PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

JUNE 24-26, 2022 | THE HOTEL HERSHEY, HERSHEY, PA

ONSITE PROGRAM

Pennsylvania Allergy & Asthma Association

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PAAA

Pennsylvania Allergy & Asthma Association

Purpose and Target Audience

Allergists, Immunologists, Pulmonologists, Family Practitioners, Certified Registered Nurse Practitionersand Physician Assistants with the most current and up-to-date treatments and scientific informationregarding allergy, asthma, and immunology.

Program Outcomes

At the conclusion of this learning activity, participants should be able to:

- Apply new knowledge in a variety of topics to improve identification and screening practices to help them choose appropriate biologics and appropriate therapies for their patients.

Accreditation

For Physicians:

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Pennsylvania Medical Society and Pennsylvania Allergy and Asthma Association. The Pennsylvania Medical Society is accredited by the ACCME to provide continuing medical education for physicians.

The Pennsylvania Medical Society designates this live activity for a maximum of *12.25 AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Faculty and all others who have the ability to control the content of continuing medical educationactivities sponsored by Pennsylvania Medical Society are expected to disclose to the audience whetherthey do or do not have any real or apparent conflict(s) of interest or other relationships related to the content of their presentation(s).

CME Program Evaluation and Credit

You will receive an email with instructions on how to access the online evaluation immediately following the course. In order to receive CME credit, you must complete the online evaluation and submit an electronic attestation form. This evaluation is necessary in order to meet CME requirements established by the Pennsylvania Medical Society. If you need to update your email address, please stop by the PAAA registration desk to do so. This information will not be shared with outside parties or companies and is for the sole use of CME evaluation purposes.

The evaluation will be available starting Monday, June 27, 2022.

CME Disclosures

Financial relationships reported by members of the Pennsylvania Allergy and Asthma Association's Planning Committee are provided below. During all phases of planning for the Annual Meeting areas of conflict were managed through a peer-review process and/or through individual recusal when appropriate.

The Planning Committee has reviewed all presenter disclosure reports, identified potential conflicts of Interest, and implemented strategies to manage those areas of conflict, where they exist

Name	Company Name	Nature of Relationship
Supinda Bunyavanich, MD, MPH, MPhil		Nothing to Disclose
Hey Chong, MD*		Nothing to Disclose
Megan Cooper, MD, PhD	Enzyvant	Consultant
Carla Davis, MD	DBV Regeneron	Researcher Researcher
Magee DeFelice, MD*		Nothing to Disclose
Alexandra Freeman, MD		Nothing to Disclose
Gisoo Ghaffari, MD*		Nothing to Disclose
Torie Grant, MD, MHS		Nothing to Disclose
Tanya Laidlaw, MD	AstraZeneca, GSK, Regeneron	Consultant
David Stukus, MD	Before Brands, Inc. DBV Technologies Novartis	Consultant Research Consultant
Paige Wickner, MD, MPH	CVS Health	Employee

** Designates a Pennsylvania Allergy and Asthma Association Program Committee member.*

Notice of Disclaimer

The information presented is that of the contributing faculty and does not necessarily represent the views of the Pennsylvania Allergy and Asthma Association, the CME accreditor, Pennsylvania Medical Society, and/or any named commercial entity providing financial support.

The Pennsylvania Allergy and Asthma Association makes every effort to ensure that speakers are knowledgeable authorities in their fields. Seminar attendees are nevertheless advised that the statements and opinions expressed by seminar speakers are those of the speakers, not that of Pennsylvania Allergy and Asthma Association. The speakers' statements and/or opinions should not be construed as Pennsylvania Allergy and Asthma Association policy or recommendations, and Pennsylvania Allergy and Asthma Association disclaims any liability or responsibility for the consequences of any actions taken in reliance upon those statements or opinions.

PAAA 2022 Annual Meeting Agenda

Thursday, June 23, 2022	
4:00 p.m. – 6:30 p.m.	**Registration & Exhibitor Set Up** Garden Terrace Lobby & Starlight Terrace Ballroom
Friday, June 24, 2022	
7:30 a.m. – 7:50 a.m.	**Registration Open/Continental Breakfast/Visit with Exhibitors** Garden Terrace Lobby & Starlight Terrace Ballroom
7:50 a.m. – 8:00 a.m.	**Welcome and Introductions** Garden Terrace Ballroom Sigrid DaVeiga, MD 2021–2022 PAAA President
8:00 a.m. – 8:45 a.m.	**COVID-19 in Primary Immune Deficiencies** Alexandra Freeman, MD
8:45 a.m. – 9:30 a.m.	**2020 Updates to Asthma Management Guidelines: SMART Dosing in Asthma** Torie Grant, MD, MHS
9:30 a.m. – 10:15 a.m.	**Asthma: Lessons from the Upper Airway** Supinda Bunyavanich, MD, MPH, MPhil
10:15 a.m. – 10:45 a.m.	**Refreshment Break/Visit Exhibitors** Starlight Terrace Ballroom
10:45 a.m. – 11:30 a.m.	**The Hyper IgE Syndromes** Alexandra Freeman, MD
11:30 a.m. – 12:15 p.m.	**The Microbiome and Food Allergy** Supinda Bunyavanich, MD, MPH, MPhil
12:15 p.m. – 1:00 p.m.	**Mayer A. Green, MD Allergy Foundation Memorial Lecture** **The Promise and Limits of Food Allergen Immunotherapy** Carla Davis, MD
1:00 p.m.	**Adjournment of PAAA Educational Activities**
1:30 p.m. – 2:30 p.m.	**Non-CME ISS Program** Tea House Room *Evidence for Using a Biologic to Treat Two Different Eosinophil-Driven Diseases: Severe Eosinophilic Asthma and Chronic Rhinosinusitis with Nasal Polyps*
6:30 p.m. – 7:30 p.m.	**Non-CME ISS Program** Tea House Room *Dual Inhibition: Targeting Systemic and Localized Type 2 Inflammation in Asthma*
8:00 p.m. – 10:00 p.m.	**Dessert Reception with Exhibitors** Starlight Veranda **Pre-Registration Required*

PAAA 2022 Annual Meeting Agenda

Saturday, June 25, 2022	
6:30 a.m. – 7:30 a.m.	**Non-CME ISS Program** Overlook Room *Challenges Associated with Respiratory Viral Infections in Patients with Primary Immunodeficiency: An Expert Discussion & Real-World Experience*
7:00 a.m. – 7:50 a.m.	**Registration Open/Continental Breakfast/Visit with Exhibitors** Garden Terrace Lobby & Starlight Terrace Ballroom
7:50 a.m. – 8:00 a.m.	**Welcome and Introductions** Garden Terrace Ballroom Hey Chong, MD 2022 Program Chair
8:00 a.m. – 8:45 a.m.	**Operationalizing an Allergy Framework for COVID-19 Vaccinations** Paige Wickner, MD, MPH
8:45 a.m. – 8:55 a.m.	**PAERF Grantee Presentation** Presenter: Stanislaw Gabryszewski, MD, PhD *Investigating epidemiologic and immunologic relationships between systemic and gastrointestinal food allergies*
8:55 a.m. – 9:00 a.m.	**Recognition of Long-Standing Attendees and In Memoriam** Janet Beausoleil, MD Historian
9:00 a.m. – 9:45 a.m.	**Recognizing Health Disparities in Food Allergy** Carla Davis, MD
9:45 a.m. – 10:15 a.m.	**Annual Business Meeting**
10:15 a.m. – 10:45 a.m.	**Refreshment Break/Visit Exhibitors**
10:45 a.m. – 11:30 a.m.	**AERD - Diagnosis and Treatment** Tanya Laidlaw, MD
11:30 a.m. – 12:15 p.m.	**Quality/Safety in the Allergy Practice** Paige Wickner, MD, MPH
12:15 p.m. – 1:00 p.m.	**Disparities in Asthma** Torie Grant, MD, MHS
1:15 p.m. – 2:45 p.m.	**WORKSHOP: Aspirin and NSAID Challenges** Tanya Laidlaw, MD
2:45 p.m.	**Adjournment of PAAA Educational Activities**
6:30 p.m. – 10:00 p.m.	**Fireside Social & Dinner*** DJ and Children's Activities with Hotel Hershey Staff Formal Gardens East **Pre-registration Required*

PAAA 2022 Annual Meeting Agenda

Sunday, June 26, 2022	
7:00 a.m. – 7:35 a.m.	**Registration Open/Continental Breakfast** Garden Terrace Lobby & Starlight Terrace Ballroom
7:35 a.m. – 7:45 a.m.	**Welcome and Introductions** Garden Terrace Ballroom Magee DeFelice, MD 2022 Assistant Program Chair
7:45 a.m. – 8:30 a.m.	**Rheumatology in the AI Clinic** Megan Cooper, MD, PhD
8:30 a.m. – 9:15 a.m. 9:15 a.m. - 9:30 a.m.	**Patient Education in the Office** David Stukus, MD Refreshment Break
9:30 a.m. – 10:15 a.m.	**Immune Dysregulation** Megan Cooper, MD, PhD
10:15 a.m. – 11:00 a.m.	**Oral Food Challenges in Infants and Toddlers** David Stukus, MD
11:00 a.m.	**Adjournment of PAAA Educational Activities**
11:15 a.m. – 12:15 p.m.	**Farewell Brunch*** Starlight Veranda *Pre-registration Required

Total CME Hours Available: 12.25

PAAA
Pennsylvania Allergy & Asthma Association

Thank you to the Faculty Participants

Supinda Bunyavanich, MD, MPH, MPhil
Mount Sinai Endowed Professor in Allergy and Systems Biology
Icahn School of Medicine at Mount Sinai
Associate Director, Jaffe Food Allergy Institute

Megan Cooper, MD, PhD
Professor, Department of Pediatrics
Washington University School of Medicine
Director, Clinical Immunology, and the Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies,
St. Louis Children's Hospital Associate Director, Medical Scientist Training Program Program Director, Pediatric Rheumatology Fellowship Washington University School of Medicine

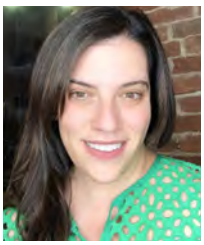
Carla Davis, MD
Professor, Department of Pediatrics and Pathology, Immunology, Allergy, and Retrovirology Director, Immunology, Allergy, and Retrovirology Division of the Department of Pediatrics
Baylor College of Medicine
Director, Texas Children's Hospital Food Allergy Program Chair, Janie and Sandra Queen Endowed in Immunology and HIV/AIDS
Chair, American Academy of Allergy, Asthma and Immunology Diversity Task Force

Alexandra Freeman, MD
Director, Primary Immune Deficiency Clinic
NIAID, NIH

Torie Grant, MD, MHS
Assistant Professor
Johns Hopkins University School of Medicine

Tanya Laidlaw, MD
Associate Professor of Medicine, Harvard Medical School Division of Allergy and Clinical Immunology Chief, Section of Clinical and Translational Sciences Director of the AERD Center
Harvard Medical School/Brigham and Women's Hospital

David Stukus, MD
Professor of Clinical Pediatrics
Director, Food Allergy Treatment Center Associate Director, Pediatric Allergy & Immunology Fellowship Program Nationwide Children's Hospital and The Ohio State University College of Medicine



Paige Wickner, MD, MPH
Assistant Professor
Division of Allergy and Clinical Immunology
Harvard Medical School/Brigham and Women's Hospital

Pennsylvania Allergy Educational Research Foundation (PAERF)

The Pennsylvania Allergy Educational Research Foundation (PAERF) is the charitable arm of the Pennsylvania Allergy & Asthma Association that funds educational and research endeavors related to the field of allergy and immunology. PAERF funds PAAA Annual Meeting fellows in training travel reimbursements that may be awarded to each training program in Pennsylvania. This fund allows the future leaders of our profession the opportunity to share their work through poster presentations and to participate in the meeting.

2022 Donors

(through May 16, 2022)

Janet L Beausoleil MD
Corinna Bowser, MD
Soheil Chegini, MD
Hey J Chong MD
Kara E Coffey MD
Robert E Coifman MD
Sigrid DaVeiga, MD
Magee L DeFelice MD
Denise A DiPrimio Kalman DO
Ishmael Faoud, MD
Tom Ferro, MD
Joel M Fiedler MD
Laura H Fisher MD
Mary E Fontana-Penn MD
Megan K Ford MD
Eugene A Gatti MD
Sandra M Gawchik DO
Gisoo Ghaffari MD
Richard L Green MD
Gretchen A Harmon MD
Sarah E Henrickson MD
Sharon L Hwang MD
Pooja B Jhaveri MD
Prakash Kaur,MD
Alana B Kekevian Jones DO
Norman L Koven, MD
Min J Ku MD
Allyson S Larkin MD
Kristen M Lutzkanin MD
Gregory V Marcotte MD
David Lee Miller, MD
Michael J Palumbo MD
Mark A Posner MD
Tracy R Prematta MD
Michael J Prematta MD
Robert P Rabinowitz DO
Thekkemadom Ramakrishnan, MD
Rejendra Singh
Karin Flynn-Rodden MD
Anthony R Rooklin MD
Melanie A Ruffner MD
Steven D Smith MD
Di Sun MD
Robert M Zemble MD

PAERF Travel Recipients 2022

Kim Nguyen, MD	Children's Hospital of Philadelphia
Anthony Lacava, MD	University of Pennsylvania
Hannah Harrison, MD	Nemours Children's Hospital/Thomas Jefferson University

Posters Submitted for Display

Ramin Beheshti, MD—Penn State Health Milton S. Hershey Medical Center
The Effectiveness of Unassigned Epinephrine Administrators Increases After The Implementation Of A Newly Developed Anaphylaxis Curriculum

Ramin Beheshti, MD—Penn State Health Milton S. Hershey Medical Center
Immunological Origins of Atopic Dermatitis Determined Through Multi-Omic Analysis

Hannah Harrison, MD—Nemours Children's Hospital/Thomas Jefferson University
Late-Onset X-Linked Chronic Granulomatous Disease: Identification of a Novel Variant in the CYBB Gene

Elisabeth Hodara, MD—St. Christopher's Hospital for Children
The Genetics of Eczema Herpeticum

Lauren Kaminsky, MD, PhD—Penn State Health Milton S. Hershey Medical Center
Clinical outcomes of bacterial pneumonia in patients with penicillin allergy label

Anthony Lacava, MD—Penn
Cyclosporine for Omalizumab-Refractory Chronic Spontaneous Urticaria—A Report of Five Cases

Sunjay Modi, MD—Milton S. Hershey Medical Center- Penn State College of Medicine
Racial and Ethnic Disparities with Allergen Immunotherapy in Patients with Allergic Rhinitis

Kim Nguyen, MD—Children's Hospital of Philadelphia
Baseline Characteristics of Patients who Fail Low-Dose Challenge and Patients who Reach Maintenance OIT to Cashew

Catherine Popadiuk, DO—Penn State Milton S Hershey Medical Center
A Case of Cutaneous Botryomycosis in a Patient with X-linked Agammaglobulinemia

Colleen Shannon, MD, MPH —Children's Hospital of Philadelphia
Asthma medication adherence during the COVID-19 pandemic in children at high risk of exacerbation

Sebastian Sylvestre, MD—Penn State Hershey Medical Center
Racial and Ethnic Disparities in Biologic Prescriptions for Moderate-to-Severe Persistent Asthma

Paulina Tran, DO—Children's Hospital of Philadelphia
Thymic Stromal Lymphopoietin Isoform Expression in Eosinophilic Esophagitis

Thank You!

Educational Grant

Mayer A. Green, MD Allergy Foundation

Industry Sponsored Symposia

GlaxoSmithKline—Respiratory Biologics
Regeneron
ADMA Biologics

Sponsors

AstraZeneca (Napkins)
DBV Technologies, Inc. (Hotel Key Cards & Napkins)

Platinum Exhibitors

GlaxoSmithKline—Respiratory Biologics
DBV Technologies, Inc.
Regeneron
CSL Behring
AstraZeneca
AstraZeneca
Aimmune

Standard Exhibitors

Genentech
ADMA Biologics
BioCryst
Horizon Therapeutics
Opitnose
Blueprint Medicines
AstraZeneca
Pfizer Immunology, Hospital
Takeda
Pfizer, Inc.
Allergy & Asthma Network
Grifols
Pharming Healthcare
Kaléo
Teva Pharmaceuticals
ALK Abello, Inc.
LEO Pharma Inc.

Sponsors as of 6.6.22

2022 Meeting Attendees

Those listed below have opted to share their contact information with vendors.
We have a total of TBD attendees registered for the meeting as of May 16, 2022.

(as of May 16, 2022)

First Name	Last Name	Degree	City	State	Zip
Schweta	Arakali	MD	Allentown	PA	18014
Elizabeth	Bailey	CRNP, MSN	Fort Washington	PA	19034
Neil	Baman	MD	West Windsor	NJ	08550
Janet	Beausoleil	MD	Media	PA	19063
Jack	Becker	MD	Willow Grove	PA	19090
Nick	Bires	PharmD	Doylestown	PA	18902
Corinna	Bowser	MD	Narberth	PA	19072
Hey	Chong	MD PhD	Pittsburgh	PA	15224
Robert	Coifman	MD	Millville	NJ	08332-2529
Megan	Cooper	MD, PhD	St Louis	MO	63110
Michael	Davies	MD	Hollidaysburg	PA	16648
Sandhya	Desai	MD	Wayne	PA	19087
Geoff	DiDario	MD	Ardmore	PA	19003
Amy	DiMase	PA-C	Middletown	NY	10941
Denise	DiPrimio Kalman	DO	Newark	DE	19711
Tracy	Estes	PhD, DNP, RN, FNP-BC	Newark	DE	19809
Neil	Feldman	DO	Allentown	PA	18104
Tom	Ferro	MD	Chester Springs	PA	19425-3729
Joel	Fiedler	MD	Voorhees Township	NJ	08043-4781
Karin	Flynn-Rodden	MD	Philadelphia	PA	19148-1003
Alexandra	Freeman	MD	Bethesda	MD	20892
Stan	Gabryszewski	MD, PhD	Philadelphia	PA	19104
Sandra	Gawchik	DO	Philadelphia	PA	19103
Patrick	Gleeson	MD	Philadelphia	PA	19130
Diane	Goldberg	GSK	McLean	VA	22101
Torie	Grant	MD	West Friendship	MD	21794
Todd	Green	MD	Pittsburgh	PA	15238
Neeti	Gupta	MD	East Windsor	NJ	08520
Sarah	Henrickson	MD/PhD	Haddonfield	NJ	08033
Shirley	Herr	PA-C	Easton	PA	18045
Shannon	Hogate	NP	Wilmington	DE	19808
Eva	Jakabovics	MD	Richboro	PA	18954
Junfang	Jiao	MD	Newark	DE	19713
Jennifer	Kannan	MD	King of Prussia	PA	19406

First Name	Last Name	Degree	City	State	Zip
Shannon	Kearney	DO	Allentown	PA	18103
Shannon	Kearney	DO	Allentown	PA	18103
John	Kim	MD	Cherry Hill	NJ	08003
Sandy	Kosmaczewski	PharmD	Woodstown	NJ	08098
Norman	Koven	MD	Philadelphia	PA	19102
Min	Ku	MD	Haddonfield	NJ	08033
John	Kuryan	MD	Huntingdon Valley	PA	19006
Tanya	Laidlaw	MD	Needham	MA	02492
Mosopefoluwa	Lanlokun	MD	Pittsburgh	PA	15219
Allyson	Larkin	MD	Pittsburgh	PA	15224
Jennifer	Lee	MD	Syosset	NY	11791
Kristen	Lutzkanin	MD	Hershey	PA	17033
Gregory	Marcotte	MD	Chadds Ford	PA	19317
Jamie	Mattern		Petersburg	NJ	08270
Sandro	Mattioli		Sewell	NJ	08080
Rickey	Miller	PharmD	Aspinwall	PA	15215
Michael	Palumbo	MD	Pittsburgh	PA	15243
Vima	Patel	MD	Philadelphia	PA	19103
Geeta	Patel	MD	Malvern	PA	19355
Sam	Patel	R.Ph., MBA	Clinton	NJ	08809
Robert	Rabinowitz	DO	Toms River	NJ	08755
Peter	Ricketti	DO	Trenton	NJ	08619
Michele	Romesberg		Berlin	PA	15530
Anthony	Rooklin	MD, MPH	Media	PA	19063
Amandeep	Sandhu	MD, MS	Philadelphia	PA	19103
Henry	Scovern	MD	Wyomissing	PA	19610
Shashank	Sheth	MD	Moorestown	NJ	08057
Rajendra	Singh	MD	Pottsville	PA	17901
Steven	Smith	MD	Philadelphia	PA	19116
John	Solic	MD	State College	PA	16803
Rosemary	Stinson	NP	Havertown	PA	19083
Erin	Toller-Artis	DO	Cherry Hill	NJ	08003
Greg	Tutko		Pearland	TX	77584
Andrew	Vayonis	MD	Pittsburgh	PA	15222
Michael	Wydila	MD	Wilmington	DE	19810
Eric	Zaccone	PhD	Abingdon	MD	21009
Robert	Zemble	MD	Allentown	PA	18104

Pennsylvania Allergy & Asthma Association

The PAERF Research Grant

Empowering the next generation!

