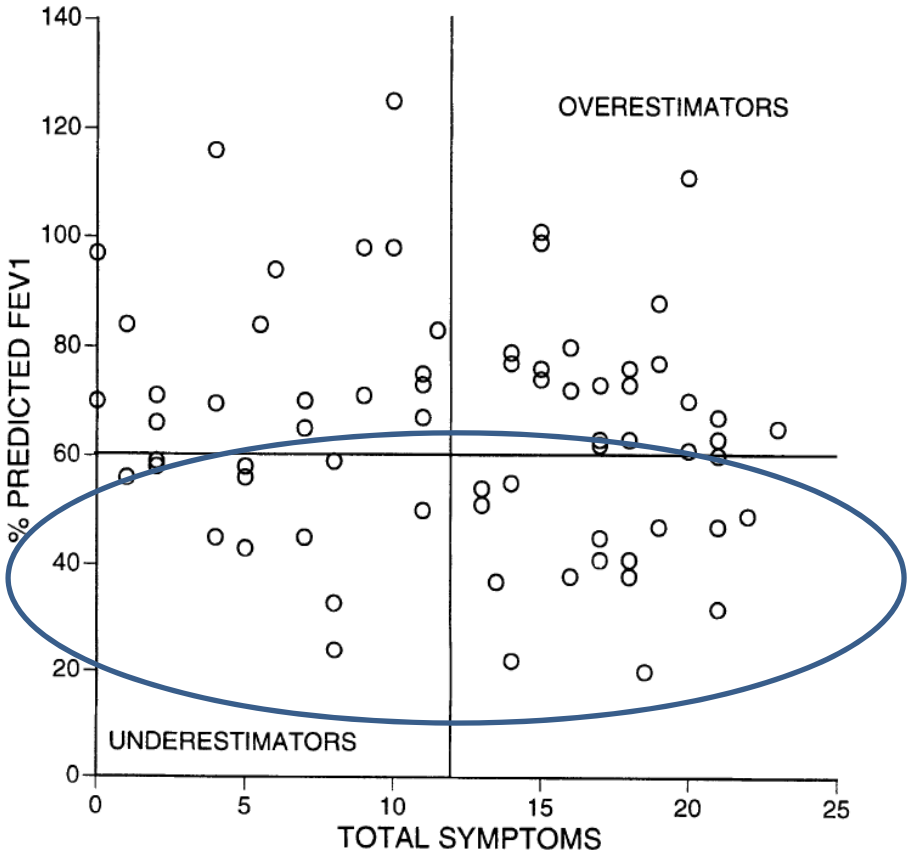
Relationship Between Airway Obstruction and Respiratory Symptoms in Adult Asthmatics*

John G. Teeter, MD, FCCP; and Eugene R. Bleecker, MD, FCCP

CHEST 1998;113(2):272-77

Table 1—*Patient Characteristics

Characteristic	No.
Age, yr	32.7±12.9
Duration of asthma, yr	18.4+13.6
Gender, % female	65
Race, %	
African-American	89.5
White	9.0
Hispanic	1.0
Hospital/ED (prior 12 mo), %	81.7
Prednisone therapy (prior 12 mo), %	73.2



Exacerbations come from down here….

r=0.143, p=0.2

New guidelines for better asthma control

Last week, the US National Asthma Education and Prevention Program issued the first comprehensive update of its clinical guidelines for the diagnosis and management of asthma in a decade. The 500-page document is rigorous and evidence-based. It integrates the latest scientific evidence into the four essential components of asthma care: assessment and monitoring, patients' education, control of factors contributing to asthma severity, and drug treatment.

There is increasing evidence that asthma is a hete
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The asthma guidelines place a lot of emphasis on monitoring lung volumes at home due to the disconnect between symptoms and volume….

side-effects, the treatment benefits far outweigh the risks. Additionally, there are now separate treatment recommendations for children aged 0–4 years, 5–11 years, and 12 years and older. The 5–11 year age group was added (earlier guidelines combined this group with adults) because of new evidence suggesting that children might respond differently from adults to asthma drugs.

The guidelines place a strong emphasis on monitoring asthma control. The new approach focuses on two related yet distinct aspects of the disease: the level of daily impairment that a patient is experiencing and the patient's future risk for exacerbations, loss of lung function, and drug side-effects. This new distinction is important because it addresses the fact that some

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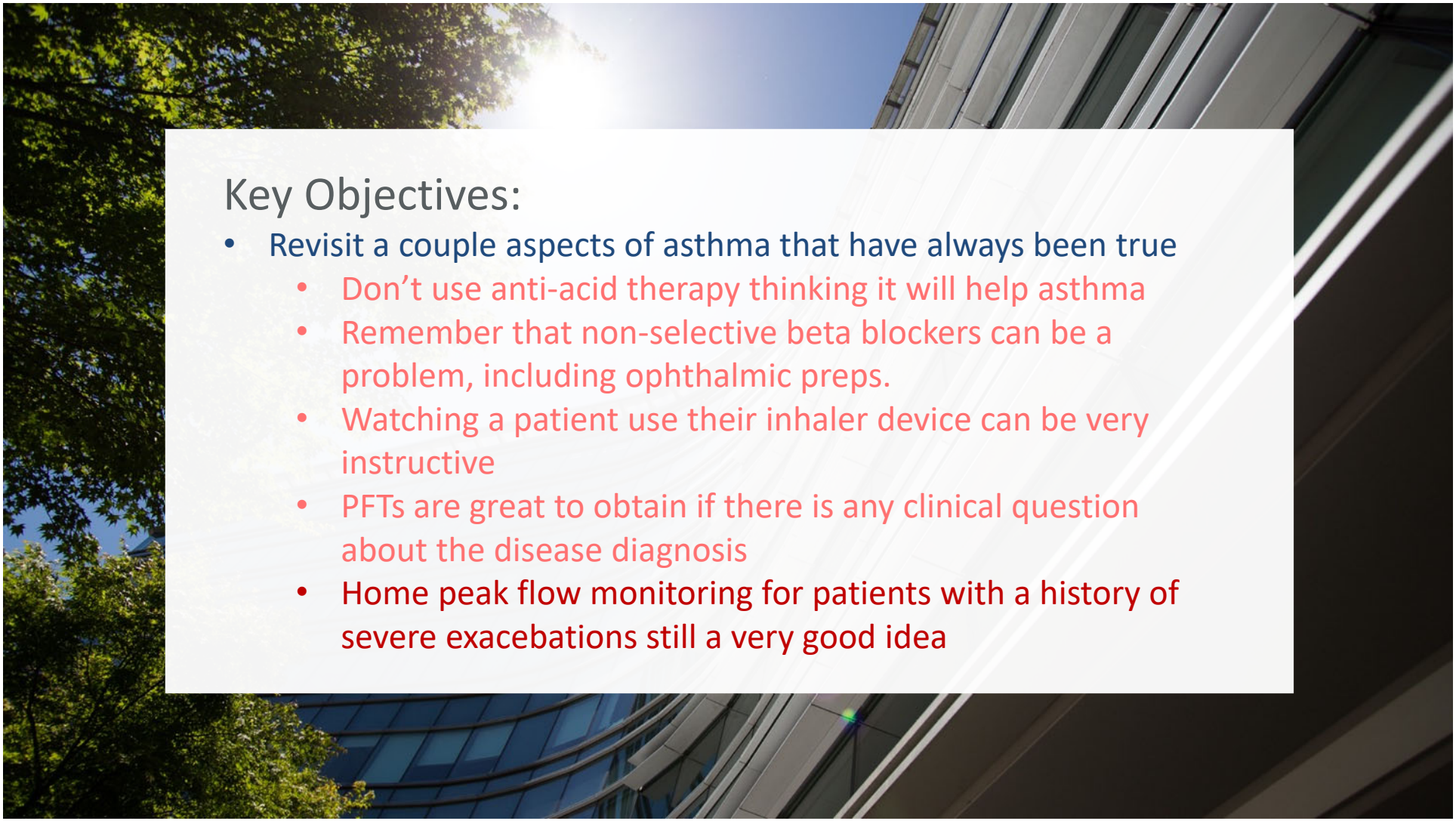
informed and empowered patients can control their asthma and live full normal active lives. These guidelines will be invaluable for clinicians and patients alike.

