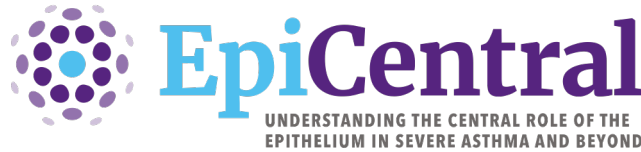


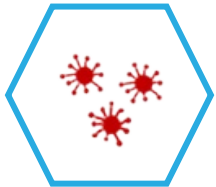


The role of the airway epithelium in asthma



Asthma is driven by interactions between the environment, epithelium and immune system¹⁻⁶

Environmental exposures^{1,2}



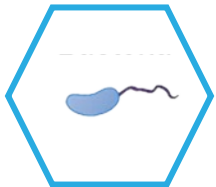
Viruses



Allergens



Pollutants
/smoke



Bacteria



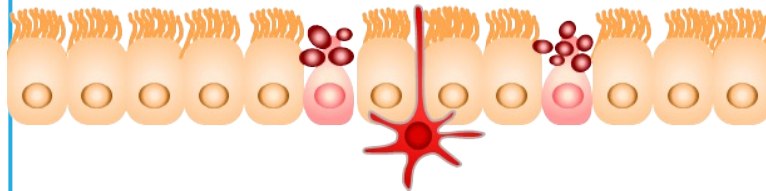
Physical
injury



Other external
stimuli (eg house
dust mites)

Epithelium²⁻⁴

- Key role in tissue homeostasis
- Mediator between environment and immune system
- Rapid production of epithelial cytokines in response to exposures



Immune system^{5,6}

- Allergic eosinophilic inflammation
- Non-allergic eosinophilic inflammation
- Non-T2 (non-eosinophilic) mechanisms
- Structural cell changes



T2, type 2

1. Pelaia G, et al. Nat Rev Drug Discov 2012;11:958–972; 2. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 3. Watson B, Gauvreau GM. Expert Opin Ther Targets 2014;18:771–785; 4. Loxham M, et al. Clin Exp Allergy 2014;44:1299–1313; 5. Brusselle G, Bracke K. Ann Am Thorac Soc 2014;11(Suppl. 5):S322–S328; 6. Gauvreau GM, et al. Expert Opin Ther Targets 2020;24:777–792

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The airway epithelium is a first point of contact for environmental exposures¹

Barrier and sensor

Protective barrier and sensor of the environment^{1,2}

Mediates immunity

Innate and adaptive immune response²

Induces inflammation

Epithelial cytokines promote airway inflammation^{1,2}

Structural changes

Can drive airway remodelling and smooth muscle pathology^{1,3,4}

Image of normal lung; bronchus by Yale Rosen, available at https://www.flickr.com/photos/pulmonary_pathology/3661529896 (Accessed 6 January 2022)

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1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Roan F, et al. J Clin Invest 2019;129:1441–1451; 3. Wang Y, et al. Respir Med 2008;102:949–955; 4. Corren J. J Allergy Clin Immunol Pract 2019;7:1394–1403

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The airway epithelium plays a fundamental role in asthma¹⁻⁴

The airway epithelium serves as a barrier/sensor and mediates airway immunity^{1,2}