"I am very grateful to the PAERF committee and sponsors, who played an instrumental role in supporting my research. The PAERF grant supported my continued training as an independent researcher, fostered fruitful collaborations, and helped enrich my knowledge about allergic disease epidemiology and mechanisms underlying systemic and gastrointestinal food allergies. Thanks to this experience, I feel empowered to continue pursuing research questions stemming from my work over the past year as I continue my training."

Stanislaw J. Gabryszewski, MD
2021 PAERF Research Grant Recipient

- When donors are asked to donate, they want to know that their donation makes a measurable difference, no matter how small or large that difference may be.
- Your donation to PAERF makes a measurable difference.
  Your contributions *"help enrich knowledge about allergic diseases."*
  Your contributions *"empower"* our recipients to "continue to pursue research questions."
- Your contribution to PAERF ensures that there is a next generation of allergy/immunologists as dedicated and as skilled as you.

Give to PAERF for the future of our profession and ever-better outcomes for our patients.

Save the Date!

PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

74th PAAA Annual Meeting

JUNE 23-25, 2023

The Hotel Hershey,
Hershey, PA

PAAA
Pennsylvania Allergy & Asthma Association

Presentations for Friday, June 24, 2022

COVID-19 in Primary Immune Deficiencies
Alexandra Freeman, MD

2020 Updates to Asthma Management Guidelines: SMART Dosing in Asthma
Torie Grant, MD, MHS

Asthma: Lessons from the Upper Airway
Supinda Bunyavanich, MD, MPH, MPhil

The Hyper IgE Syndromes
Alexandra Freeman, MD

The Microbiome and Food Allergy
Supinda Bunyavanich, MD, MPH, MPhil

Mayer A. Green, MD Allergy Foundation Memorial Lecture
The Promise and Limits of Food Allergen Immunotherapy
Carla Davis, MD

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

COVID-19 in Primary Immune Deficiencies

Presented by:
Alexandra Freeman, MD

Friday, June 24, 2022
8:00 a.m. – 8:45 a.m.

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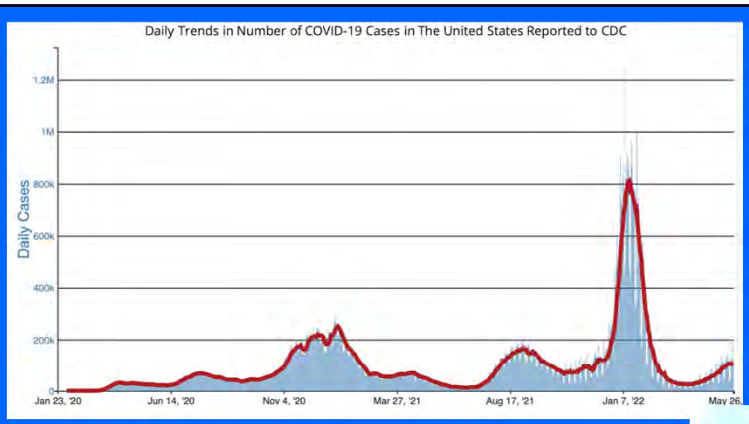
Pennsylvania Allergy & Asthma Association

COVID-19 in Inborn Errors of Immunity

Alexandra Freeman MD
Director, Primary Immunodeficiency Clinic
NIAID, NIH
June, 2022

1



CDC.gov

Difficulties of Counseling patients in a Constantly Evolving Field

2

COVID-19 in STAT3 HIES in the pre-vaccine era

Age (years)	Gender	SARS-CoV2 PCR	Exposure	Duration (Days)	COVID-19 Severity	Complications	Outcome
12	F	+	PCR + Family Member	14	Mild	None	Recovered
14	F	Not Tested	PCR + Family member	14	Mild	None	Recovered
17	M	--	PCR + Family member	6	Mild	Residual Fatigue; 21 days	Recovered
24	F	--	PCR+ Work exposure	18	Mild	None	Recovered
26	M	+	High exposure work environment	14	Mild	Clinical worsening on day 7, treated with additional antibiotics	Recovered
27	F	+	Unknown	0	Asymptomatic	None	
41	M	+	Unknown	26	**Severe**	Pseudomonas co-infection; Multiorgan failure	**Died**
45	M	Not Tested	PCR + Work and family exposures	20	Mild	None	Recovered
28	M	+	Family member	10	moderate	Received antibiotics	Recovered; received monoclonal plus remdesivir

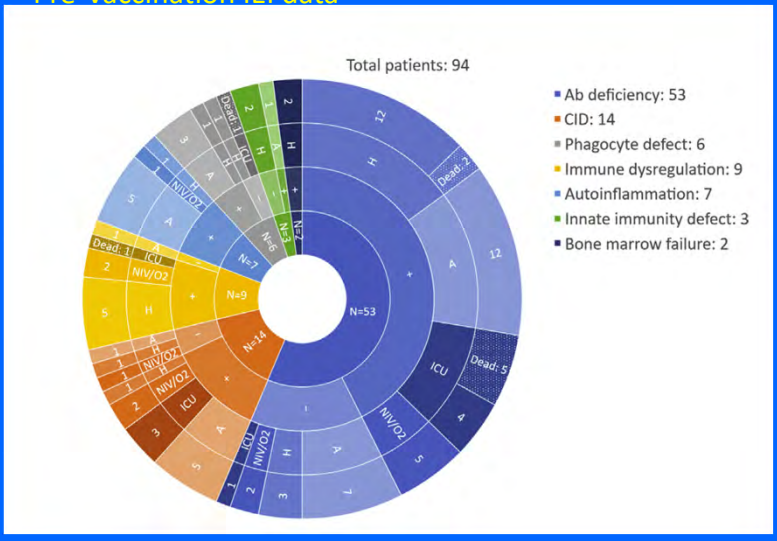
Post- vaccination: No hospitalizations yet
Also first year or so, less pulmonary infections with the major decrease in circulating respiratory viruses!

Fatality
41 year old Hispanic male
-obesity
-Bronchiectasis/pneumato-celes with MRSA and Pseudomonas chronic infection
-hypertension, prior MI with coronary artery aneurysms
-Busy hospital with many COVID cases

Hospitalized non-fatality:
s/p pneumonectomy, remaining lung with bronchiectasis/pneumatoceles
Chronic liver disease
Received oxygen by NC briefly

3

Pre-Vaccination IEI data

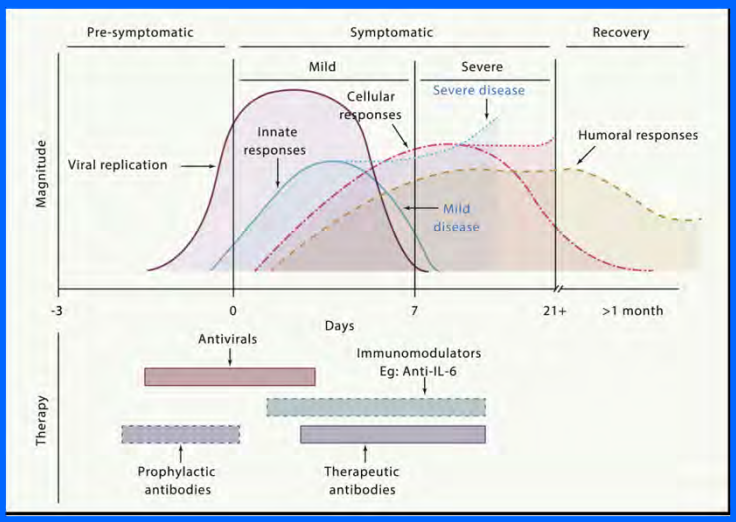


94 patients from around the world with varying IEIs
-CVID most common, than CID
->30% mild disease, and many more likely un-recognized or reported
-Case fatality 10% (not that different than reports at the time, not all causal)
-Increased severe disease in male
-Increased severe disease and mortality for those with other underlying disease
- Some with Interferonopathies on therapies had mild disease

Meyts et al, JACI 2021

4

Immune deficiency vs Immune dysregulation



First year saw evolving therapies for Severe COVID-19

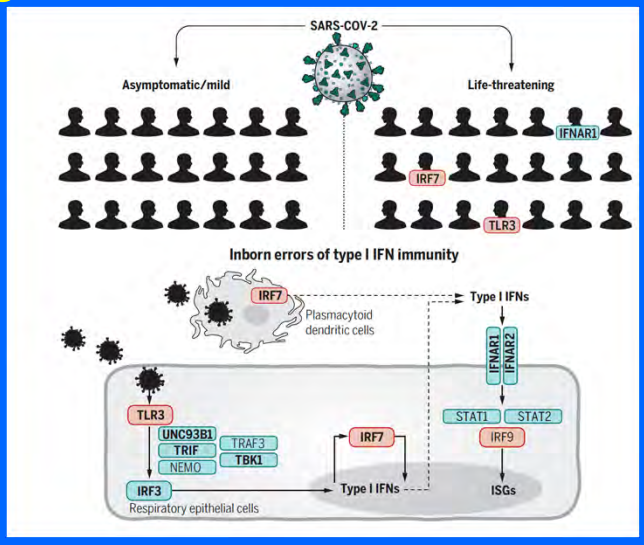
- Dexamethasone
- Tocilizumab
- Jak inhibitors

Subbaro, Immunity 2020

5

Searching for Immune defects in those with severe COVID-19

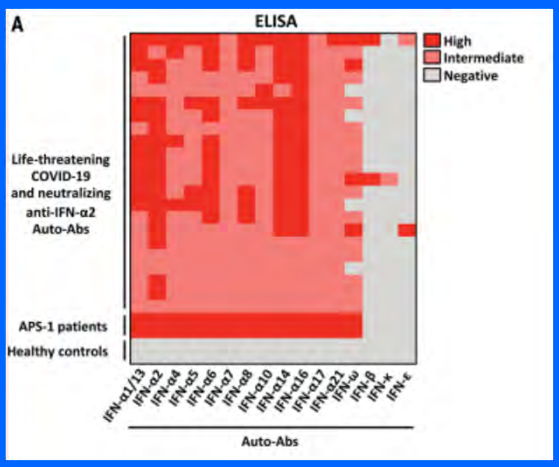
Type 1 IFN immunity Defects identified in 3.5% of 659 pts screened with severe disease compared to 534 with asymptomatic or mild



Zhang et al, Science 2020

6

Searching for Immune defects in those with severe COVID-19



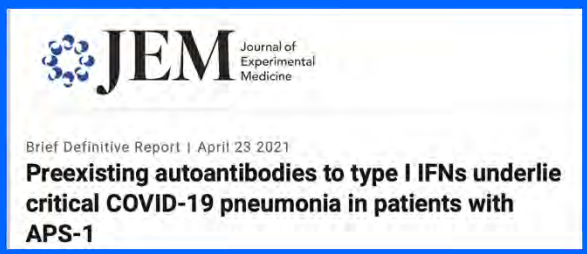
About 10% of those with severe COVID-19 were found to have neutralizing auto-abs against Type 1 IFNs
Increased in males, older patients. Most clinically silent until COVID-19.

Bastard, Rosen et al.
Science 2020

7

IEIs with IFN auto-antibodies, and immune dysregulation

- APECED
- Thymoma?
- CTLA4 Deficiency



22 patients, 21 checked and positive for anti-IFN auto-abs
86% hospitalized, 65% to ICU, 18% died

8

Concern of Persistent Shedding of Virus

16 year old with STAT1 GOF, s/p failed HSCT, bronchiectasis, IDDM, enteropathy. On ruxolitinib with reasonable control of disease.

October with mild COVID-19 symptoms (Delta wave) after one dose of mRNA vaccine.

Received monoclonal antibody infusion, with quick resolution of symptoms.

About 100 days later, lung pulmonary infection.

-NP swab SARS-CoV2 PCR negative, NP wash SARS-CoV2 PCR positive, BAL PCR negative…into isolation, symptoms improved with treatment of bacterial infections. Sequence of SARS-CoV2 : Delta variant

-5 months after COVID19 infection, NP swab PCR negative, saliva SARS-CoV2 PCR positive. Delta variant.

-Repeat vaccinations and Evusheld™ given for protection.

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The Journal of Infectious Diseases

BRIEF REPORT

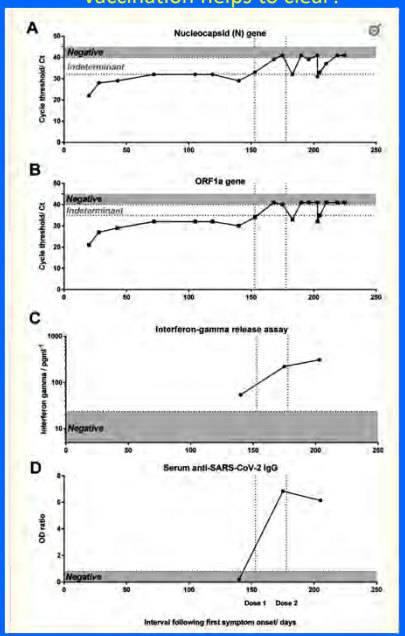
Yearlong COVID-19 Infection Reveals Within-Host Evolution of SARS-CoV-2 in a Patient With B-Cell Depletion

Veronique Nussenblatt,[1,a] Allison E. Roder,[2,a] Sanchita Das,[3] Emmie de Wit,[4,a] Jung-Ho Youn,[3] Stephanie Banakis,[2] Alexandra Mushegian,[2] Christopher Mederos,[2] Wei Wang,[2] Matthew Chung,[2] Lizzette Pérez-Pérez,[4] Tara Palmore,[5] Jennifer N. Brudno,[6] James N. Kochenderfer,[6] and Elodie Ghedin[2]

Therapy for persistent positivity??

- Convalescent serum is not the answer
  - Evasion with variants
- Repeat antivirals?
- Vaccination?
  - Patient with WAS reported to clear following vaccination

Vaccination helps to clear?

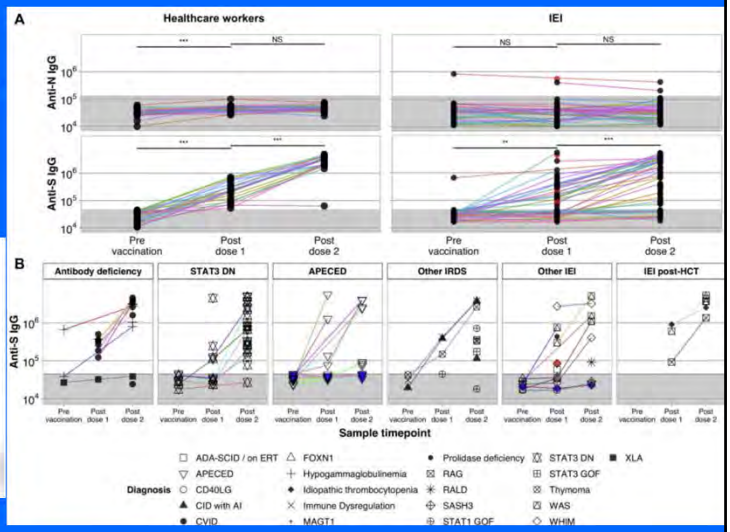


Bradley et al, J Clin Immunol 2022

10

Current Preventive Therapies Available

- VACCINATION!!!
  - 4 doses (>12 years) for those with immune suppression.



Delmonte, Bergerson et al, JACI 2021.

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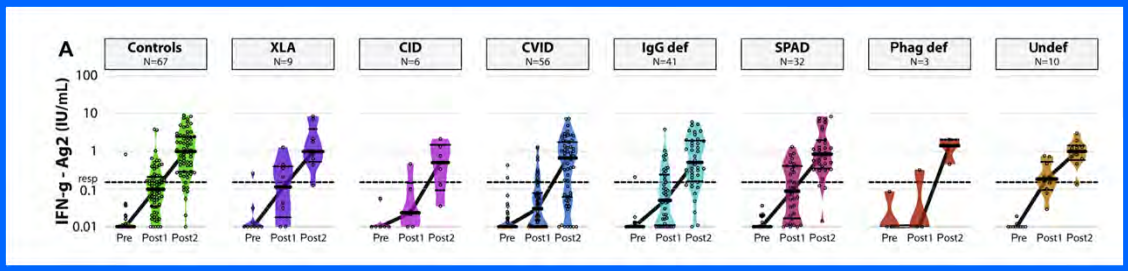
T cell responses post Vaccine too!



T cell response by Quantiferon assay. Leanne et al, JACI 2022

Important to still vaccine those without antibody responses, such as XLA.

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Current Preventive Therapies Available

- Tixagevimab/cilgavimab (Evusheld)
  - 12 years and older, 40kg
  - Two shots given, well tolerated
  - Moderate to severe immune suppression
  - Seems to have activity against omicron, subvariants
  - Some activity for about 6 months?
  - Risk: slight increase in cardiac events for those with underlying cardiac history

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Tixagevimab/cilgavimab during omicron pre-review, VA population

	Matched Controls N=6,354	Tixagevimab/cilgavimab recipients N=1,733	Propensity Score Survival Analysis	Difference in Difference^ Analysis
	Number of Events (%)	Number of Events (%)	Hazard Ratio (95% CI)	Incidence Rate Ratio (95% CI)
Composite outcome (COVID-19 infection, COVID-19 hospitalization, and all-cause mortality)				
Overall Cohort	206 (3.2%)	17 (1.0%)	0.31 (0.18-0.53)	
Immunocompromised	147 (3.5%)	12 (1.0%)	0.32 (0.18-0.62)	
Severely Immunocompromised	87 (3.7%)	11 (1.4%)	0.44 (0.21-0.93)	
Not Immunocompromised* but at High Risk	59 (2.8%)	(<1%)[&]	0.27 (0.13-0.56)	
Individual Outcome (Overall Cohort)				
COVID-19 Infection	69 (1%)	(<0.5%)[&]	0.34 (0.13-0.87)	0.32 (0.24-0.44)
COVID-19 related hospitalization	38 (0.5%)	(<0.5%)[&]	0.13 (0.02-0.99)	0.10 (0.05-0.22)
All-cause Mortality	99 (2%)	(<0.5%)[&]	0.36 (0.18-0.73)	
Falsification: Urinary Tract Infection	127 (2%)	36 (2%)	1.05 (0.68-1.62)	

^ DiD analysis was not performed on outcomes involving mortality data because matched cohorts were all alive at index dates.
* Electronic data regarding immunocompromised conditions or immunosuppressant use were found.
& Numbers not shown to protect patient information.

Young-Xu et al, 2022

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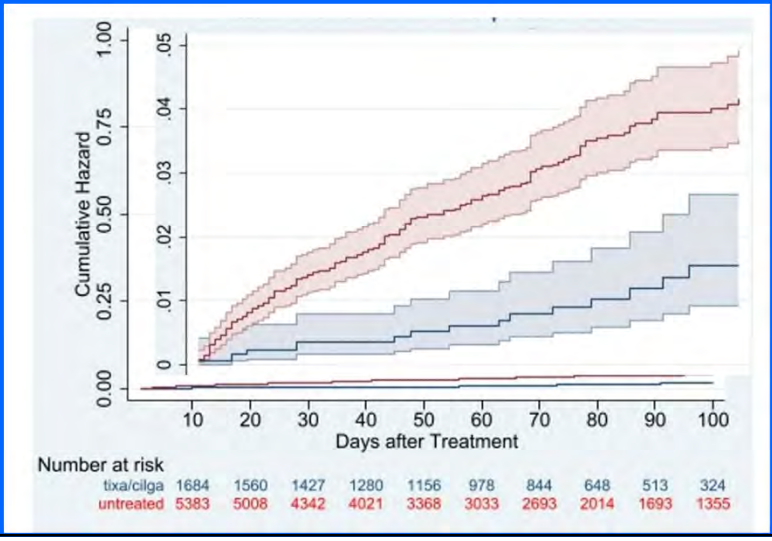
Tixagevimab/cilgavimab during omicron pre-review



Young-Xu et al, 2022

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Current Therapeutics for Outpatients

- Monoclonals
  - Rapidly changing with variants
    - Bebtelovimab- currently available for omicron and subvariants
- Anti-virals, oral
  - Nirmatrelvir plus ritonavir (Paxlovid)
    - Protease inhibitors (ritonavir boosts levels)
    - Decrease risk of hospitalization by 88% in phase 2/3 study
      - No deaths in study compared to 12 in placebo
    - Approved for 12 years and older with significant risk of severe disease
    - Start within 5 days of symptoms, give for 5 days
    - Dose adjusted for GFR 30-60, and not for use <30 GFR
    - Check for drug-drug interactions
    - Main side effect: Metallic taste in mouth

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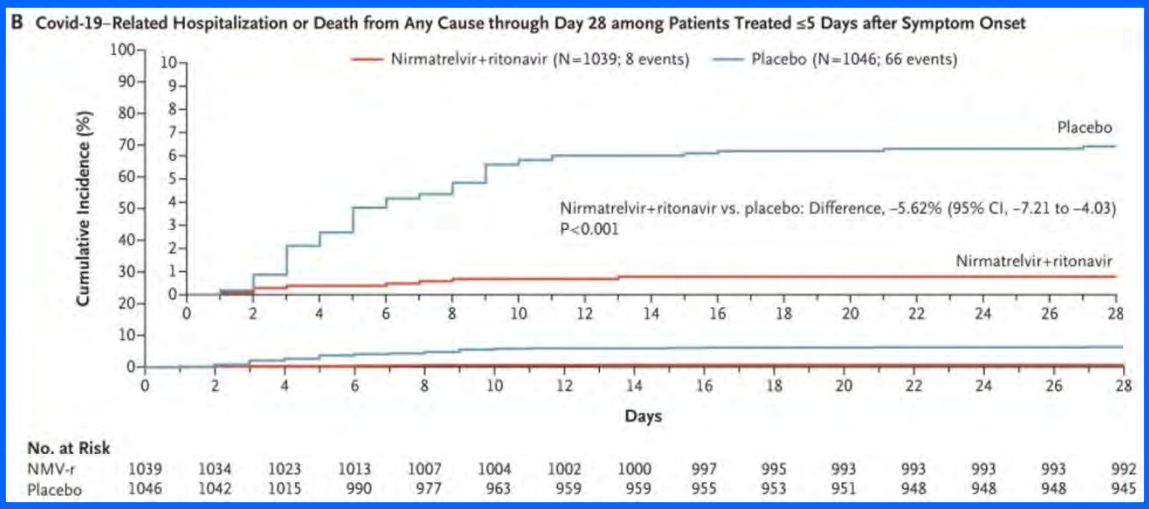

Hammond et al, NEJM 2022

17

Paxlovid™ rebound?