■ *The Lancet*



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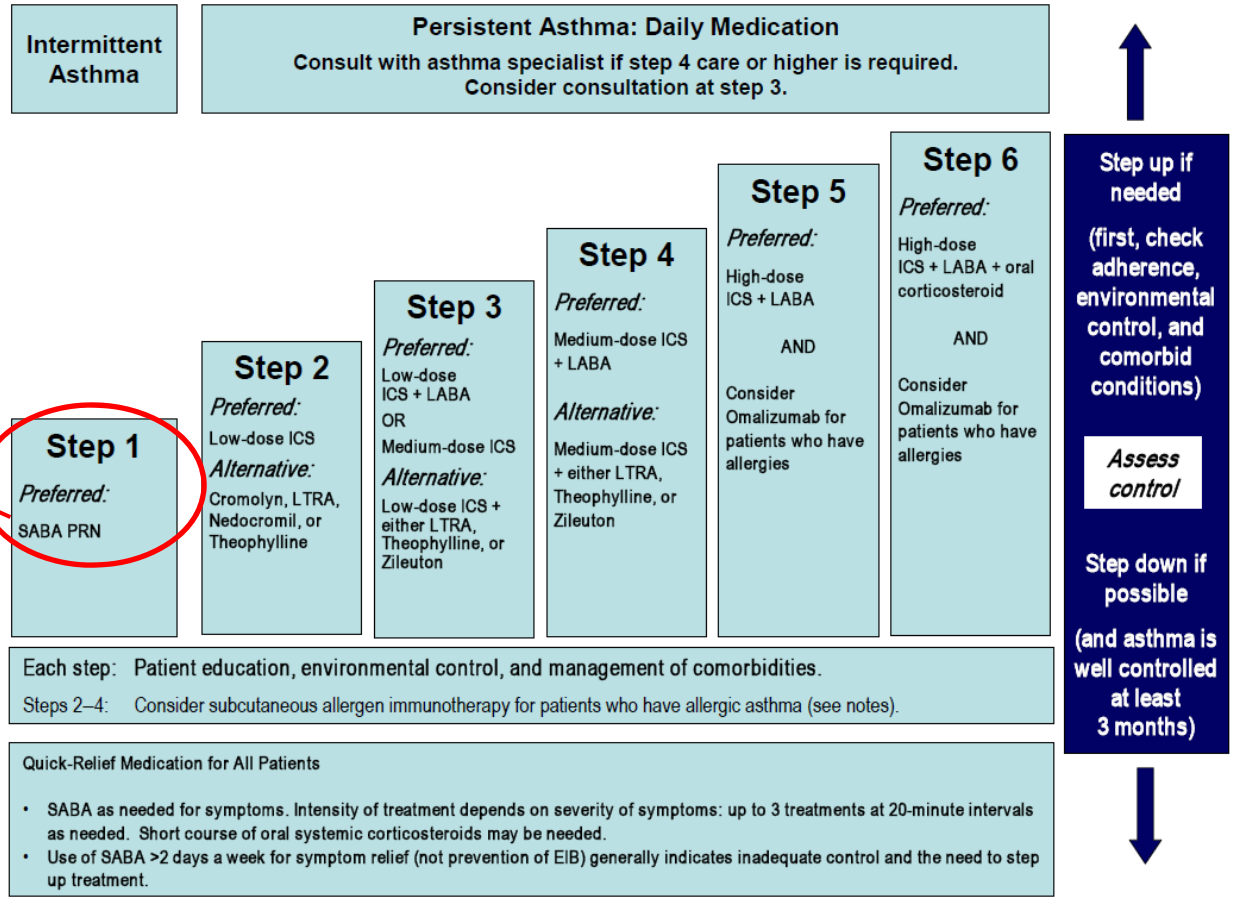
  - Watching a patient use their inhaler device can be very instructive
  - PFTs are great to obtain if there is any clinical question about the disease diagnosis
  - Home peak flow monitoring for patients with a history of severe exacebations still a very good idea

So a number of things about asthma management have NOT changed but "Treatment Approach" is no longer one of them….

NAEPP page 343

FIGURE 4–5. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS



GINA 2019 guidelines say first line: formoterol+ICS

Symbicort is with budesonide

Dulera is with mometasone

"SMART" approach: Single Maintenace and Reliever Therapy

Who are the GINA guidelines authors?

"In 1993, NIH/NHLBI convened the NAEPP work group....."

Preface

"…This was followed by the establishment of GINA, a network of individuals, organizations and public health officials…..to provide a mechanism to translate scientific evidence into improved asthma care….The GINA assembly was subsequently initiated, as an ad hoc group of dedicated asthma care experts from many countries…."

workshop that led to a Workshop Report: Global Strategy for Asthma Management and Prevention.[1] This was followed by the establishment of the Global Initiative for Asthma (GINA), a network of individuals, organizations, and public health officials to disseminate information about the care of patients with asthma, and to provide a mechanism to translate scientific evidence into improved asthma care. The GINA Assembly was subsequently initiated, as an *ad hoc* group of dedicated asthma care experts from many countries. The Assembly works with the Science Committee, the Board of

There are 15 members of their scientific writing Board and 12 members of the Board of Directors (many overlap)

Here are financial disclosure statements for first 4 GINA co-authors. The total COI document is 25 pages long.

Name of Entity	Grant ?	Personal Fee?	Non-Financial Support?	Other ?	Nature of involvement:
AstraZeneca	X				Investigator
AstraZeneca		X to my group			Conferences and Advisory Board
Boston Scientific	X				Co-investigator
GlaxoSmithKline		X to my group			Conferences
Novartis		X to my group			Conferences
Novartis	X				Investigator
Sanofi	X				Investigator
GlaxoSmithKline	X				Investigator
Merck		X to my group			Conferences
Teva		X to my group			Conferences
AstraZeneca, GlaxoSmithKline, Novartis, Boehringer-Ingelheim, Merck		X to University Chair			Independent production of educational material

Name of Entity	Grant?	Personal Fee?	Non-Financial Support?	Other?	Nature of involvement:
AstraZeneca		X			Advisory board, lecture fees, consultancy
ALK		X			Advisory board, lecture fees, consultancy
Novartis		X			Advisory board, lecture fees, consultancy
Sanofi		X			Advisory board, lecture fees
Regeneron		X			Advisory board, lecture fees
Orion		X			Lecture fee
Menarini		X			Lecture fee
Medscape		X			Lecture feee

Name of Entity	Grant?	Personal Fee?	Non-Financial Support?	Other?	Nature of involvement:
GlaxoSmithKline	X				Research grants paid to Institu
AstraZeneca/MedImmune	X	X			Research grants and consultanc paid to Institution
Novartis	X	X			Research grants and consultancy paid to Institution
Chiesi	X				Research grants paid to Institution
Boehringer-Ingelheim	X	X			Research grants and consultancy paid to Institution
Mologic	X	X			Research grants and consultancy paid to Institution
TEVA		X			Consultancy paid to Institution
4DPharma	X	X			Research grants and consultancy paid to Institution
Sterna		X			Consultancy paid to Institution
Gossamer	X	X			Research grants and consultancy paid to Institution
Merck	X				Research grant paid to Institution
Quench		X			Consultancy paid to Institution
Regeneron		X			Consultancy paid to Institution
Sanofi		X			Consultancy paid to Institution
Roche/Genentech	X				Consultancy paid to Institution

Name of Entity	Grant?	Personal Fee?	Non-Financial Support?	Other?	Nature of involvement:
AstraZeneca	NO	Yes	No	No	Speaking fees, advisory board fees
Regeneron	No	Yes	No	No	Speaking fees, advisory board fees
Sanofi	No	Yes	No	No	Speaking fees, advisory board fees
GlaxoSmithKline	No	Yes	No	No	Speaking fees
DBV Technologies	No	Yes	No	No	DSMB
Novartis	No	Yes	No	No	Speaking fees, advisory board fees
AAAAI	No	Yes	No	No	Associate Editor, JACI
ACAAI	No	Yes	No	No	Development of Asthma Yardstick documents
CF Foundation	No	Yes	No	No	DSMB
American Board of Allergy and Immunology	No	Yes	No	No	Vice Chair

How were financial COI handled as "GINA" authors voted that everyone should use $300-400 *Dulera* or *Symbicort*?

Compared to NIH NAEPP guideline, less clear how GINA guidelines handle financial COI. Conflicted members of the 15-person scientific writing board appear to retain ability to vote on pathway updates….