In severe asthma, the epithelium is significantly altered¹⁻⁴

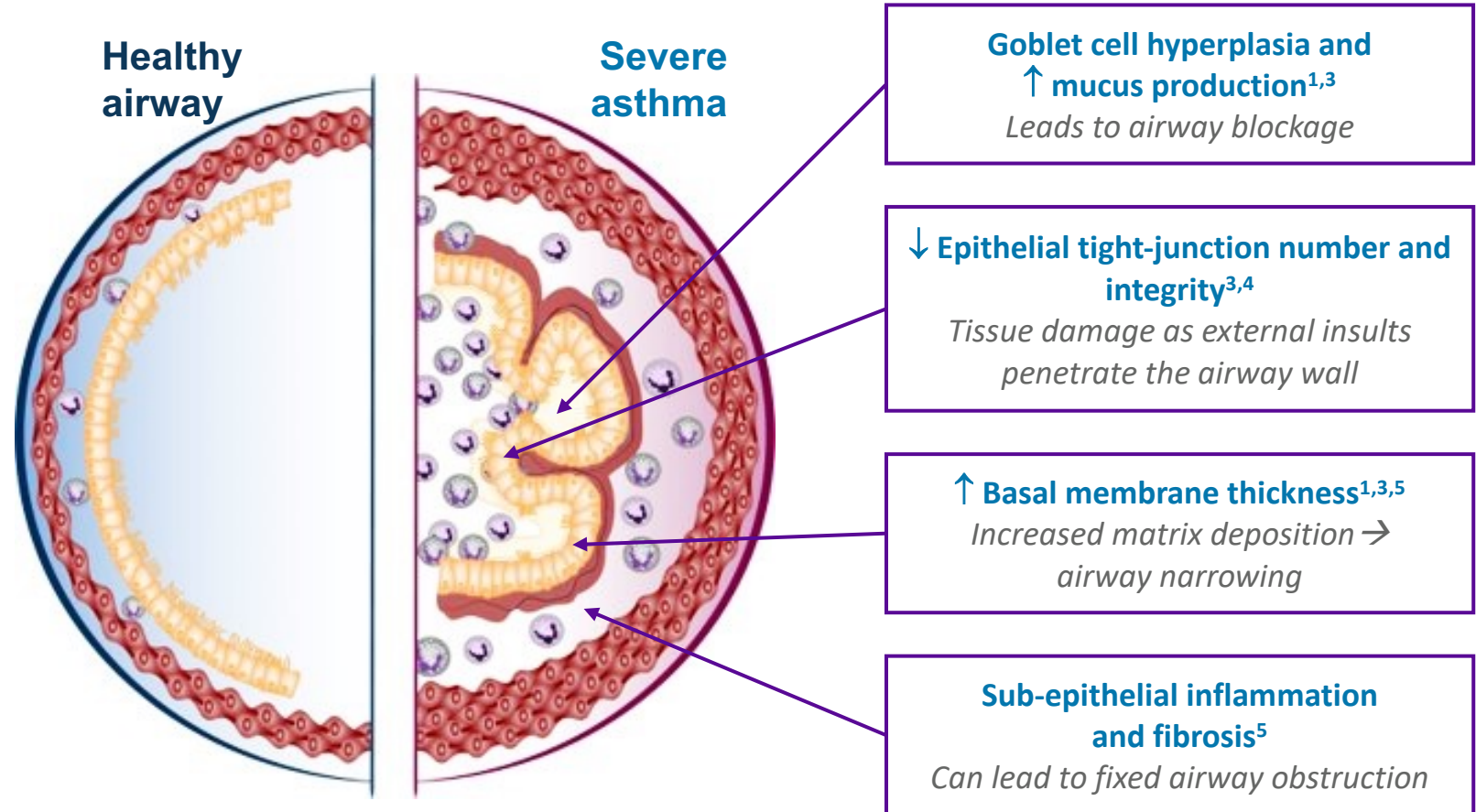


Figure adapted from the Centre of Excellence in Severe Asthma as part of the Centre of Research Excellence in Severe Asthma (<https://toolkit.severeasthma.org.au>) (Accessed 6 January 2022).

1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Roan F, et al. J Clin Invest 2019;129:1441–1451; 3. Holgate ST. Immunol Rev 2011;242:205–219; 4. Heijink IH, et al. Clin Exp Allergy 2014;44:620–630; 5. Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145

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The airway epithelium structure is significantly altered in severe asthma¹⁻⁵

In bronchial biopsies of patients with severe asthma versus healthy controls:⁵

↑ Epithelial thickness versus normal airway (A)

↑ Epithelial cell proliferation versus normal airway (B)

