ASPIRE

SHARING BEST PRACTICE AND
ENRICHING EXCELLENCE

Meeting starts at 7.00 pm

Managing asthma in Australia, what should we aspire to?

MAT-AU-2302629-1 | Date of preparation November 2023 | Sanofi Australia (Macquarie Park, NSW)

RESPIRATORY ADVENT
ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

John Harrington (Chair)

Clinical Nurse Consultant for Airway Disease, Hunter New England Area Health

John Harrington is a Registered Nurse leading respiratory nursing for Hunter New England Area Health as the Clinical Nurse Consultant for Airway Disease. John brings extensive experience from senior nursing roles in the UK's NHS and Australia. John's focus is to develop a world-class respiratory service at HNELHD, providing leadership in airway disease. Significant roles are developing a multi-disciplinary approach to airway disease, developing new models of care for COPD & asthma, and focusing on better integration with primary health providers to enhance patient self-management.

Disclosures

I have received honoraria from Sanofi, Astra Zeneca, GSK and Novartis for the development of patient support materials and educational meetings.
I have no conflicts of interest in this subject matter

A/Prof. John Blakey

Clinical Lead – Asthma, Sir Charles Gairdner Hospital,
Adjunct Associate Professor, Medical School, Curtin University

A/Prof. John Blakey is a consultant in Respiratory and Sleep Medicine at Sir Charles Gairdner Hospital where he is the lead for asthma. John has a record of award-winning quality improvement activities and highly-cited collaborative research. He is a medical advisor for Asthma Australia & Asthma WA, and current WA TSANZ branch president.

Disclosures

Grants: Avant
FHRI
IPCRG
MRFF
Novartis
Educational activity and advisory:
Asthma Australia
AstraZeneca
Boehringer Ingelheim
Chiesi
GSK
Sanofi

Brooke Kyle

Clinical Nurse Consultant for Asthma & Airways, Sir Charles Gairdner Osborne Park Health Care Group

Brooke is the Clinical Nurse Consultant for Asthma and Airways for the Sir Charles Gairdner Osborne Park Health Care Group, where she provides clinical consultation, management, support, and education to patients with asthma and airways disease. Brooke has been a Respiratory Nurse for 13 years, working in the both the hospital and community setting covering all aspects of Respiratory Medicine. Brooke values the importance of multidisciplinary care, lifelong learning and is a passionate patient advocate who believes in supporting and empowering patients in managing their health. She is a member of the Thoracic Society of Australia and New Zealand and has recently commenced a Masters of Nurse Practitioner.

Disclosures

Grants: Avant
FHRI
IPCRG
MRFF
Novartis
Educational activity and advisory:
Asthma Australia
AstraZeneca
Boehringer Ingelheim
Chiesi
GSK
Sanofi

Prof. Peter Wark

Director of Cystic Fibrosis Service, AIRMed, Alfred Health & Professor of Medicine, Monash University

Professor Peter Wark is the newly appointed Director of Cystic Fibrosis at AIRMed (Allergy, Immunology & Respiratory) at Alfred Health, Melbourne, and Professor of Medicine at Monash University. His research interests are airway inflammation in the context of chronic airways disease, innate immunity, and the role of infection in chronic airways disease. His group has developed expertise in identifying respiratory viruses in airway secretions and developing an in-vitro cell culture model of the airway epithelium that we use to model the effect of infection and inflammation. His research focuses upon factors that increase susceptibility to virus infection in asthma, COPD, cystic fibrosis (CF) and bronchiectasis. Characterising airway inflammation and innate immune responses in chronic airways disease and applying this to clinical care, as well as the development of precise individualised management strategies.

Disclosures

Requested to speak and will receive an honorarium at this Sanofi sponsored symposium
Employee NSW Health
Spoken or organised meetings sponsored by:
AstraZeneca, GSK, Boehringer Ingelheim, Mundipharma, Menarini, Novartis, CSL, Chiesi, Sanofi, Vertex.
Advisory boards; Astra Zeneca, Boehringer, Novartis, Sanofi, Vertex. PBAC Australia.

PANEL FOR TONIGHT'S MEETING

John Harrington (Chair)
Clinical Nurse Consultant for Airway Disease, Hunter New England Area Health

Brooke Kyle
Clinical Nurse Consultant for Asthma & Airways, Sir Charles Gairdner Osborne Park Health Care Group

Eddie Weber
Clinical Nurse Coordinator Allergy, Asthma and Clinical Immunology Service, Alfred Health

A/Prof. John Blakey
Clinical Lead – Asthma, Sir Charles Gairdner Hospital, Adjunct Associate Professor, Medical School, Curtin University

Prof. Peter Wark
Director of Cystic Fibrosis Service, AIRMed, Alfred Health & Professor of Medicine, Monash University

Adriana Avram
Clinical Nurse Consultant, Monash Health, Melbourne

AGENDA

RESPIRATORY ADVENT ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

19:00	**Welcome and speaker introductions**	John Harrington (Chair)
19:05	**Current landscape of asthma in Australia: The new normal that we shouldn't accept**	John Harrington
19:25	**Q&A and panel discussion**	Expert panel
19:30	**Success in asthma therapies: Remission in asthma; definitions, directions and disagreements**	A/Prof. John Blakey and Brooke Kyle
19:50	**Q&A and panel discussion**	Expert panel
19:55	**Which biologic and why? When to switch to another one?**	Prof. Peter Wark
20:15	**Q&A and panel discussion**	Expert panel
20:25	**Final Remarks**	John Harrington (Chair)
20:30	**Meeting Close**	

ASPIRE

SHARING BEST PRACTICE AND
ENRICHING EXCELLENCE

Current Landscape of asthma in Australia “The New Normal” that we shouldn’t accept

John Harrington

Respiratory CNC John Hunter Hospital

RESPIRATORY
ADVENT
ADVANCES IN
TYPE 2 INFLAMMATORY DISEASES

Disclosures

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- I have no conflicts of interest in this subject matter

Objectives

Understand disease burden of asthma.

Current management of asthma in Australia in the “New Normal”

- Prevalence of asthma in Australia
- Management and outcomes of asthma pre and post pandemic
- Asthma diagnostics
- Benefits of Treatable Traits approach
- Sustainability of asthma treatment

Burden of asthma - Australia

Approximately 11% of Australians have asthma (2.7 million)[1]

3-10% of people with asthma are defined as severe asthma[2] (81,000 – 270,000) - for HNE LHD as many as 3222

Asthma costs the Australian health system $1.2 billion per year, with over 60% of that attributed to severe asthma[3,4]

Treatment failures frequently result in OCS burst therapies and/or maintenance OCS treatment. This could be as high as 60% of people on high dose ICS[5]

OCS, oral corticosteroids; **HNE LHD**, Hunter-New England Local Health District; **ICS**, inhaled corticosteroids

1. AIHW 2022. 2. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, 2023. Available at www.ginasthma.org (accessed August 2023). 3. Asthma Australia and National Asthma Council Australia. The Hidden Cost of Asthma. 2015. Available at: https://asthma.org.au/wp-content/uploads/2022/03/HIdden-cost-of-asthma-final-report-revised-181115-v2-2.pdf. Accessed November 2023. 4. Centre of Excellence in Severe Asthma. Available at: https://www.severeasthma.org.au/. Accessed November 2023. 5. Wang E, et al. Chest. 2020;157(4):790-804.

Asthma – a very common disease in Australia

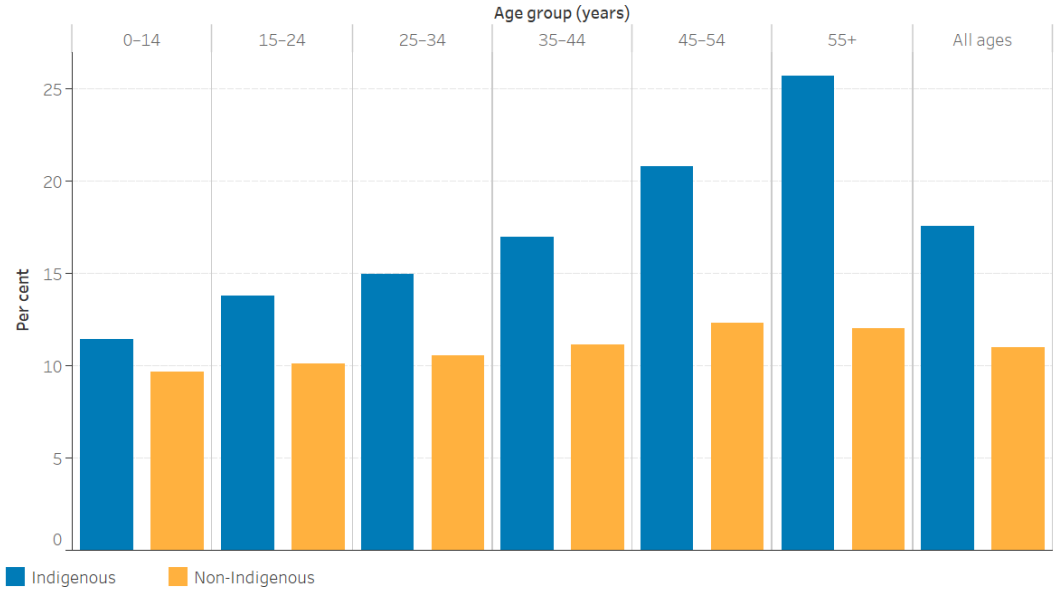
Overview | Age and Sex | Click to select tab

9% (1.2 million)
of **Males** have asthma
(2020–21)

12% (1.5 million)
of **Females** have asthma
(2020–21)

11% (2.7 million)
of **People** have asthma
(2020–21)

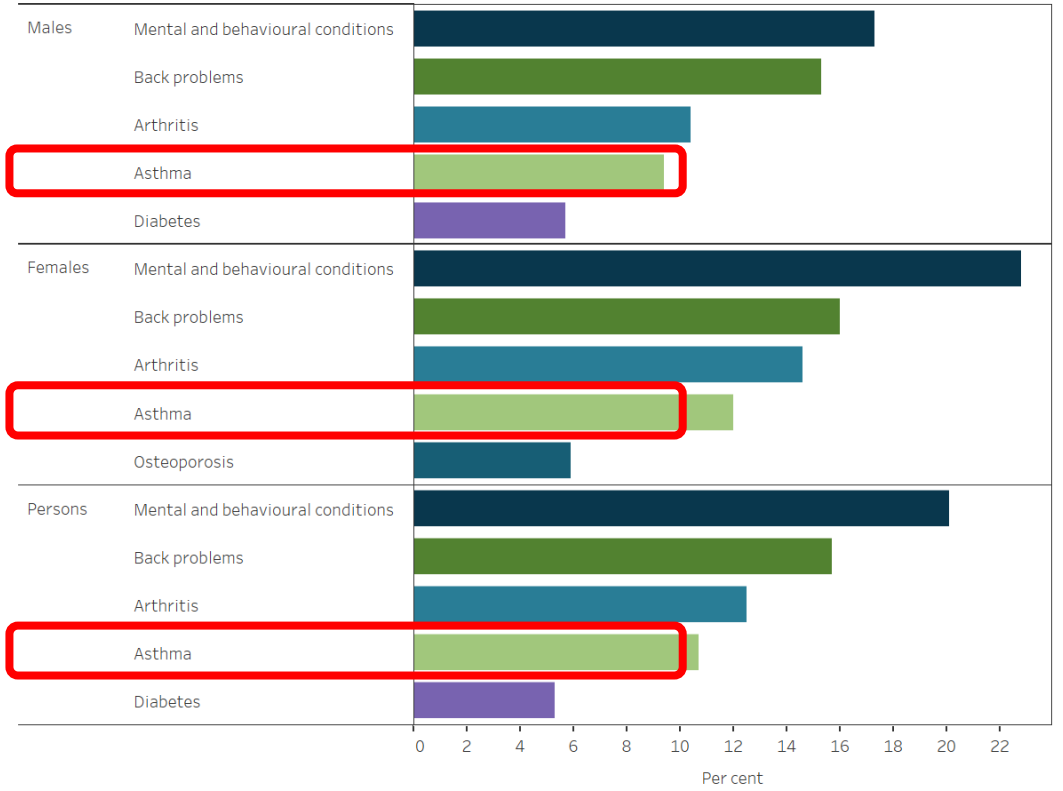
Prevalence of asthma by Indigenous status and age group | 2018–19



Note: People with asthma refers to people who self-reported that they were diagnosed by a doctor or nurse as having asthma (current and long-term). For more details please refer to the Technical specifications.
Source: AIHW analysis of ABS Microdata: National Health Surveys (NHS) 2020–21; ABS National Aboriginal and Torres Strait Islander Health Survey, 2018–19.
http://www.aihw.gov.au

Figure 1: Most common chronic conditions by sex and age, 2020–21

Filter
Age group
Sex

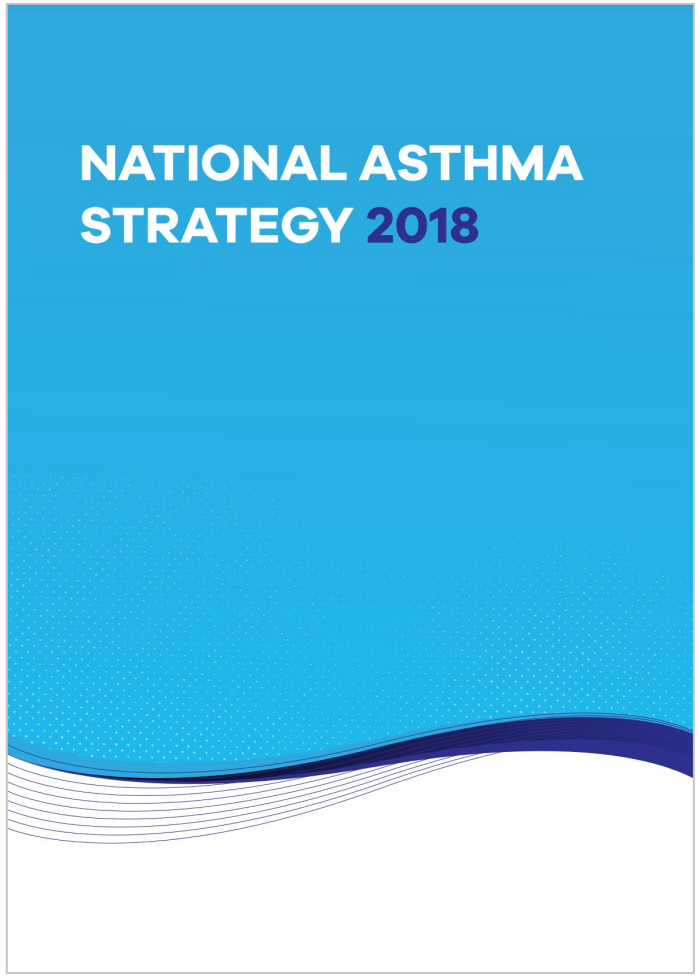


[Notes]

Source: ABS 2022b.
http://www.aihw.gov.au/

Australian Institute of Health and Welfare (AIHW), 2023. Available from https://www.aihw.gov.au/reports/chronic-respiratory-conditions/chronic-respiratory-conditions/contents/asthma-1 and https://www.aihw.gov.au/reports/australias-health/chronic-conditions-and-multimorbidity Accessed November 2023.

National Asthma Strategy

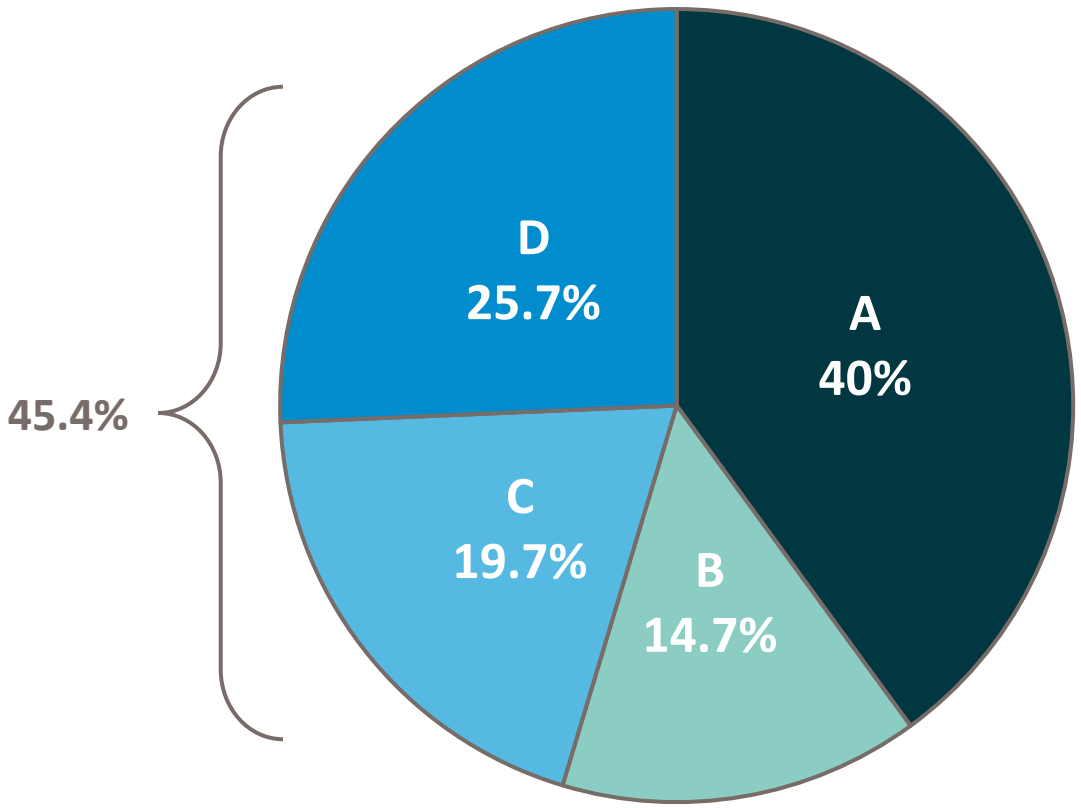


To reduce the health, social and economic impacts of asthma with a targeted and comprehensive approach to optimise asthma diagnosis and management

1. To support effective self-management practices through increasing patient knowledge, confidence and skills
2. To ensure consistent, best-practice asthma care through improving health professional adherence to treatment guidelines for asthma diagnosis and management
3. To enhance asthma care and management by creating an integrated, equitable and accessible healthcare system
4. To promote health and reduce asthma risk through supportive community environments
5. To improve asthma prevention, diagnosis and management through increased support for research, evidence and data

Commonwealth of Australia. National Asthma Strategy 2018. Canberra: Commonwealth of Australia, 2018.
Available from: https://www.health.gov.au/sites/default/files/documents/2019/09/national-asthma-strategy-2018_0.pdf Accessed November 2023

Asthma landscape 2015



2686 participants (> 16 years of age) completed the survey (57.1% female; median age group, 40-49 years)

A. ‘Well-controlled’ asthma with no preventer or with poor adherence

B. ‘Well-controlled’ asthma with good self-reported preventer adherence

C. Uncontrolled symptoms despite good self-reported adherence

D. Uncontrolled symptoms with no preventer or poor adherence

Adapted from Reddel et al. 2015

Reddel, HK et al. Med J Aust. 2015; 202(9):492-496

2023 update

Major changes in asthma outcomes 2012-2021

	2012 (*n* = 2686)	2021 (*n* = 5435)	*P*-value
ACT score, mean ± SD	19.12 ± 4.63	18.46 ± 4.58	<0.001
Poorly controlled asthma (ACT <20), *n* (%)	1225 (45.6)	2823 (52.0)	<0.001
Urgent health care for asthma in past 12 months, *n* (%)			
Urgent GP visit for asthma	628 (23.3)	1902 (35.0)	<0.001
Hospital or ED visit for asthma	269 (10.0)	1316 (24.3)	<0.001
Spent at least one night in hospital for asthma	98 (3.7)	920 (16.9)	<0.001
Any urgent visit for asthma	769 (28.6)	2004 (36.9)	<0.001

Table adapted from Reddel et al. 2023

- Prof Reddel's team used population-based cross-sectional web survey of 5427 people ≥ 18 years with current asthma in Australia, using similar methodology as in a survey of 2686 persons (≥ 16 years) in Nov 2012[1,2]
- Despite a similar symptom score (ACT) and a 16% increase in annual asthma reviews many significant outcomes were worse[2]

ACT, asthma control test; **GP**, general practitioner; **ED**, emergency department; **SD**, standard deviation

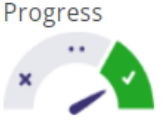
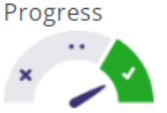
1.Reddel, HK et al. Med J Aust. 2015; 202(9):492-496. 2. Reddel et al. Respirology. 2023;28(S2):110-246.

Areas for improvement

Outcome measure	Indicator	Baseline value	Latest value	Progress status	Last updated
Decrease in suboptimal asthma control	5: Asthma control medication use	17% of people dispensed at least 1 SABA, were dispensed 3 or more SABA in 2017–18	18% of people dispensed at least 1 SABA, were dispensed 3 or more SABA in 2021–22	No change 	30 June 2023 View data source for asthma control medications
Improved adherence with appropriate preventer medicines	6: Preventer medication use for asthma	34% dispensed at least 1 preventer, were dispensed 3 or more preventers in 2017–18	33% dispensed at least 1 preventer, were dispensed 3 or more preventers in 2021–22	No change 	30 June 2023 View data source for preventer medication
Increase in annual General Practitioner (GP) reviews of people with asthma	7: Asthma cycle of care claims	0.3% of Australians claimed in 2017–18	0.1% of Australians claimed in 2021–22	Regress 	30 June 2023 View data source for asthma cycle of care claims
Reduced costs of asthma to patients, the healthcare system and government, including indirect costs such as reduced productivity	2: Annual health expenditure on asthma	$770 million in 2015–16	$900 million in 2019–20	Regress 	30 June 2023 View data source for health expenditure

1. AIHW 2023 https://www.aihw.gov.au/reports/chronic-respiratory-conditions/asthma-indicators

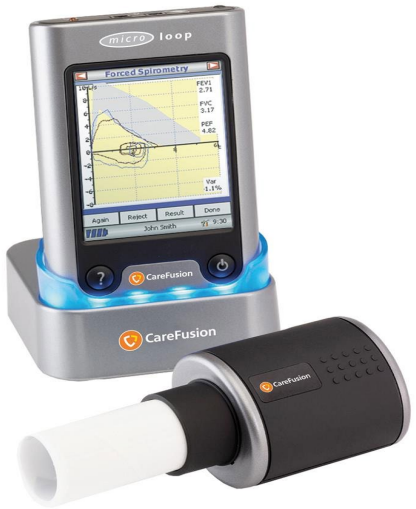
Progress

Outcome measure	Indicator	Baseline value	Latest value	Progress status	Last updated
Reduced asthma-related deaths	4: Deaths due to asthma	1.9 deaths per 100,000 for all ages in 2017 (456 deaths)	1.4 deaths per 100,000 people for all ages in 2021 (351 deaths)	Progress 	30 June 2023 View data source for deaths
		The death rate due to asthma for people aged 5–34, was 0.3 per 100,000 in 2017	The death rate due to asthma for people aged 5–34, was 0.2 per 100,000 in 2021	Progress 	30 June 2023 View data source for deaths
		The death rate due to asthma for people aged 35–54, was 1.0 per 100,000 in 2017	The death rate due to asthma for people aged 35–54, was 0.4 per 100,000 in 2021	Progress 	30 June 2023 View data source for deaths
		The death rate due to asthma for people aged 55 and over, was 5.5 per 100,000 in 2017	The death rate due to asthma for people aged 55 and over, was 4.1 per 100,000 in 2021	Progress 	30 June 2023 View data source for deaths
Reduced asthma-related hospitalisations	9: Hospital admissions due to asthma	175 per 100,000 asthma hospitalisations in 2016–17	100 per 100,000 asthma hospitalisations in 2020–21	Progress 	30 June 2023 View data source for asthma hospitalisations
Reduced asthma-related hospitalisations	10: Emergency department presentations	297 per 100,000 ED presentations in 2018–19 due to asthma	232 per 100,000 ED presentations in 2020–21 due to asthma	Progress 	30 June 2023 View data source for asthma ED presentations

1. AIHW 2023 https://www.aihw.gov.au/reports/chronic-respiratory-conditions/asthma-indicators

Asthma diagnostics

- Clinic spirometry is a simple, non-invasive test for basic lung function
- Reimbursable via MBS (11506)
- Training
  https://www.nationalasthma.org.au/health-professionals/education-training/face-to-face-workshops



MBS, Medical Benefits Schedule

Image problem or just the wrong time?

Wiley – Personal reflection

Spirometry, you have an image problem!

Peter G. Gibson

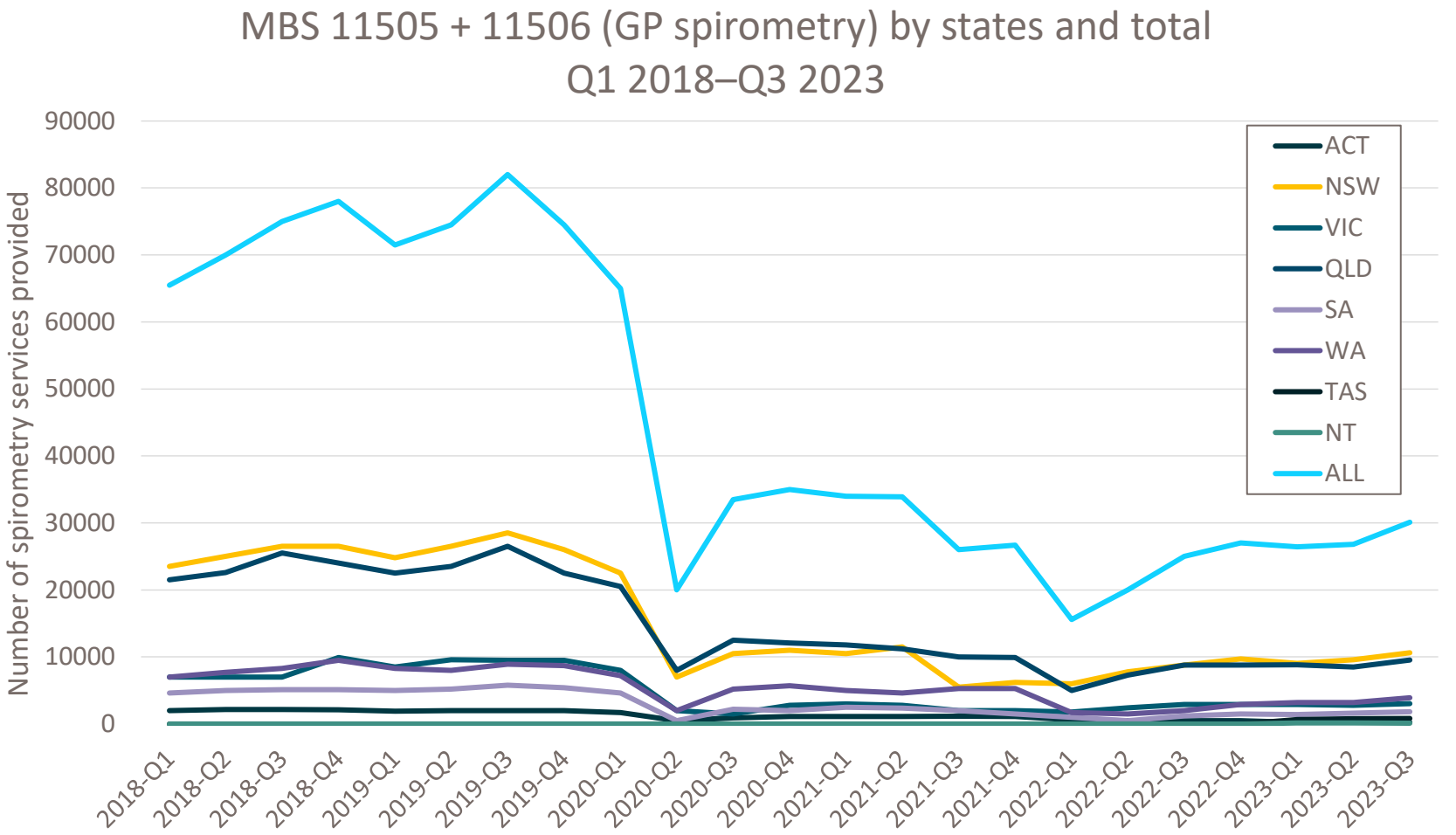


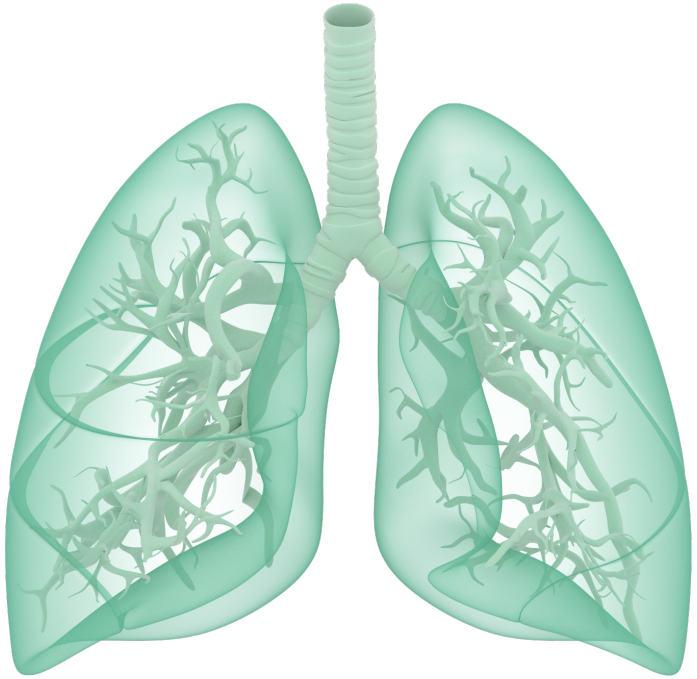
Chart generated by: http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp

Gibson PG. Respirology. 2023;28(6):577.

MBS, Medical Benefits Schedule

What can the pulmonary function lab offer?

- Spirometry
- Gas transfer
- Lung volumes
- FeNO
- Broncho-provocation test
- (FOT, CPET, oximetry, sleep studies, 6-minute walk test etc.)