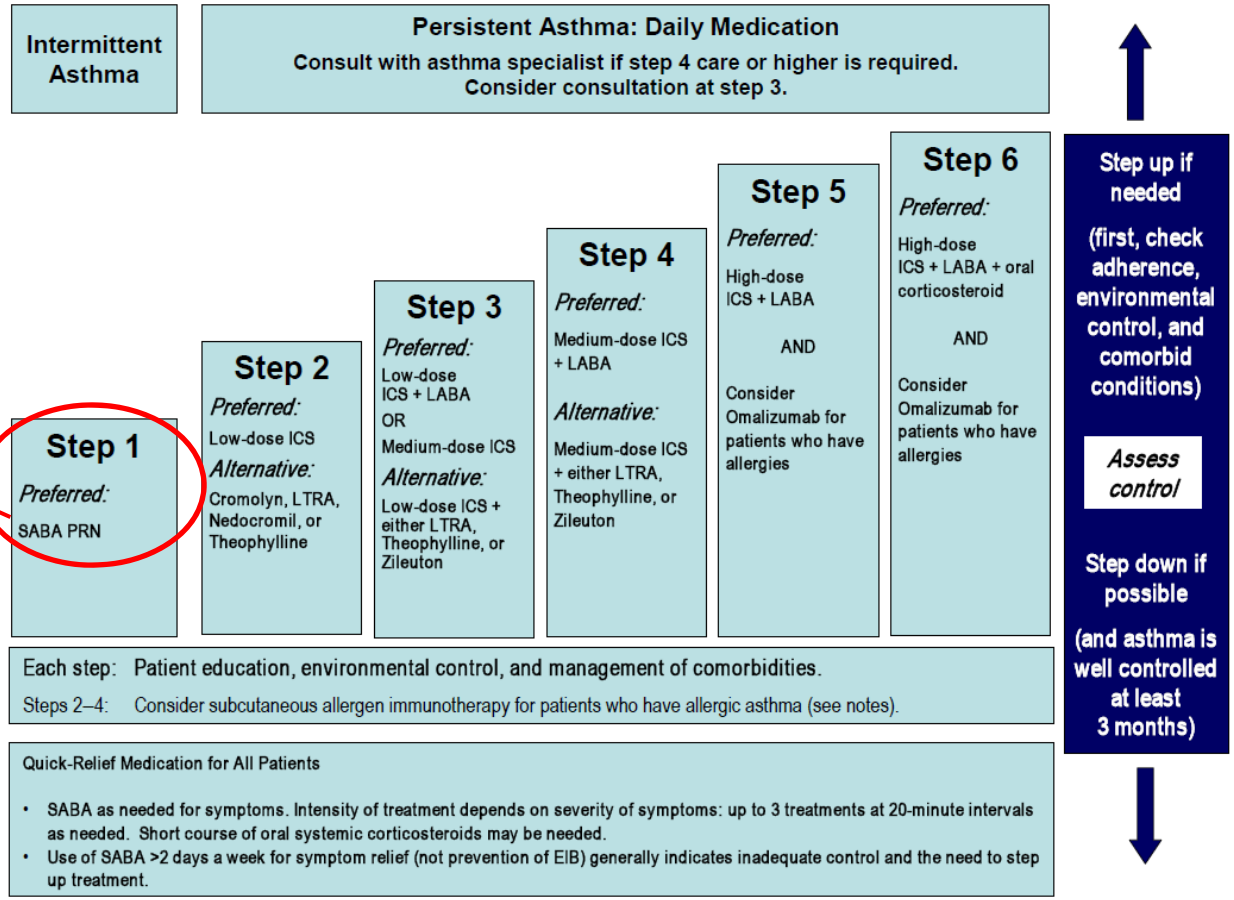
Screening and review

After initial screening of articles identified by a cumulative search of the literature by the Editorial Assistant and Chair of the Science Committee, each publication identified by the above search is reviewed for relevance and quality by members of the Science Committee. Each publication is allocated to at least two Committee member reviewers, neither of whom may be an author (or co-author) or declare a conflict of interest in relation to the publication. All members receive a copy of all of the abstracts and non-conflicted members have the opportunity to provide comments during the pre-meeting review period. Members evaluate the abstract and, by their judgment, the full publication, and answer written questions about whether the scientific data impact on GINA recommendations, and if so, what specific changes should be made. A list of all publications reviewed by the Committee is posted on the GINA website (www.ginasthma.org).

So, "GINA" authors say no more prn SABA for any asthmatic….

NAEPP page 343

FIGURE 4–5. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS



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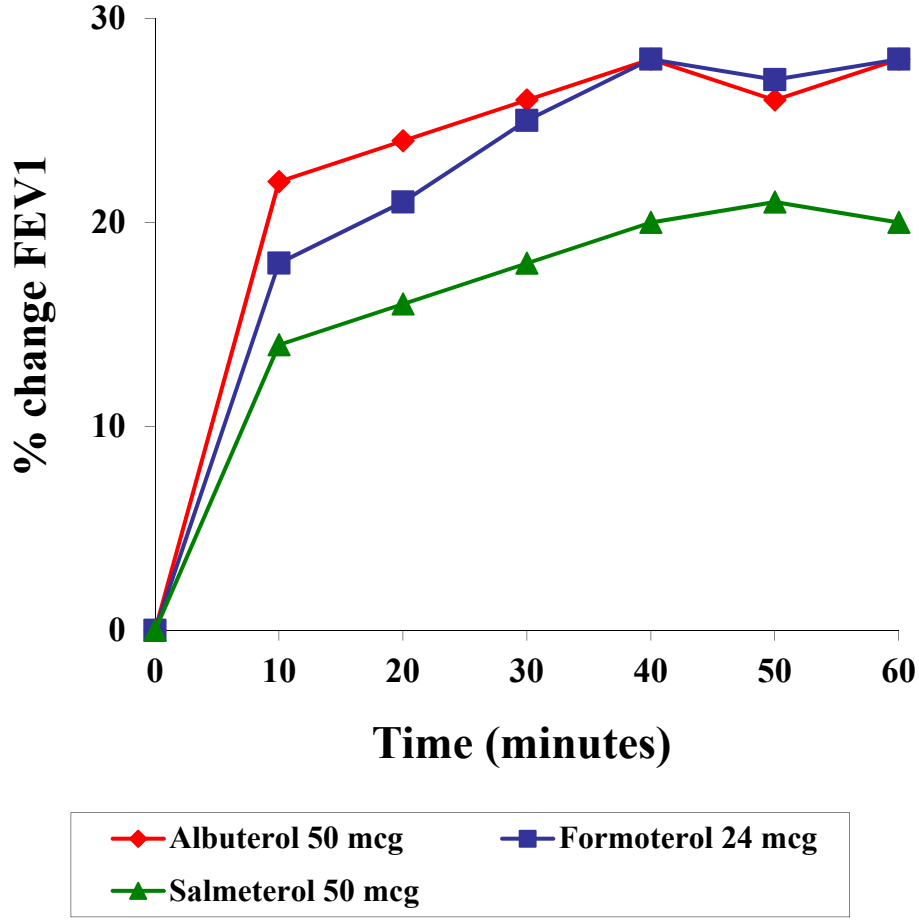
"SMART" approach: Single Maintenace and Reliever Therapy

% Change in FEV1 in first hour

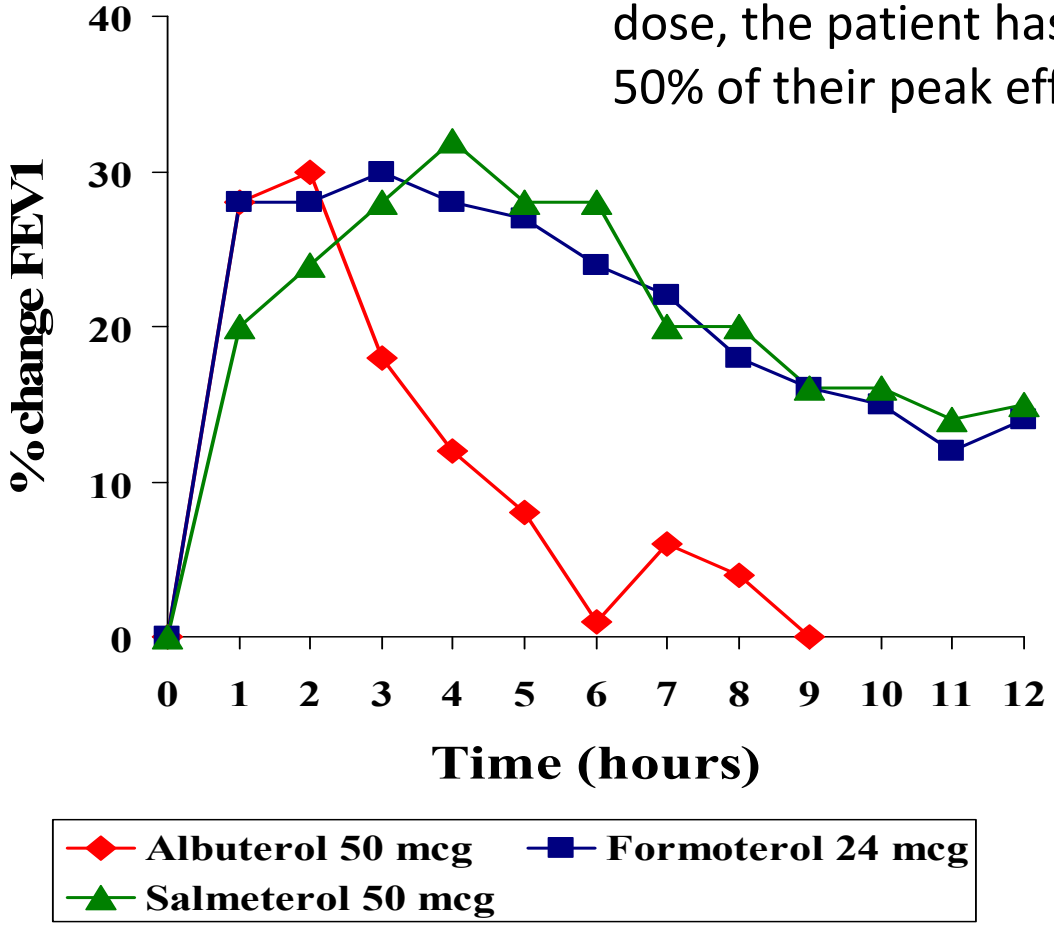


Onset of albuterol: < 2 min

Effective clinical duration: 4 hours

% Change in FEV1 over 12 hours

At the 12th hour after a LABA dose, the patient has about 50% of their peak effect



Why the "SMART" approach from GINA?

1. Asthmatics that are pretty healthy often only use their "reliever" because that's the one that makes them acutely feel better….but that's a problem

2. The inflammation in asthma is very amenable to corticosteroid therapy and missed use of ICS (inhaled corticosteroid) misses the opportunity to control the disease

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Controversies settled in asthma: Scheduled, daily use of SABA?: NO
- NAEPP 2007 guidelines, page 236

KEY POINTS: SAFETY OF INHALED SHORT-ACTING BETA$_2$-AGONISTS

- SABAs are the most effective medication for relieving acute bronchospasm (Evidence A).
- Increasing use of SABA treatment or using SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control of asthma and the need for initiating or intensifying anti-inflammatory therapy (Evidence C).
- Regularly scheduled, daily, chronic use of SABA is not recommended (Evidence A).