- Treated patients tested negative post therapy, and then tested positive again with some return of symptoms typically 2-8 days later
- Most with symptom resolution and test negativity again about 3 days later
- For most, mild symptoms, no need for repeat therapy.
- Evolving knowledge….will this be a bigger concern for our patients?

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Current Therapeutics for Outpatients

- Molnupiravir
  - Cytidine nucleoside analogue that gets incorporated into the SARS-CoV2 RNA leading to errors in the RNA genome and inhibits replication
  - Decreased risk of hospitalization by 30%, and death by 89% in phase 2/3 study
  - Approved for 18 years old older with significant risk for severe disease
  - Start within 5 days of symptoms
  - 800mg BID x 5 days
  - No drug interactions.
  - No dose adjustments for renal or liver disease
  - Well tolerated
  - Mutagenicity potential- don't use in pregnancy!
  - Not approved for kids- may cause bone/cartilage issues

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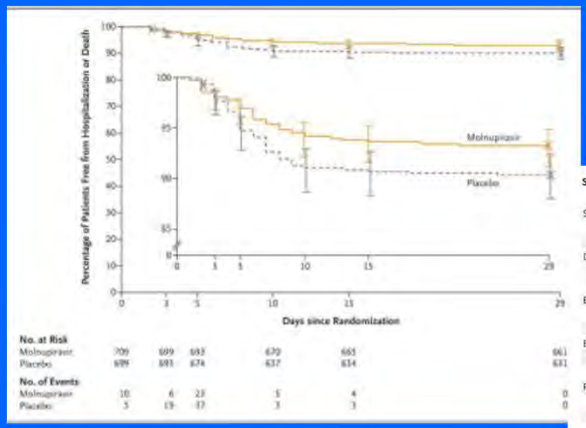

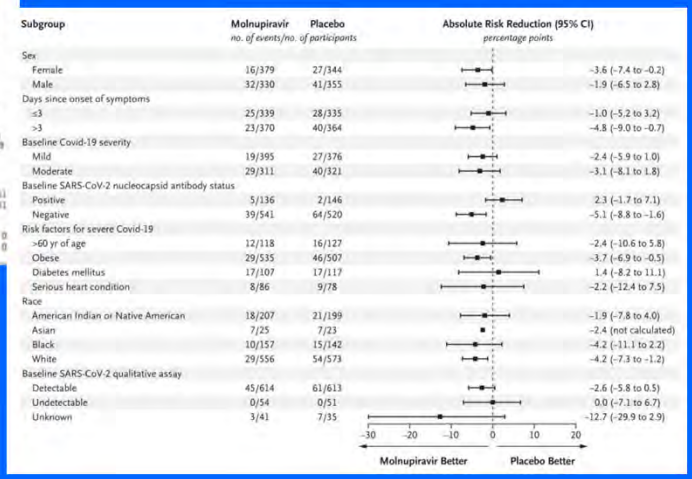

Jayk Bernal et al, NEJM 2022.

20

Current OutpatientTherapeutics

Remdesivir IV therapy

- Inhibits RNA polymerase
- 3 day therapy for outpatients to decrease need for hospitalization, mortality
- Well tolerated
- Not studied for GFR less than 30- but can be considered
- Dosing for children and adults
- Minimal drug interactions
- Well tolerated- can increase LFTs

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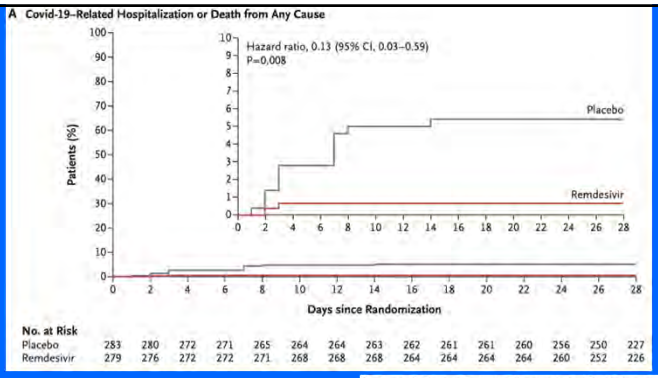
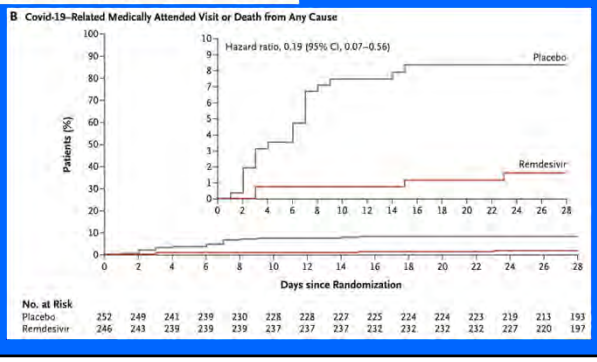


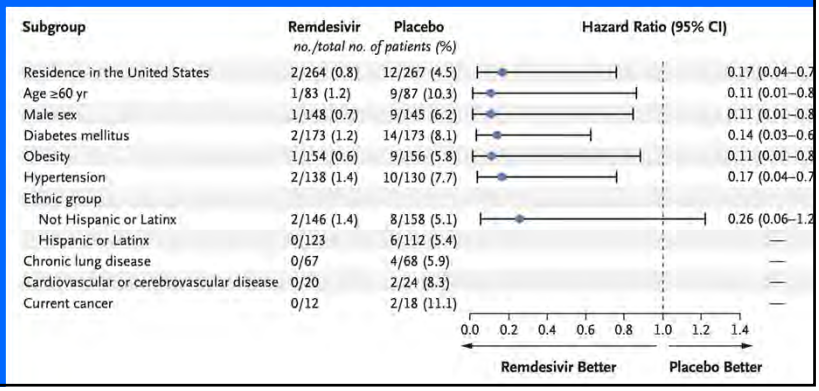


Gottlieb et al, NEJM 2021

22

Outpatient Remdesivir

Coexisting conditions — no. (%)			
Diabetes mellitus	173 (62.0)	173 (61.1)	346 (61.6)
Obesity	154 (55.2)	156 (55.1)	310 (55.2)
Hypertension	138 (49.5)	130 (45.9)	268 (47.7)
Chronic lung disease	67 (24.0)	68 (24.0)	135 (24.0)
Current cancer	12 (4.3)	18 (6.4)	30 (5.3)
Cardiovascular or cerebrovascular disease	20 (7.2)	24 (8.5)	44 (7.8)
Immune compromise	14 (5.0)	9 (3.2)	23 (4.1)
Chronic kidney disease, mild or moderate	7 (2.5)	11 (3.9)	18 (3.2)
Chronic liver disease	1 (0.4)	1 (0.4)	2 (0.4)



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Important therapy websites to help with therapy

- Drug interactions: https://www.covid19-druginteractions.org
- Finding medications: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com
- Evolving treatment guidelines: https://www.covid19treatmentguidelines.nih.gov

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Thank you!! Questions?

- Luigi Notarangelo, Ottavia Delmonte and Lab
- Steve Holland and lab
- Emily Ricotta
- HIES team: Amanda Urban, Christine Lafeer, Jean Ulrick, Susan Roy
- PID team: Jenna Bergerson, Ana Agharahimi, Justina Pfister
- Stuart Tangye, Garvan Institute, Australia

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

2020 Updates to Asthma Management Guidelines: SMART Dosing in Asthma

Presented by:
Torie Grant, MD, MHS

Friday, June 24, 2022
8:45 a.m. – 9:30 a.m.

PAAA
Pennsylvania Allergy & Asthma Association

2020 Updates to Asthma Management Guidelines: SMART Dosing in Asthma

Torie Grant, MD, MHS
Assistant Professor of Medicine and Pediatrics
Johns Hopkins University School of Medicine

1

Disclosures

- Current Funding
  - National Institutes of Health K23 Mentored Patient-Oriented Research Career Development Award
  - American Academy of Allergy, Asthma, and Immunology Foundation Faculty Development Award

2

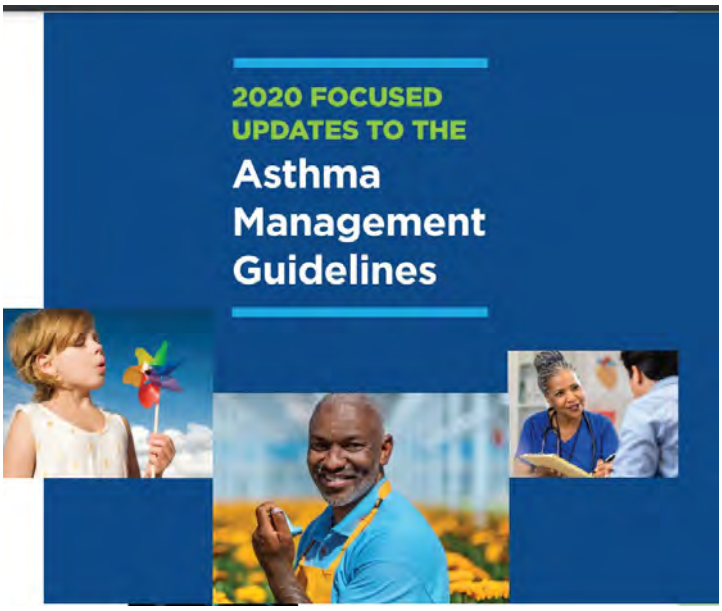
Objectives

1. Understand changes to the 2020 Asthma Management Guidelines regarding single maintenance and relieve therapy (SMART)

2. Review the literature supporting SMART

3. Identify the target population and patients who would benefit from SMART

3



https://www.nhlbi.nih.gov/resources/2020-focused-updates-asthma-management-guidelines

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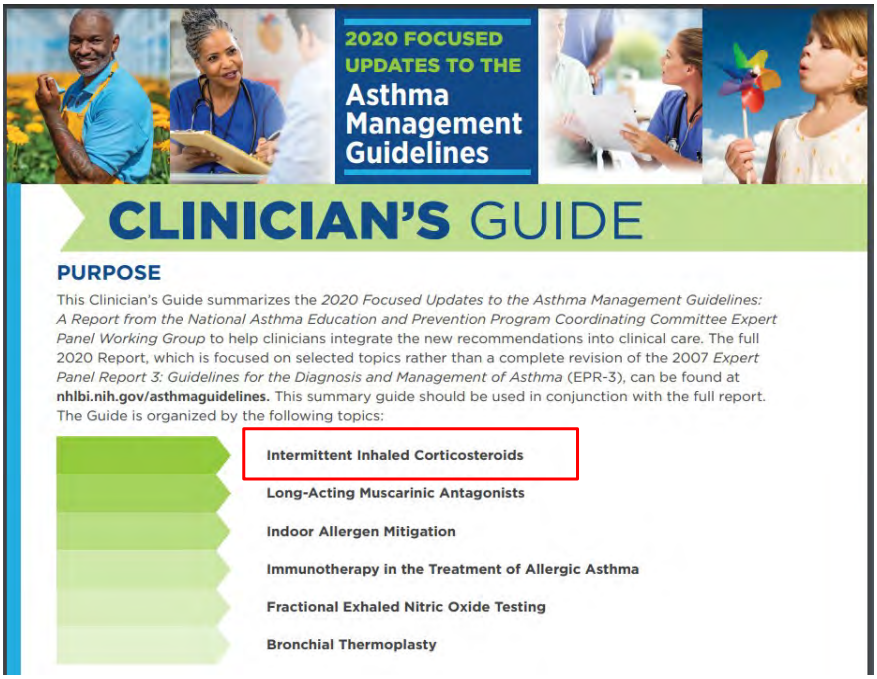

5

In a Nutshell…

- "In individuals ages 4 years and older, the preferred Step 3 (low-dose ICS) and Step 4 (medium-dose ICS) therapy is single-inhaler ICS-formoterol both daily and as needed. In the literature, inhaled ICS-formoterol is referred to as 'single maintenance and reliever therapy (SMART).'"

https://www.nhlbi.nih.gov/resources/2020-focused-updates-asthma-management-guidelines

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In Summary

"In individuals ages ***4 years and older***, the preferred **Step 3 (low-dose ICS) and Step 4 (medium-dose ICS) therapy is single-inhaler ICS-formoterol both daily and as needed.** In the literature, inhaled ICS-formoterol is referred to as 'single maintenance and reliever therapy (SMART)." This form of therapy has only been used with ***formoterol as the LABA***. Formoterol has a *rapid onset and a maximum total daily dose that allows it to be used more than twice daily*. The maximum total daily dose of formoterol should not exceed **eight puffs (36 mcg) for ages 4–11 years** and **12 puffs (54 mcg) for ages 12 years and older**. SMART is administered with a single inhaler containing both formoterol and an ICS (primarily budesonide in the reviewed studies, but one study used beclomethasone). The regimens compared to address this key question required two inhalers: the controller (ICS or ICS-LABA) and the reliever (SABA). The recommended alternate therapy of maintenance *ICS-LABA with SABA as quick-relief therapy does not need to be changed if it is providing adequate control*. However, **patients whose asthma is uncontrolled on such therapy should receive the preferred SMART if possible before moving to a higher step of therapy**."

https://www.nhlbi.nih.gov/resources/2020-focused-updates-asthma-management-guidelines

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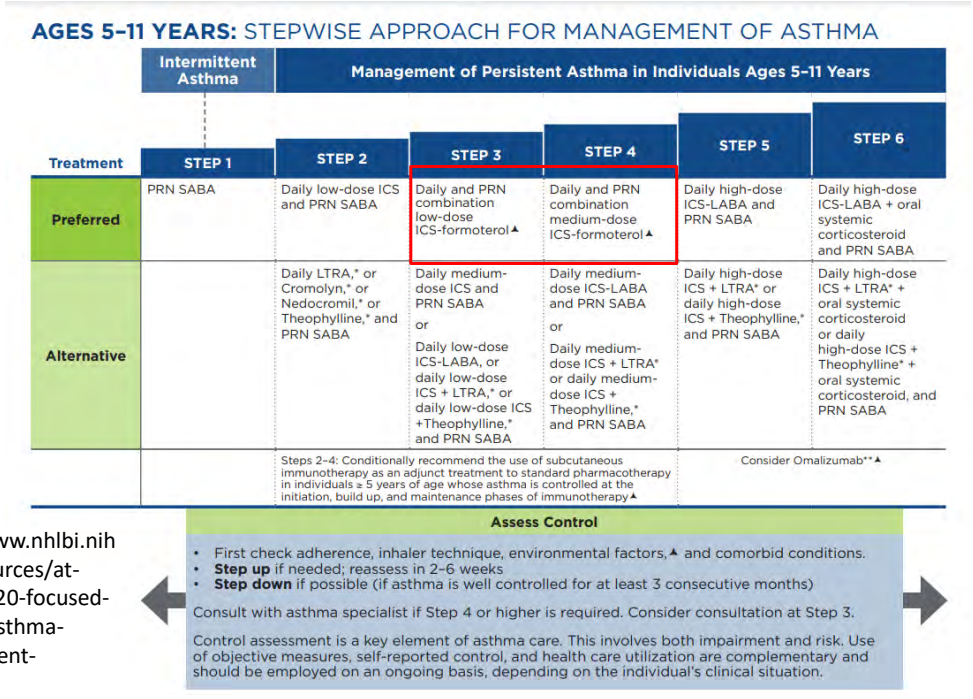

https://www.nhlbi.nih.gov/resources/at-glance-2020-focused-updates-asthma-management-guidelines

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ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL

	0–4 years of age			5–11 years of age			≥12 years of age		
Daily Dose	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***
MEDICATION									
Beclomethasone MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	80–240 mcg	>240–480 mcg	>480 mcg
40 mcg/puff				1–2 puffs 2x/day	3–4 puffs 2x/day		1–3 puffs 2x/day	4–6 puffs 2x/day	
80 mcg/puff				1 puff 2x/day	2 puffs 2x/day	≥3 puffs 2x/day	1 puff am, 2 puffs pm	2–3 puffs 2x/day	≥4 puffs 2x/day
Budesonide DPI†	N/A	N/A	N/A	180–360 mcg	>360–720 mcg	>720 mcg	180–540 mcg	>540–1,080 mcg	>1,080 mcg
90 mcg/inhalation				1–2 inhs† 2x/day	3–4 inhs† 2x/day		1–3 inhs† 2x/day		
180 mcg/ inhalation					2 inhs† 2x/day	≥3 inhs† 2x/day	1 inh† am, 2 inhs† pm	2–3 inhs† 2x/day	≥4 inhs† 2x/day
Budesonide Nebules	0.25–0.5 mg	>0.5–1.0 mg	>1.0 mg	0.5 mg	1.0 mg	2.0 mg	N/A	N/A	N/A
0.25 mg	1–2 nebs†/day			1 neb† 2x/day					
0.5 mg	1 neb†/day	2 nebs†/day	3 nebs†/day	1 neb†/day	1 neb† 2x/day				
1.0 mg		1 neb†/day	2 nebs†/day		1 neb†/day	1 neb† 2x/day			
Ciclesonide MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	160–320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1–2 puffs/day	1 puff am, 2 puffs pm–2 puffs 2x/day	≥3 puffs 2x/day	1–2 puffs 2x/day	3–4 puffs 2x/day	
160 mcg/puff				1 puff/day	1 puff 2x/day	≥2 puffs 2x/day		2 puffs 2x/day	≥3 puffs 2x/day
Flunisolide MDI†	N/A	N/A	N/A	160 mcg	320–480 mcg	≥480 mcg	320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1 puff 2x/day	2–3 puffs 2x/day	≥4 puffs 2x/day	2 puffs 2x/day	3–4 puffs 2x/day	≥5 puffs 2x/day

* It is preferable to use a higher mcg/puff or mcg/inhalation formulation to achieve as low a number of puffs or inhalations as possible.
† **Abbreviations:** DPI, dry powder inhaler (requires deep, fast inhalation); inh, inhalation; MDI, metered dose inhaler (releases a puff of medication); neb, nebule.

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

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ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL *(continued)*

	0–4 years of age			5–11 years of age			≥12 years of age		
Daily Dose	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***
MEDICATION									
Fluticasone MDI†	176 mcg	>176–352 mcg	>352 mcg	88–176 mcg	>176–352 mcg	>352 mcg	88–264 mcg	>264–440 mcg	>440 mcg
44 mcg/puff	2 puffs 2x/day	3–4 puffs 2x/day		1–2 puffs 2x/day	3–4 puffs 2x/day		1–3 puffs 2x/day		
110 mcg/puff		1 puff 2x/day	≥2 puffs 2x/day		1 puff 2x/day	≥2 puffs 2x/day		2 puffs 2x/day	3 puffs 2x/day
220 mcg/puff								1 puffs 2x/day	≥2 puffs 2x/day
Fluticasone DPI†	N/A	N/A	N/A	100–200 mcg	>200–400 mcg	>400 mcg	100–300 mcg	>300–500 mcg	>500 mcg
50 mcg/inhalation				1–2 inhs† 2x/day	3–4 inhs† 2x/day		1–3 inhs† 2x/day		
100 mcg/inhalation				1 inh† 2x/day	2 inhs† 2x/day	>2 inhs† 2x/day		2 inhs† 2x/day	≥3 inhs† 2x/day
250 mcg/inhalation						1 inh† 2x/day		1 inh† 2x/day	≥2 inhs† 2x/day
Mometasone DPI†	N/A	N/A	N/A	110 mcg	220–440 mcg	>440 mcg	110–220 mcg	>220–440 mcg	>440 mcg
110 mcg/inhalation				1 inh†/day	1–2 inhs† 2x/day	≥3 inhs† 2x/day	1–2 inhs† pm	3–4 inhs† pm or 2 inhs† 2x/day	≥3 inhs† 2x/day
220 mcg/inhalation					1–2 inhs†/day	≥3 inhs† divided in 2 doses	1 inh† pm	1 inh† 2x/day or 2 inhs† pm	≥3 inhs† divided in 2 doses

* It is preferable to use a higher mcg/puff or mcg/inhalation formulation to achieve as low a number of puffs or inhalations as possible.
† **Abbreviations:** DPI, dry powder inhaler (requires deep, fast inhalation); inh, inhalation; MDI, metered dose inhaler (releases a puff of medication); neb, nebule.