FeNO, fractional exhaled nitric oxide; **FOT**, forced oscillation technique; **CPET**, cardiopulmonary exercise testing

Assessment

Good control	Partial control	Poor control
All of: • Daytime symptoms ≤ 2 days per week • Need for SABA reliever ≤ 2 day per week* • No limitation of activities • No symptoms during night or on waking	One or two of: • Daytime symptoms > 2 days per week • Need for SABA reliever > 2 days per week* • Any limitation of activities • Any symptoms during night or on waking	Three or more off: • Daytime symptoms > 2 days per week • Need for SABA reliever > 2 days per week* • Any limitation of activities • Any symptoms during night or on waking

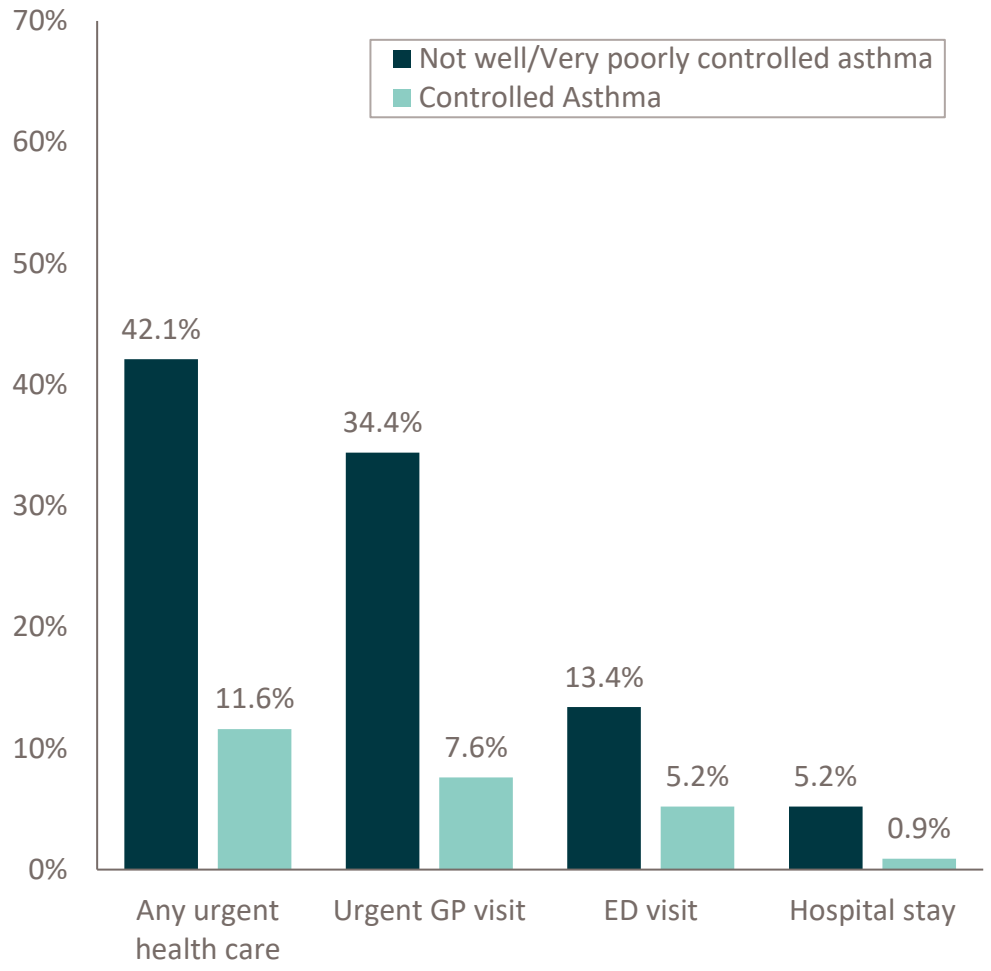
- Baseline lung function
- Level of recent asthma symptom control
- Risk factors for flare-ups, life-threatening asthma, accelerated decline in lung function, or adverse effects of treatment

*SABA, not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

SABA, short-acting beta agonist

1. National Asthma Council Australia. Australian Asthma Handbook, Version 2.2. National Asthma Council Australia, Melbourne, 2022. Available from: http://www.asthmahandbook.org.au Accessed November 2023.

Ending SABA-only treatment



SABA only treatment is an outdated treatment modality[1]

It can lead to:

- Persistent symptoms
- SABA reliance & loss of efficacy
- Exacerbations & OCS exposure
- Poor quality of life

Price et al[2] analysed 720 people prescribed SABA Patients who self-reported ≥ 3 canisters/yr

- 2.07 times severe exacerbations ($p < 0.001$)
- 3.53 times more likely to have poorly controlled asthma than those < 3 canisters a year ($p < 0.001$)

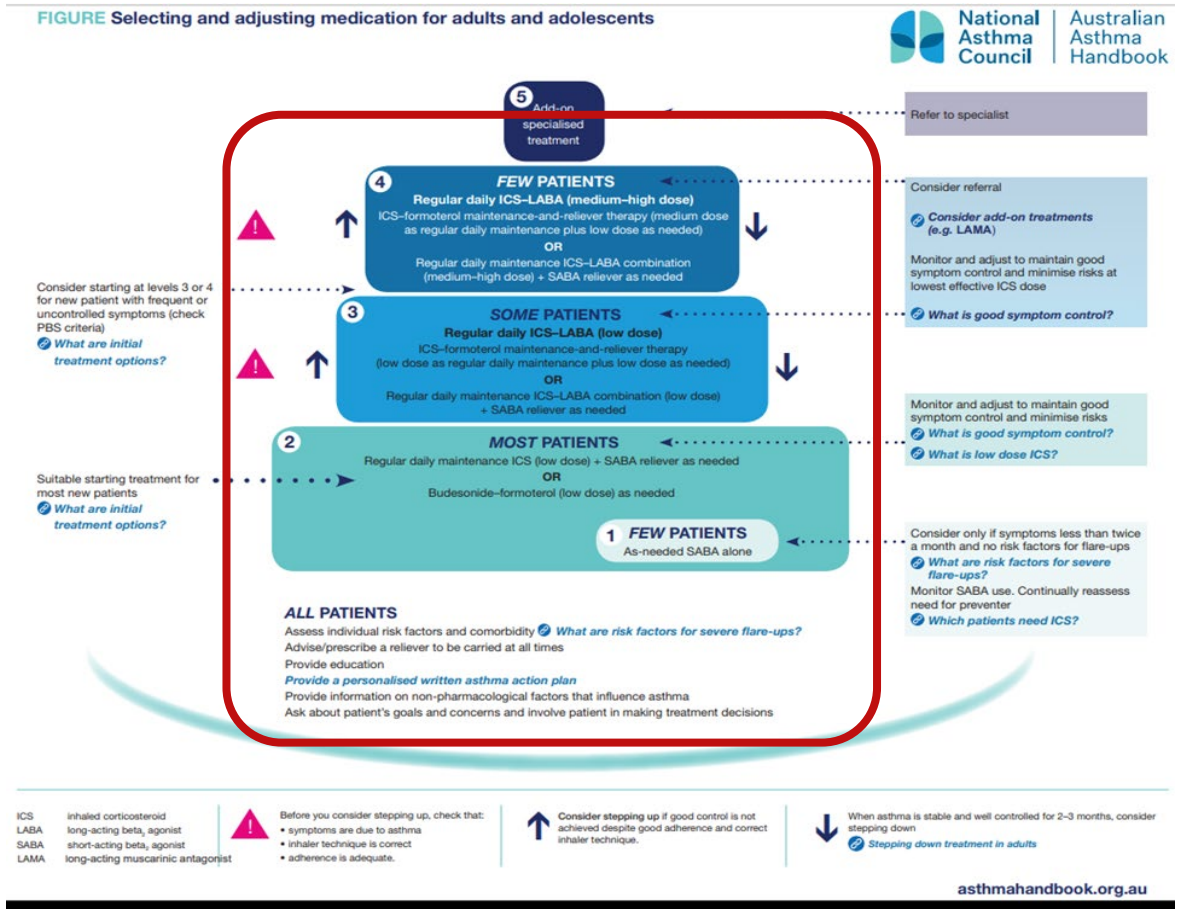
Every patient with asthma should be on an ICS

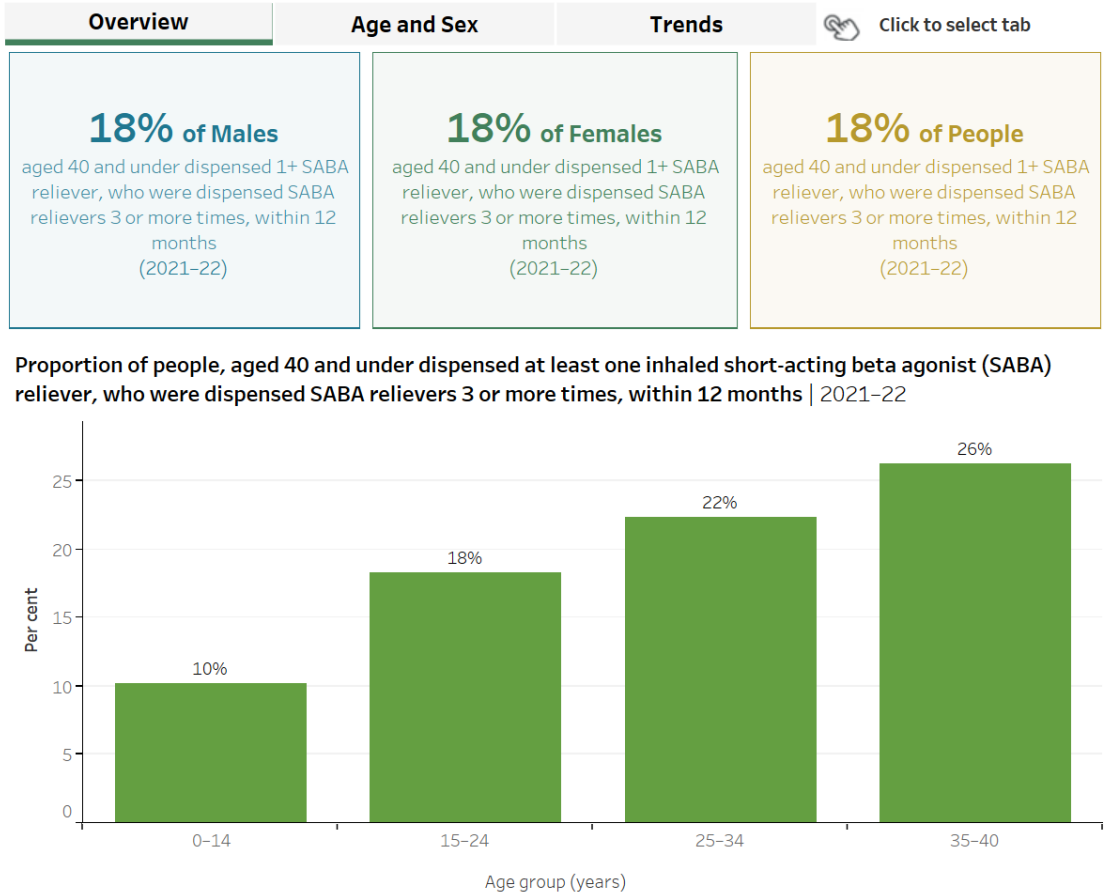
Figure adapted from Reddel et al. 2017

SABA, short-acting beta agonist; **OCS**, oral corticosteroids; **GP**, general practitioner; **ED**, emergency department; **ICS**, inhaled corticosteroids

1. Reddel HK, et al. BMJ Open. 2017;7(9):e016688. 2. Price D et al. 2023 Respirology, 28(S1):22-23.

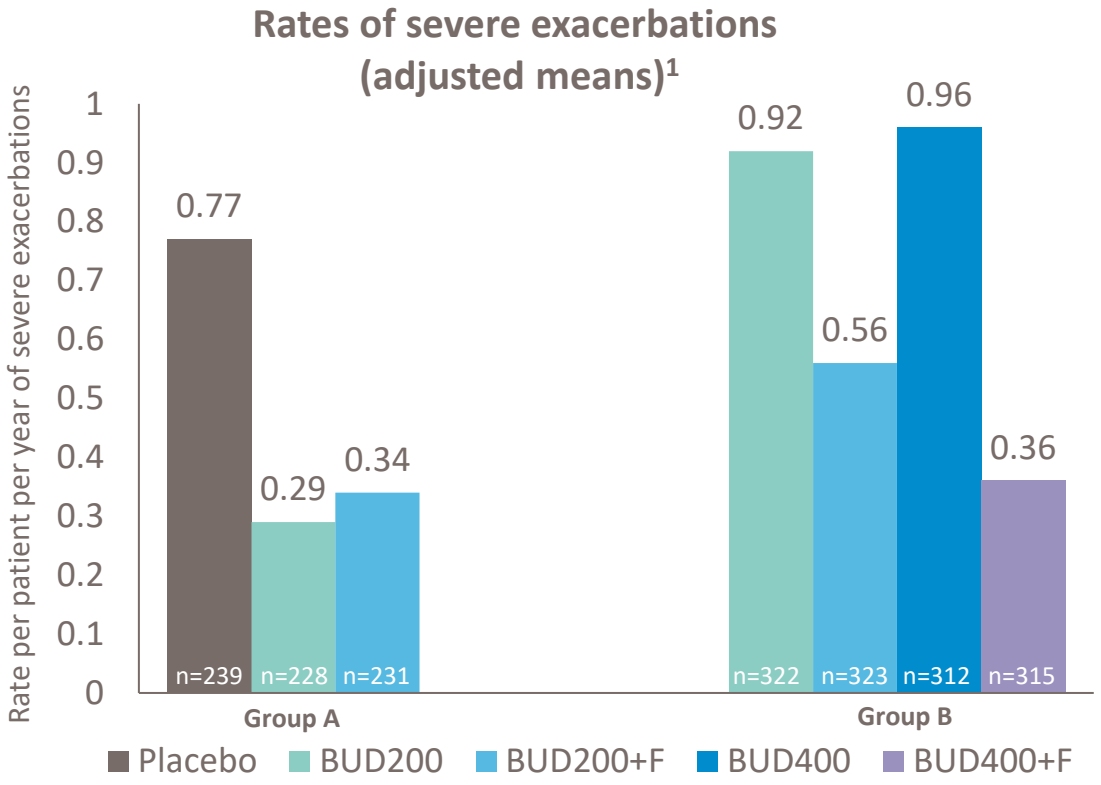
Guideline therapy

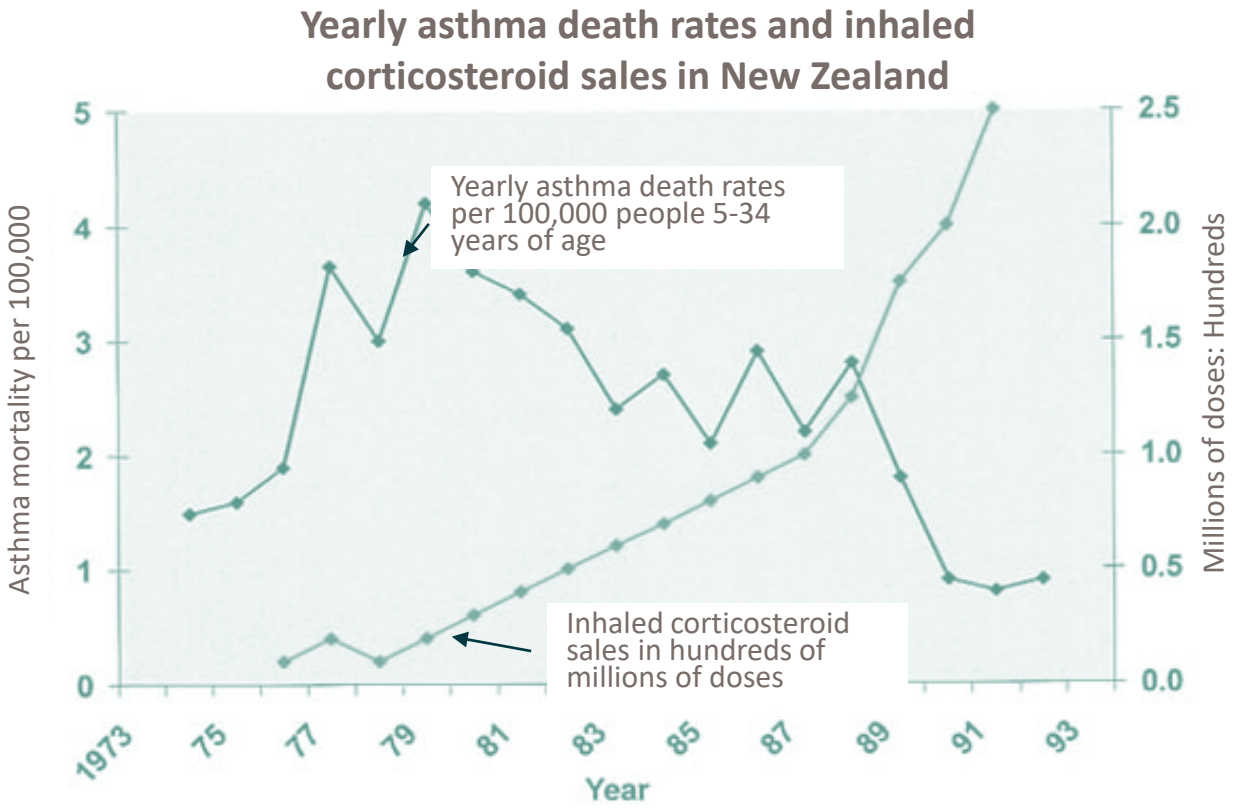




1. National Asthma Council Australia. Australian Asthma Handbook, Version 2.2. National Asthma Council Australia, Melbourne, 2022. Available from: http://www.asthmahandbook.org.au Accessed November 2023. 2. Australian Institute of Health and Welfare (AIHW), 2023. Available from https://www.aihw.gov.au/reports/chronic-respiratory-conditions/chronic-respiratory-conditions/contents/asthma-1
Accessed November 2023.

Inhaled corticosteroid efficacy





Patients ≥ 12 years of age with mild asthma. **Group A patients (N=698) (corticosteroid- free)** had not used inhaled corticosteroid for 3 months, and FEV1 ≥80% predicted normal after inhaling 1 mg terbutaline. **Group B patients (N=1272)** were taking **up to 400 µg/d of inhaled budesonide** or its equivalent for over 3 months, with a FEV1 ≥ 70% predicted normal after terbutaline, at baseline.
Non-significant p Values found for BUD200+F vs BUD200 (p =0.5) in group A, and BUD 400 vs 200 (p=0.069) for all other comparisons, including BUD200+F vs BUD 400, p = 0.0001 showing significant difference

Adapted from O'Byrne 2001[1]

Adapted from Suissa & Ernst, 2001[2]

BUD, budesonide**; F,** formoterol**; FEV_1,** Forced Expiratory Volume in one second;

1. O'Byrne PM et al. Am J Respir Crit Care Med 2001;164:1392-7. 2. Suissa, S and Ernst P. J Allergy Clin Immunol 2001;107:937-44.

(S)MART & Ad hoc

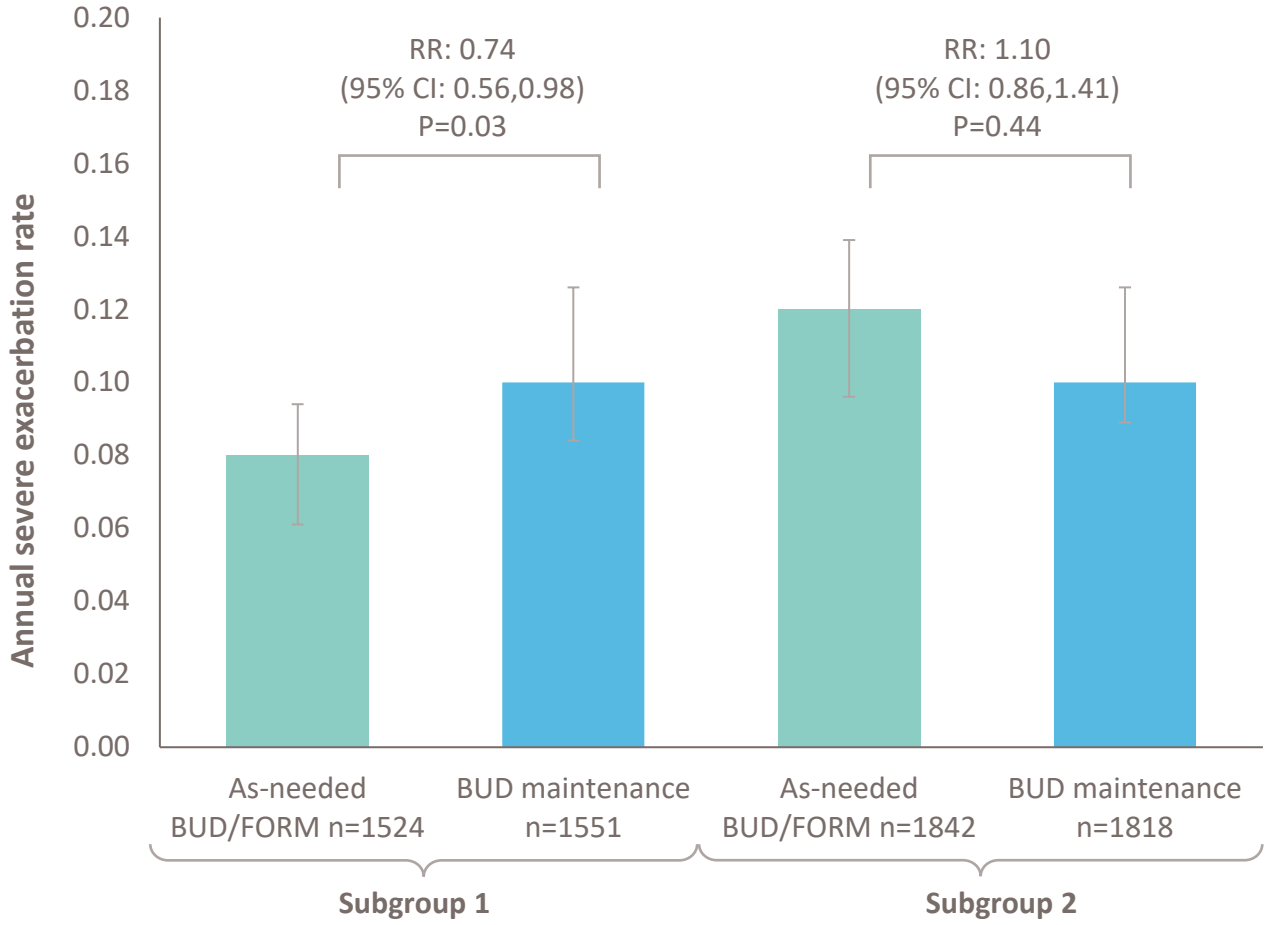


Figure adapted from Bateman et al., 2021[1]

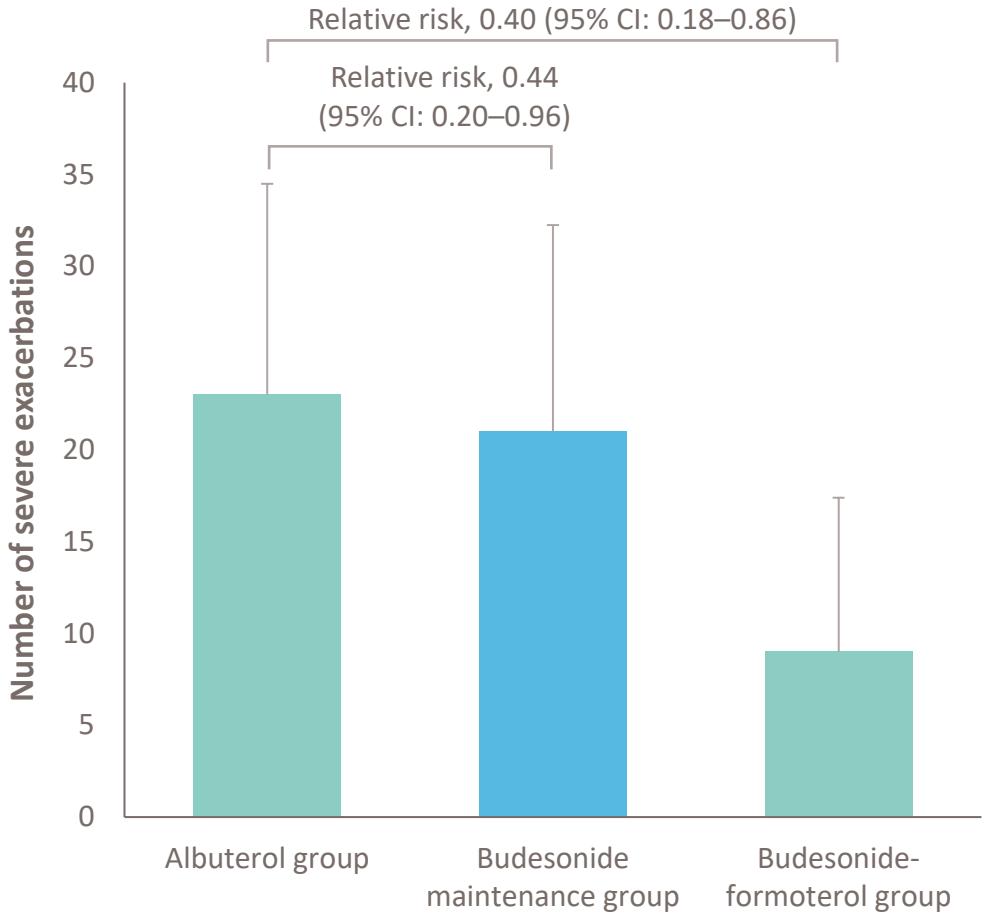


Figure adapted from Beasley et al., 2019[2]

BUD; budesonide; **CI**, confidence interval; **FOR**, formoterol; **RR**, risk ratio.

1. Bateman ED, et al. Ann Am Thorac Soc. 2021;18(12):2007-17. 2. Beasley R, et al. N Engl J Med. 2019;380(21):2020-30.

Meta-analysis of 4 trials

- A total of four RCTs (n=8065) were used to compare as-needed ICS/FOR (n=4023) with maintenance ICS + SABA (n=4042) in patients ≥ 12 years of age
- As-needed combination low-dose BUD-FOR reduced the risk of severe exacerbations by ≥60% compared to SABA reliever therapy in mild asthma
- Similar risks of at least one serious adverse event between both treatment arms
- 35% reduction in ED visits with those taking as-needed ICS/FOR compared to maintenance ICS + SABA*
- Lower risk of severe exacerbations with ad-hoc ICS/FOR vs daily ICS + SABA reliever

*no statistically significant difference in hospitalisation or ED visits/hospitalisation combined between the two treatment arms

ED, emergency department; **FOR**, formoterol; **ICS**, inhaled corticosteroid; **SABA**, short-acting beta agonist

Hatter L, et al. ERJ Open Research. 2021;7(1):00701-2020.

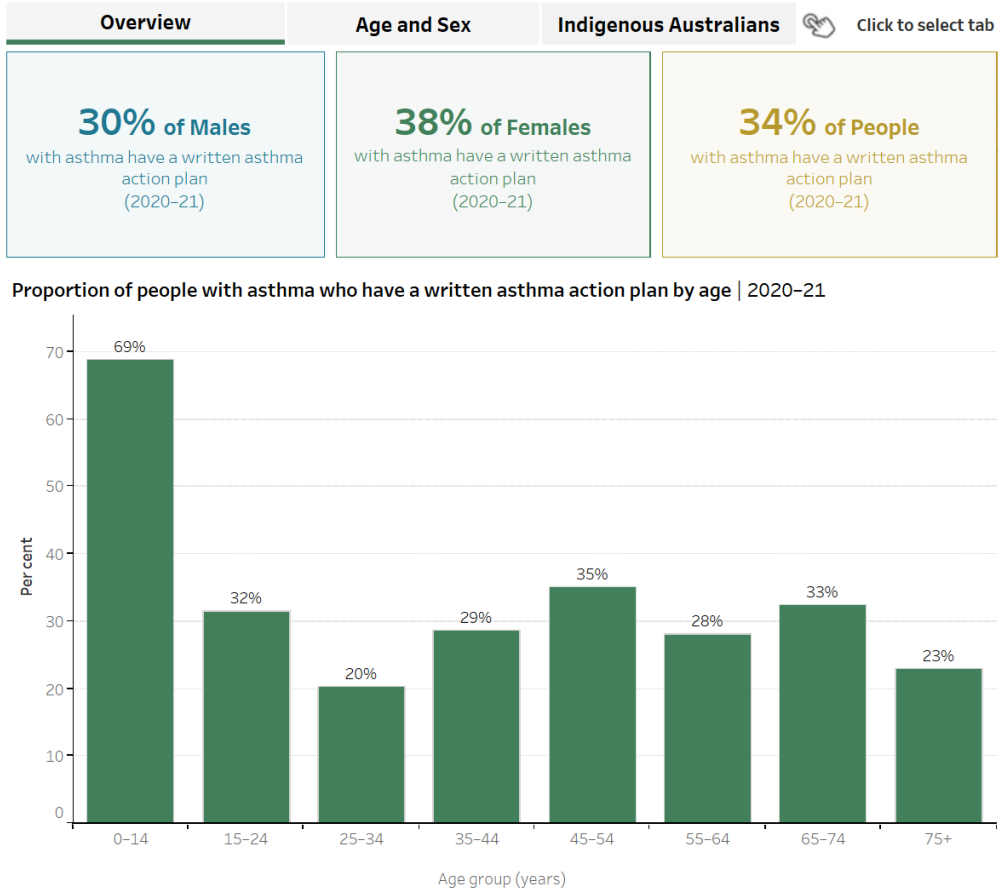
Treatable traits (TT) [1]

- TT is agnostic to the traditional diagnostic labels of asthma or COPD
- TTs can be identified by their observable clinical characteristics (i.e., phenotypes) or through validated biomarkers that indicate the presence/absence of distinct molecular mechanisms (i.e., endotypes)
- TT can be pulmonary (e.g., airflow limitation, chronic bronchitis, emphysema, among others)
- Extra-pulmonary (e.g., obesity, cardiovascular disease or gastroesophageal reflux, among others)
- behavioural/environmental domains (e.g., smoking, treatment compliance, familiar/social support among others).

COPD; chronic obstructive pulmonary disease; **TT**; treatable trait

Agustí A, et al. Respirology. 2022;27(11):929-40.

Written Action Plan (WAP)



Note: People with asthma refer to people who self-reported that they were diagnosed by a doctor or nurse as having asthma (current and long-term).
Source: AIHW analysis of ABS Microdata: National Health Surveys (NHS) 2020–21.
http://www.aihw.gov.au

Action plan variation	Result
Action point	
Symptoms v PEF triggered	Equivalent
Standard written instruction	Consistently beneficial
Traffic light configuration	Not clearly better than standard instruction
2-3 action points	Consistently beneficial
4 action points	Not clearly better than < 4 points
PEF based on personal best PEF	Consistently beneficial
PEF based on % predicted PEF	Not consistently better than usual care
Treatment instruction	
Individualised WAP using ICS & OCS	Consistently beneficial
Individualised WAP using OCS only	Insufficient data to evaluate
Individualised WAP using OCS only	Insufficient data to evaluate

Table adapted from Gibson & Powell, 2004.

1. Australian Institute of Health and Welfare (AIHW), 2023. Available from https://www.aihw.gov.au/reports/chronic-respiratory-conditions/chronic-respiratory-conditions/contents/asthma-1 Accessed November 2023. 2. Gibson PG, Powell H. Thorax. 2004;59(2):94-9.

Biological therapy

For patients with eosinophilic Th2 high asthma biological therapies such as omalizumab, mepolizumab, benralizumab and dupilumab have shown significant improvement in outcomes[1,2]

- Omalizumab (Xolair) PBS listed for severe asthma 2011
- Mepolizumab PBS listed for severe asthma 2017
- Benralizumab PBS listed for severe asthma 2018
- Dupilumab PBS listed for severe asthma 2021

All biological therapies approved via S100 Authority. PRODA on-line portal has reduced application times.

Please refer to Product Information before prescribing

1. Assaf SM, Hanania NA. Curr Opin Allergy Clin Immunol. 2019;19(4):379-86. 2. Eger K, et al. J Allergy Clin Immunol Pract. 2021;9(3):1194-200.

New Hope(s)

European Respiratory Journal

Asthma remission – what is it and how can it be achieved?

Dennis Thomas, Vanessa McDonald, Ian Pavord and Peter Gibson

Rostrum

An expert consensus framework for asthma remission as a treatment goal

Andrew Menzies-Gow, Mona Bafadhel, William Busse, Thomas Casale, Janwillem Kocks, Ian Pavord, Stanley Szefler, Prescott Woodruff, Alaxander Girgio-Miller, Frank Trudo, Malan Fageras and Christopher Ambrose.

