Asthma: Resolving the NIH vs GINA Guidelines



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54th Annual Primary Care Review

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Roadmap for today



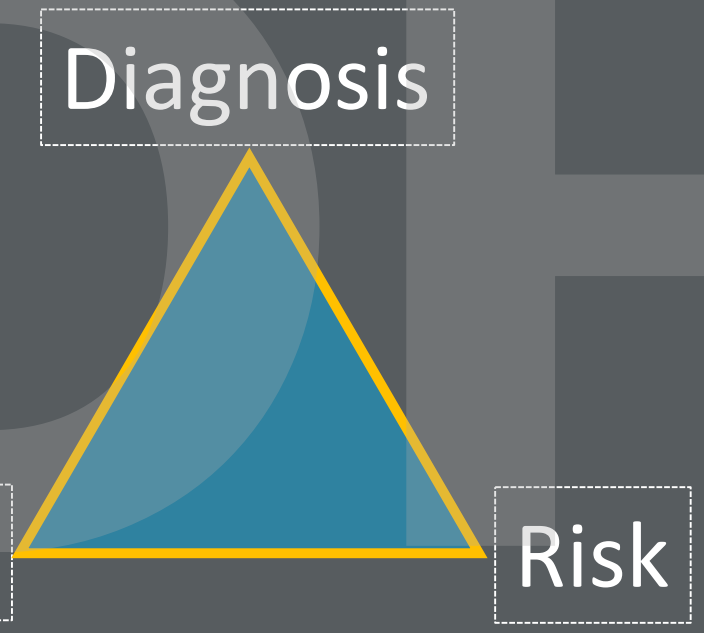
Approach to initial workup of asthma

Recent updates to asthma guidelines

Compare/contrast treatment strategies

32 yo female presents for her initial visit for asthma

How do you approach this visit?





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Asthma Diagnosis Often Requires a Multifaceted Assessment

No Gold Standard for Diagnosis

Highly Suspicious if:

- Hx of intermittent symptoms typical of asthma
- Physical examination findings: wheezing

+

Confirmed by:

- Presence of variable airflow obstruction
- Exclusion of alternative diagnoses



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Spirometry

Obstruction Present

Bronchodilator

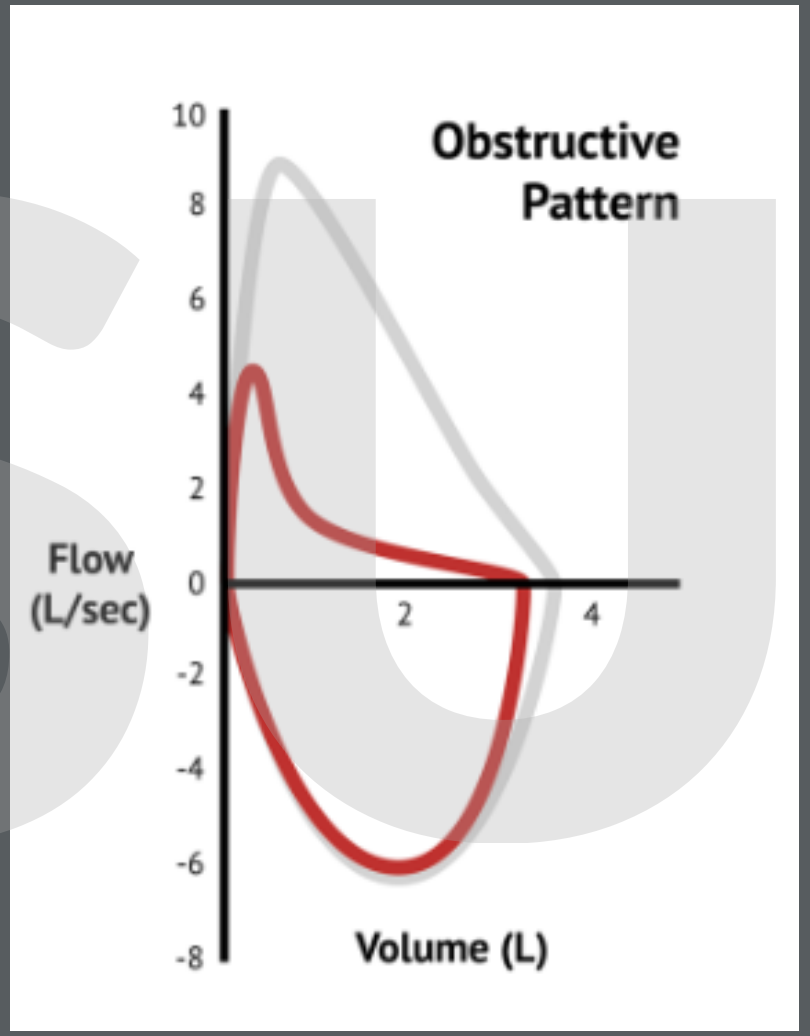
Completely Reverses

Asthma Confirmed

Incomplete or No Reversal

$\Delta zFEV_1 > 0.78$ or $\Delta zFVC > 0.64$

Possible Asthma consider ddx

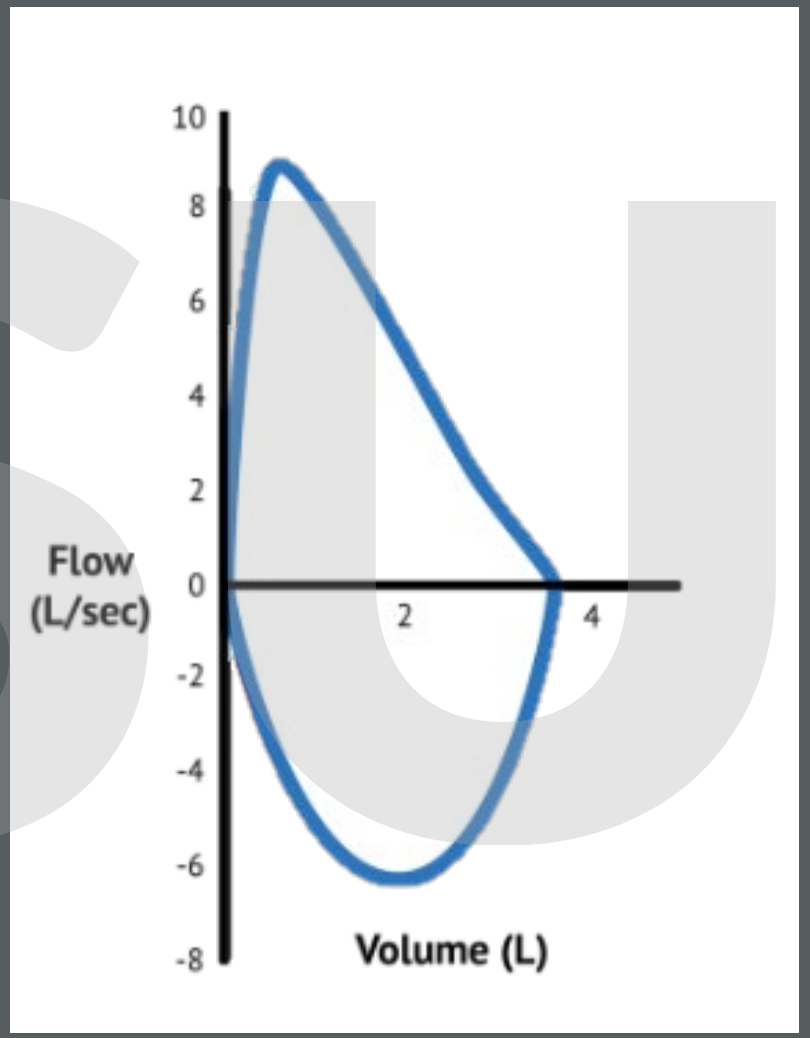


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Spirometry