Adverse effects:

These drugs are related to adrenaline (epinephrine) and are mild stimulants but most importantly, overuse can mask progressing, underlying disease

LABA (long-acting beta agonist): Manufacturer of Salmeterol did a trial of that drug as the “controller” for mild persistent asthma and it failed

FDA put a black box warning on LABA for asthma without a controller

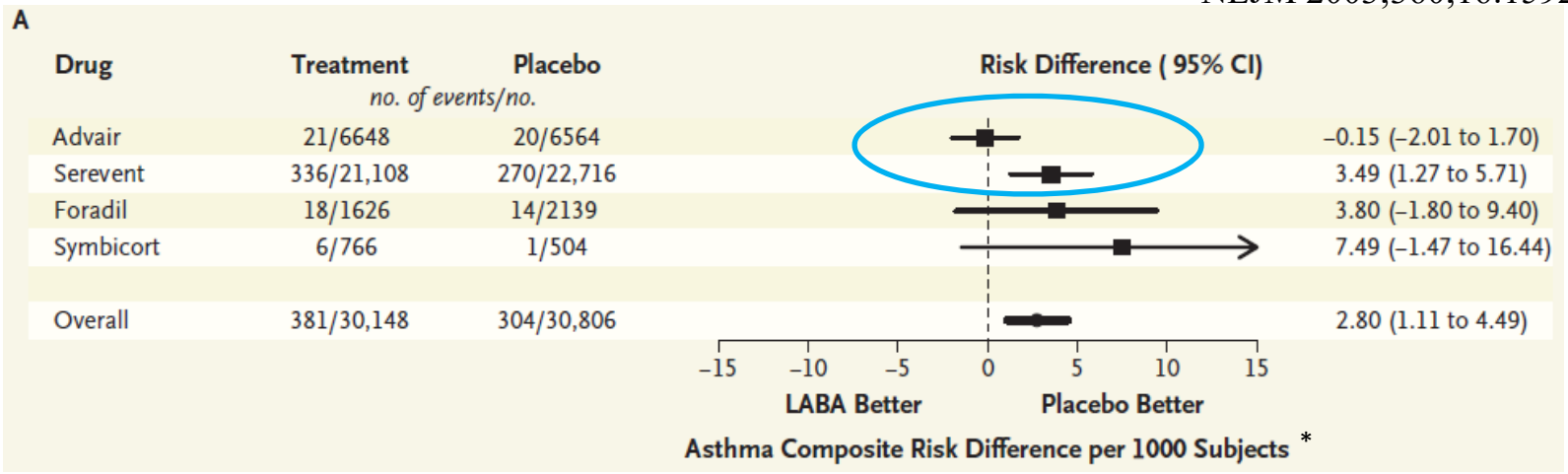
WARNING: ASTHMA-RELATED DEATH

See full prescribing information for complete boxed warning.

- **Long-acting beta$_2$-adrenergic agonists (LABA), such as salmeterol, the active ingredient in SEREVENT DISKUS, increase the risk of asthma-related death. A U.S. trial showed an increase in asthma-related deaths in subjects receiving salmeterol (13 deaths out of 13,176 subjects treated for 28 weeks on salmeterol versus 3 out of 13,179 subjects on placebo). Currently available data are inadequate**

Controversies in Asthma: LABA not harmful when added to a controller

NEJM 2003;360;16:1592



*Asthma composite risk: death from asthma, intubation, hospitalization

- **LABAs:** Salmeterol and formoterol are bronchodilators that have a duration of bronchodilation of at least 12 hours after a single dose.
  - LABAs are not to be used as monotherapy for long-term control of asthma (Evidence A).
  - LABAs are used in combination with ICSs for long-term control and prevention of symptoms in moderate or severe persistent asthma (step 3 care or higher in children ≥5 years of age and adults) (Evidence A for ≥12 years of age, Evidence B for 5–11 years of age).

NAEPP, page 213

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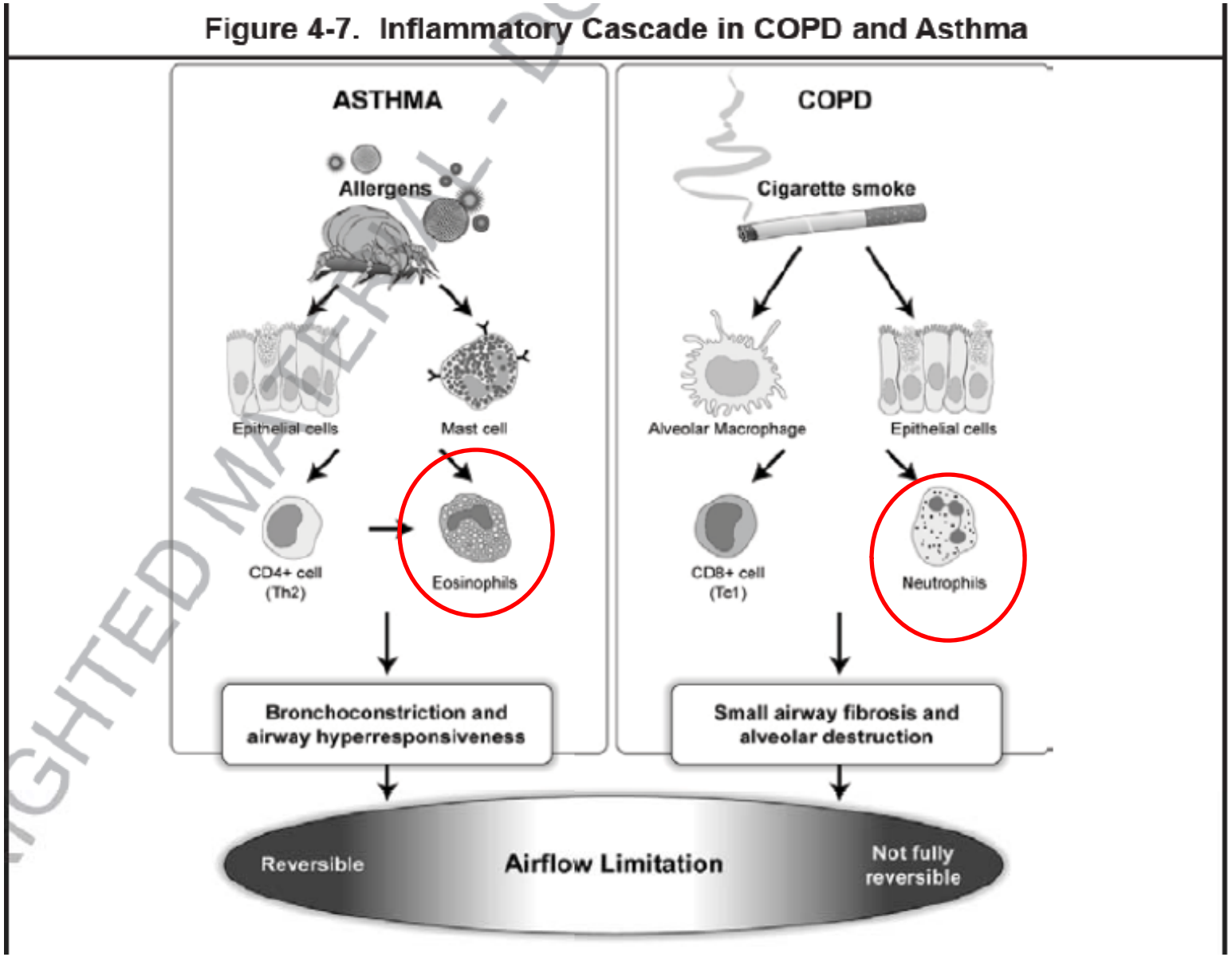
N Engl J Med; Sept. 19, 2002

Editorials

Eat Dirt — The Hygiene Hypothesis and Allergic Diseases

THERE has been an epidemic of both autoimmune diseases (in which the immune response is dominated by type 1 helper T [Th1] cells, such as type 1 diabetes, Crohn's disease, and multiple sclerosis) and allergic diseases (in which the immune response is dominated by type 2 helper T [Th2] cells, such as asthma, allergic rhinitis, and atopic dermatitis), as documented in the article by Bach in this issue of the *Journal*.[1] The occurrence of these diseases is higher

The inflammation in asthma is different from COPD and more amenable to steroid therapy….