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

10

SMART for ages 5-11

- For individuals with moderate to severe persistent asthma already taking low- or medium-dose ICS (Steps 3 and 4) the **preferred treatment** is a single inhaler with **ICS-formoterol** used both daily and as needed.
- In Steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of **8 puffs (36 mcg)**
- *Individuals with a severe exacerbation* in the prior year are particularly good candidates for SMART to reduce exacerbations.
- Do not use ICS-formoterol as reliever therapy in individuals taking ICS-salmeterol as maintenance therapy.
- Individuals whose asthma is uncontrolled on maintenance ICS-LABA with SABA as quick-relief therapy should receive the preferred SMART if possible *before moving to a higher step of therapy.*
- In children ages 4–11 years, there may be a lower risk of growth suppression among those taking SMART versus daily higher-dose ICS treatment.

https://www.nhlbi.nih.gov/resources/at-glance-2020-focused-updates-asthma-management-guidelines

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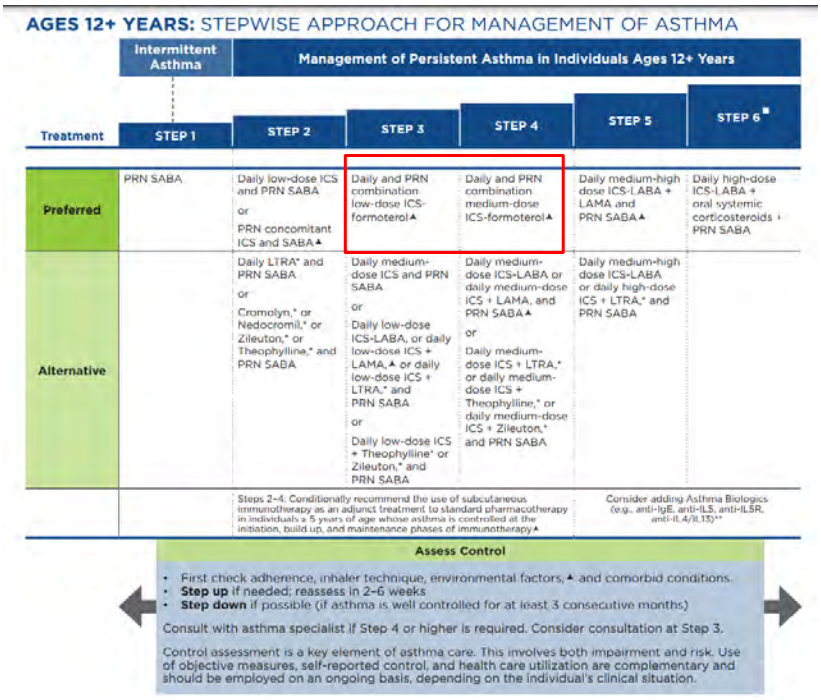

12

ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL

	0–4 years of age			5–11 years of age			≥12 years of age		
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MEDICATION									
Beclomethasone MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	80–240 mcg	>240–480 mcg	>480 mcg
40 mcg/puff				1–2 puffs 2x/day	3–4 puffs 2x/day		1–3 puffs 2x/day	4–6 puffs 2x/day	
80 mcg/puff				1 puff 2x/day	2 puffs 2x/day	≥3 puffs 2x/day	1 puff am, 2 puffs pm	2–3 puffs 2x/day	≥4 puffs 2x/day
Budesonide DPI†	N/A	N/A	N/A	180–360 mcg	>360–720 mcg	>720 mcg	180–540 mcg	>540–1,080 mcg	>1,080 mcg
90 mcg/inhalation				1–2 inhs† 2x/day	3–4 inhs† 2x/day		1–3 inhs† 2x/day		
180 mcg/ inhalation					2 inhs† 2x/day	≥3 inhs† 2x/day	1 inh† am, 2 inhs† pm	2–3 inhs† 2x/day	≥4 inhs† 2x/day
Budesonide Nebules	0.25–0.5 mg	>0.5–1.0 mg	>1.0 mg	0.5 mg	1.0 mg	2.0 mg	N/A	N/A	N/A
0.25 mg	1–2 nebs†/day			1 neb† 2x/day					
0.5 mg	1 neb†/day	2 nebs†/day	3 nebs†/day	1 neb†/day	1 neb† 2x/day				
1.0 mg		1 neb†/day	2 nebs†/day		1 neb†/day	1 neb† 2x/day			
Ciclesonide MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	160–320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1–2 puffs/day	1 puff am, 2 puffs pm–2 puffs 2x/day	≥3 puffs 2x/day	1–2 puffs 2x/day	3–4 puffs 2x/day	
160 mcg/puff				1 puff/day	1 puff 2x/day	≥2 puffs 2x/day		2 puffs 2x/day	≥3 puffs 2x/day
Flunisolide MDI†	N/A	N/A	N/A	160 mcg	320–480 mcg	≥480 mcg	320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1 puff 2x/day	2–3 puffs 2x/day	≥4 puffs 2x/day	2 puffs 2x/day	3–4 puffs 2x/day	≥5 puffs 2x/day

* It is preferable to use a higher mcg/puff or mcg/inhalation formulation to achieve as low a number of puffs or inhalations as possible.
† **Abbreviations:** DPI, dry powder inhaler (requires deep, fast inhalation); inh, inhalation; MDI, metered dose inhaler (releases a puff of medication); neb, nebule.

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

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ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL *(continued)*

	0–4 years of age			5–11 years of age			≥12 years of age		
Daily Dose	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***
MEDICATION									
Fluticasone MDI†	176 mcg	>176–352 mcg	>352 mcg	88–176 mcg	>176–352 mcg	>352 mcg	88–264 mcg	>264–440 mcg	>440 mcg
44 mcg/puff	2 puffs 2x/day	3–4 puffs 2x/day		1–2 puffs 2x/day	3–4 puffs 2x/day		1–3 puffs 2x/day		
110 mcg/puff		1 puff 2x/day	≥2 puffs 2x/day		1 puff 2x/day	≥2 puffs 2x/day		2 puffs 2x/day	3 puffs 2x/day
220 mcg/puff								1 puffs 2x/day	≥2 puffs 2x/day
Fluticasone DPI†	N/A	N/A	N/A	100–200 mcg	>200–400 mcg	>400 mcg	100–300 mcg	>300–500 mcg	>500 mcg
50 mcg/inhalation				1–2 inhs† 2x/day	3–4 inhs† 2x/day		1–3 inhs† 2x/day		
100 mcg/inhalation				1 inh† 2x/day	2 inhs† 2x/day	>2 inhs† 2x/day		2 inhs† 2x/day	≥3 inhs† 2x/day
250 mcg/inhalation						1 inh† 2x/day		1 inh† 2x/day	≥2 inhs† 2x/day
Mometasone DPI†	N/A	N/A	N/A	110 mcg	220–440 mcg	>440 mcg	110–220 mcg	>220–440 mcg	>440 mcg
110 mcg/inhalation				1 inh†/day	1–2 inhs† 2x/day	≥3 inhs† 2x/day	1–2 inhs† pm	3–4 inhs† pm or 2 inhs† 2x/day	≥3 inhs† 2x/day
220 mcg/inhalation					1–2 inhs†/day	≥3 inhs† divided in 2 doses	1 inh† pm	1 inh† 2x/day or 2 inhs† pm	≥3 inhs† divided in 2 doses

* It is preferable to use a higher mcg/puff or mcg/inhalation formulation to achieve as low a number of puffs or inhalations as possible.
† **Abbreviations:** DPI, dry powder inhaler (requires deep, fast inhalation); inh, inhalation; MDI, metered dose inhaler (releases a puff of medication); neb, nebule.

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

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SMART for ages 12+

- For individuals with moderate to severe persistent asthma already taking low- or medium-dose ICS (Steps 3-4), the **preferred treatment is a single inhaler with ICS-formoterol (SMART)** used both daily and as needed.
- In steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of **12 puffs (54 mcg).**
- *Individuals with a severe exacerbation in the prior year* are particularly good candidates for SMART to reduce exacerbations.
- Do not use ICS-formoterol as reliever therapy in individuals taking ICS-salmeterol as maintenance therapy.
- Individuals whose asthma is uncontrolled on maintenance ICS-LABA with SABA as quick-relief therapy should receive the preferred *SMART if possible before moving to a higher step of therapy*

https://www.nhlbi.nih.gov/resources/at-glance-2020-focused-updates-asthma-management-guidelines

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NAEEP vs. GINA?

- GINA = Global Initiative for Asthma
- More of a living document with frequent updates
- Adopted SMART in 2014
- In 2019, low-dose ICS-formoterol became the preferred reliever or 12+ and is an option for 6-11 years

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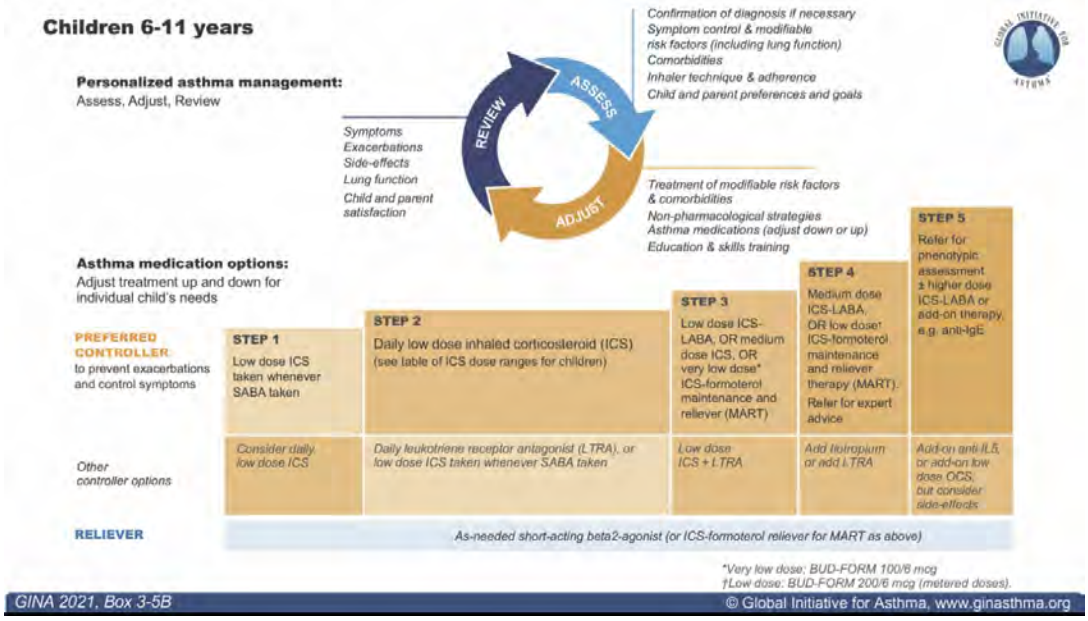

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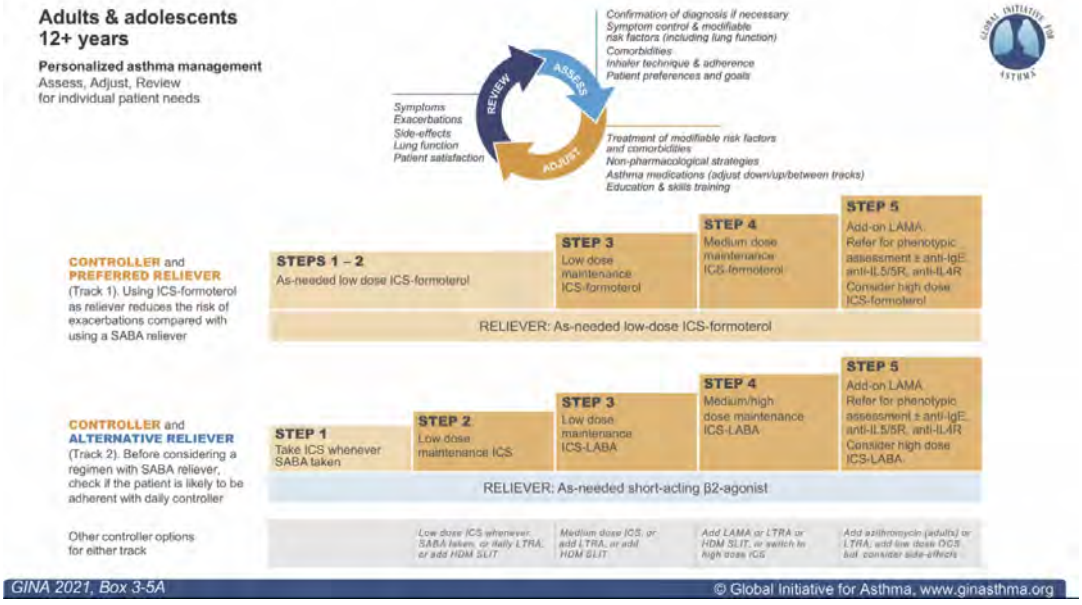

https://www.guidelinesinpractice.co.uk/respiratory/gina-asthma-strategy-whats-new-for-2021/

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Why SMART?

- Let's review the evidence

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Why formoterol?

- Onset of action is rapid like albuterol
- Patients get quick relief
- Has the added advantage of a longer duration of action

Reddel HK, *J Allergy Clin Immunol Pract.* 2022

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Budesonide/Formoterol Combination Therapy as Both Maintenance and Reliever Medication in Asthma

Paul M. O'Byrne, Hans Bisgaard, Philippe P. Godard, Massimo Pistolesi, Mona Palmqvist, Yuanjue Zhu, Tommy Ekström, and Eric D. Bateman

Firestone Institute for Respiratory Health, St. Joseph's Hospital, Hamilton, Ontario, Canada; COPSAC Clinical Research Unit, University Hospital of Copenhagen, Gentofte, Denmark; Hôpital Arnaud de Villeneuve, Service des Maladies Respiratoires and Bronchomotricité, Montpellier, France; Department of Critical Care, Section of Respiratory Medicine, University of Florence, Florence, Italy; Department of Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden; Respiratory Department, Peking Union Medical College Hospital, Beijing, China; AstraZeneca R&D, Lund, Sweden; and University of Cape Town, Cape Town, South Africa

Am J Respir Crit Care Med. 2005 Jan 15;171(2):129-36

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TABLE 1. PATIENTS' BASELINE CHARACTERISTICS

Characteristic	Bud + SABA (*n* = 926)	Bud/form + SABA (*n* = 909)	Bud/form Maintenance + Relief (*n* = 925)
Male/female, n	416/510	394/515	421/504
Age, yr	36 (4–79)	36 (4–79)	35 (4–77)
4–11 years, n (%)	106 (11)	117 (13)	118 (13)
Asthma duration, yr	9 (0–69)	9 (0–65)	9 (0–63)
FEV_1, L	2.14 (0.64–4.02)	2.10 (0.62–4.50)	2.13 (0.65–4.28)
FEV_1, % predicted normal	73 (49–100)	73 (46–108)	73 (43–108)
FEV_1 reversibility, %	21 (3–77)	21 (12–75)	21 (2–89)
ICS dose at entry,* μg/day	620 (100–1000)	598 (200–1,000)	619 (200–1,200)
Inhaled LABA use at study entry†	256 (28)	258 (29)	250 (27)
Reliever use, number of inhalations/day	1.69 (0.0–7.0)	1.69 (0.0–9.4)	1.74 (0.0–8.0)
Reliever use, number of inhalations/night	0.72 (0.0–3.7)	0.73 (0.0–6.6)	0.72 (0.0–5.7)
Asthma symptom score (scale 0–6)	1.5 (0.0–5.6)	1.4 (0.0–5.2)	1.5 (0.0–6.0)
Symptom-free days, %	23.5 (0–100)	24.0 (0–100)	23.1 (0–100)
Reliever-free days, %	8.8 (0–100)	8.3 (0–100)	8.2 (0–100)
Asthma control days, %	5.6 (0–90)	5.9 (0–80)	5.4 (0–90)
Awakenings, % of nights	20.6 (0–100)	20.2 (0–100)	21.8 (0–100)

Definition of abbreviations: Bud = budesonide; form = formoterol; ICS = inhaled corticosteroids; LABA = long-acting β_2-agonist; SABA = short-acting β_2-agonist.

All values are presented as absolute numbers or as mean (range), except asthma duration (median).

*Values are a combination of metered and delivered doses.

† Includes combinations of ICS/LABA and LABA.

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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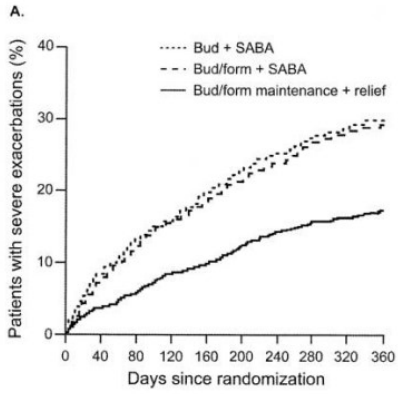

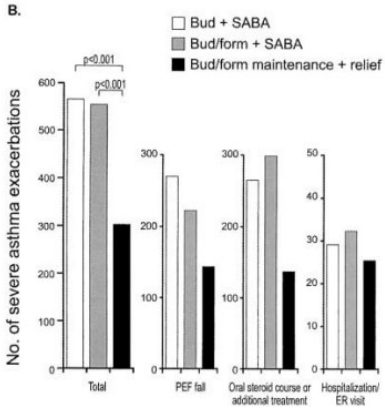

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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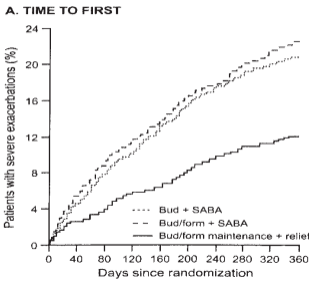

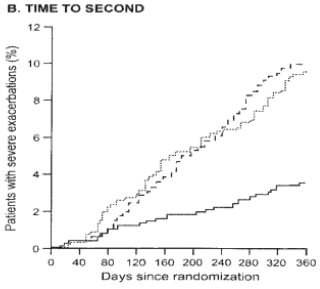

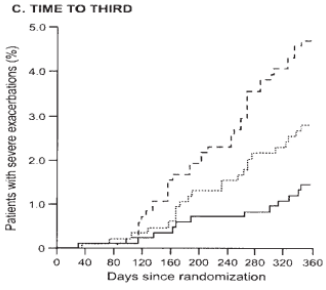

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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TABLE 2. CLINICAL OUTCOMES

Variable	Bud + SABA	Bud/form + SABA	Bud/form Maintenance + Relief	p Values: Bud/form + SABA vs. Bud + SABA	p Values: Bud/form Maintenance + Relief vs. Bud + SABA	p Values: Bud/form Maintenance + Relief vs. Bud/form + SABA
Severe exacerbations including PEF falls						
Patients with event, %*	28	27	16	0.74	< 0.001	< 0.001
Events/patient/year†	0.68	0.68	0.36	0.98	< 0.001	< 0.001
Severe exacerbations resulting in medical intervention						
Patients with event, %*	19	21	11	0.37	< 0.001	< 0.001
Events/patient/year†	0.35	0.40	0.19	0.11	< 0.001	< 0.001
Daily control measures						
Daytime symptom score‡	0.59	0.50	0.48	< 0.001	< 0.001	0.12
Night-time symptom score‡	0.42	0.36	0.31	0.01	< 0.001	< 0.001
Reliever use, inhs/day	1.03	0.84	0.73	< 0.001	< 0.001	< 0.001
Reliever use, inhs/night	0.43	0.37	0.28	0.003	< 0.001	< 0.001
Symptom-free days, %	46	53	54	< 0.001	< 0.001	0.52
Reliever-free days, %	45	54	55	< 0.001	< 0.001	0.60
Asthma control days, %§	37	44	45	< 0.001	< 0.001	0.64
Awakenings, % of nights	12	12	9	0.60	< 0.001	< 0.001
Mild exacerbation days, %¶	20	23	17	0.06	0.03	< 0.001
Morning PEF, L/min	339	346	355	< 0.001	< 0.001	< 0.001
Evening PEF, L/min	345	349	360	< 0.001	< 0.001	< 0.001
FEV_1, L	2.41	2.43	2.51	0.09	< 0.001	< 0.001

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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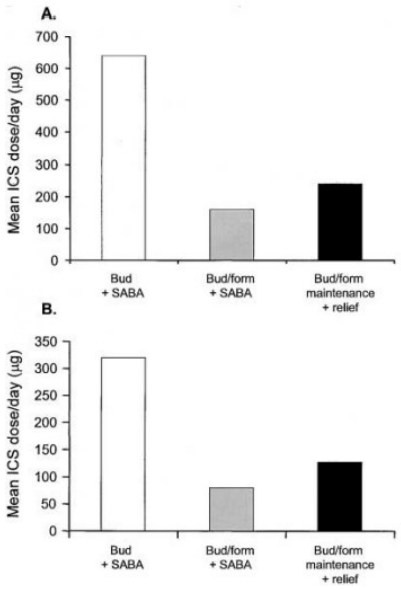

A: Patients 12-80 years
B: Patients 4-11 years

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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TABLE 3. COMMON ADVERSE EVENTS BY TYPE (≥ 5% INCIDENCE) AND ANY PHARMACOLOGICALLY PREDICTABLE ADVERSE EVENTS

	Number of Patients (%)		
	Bud + SABA (*n* = 925)	Bud/form + SABA (*n* = 906)	Bud/form Maintenance + Relief (*n* = 922)
Respiratory infection	182 (20)	144 (16)	158 (17)
Pharyngitis	86 (9)	88 (10)	88 (10)
Rhinitis	76 (8)	72 (8)	80 (9)
Bronchitis	76 (8)	61 (7)	51 (6)
Sinusitis	33 (4)	39 (4)	43 (5)
Headache	42 (5)	35 (4)	31 (3)
Pharmacologically predictable events			
Tremor	19 (2)	18 (2)	20 (2)
Palpitation	3 (< 0.5)	11 (1)	10 (1)
Tachycardia	3 (< 0.5)	4 (< 0.5)	5 (0.5)
Candidiasis	10 (1)	6 (1)	9 (1)
Dysphonia	12 (1)	13 (1)	11 (1)

Definition of abbreviations: Bud = budesonide; form = formoterol; SABA = short-acting β_2-agonist.