No Obstruction

- Repeat Testing
- Measure AM Peak Flow
- Broncho-provocation

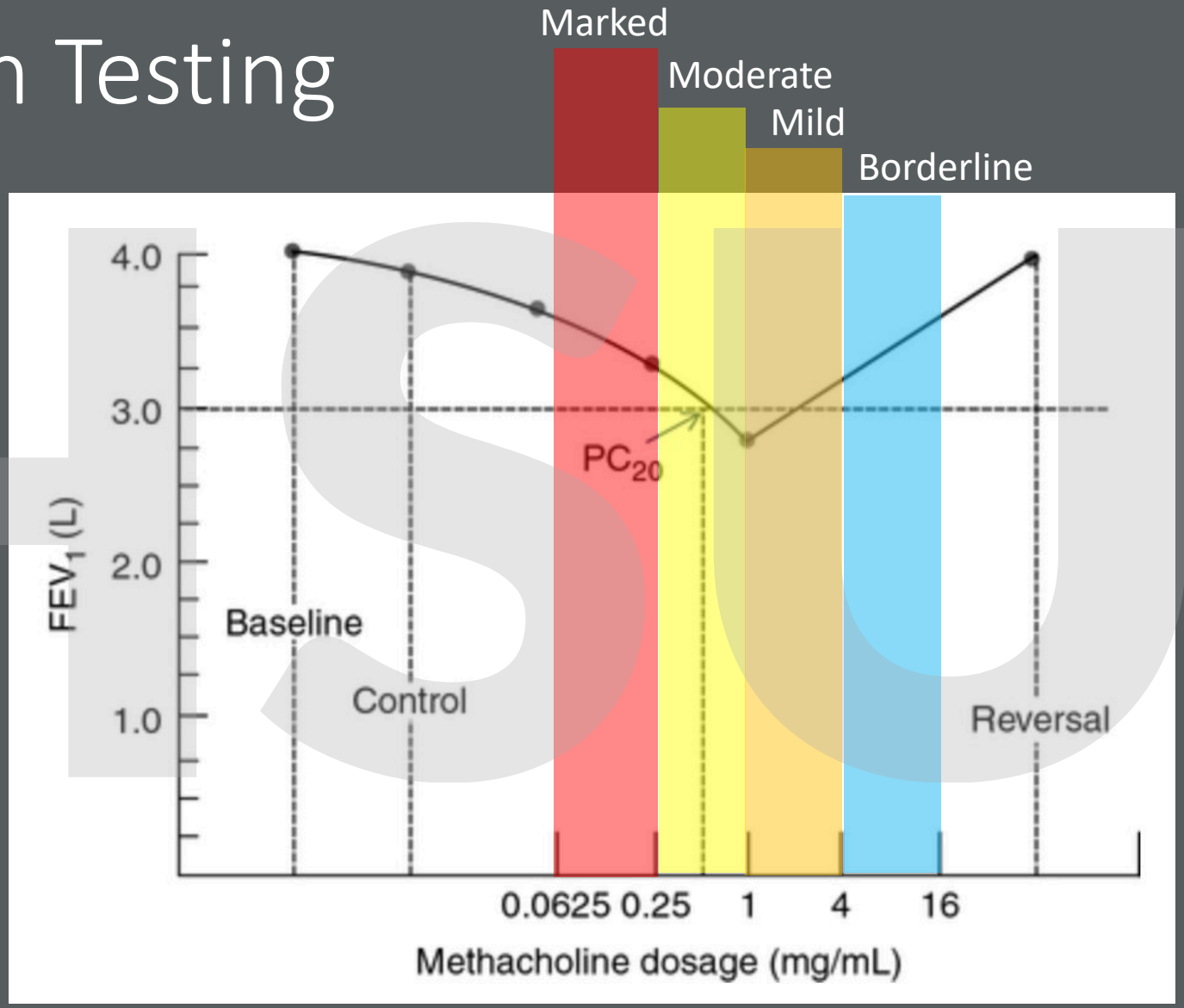


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Bronchoprovocation Testing

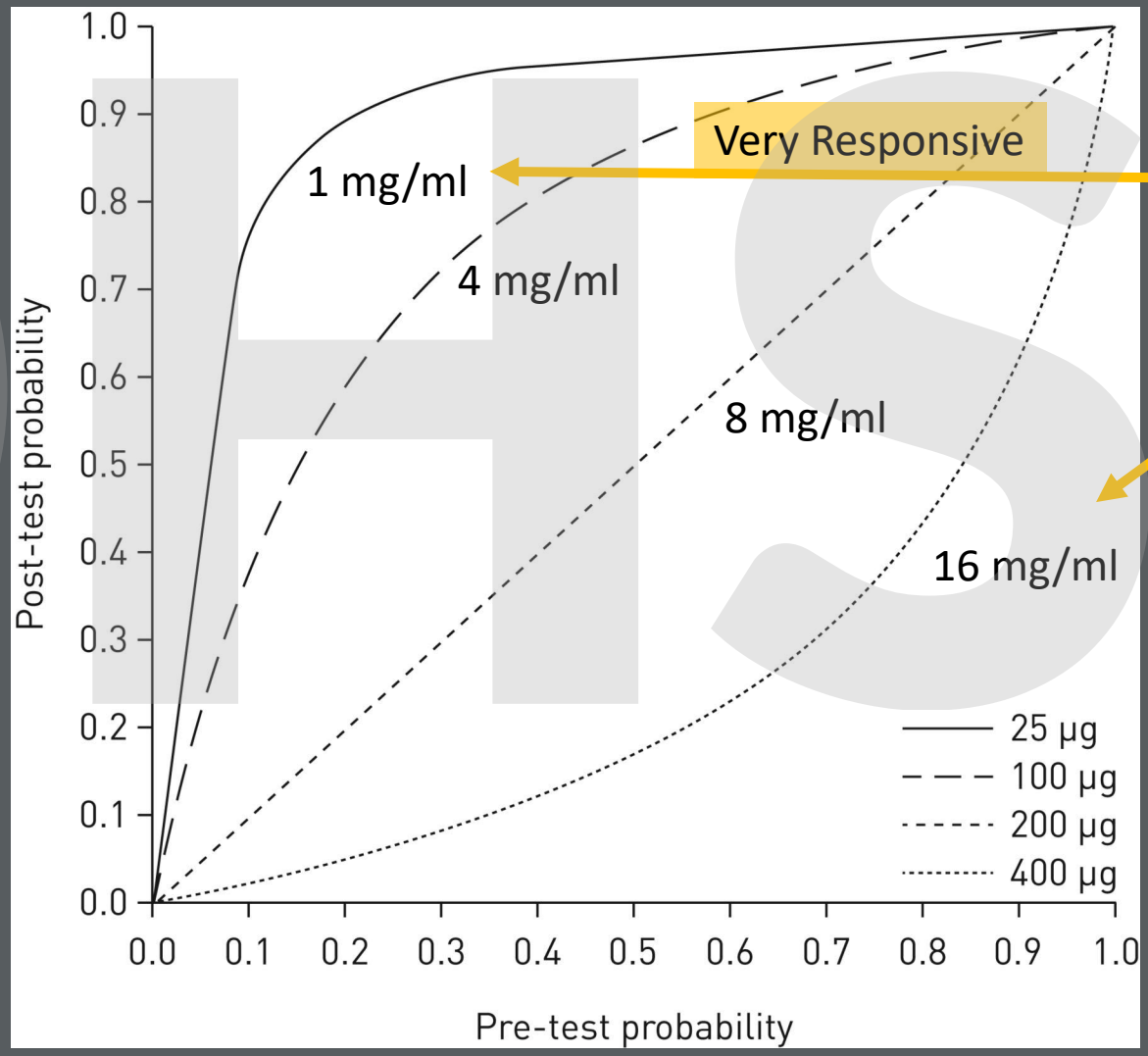
Methods

- Methacholine
- Mannitol
- Dry air
- Exercise



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Interpretation of Bronchoprovocation Test Depends on Airway Responsiveness + Pre-test Probability