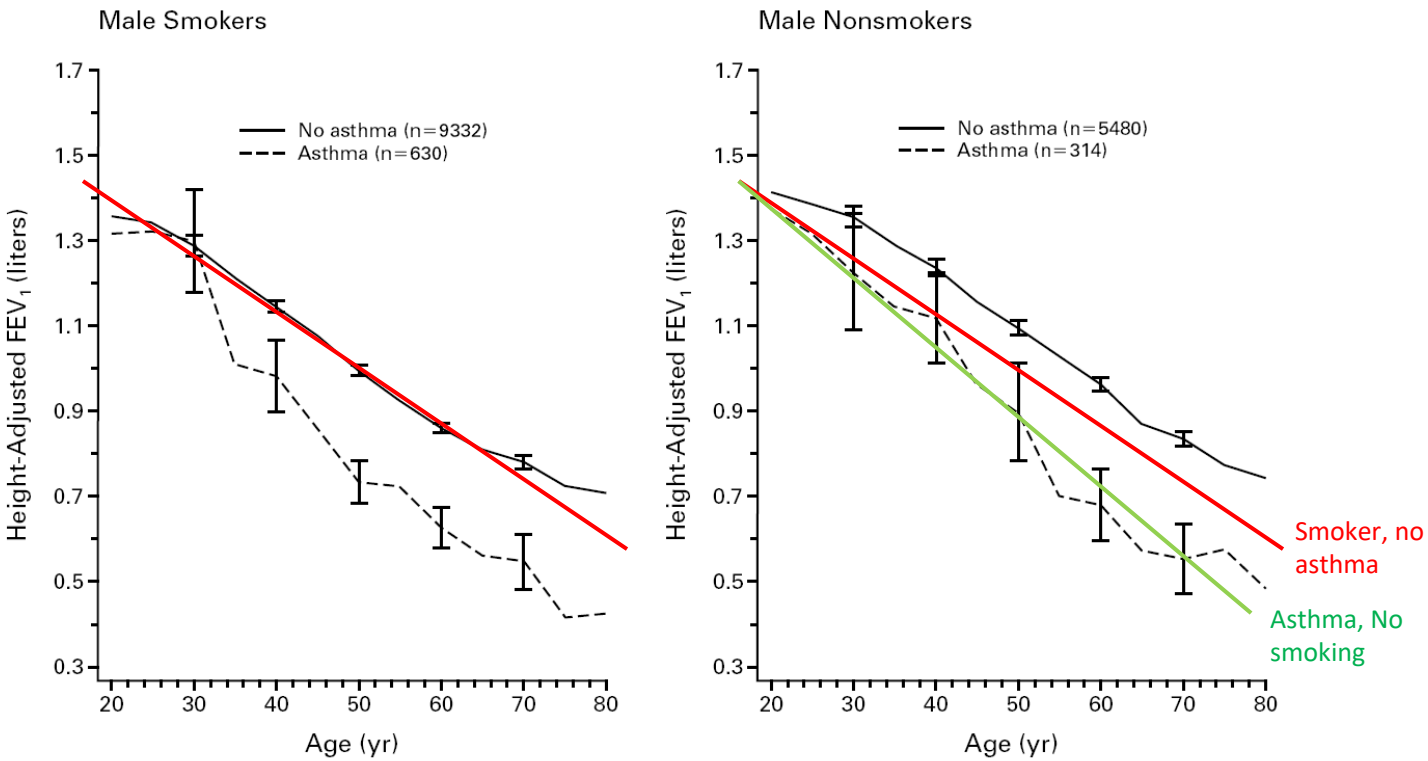


Why control: Poorly controlled asthmatics with moderate-severe disease lose lung volume faster than smokers

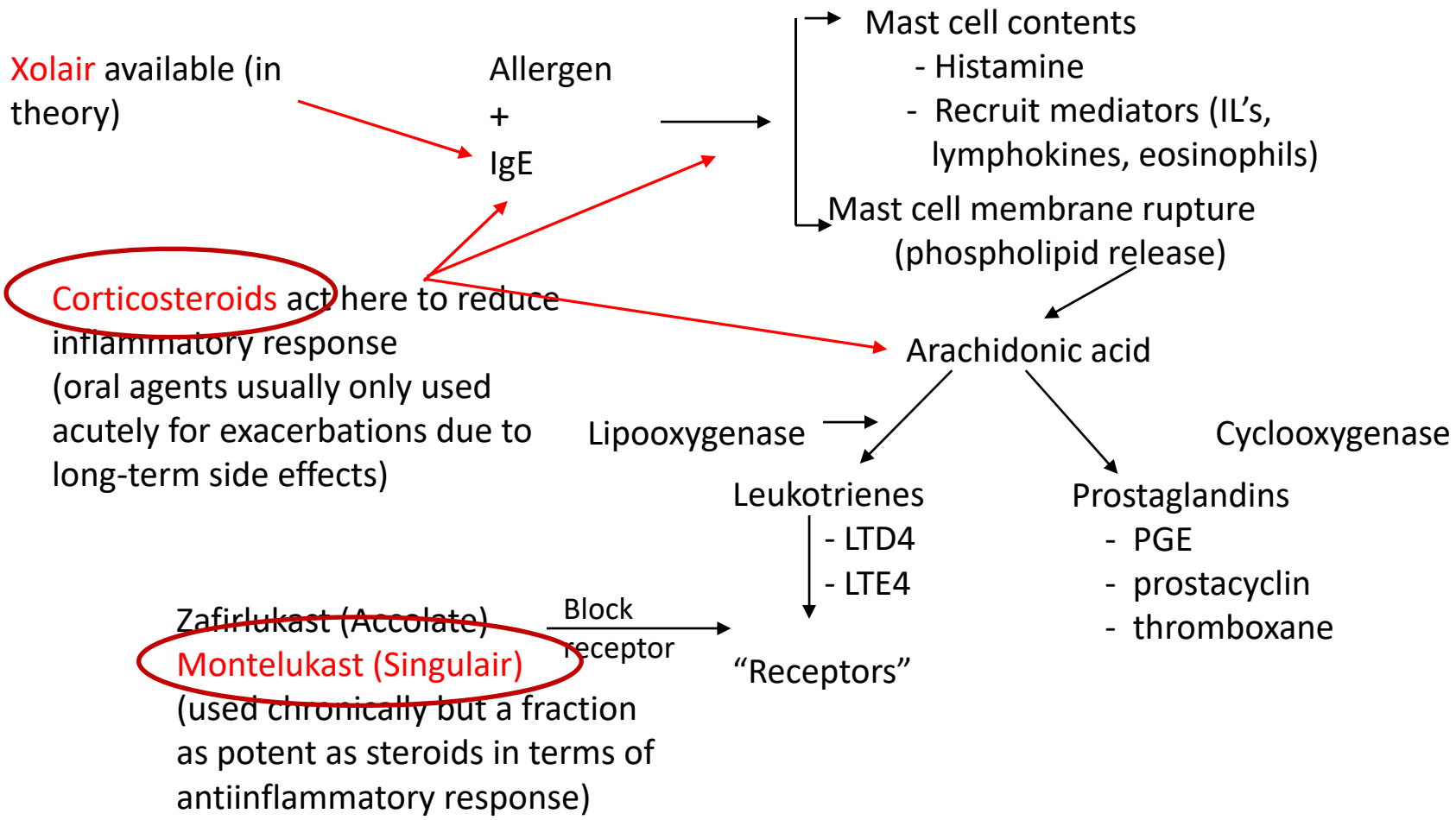
NEJM 1998;339:1194-200

A 15-YEAR FOLLOW-UP STUDY OF VENTILATORY FUNCTION IN ADULTS WITH ASTHMA

PETER LANGE, M.D., PH.D., JAN PARNER, JØRGEN VESTBO, M.D., PH.D., PETER SCHNOHR, M.D., AND GORM JENSEN, M.D., PH.D.



"Controllers" help bend the disease curve and slow the rate of loss of lung function

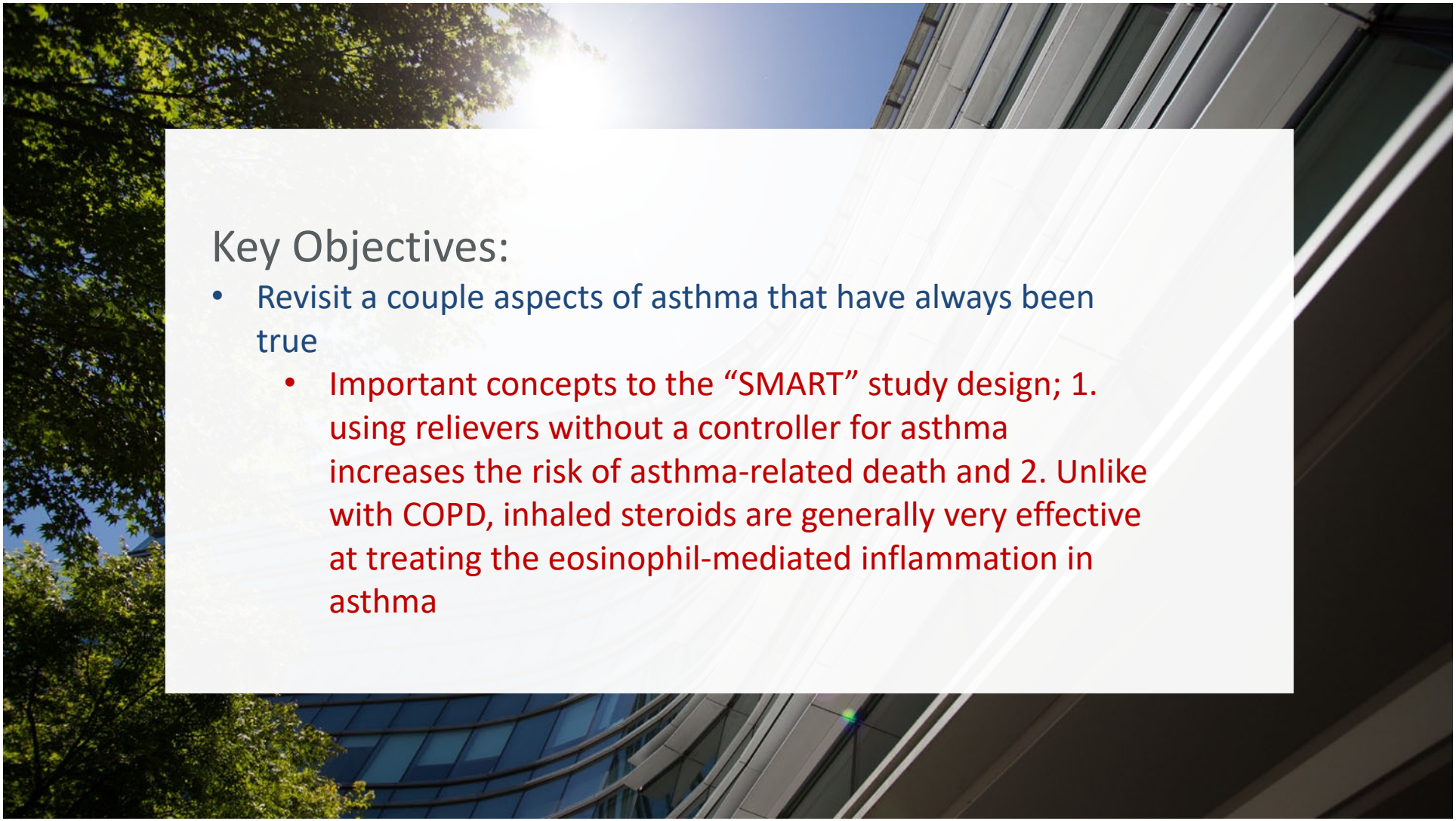


In terms of comparative efficacy of controllers for asthma:

Efficacy of Inhaled Corticosteroids as Compared to Other Long-Term Control Medications as Monotherapy

The Expert Panel concludes that studies demonstrate that ICSs improve asthma control more effectively in both children and adults than LTRAs or any other single long-term control medication (Evidence A).