↑ Apoptosis versus normal airway

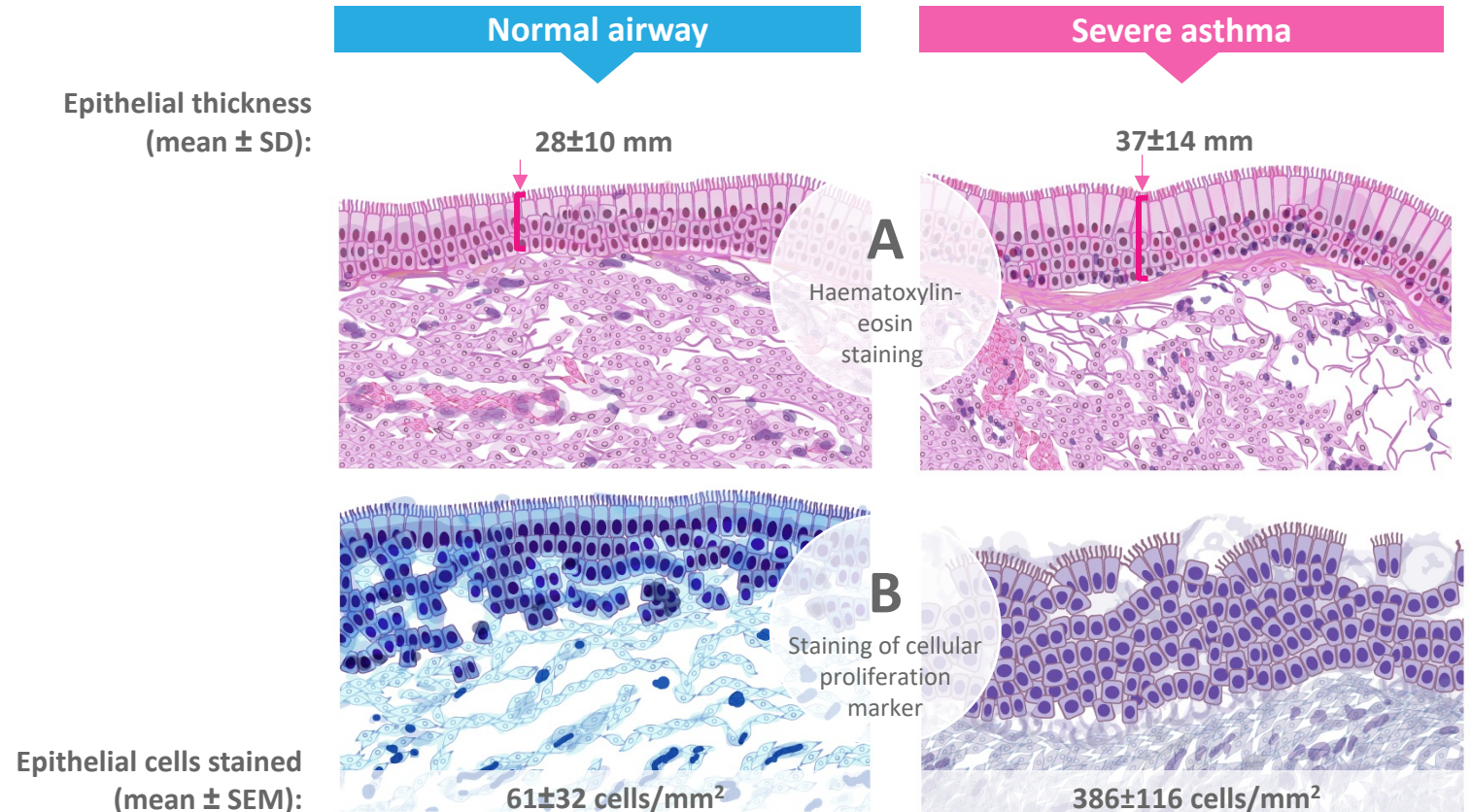


Figure adapted from Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145

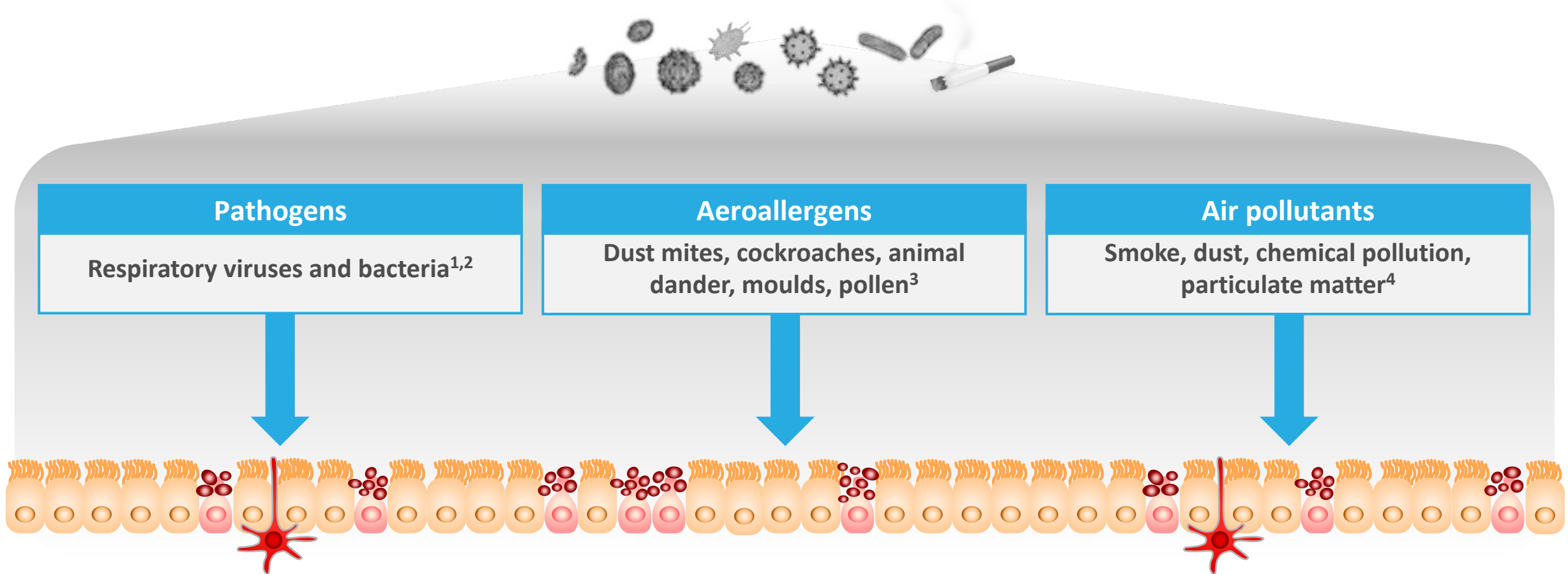
SD, standard deviation; SEM, standard error of the mean