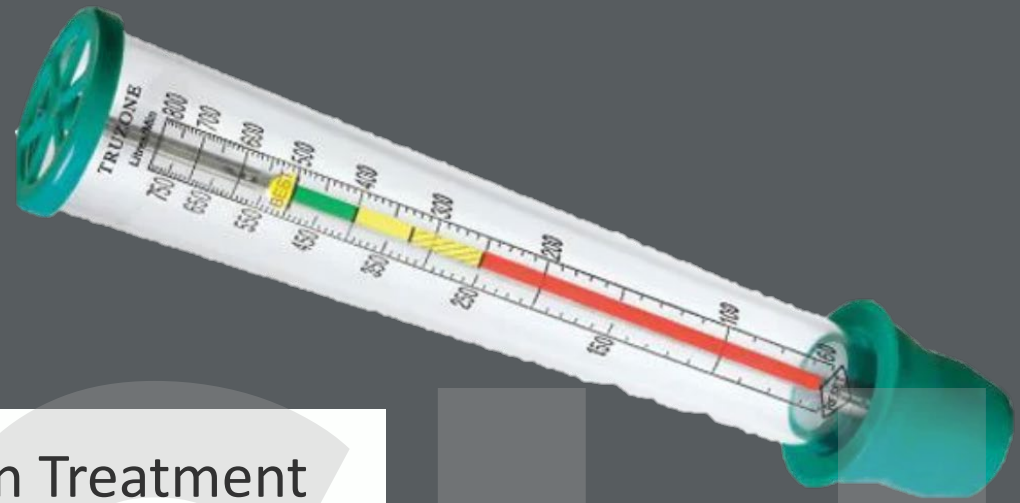
Very Responsive

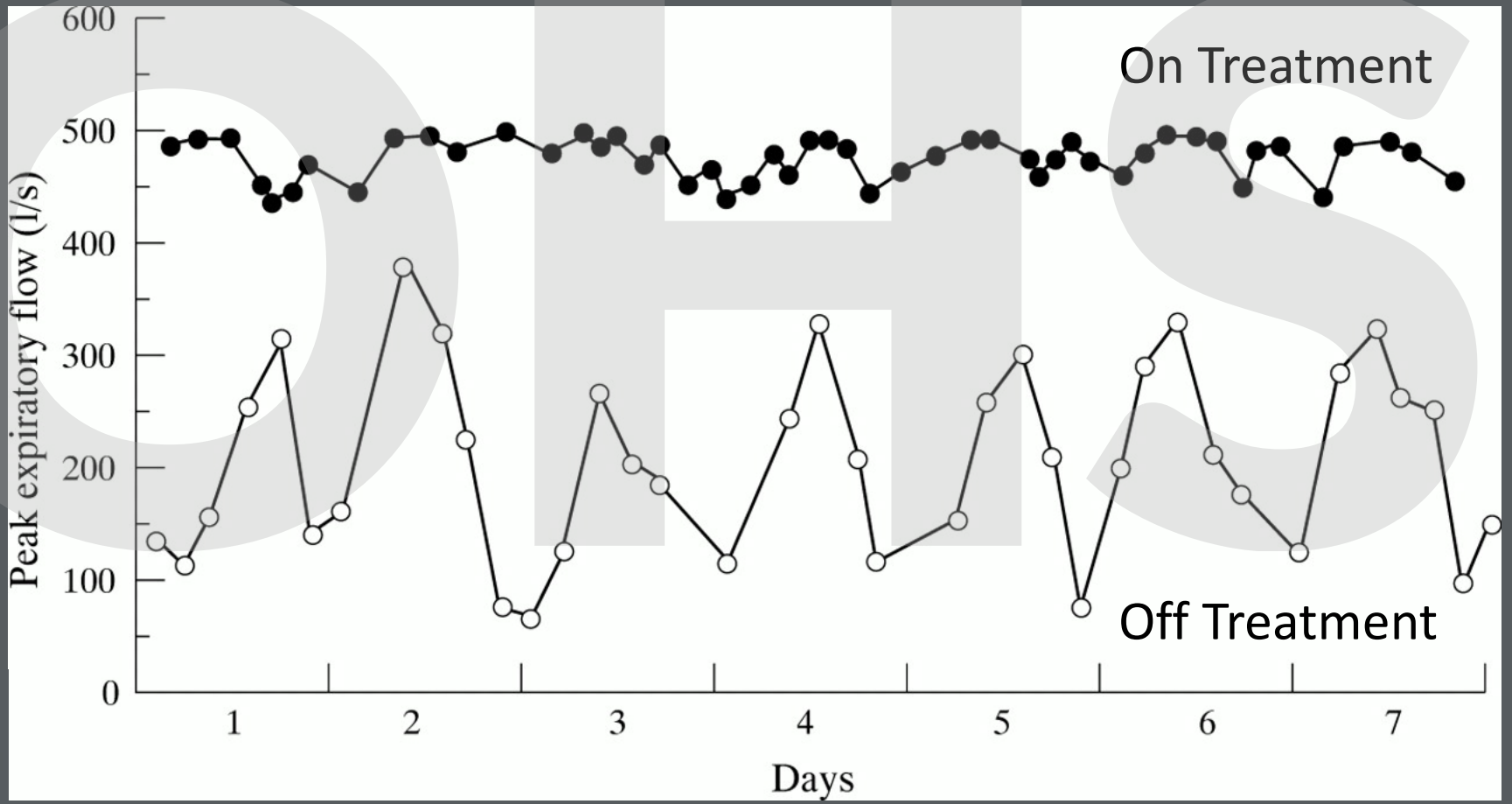
Methacholine Dose

Not Very Responsive

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AM Peak Flow Testing

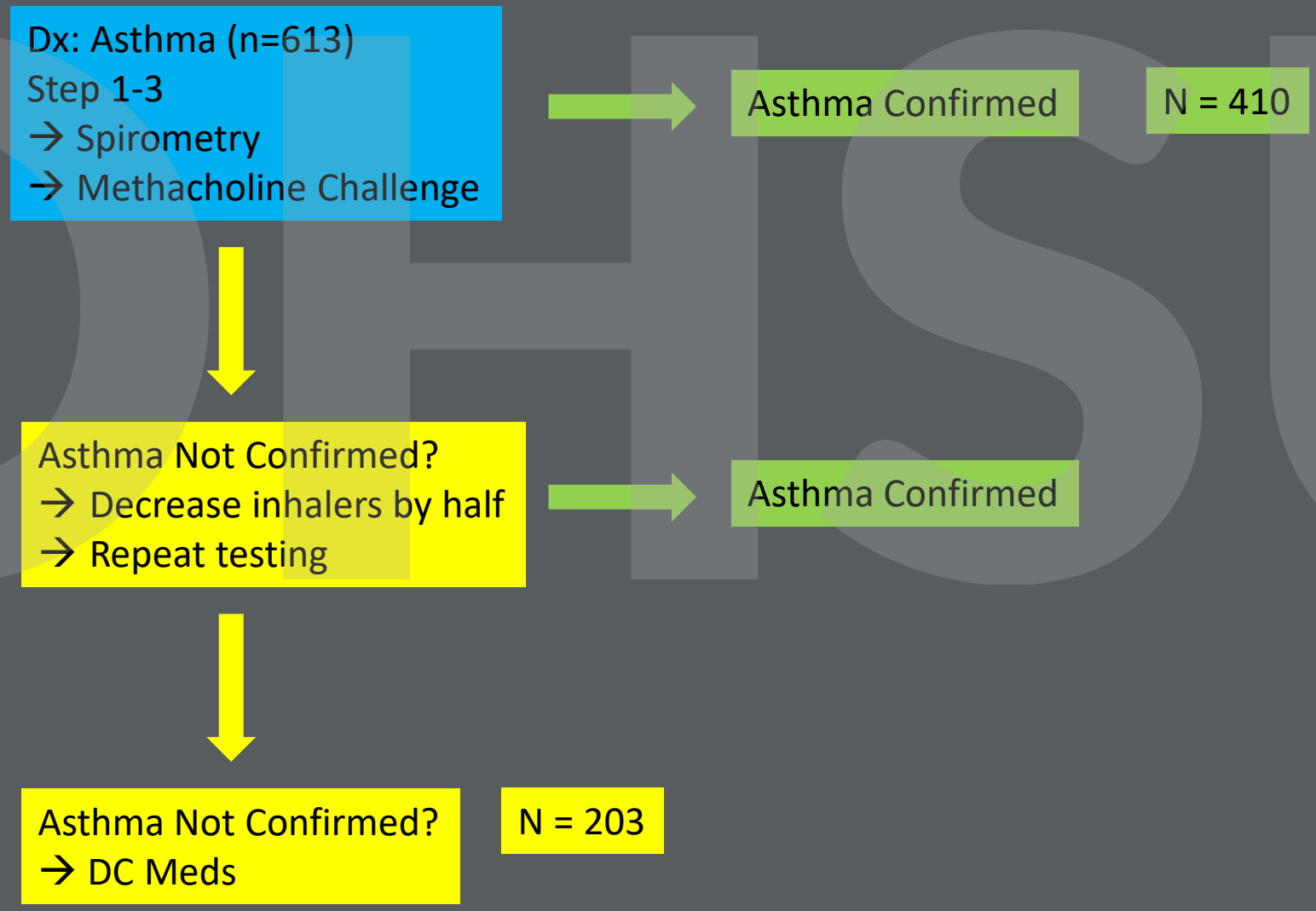




> 20% variability = significant
Correlate with sx

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Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma



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JAMA. 2017;317(3):269-279.

Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma

Dx: Asthma (n=613)
Step 1-3
→ Spirometry
→ Methacholine Challenge

→ Asthma Confirmed — N = 410

Associated with Correct Dx:
Spirometry at time of diagnosis
Wheezing in past year
Daily use of medications

Asthma Not Confirmed?
→ Decrease inhalers by half
→ Repeat testing

Asthma Not Confirmed?
→ DC Meds

N = 203

Not Associated
Dyspnea
Specialist involvement

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JAMA. 2017;317(3):269-279.

32 yo female presents for her initial visit for asthma

Asthma Control

Frequency of daytime symptoms (>2 days/wk)

- Wheezing, cough, sob

Nighttime symptoms?

Reliever inhaler > twice/week?

Any activity limitations due to asthma?

Validated Metric: ACT, AIRQ, CACT, others



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32 yo female presents for her initial visit for asthma

Asthma Risk

Hx of life-threatening exacerbation
-intubation or ICU admission
Currently on OCS
1+ asthma hospitalization past year
3+ ER visits for asthma
>1 albuterol MDI/month
Comorbidities: CAD, lung disease
Illicit drug use
Major psychosocial problems
Food allergy



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Asthma Action Plan

For: _____ Doctor: _____ Date: _____

Doctor's Phone Number _____ Hospital/Emergency Department Phone Number _____

GREEN ZONE

Doing Well

- No cough, wheeze, chest tightness, or shortness of breath during the day or night
- Can do usual activities

And, if a peak flow meter is used,

Peak flow: more than _____
(80 percent or more of my best peak flow)

My best peak flow is: _____

Before exercise

Take these long-term control medicines each day (include an anti-inflammatory).

Medicine	How much to take	When to take it
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
❒ _____	❒ 2 or ❒ 4 puffs _____	5 minutes before exercise

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Asthma Action Plan

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Medicine	How much to take	When to take it
Before exercise ❒ _____	❒ 2 or ❒ 4 puffs _____	5 minutes before exercise





Measure Peak Flow 2-3 times daily
Same time of day

Decrease > 20% from baseline may indicate an asthma exacerbation

Amount of decrease indicates severity

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Updates to Guideline-based Asthma Therapy

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GINA



NAEPP / EPR4

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

2020 FOCUSED UPDATES TO THE

Asthma Management Guidelines

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GINA

- Updated yearly
- Twice-yearly cumulative review of new evidence across the whole asthma strategy
- Uses GRADE reviews (Grading of Recommendations Assessment, Development, and Evaluation), when available
- Priority based on clinical relevance of study designs and generalizability of populations
- Extensive external review before publication

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

NAEPP / EPR4

- Agency for Healthcare Research and Quality (AHRQ)
- Focused on 6 topics decided upon in 2015
- Comprehensive literature review of studies 2018 and prior
- Panel composed of asthma content experts, primary care clinicians, and experts in implementation of health care policy
- Strict COI, recusal for high conflicts of interest.
- Uses GRADE (Grading of Recommendations Assessment, Development, and Evaluation)

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Step-wise Approach to Therapy:
Adults and Adolescents 12+

GINA

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
As-needed low dose ICS-formoterol

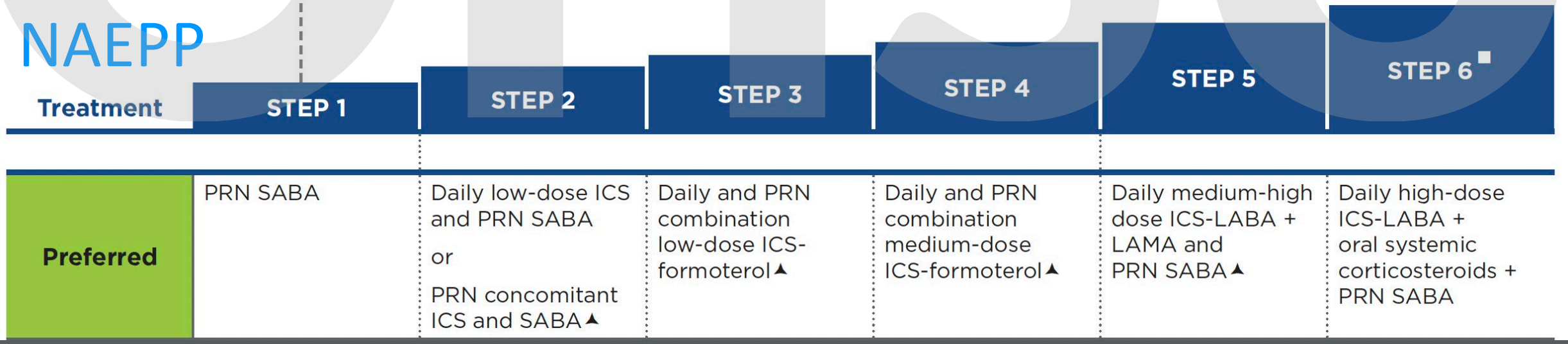
STEP 3
Low dose maintenance ICS-formoterol

STEP 4
Medium dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

NAEPP



Children 0-4: Viral URI

3+ episodes wheezing after URI + 2 episodes in the past year

NAEPP

- A short course (7-10 days) of high dose inhaled ICS daily + SABA prn for quick-relief therapy

GINA

- Inhaled SABA with a facemask from 0 to 3 years of age and
- Inhaled SABA with a mouthpiece from 3 to 4 years of age.
- SABA use > 2x/week indicates need for a trial of controller therapy
- Reserve nebulizer for children who cannot be taught effective use spacer use

Concerns in young children about adverse long-term effects of intermittent high-dose ICS

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Adults and Adolescents 12+: Intermittent ICS Use

NAEPP (step 2)

Low-dose ICS daily + SABA prn

or

ICS + SABA prn taken sequentially

GINA (step 1-2)

Track 1 (preferred):

Low-dose ICS-formoterol prn

Track 2 (alternative):