NAEPP page 217

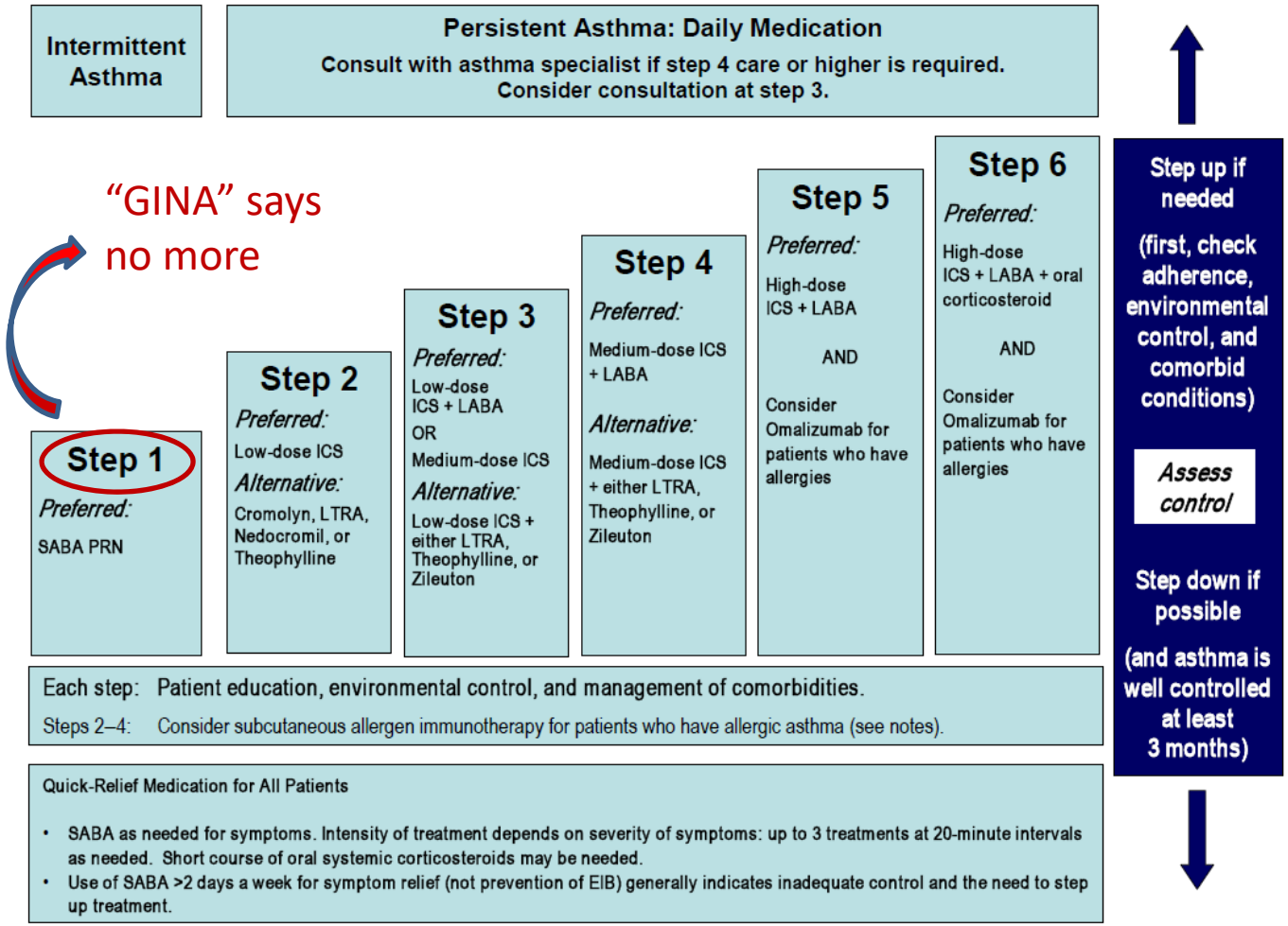


Key Objectives:

- Revisit a couple aspects of asthma that have always been true
  - Important concepts to the “SMART” study design; 1. using relievers without a controller for asthma increases the risk of asthma-related death and 2. Unlike with COPD, inhaled steroids are generally very effective at treating the eosinophil-mediated inflammation in asthma

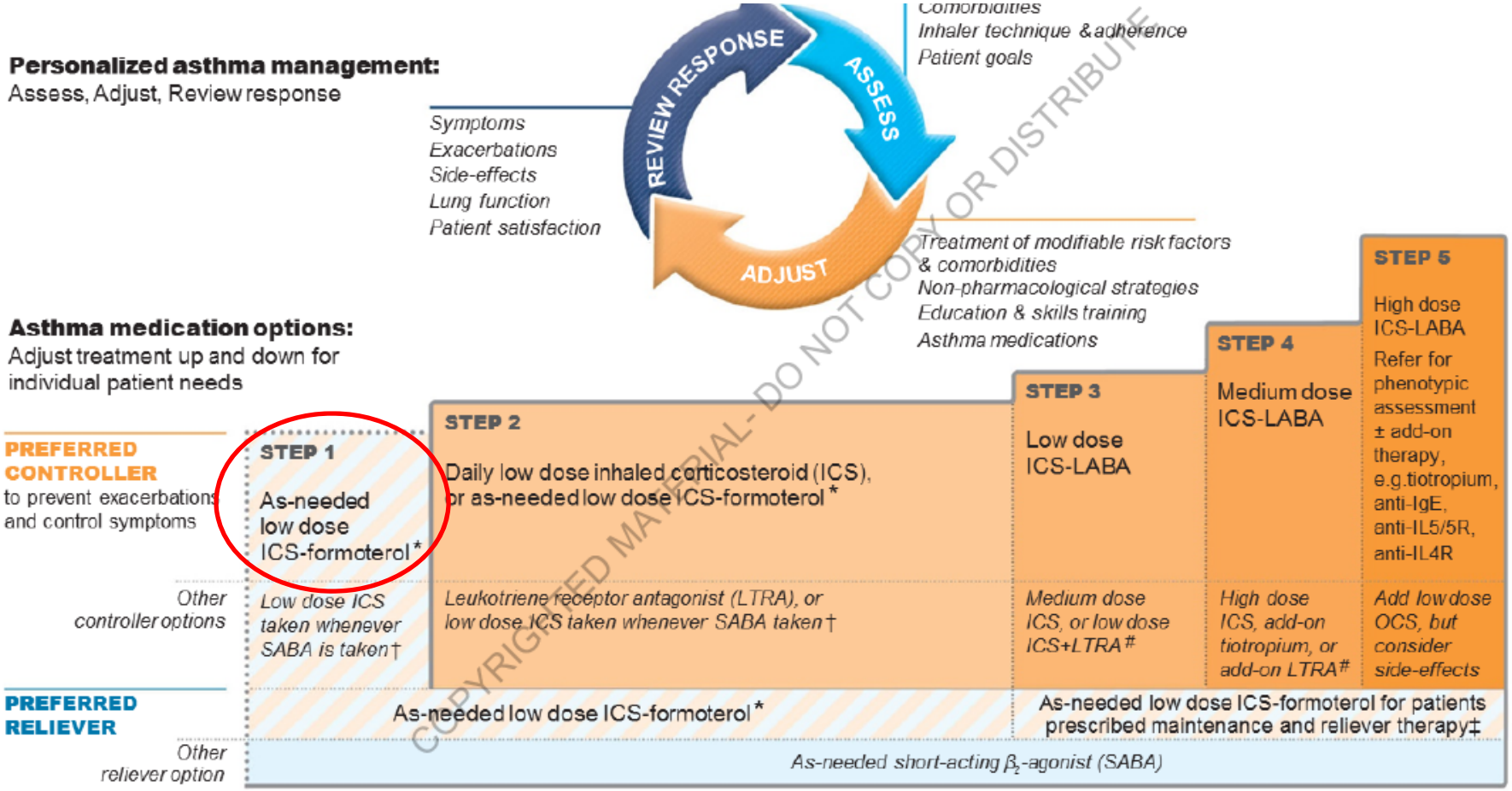
Therapeutic strategies. Optimizing asthma control: Adults/adolescents

FIGURE 4–5. STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥12 YEARS OF AGE AND ADULTS



NAEPP page 343

GINA guidelines, 2019:



"SMART" approach: Single Maintenace and Reliever Therapy

NIH Update 2020…..

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines

A Report from the National
Asthma Education and Prevention
Program Coordinating Committee
Expert Panel Working Group

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

NIH NAEPP guidelines in 2020 retained the prn SABA approach for intermittent asthma patients (2 or fewer uses of reliever per week).....

Figure I.d: Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and 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 Zileuton,* 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 low-dose ICS + 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▲ or Daily medium-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	

Why did NAEPP in 2020 NOT endorse the "S.M.A.R.T" approach to intermittent asthma?