O'Byrne PM, et al. *Am J Respir Crit Care Med*. 2005

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Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study

Klaus F Rabe, Tito Atienza, Pál Magyar, Per Larsson, Carin Jorup, Umesh G Lalloo

Lancet. 2006 Aug 26;368(9537):744-53

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	Terbutaline as-needed group (n=1141)	Formoterol as-needed group (n=1140)	Budesonide-formoterol as-needed group (n=1113)
Men, n (%)	450 (39%)	458 (40%)	437 (39%)
Age, years	43 (12–83)	42 (12–81)	42 (12–89)
Median (range) asthma duration, years	10 (1–69)	10 (1–77)	9 (0–64)
FEV_1, L	2·16 (0·68–4·58)	2·20 (0·74–4·58)	2·21(0·61–4·68)
FEV_1 (pre-terbutaline), % predicted	72 (39†–100)	72 (38†–115†)	72 (30†–110†)
FEV_1 reversibility, %	24 (11†–90)	24 (0†–96)	24 (6†–132)
ICS dose at entry, µg/day	751 (250†–1600)	758 (320†–1600)	757 (160†–1600)
Inhaled LABA use at entry, % of patients	59%	59%	59%
Mean daily asthma control measures ‡			
Total asthma symptom score (scale 0–6)	1·74 (0·00–6·00)	1·70 (0·00–6·00)	1·71 (0·00–5·71)
Reliever use, number of inhalations per 24 h	1·9 (0·3–9·7)	1·9 (0·0–9·1)	1·8 (0·0–8·9)
Nights with awakenings, %	30·3 (0–100)	28·0 (0–100)	31·1 (0–100)
Asthma-control days§, %	8·3 (0–50)	8·3 (0–80)	9·2 (0–90)
ACQ-5¶	1·9 (0–4·8)	1·9 (0–5·4)	1·9 (0–4·8)

Data are mean (range) unless otherwise indicated. ACQ-5=Asthma control questionnaire (5-item symptom and activity version). FEV_1=forced expiratory volume in 1 s. ICS=inhaled corticosteroid. LABA=long-acting β2 agonist. *All patients received budesonide-formoterol 160/4·5 µg one inhalation twice daily for maintenance therapy. †Deviation from inclusion criteria (included in all statistical analyses). ‡Average over the past 10 days of run-in. §A night and day with no asthma symptoms (symptom score=0), a night with no awakenings due to asthma symptoms, and a night and day with no use of as-needed medication. ¶ACQ-5 was measured at visit 2.

Table 1: **Baseline characteristics of patients using maintenance budesonide-formoterol plus alternative reliever medications***

Rabe KF, et al. *Lancet*. 2006

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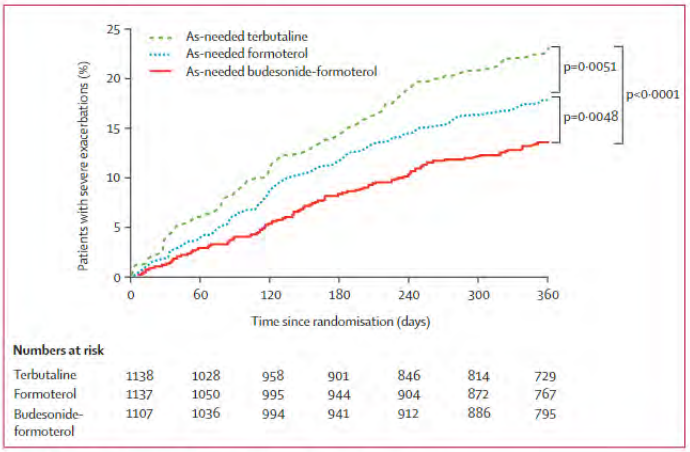

Numbers at risk

Terbutaline	1138	1028	958	901	846	814	729
Formoterol	1137	1050	995	944	904	872	767
Budesonide-formoterol	1107	1036	994	941	912	886	795

Figure 2: **Kaplan–Meier plot of time to first severe asthma exacerbation**
Time to first severe asthma exacerbation defined as a deterioration in asthma resulting in hospitalisation, emergency room treatment, or the need for oral steroids for 3 days or more because of asthma (as judged by investigator). Patients received maintenance budesonide-formoterol 160/4·5 µg, one inhalation twice daily, plus one of the following for as-needed relief: additional inhalations of budesonide-formoterol 160/4·5 µg; formoterol 4·5 µg; or terbutaline 0·4 mg. Significant between-group differences were derived from a log-rank test.

Rabe KF, et al. *Lancet*. 2006

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	Reliever medication group			Treatment comparison of hazard ratios (95% CI)		
	Terbutaline as-needed (n=1138)	Formoterol as-needed (n=1137)	Budesonide–formoterol as-needed (n=1107)	Formoterol versus terbutaline	Budesonide-formoterol versus terbutaline	Budesonide-formoterol versus formoterol
Severe exacerbations (all definitions)						
Patients with event, n (%)	245 (22%)	195 (17%)	143 (13%)	0·76* (0·63–0·92); p=0·004	0·55* (0·45–0·68); p<0·0001	0·73* (0·59–0·90); p=0·0038
Total events (days with events)	377 (3030)	296 (2214)	194 (1353)			
Rate, events per 100 patients per year	37	29	19	0·78† (0·67–0·91); p=0·0012	0·52† (0·44–0·62); p<0·0001	0·67† (0·56–0·80); p<0·0001
Emergency room visits or hospitalisations						
Patients with event, n (%)	91 (8%)	75 (7%)	54 (5%)	0·79* (0·58–1·07); p=0·12	0·57* (0·41–0·81); p=0·0013	0·73* (0·51–1·04); p=0·079
Total events (days with events)	115 (392)	98 (282)	70 (218)			
Rate, events per 100 patients per year	7	5	4	0·83† (0·63–1·08); p=0·17	0·61† (0·45–0·82); p=0·0010	0·73† (0·54–0·99); p=0·046
Mild exacerbations						
Patients with event, n (%)	887 (78%)	873 (77%)	811 (74%)	0·97* (0·88–1·06); p=0·47	0·88* (0·80–0·97); p=0·0075	0·91* (0·83–1·00); p=0·050
Rate, days per patient per year	69	63	57	0·91† (0·83–1·00); p=0·058	0·82† (0·74–0·91); p=0·0001	0·90† (0·81–1·00); p=0·043

All patients received budesonide-formoterol 160/4·5 µg one inhalation twice daily for maintenance therapy. *Treatment comparisons of hazard ratios from a Cox proportional hazards model of time to first severe exacerbation. †Comparisons of relative rates from a Poisson regression.

Table 2: **Severe and mild asthma exacerbations in patients using maintenance budesonide–formoterol plus alternative reliever medications**

Rabe KF, et al. *Lancet*. 2006

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	Change from run-in			Treatment comparison (95% CI); p*		
	Terbutaline as-needed (n=1138)	Formoterol as-needed (n=1137)	Budesonide-formoterol as-needed (n=1107)	Formoterol versus terbutaline	Budesonide-formoterol versus terbutaline	Budesonide-formoterol versus formoterol
Symptom control						
Asthma symptom score (scale 0–6)†	−0·58	−0·57	−0·69	0·01 (−0·05 to 0·07); p=0·72	−0·11 (−0·17 to −0·05); p=0·0007	−0·12 (−0·18 to −0·06); p=0·0002
Reliever use, number of inhalations per 24 h†	−0·64	−0·67	−0·84	−0·03 (−0·11 to 0·05); p=0·48	−0·20 (−0·28 to −0·11); p<0·0001	−0·17 (−0·25 to −0·08); p<0·0001
Nights with awakenings, %†	−13·5%	−14·0%	−16·0%	−0·6 (−2·2 to 1·1); p=0·51	−2·6 (−4·3 to −0·9); p=0·0025	−2·0 (−3·7 to −0·4); p=0·018
Asthma-control days, %†	29·3%	28·8%	31·2%	−0·5 (−3·1 to 2·2); p=0·74	1·9 (−0·7 to 4·6); p=0·16	2·4 (−0·3 to 5·1); p=0·079
ACQ-5‡	−0·49	−0·53	−0·63	−0·04 (−0·10, 0·02); p=0·21	−0·15 (−0·21, −0·08); p<0·0001	−0·11 (−0·17, −0·04); p=0·0009
Lung function¶						
FEV_1 (L)‡	−0·02	0·01	0·06	0·03 (0·001 to 0·05); p=0·043	0·08 (0·05 to 0·10); p<0·0001	0·05 (0·02 to 0·08); p=0·00014
Morning PEF (L/min)†	7·9	10·6	15·3	2·7 (−0·6 to 5·9); p=0·11	7·5 (4·2 to 10·7); p<0·0001	4·8 (1·5 to 8·0); p=0·0040
Evening PEF (L/min)†	7·5	8·5	13·8	0·9 (−2·3 to 4·1); p=0·57	6·3 (3·1 to 9·5); p=0·00014	5·4 (2·1 to 8·6); p=0·0011

All patients received budesonide-formoterol 160/4·5 µg one inhalation twice daily for maintenance therapy. ACQ-5=Asthma Control Questionnaire (5-item symptom and activity version); FEV_1=forced expiratory volume in 1 s. PEF=peak expiratory flow. *ANOVA. †Data are presented as adjusted mean change from run-in to the treatment period. ‡Data are presented as adjusted mean change from visit 2 (day 0) to the average value of available data during clinic visits.

Table 3: **Changes from run-in in symptom control and lung function in patients using maintenance budesonide-formoterol plus alternative reliever medications**

Rabe KF, et al. *Lancet*. 2006

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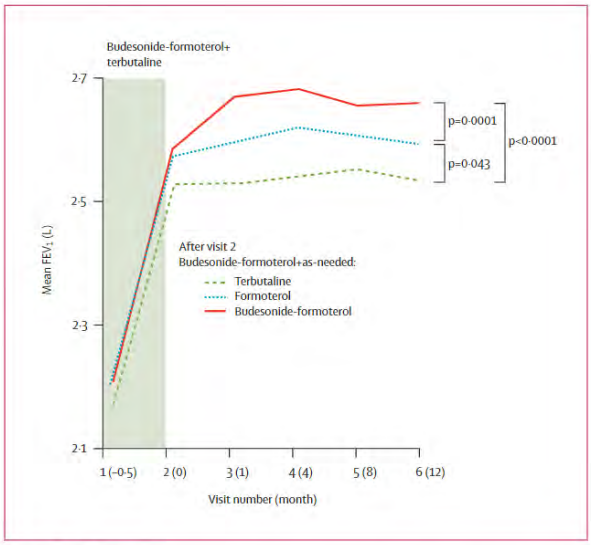

Figure 3: **Mean FEV_1 over time**
The shaded area represents the run-in period. Patients received maintenance budesonide-formoterol 160/4·5 µg, one inhalation twice daily, plus as-needed terbutaline during run-in. Post-randomisation, patients received budesonide-formoterol 160/4·5 µg 1 inhalation twice daily plus one of the following for as-needed relief: additional inhalations of budesonide-formoterol 160/4·5 µg; formoterol 4·5 µg; or terbutaline 0·4 mg. FEV_1=forced expiratory volume in 1 s.

Rabe KF, et al. *Lancet*. 2006

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	Number of patients with event (%)		
	Terbutaline as-needed group (n=1138)	Formoterol as-needed group (n=1137)	Budesonide-formoterol as-needed group (n=1107)
SAEs reported as asthma	26 (2%)	23 (2%)	16 (1%)
DAEs reported as asthma	10 (1%)	14 (1%)	1 (0·1%)
Pharmacologically predictable adverse events			
Tremor	2 (0·2%)	4 (0·4%)	1 (0·1%)
Palpitation/tachycardia	4 (0·4%)	6 (0·5%)	7 (0·6%)
Hoarseness	7 (0·6%)	11 (1%)	7 (0·6%)
Oral candidosis*	10 (1%)	11 (1%)	22 (2%)
Dysphonia	0 (0)	1 (0·1%)	0 (0)

SAE=serious adverse event. DAE=adverse event leading to discontinuation of the patient from the study. *Includes oral candidosis and any adverse event considered closely related to oral candidosis (ie, pharyngeal candidosis, oropharyngitis fungal, or oral fungal infection).

Table 4: **Adverse events reported as asthma and pharmacologically predictable adverse events**

Rabe KF, et al. *Lancet*. 2006

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ORIGINAL ARTICLE

Controlled Trial of Budesonide–Formoterol as Needed for Mild Asthma

Richard Beasley, D.Sc., Mark Holliday, B.Sc., Helen K. Reddel, Ph.D., Irene Braithwaite, Ph.D., Stefan Ebmeier, B.M., B.Ch., Robert J. Hancox, M.D., Tim Harrison, M.D., Claire Houghton, B.M., B.S., Karen Oldfield, M.B., Ch.B., Alberto Papi, M.D., Ian D. Pavord, F.Med.Sci., Mathew Williams, Dip.Ex.Sci., and Mark Weatherall, F.R.A.C.P., for the Novel START Study Team*

N Engl J Med. 2019 May 23;380(21):2020-2030

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Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Albuterol Group (N=223)	Budesonide Maintenance Group (N=225)	Budesonide–Formoterol Group (N=220)
Age — yr	35.8±14.0	34.9±14.3	36±14.1
Female sex — no. (%)	113 (50.7)	129 (57.3)	122 (55.5)
Current smoker — no. (%)	24 (10.8)	22 (9.8)	18 (8.2)
Patient-reported SABA use in the 4 weeks before enrollment			
No. of occasions per wk			
Mean	3.4±3.3	3.2±3.0	3.8±3.5
Median (IQR)	2 (1–4)	2 (1–4)	3 (1–5)
Range	0–14	0.5–14	0.5–14
Patients who had ≤2 occasions per wk — no. (%)	127 (57.0)	132 (58.7)	105 (47.7)
Puffs per wk			
Mean	6.52±7.83	5.82±5.25	6.98±6.91
Median (IQR)	4 (2–8)	4 (2–7)	4 (2–8)
Range	0–84	0.5–28	0.5–42
No. of hospital admissions for asthma at any time before enrollment — mean per patient	0.3±0.9	0.3±0.9	0.3±1.3
No. of severe exacerbations in the previous 12 mo. — no. (%)			
0	203 (91.0)	208 (92.4)	208 (94.5)
1	20 (9.0)	15 (6.7)	12 (5.5)
2	0	2 (0.9)	0
Any	20 (9.0)	17 (7.6)	12 (5.5)
ACQ-5 score†	1.1±0.7	1.1±0.7	1.1±0.7
On-treatment FEV_1 — % of predicted value‡	89.2±13.7	90.3±13.6	89.8±14.1
Median F_{ENO} (range) — ppb	40 (5–235)	38 (5–200)	37 (3–300)
Periostin — ng/ml	69.3±28.9	70.6±27.8	70.8±27.0
Blood eosinophil count — $\times 10^{-9}$ per liter	0.3±0.2	0.3±0.2	0.3±0.2

Beasley R, et al.
N Engl J Med. 2019

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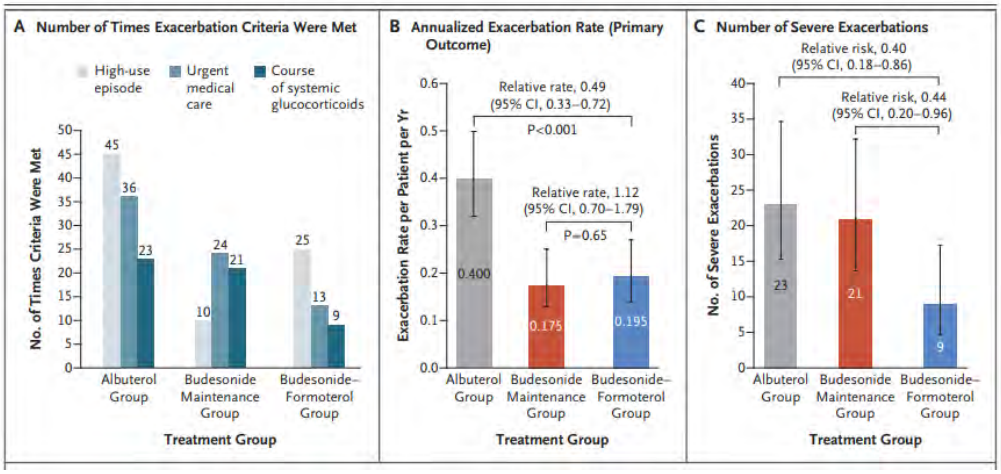

Beasley R, et al. *N Engl J Med*. 2019

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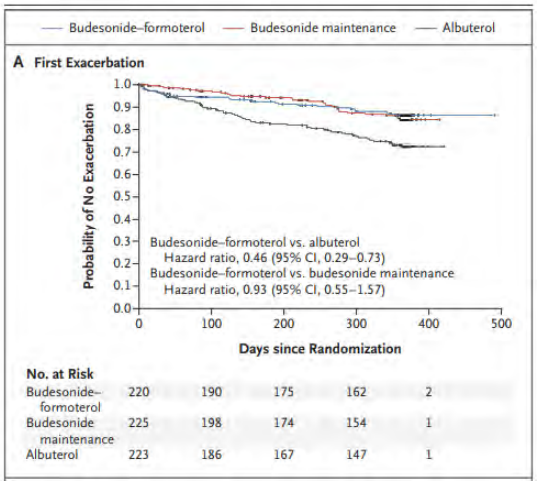

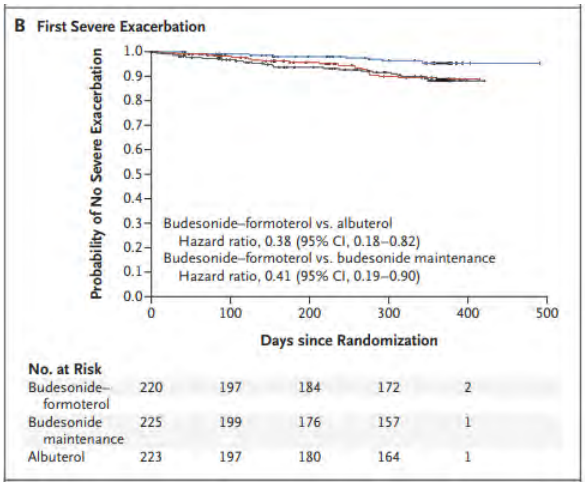

Beasley R, et al. *N Engl J Med*. 2019

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Table 2. Medication Outcomes.*

Outcome	Albuterol Group (N=223)	Budesonide Maintenance Group (N=225)	Budesonide–Formoterol Group (N=220)
Glucocorticoid use			
No. of inhaled glucocorticoid-containing actuations per day			
Mean	NA	1.11±0.56	0.53±0.54
Median (IQR)	NA	1.23 (0.66–1.57)	0.37 (0.15–0.73)
Range	NA	0–2.01	0–3.95
Daily budesonide dose — μg			
Mean	NA	222±113	107±109
Median (IQR)	NA	247 (132–314)	73 (31–146)
Range†	NA	0–402	0–790
Oral glucocorticoid use, prednisone — mg	17.4±59.8	14.5±51.0	7.5±40.2
No. of β_2-agonist–containing actuations per day			
Mean	1.01±1.60	0.52±1.03	0.53±0.54
Median (IQR)	0.50 (0.18–1.18)	0.18 (0.06–0.46)	0.37 (0.15–0.73)
Range	0.0–16.3	0.0–8.7	0–3.95

* Plus–minus values are means ±SD. Inhaled glucocorticoid and β_2-agonist use was determined with the use of electronic monitoring of the trial inhalers. NA denotes not applicable.
† The range refers to the minimum mean daily dose and the maximum mean daily dose.

Beasley R, et al. *N Engl J Med*. 2019

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JAMA Network Open

Original Investigation | Pulmonary Medicine

Evaluation of Budesonide-Formoterol for Maintenance and Reliever Therapy Among Patients With Poorly Controlled Asthma

A Systematic Review and Meta-analysis

Richard Beasley, DSc; Tim Harrison, MD; Stefan Peterson, PhD; Per Gustafson, MD, PhD; Angus Hamblin, BA; Thomas Bengtsson, MSc; Malin Fageråas, PhD

JAMA Netw Open. 2022 Mar 1;5(3).