- Asthma treatment goals focus on symptom and exacerbation control – whilst not a cure remission is a major step[1]
- Prior to 2005 asthma remission in adults with asthma was estimated to be 6%[2]
- Measures of remission vary but have commonalities[3]
- Advent of biological treatments has increased the number of patients achieving remission significantly[4]

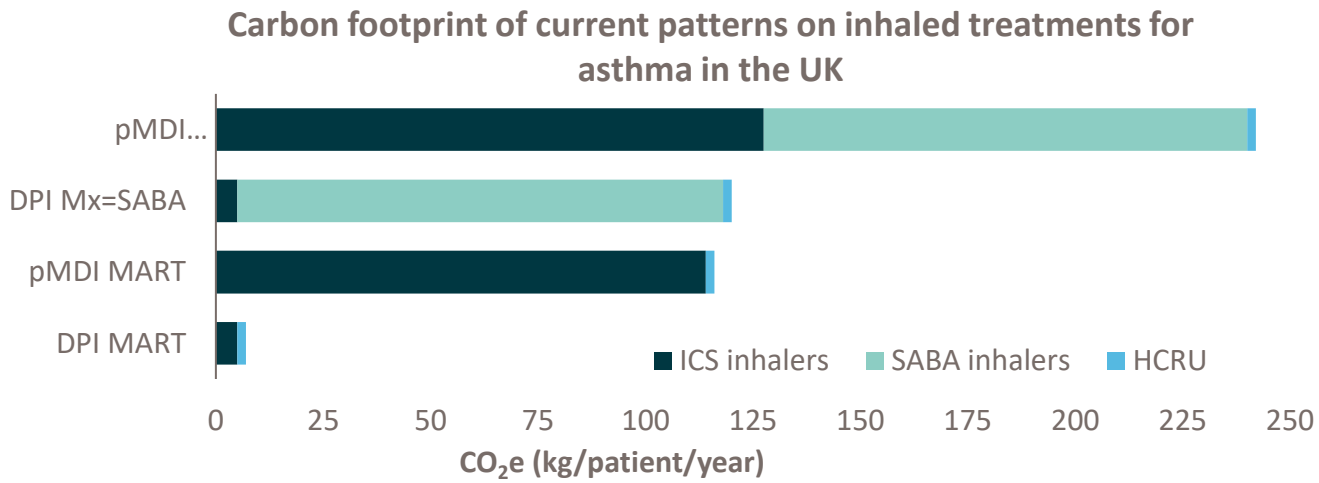
1. Thomas D, et al. Eur Respir J. 2022;60(5). 2. Rönmark E, et al. Thorax. 1999;54(7):611-3. 3. Menzies-Gow A, et al. J Allergy Clin Immunol. 2020;145(3):757-65. 4. Pavord I, et al. J Allergy Clin Immunol. 2021;147(2):AB4.

Asthma treatments and climate change

- MDI have been on the wrong side of the environment on more than one occasion with early MDIs being propelled by CFCs[1]
- New delivery systems are in development with reduced impact
- SABA use is largest proportion of carbon footprint[2]
- Carbon footprint of a severe AE = 2.38-166.5 $kgCO_2e$[3]

Name	Global warming potential
CO_2 (carbon dioxide)	1
HFO 1234ze (potential new propellant in future MDIs)	<1
HFA152a (potential new propellant in future MDIs)	138
HFA-134a (used in most current MDIs)	1300
HFA-227ea (used in some current MDIs)	3350
CFC-11 (previously used in MDIs)	4660
CFC-12 (previously used in MDIs)	10200

Adapted from Bell et al., 2022



Adapted from Wilkinson and Woodcock, 2022

1. Wilkinson A, Woodcock A. Br J Clin Pharmacol. 2022;88(7):3016-22. 2. Bell J, et al. Eur Resp J. 2022;60(suppl 66):4578. 3. Beeh KM, et al. Eur Resp J. 2021;58(suppl 65):OA102

Dupilumab PBS Information: Refer to PBS schedule for full authority information. Authority required for patients aged ≥12 years with: chronic severe atopic dermatitis; OR uncontrolled severe asthma. This product is not listed on the PBS for: children 6 months to 11 years of age with severe atopic dermatitis; children 6-11 years of age with moderate to severe asthma; adults with uncontrolled chronic rhinosinusitis with nasal polyps; or adults with moderate-to-severe prurigo nodularis.

Please review full Product Information before prescribing. Full Product Information is available from sanofi-aventis australia pty ltd at the QR code below, or by contacting 1800 818 806.

Scan for more information

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

ASPIRE

SHARING BEST PRACTICE AND ENRICHING EXCELLENCE

Remission in asthma therapies: Definitions, directions and disagreements

Brooke Kyle, Asthma and Airways CNC &
A/Prof. John Blakey, Consultant in Respiratory Medicine
Sir Charles Gairdner Hospital, Perth

RESPIRATORY ADVENT
ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

Disclosures

Grants

- Avant
- FHRI
- IPCRG
- MRFF
- Novartis

Educational activity and advisory

- Asthma Australia
- Astra Zeneca
- Boehringer Ingelheim
- Chiesi
- GSK
- Sanofi

We've all given the same kinds of answers in interviews

Why do you want to be a….?

Why do you want to be a CNC?

So people *feel* better

CNC, Clinical Nurse Consultant

Why do you want to be a CNC?

So people *feel* better

To make people better

CNC, Clinical Nurse Consultant

Why do you want to be a CNC?

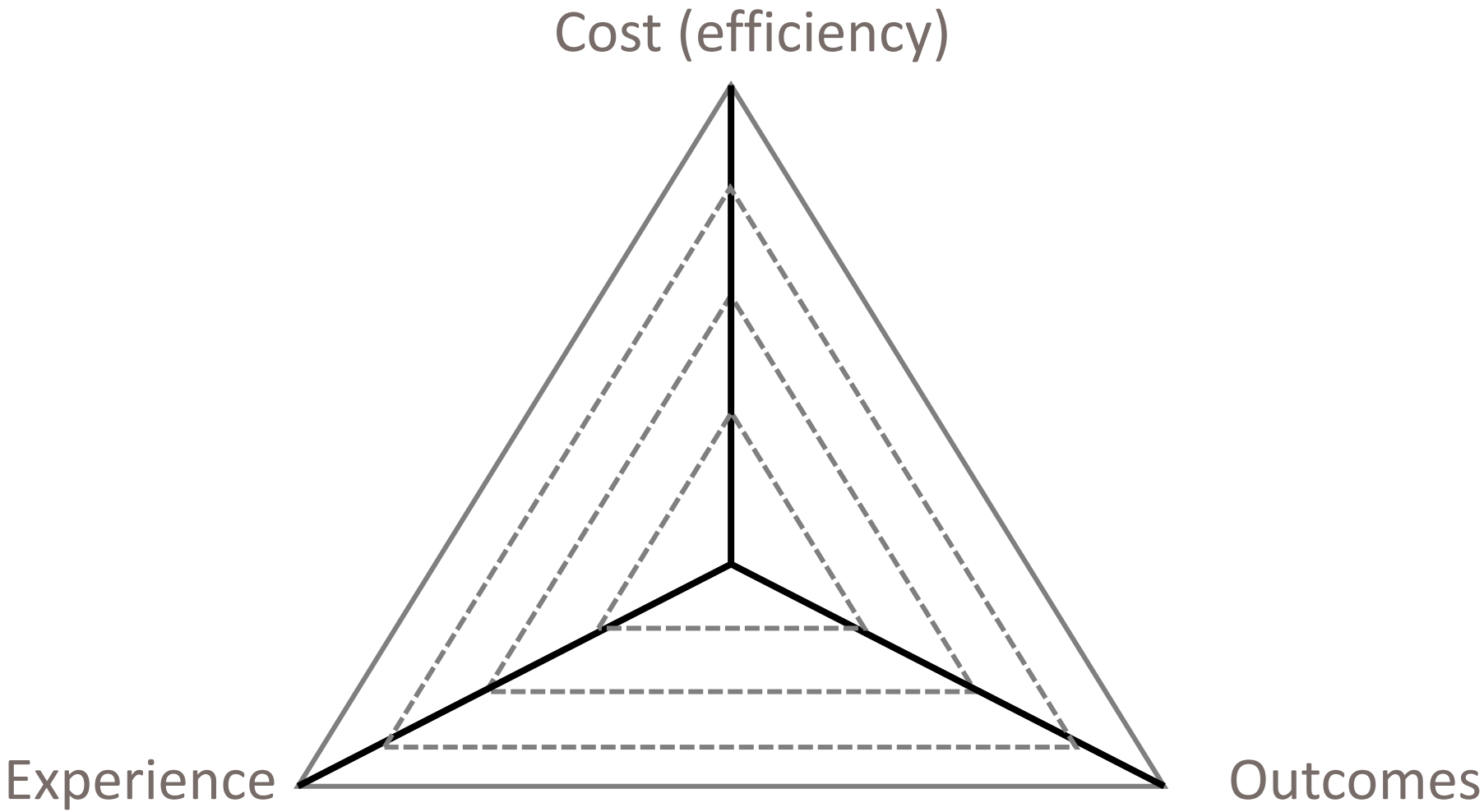
So people *feel* better

To improve efficiency

To make people better

CNC, Clinical Nurse Consultant

Triple aim



Outcomes

- Some progress
- Ongoing serious preventable harm
- Unacceptable variation

Perspectives

Sleepwalking towards more harm from asthma

The burden of asthma for patients and doctors can be reduced through simple evidence-based approaches to care and self-management

Asthma continues to be a major but avoidable burden on the Australian health care system.[1] It is a treatable and responsive disease, and much has been achieved in the years since asthma was declared a National Health Priority. However, we are locked into an old paradigm of care that does not serve the best interests of either patients or doctors and is long past its use-by date.[2] Several key issues need urgent attention and action: fragmented and suboptimal care,[3] over-reliance on reliever therapies,[4] neglect of rural and remote populations,[5] and overprescription of oral corticosteroids.[6,7] Add to this the impact of environmental threats such as climate change, wildfires,[8] thunderstorm asthma, and respiratory viral pandemics,[9] with the increasing association of asthma with obesity and sedentary lifestyle,[10] and we have the ingredients of a perfect storm.

In 2017–18, there were almost 40 000 hospitalisations for asthma, up to 80% of which could have been avoided with better asthma care and resources in the community.[11-13] In 2020–21, the numbers were reduced, paradoxically thanks to the COVID-19 pandemic.[14] However, children aged under 15 years still constitute the largest proportion of people presenting to emergency departments in Australia with a respiratory condition, and asthma is the leading preventable cause of these presentations.[15-17] Respiratory conditions generally account for the highest proportion of emergency department presentations in relation to other disease systems, and around one-third of these people are admitted to hospital.[5] These presentations and admissions for asthma comprise a large group of patients with a readily treatable disease.[12] Further, there is a tenfold variation in hospitalisation rate between the highest and the lowest socio-economic regions, and people with asthma in low income settings and in rural Australia are doing worst of all.[5,18] This is not inevitable — much of it can be prevented by simple evidence-based approaches to asthma care, including assessing triggers, performing spirometry, devising a written action plan, and checking device use and adherence.

Although asthma is eminently treatable, suboptimal asthma control is prevalent in Australia.[19] Greater awareness and more options for effective management in the community can prevent asthma flare-ups, persistent symptoms, permanent airway remodelling, psychological stress, and even death.[12,20] Indeed, people with asthma are more likely to experience high (15%) and very high (11%) levels of psychological distress compared with those without asthma, and better asthma control can help alleviate this burden.[21] Lower quality of life, reduced workforce participation, and likelihood of an emergency hospital admission are also all strongly linked to poorly controlled asthma.[22-24]

Although death rates from asthma have fallen markedly in Australia over the past 10 years, there is more to achieve. Asthma death rates are higher among people living in regional and remote areas, in low compared with high socio-economic areas, and among Aboriginal and Torres Strait Island people. People aged over 65 years now predominate, possibly reflecting the fact that older adults tend to understate their symptoms and may not regard their asthma as a priority.

Current models of care are failing people with asthma, resulting in management that does not align with the evidence clearly articulated in guidelines recommending inhaled corticosteroids as a starting therapy, and by dispensing excessive burst oral corticosteroid therapy.[6,7] The time pressures on primary care physicians might limit their capacity to have a detailed discussion with patients about asthma and the many issues that need attention. It behoves us to develop better tools and strategies to help facilitate this and achieve better asthma outcomes on low doses of preventer and controller medication[25,26] to avoid excessive exposure to oral corticosteroids. It is hoped that the proposed review and strengthening of Medicare[27] will more appropriately reimburse clinicians for a systematic, evidence-based approach to patients with chronic disease such as poorly controlled asthma, and address the disproportionate financial reimbursement for hospital admissions compared with prevention via optimal community care. Spirometry is underfunded given its time and complexity, and solutions using innovative technologies or referral to a community respiratory service need to be developed. Several studies[28,29] suggest that training and engagement of pharmacists in asthma care can deliver significant benefits in device use, asthma control and self-management, and training standards and reimbursement for pharmacy-based care are needed to encourage shared asthma support between primary care and pharmacy.

Nationally at a regulatory level, as matter of extreme urgency, Australia needs to re-examine its approach to over-the-counter availability of short-acting β2-agonist (SABA) medications and the excessive number of inhalers available on prescription.[30] Over-the-counter availability was put in place over 30 years ago as a stop-gap measure when asthma death rates were high and community awareness of asthma as a potentially life-threatening disease was low, meaning patients sought help far too late. Since then, asthma research findings and management recommendations[31] have shown that this practice is no longer fit for purpose, indeed it is antiquated and harmful.[30,32] There are few diseases that are still treated as they were 30 years ago, yet that is what is happening for many patients with asthma. In addition

hristine R Jenkins[1,2]
Philip G Bardin[3]
John Blakey[4,5]
Kerry L Hancock[6]
Peter Gibson[7]
Vanessa M McDonald[8]

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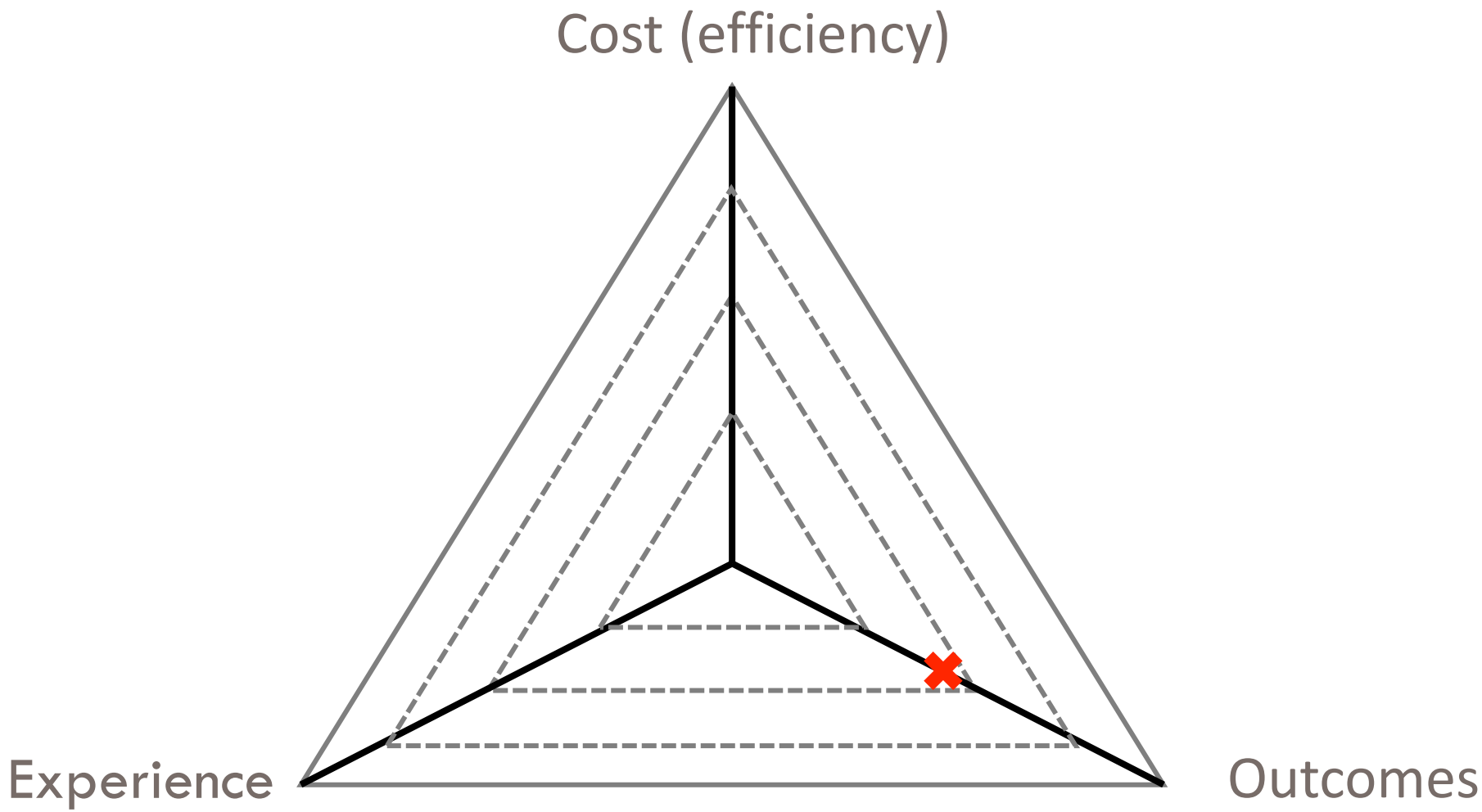
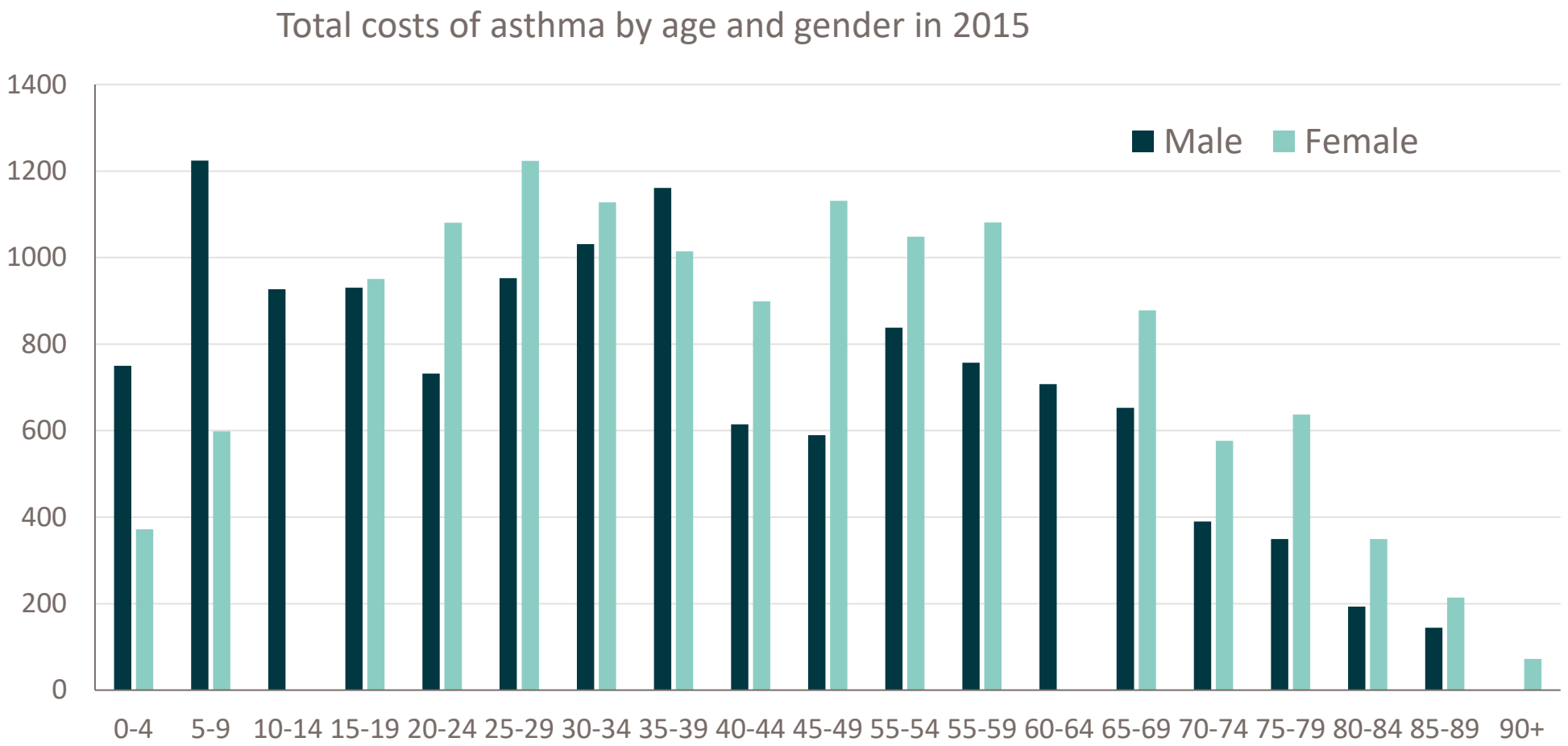
doi: 10.5694/mja2.52000

Jenkins CR. et al. Med J Aust 2023; 219(2):49-52.

Triple aim

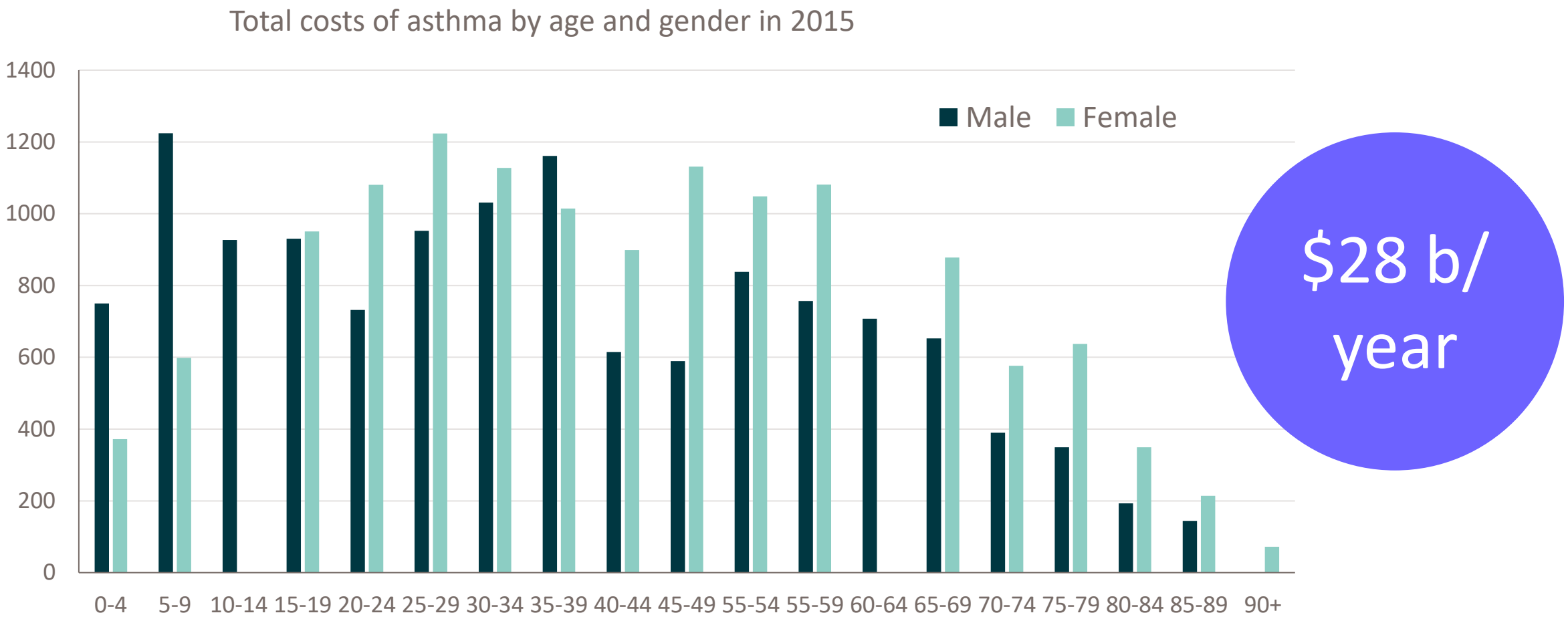


Cost (efficiency)



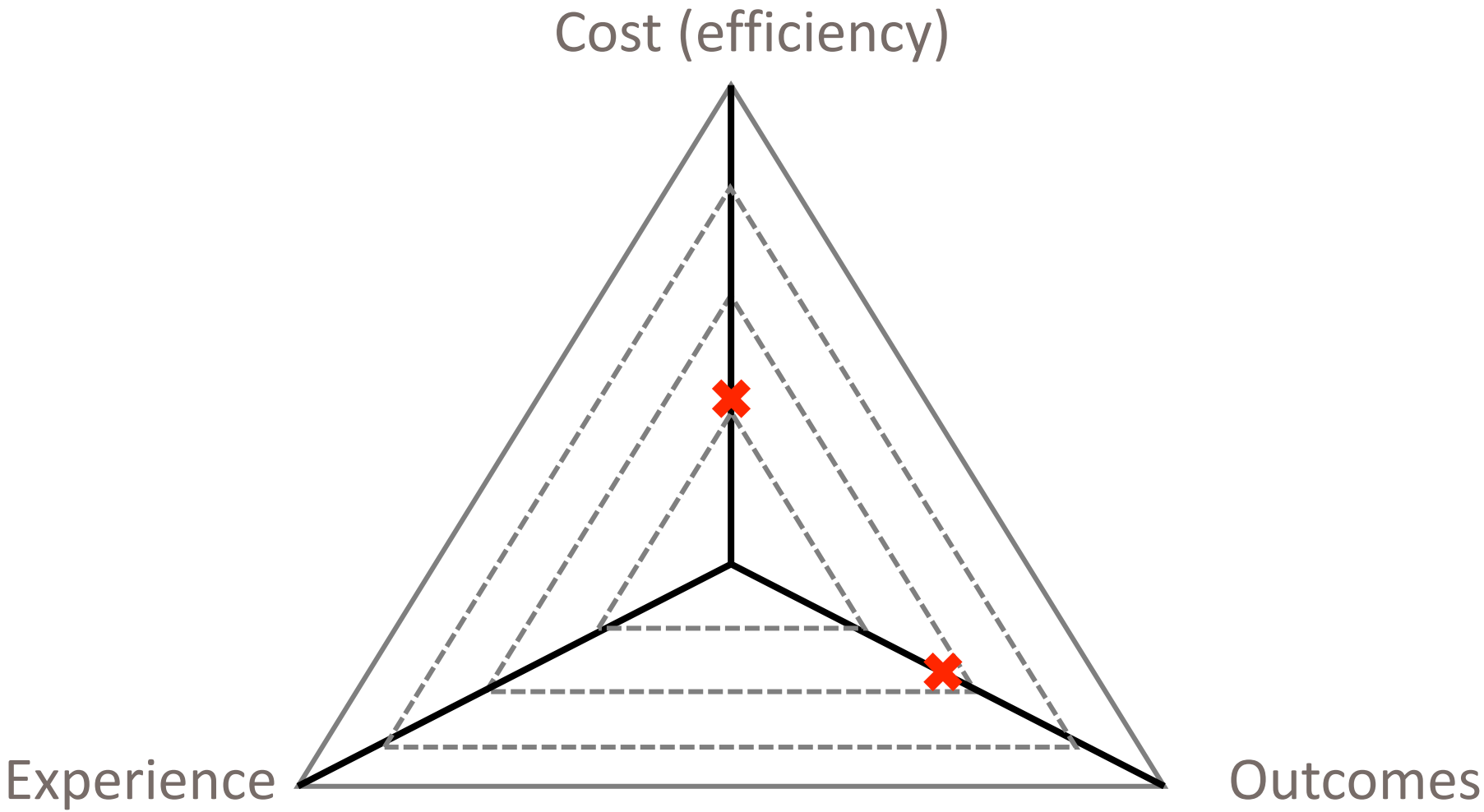
Adapted from Deloitte Access Economics. Asthma Australia and National Asthma Council Australia. The hidden cost of asthma. Published November 2015. https://asthma.org.au/wp-content/uploads/2022/03/HIdden-cost-of-asthma-final-report-revised-181115-v2-2.pdf Accessed November 2023

Cost (efficiency)

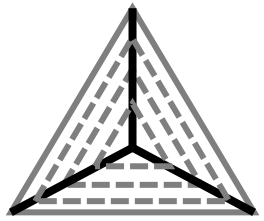


$28 b/ year

Adapted from Deloitte Access Economics. Asthma Australia and National Asthma Council Australia. The hidden cost of asthma. Published November 2015. https://asthma.org.au/wp-content/uploads/2022/03/HIdden-cost-of-asthma-final-report-revised-181115-v2-2.pdf Accessed November 2023