1. Dulera or Symbicort are expensive ($300-400 each) and

2. The trials in 2018 which led to the GINA update in 2019 studied patients who mostly had persistent asthma and therefore should have already been on a controller. Not surprisingly, low dose ICS + formoterol beat prn albuterol

least 6 months previously were eligible if they had been assessed by the investigator as needing GINA step 2 treatment[16] for the 30 days before visit 2. Step 2 treatment is considered to be appropriate in patients with asthma that is uncontrolled while the patient is taking inhaled short-acting bronchodilators on an as-needed basis

GINA step 2 means symptoms "at least" twice monthly but less than daily.

But, on average…….

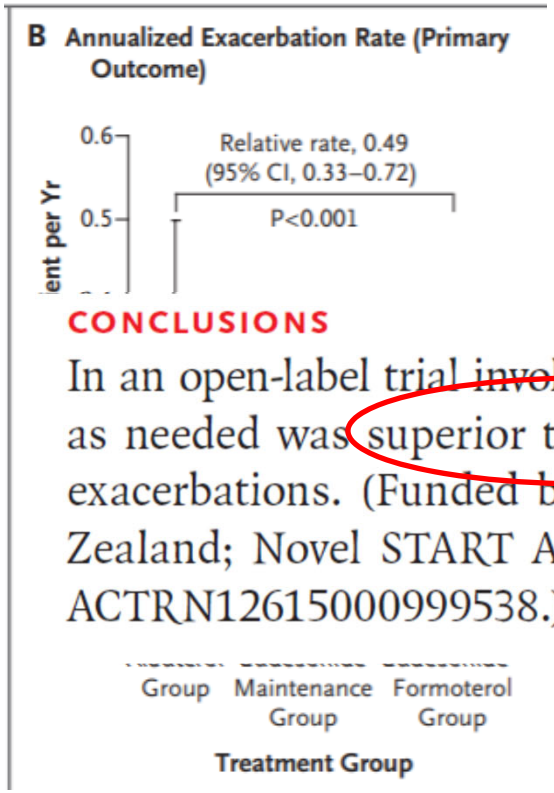
Patient-reported SABA use in the 4 weeks before enrollment			
No. of occasions per wk			
Mean	3.4±3.3	3.2±3.0	3.8±3.5
Median (IQR)	2 (1–4)	2 (1–4)	3 (1–5)
Range	0–14	0.5–14	0.5–14

The “SMART” trials overwhelmingly studied patients with persistent asthma who already qualified for a daily controller per the 2007 NIH EPR 3 guidelines

What did they find in that persistent asthma population?

ESTABLISHED IN 1812 MAY 17, 2018 VOL. 378 NO. 20

Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma



In the trials, exacerbation rates are the same with scheduled low dose ICS or prn ICS+formoterol but…..

CONCLUSIONS

In an open-label trial involving adults with mild asthma, budesonide–formoterol used as needed was superior to albuterol used as needed for the prevention of asthma exacerbations. (Funded by AstraZeneca and the Health Research Council of New Zealand; Novel START Australian New Zealand Clinical Trials Registry number, ACTRN12615000999538.)

ESTABLISHED IN 1812 MAY 17, 2018 VOL. 378 NO. 20

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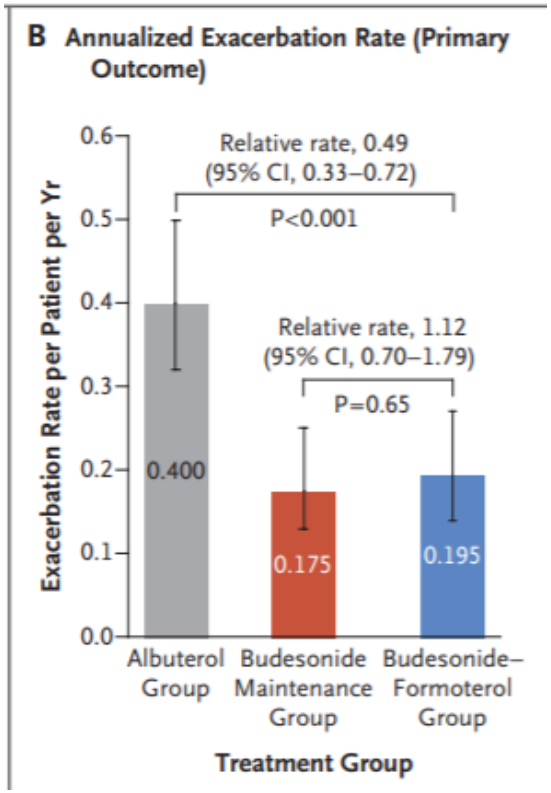


In the trials, exacerbation rates are the same with scheduled low dose ICS or prn ICS+formoterol but…..

But, overall, # weeks of controlled asthma were actually better with scheduled controller

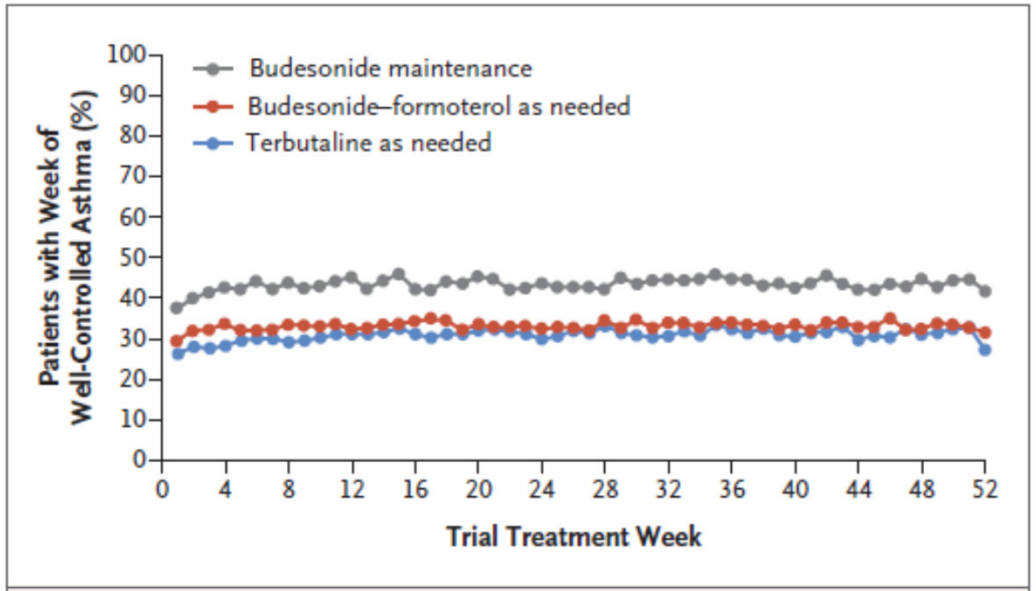
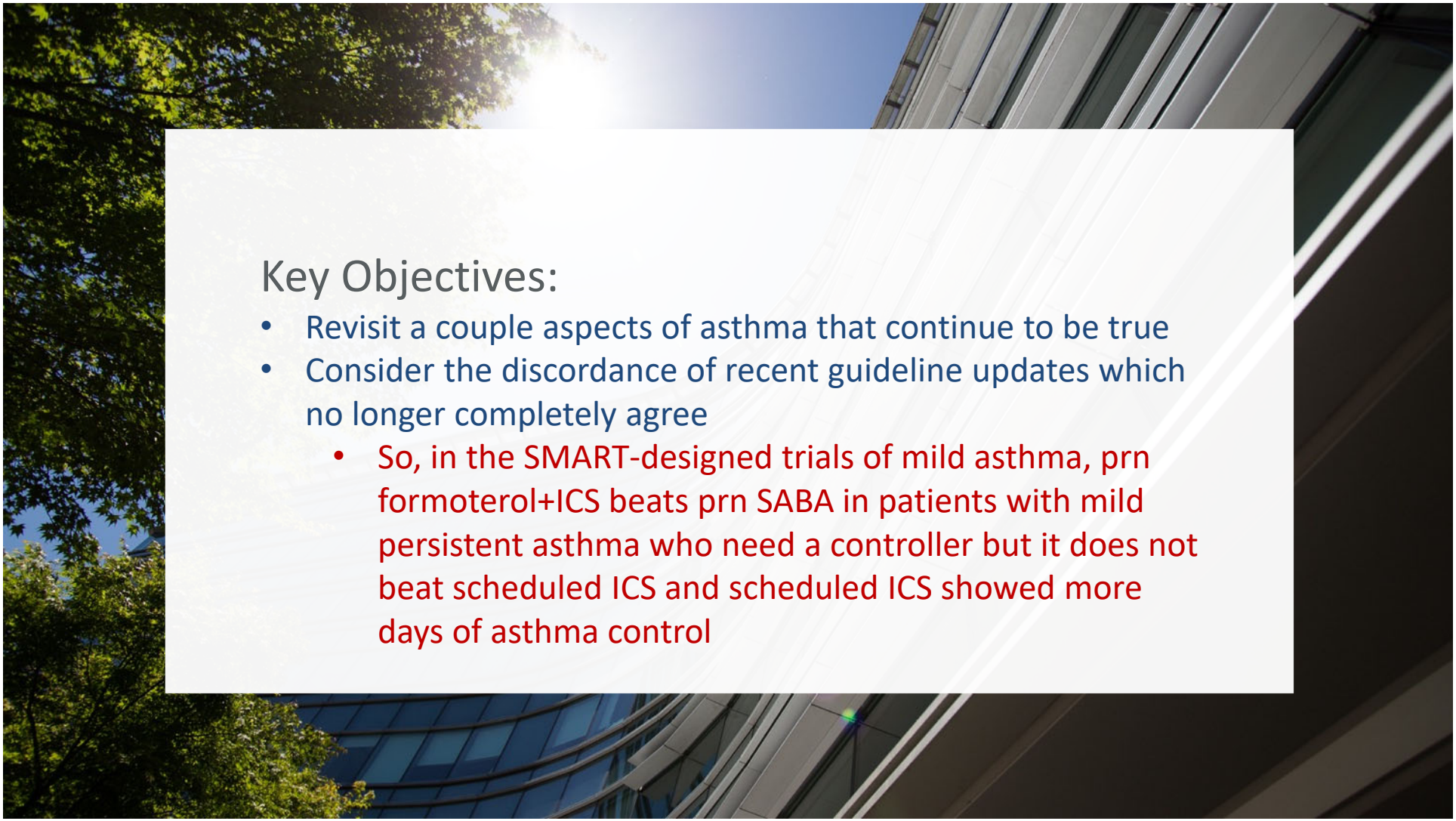