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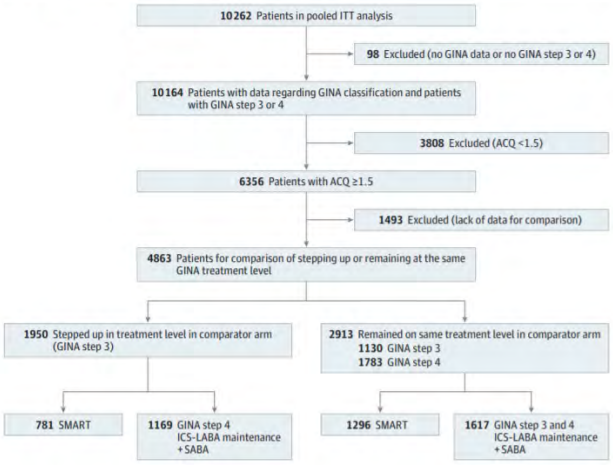
Figure 1. Flow Diagram of Patients Included in the Analysis



The initial total of 10 262 patients excludes the patients in the as-needed formoterol-only arm of the SMILE trial.[11] The 1493 patients excluded because of lack of data for comparison refers to patients receiving Global Initiative for Asthma (GINA) step 4 treatment in the SMILE[11] and SAKURA[12] trials, who corresponded to a step down in treatment level. ACQ indicates Asthma Control Questionnaire; ICS, inhaled corticosteroid; ITT, intention to treat; LABA, long-acting β_2-agonist; SABA, short-acting β_2-agonist; SMART, single maintenance and reliever therapy.

Beasley R, et al. *JAMA Netw Open*. 2022

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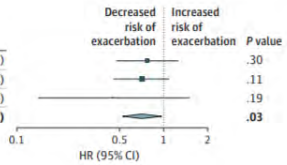
Figure 2. Meta-analysis of the Association of Single Inhaler Maintenance and Reliever Therapy (SMART) vs Inhaled Corticosteroid–Long-acting β_2-Agonist (ICS-LABA) Maintenance Plus Short-acting β_2-Agonist (SABA) Reliever With Time to First Severe Exacerbation

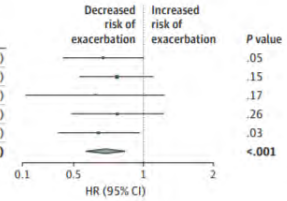
A SMART vs step up to GINA step 4

Trial	No. exacerbation, No./total No. (%) SMART	GINA step 4	HR (95% CI)	P value
AHEAD[10]	29/371 (7.8)	38/373 (10.2)	0.77 (0.48-1.25)	.30
COMPASS[8]	29/372 (7.8)	84/774 (10.9)	0.71 (0.46-1.08)	.11
Patel et al,[9]	5/38 (13.2)	6/22 (27.3)	0.45 (0.14-1.49)	.19
Total	**63/781 (8.1)**	**128/1169 (10.9)**	**0.71 (0.52-0.97)**	**.03**



B SMART vs same GINA step 3

Trial	No. exacerbation, No./total No. (%) SMART	GINA step 3 or 4	HR (95% CI)	P value
AHEAD[10]	40/327 (12.2)	61/348 (17.5)	0.67 (0.45-1.00)	.05
COMPASS[8]	41/333 (12.3)	108/681 (15.9)	0.77 (0.53-1.10)	.15
Patel et al,[9]	13/46 (28.3)	21/48 (43.8)	0.62 (0.31-1.23)	.17
SAKURA[12]	35/251 (13.9)	38/215 (17.7)	0.77 (0.49-1.22)	.26
SMILE[11]	42/339 (12.4)	58/325 (17.8)	0.64 (0.43-0.96)	.03
Total	**171/1296 (13.2)**	**286/1617 (17.7)**	**0.70 (0.58-0.85)**	**<.001**



In the COMPASS trial,[8] the 2 comparator arms were pooled into 1 fixed ICS-LABA treatment arm. GINA indicates Global Initiative for Asthma; HR, hazard ratio.

Beasley R, et al. *JAMA Netw Open*. 2022

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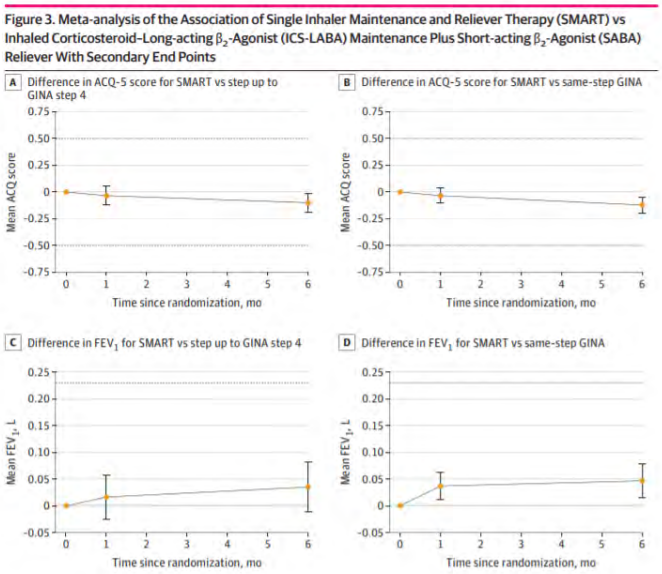

Figure 3. Meta-analysis of the Association of Single Inhaler Maintenance and Reliever Therapy (SMART) vs Inhaled Corticosteroid–Long-acting β_2-Agonist (ICS-LABA) Maintenance Plus Short-acting β_2-Agonist (SABA) Reliever With Secondary End Points

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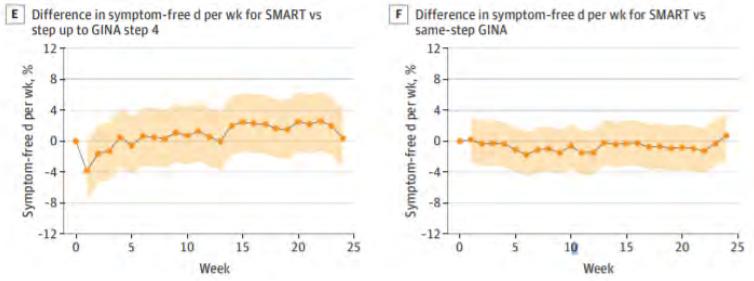

Whiskers and shading represent 95% CIs; and dotted lines, the minimal clinically important differences. ACQ-5 indicates Asthma Control Questionnaire 5-item version; FEV_1, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma.

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 2, 2022 VOL. 386 NO. 22

Albuterol–Budesonide Fixed-Dose Combination Rescue Inhaler for Asthma

Alberto Papi, M.D., Bradley E. Chipps, M.D., Richard Beasley, D.Sc., Reynold A. Panettieri, Jr., M.D., Elliot Israel, M.D., Mark Cooper, M.Sc., Lynn Dunsire, M.Sc., Allison Jeynes-Ellis, M.D., Eva Johnsson, M.D., Robert Rees, Ph.D., Christy Cappelletti, Pharm.D., and Frank C. Albers, M.D.

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Table 1. Demographic and Clinical Characteristics of the Patients at Screening.*

Characteristic	Albuterol (180 μg)–Budesonide (160 μg) (N=1013)	Albuterol (180 μg)–Budesonide (80 μg) (N=1054)	Albuterol (180 μg) (N=1056)	All Patients (N=3123)
Age				
Mean — yr	50.6±15.1	48.5±16.7	49.1±17.2	49.4±16.4
Distribution — no. (%)				
≥4 to <12 yr	0	41 (3.9)	42 (4.0)	83 (2.7)
≥12 to <18 yr	34 (3.4)	32 (3.0)	34 (3.2)	100 (3.2)
≥18 to <65 yr	787 (77.7)	804 (76.3)	783 (74.1)	2374 (76.0)
≥65 yr	192 (19.0)	177 (16.8)	197 (18.7)	566 (18.1)
Female sex — no. (%)	645 (63.7)	685 (65.0)	694 (65.7)	2024 (64.8)
Race or ethnic group — no. (%)				
White	818 (80.8)	847 (80.4)	868 (82.2)	2533 (81.1)
Black	139 (13.7)	141 (13.4)	137 (13.0)	417 (13.4)
Asian	29 (2.9)	33 (3.1)	23 (2.2)	85 (2.7)
American Indian or Alaska Native	1 (0.1)	1 (0.1)	0	2 (0.1)
Other	26 (2.6)	32 (3.0)	28 (2.7)	86 (2.8)
Hispanic or Latinx — no. (%)				
Yes	233 (23.0)	260 (24.7)	315 (29.8)	808 (25.9)
No	780 (77.0)	794 (75.3)	741 (70.2)	2315 (74.1)

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Geographic region — no. (%)				
North America, Western Europe, and South Africa	536 (52.9)	556 (52.8)	563 (53.3)	1655 (53.0)
South America and rest of Europe	477 (47.1)	498 (47.2)	493 (46.7)	1468 (47.0)
Prebronchodilator FEV_1				
Mean volume — liters†	1.9±0.6	1.9 ±0.6	1.9±0.6	1.9±0.6
Mean percent of predicted value†	63.4±12.8	64.0±13.7	64.4±13.3	63.9±13.3
Mean reversibility in FEV_1 — %‡	27.7±17.2	27.2±14.2	27.8±15.9	27.6±15.8
Maintenance treatment — no. (%)				
Low-dose inhaled glucocorticoid–LABA or medium-dose inhaled glucocorticoid	314 (31.0)	334 (31.7)	308 (29.2)	956 (30.6)
Medium-dose inhaled glucocorticoid–LABA or high-dose inhaled glucocorticoid	385 (38.0)	435 (41.3)	441 (41.8)	1261 (40.4)
High-dose inhaled glucocorticoid–LABA	295 (29.1)	267 (25.3)	285 (27.0)	847 (27.1)
Missing	19 (1.9)	18 (1.7)	22 (2.1)	59 (1.9)
Severe asthma exacerbations in the 12 mo before screening — no. (%)				
1	788 (77.8)	822 (78.0)	840 (79.5)	2450 (78.5)
2	185 (18.3)	185 (17.6)	164 (15.5)	534 (17.1)
3	27 (2.7)	38 (3.6)	45 (4.3)	110 (3.5)
≥4	13 (1.3)	9 (0.9)	7 (0.7)	29 (0.9)

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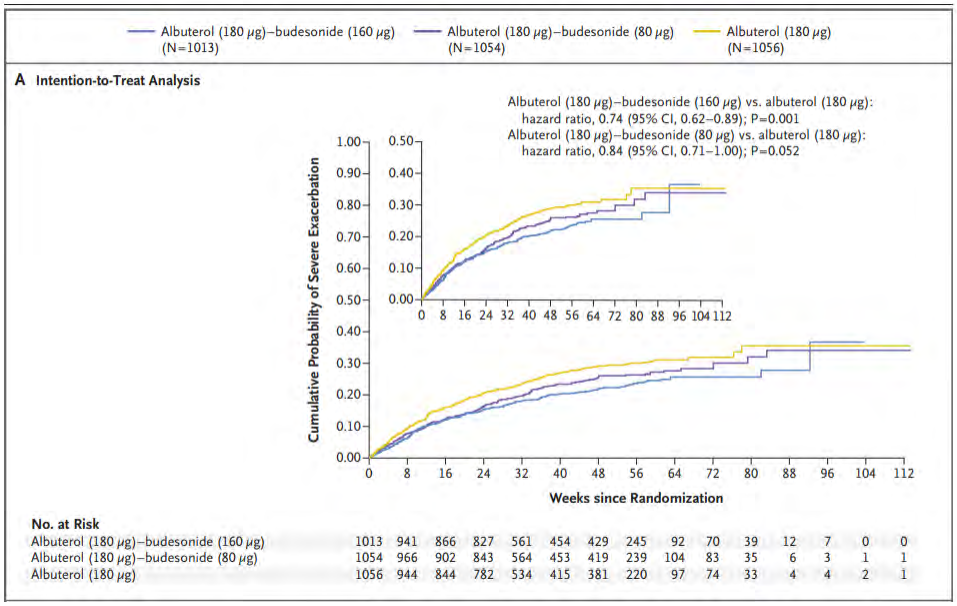

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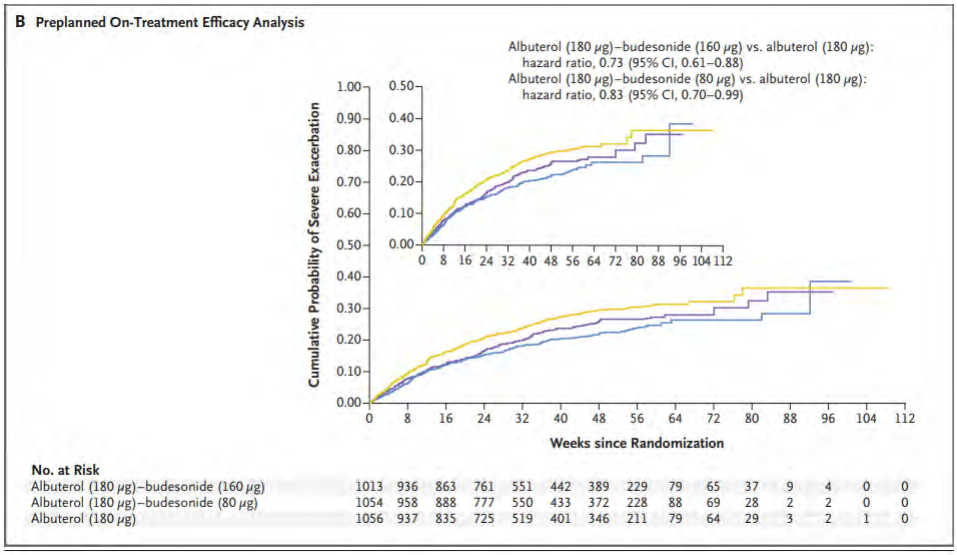

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Table 2. Intention-to-Treat and Preplanned On-Treatment Efficacy Analyses of the Secondary End Points.*

Analysis	Intention-to-Treat Analysis				Preplanned On-Treatment Efficacy Analysis			
	Adults and Adolescents†		Adults, Adolescents, and Children‡		Adults and Adolescents†		Adults, Adolescents, and Children‡	
	Albuterol (180 μg)–Budesonide (160 μg)	Albuterol (180 μg)	Albuterol (180 μg)–Budesonide (80 μg)	Albuterol (180 μg) Alone	Albuterol (180 μg)–Budesonide (160 μg)	Albuterol (180 μg)	Albuterol (180 μg)–Budesonide (80 μg)	Albuterol (180 μg)
Annualized rate of severe asthma exacerbation								
Patients — no.	1013	1014	1054	1056	1013	1014	1054	1056
Severe exacerbations — no.	345	427	372	441	334	413	354	426
Annualized rate (95% CI)	0.43 (0.33–0.58)	0.58 (0.44–0.77)	0.48 (0.37–0.63)	0.60 (0.46–0.79)	0.45 (0.34–0.60)	0.59 (0.44–0.78)	0.49 (0.37–0.64)	0.61 (0.46–0.80)
Rate ratio (95% CI)	0.75 (0.61–0.91)	Reference	0.81 (0.66–0.98)	Reference	0.76 (0.62–0.93)	Reference	0.80 (0.66–0.98)	Reference
Annualized total dose of systemic glucocorticoid§								
Patients — no.	1012	1011	1052	1052	1012	1011	1052	1052
Median value (5th–95th percentile) — mg/yr	0.0 (0.0–459.2)	0.0 (0.0–484.3)	0.0 (0.0–494.4)	0.0 (0.0–600.8)	0.0 (0.0–496.1)	0.0 (0.0–622.1)	0.0 (0.0–487.0)	0.0 (0.0–615.9)
Mean value — mg/yr	83.6±247.7	130.0±630.3	94.7±318.2	127.6±619.8	86.2±262.9	129.3±657.2	95.5±335.4	127.1±646.2
Response analysis at wk 24¶								
ACQ-5								
Patients — no.	1013	1014	1052	1055	1013	1014	1052	1055
Patients with response — no. (%)	682 (67.3)	636 (62.7)	690 (65.6)	656 (62.2)	677 (66.8)	630 (62.1)	681 (64.7)	650 (61.6)
Odds ratio (95% CI)	1.22 (1.01–1.46)	Reference	1.15 (0.96–1.37)	Reference	1.22 (1.02–1.47)	Reference	1.13 (0.95–1.35)	Reference
AQLQ+12								
Patients — no.	994	993	987	NA	994	993	987	NA
Patients with response — no. (%)	515 (51.8)	464 (46.7)	496 (50.3)	NA	508 (51.1)	461 (46.4)	489 (49.5)	NA
Odds ratio (95% CI)	1.25 (1.04–1.50)	Reference	1.13 (0.94–1.36)	NA	1.23 (1.02–1.48)	Reference	1.11 (0.93–1.34)	NA

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Table 3. Adverse Events Occurring in at Least 2% of Patients in Any Trial Group.*

Event	Albuterol (180 μg)–Budesonide (160 μg) (N=1015)	Albuterol (180 μg)–Budesonide (80 μg) (N=1055)	Albuterol (180 μg) (N=1057)
	number of patients (percent)		
Any adverse event	469 (46.2)	497 (47.1)	490 (46.4)
Nasopharyngitis	76 (7.5)	61 (5.8)	54 (5.1)
Headache	44 (4.3)	50 (4.7)	50 (4.7)
Covid-19	43 (4.2)	52 (4.9)	46 (4.4)
Upper respiratory tract infection	26 (2.6)	31 (2.9)	26 (2.5)
Bronchitis	25 (2.5)	27 (2.6)	28 (2.6)
Hypertension	22 (2.2)	27 (2.6)	26 (2.5)
Asthma	18 (1.8)	20 (1.9)	35 (3.3)
Back pain	27 (2.7)	23 (2.2)	20 (1.9)
Influenza	21 (2.1)	23 (2.2)	14 (1.3)
Sinusitis	15 (1.5)	17 (1.6)	24 (2.3)

* Adverse events are sorted in decreasing total frequency of preferred term in the *Medical Dictionary for Regulatory Activities*, version 24.0. Patients with multiple events in the same category are counted only once in that category.

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Take home points

- SMART works
- It is associated with a reduction in time to severe exacerbation, reduced rate of severe exacerbations, improvements in FEV_1
- Overall, patients get lower doses of ICS and OCS

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

The Hyper IgE Syndromes

Presented by:
Alexandra Freeman, MD

Friday, June 24, 2022
10:45 a.m. – 11:30 a.m.

PAAA
Pennsylvania Allergy & Asthma Association

The Patient with Eczema and an elevated Serum IgE: when to suspect a Hyper IgE Syndrome

Alexandra Freeman MD
Director, Primary Immune Deficiency Clinic
Laboratory of Clinical Immunology and Microbiology

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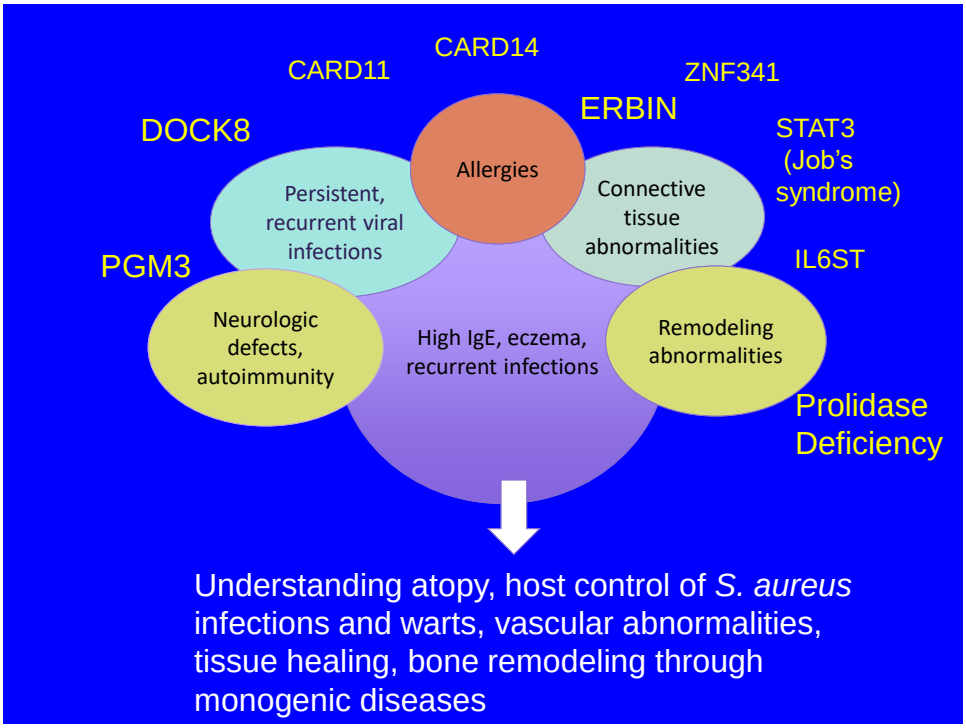
Approach to the patient with Elevated Serum IgE and eczema

- Most of the time atopy, without a "hyper IgE syndrome"
- Monogenic causes related to Primary immune deficiencies
  - Many causes of immune dysregulation can cause mildly elevated IgE (IgE hundreds)
  - The Hyper IgE syndromes are associated with eczema, recurrent skin and lung infections
  - Unique features to consider in the evaluation.