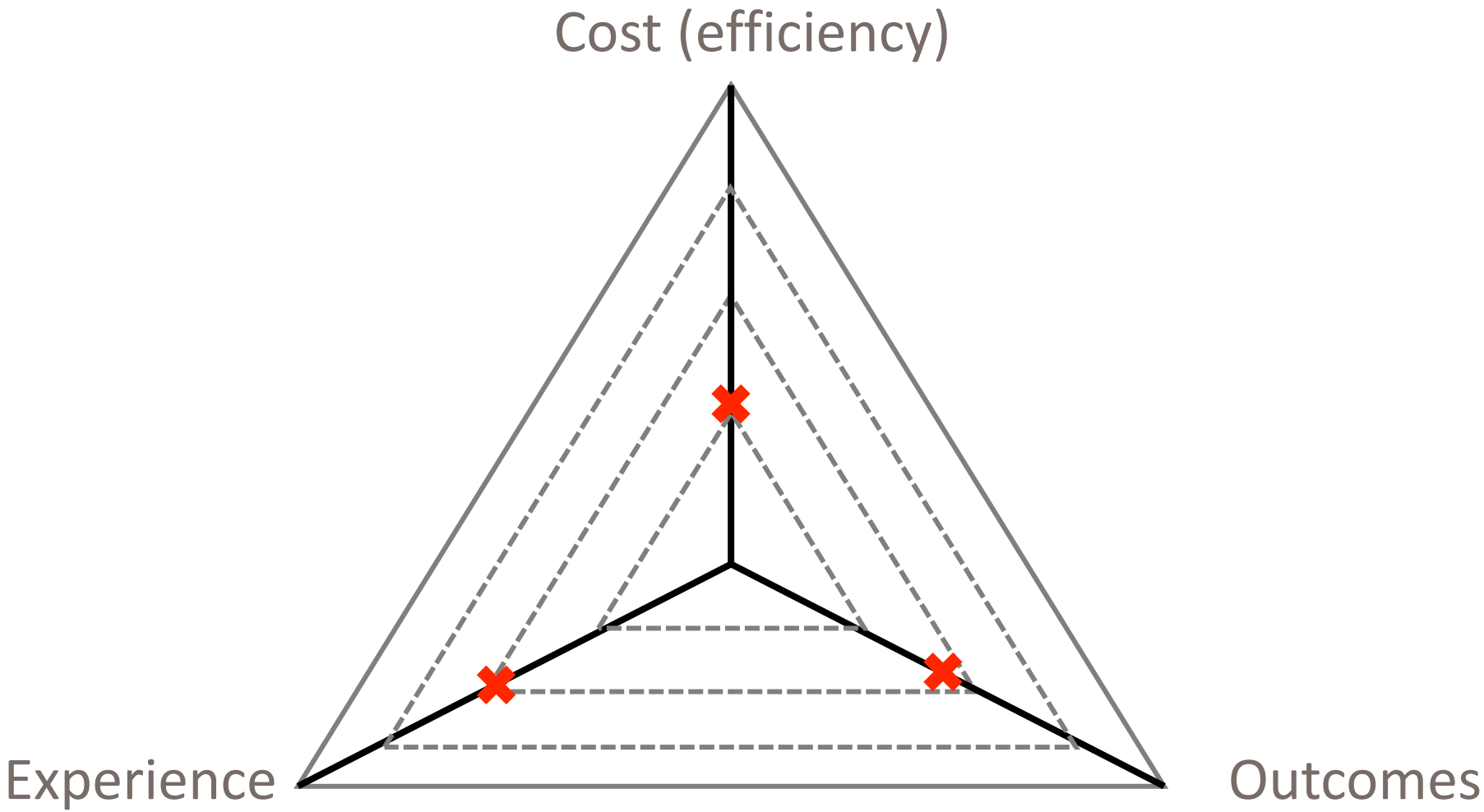


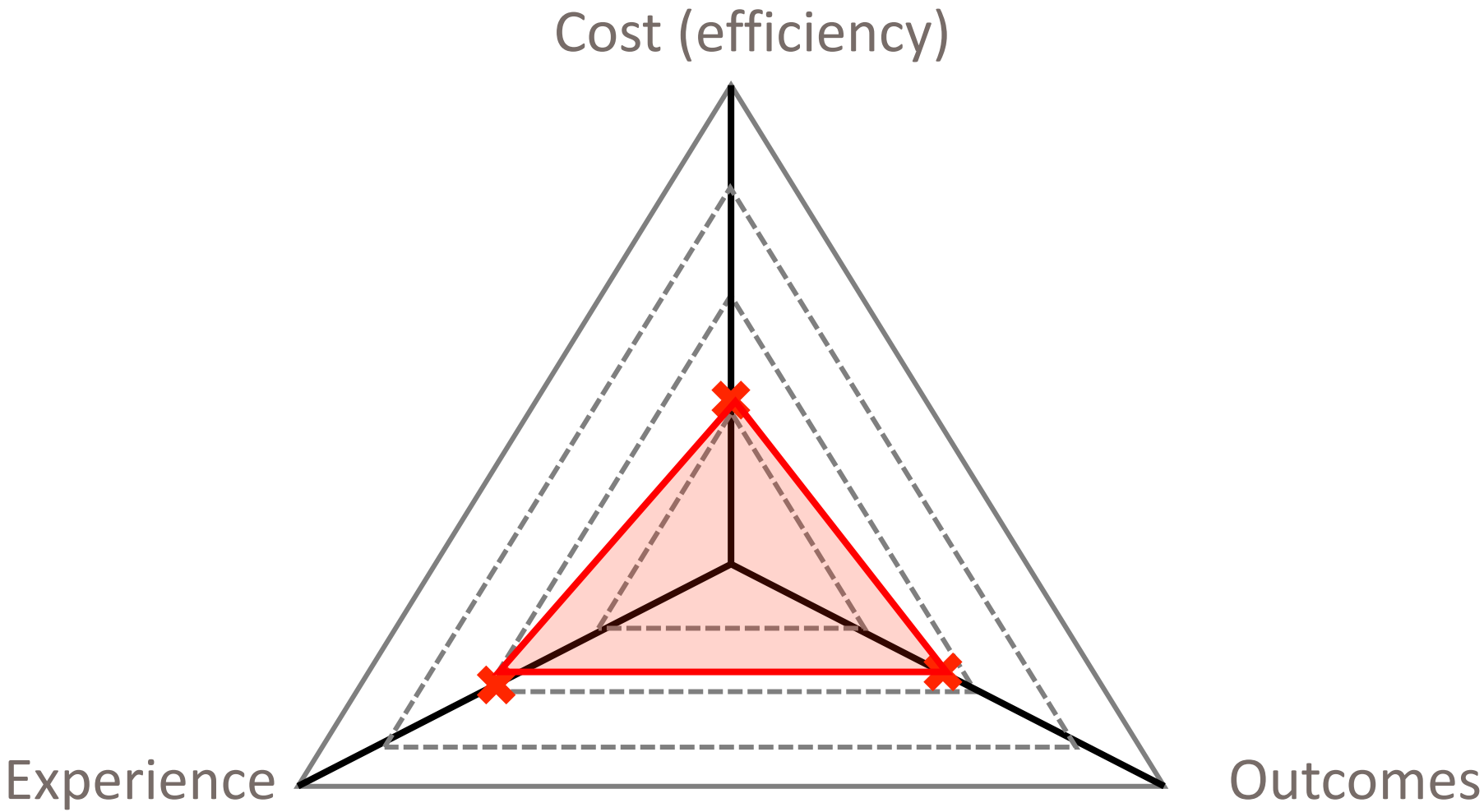
Experience



- Challenges of asthma itself[1-4]
- Lack of support is common[5]
- Disappointing acute care is the norm[6]

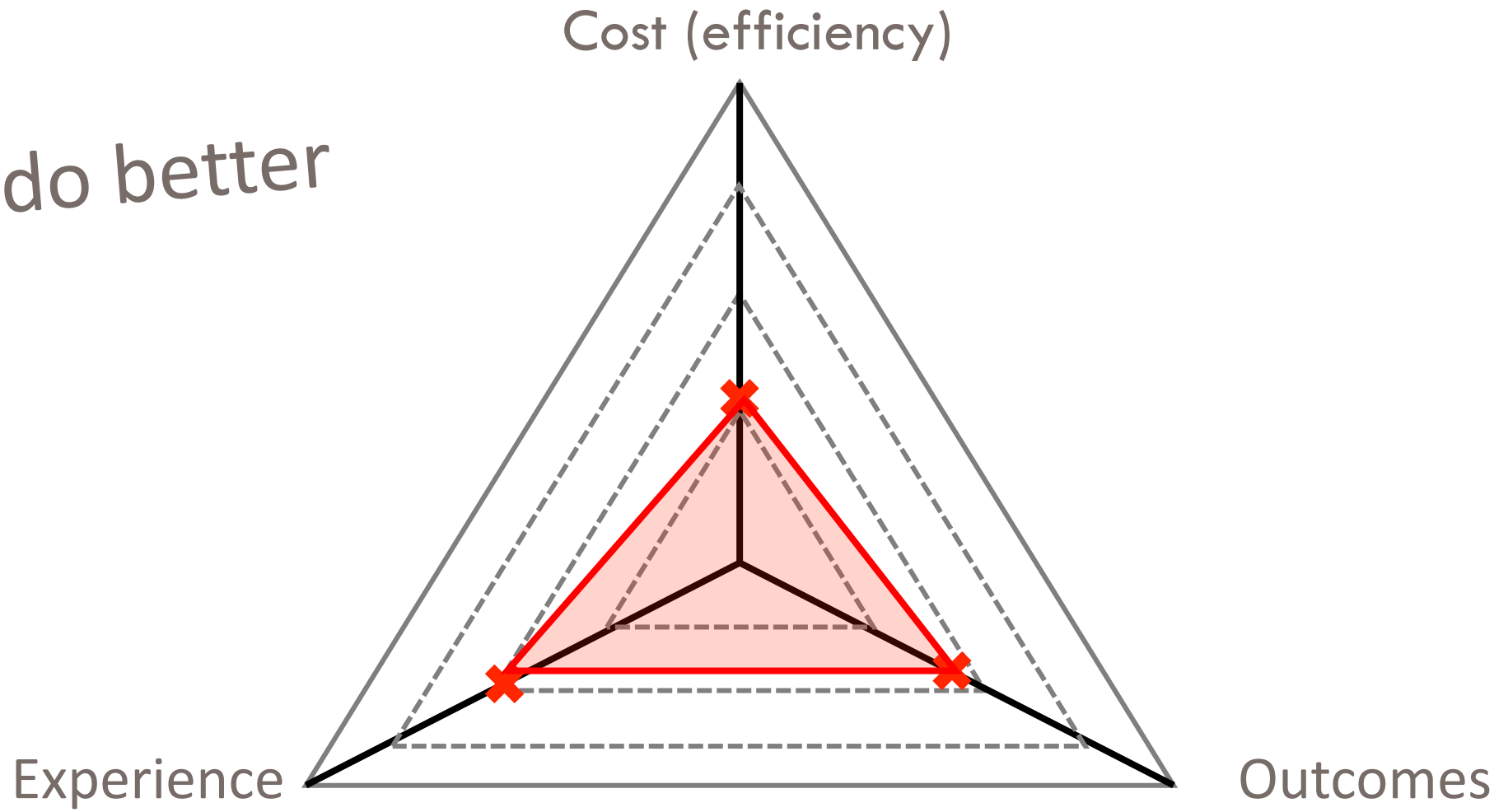
1. Foster JM, et al. Eur Respir J. 2017;50(3):1700765. **2.** Kelada L, et al. NPJ Prim Care Respir Med. 2021;31(1):42. **3.** Moffat M, et al. Prim Care Respir J. 2006;15(3):159-65.
4. Shulhan-Kilroy J, et al. PEC Innov. 2022;1:100006. **5.** The Royal College of Emergency Medicine. Moderate and acute severe asthma. Clinical audit 2016/17 National Report Published 2017. Available at https://rcem.ac.uk/wp-content/uploads/2021/11/Moderate_and_Acute_Severe_Asthma_Clinical_Audit_2016_17.pdf Accessed November 2023. **6.** Reddel. Respirology. 2023;28(S2):110-246.





C+

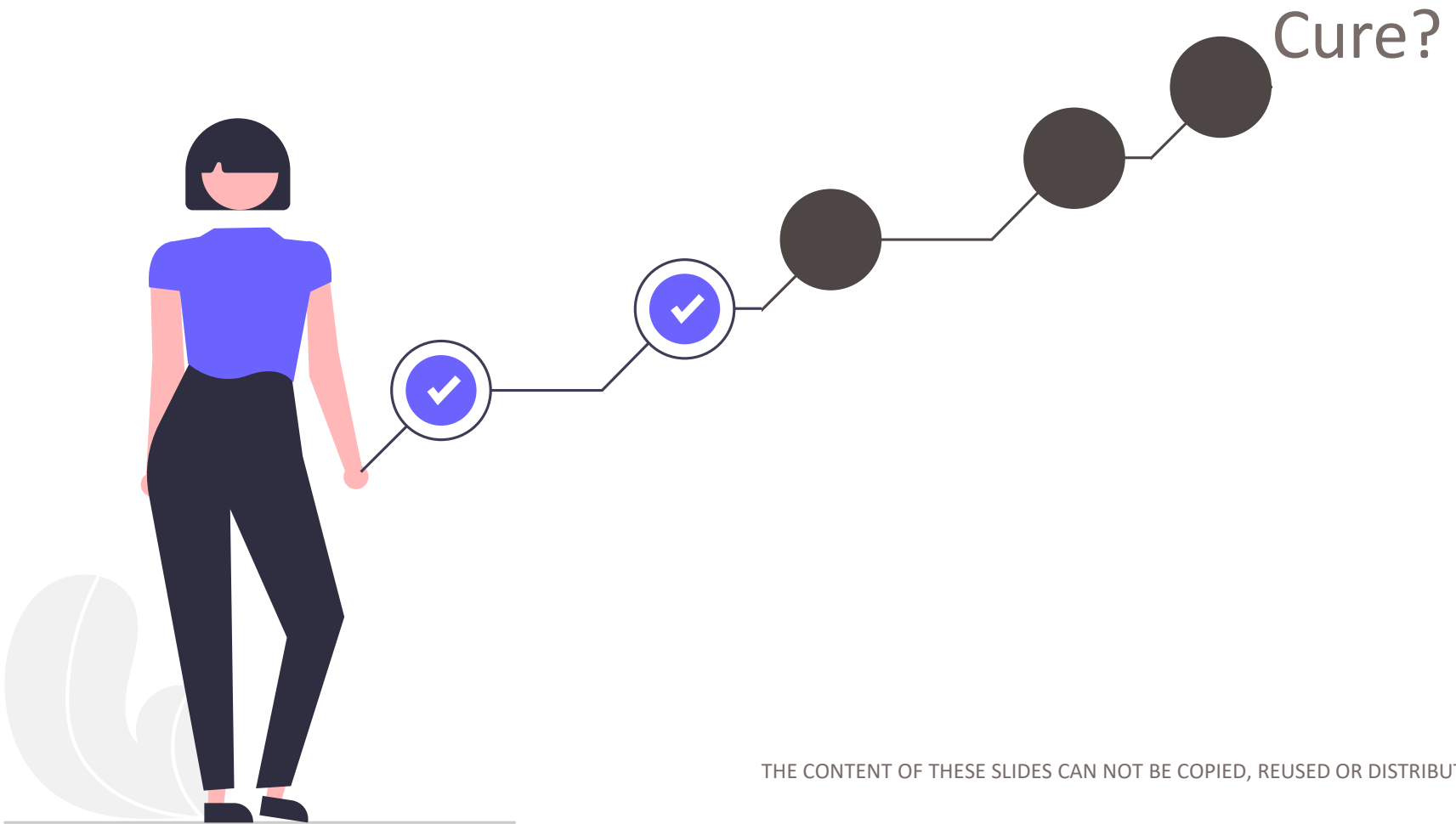
Must do better



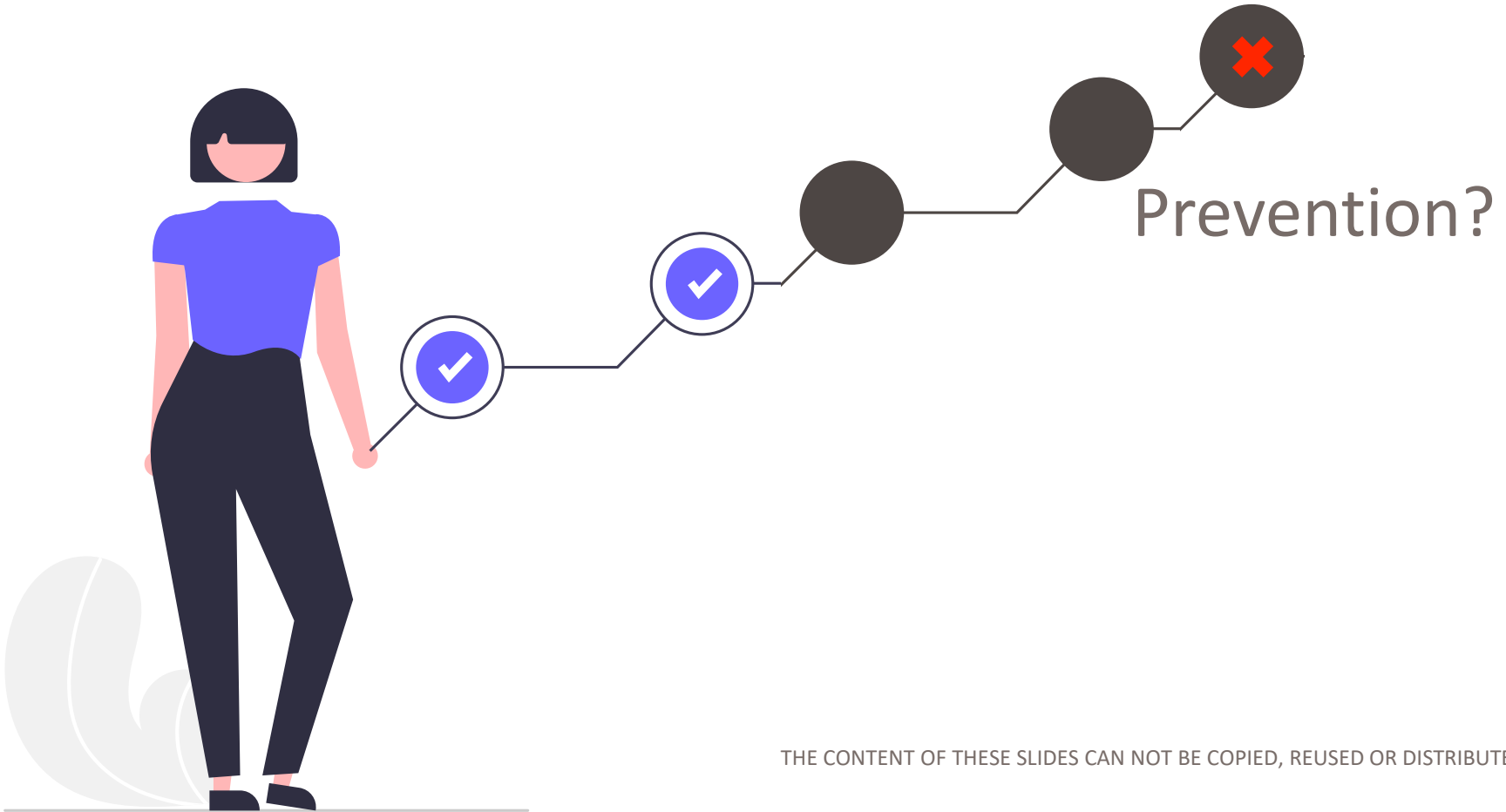
How are we going to make substantial progress?

(some) Control

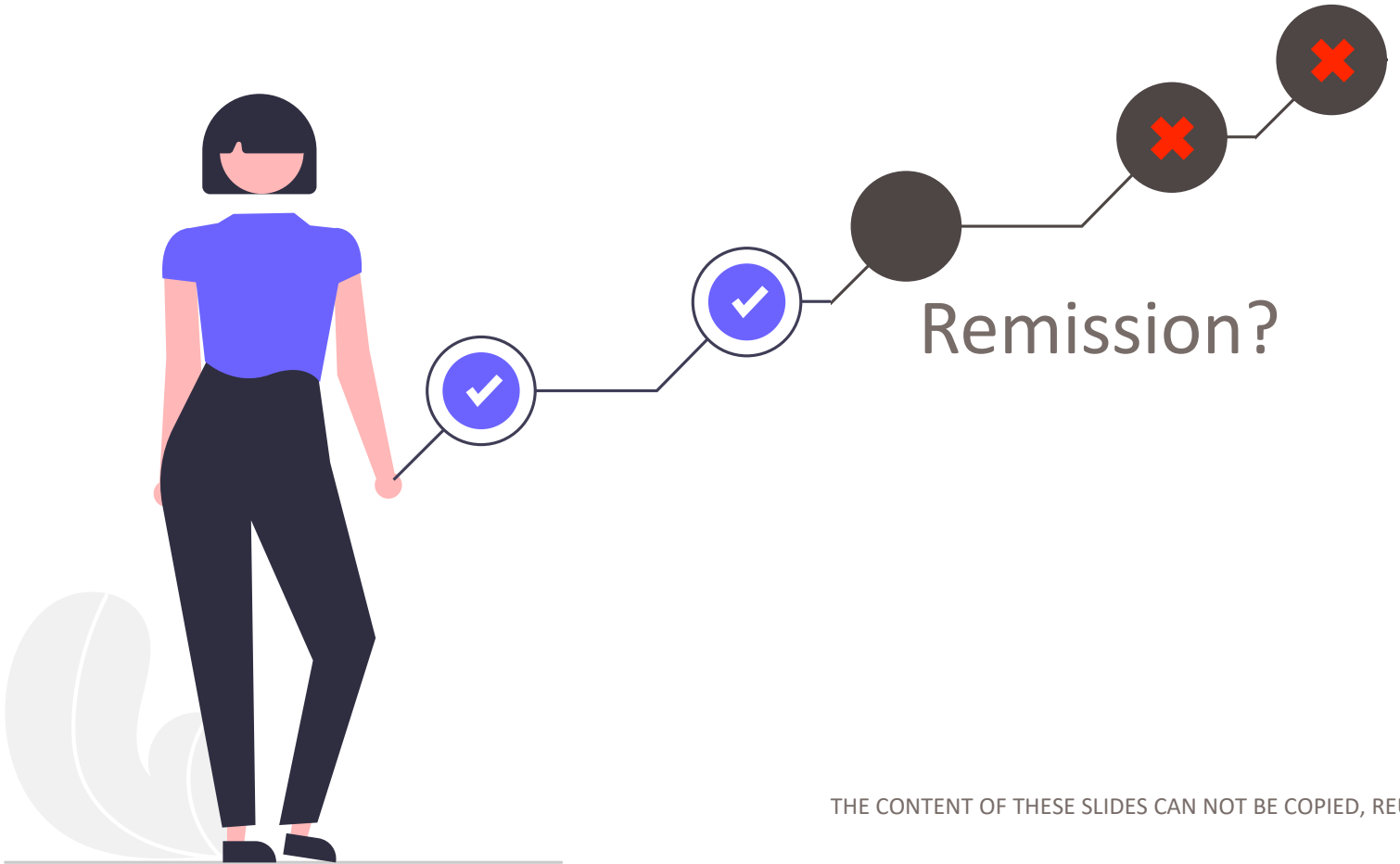
How are we going to make substantial progress?



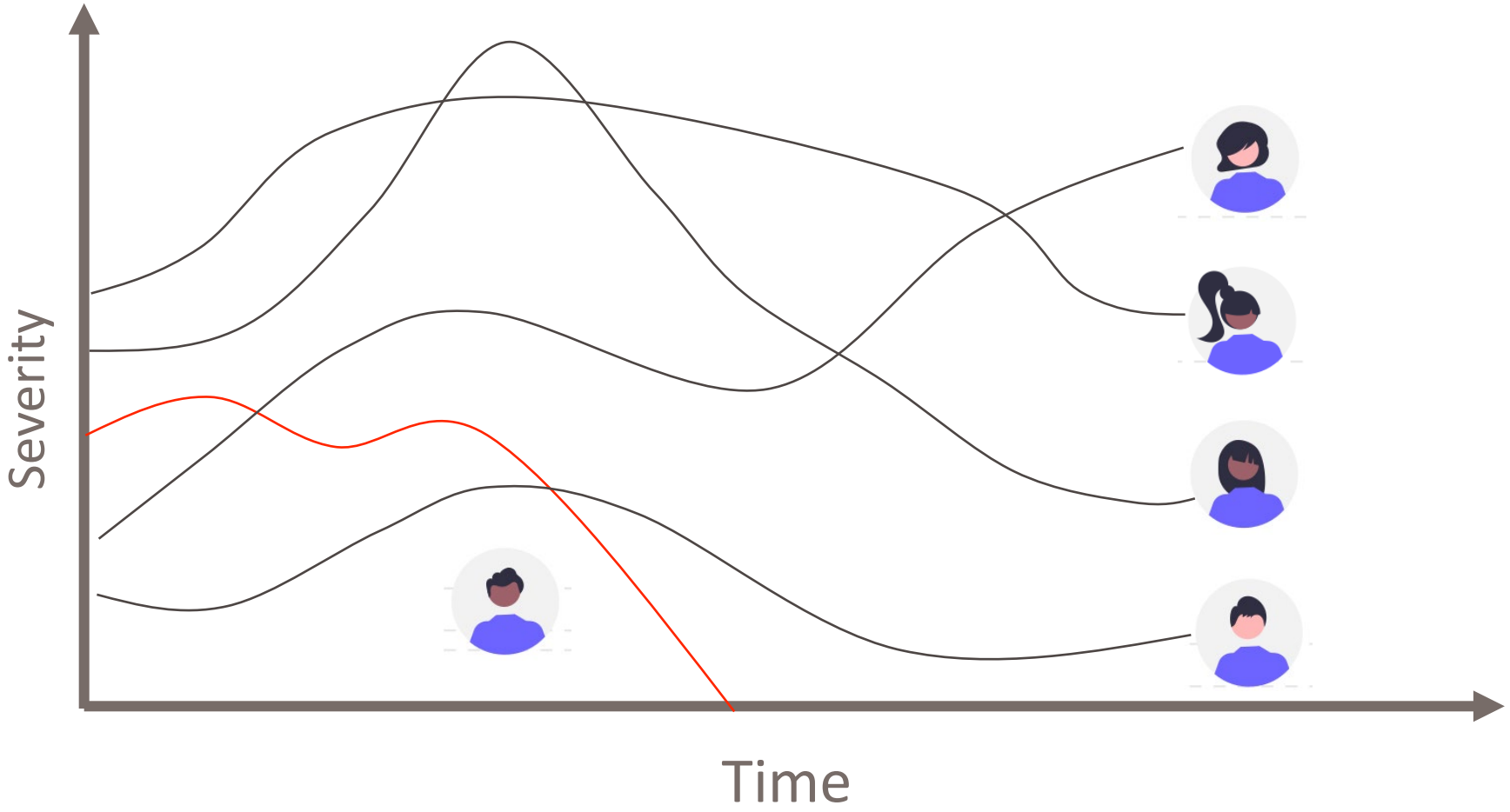
How are we going to make substantial progress?



How are we going to make substantial progress?

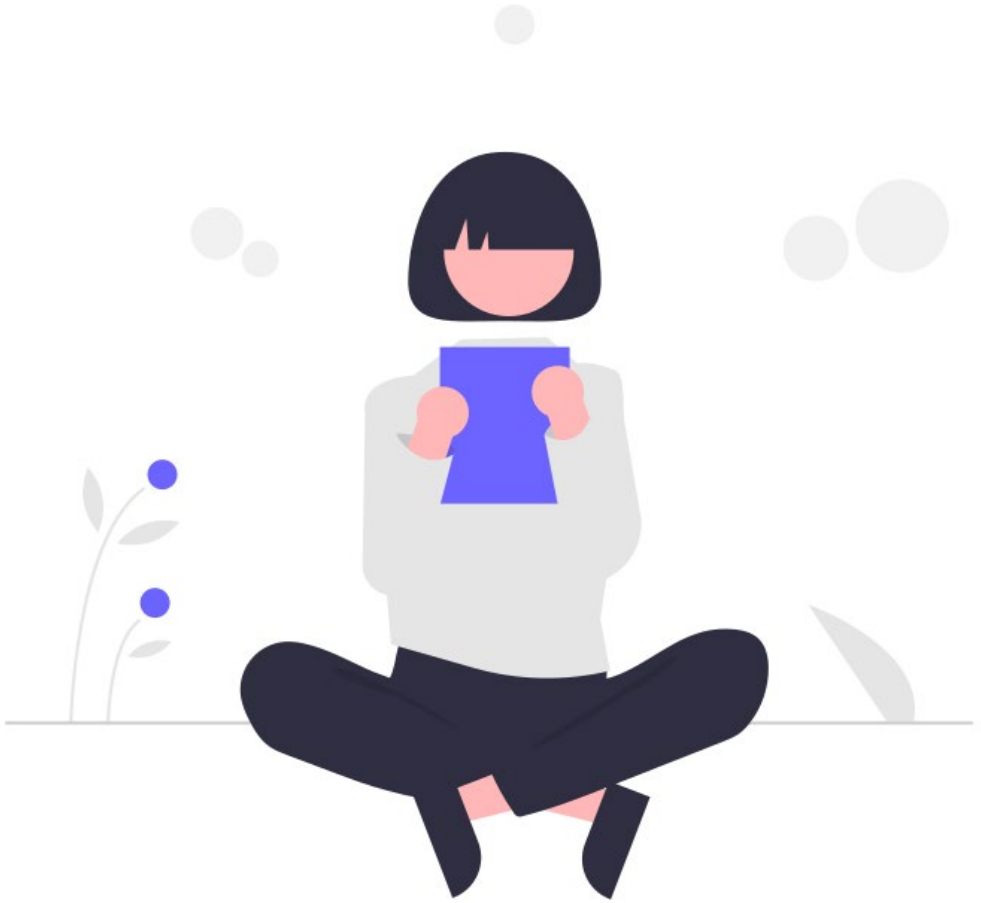


Spontaneous remission does occur



Examples of possible different asthma trajectories

Some light reading for after the webinar



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- Holm M, et al. Eur Respir J. 2007;30(1):62-5.
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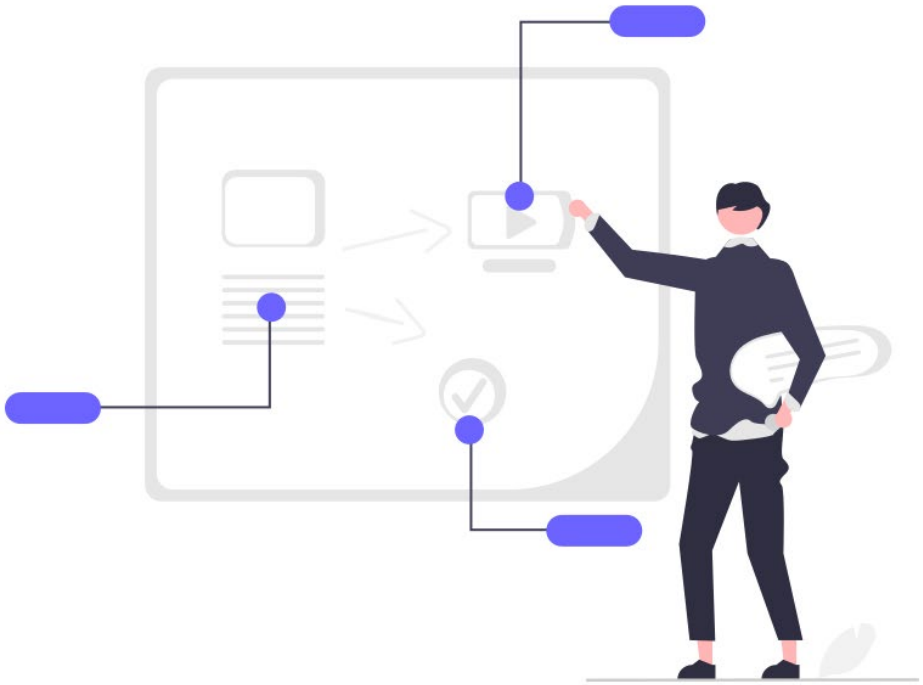
- Rönmark E, et al. Thorax. 1999;54(7):611-3.

A reference list from this meeting is available by scanning the QR code and includes the references above

What lessons can we learn from other areas of medicine?



1 Agreement won’t happen overnight

1 Agreement won't happen overnight

2

Framework[1,2,3]	On treatment	Off treatment
Clinical		
Complete		

1. Wechsler ME, et al. N Engl J Med. 2017;376(20):1921-32. 2. Dejaco C, et al. Ann Rheum Dis. 2011;70(3):447-53. 3. van Vollenhoven R, et al. Ann Rheum Dis. 2017;76(3):554-61.

1 Agreement won't happen overnight

2

Framework[1,2,3]	On treatment	Off treatment
Clinical		
Complete		

3 Remission now → Better outcomes later[3,4]

1. Wechsler ME, et al. N Engl J Med. 2017;376(20):1921-32. 2. Dejaco C, et al. Ann Rheum Dis. 2011;70(3):447-53. 3. van Vollenhoven R, et al. Ann Rheum Dis. 2017;76(3):554-61. 4. Radner H, et al. Arthritis Res Ther. 2014;16(1):R56.

What progress has there been in asthma?

Review
Pharmacol Ther 2011 Apr;130(1):38-45. doi: 10.1016/j.pharmthera.2011.01.002. Epub 2011 Jan 11.

Remission of asthma: The next therapeutic frontier?

John W Upham, Alan L James

Abstract

Asthma treatment goals focus on disease control rather than remission as a therapeutic aim. This is in contrast to diseases where remission is frequently discussed and has well-defined criteria. In this review, we consider the similarities and differences between remission in asthma and another chronic inflammatory disease, rheumatoid arthritis, where new therapies have made remission a realistic treatment goal. Clinical remission of asthma is often defined as prolonged absence of asthma symptoms without requirement for medication while others insist on the demonstration of normal lung function and airway responsiveness. Even in those who develop a symptomatic remission of asthma, persistent physiological abnormalities and airway inflammation are common. There is a clear need to develop a precise, internationally accepted, definition of asthma remission that can be used as a therapeutic endpoint in studies of new asthma treatments. Spontaneous remission of asthma symptoms is relatively common, especially during adolescence. It is more likely in males, those with mild symptoms and normal lung function and in those who quit smoking, and may be linked to normalisation of immune function. Remission is less likely in severe asthma, atopy, eosinophilia, airflow obstruction, continued smoking and weight gain.

Upham JW, James AL. Pharmacol Ther. 2011;130(1):38-45.

What progress has there been in asthma?