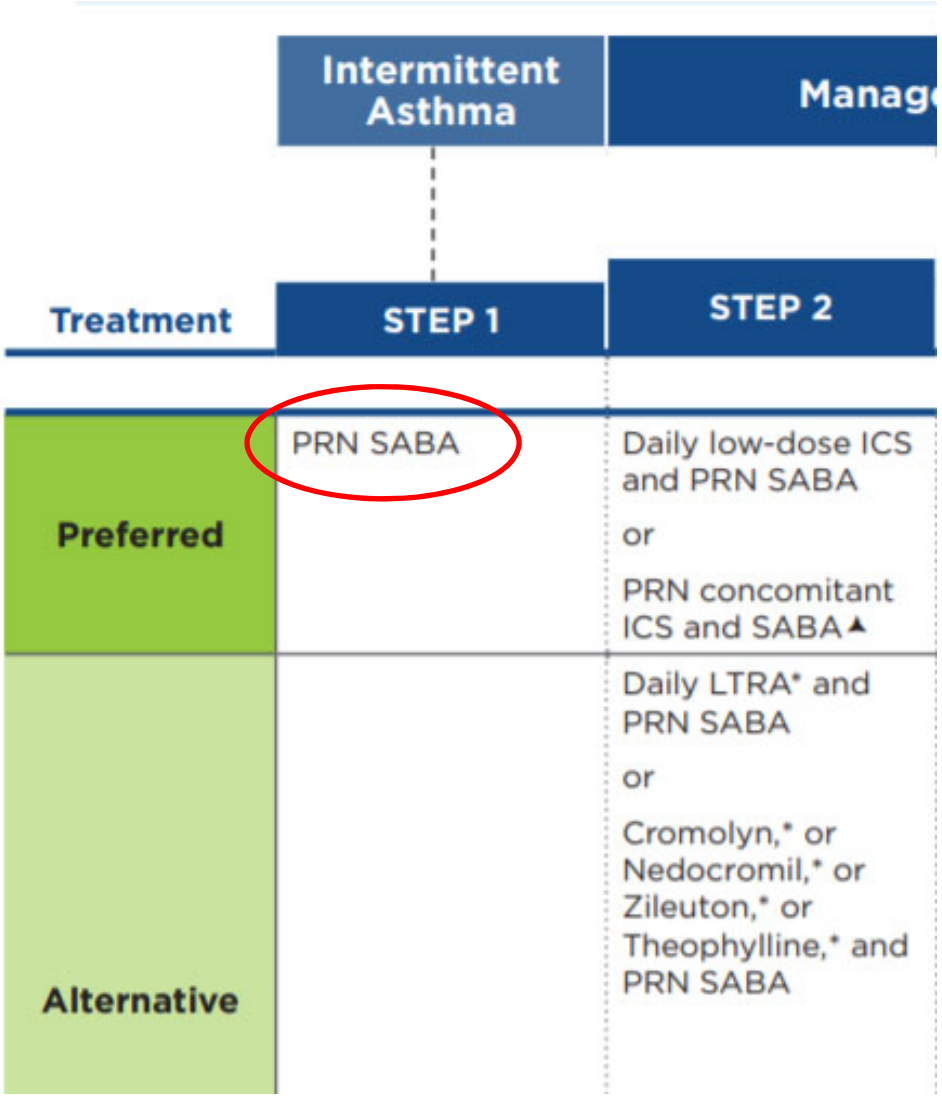
Figure 2. Overall Weeks of Well-Controlled Asthma, According to Data in the Electronic Diary.



Key Objectives:

- Revisit a couple aspects of asthma that continue to be true
- Consider the discordance of recent guideline updates which no longer completely agree
  - So, in the SMART-designed trials of mild asthma, prn formoterol+ICS beats prn SABA in patients with mild persistent asthma who need a controller but it does not beat scheduled ICS and scheduled ICS showed more days of asthma control

So again, NAEPP in 2020 didn't change their recommendation for Intermittent asthma patients….



	Intermittent Asthma	Manag
Treatment	STEP 1	STEP 2
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA

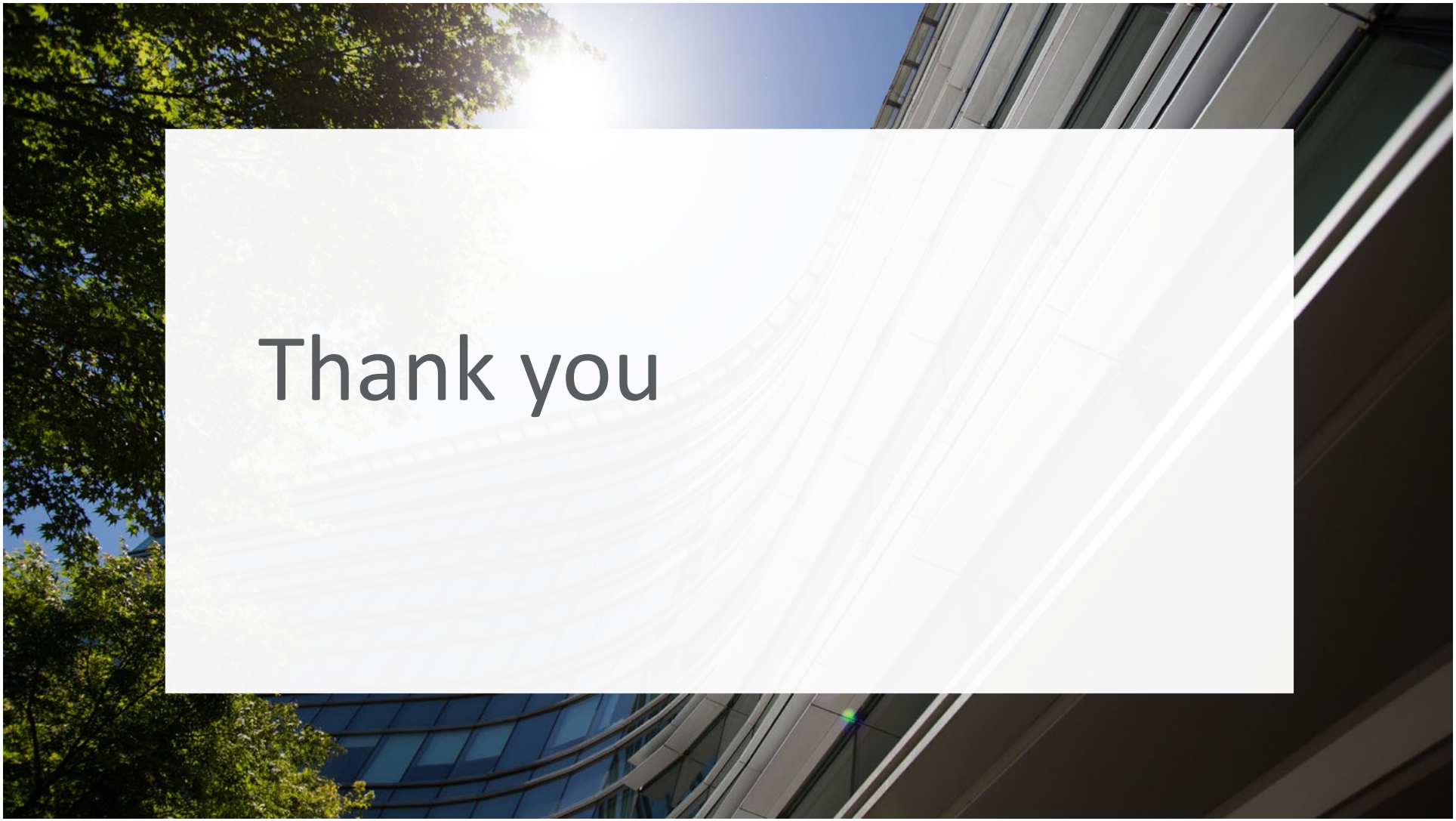
https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines

Just a reminder WHO those “intermittent” patients are….

Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20 –39 yr 80% 40 –59 yr 75% 60 –80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1			

Summary of the "SMART" approach to asthma care:

1. Not yet proven if necessary for truly "intermittent" asthma patients and prn SABA still endorsed by NIH NAEPP 2020 update
2. The S.M.A.R.T. approach must use a formoterol-containing MDI and they are expensive (check insurance)
3. The S.M.A.R.T. approach is clearly superior to SABA alone in persistent asthma but no better than scheduled ICS with a separate reliever in those patients
4. For patients who cannot manage multiple inhalers and are only using their "reliever," a S.M.A.R.T. approach can be an attractive option (if affordable) to ensure some use of ICS


Thank you