2



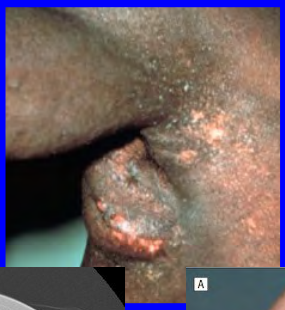
3

STAT3 deficient Hyper IgE Syndrome (Autosomal dominant HIES; Job's syndrome)

"So Satan went forth from the presence of the Lord, and smote Job with sore boils from the sole of his foot unto his crown."

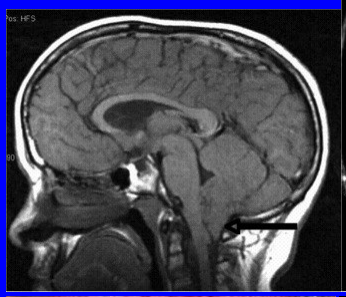
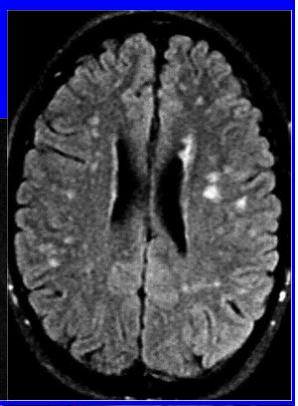
4

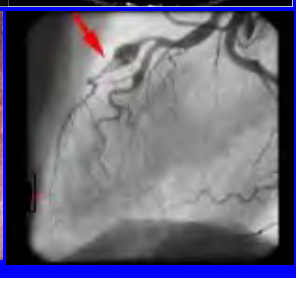
Staphylococcus aureus and *Candida* epithelial infections in LOF STAT3



5

Skeletal, joint, dental, vascular abnormalities



6

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

STAT3 Mutations in the Hyper-IgE Syndrome

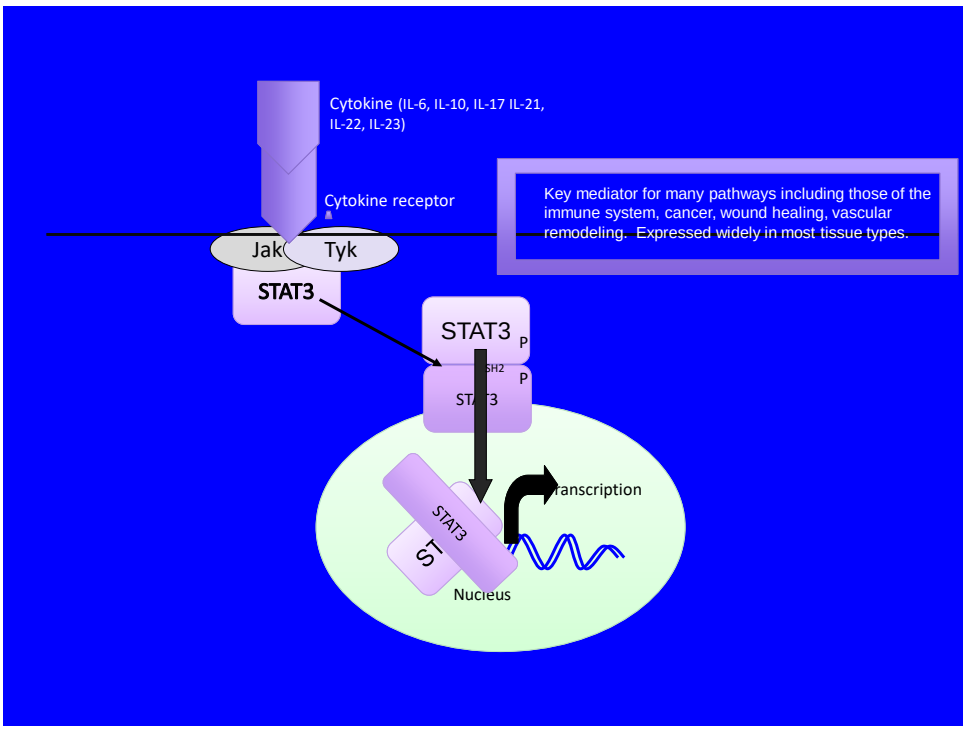
Steven M. Holland, M.D., Frank R. DeLeo, Ph.D., Houda Z. Elloumi, Ph.D., Amy P. Hsu, B.A., Gulbu Uzel, M.D., Nina Brodsky, B.S., Alexandra F. Freeman, M.D., Andrew Demidowich, B.A., Joie Davis, A.P.R.N., Maria L. Turner, M.D., Victoria L. Anderson, C.R.N.P., Dirk N. Darnell, M.A., Pamela A. Welch, B.S.N., Douglas B. Kuhns, Ph.D., David M. Frucht, M.D., Harry L. Malech, M.D., John I. Gallin, M.D., Scott D. Kobayashi, Ph.D., Adeline R. Whitney, B.A., Jovanka M. Voyich, Ph.D., James M. Musser, M.D., Ph.D., Cristina Woellner, M.Sc., Alejandro A. Schäffer, Ph.D., Jennifer M. Puck, M.D., and Bodo Grimbacher, M.D.

Dominant-negative mutations in the DNA-binding domain of STAT3 cause hyper-IgE syndrome

Yoshiyuki Minegishi[1], Masako Saito[1], Shigeru Tsuchiya[2], Ikuya Tsuge[3], Hidetoshi Takada[4], Toshiro Hara[4], Nobuaki Kawamura[5], Tadashi Ariga[5], Srdjan Pasic[6], Oliver Stojkovic[7], Ayse Metin[8] & Hajime Karasuyama[1]

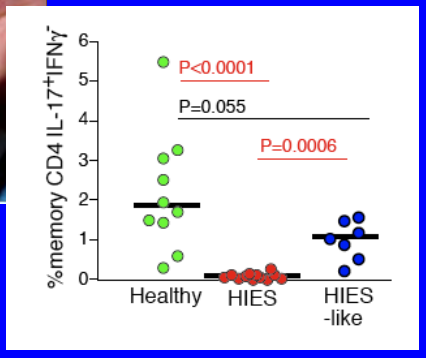
nature 2007

7



8

Epithelial/mucosal infection susceptibility: Lack of Th17 cells

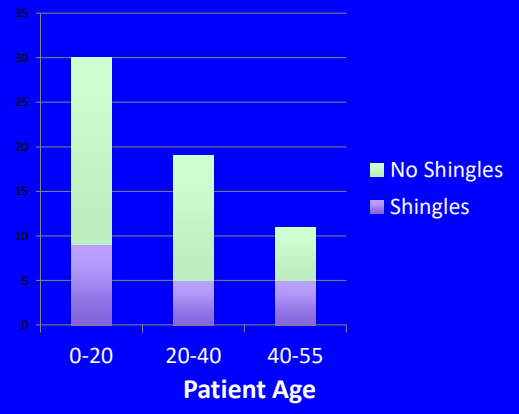


Milner et al, Nature, 2008

9

Decreased memory T and B Cells

Zoster reactivation is increased in HIES patients and occurs at young ages

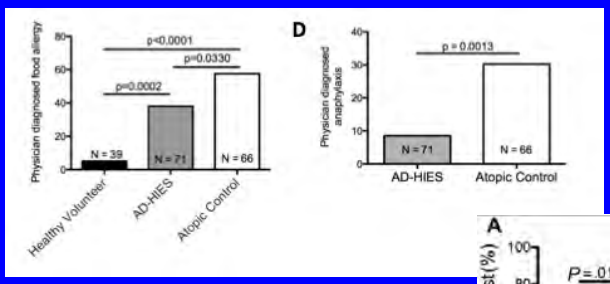


Minimum lifetime prevalence 19/60=31.7%

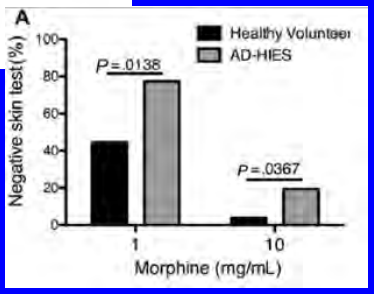
Siegel et al, Immunity 2011

10

AD-HIES with less food allergy and anaphylaxis

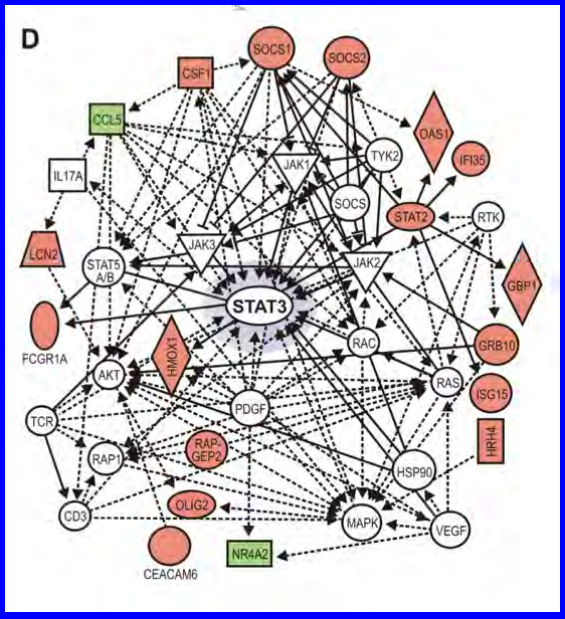


Similar levels of IgE



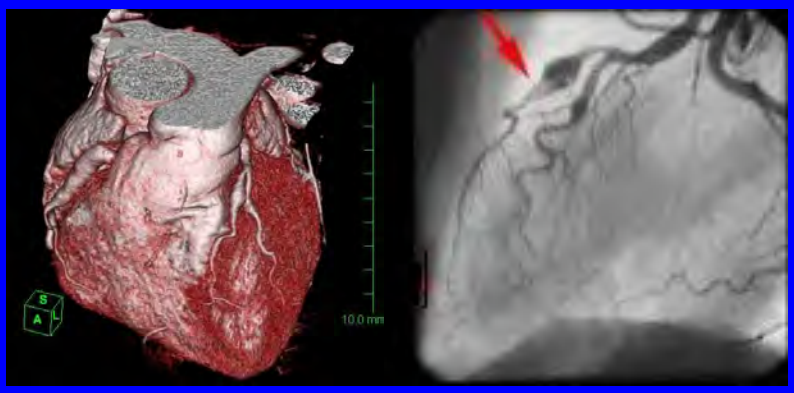
11

STAT3 is expressed widely and involved in many pathways making understanding the diverse clinical features difficult



12

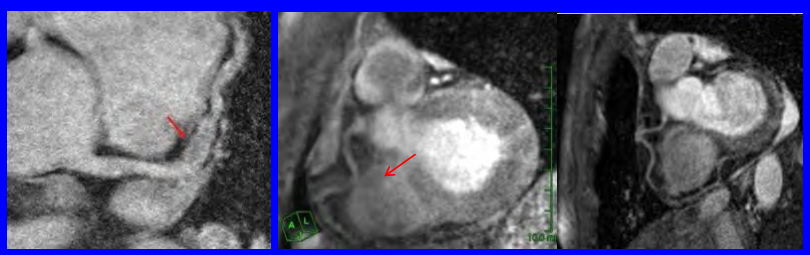
A 43 year old with an MI



Then, 10 years later with a life threatening GI bleed from a mesenteric artery aneurysm
Now, 4 years since GI bleed…..surgery for severe spine disease…

13

Middle sized arterial aneurysm



Left anterior descending artery dilation and aneurysm, and RCA Tortuosity

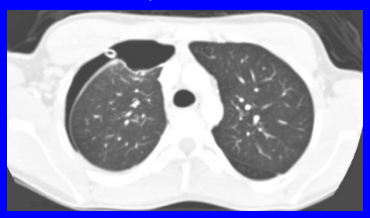
Coronary arteries: myocardial infarction
Cerebral arteries: subarachnoid hemorrhages
Bronchial arteries: massive pulmonary bleeds
Mesenteric arteries: GI bleeds

14

AD-HIES abnormal tissue remodeling

Pneumatocoele with aspergilloma

Bronchopleural fistulae

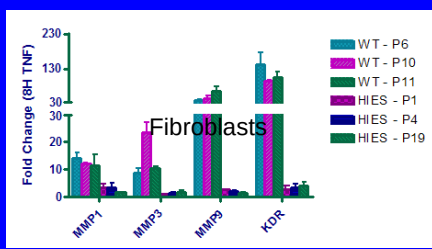


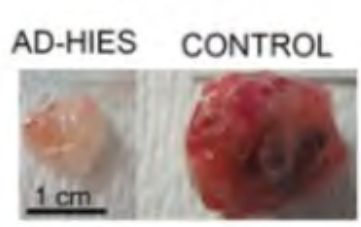
Freeman et al, J of Clin Immunology 2013

15

Disordered Tissue Remodeling

- STAT3 important for angiogenesis and extracellular remodeling





iPSC Teratomas

Impaired angiogenesis and extracellular matrix metabolism in autosomal-dominant hyper-IgE syndrome

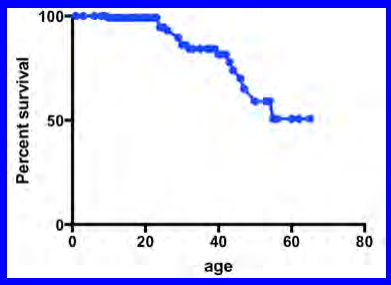
Natalia I. Dmitrieva, … , Guibin Chen, Manfred Boehm

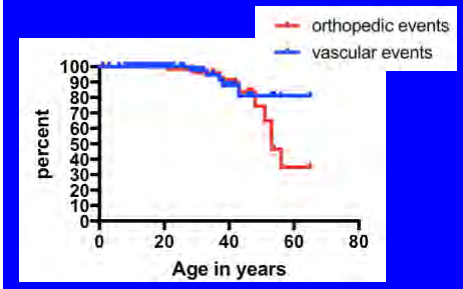
J Clin Invest. 2020;130(8):4167–4181. https://doi.org/10.1172/JCI135490.

16

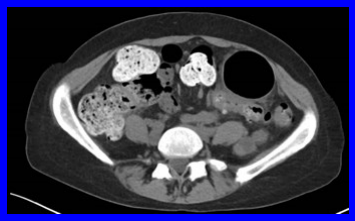
Evolving Prognosis

Overall survival





Early diagnosis changing natural history



Contained GI perforation

17

STAT3 deficient HIES

- Infection susceptibility (Candida, Staph) PLUS connective tissue abnormalities- teeth, bones, joints
- Destructive lung disease
- Less allergy than expected for height of serum IgE

Diagnosis: Sequence STAT3 in setting of infections/connective tissue phenotype

18

Approach to Care

- Supportive with suppressive antimicrobials
  - TMP/SMX typically, antifungals
- Antiseptics (i.e.dilute bleach baths) to control eczema, reduce *S. aureus* colonization
- Consideration of dupilumab for significant eczema
  - James et al, JACI: in practice, 2022. With UPMC!
- Consideration of IgG supplementation- normal IgG levels, poor specific antibody
- Bone and dental health
- Low suspicion of infection

19

What is the role for HSCT?

Bone Marrow Transplantation (2000) 25, 1303–1305
© 2000 Macmillan Publishers Ltd All rights reserved 0268-3369/
www.nature.com/bmt

Case report

Bone marrow transplantation does not correct the hyper IgE syndrome

AR Gennery, TJ Flood, M Abinun and AJ Cant

Department of Paediatric Immunology, Newcastle General Hospital, Newcastle upon Tyne, UK

J Allergy Clin Immunol. 2010 Aug;126(2):392-4. doi: 10.1016/j.jaci.2010.05.005. Epub 2010 Jul 2.

Successful long-term immunologic reconstitution by allogeneic hematopoietic stem cell transplantation cures patients with autosomal dominant hyper-IgE syndrome.

Goussetis E, Peristeri I, Kitra V, Traeger-Synodinos J, Theodosaki M, Psarra K, Kanariou M, Tzortzatou-Stathopoulou F, Petrakou E, Fylaktou I, Kanavakis E, Graphakos S.

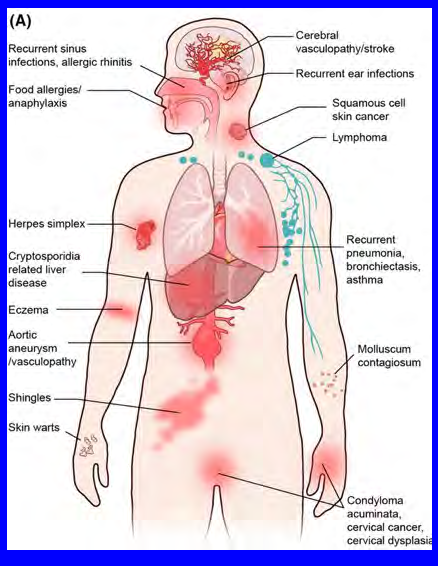
20

What is the role for HSCT?

- Seems to make sense in some cases
  - four patients transplanted at NIH- all at worse end of spectrum
  - About 15-20 patients transplanted worldwide
  - Some good outcomes being reported
    - Worse with mixed chimerism?
- Hard to predict from mutation who will do well and who won't
- But understanding what is driving the different parts of the clinical phenotype is important
  - Will the infection phenotype be improved? Probably
  - Will the bone phenotype be improved? Maybe
  - Will the vascular phenotype be improved? Maybe not
  - Lung healing if there a post- transplant pneumonia? Unknown

21

DOCK8 Deficiency: Formerly known as a "HIES"



Combined B and T cell defect with progressive T lymphopenia over time , and worsening specific antibody function

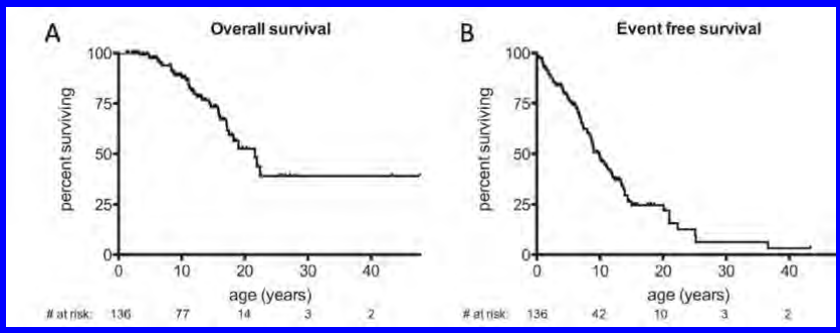
22

DOCK8 Pathogenesis

- DOCK8: involved in actin cell cytoskeleton
- Highly expressed immune system- very low levels in other organs, and not in endothelial cells
- Lymphocytes and dendritic cells have trouble with movement in matrices such as skin (vasculature?) due to abnl cytoskeleton
  - Cytothripsis: Cells fragment in tissues
  - Prevents generation of memory CD8 T cells in the skin

23

High Morbidity and Mortality



136 patients from around the world
Aydin et al, JOCI, 2015

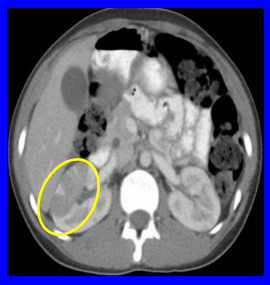
24

Complications with age

15 year old with bronchiectasis

17 year old with persistent HSV

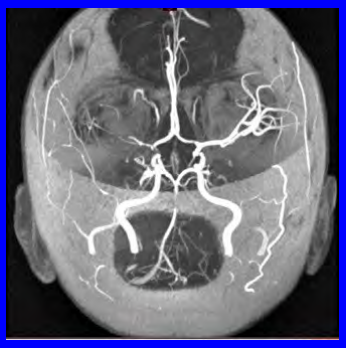
11 year old with cryptosporidia related liver disease, portal hypertension (Liver disease in about 25% of cohort)



15 year old with Burkitt's lymphoma Malignancy in about 25% of cohort

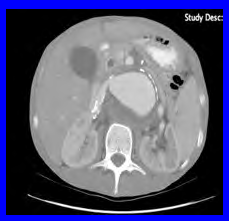
25

Vascular Complications with age: about 15% in our cohort



19 year old with cerebral vasculopathy and stroke

19 year old with bilateral renal artery stenosis



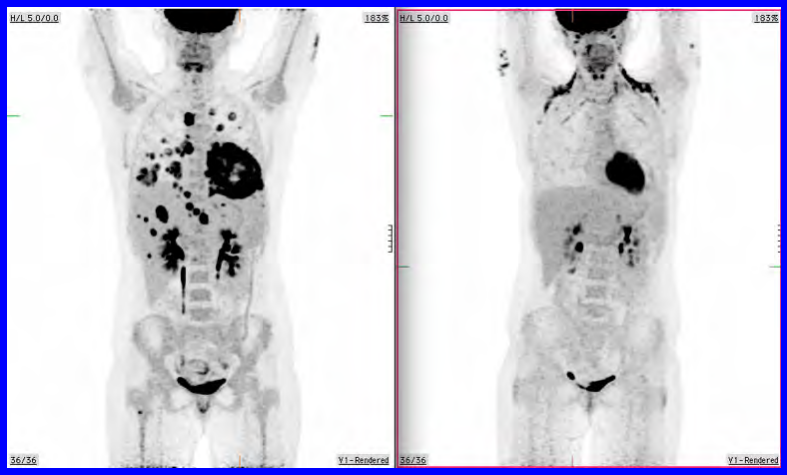
24 year old with large aortic aneurysm

26

Bone marrow transplant for DOCK8 deficiency

27

EBV Driven Lymphoproliferation Improved After Transpla



28

Resolution of eczema: wrapping pre-transplant to improve skin barrier, diminish infection risk

29

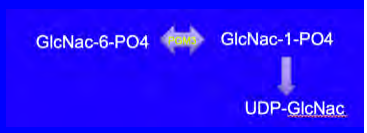
DOCK8 Deficiency

- Variable IgE, eczema, allergies
- Poor control of skin viral control, EBV viremia
- Malignancy risk increases through teen years, young adulthood
- T lymphopenia, poor specific antibodies
- Can be difficult to diagnosis at younger ages
- Genetics- need to look for mutations and deletions

30

Recessive hypomorphic mutations in *PGM3* glycosylation disorder

- Allergy
  - high IgE; atopic dermatitis; asthma; food and environmental allergies; EGID; ABPA
- Infections
  - chronic otitis externa
  - staph and URI/pneumonia
  - lung, cutaneous, parotid, periodontal abscesses
- Autoimmunity
  - increased T_H17; elevated IgG; psoriatic lesions
- Lymphoproliferative disease
  - Evan's syndrome
  - lymphoma
- Neurocognitive impairment
  - developmental delay, ataxia, discoordination and speech abnormalities/dyspraxia
  - febrile seizures



31

Think about PGM3 Deficiency

- Eczema, recurrent bacterial and viral infections
- Developmental delays
- Lymphopenia and neutropenia

TREATMENT

- Supportive
- Consideration of HSCT (maybe 4 known cases?)
  - Partially corrective
- Sugar supplementation?