Low-dose ICS daily + SABA prn

Reliever Therapy (All Steps)

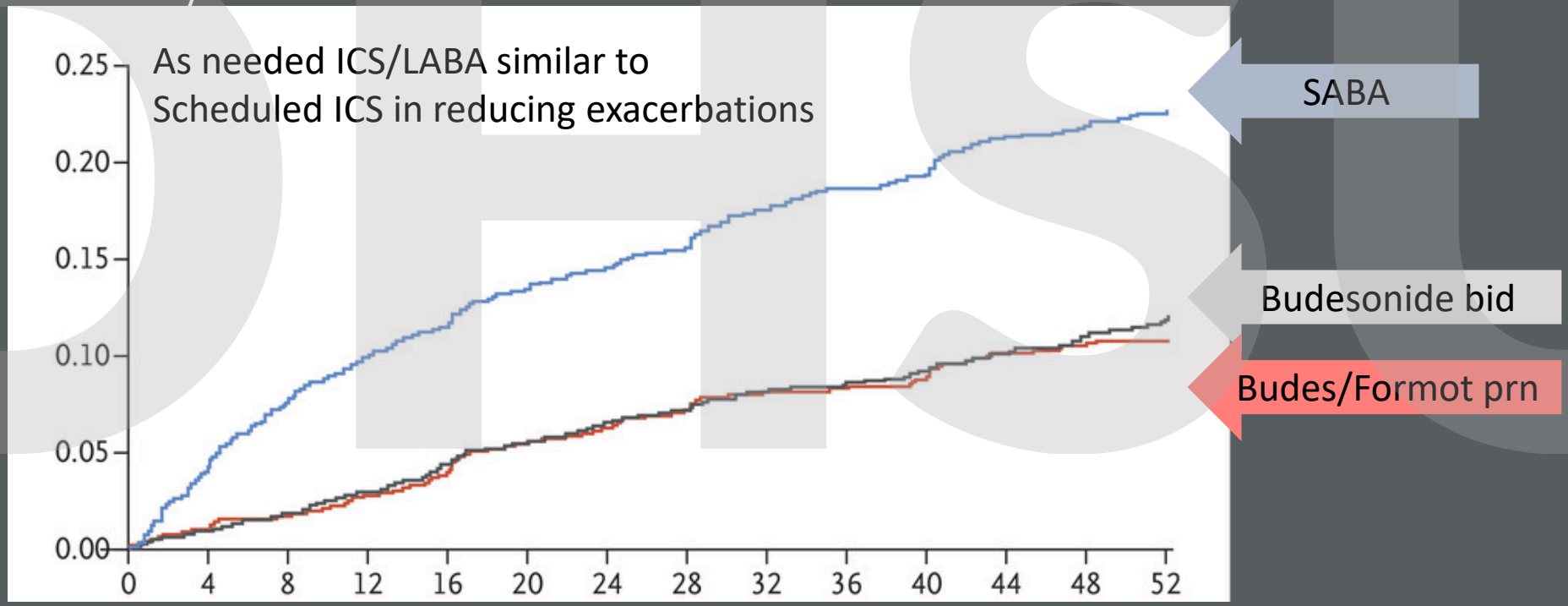
Low-dose ICS-formoterol prn > SABA prn

ICS-LABA prn reduced overall steroid exposure

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Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

O'Byrne, et al. NEJM. 2018, 378(20):1865-1876



Similar results in:
R Beasley et al. N Engl J Med 2019;380:2020-2030.
ED Bateman et al. NEJM 2018;378:1877-1887.

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Rationale for SMART

- Inhaled steroids reduce the risk of asthma exacerbation and deaths
- Intermittent dosing aligns with real-world use
- Formoterol (LABA) has similar on-time to albuterol but much longer duration of action
- Uses single inhaler for daily use and rescue use
- Mild asthmatics still have airway inflammation

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“Mild Asthma” Carries Risk

- Mild asthma still carries risk of serious adverse events
  - 30–37% acute asthma exacerbations
  - 16% adults with near-fatal asthma
  - 15–27% adults asthma deaths

  } symptoms < weekly in previous 3 months
- Exacerbation triggers are unpredictable
  - viruses, pollens, pollution, poor adherence
- Even 4–5 lifetime OCS courses increases the risk of osteoporosis, diabetes, cataract

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Dusser, Allergy 2007; Bergstrom, 2008; Price, J Asthma Allergy 2018)