REVIEWS AND FEATURE ARTICLE| VOLUME 145, ISSUE 3, P757-765, MARCH 2020

An expert consensus framework for asthma remission as a treatment goal

Andrew Menzies-Gow, PhD, Mona Bafadhel, PhD, William W. Busse, MD, Thomas B. Casale, MD, Janwillem, W.H. Kocks, MD, PhD, Ian D. Pavord, MD, Stanley J. Szefler, MD, Prescott G. Woodruff, MD, Alexander de Giorgio-Miller, PhD, Frank Trudo, MD, Malin Fageras, PhD, Christopher S. Ambrose, MD

Abstract

With novel therapies in development, there is an opportunity to consider asthma remission as a treatment goal. In this Rostrum, we present a generalized framework for clinical and complete remission in asthma, on and off treatment, developed on the basis of medical literature and expert consensus. A modified Delphi survey approach was used to ascertain expert consensus on core components of asthma remission as a treatment target. Phase 1 identified other chronic inflammatory diseases with remission definitions. Phase 2 evaluated components of those definitions as well as published definitions of spontaneous asthma remission. Phase 3 evaluated a remission framework created using consensus findings. Clinical remission comprised 12 or more months with (1) absence of significant symptoms by validated instrument, (2) lung function optimization/stabilization, (3) patient/provider agreement regarding remission, and (4) no use of systemic corticosteroids. Complete remission was defined as clinical remission plus objective resolution of asthma-related inflammation and, if appropriate, negative bronchial hyperresponsiveness. Remission off treatment required no asthma treatment for 12 or more months. The proposed framework is a first step toward developing asthma remission as a treatment target and should be refined through future research, patient input, and clinical study.

Menzies-Gow A, et al. J Allergy Clin Immunol. 2020;145(3):757-65.

What progress has there been in asthma?

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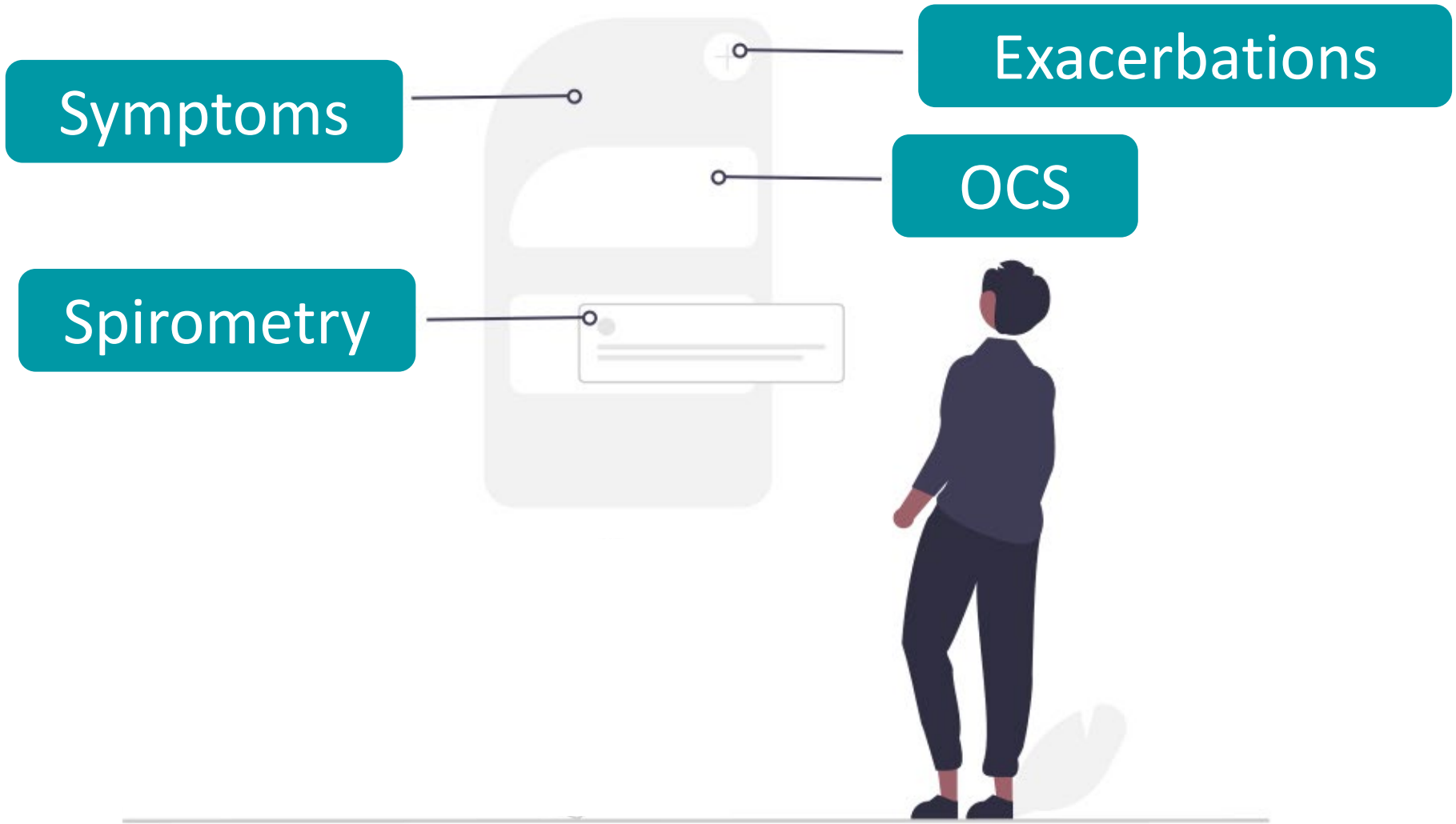
Diverse expertise?

Consensus amongst experts?

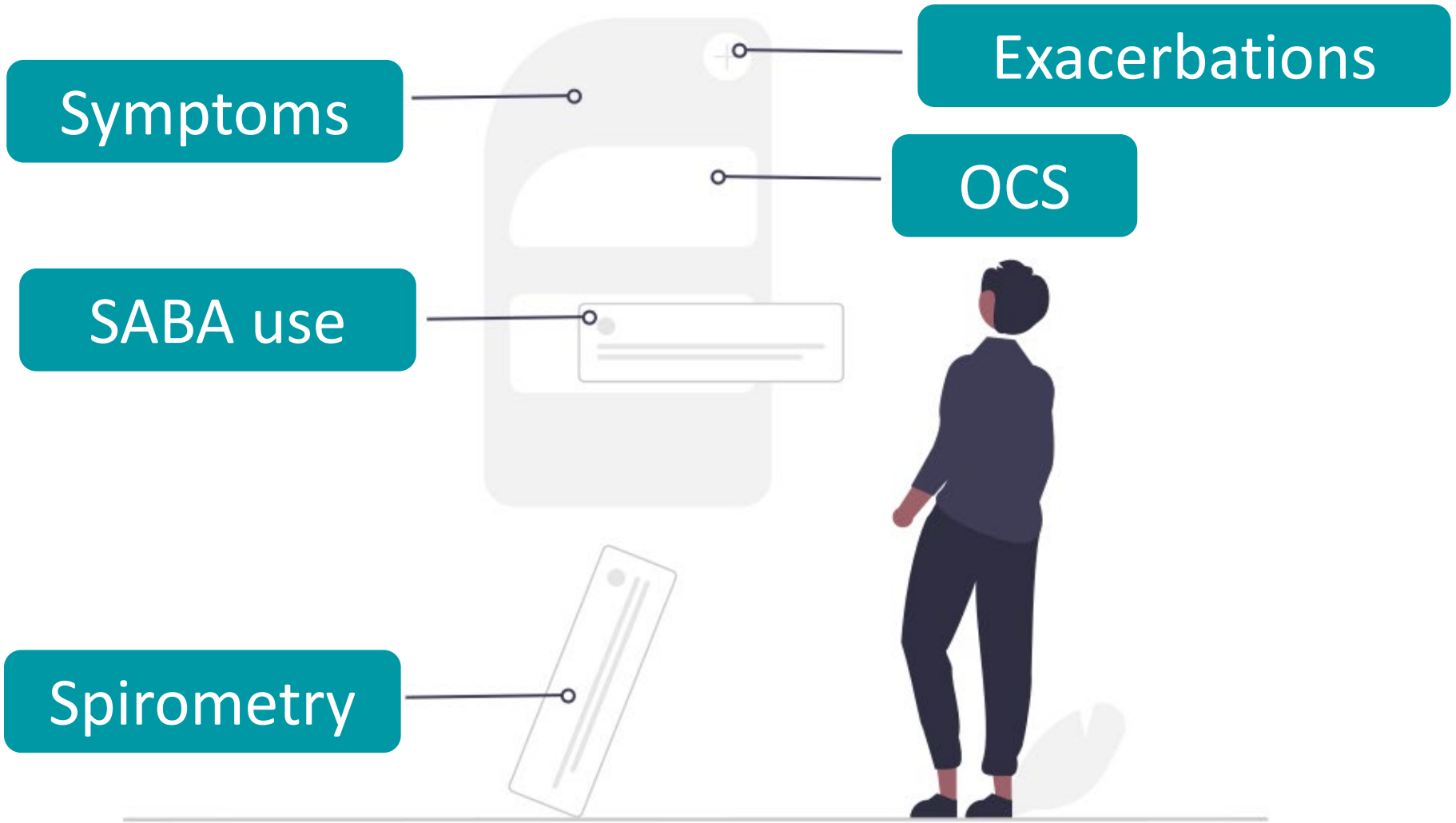
Menzies-Gow A, et al. J Allergy Clin Immunol. 2020;145(3):757-65.

Multiple definitions used since



OCS, oral corticosteroid

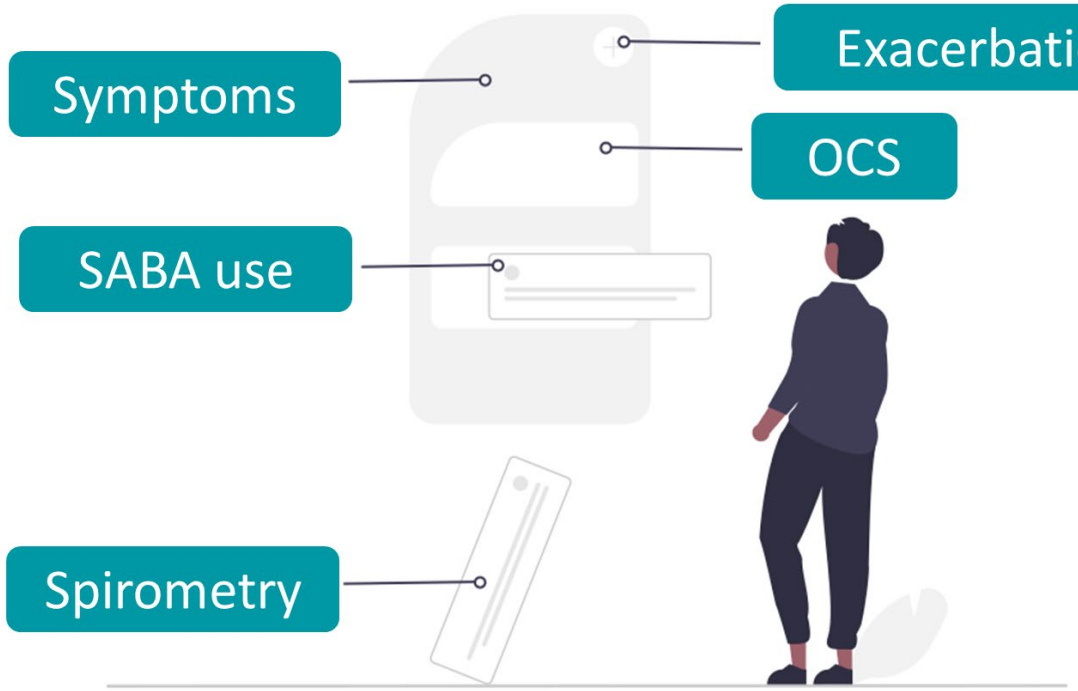
Multiple definitions used since



OCS, oral corticosteroid; **SABA**, short-acting beta-agonist

Multiple definitions used since

Different questionnaires



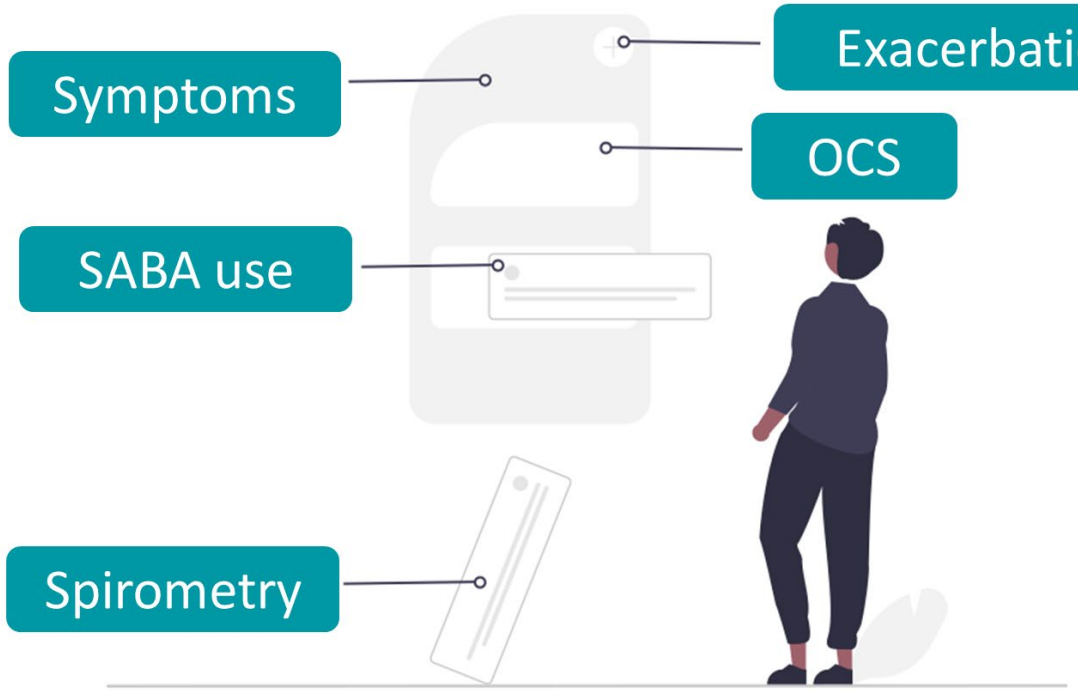
Different thresholds

Normal or “optimised”?

OCS, oral corticosteroid; **SABA**, short-acting beta-agonist

Multiple definitions used since

Different questionnaires



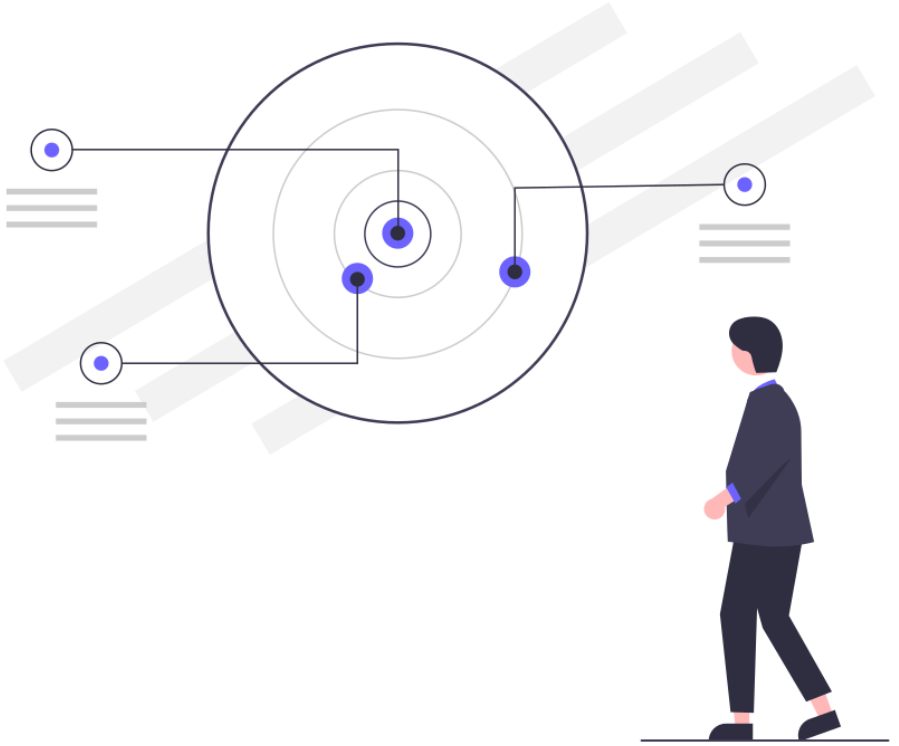
Different thresholds

Normal or “optimised”?

What about other measures?

OCS, oral corticosteroid; **SABA**, short-acting beta-agonist

How realistic is remission as a goal?



With a monoclonal antibody?

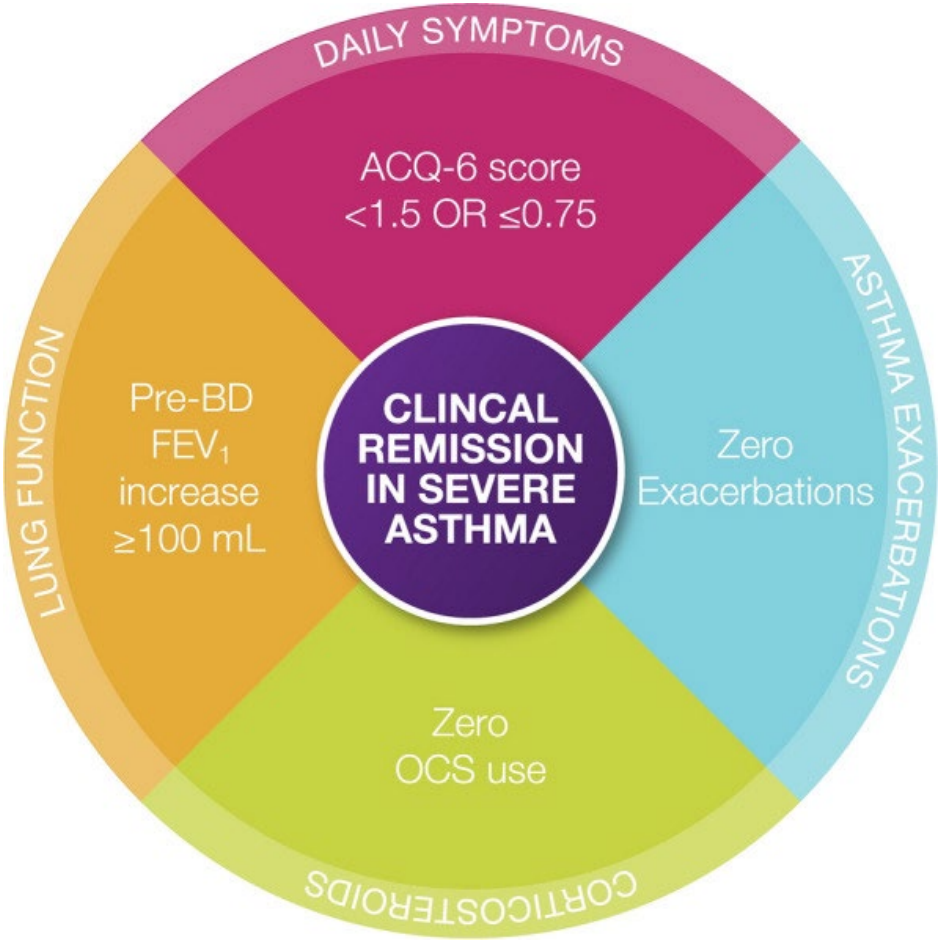


Image from Menzies-Gow et al. 2022.
Attribution-Non-Commercial 4.0 International (CC BY-NC 4.0)

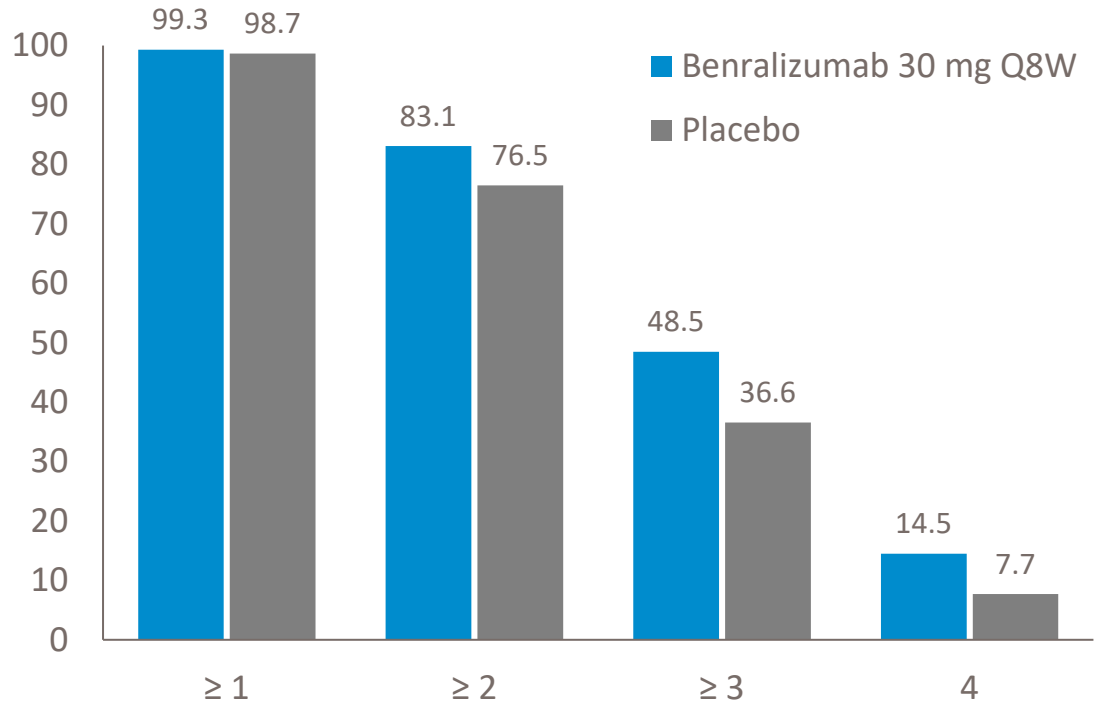
ACQ-6, 6-item Asthma Control Questionnaire; **BD**, bronchodilator; **FEV_1**, forced expiratory volume in 1 second; **OCS**, oral corticosteroid

Menzies-Gow A, et al. Adv Ther. 2022;39(5):2065-84.

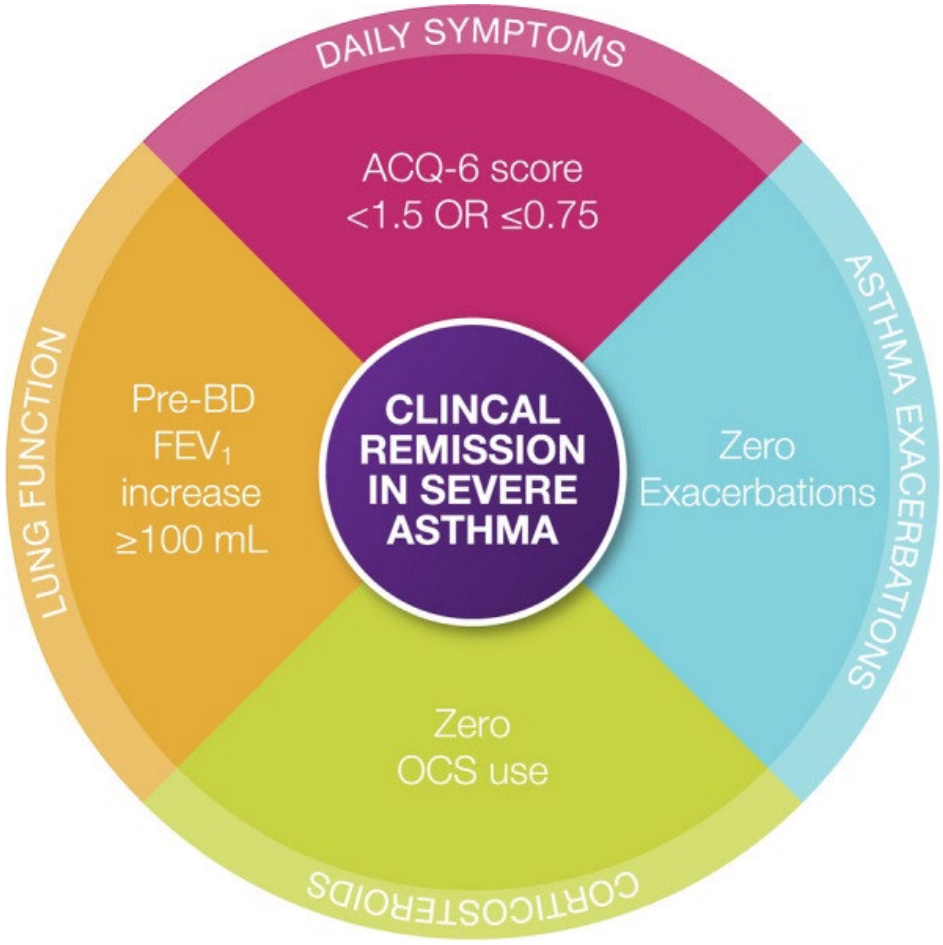
With a monoclonal antibody?

Proportion of patients in SIROCCO/CALIMA studies achieving given number of remission components

Adapted from Menzies-Gow et al. 2022



n	582	612	487	474	284	227	85	48
Total patients (N)	586	620	586	620	586	620	586	620

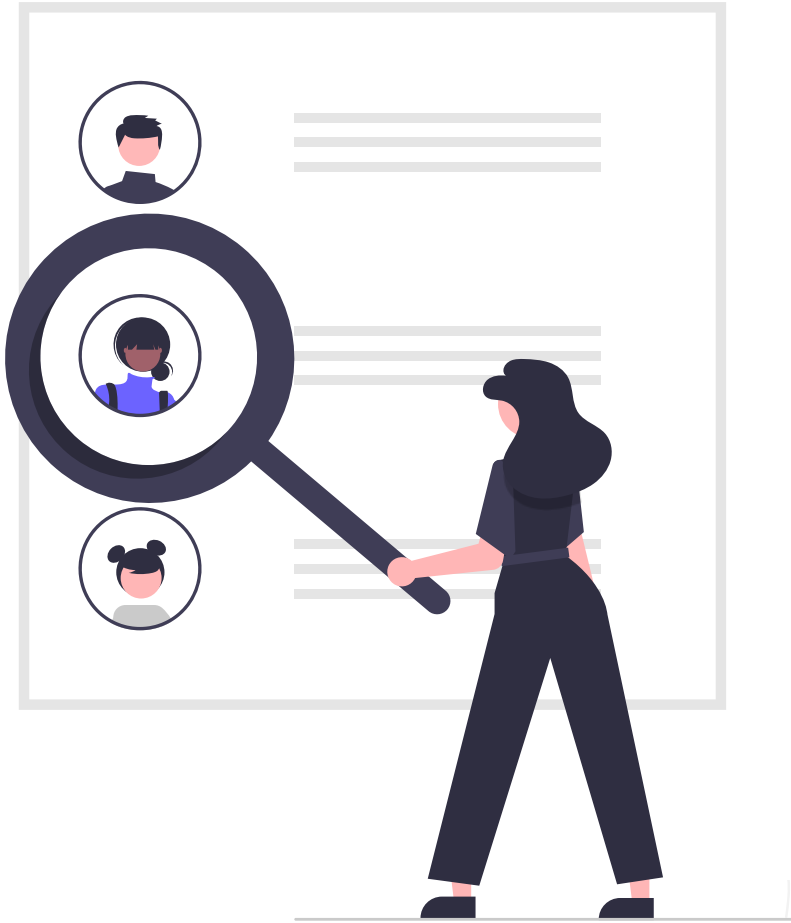


ACQ-6, 6-item Asthma Control Questionnaire; **BD**, bronchodilator; **FEV_1**, forced expiratory volume in 1 second; **OCS**, oral corticosteroid; **Q8W**; once every 8 weeks

Menzies-Gow A, et al. Adv Ther. 2022;39(5):2065-84.

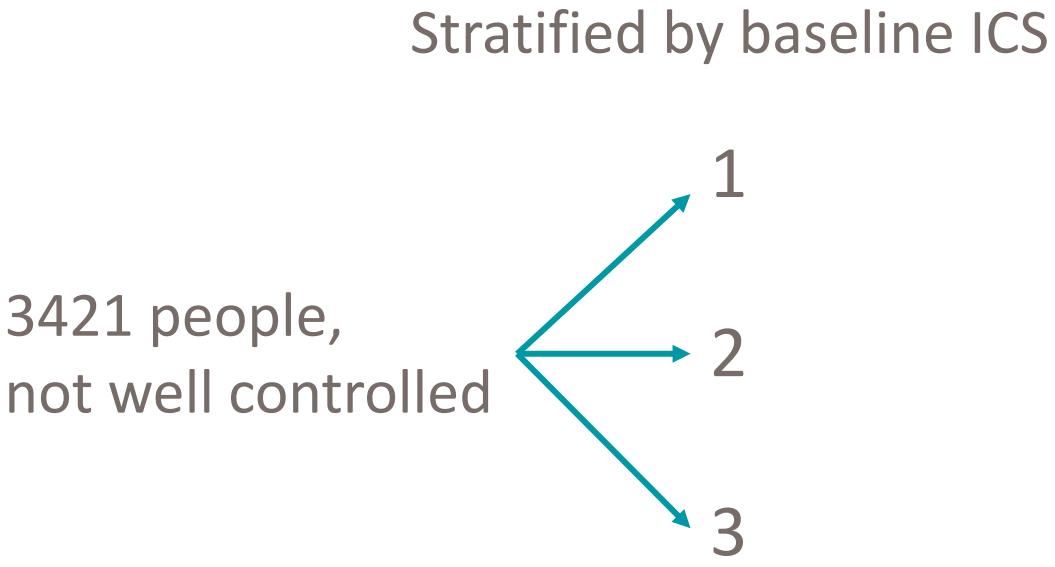
Perhaps difficult to treat asthma is the wrong place to start

- Disease type
- Disease duration
- Treatment effects
- Comorbidities
- Behaviours
- Environment/occupation



Pavord ID, et al. Lancet. 2018;391(10118):350-400.

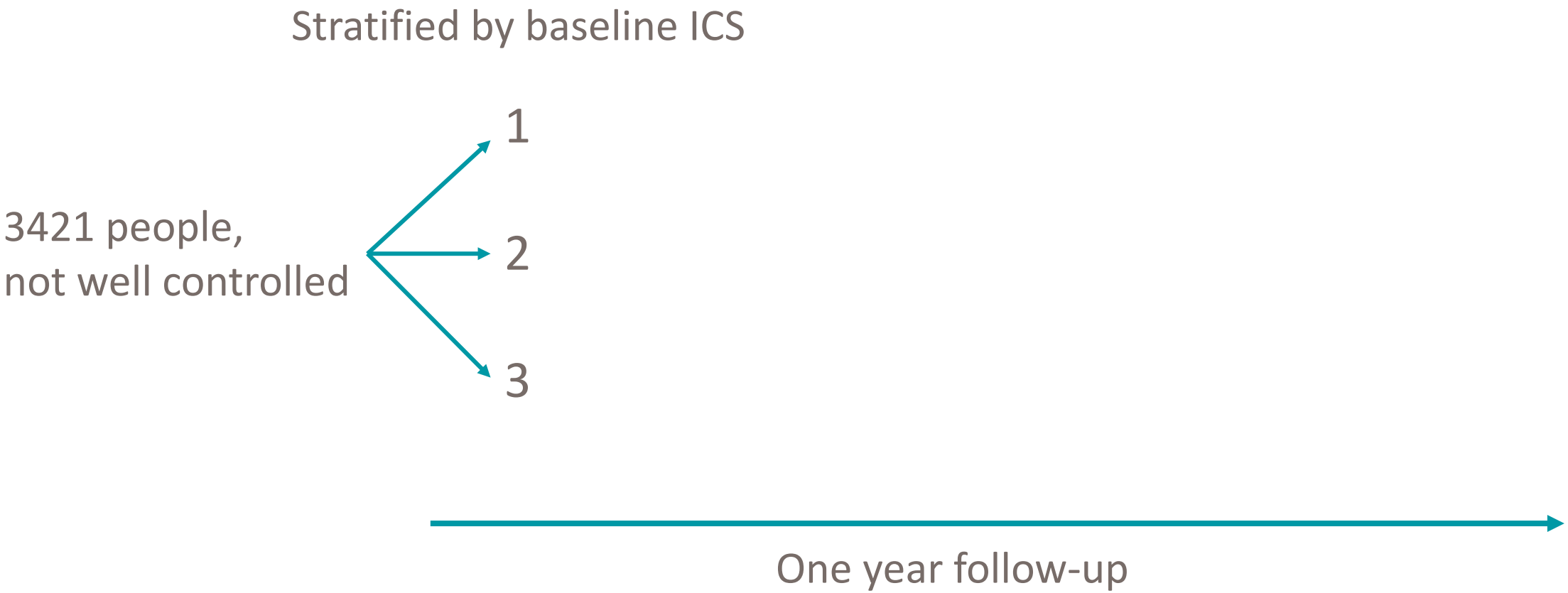
With inhaled therapy?