1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Holgate ST. Immunol Rev 2011;242:205–219; 3. Heijink IH, et al. Clin Exp Allergy 2014;44:620–630; 4. Caminati M, et al. World Allergy Organ J 2018;11:13;

5. Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145

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Environmental exposures trigger airway inflammation at the epithelium¹⁻⁴



1. Wark PA, Gibson PG. Thorax 2006;61:909–915; 2. Iikura M, et al. PLoS One 2015;10:e0123584; 3. Baxi SN, Phipatanakul W. Adolesc Med State Art Rev 2010;21:57–71; 4. Lambrecht BN, et al. Immunity 2019;50:975–991

The triggers of asthma are diverse¹

Self-reported asthma triggers (N=1202)

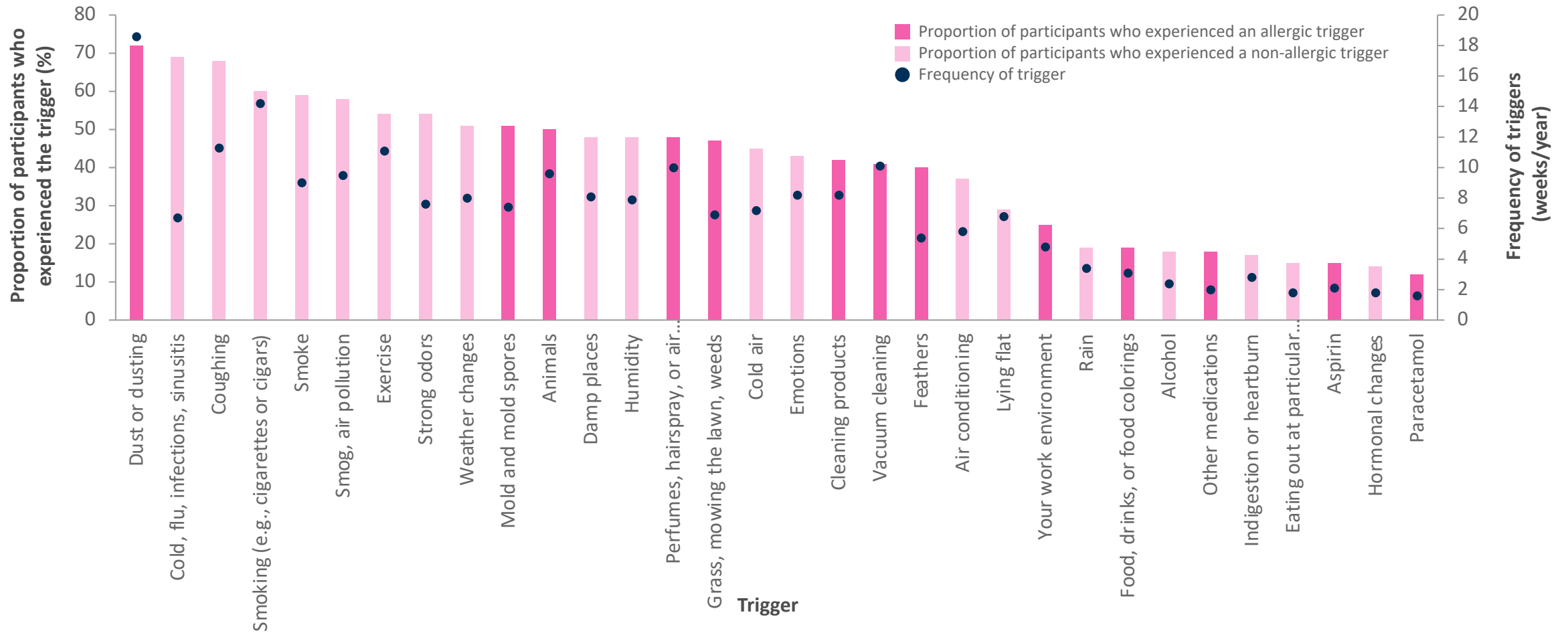


Figure adapted from Price D, et al. J Asthma. 2014;51:127–135 (<http://creativecommons.org/licenses/by/3.0>) (Accessed 6 January 2022).

1. Price D, et al. J Asthma 2014;51:127–135