Arguments against SABA monotherapy

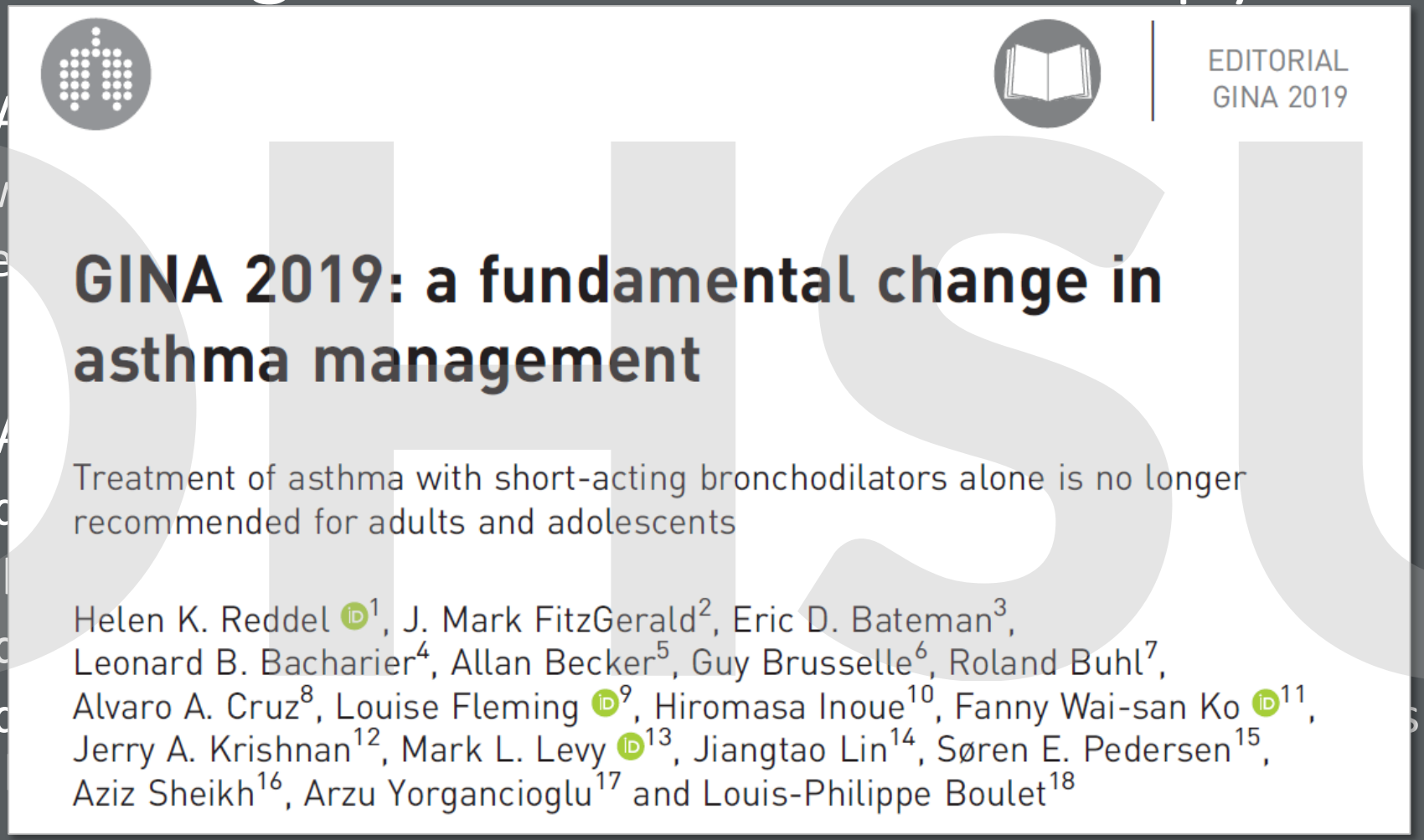
Inhaled SABA

- Asthma w
- SABA use

Regular SABA

- increased
- reduced
- increased
- increased
  ↑ morta

s and



EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

Hancox, 2000; Aldridge, 2000; Suissa 1994, Nwaru 2020



NAEPP / EPR4

NAEPP excluded studies of ICS-LABA for step 2

- Cost
  - Generic now available: Breyna=budesonide/formoterol
  - Alternative: Airsupra=budesonide/albuterol
- Potential COIs involved in formoterol specific recommendation
- Formulary restrictions
- Effect on refill availability with increased inhaler use

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SMART: Single Maintenance and Reliever Therapy

NAEPP (step 3-4, age 4+)

- Recommend ICS-formoterol for both daily use and prn rather than:
  - higher-dose ICS daily + SABA prn
  - same-dose ICS-LABA daily + SABA prn

GINA (step 3-4)

- Step 3 18+: low dose ICS-formoterol MART
- Step 3 6-11:
  - Medium dose ICS + SABA prn
  - low-dose ICS-LABA + SABA prn
  - SMART with very low dose ICS-formoterol

Max daily formoterol dose:
= 8 puffs (48 mg MDI) ages 4 - 11 years
= 12 puffs (72 mg MDI) ages 12 +

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Increasing ICS Dose for Increased Symptoms

NAEPP

- Recommends against increased ICS dose for increased symptoms or decreased peak flow in age 12+ with mild to moderate persistent asthma who are likely to be adherent to daily ICS treatment
- Consider 4X ICS dose for age 16+ whose adherence to daily therapy is not assured

GINA

- Consider 4X regular dose of ICS for aged 16+ whose adherence to daily therapy is not assured.

Both NAEPP and GINA recommend a short-term increase in ICS dose when asthma worsens, particularly when background adherence is low

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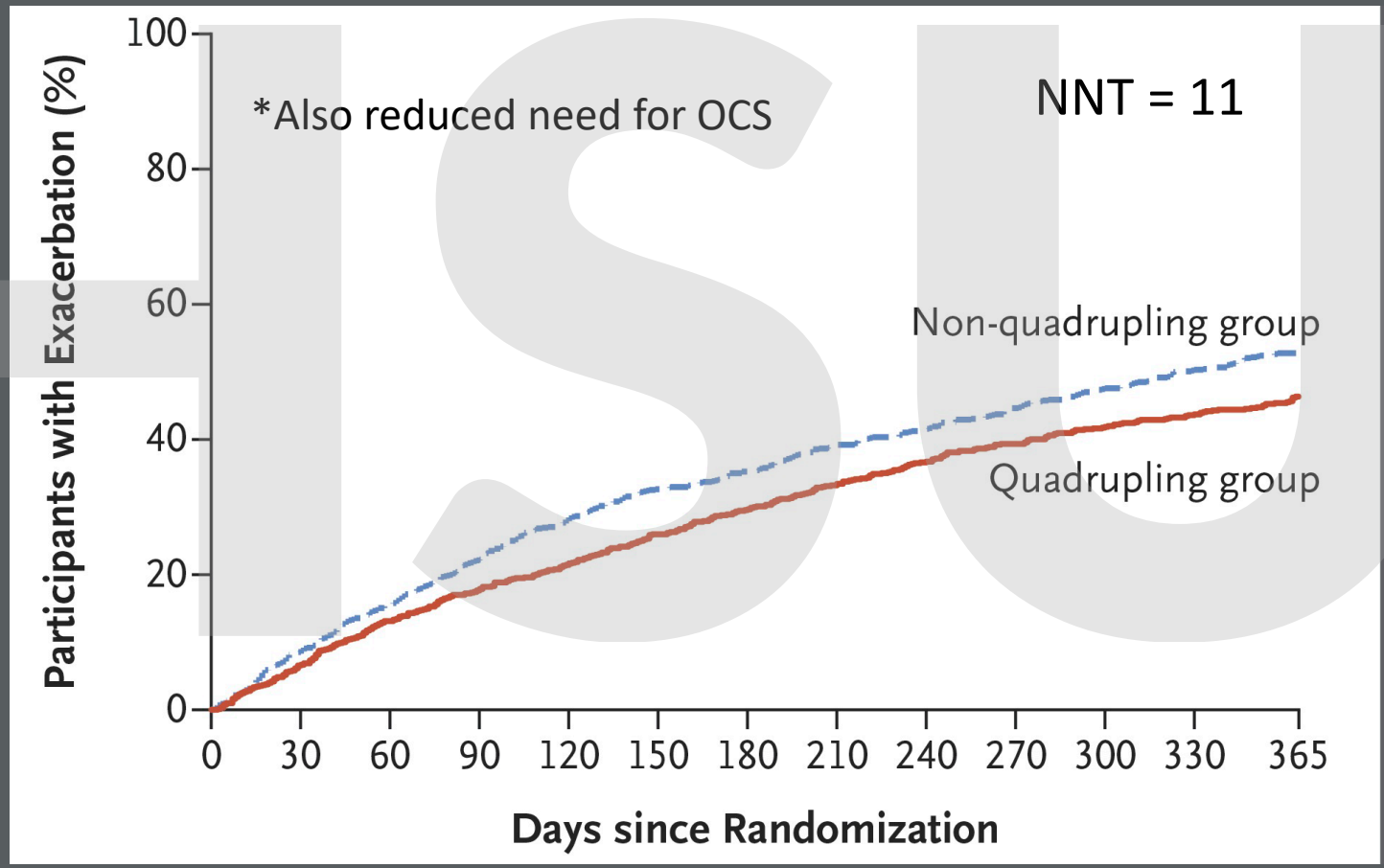
Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations

N=1,871 Asthmatics
Step 2 or greater
1+ Exacerbation/year

Yellow Zone

↑ICS 4X
N= 933

No Change
N= 938



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McKeever T et al. NEJM 2018;378:902-910

Long Acting Muscarinic Antagonists

NAEPP

- Step 3-4 Recommend ICS-LABA > ICS-LAMA
- Step 5 Recommend ICS-LABA + LAMA

GINA

- Step 4 Recommend ICS-LABA > ICS-LAMA
- Step 4-5 Recommend ICS-LABA + LAMA (triple therapy in adults)

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Fraction of Exhaled Nitric Oxide (FeNO)

NAEPP

- Age 5+
  - FeNO testing when dx unclear
  - FeNO for monitoring adherence
  - Cannot be used in isolate
- Age 0-4
  - Avoid FeNO testing

GINA

- FeNO cannot be used to rule in or out an asthma diagnosis
- Elevated in
  - asthma with type 2 inflammation
  - eosinophilic bronchitis
  - Allergic rhinitis
  - eczema,
- Low
  - smokers an
- Variable
  - during bronchoconstriction and allergic response
  - obesity
  - viral infections

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Allergen Mitigation





NAEPP

- single-component allergen mitigation, including dust mite, are rarely effective,
- tailored allergen mitigation only for individuals exposed to specific allergens with symptoms or + allergy testing (skin testing or specific IgE)
- potential benefit from multicomponent allergen mitigation

GINA

- Evaluated studies on individual allergen mitigation
- potential benefit from multicomponent allergen mitigation

Mitigation may be cost prohibitive and difficult to maintain
No validated metric identifies who is most likely to benefit

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Immunotherapy (SCIT and SLIT)

NAEPP

- Recommends SCIT as adjunct to standard pharmacotherapy
- Recommends against SLIT

GINA

- Recommends against SCIT
- Conditional recommendation for SLIT for house dust mite with AR

Poor study design limits certainty of recommendation and likely drives discordant recommendations

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Bronchial Thermoplasty (BT)

NAEPP

- BT should be considered only in expert centers as part of IRB registered trial or registry studies

GINA

- BT should be considered only in expert centers as part of IRB registered trial or registry studies

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Summary of Updates

Viral URI Wheezing:

- consider short course ICS + SABA age 0-4

ICS-LABA:

- daily + prn use in step 2+ (consider for step 1

LAMA

- LABA>LAMA
- Consider LAMA add on to LABA-ICS in step 4-5

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Step-wise Approach to Therapy:
Adults and Adolescents 12+

GINA

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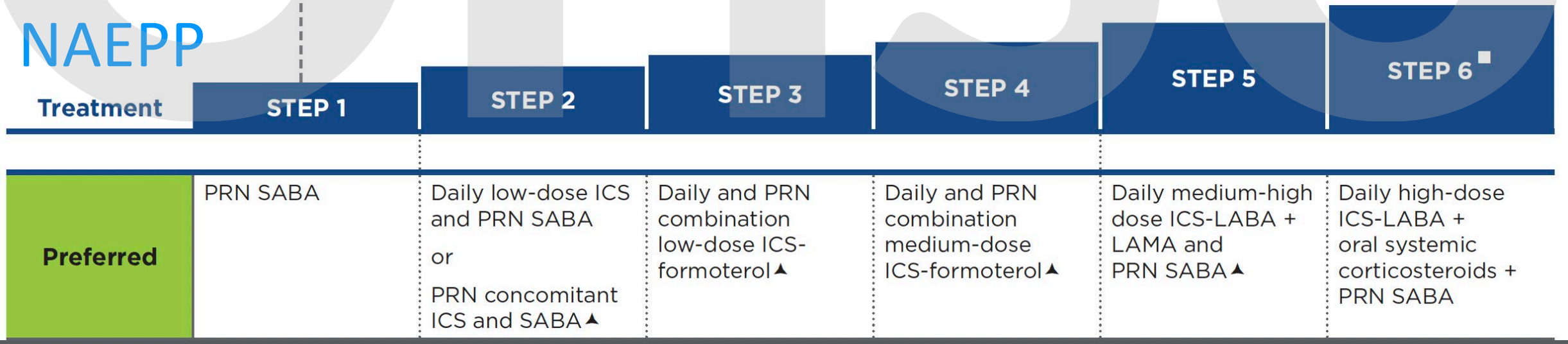
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RELIEVER: As-needed low-dose ICS-formoterol

NAEPP



Summary of Updates cont.

FENO

- Limited utility as isolated test for asthma

Allergen Mitigation

- Single allergen mitigation lacks benefit except in rare circumstances

Allergen Immunotherapy

- Mixed reviews, consider on individual basis and consult allergist

Bronchial Thermoplasty

- Limited use except in specialized centers

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Myriad Inhalers Complicates Adherence As Does Cost













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Videos available online

https://www.thoracic.org/professionals/clinical-resources/video-lecture-series/obstructive-lung-disease/asthma/inhaler-device-selection-and-technique.php

Thank You

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