ICS, Inhaled corticosteroid

Bateman ED, et al. Am J Respir Crit Care Med. 2004;170(8):836-44.

With inhaled therapy?



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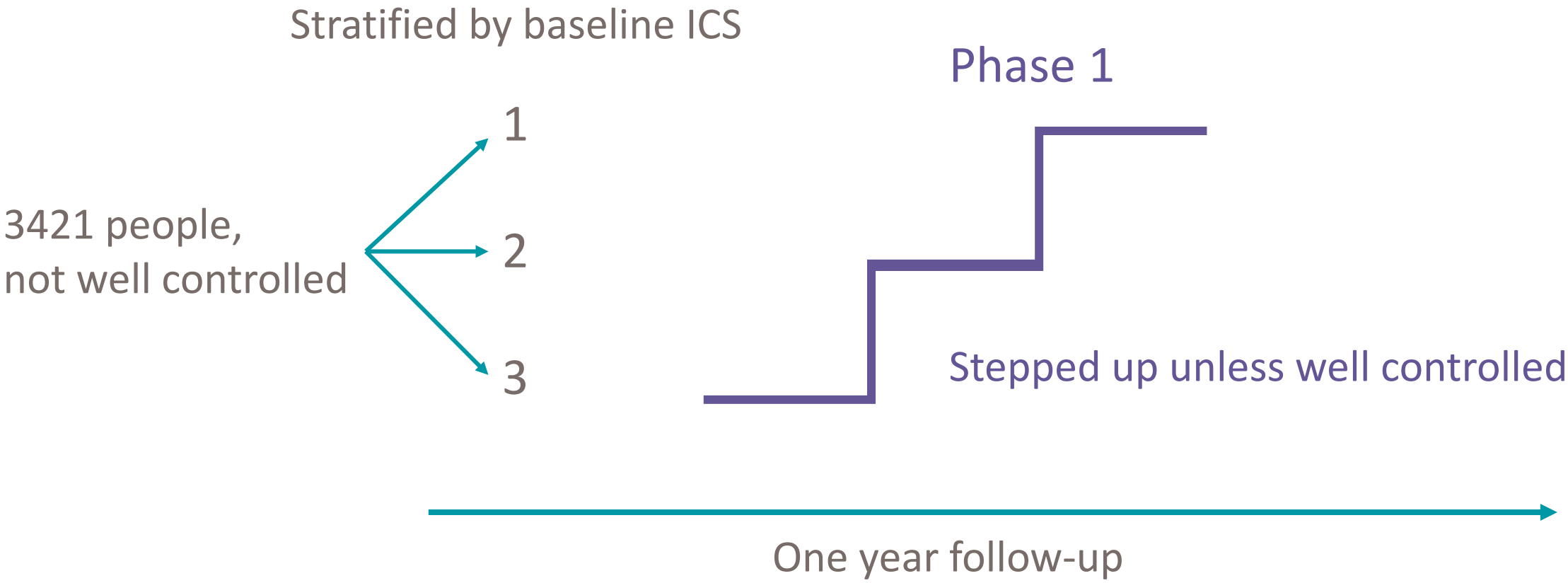
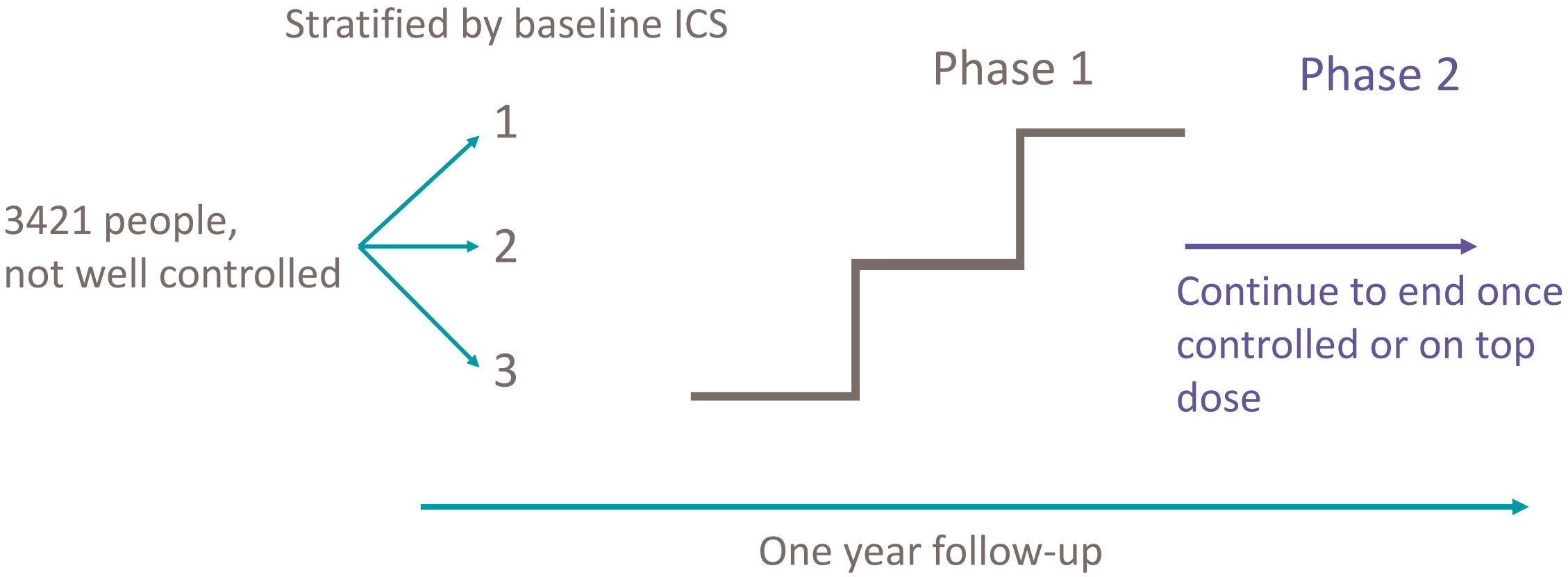
With inhaled therapy?



ICS, Inhaled corticosteroid

Bateman ED, et al. Am J Respir Crit Care Med. 2004;170(8):836-44.

With inhaled therapy?



ICS, Inhaled corticosteroid

Bateman ED, et al. Am J Respir Crit Care Med. 2004;170(8):836-44.

With inhaled therapy?

"Total control"

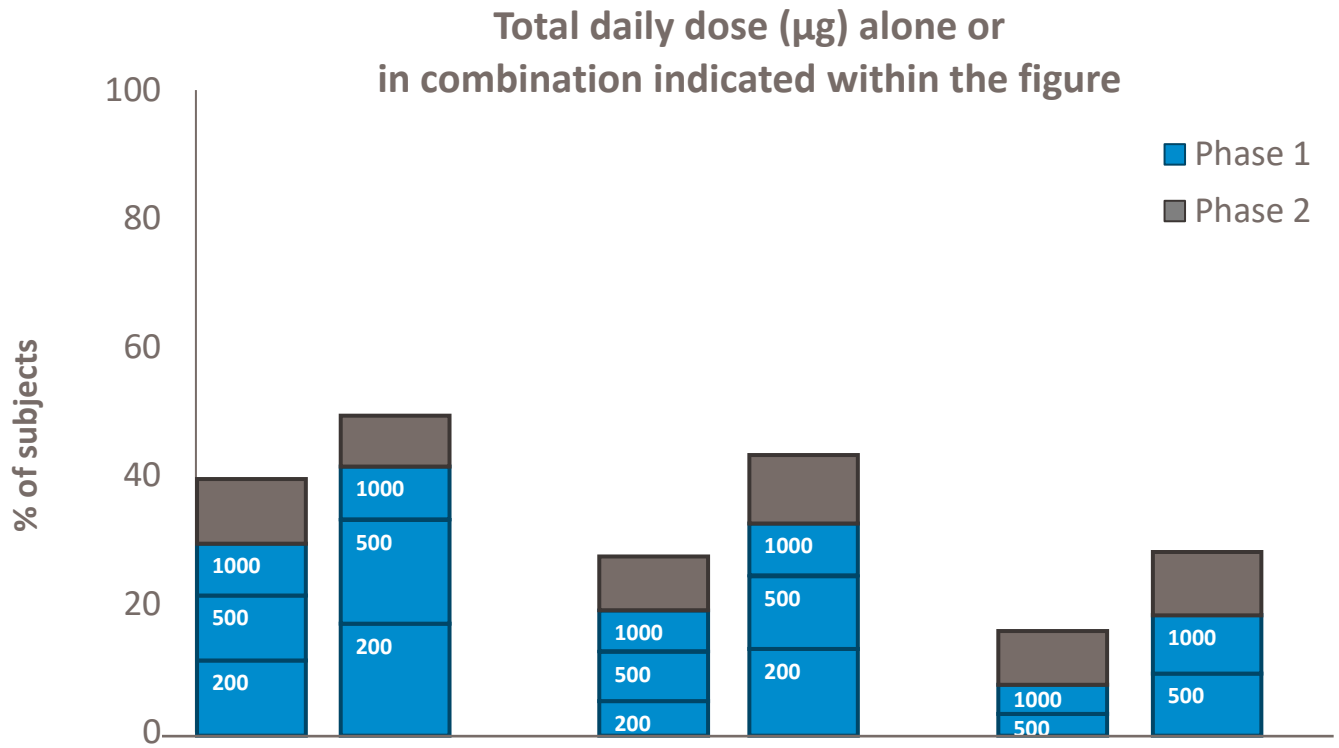
No symptoms day or night

No SABA use

PEF > 80% predicted

No exacerbations

Adapted from Bateman et al. 2004



Stratum	1		2		3	
Treatment group (n*)	FP (544)	SFC (539)	FP (577)	SFC (583)	FP (567)	SFC (568)
ICS use in previous 6 months	No ICS		BDP 500 µg/day		BDP > 500 – ≤ 1000 µg/day	

ICS, Inhaled corticosteroid; **BDP**, beclomethasone dipropionate; **SABA**, short-acting beta-agonist; **PEF**, peak expiratory flow; **SFC**, salmeterol/fluticasone combination; **FP**, fluticasone propionate

Bateman ED, et al. Am J Respir Crit Care Med. 2004;170(8):836-44.

If we can do that with an older combination, what about…

- Maintenance and reliever LABA-ICS?
- Single inhaler triple therapy?
- Earlier use of biologics or azithromycin?
- Treatable traits approach?
- Newer products in late phase trials?

……in moderate asthma.

(a question for you to ponder, not encouragement to use products outside their indications)

ICS, Inhaled corticosteroid; **LABA**, long-acting beta agonist

We can’t leave patients out of this process

1. Harvey DJR, Gardiner D. BJA Educ. 2019;19(3):68-73. 2. Farr RS. J Allergy Clin Immunol. 1999;103(1 Pt 1):29-35.

Summary

- We need to take action in asthma
- We should set standards higher
- Aiming for remission may activate stakeholders
- There is plenty of work to be done in this area, but progress is being made

ASPIRE

SHARING BEST PRACTICE AND
ENRICHING EXCELLENCE

Biologic agents in severe asthma, how to choose and when to switch?

Prof. Peter Wark

Alfred Health

Conjoint Professor Monash University, Melbourne AUSTRALIA

Adjunct Professor University of Newcastle, affiliate Immune Health, HMRI.

Honorary Consultant HNE LHD

RESPIRATORY
ADVENT
ADVANCES IN
TYPE 2 INFLAMMATORY DISEASES

Disclosures

Requested to speak and will receive an honorarium at this Sanofi sponsored symposium

Employee NSW health

Spoken or organised meetings sponsored by: Astra Zeneca, GSK, Boehringer Ingelheim, Mundipharma, Menarini, Novartis, CSL, Chiesi, Sanofi, Vertex.

Advisory boards; Astra Zeneca, Boehringer, Novartis, Sanofi, Vertex. PBAC Australia.

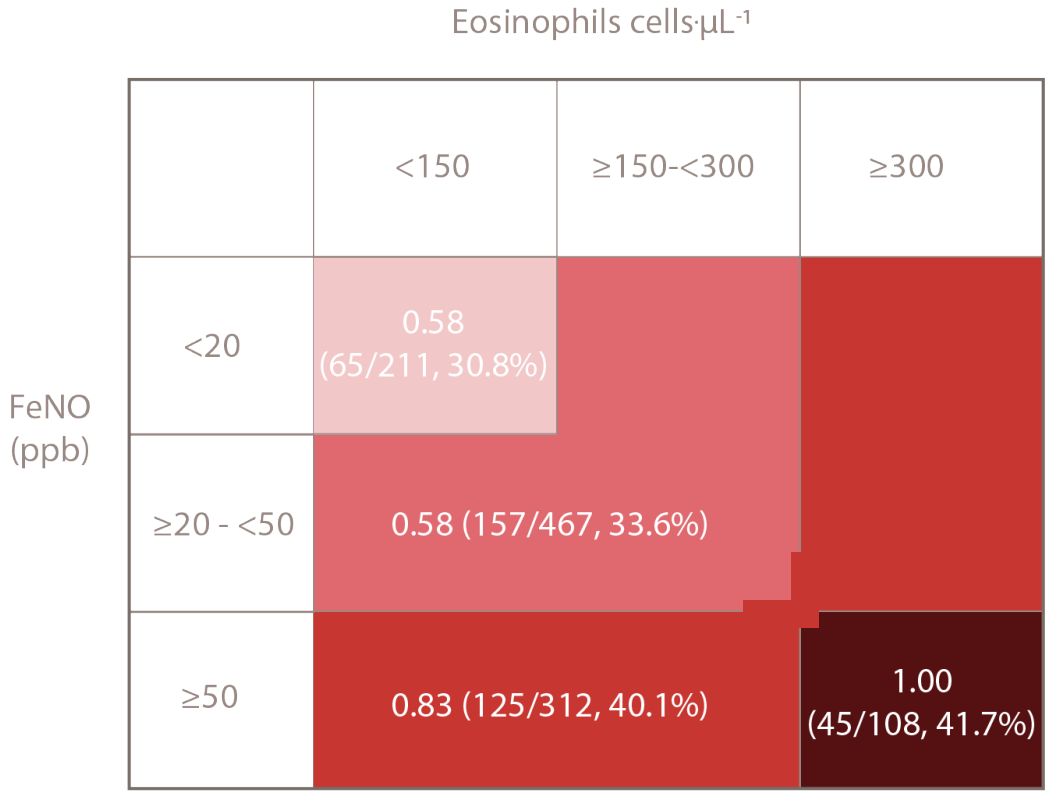
Severe asthma, refractory type 2 airway inflammation and the role of biologic therapy

Patient characteristics, biomarkers and exacerbation risk in severe, uncontrolled asthma

- Seven phase 2/3 randomised controlled trials of moderate to severe asthma
- All had medium-high ICS + LABA,
- Assessed annual exacerbations
- 48–56 weeks

AAERs by eosinophil and FeNO subgroups

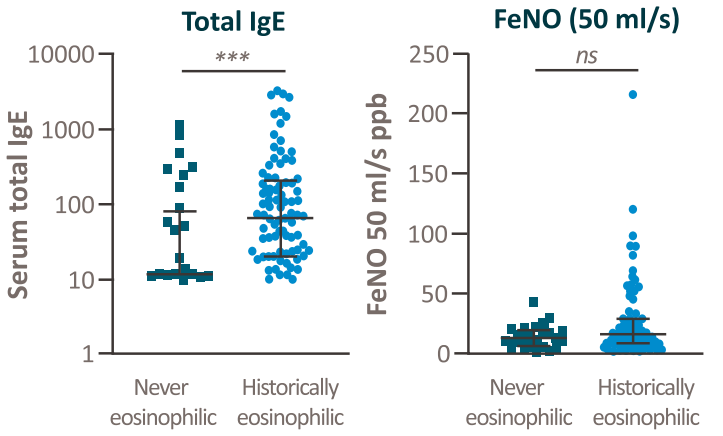
Image adapted from Kraft M, et al. 2021.

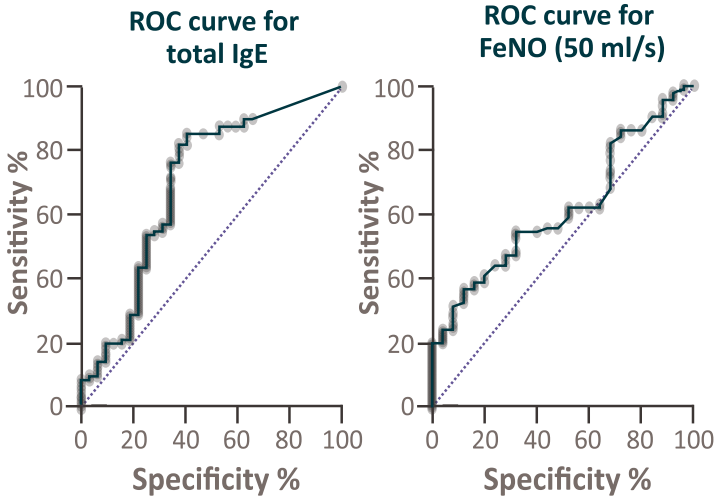


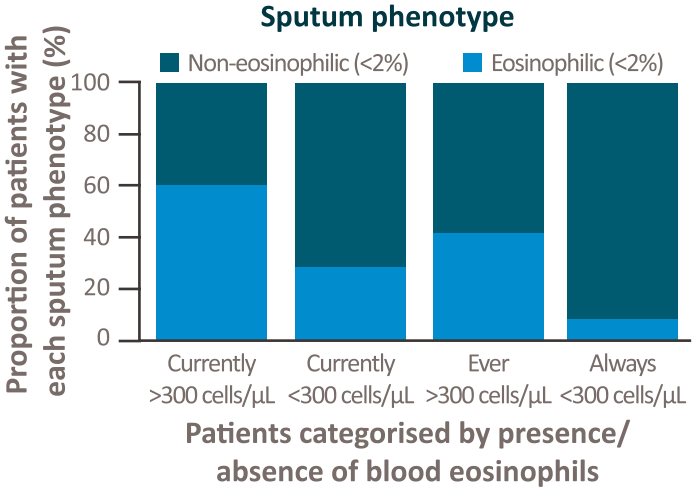
ICS, inhaled corticosteroid; **LABA**: long-acting beta agonist; **FeNO**, fractional exhaled nitric oxide; **RCT**, randomised controlled trial; **ppb**, parts per billion; **CI**, confidence interval; **AAER**, annual asthma exacerbation rate
Kraft M, et al. Eur Respir J. 2021;58(6).

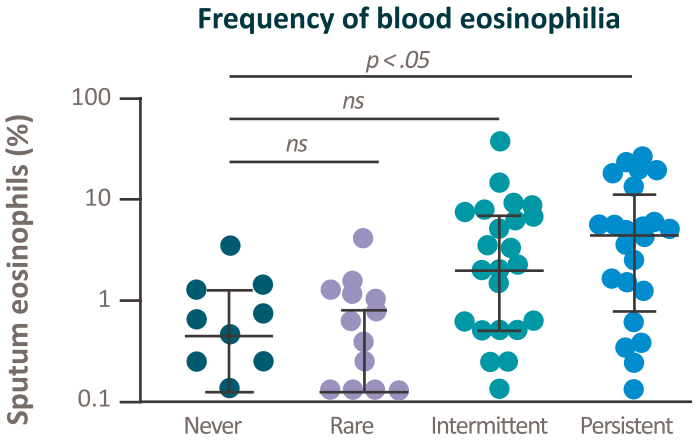
How many really have type two inflammation in a severe asthma clinic? The Wessex Asthma Cohort

- 235 severe asthma, biologic naïve
- How many had blood eosinophilia ≥ 300 cells/µL?
- At baseline
  - 40.3% had eosinophilia
  - Further 43% were eosinophilic in the previous decade
- Persistent eosinophilia, more airflow obstruction and higher FeNO









Images adapted from Azim et al. 2021.

FeNO, fractional exhaled nitric oxide; **ROC**, Receiver Operating Characteristic; **IgE**, immunoglobulin E

Azim A, et al. Clin Exp Allergy. 2021;51(6):811-20.

***p<0.001, ns – not significant

Anti-IL-5 (mepolizumab, benralizumab, reslizumab) for severe asthma

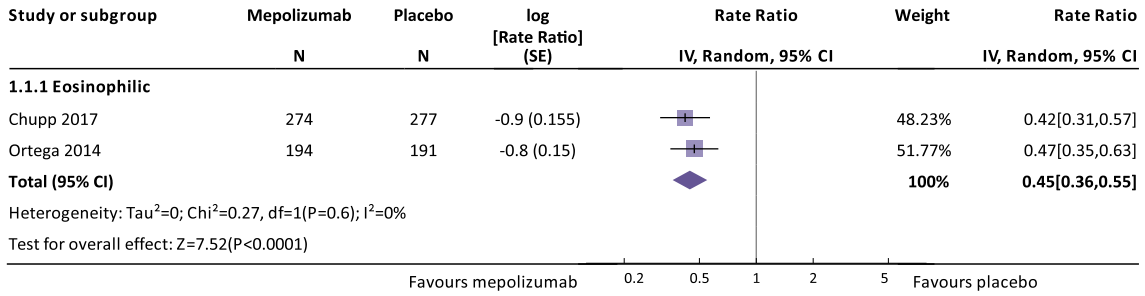
- Studies
  - N=13 studies, 6000 participants
  - 8 trials > 12 yrs
  - 4 mepolizumab, 5 benralizumab, 4 reslizumab
  - 24 to 32 weeks
- Mepolizumab trials
  - Blood eosinophils > 150 μL at randomisation and 300 μL in the last 12 months
  - FEV_1 < 80% predicted
  - Fluticasone > 500 μg + LABA
  - 2 exacerbations needing OCS > 3 d

LABA, long-acting beta agonist; **OCS**, oral corticosteroid; **FEV_1**, forced expiratory volume in 1 second
Farne et al Cochrane Database Syst Rev 2017 Sep 21;9(9):CD010834.

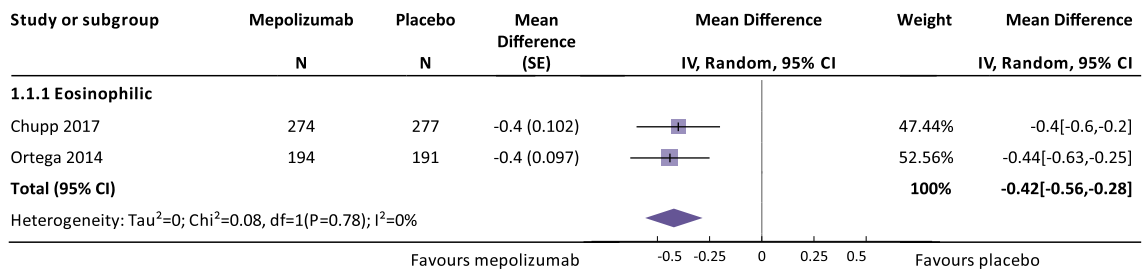
Mepolizumab

- Exacerbations requiring OCS OR 0.45 (95% CI 0.36 to 0.55)
- ED visits, OR 0.36 (95% CI 0.20 to 0.66)

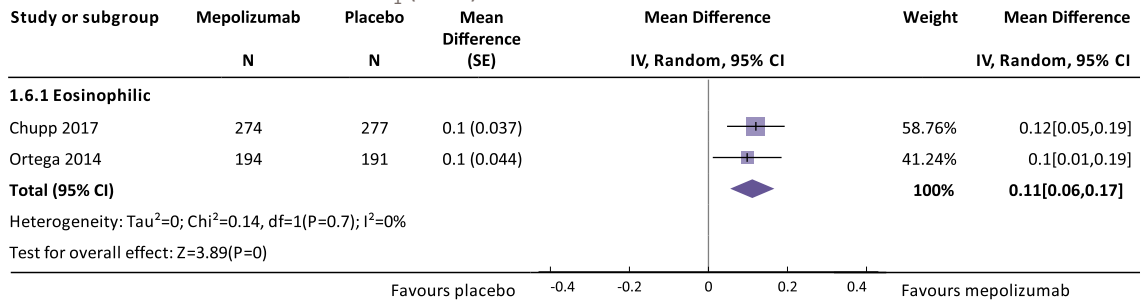
Comparison 1: Mepolizumab (SC) versus placebo
Outcome 1: Rate of exacerbations requiring systemic corticosteroids



Comparison 1: Mepolizumab (SC) versus placebo
Outcome 4: Health-related quality of life



Comparison 1: Mepolizumab (SC) versus placebo
Outcome 6: Pre-bronchodilator FEV_1 (litres)



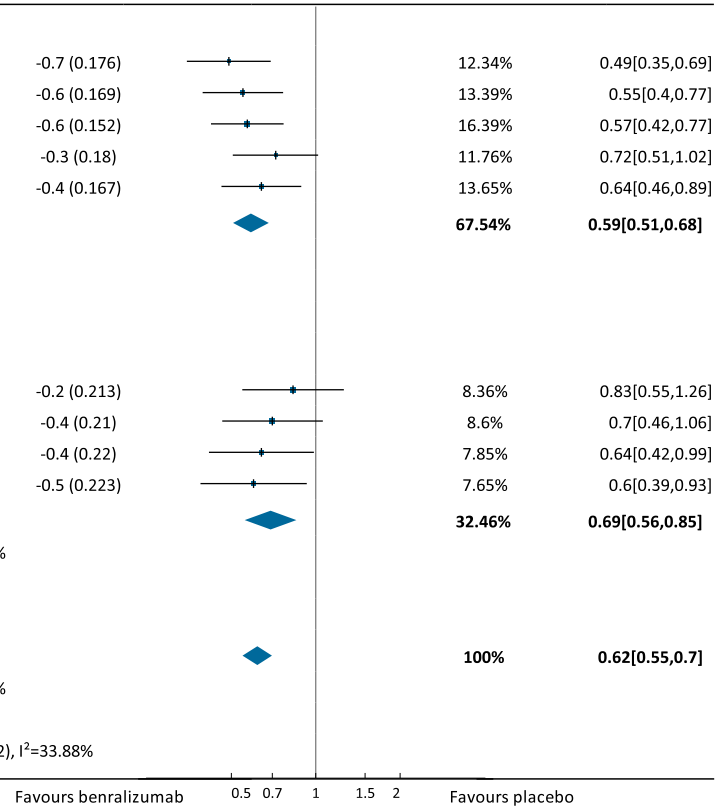
LABA, long-acting beta agonist; **OCS**, oral corticosteroid; **FEV_1**, forced expiratory volume in 1 second
Farne et al Cochrane Database Syst Rev 2017 Sep 21;9(9):CD010834.

Image adapted from Farne et al. 2017

Benralizumab

Comparison 4: Benralizumab (SC) versus placebo
Outcome 1: Rate of exacerbations requiring systemic corticosteroids

Study or subgroup	Benralizumab N	Placebo N	Log [Rate Ratio] (SE)	Rate Ratio IV, Fixed, 95% CI	Weight	Rate Ratio IV, Fixed, 95% CI
4.1.1 Eosinophilic						
Bleecker 2016	275	133	-0.7 (0.176)		12.34%	0.49[0.35,0.69]
Bleecker 2016	275	134	-0.6 (0.169)		13.39%	0.55[0.4,0.77]
Castro 2014a	70	83	-0.6 (0.152)		16.39%	0.57[0.42,0.77]
FitzGerald 2016	239	124	-0.3 (0.18)		11.76%	0.72[0.51,1.02]
FitzGerald 2016	241	124	-0.4 (0.167)		13.65%	0.64[0.46,0.89]
Subtotal (95% CI)					**67.54%**	**0.59[0.51,0.68]**
Heterogeneity: Tau^2=0; Chi^2=2.8, df=4(P=0.59); I^2=0%						
Test for overall effect: Z=7.1(P<0.0001)						
4.1.2 Non-eosinophilic						
Bleecker 2016	131	70	-0.2 (0.213)		8.36%	0.83[0.55,1.26]
Bleecker 2016	124	70	-0.4 (0.21)		8.6%	0.7[0.46,1.06]
FitzGerald 2016	116	61	-0.4 (0.22)		7.85%	0.64[0.42,0.99]
FitzGerald 2016	125	61	-0.5 (0.223)		7.65%	0.6[0.39,0.93]
Subtotal (95% CI)					**32.46%**	**0.69[0.56,0.85]**
Heterogeneity: Tau^2=0; Chi^2=1.27, df=3(P=0.74); I^2=0%						
Test for overall effect: Z=3.43(P=0)						
Total (95% CI)					**100%**	**0.62[0.55,0.7]**
Heterogeneity: Tau^2=0; Chi^2=5.58, df=8(P=0.69); I^2=0%						
Test for overall effect: Z=7.79(P<0.0001)						
Test for subgroup differences: Chi^2=1.51, df=1 (P=0.22), I^2=33.88%						



Comparison 4: Benralizumab (SC) versus placebo
Outcome 4: Health-related quality of life (ACQ mean difference)

Study or subgroup	Benralizumab N	Placebo N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
4.4.1 Eosinophilic						
Bleecker 2016	263	133	-0.3 (0.119)		15.38%	-0.29[-0.52,-0.06]
Bleecker 2016	274	134	-0.1 (0.119)		15.35%	-0.15[-0.38,0.08]
Castro 2014a	35	38	-0.4 (0.246)		3.58%	-0.44[-0.92,0.04]
FitzGerald 2016	239	123	-0.2 (0.112)		17.18%	-0.25[-0.47,-0.03]
FitzGerald 2016	241	124	-0.2 (0.112)		17.24%	-0.19[-0.41,0.03]
Subtotal (95% CI)					**68.72%**	**-0.23[-0.34,-0.12]**
Heterogeneity: Tau^2=0; Chi^2=1.6, df=4(P=0.81); I^2=0%						
Test for overall effect: Z=4.12(P<0.0001)						
4.4.2 Non-eosinophilic						
Bleecker 2016	130	69	-0.2 (0.168)		7.68%	-0.22[-0.55,0.11]
Bleecker 2016	124	69	0 (0.167)		7.75%	0[-0.33,0.33]
FitzGerald 2016	116	61	-0.2 (0.168)		7.68%	-0.24[-0.57,0.09]
FitzGerald 2016	125	61	-0.1 (0.163)		8.17%	-0.1[-0.42,0.22]
Subtotal (95% CI)					**31.28%**	**-0.14[-0.3,0.02]**
Heterogeneity: Tau^2=0; Chi^2=1.34, df=3(P=0.72); I^2=0%						
Test for overall effect: Z=1.67(P=0.09)						
Total (95% CI)					**100%**	**-0.2[-0.29,-0.11]**
Heterogeneity: Tau^2=0; Chi^2=3.79, df=8(P=0.88); I^2=0%						
Test for overall effect: Z=4.35(P<0.0001)						
Test for subgroup differences: Chi^2=0.85, df=1 (P=0.36), I^2=0%						

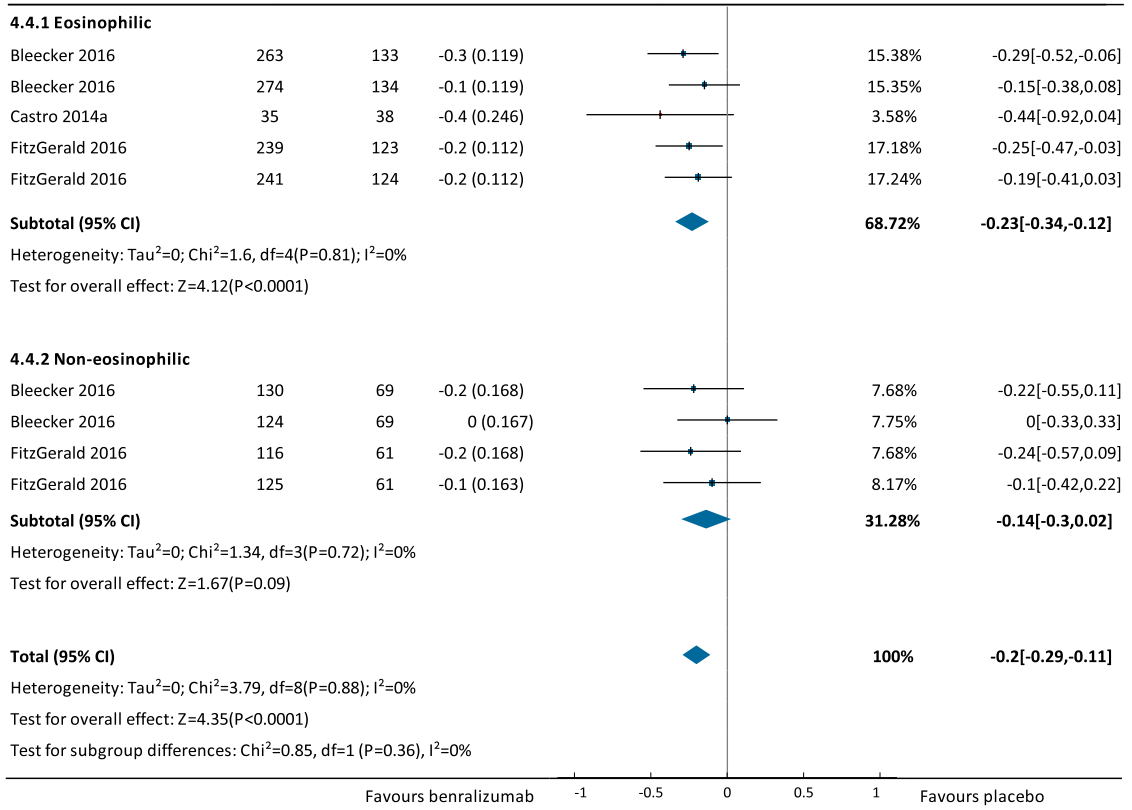


Image adapted from Farne et al. 2017

LABA, long-acting beta agonist; **OCS**, oral corticosteroid; **FEV_1**, forced expiratory volume in 1 second; **IL-5**, interleukin 5; **SC**, subcutaneous; **IV**, intravenous; **OR**, odds ratio; **CI**, confidence interval; **SE**, standard error; **ACQ**; asthma control questionnaire

Farne et al Cochrane Database Syst Rev 2017 Sep 21;9(9):CD010834.

Response to mepolizumab, stratified by baseline blood eosinophils

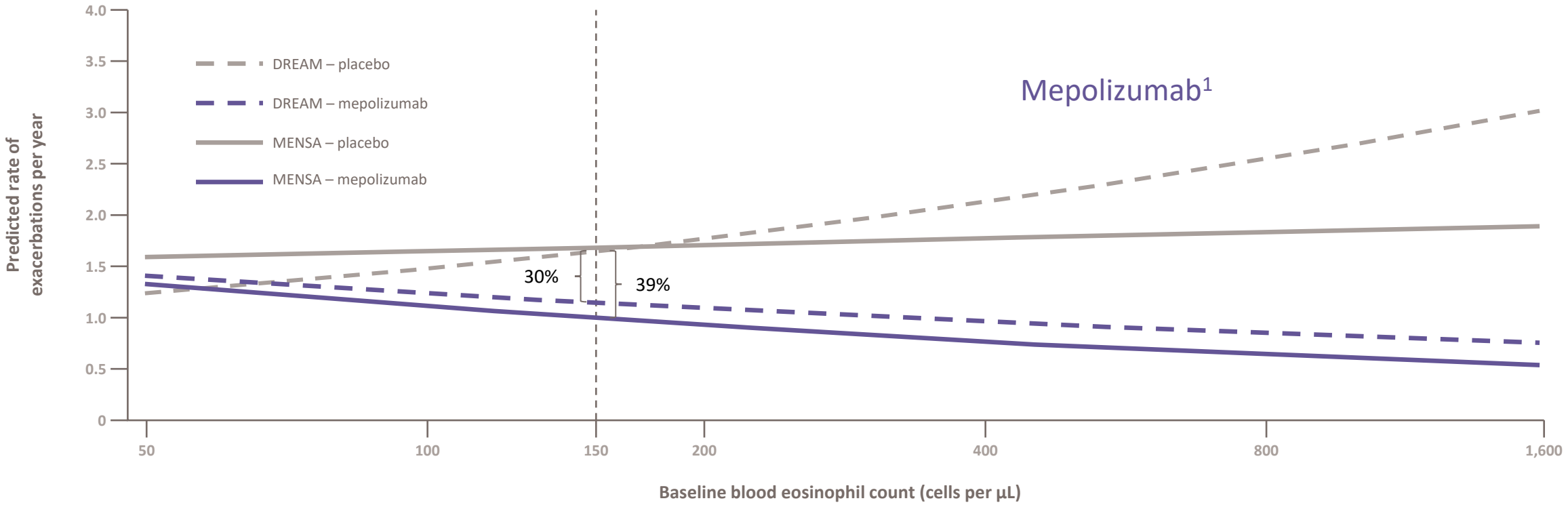


Image adapted from: Ortega et al., 2016

Ortega et al., Lancet Respir Med. 2016 Jul;4(7):549-556.

Sustained response to benralizumab

At least 75% of patients on Q8W* had zero exacerbations per year
59% of patients had zero exacerbations during the extension studies (up to 4 years)

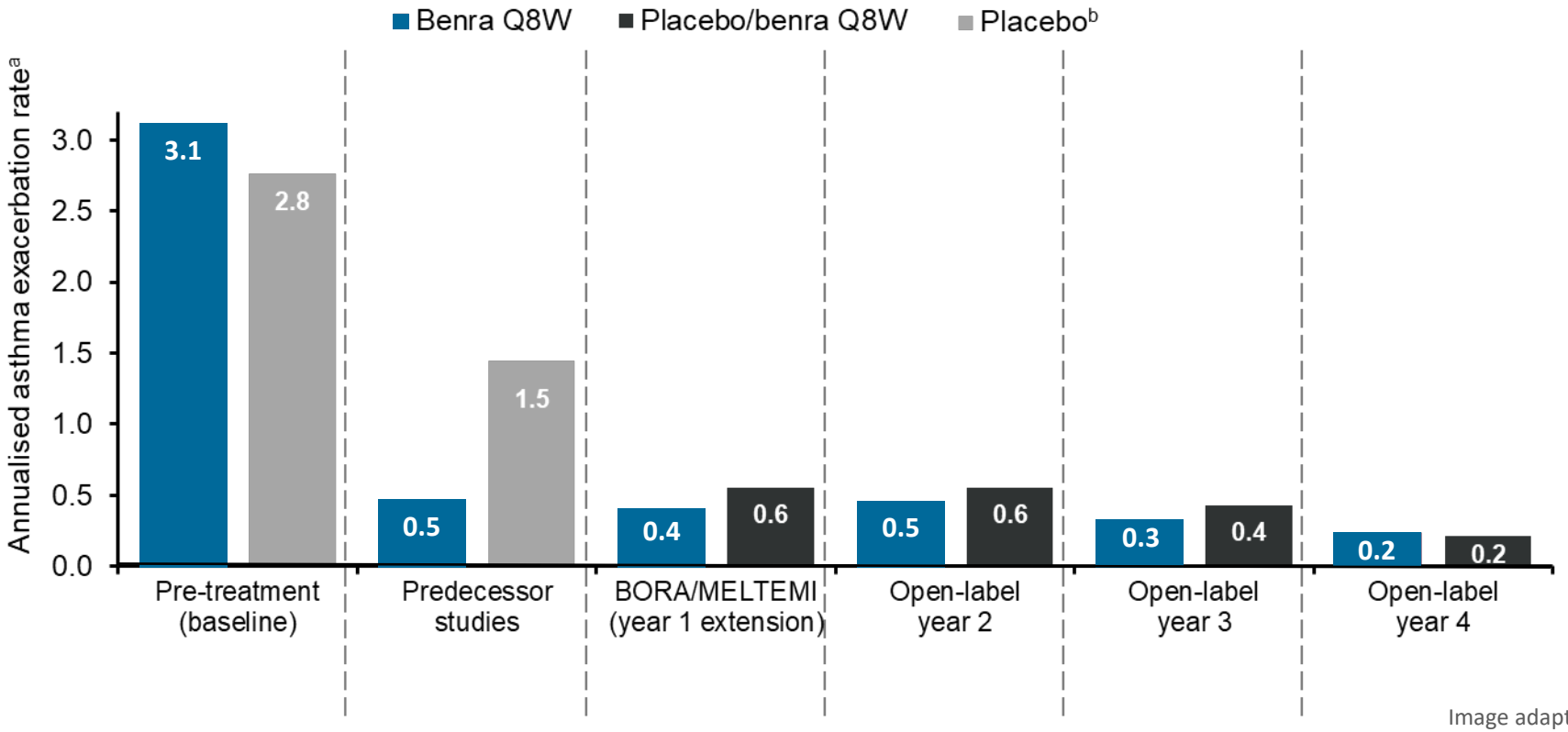


Image adapted from Korn S, et al. 2021

[a]Annual exacerbation rate defined as 365.25 x total number of exacerbations/total duration of on-treatment follow-up within the treatment group and time interval (days).
[b]Placebo includes N=49 patients in the placebo/benra Q4W group and N=42 patients in the placebo/benra Q8W group during the extension studies (BORA and MELTEMI).
*First 3 doses Q4W. Q8W, every 8 weeks; Q4W, every 4 weeks.

Korn S, et al. J Allergy Clin Immunol Pract. 2021;9(12):4381-92.e4.

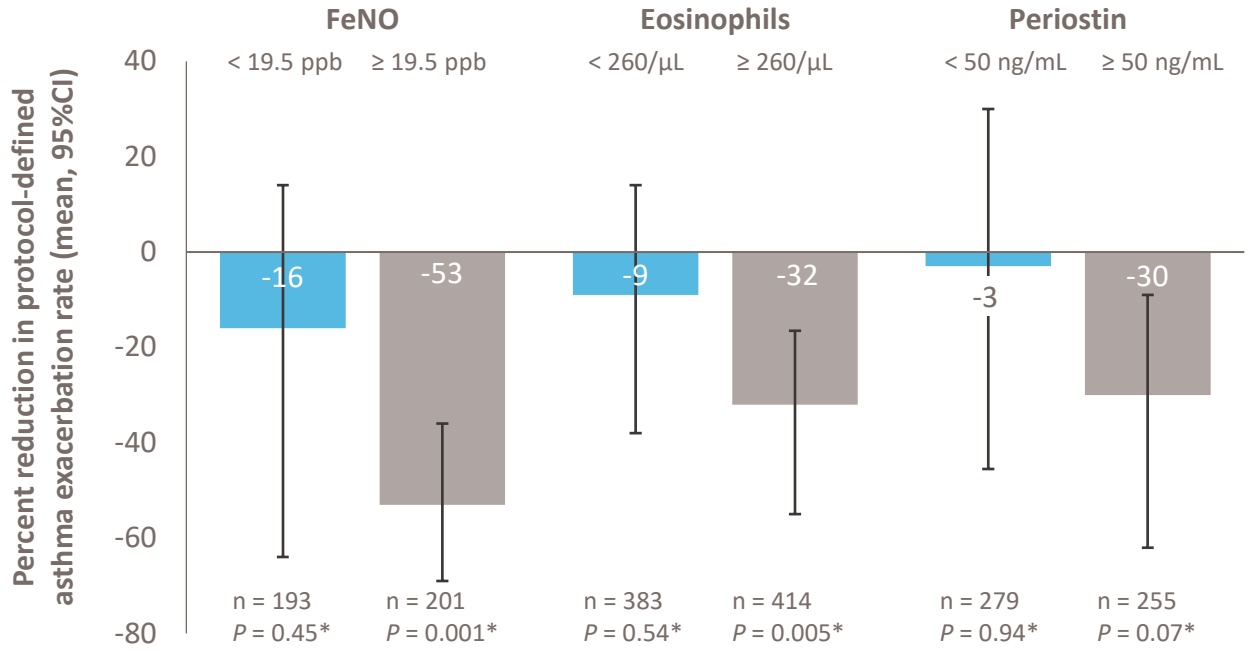
Who benefits most from omalizumab?

Allergic moderate to severe asthmatics n=850[1]

- Th2 persistent inflammation, high FeNO, blood EOS or blood periostin

Non-allergic severe asthma; n=41[2]

- Improved lung function
- No reduction in exacerbations



Exacerbation rates

	Low FeNO at baseline	High FeNO at baseline	Low eosinophils at baseline	High eosinophils at baseline	Low periostin at baseline	High periostin at baseline
Omalizumab	0.60	0.50	0.65	0.70	0.73	0.66
Placebo	0.71	1.07	0.72	1.03	0.72	0.93

Exacerbation reduction P values; omalizumab vs placebo in each biomarker subgroup

Image adapted from: Hanania et al. 2013.

FeNO, fraction of exhaled nitric oxide; CI, confidence interval; EOS, eosinophils

1. Hanania et al., Am J Respir Crit Care Med. 2013;187(8):804-11; **2.** Garcia et al., Chest. 2013 144(2):411–419.

Australian Xolair registry

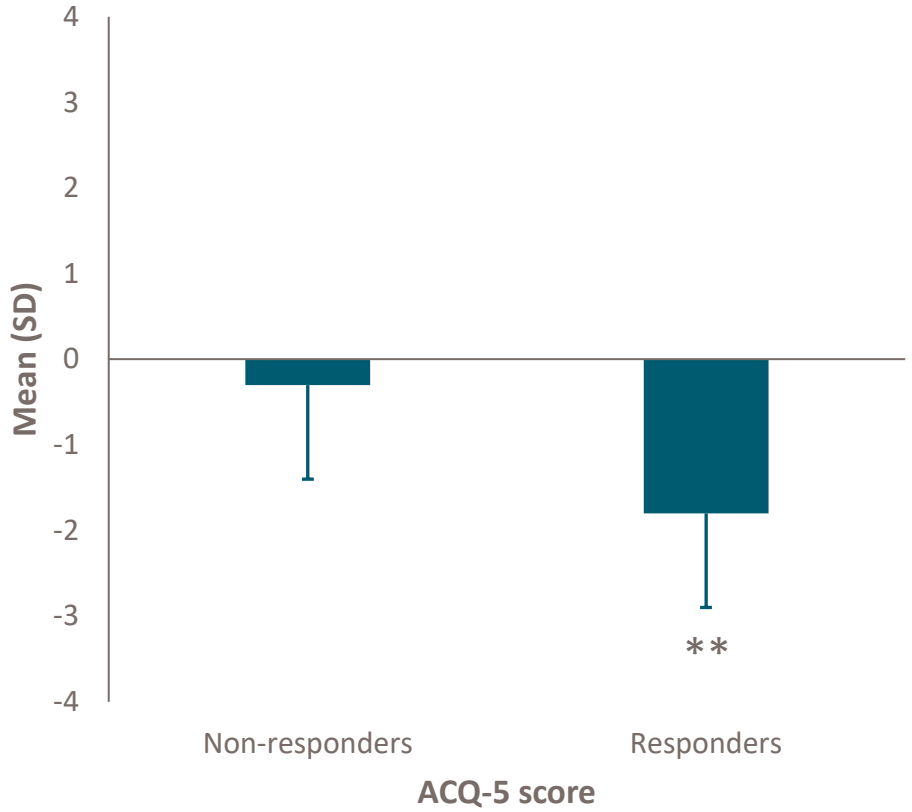
180 patients approved assessed after 6 months

Characteristics:

- Mean age 51.4 (range 12-85)
- Mean FEV_1pp 64 (SD 21%)
- 52% on regular OCS, median 10 mg/d

Response:

- 83% responded (PBS)
- Mean ACQ-5 fell from 3.5 to 2 ($p < 0.001$)
- 19% ACQ < 0.75
- 22/80 (27.5%) had a 25% reduction in OCS



Adapted from Gibson et al. 2016
**P < 0.0001

ACQ-5, 5-Item Asthma Control Questionnaire; **FEV_1pp**, forced expiratory volume in 1 second, percent predicted; **OCS**, oral corticosteroid; **PBS**, Pharmaceutical Benefits Scheme; **SD**, standard deviation
Gibson et al., Intern Med J. 2016 Sep;46(9):1054-62.

Dupilumab efficacy and safety in moderate to severe asthma

N=1902, > 12 years of age

FP > 500 µg/d + LABA

ACQ-5 > 1.5

X 1 exacerbation needing OCS

Exacerbations

- Placebo 0.87 (95% CI 0.72, 1.05)
- Dupilumab 200 mg; 0.46 (95% CI 0.39, 0.53)
- 47% reduction, p < 0.001

Dupilumab, 200 mg Every 2 Wk, vs. Matched Placebo

Subgroup	No. of Patients		Relative Risk vs. Placebo (95% CI)
	Placebo	Dupilumab	
Overall	317	631	0.52 (0.41–0.66)
Eosinophil count			
≥300 cells/mm^3	148	264	0.34 (0.24–0.48)
≥150 to <300 cells/mm^3	84	173	0.64 (0.41–1.02)
<150 cells/mm^3	85	193	0.93 (0.58–1.47)
FeNO			
≥50 ppb	71	119	0.31 (0.18–0.52)
≥25 to <50 ppb	91	180	0.39 (0.24–0.62)
<25 ppb	149	325	0.75 (0.54–1.05)

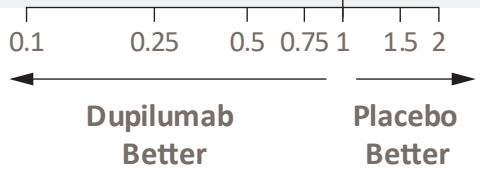


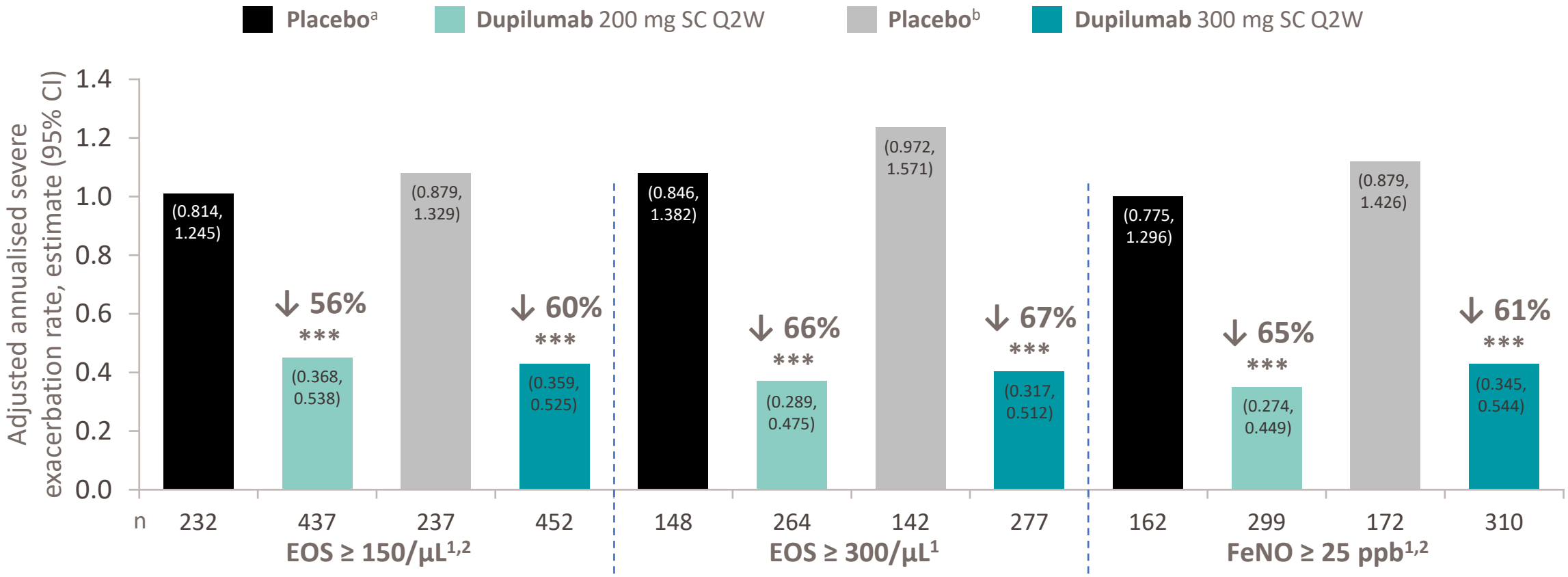
Image adapted from: Castro M, et al. 2018.

ACQ-5, 5-Item Asthma Control Questionnaire; **FDP**, fluticasone propionate; **OCS**, oral corticosteroid; **LABA**, long-acting beta agonist; **CI**, confidence interval.

Castro M, et al. N Engl J Med. 2018;378:2486–2496.

Exacerbation rates with dupilumab, an anti-IL-4Rα

Exacerbation rate



*** Reduction vs placebo, P < 0.001, 95% CI a,b: placebo + standard of care

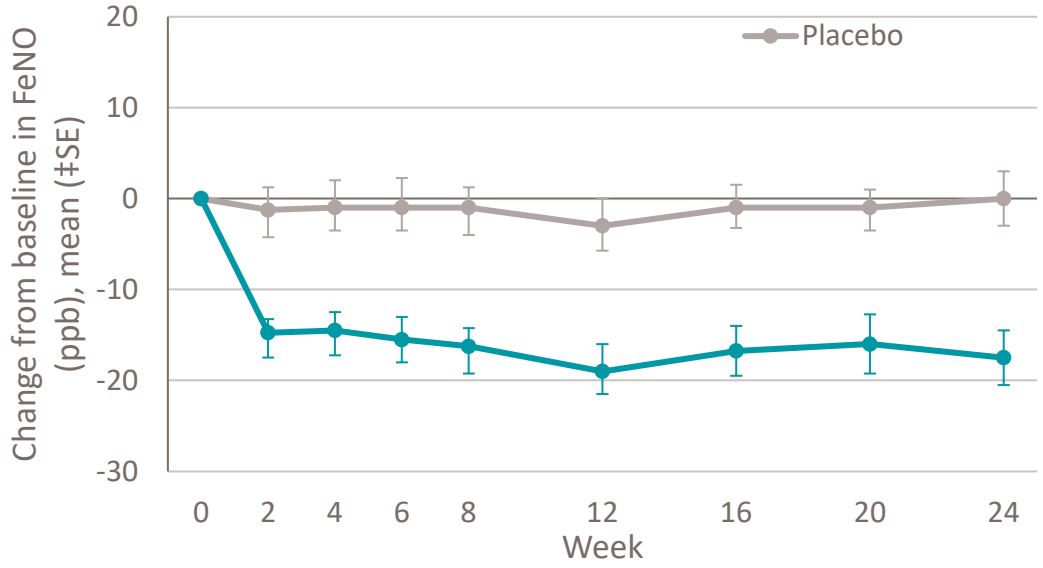
Image adapted from: Ford LB, et al. 2018 (poster).

IL-4Rα, interleukin 4 receptor alpha-subunit; **SC**, subcutaneous; **FeNO**, fractional exhaled nitric oxide; **ppb**, parts per billion; **EOS**, eosinophil; **CI**, confidence interval; **Q2W**, every 2 weeks; **RRR**, relative risk reduction; **SC**, standard of care

1. Castro M, et al. N Engl J Med. 2018;378:2486–2496. 2. Ford EB, et al. EAACI. 2018.

Dupilumab blocks IL-4/13 signalling and reduces FeNO in severe asthma

Change in FeNO (ppb) during 24-week treatment period*[1]



No. of patients									
Placebo	103	90	95	98	95	93	98	93	89
Dupilumab 300 mg q2w	101	90	90	92	93	83	91	86	88

*ITT population, exploratory analysis and data not controlled for multiplicity

Effect of dupilumab on blood eosinophil levels†[2,3]

- EOS increased from baseline at Week 4
  - Increase of 9.2% (4.3–14.3); P=0.001
- EOS returned to baseline by Week 24
- EOS fell below baseline by Week 52
  - −12.3% (−15.9 to −7.7); P=0.03

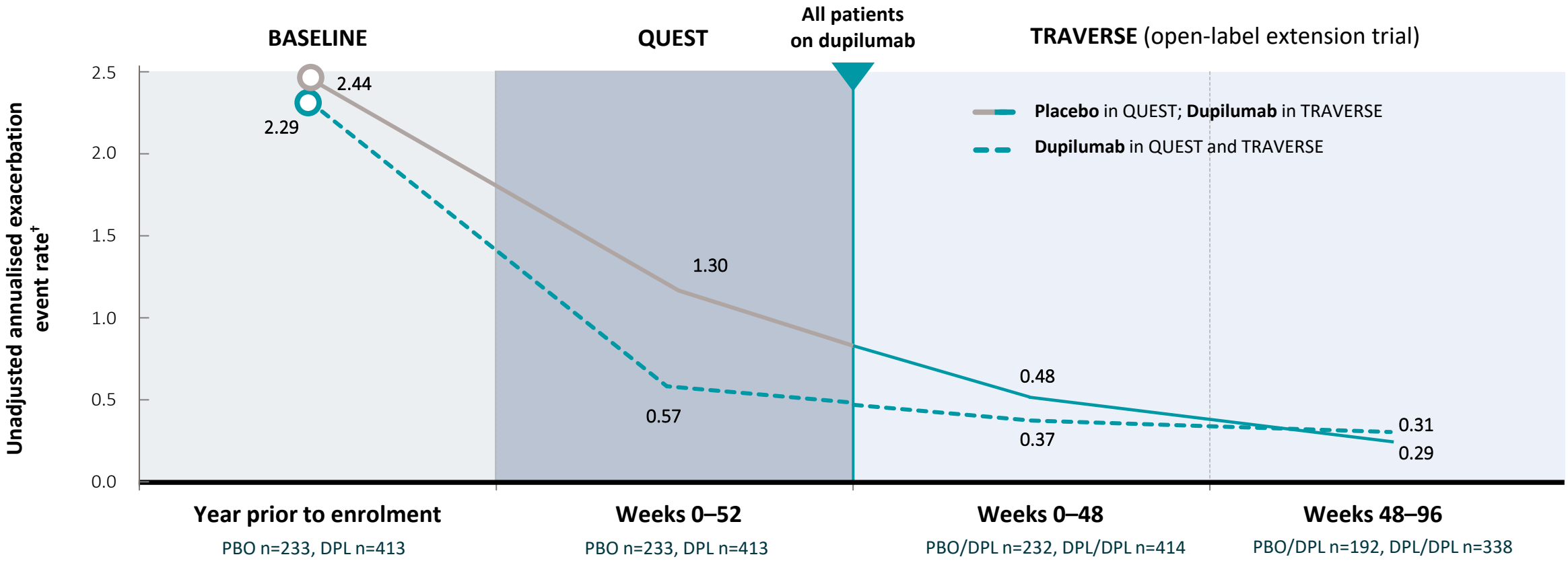
†Data from dupilumab-treated uncontrolled moderate-to-severe asthma trials: QUEST, NCT02414854, N=1,902 and TRAVERSE, NCT02134028, dupilumab/dupilumab-arm: N=1,013

FeNO, fractional exhaled nitric oxide; **ppb**, parts per billion; **SE**, standard error; **IL**, interleukin; **Q2W**, every 2 weeks; **EOS**, blood eosinophils

1. Rabe KF et al. N Engl J Med 2018; 378(26): 2475–85; **2.** Wechsler M et al. J Allergy Clin Immunol. 2021;147 (2suppl):AB140; **3.** Wechsler ME, et al. J Allergy Clin Immunol Pract. 2022;10(10):2695-709.

Reduction in exacerbation rate was sustained over ~3 years of follow-up with dupilumab in patients with high-dose ICS at baseline

Unadjusted annualised rate of severe exacerbations† in patients receiving high-dose ICS at baseline (type 2 population)



† The total number of events that occurred during the treatment period divided by the total number of patient-years followed in the treatment period.

ICS, inhaled corticosteroid; **PBO**, placebo; **DPL**, dupilumab

Pavord ID, et al. Allergy 2023;78(11):2921–32.

Adapted from Pavord et al. 2023

Biologic agents for severe type 2 high asthma

	Omalizumab[1-4]	Mepolizumab[5,6]	Benralizumab[7,8]	Dupilumab[9,10]
Blood EOS > 150 mm^3	Responder	Needed	Needed	Needed or FeNO
FeNO > 20 ppb on ICS	Responder	N/A	N/A	Needed or EOS
IgE sensitised	Needed	N/A	N/A	N/A
Age	12 years and above	12 years and above	12 years and above	12 years and above
Results				
Fall in ACQ-5	1.8[3]	0.44-0.52	0.55	0.19*-0.47
Exacerbations (% reduction)	25-53%	32-53%	49-70%	48-59%
FEV$_1$ diff placebo	94 mL	98–100 mL	159 mL	130–220 mL
Reduced OCS at least by 25%	28% (only phase 4)[3]	64%	78%	80%

Disclaimer: as head-to-head studies have not yet been conducted, these results should be interpreted with caution

*at 24 weeks

EOS, eosinophils; **ACQ-5**, asthma control questionnaire – 5; **ppb**, parts per billion; **FEV$_1$**, forced expiratory volume in 1 second; **IgE**, Immunoglobulin E; **FeNO**, fractional exhaled nitric oxide; **OCS**, oral corticosteroids; **T2**, type 2

1.Humbert M, et al. Allergy. 2005;60(3):309-16. **2**. Hanania NA, et al. Ann Intern Med. 2011;154(9):573-82. **3**. Hanania NA, et al. Am J Respir Crit Care Med. 2013;187(8):804-11. **4**. Gibson PG, et al. Int Med J. 2016;46(9):1054-62. **5**. Ortega HG, et al. N Engl J Med. 2014;371(13):1198-207. **6**. Bel EH, et al. N Engl J Med. 2014;371(13):1189-97. **7**. Bleecker ER, et al. Lancet. 2016;388(10056):2115-27. **8**. Nair P, et al. N Engl J Med. 2017;376(25):2448-58. **9**. Castro M, et al. N Engl J Med. 2018;378(26):2486-96. **10**. Rabe KF, et al. N Engl J Med. 2018;378(26):2475-85.

“Choosebetweenamab” study (ACTRN12618000850279)

Hypothesis

In patients with the dual phenotypes of severe allergic and eosinophilic asthma, mepolizumab is as effective as omalizumab.

Aims

Aim 1: To determine if mepolizumab is as effective as omalizumab in adults with severe refractory asthma who exhibit a dual allergic/eosinophilic phenotype in terms of improvement in asthma symptom control.

Aim 2: To determine which patients are more likely to respond to one agent or the other and to clarify the clinical and/or biological features that predict this response. This may allow the development of a clinical algorithm to select a clinically preferable treatment option.

theAlfred

MONASH University

Methods

- A non-inferiority unblinded “pragmatic” randomised control trial
- 18 sites in Australia and New Zealand

Inclusion criteria:

- 12 years and older, asthma present > 1 year
- Asthma with demonstrable variable airflow obstruction, under the care of respiratory/immunology for > 6 months with optimised treatment
- On high dose ICS/LABA for at least 6 months
- Allergic (documented atopy, SPT or RAST)
- Blood eosinophil count ≥ 150 cells/µL on OCS or ≥ 300 cells/µL
- ACQ-5 > 2.0 and at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (OCS initiated or increased for at least 3 days, or parenteral corticosteroids)

EOS, eosinophils; **ACQ-5**, 5-item asthma control questionnaire; **RAST**, radioallergosorbent test; **SPT**, skin prick test; **ICS**, inhaled corticosteroids; **OCS**, oral corticosteroid; **LABA**, long-acting beta agonist

Primary outcome

- Change in ACQ-5 after 6 months of treatment, adjusted for baseline ACQ-5
- Mean ACQ-5 in the mepolizumab group will be compared to that in the omalizumab group using a pre-specified non-inferiority margin (Δ) of 0.35

ACQ-5, 5-item Asthma Control Questionnaire

Secondary outcomes

- Number of exacerbations, requiring change in OCS, with either a course of prednisone for at least 3 days or, for those subjects on maintenance OCS, an increase in dose of at least 50% for at least 3 days
- Time to first exacerbation
- Number of admissions to hospital and/or ED presentations
- Reduction in dose of regular OCS
- Reduction in total OCS use during the 6-month treatment period
- Changes in spirometry (FEV_1 or FVC)
- Change in blood eosinophil count
- Proportion continuing on Australian PBS treatment (successful treatment)
- Adverse events

ACQ-5, 5-Item Asthma Control Questionnaire; **FEV_1**, forced expiratory volume in 1 second; **FVC**, forced vital capacity; **OCS**, oral corticosteroid; **PBS**, Pharmaceutical Benefits Scheme; **ED**, Emergency Department

Non-responder

- After 6 months of treatment, subjects will be clinically assessed to determine if the treatment has succeeded or failed

The following criteria will be used and regarded as the treatment having failed:

- No improvement in ACQ-5 of at least 0.5 (minimum clinically important difference) from baseline, **and**
- No reduction in regular prednisone dose or intermittent prednisone usage by at least 15%, **and**
- An intolerance to the agent or the emergence of clinically significant side effects.

ACQ-5, 5-Item Asthma Control Questionnaire

Clinical remission at 6 months of treatment

- ACQ-5 < 0.8
- No exacerbations
- No use of systemic corticosteroids
- No exacerbations
- FEV_1 stable or unchanged (no deterioration in FEV_1 > 3%)

Unpublished data provided by Prof. Peter Wark

ACQ-5, 5-Item Asthma Control Questionnaire; **FEV_1**, forced expiratory volume in 1 second

Baseline demographics

	Omalizumab	Mepolizumab	Analysis
Number	36	36	
Gender (M:F)	18:18	18:14	P=0.8
Age (SD)	54.2 (18)	56.3 (18)	P=0.8
Baseline ACQ-5	3.3 (1.1)	3.2 (1.0)	P=0.6
Prednisolone use in the previous 12 months (mg)	1367 (1078)	1468 (1912)	P=0.7
Number of exacerbations in the previous 12 months	4.2 (2.5)	4.4 (3.1)	P=0.7
FEV_1pp	69.2 (22)	65.9 (26)	P=0.6

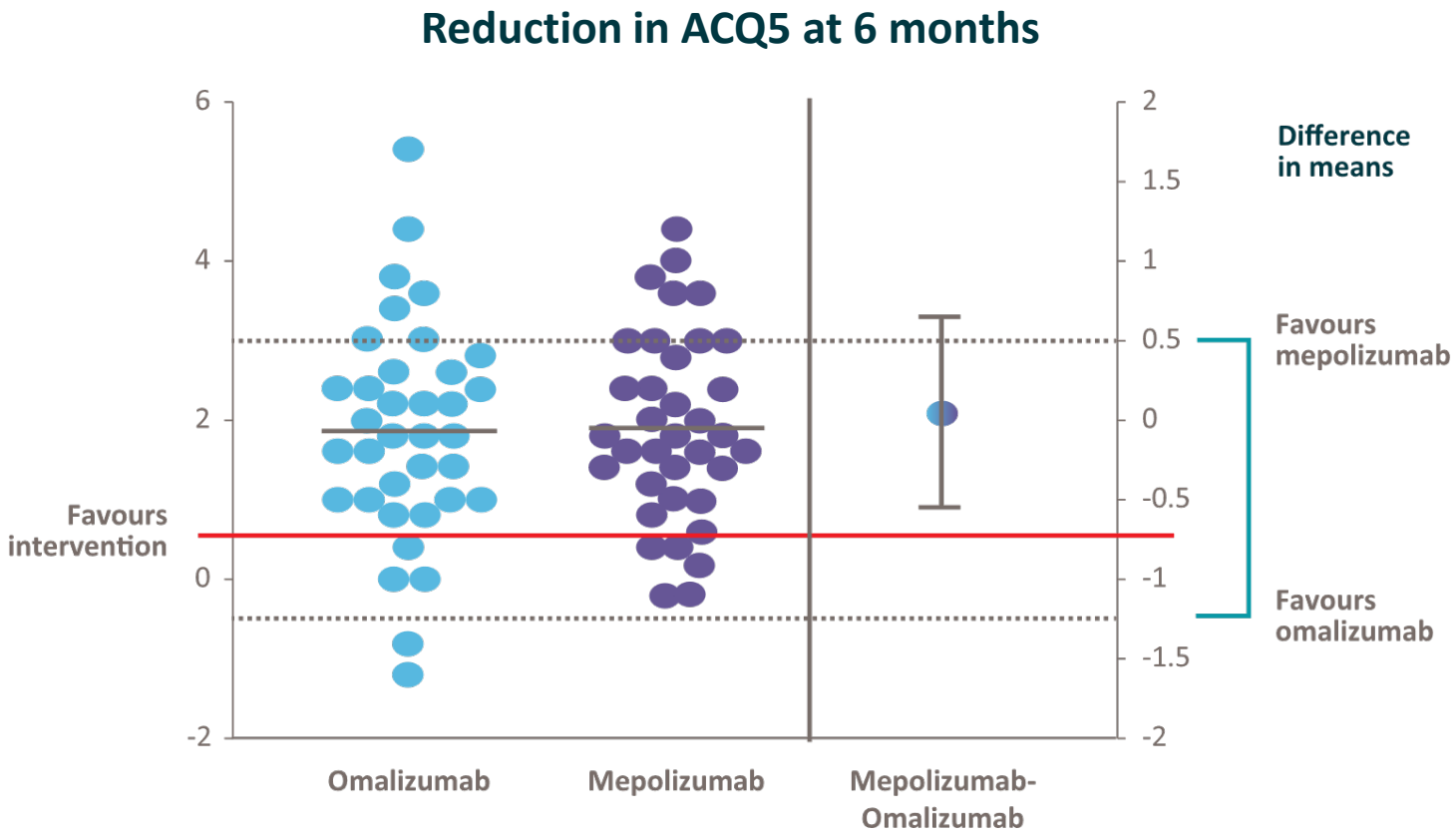
Unpublished data provided by Prof. Peter Wark.

ACQ-5, 5-Item Asthma Control Questionnaire; **FEV_1pp**, forced expiratory volume in 1 second, percent predicted; **SD**, standard deviation

Interim analysis

- Interim analysis, (n=36 omalizumab, n=36 mepolizumab)
- Difference in mean ACQ-5 at 6 months, adjusted for baseline (per protocol)

➢ 0.015 (−0.457, 0.487)



Unpublished data provided by Prof. Peter Wark.
ACQ-5, 5-Item Asthma Control Questionnaire

Baseline demographics

	Omalizumab	Mepolizumab	Analysis
Reduction in ACQ-5 (ITT)	1.8 (1.4)	1.9 (1.2)	P=0.6
Reduction in ACQ-5 (per protocol)	2.0 (0.99)	1.9 (1.4)	P=0.1
Reduction in exacerbations	2.8 (2.6)	3.1 (2.9)	P=0.9
Failed to respond	5 (13%)	2 (5%)	
Responder	25 (68%)	32 (86%)	
Clinical remission	7 (19%)	3 (8%)	p=0.8*
Changed to another* monoclonal antibody	7	1	P=0.03
Adverse event potentially due to Mab*	10	11	P=0.6

*Fisher's exact test
Clinical remission defined as: ACQ-5 < 0.8; no oral corticosteroid use; no exacerbations; FEV_1 increased or stabilised (no change < 5% from baseline).
Unpublished data provided by Prof. Peter Wark.

ITT, intention to treat; **Mab**, monoclonal antibody; **ACQ-5**, 5-Item Asthma Control Questionnaire; **FEV_1**, forced expiratory volume in 1 second, percent predicted

How do you choose between the biologics?

When do you switch?

Factors to consider when choosing between the biologics

1. Co-morbidities that worsen asthma and are serious problems themselves
2. A dominant phenotype of T2 asthma?

Comorbidities of severe asthma

1. **Chronic rhinosinusitis +/- nasal polyposis (CRSwNP)**
   - Mepolizumab[1] improved nasal polyp score and quality of life
   - Benralizumab[*2], severe asthma + CRSwNP, improved symptom scores
   - Dupilumab[3], improved nasal symptoms and CT scores
2. **Atopic dermatitis**
   - Dupilumab[4] improved symptoms and quality of life

*Benralizumab is not indicated for the treatment of CRSwNP

CRSwNP, chronic rhinosinusitis with nasal polyposis, **CT,** computerised tomography

1. Han JK, et al. Lancet Respir Med. 2021;9(10):1141-53. **2.** Canonica GW, et al. Allergy. 2022;77(1):150-61.. **3.** Bachert et al Lancet. 2019;394(10209):1638-1650; **4.** Simpson et al. N Engl J Med 2016; 375:2335-2348.

When is it time to switch?

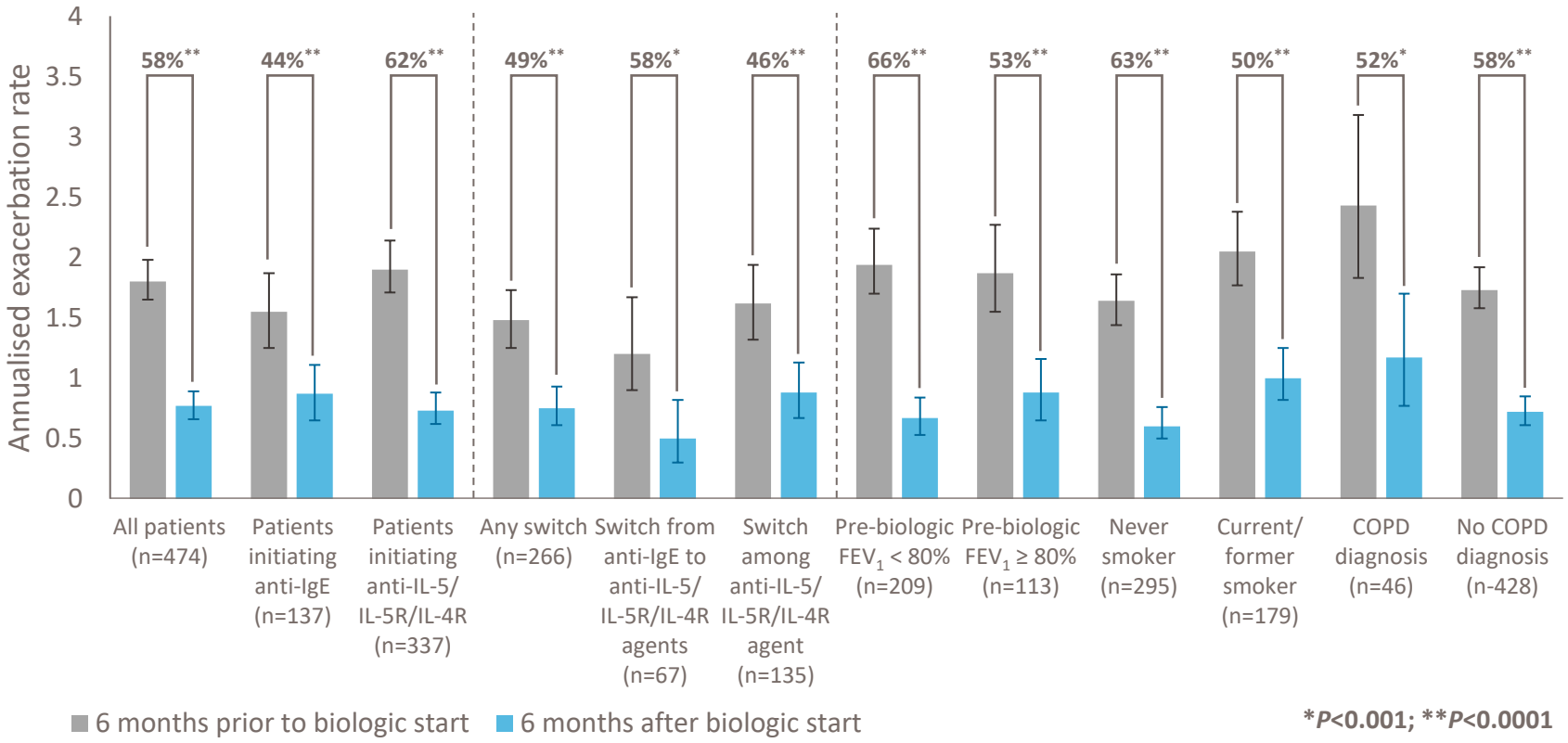
CHRONICLE: observational cohort of US adults with severe asthma

Biologic usage

- Of 2793 adult patients, n = 1832 (66%) on biologics:
  - Omalizumab, 47%
  - Benralizumab, 27%
  - Mepolizumab, 26%
  - Dupilumab, 18%
  - Reslizumab, 3%
- 13% stopped
- 16% switched
  - Reasons: worsening control or waning efficacy

Exacerbation rates for patients 6 months before and after biologic initiations

Presented as overall and by class, biologic switches overall and by class, and biologic initiations for clinical groups of interest



***P*<0.001; ****P*<0.0001

Adapted from Panettieri et al. 2022

IgE, Immunoglobulin E; **IL,** interleukin; **FEV_1**, forced expiratory volume in 1 second, **COPD,** chronic obstructive pulmonary disease

Panettieri RA, Jr., et al. Ann Allergy Asthma Immunol. 2022;129(4):467-74.e3.

Switch from omalizumab to mepolizumab

Participants

- Multicentre, open-label, single-arm, 32-week trial in patients with:
  - ≥ 2 asthma exacerbations in the year prior despite high-dose ICS/LABA, plus omalizumab (≥ 4 months)
  - Blood eosinophil counts ≥ 150 cells/µL (or ≥ 300 cells/µL in the prior year), and
  - ACQ-5 score ≥ 1.5
- Patients discontinued omalizumab and immediately commenced mepolizumab 100 mg subcutaneously every 4 weeks

Results

- ACQ-5 mean change (SE) was −1.45 (0.107)
- Annualised rate of clinically significant exacerbations was 1.18 events/year, a 64% reduction from 3.26 events/year during the previous year

ACQ-5, 5-item Asthma Control Questionnaire; **ICS**, inhaled corticosteroids; **LABA,** long-acting beta-agonist; **SE**, standard error

Chapman et al. Allergy. 2019;74(9):1716-1726.

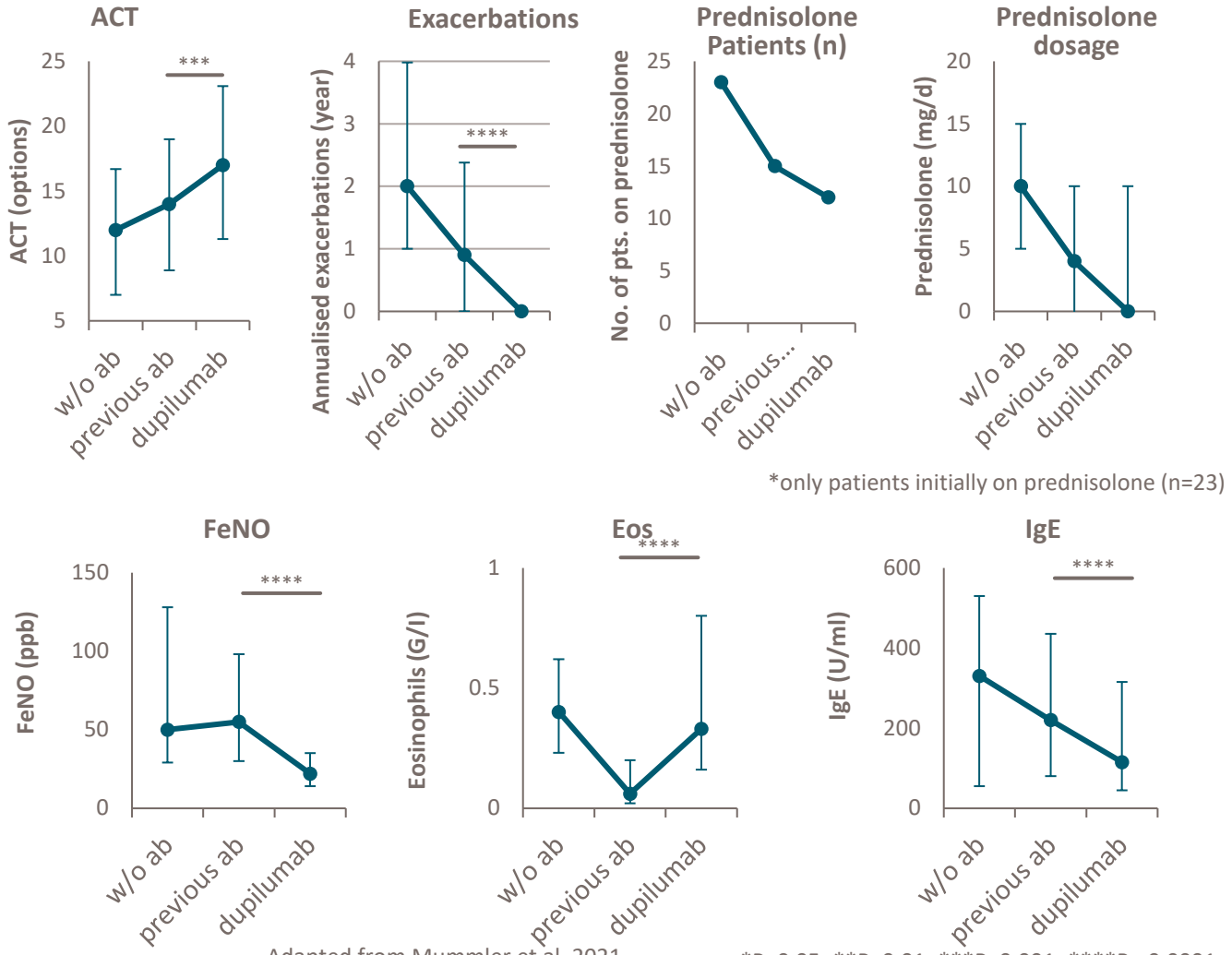
Switch from anti-IL-5 or anti-IgE therapy to dupilumab

Participants

- Retrospective analysis at 2 centres
- 38 of 454 patients with severe asthma were switched to dupilumab
  - 64% on OCS at baseline
  - Persistent T2 inflammation, mean FeNO of 52 ppb & blood eosinophils of 0.41 G/L
  - 32 switched from anti-IL-5
  - 6 switched from anti-IgE

Results

- 5 developed asymptomatic hypereosinophilia
- 29/38 were responders
  - Improved ACT, reduced OCS
- High FeNO > 24 ppb more likely to respond



Adapted from Mummler et al. 2021

*P<0.05, **P<0.01, ***P<0.001, ****P< 0.0001.

EOS, eosinophil; **FeNO**, fractional exhaled nitric oxide; **ppb**, parts per billion; **IgE**, immunoglobulin E; **IL**, interleukin; **OCS**, oral corticosteroid; **ab**, antibody; **ACT**, Asthma Control Test

Mummler C et al. J Allergy Clin Immunol Pract. 2021;9(3):1177-85.e4.

Refractory T2 asthma, refractory to ICS, needs biologic therapy

Speaker's own content

Consider add on biologic therapy[1]

Asthma, despite ICS/LABA, have exacerbations or poor asthma control or require regular OCS

+ T2 inflammation

- Blood EOS ≥150 cells/µL
  and/or
- FeNO ≥20 ppb
  and/or
- Sputum EOS ≥2%
  and/or
- Asthma clinically allergen driven

Eligibility for *anti-IgE* for *severe allergic asthma*

- Sensitization on skin prick testing or elevated specific IgE
- Elevated total serum IgE
- Exacerbations in last year
- 6yrs+

Eligibility for *anti-IL-5/anti-IL-5R* for *severe eosinophilic asthma*

- Exacerbations in last year
- Blood EOS ≥150/µL
- Mepolizumab 6yr+, Benralizumab 12yr+

Eligibility for *anti-IL-4R*

… for severe eosinophilic/type 2 asthma

- Exacerbations in last year
- Blood EOS ≥150 cells/µL or FeNO ≥25 ppb
- 12yr+

… or because of need for maintenance OCS

Factors that may predict response[1]

- Blood EOS ≥260 cells/µL **++**
- FeNO ≥20 ppb **+**
- Allergen-driven symptoms **+**
- Childhood-onset asthma **+**

- Higher blood EOS **+++**
- More exacerbations in the previous year **+++**
- Adult-onset of asthma **++**
- CRSwNP/nasal polyposis **++**

- Higher blood EOS **+++**
- Higher FeNO **+++**

Anti-IL-4R may also be used to treat: [3]

- Moderate/severe AD
- CRSwNP/nasal polyposis

Efficacy[2]

1. **Exacerbations reduced 25–50%**
2. **FEV_1 min change**
3. **? Reduced OCS**

1. **Exacerbations reduced 50%**
2. **FEV_1 98–160 mL**
3. **Reduced OCS**

1. **Exacerbations reduced 70%**
2. **FEV_1 150–240 mL**
3. **Reduced OCS**

Adapted from GINA, 2023

EOS, eosinophil; **FeNO**, fractional exhaled nitric oxide; **IgE**, immunoglobulin E; **IL**, interleukin; **ICS**, inhaled corticosteroid; **LABA**, long-acting beta-agonist; **OCS**, oral corticosteroid; **ppb**, parts per billion; **CRSwNP**, chronic rhinosinusitis with nasal polyposis; **FEV_1**, forced expiratory volume in 1 second; **AD**, atopic dermatitis

1. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention, 2023. Available at www.ginasthma.org (accessed August 2023). 2. Jin HJ. Yeungnam Univ J Med. 2020; 37(4):262–68. 3. Buhl R, et al. J Allergy Clin Immunol Pract. 2022;10(2):422–32.

“Choosebetweenamab" for severe asthma: recent findings

- Odds ratio of having to change to another Mab if treated initially with omalizumab
  - **OR 2.2 (95%CI: 0.99 to 2.6)**

- Reasons for change to another Mab within the first 6 months of treatment
  - Omalizumab adverse event (n=1)
  - Clinician/subject dissatisfaction with the clinical response (all others), all had achieved a reduction in ACQ-5 > 0.5

- Relative risk of failing to respond, not meeting criteria or deciding to change to another mab if treated with omalizumab vs mepolizumab
  - **RR 0.88 (95%CI; 0.70-1.07), Fisher’s exact p=0.3**

- Relative risk of omalizumab inducing clinical remission compared to mepolizumab
  - **RR 2.3 (95%CI; 0.7 to 7.9), Fisher’s exact p=0.3**

Unpublished data provided by Prof. Peter Wark.

ACQ-5, 5-Item Asthma Control Questionnaire; **OR**, odds ratio; **RR**, relative risk

“Choosebetweenamab" for severe asthma: conclusions

- LPLV: August 31st
- N=89, final analysis complete Q4 2023
- Unlikely there will be a difference in terms of the primary outcome (change in ACQ-5)
- More consistent response from mepolizumab
- Possibly more people are likely to achieve remission of clinical symptoms at 6 months with omalizumab, but also more likely to request switching at 6 months

Unpublished data provided by Prof. Peter Wark.
ACQ-5, 5-Item Asthma Control Questionnaire; **LPLV**, last patient last visit

Dupilumab PBS Information: Refer to PBS schedule for full authority information. Authority required for patients aged ≥12 years with: chronic severe atopic dermatitis; OR uncontrolled severe asthma. This product is not listed on the PBS for: children 6 months to 11 years of age with severe atopic dermatitis; children 6-11 years of age with moderate to severe asthma; adults with uncontrolled chronic rhinosinusitis with nasal polyps; or adults with moderate-to-severe prurigo nodularis.

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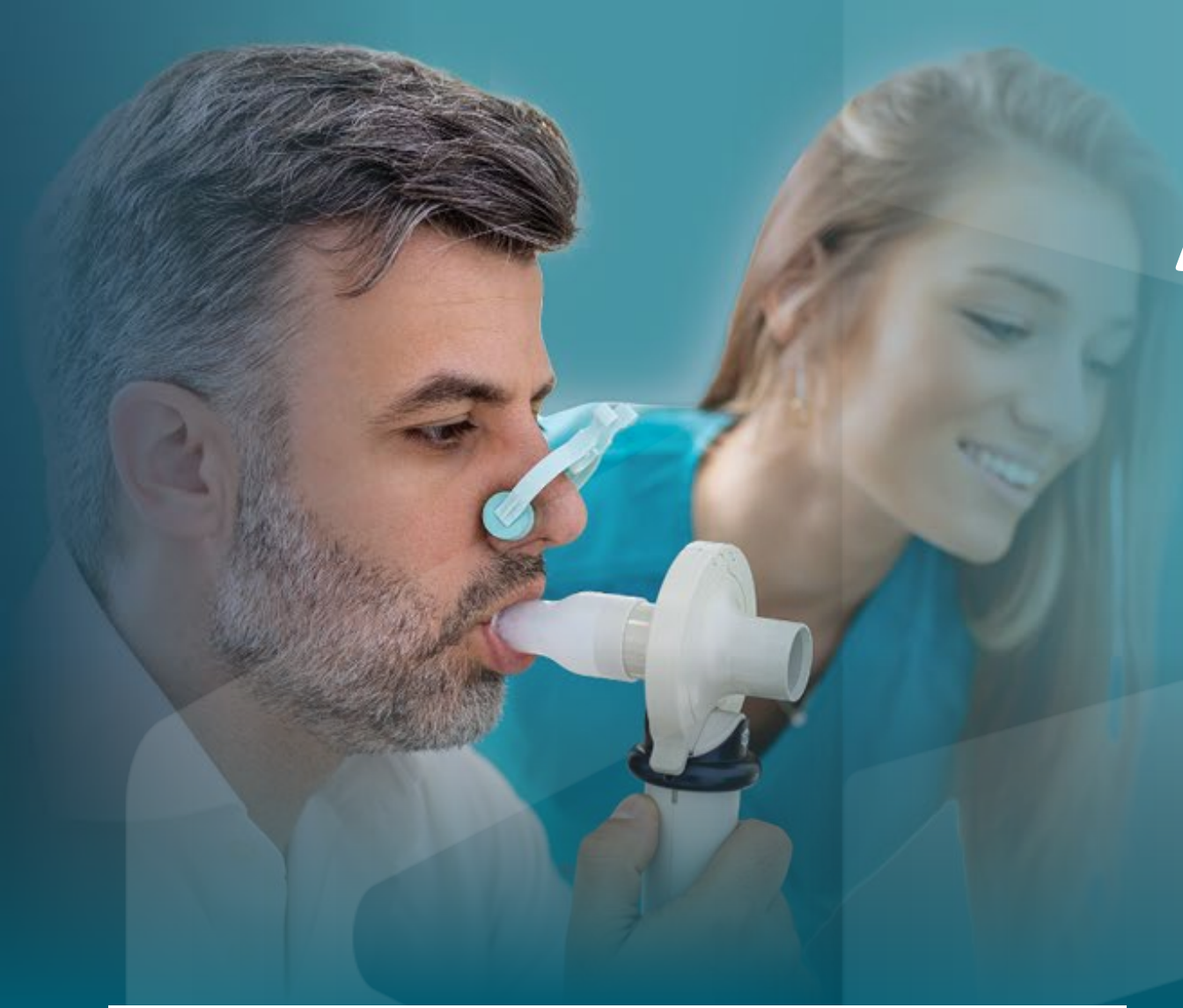

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Concluding remarks

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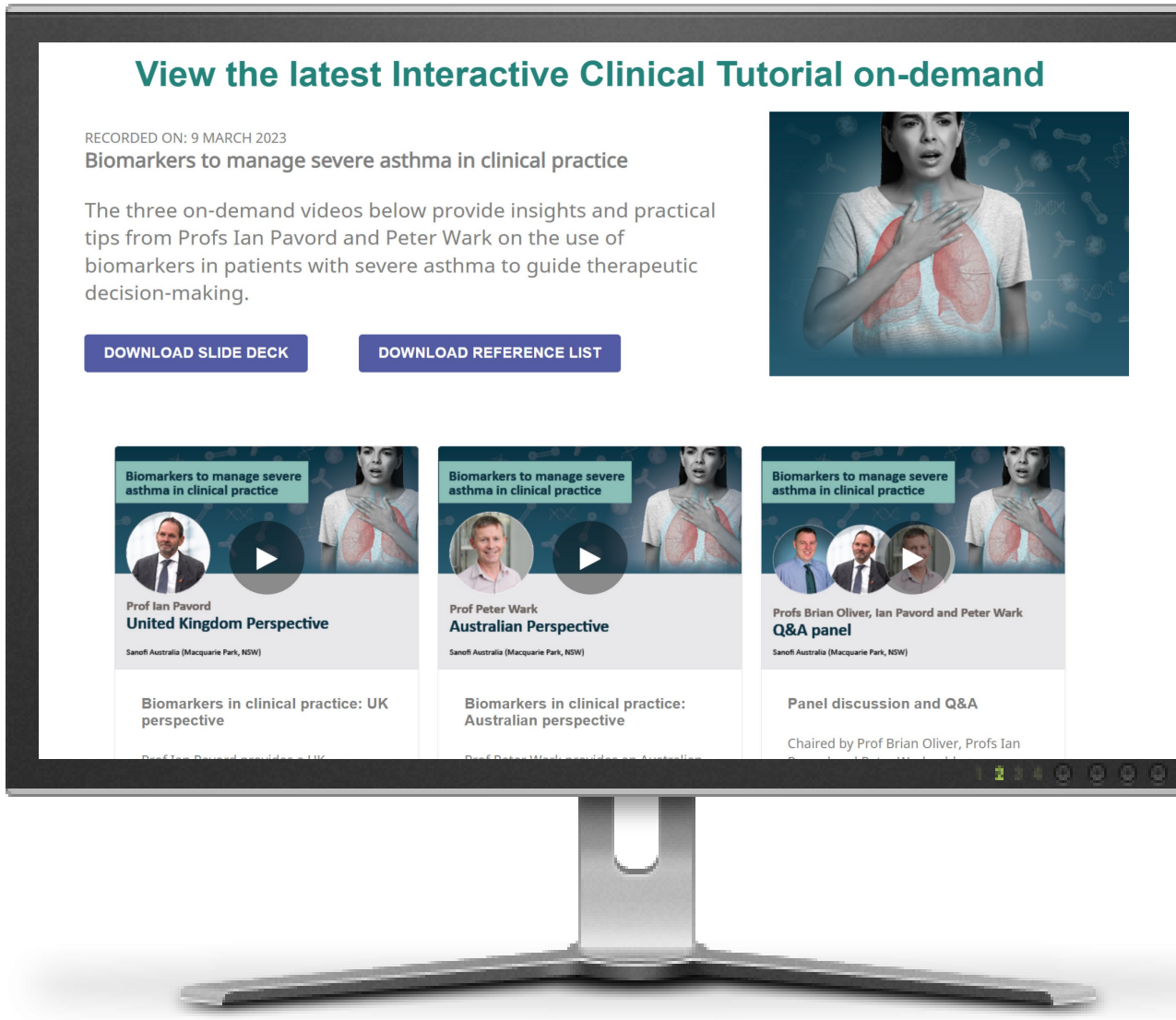

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