32

CARD11/14 Defects Causing Hyper IgE Phenotypes

Hypomorphic caspase activation and recruitment domain 11 *(CARD11)* mutations associated with diverse immunologic phenotypes with or without atopic disease

JACI 2018

Batsukh Dorjbal, PhD,[a] Jeffrey R. Stinson, PhD,[a] Chi A. Ma, PhD,[b] Michael A. Weinreich, MD,[b] Bahar Miraghazadeh, PhD,[c,d] Julia M. Hartberger,[e] Stefanie Frey-Jakobs, PhD,[e] Stephan Weidinger, MD,[f] Lena Moebus, MSc,[f] Andre Franke, PhD,[g] Alejandro A. Schäffer, PhD,[h] Alla Bulashevska, PhD,[a] Sebastian Fuchs, PhD,[a] Stephan Ehl, MD, PhD,[a] Sandhya Limaye, PhD,[i] Peter D. Arkwright, FRCPCH, DPhil,[j] Tracy A. Briggs, MBChB, PhD,[j] Claire Langley, PhD,[j] Claire Bethune, MRCP, MRCPath,[k] Andrew F. Whyte, MBBS,[k] Hana Alachkar, MD,[l] Sergey Nejentsev, MD, PhD,[m] Thomas DiMaggio, RN,[n] Celeste G. Nelson, CRNP,[n] Kelly D. Stone, MD,[n] Martha Nason, PhD,[o] Erica H. Brittain, PhD,[o] Andrew J. Oler, PhD,[o] Daniel P. Velthi, PhD,[o] T. Ronan Leahy, PhD,[p] Niall Conlon, FRCPath, PhD,[q] Maria C. Poli, MD,[r] Arturo Borzutzky, MD,[s] Jeffrey I. Cohen, MD,[t] Joie Davis, APRN, APRG,[u] Michele P. Lambert, MD,[v] Neil Romberg, MD,[v] Kathleen E. Sullivan, MD, PhD,[v] Kenneth Paris, MD, PhD,[w] Alexandra F. Freeman, MD,[x] Laura Lucas, RN,[x] Shanmuganathan Chandrakasan, MD,[y] Sinisa Savic, MRCP, FRCPath,[y] Sophie Hambleton, MD, PhD,[z] Smita Y. Patel, MD, PhD, FRCPath,[aa] Michael B. Jordan, MD,[bb] Amy Theos, MD,[cc] Jeffrey Lebensburger, MD,[dd] T. Prescott Atkinson, MD,[ee] Troy R. Torgerson, MD, PhD,[f] Ivan K. Chinn, MD,[f] Joshua D. Milner, MD,[f,s] Bodo Grimbacher, MD,[f,s] Matthew C. Cook, MBBS, PhD,[c,d,s] and Andrew L. Snow, PhD[a,s]

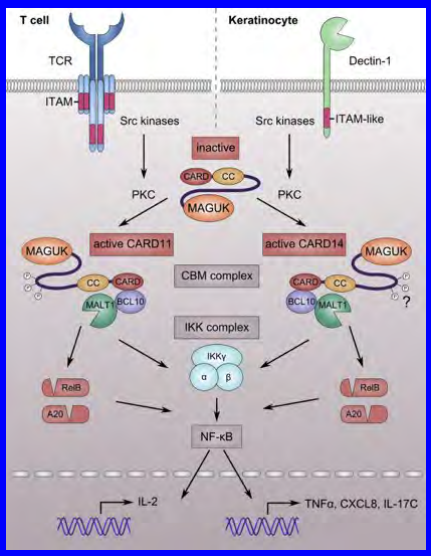
Bethesda, Md; Canberra and Concord, Australia; Freiburg and Kiel, Germany; Manchester, Plymouth, Cambridge, Leeds, Newcastle upon Tyne, and Oxford, United Kingdom; Dublin, Ireland; Houston, Tex; Santiago, Chile; Philadelphia, Pa; New Orleans, La; Atlanta, Ga; Cincinnati, Ohio; Birmingham, Ala; and Seattle, Wash

Loss-of-function mutations in caspase recruitment domain-containing protein 14 *(CARD14)* are associated with a severe variant of atopic dermatitis

JACI 2018

Alon Peled, BMedSci,[a,b] Ofer Sarig, PhD,[a] Guangping Sun, MD,[c] Liat Samuelov, MD,[a,b] Chi A. Ma, PhD,[c] Yuan Zhang, PhD,[c] Tom Dimaggio, RN,[c] Celeste G. Nelson, CRNP,[c] Kelly D. Stone, MD,[c] Alexandra F. Freeman, MD,[c] Liron Malki, BSc,[a] Lucia Seminario Vidal, MD, PhD,[a] Latha M. Chamarthy, MD,[1,c] Valeria Briskin, PhD,[a] Janan Mohamad, BMedSci,[a,b] Mor Pavlovski, MD,[a] Jolan E. Walter, MD, PhD,[c] Joshua D. Milner, MD,[c] and Eli Sprecher, MD, PhD[a,b]

Tel Aviv, Israel; Bethesda, Md; Tampa Bay, St Petersburg, and Pinellas Park, Fla; and Busan, Mass



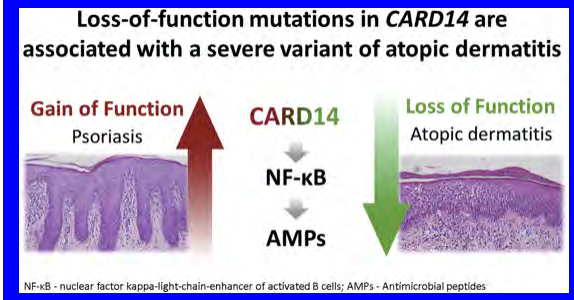
33

CARD11: one gene, multiple phenotypes

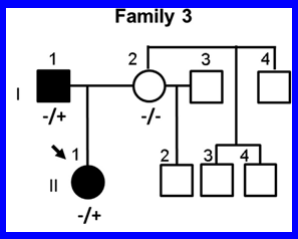
- GOF mutations: B cell lymphoproliferative disease
- Somatic GOF: lymphoma
- Bi-allelic LOF: SCID phenotype
- Hypomorphic heterozygous LOF Mutations- ATOPY!
  - Increased skin viral infections (molluscum), sinopulmonary infections
  - Some with hypogammaglobulinemia, autoimmunity, infrequent lymphoma

34

Dermatologic Conditions with CARD14 mutations



Peled et al, JACI 2018



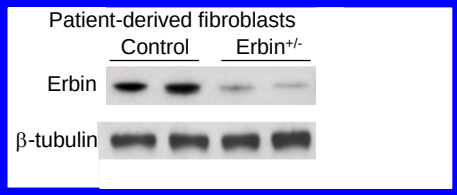
Severe eczema
Asthma, pneumonias?
Anaphylaxis, food allergy
IgE thousands
Cutaneous infections
Retained primary teeth
Fractures (steroids-osteoporosis?)

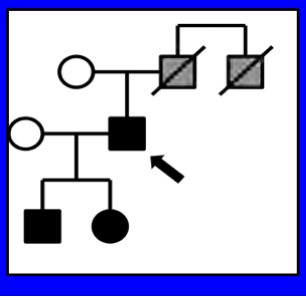
35

ERBIN deficiency links STAT3 and TGF-β pathway defects with atopy in humans

J.J. Lyons,[1] Y. Liu,[1] C.A. Ma,[1] X. Yu,[1] M.P. O'Connell,[1] M.G. Lawrence,[5] Y. Zhang,[1] K. Karpe,[1] M. Zhao,[2] A.M. Siegel,[1] K.D. Stone,[1] C. Nelson,[1] N. Jones,[6] T. DiMaggio,[1] D.N. Darnell,[3] E. Mendoza-Caamal,[7] L. Orozco,[7] J.D. Hughes,[8] J. McElwee,[8] R.J. Hohman,[2] P.A. Frischmeyer-Guerrerio,[4] M.E. Rothenberg,[9] A.F. Freeman,[3] S.M. Holland,[3] and J.D. Milner[1]

J. Exp. Med. 2017 Vol. 214 No. 3 669–680





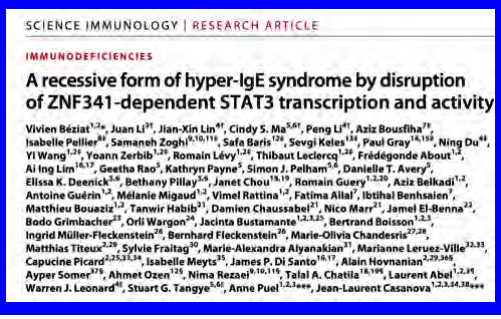
Dilated aortic root
Joint hyper-extensibility
Eosinophilic esophagitis
Mild increase in infections

STAT3 ↓
Erbin ↓
TGFb ↑

36

ZNF341 Deficiency

- Autosomal recessive
- Transcription factor that binds to a STAT3 promoter, thus causes decreased STAT3 transcription when present.
- More inflammatory, less connective tissue phenotype



SCIENCE IMMUNOLOGY | RESEARCH ARTICLE

IMMUNODEFICIENCIES

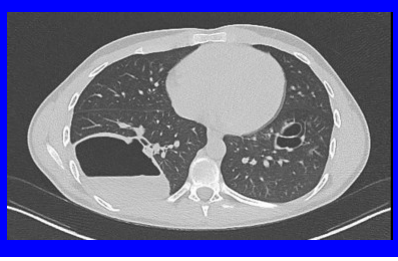
A recessive form of hyper-IgE syndrome by disruption of ZNF341-dependent STAT3 transcription and activity

Vivien Béziat[1,2]*, Juan Li[3†], Jian-Xin Lin[4†], Cindy S. Ma[5,6†], Peng Li[4†], Aziz Bousfiha[7†], Isabelle Pellier[8†], Samaneh Zoghi[9,10,11†], Safa Baris[12†], Sevgi Keles[13†], Paul Gray[14,15†], Ning Du[4†], Yi Wang[1,2†], Yoann Zerbib[1,2†], Romain Lévy[1,2†], Thibaut Leclercq[1,2†], Frédégonde About[1,2], Ai Ing Lim[16,17], Geetha Rao[5], Kathryn Payne[5], Simon J. Pelham[5,6], Danielle T. Avery[5], Elissa K. Deenick[5,6], Bethany Pillay[5,6], Janet Chou[18,19], Romain Guery[1-2,20], Aziz Belkadi[1,2], Antoine Guérin[1,2], Mélanie Migaud[1,2], Vimel Rattina[1,2], Fatima Allaf[7], Ibtihal Benhsaien[7], Matthieu Bouaziz[1,2], Tanwir Habib[21], Damien Chaussabel[21], Nico Marr[21], Jamel El-Benna[22], Bodo Grimbacher[23], Orli Wargon[24], Jacinta Bustamante[1,2,3,25], Bertrand Boisson[1,2,3], Ingrid Müller-Fleckenstein[26], Bernhard Fleckenstein[26], Marie-Olivia Chandesris[27,28], Matthias Titeux[2,29], Sylvie Fraitag[30], Marie-Alexandra Alyanakian[31], Marianne Leruez-Ville[32,33], Capucine Picard[2,25,33,34], Isabelle Meyts[35], James P. Di Santo[16,17], Alain Hovnanian[2,29,36§], Ayper Somer[37§], Ahmet Ozen[12§], Nima Rezaei[9,10,11§], Talal A. Chatila[18,19§], Laurent Abel[1,2,3§], Warren J. Leonard[4§], Stuart G. Tangye[5,6§], Anne Puel[1,2,3***], Jean-Laurent Casanova[1,2,3,34,38***]

37

IL6ST Loss of function mutations

- Heterozygous and homozygous LOF Mutations described in several patients.
- IL-6 receptor that then signals through STAT3
- Significant ABPA, destructive lung disease
- Some connective tissue phenotype



38

	DN STAT3	DOCK8	PGM3	LOF CARD11	LOF CARD14*	ZNF341*	IL6ST Biallelic*	DN IL6ST*	IL6R*
Allergic hypersensitivity	++	+/+++	+++	+++	+++	+	ND	+	+
Eczema	++	+/+++	++	+++	+++	+++	++	+	+++
Bronchiectasis/ pneumatoceles	++	++	++	+	-	++	+++	+++	+
Mucocutaneous candidiasis	+++	+	-	-	-	+++	ND	+	-
Cutaneous viral infections	+	+++	++	++	+	-	-	-	-
Neurologic deficits	+/-	+/-	+++	-	-	-	-	-	-
Vascular abnormalities	++	+	+	-	-	-	-	-	-
Skeletal/connective tissue changes	+++	-	++	-	-	+	+++	+	-
Retained primary teeth	+++	-	-	-	-	-	ND	++	-
Immunoglobulins (except IgE)	Typically normal	Low IgM	High	Some low IgG	Some low IgG	Some increased IgG	Normal	Normal	Low normal/slight decreased IgG
T Lymphopenia	+	++	++	+	-	-	-	-	-
Lymphoma	+	++	+	++	-	-	-	-	-

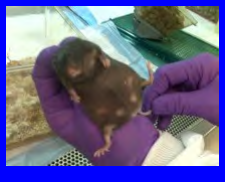
39

Thanks

Steve Holland and Lab
Joie Davis
Amy Hsu
Jenna Bergerson
Amanda Urban
Christine Lafeer
Amanda Urban
Dirk Darnell
Ana Agharahimi
Justina Pfister

- Ken Olivier, NHLBI
- Josh Milner, Columbia Hospital
- Jon Lyons, NIAID
- Helen Su and Lab, NIAID
- Nirali Shah, Corina Gonzalez and Dennis Hickstein, NCI
- Ian Myles, NIAID
- Manfred Boehm, NHLBI
- Ahmed Gharib, NIDDK
- Heidi Kong, NCI
- Theo Heller, NIDDK
- Niki Moutsopoulos, NIDCR

All of the patients with HIES and their families



Deletion of STAT3 V463, 1387delGTG

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

The Microbiome and Food Allergy

Presented by:
Supinda Bunyavanich, MD, MPH, MPhil

Friday, June 24, 2022
11:30 a.m. – 12:15 p.m.

PAAA does not have permission to share slides.

PAAA
Pennsylvania Allergy & Asthma Association

PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Mayer A. Green, MD Allergy Foundation Memorial Lecture
The Promise and Limits of Food Allergen Immunotherapy

Presented by:
Carla Davis, MD

Friday, June 24, 2022
12:15 p.m. – 1:00 p.m.

PAAA
Pennsylvania Allergy & Asthma Association

The Promise and Limits of Food Allergen Immunotherapy

Mayer A. Green Allergy Foundation Memorial Lecture
Pennsylvania Allergy and Asthma Association

June 24, 2022

Carla M. Davis, MD
Professor of Pediatrics
Chief, Immunology, Allergy, and Retrovirology Division
Director, Food Allergy Program
Texas Children's Hospital
Baylor College of Medicine

Texas Children's Hospital
BCM Baylor College of Medicine

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Disclosures

- **In relation to this presentation, I declare the following, real or perceived conflicts of interest:**
  - Research Grants: National Institute of Allergy and Infectious Disease, DBV Technologies, Aimmune Therapeutics, Food Allergy Research and Education, Allergenis, Regeneron Pharmaceuticals, Pfizer, The Scurlock Foundation
  - Consultant/Advisory Board: Moonlight Therapeutics

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2

Outline

- History of Food Allergen Immunotherapy
- Current Protocols
  - Oral, Sublingual, and Epicutaneous Food Immunotherapy
- Evaluation of Sustained Unresponsiveness to Food
- Limitations of Immunotherapy Protocols
- Promise for the Future of Immunotherapy

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History of Allergen Immunotherapy

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History of Modern Food Allergen Immunotherapy

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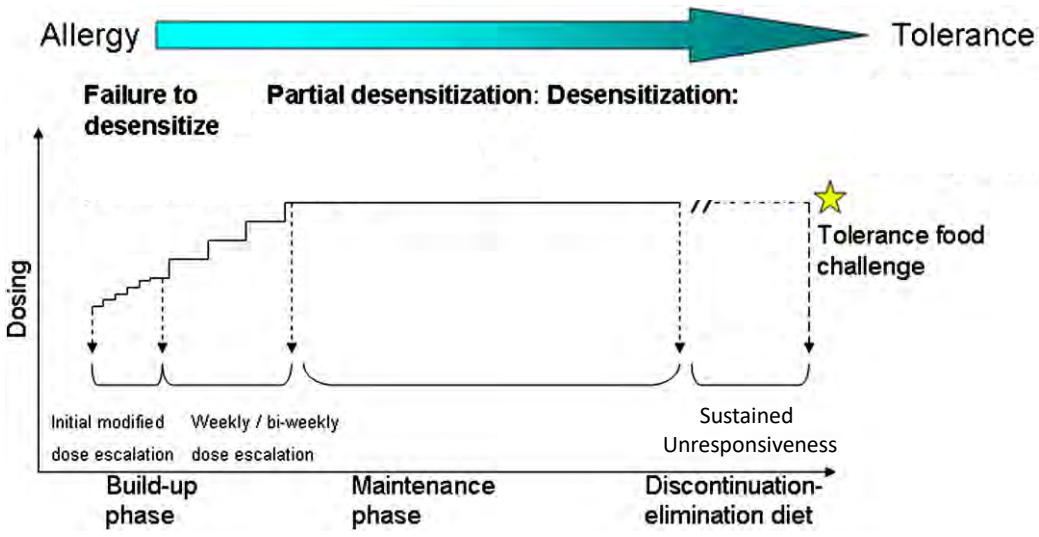
5

Schematic of Food IT Protocols



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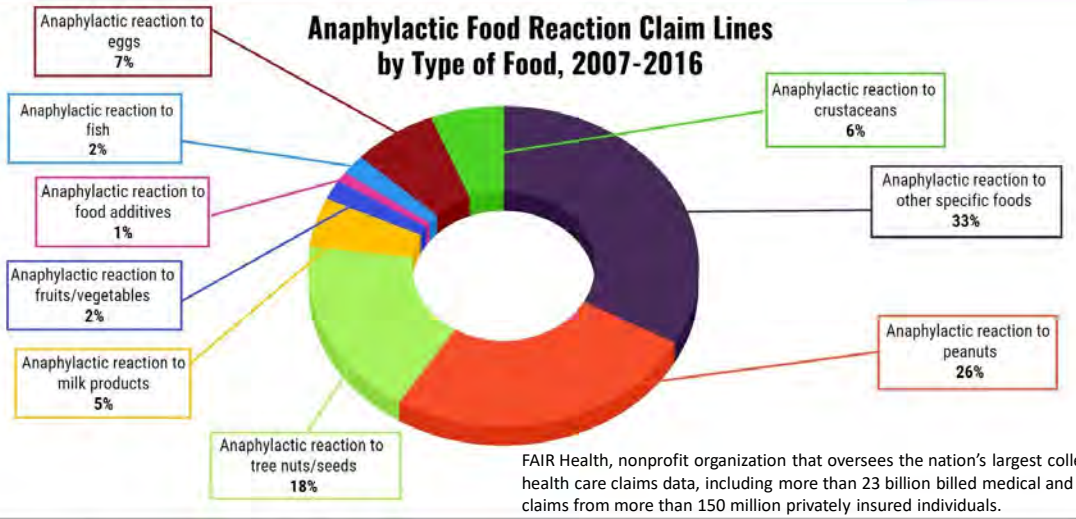
Nowak-Węgrzyn A, Sampson HA. J Allergy Clin Immunol. 2011 Mar;127(3):558-73

6

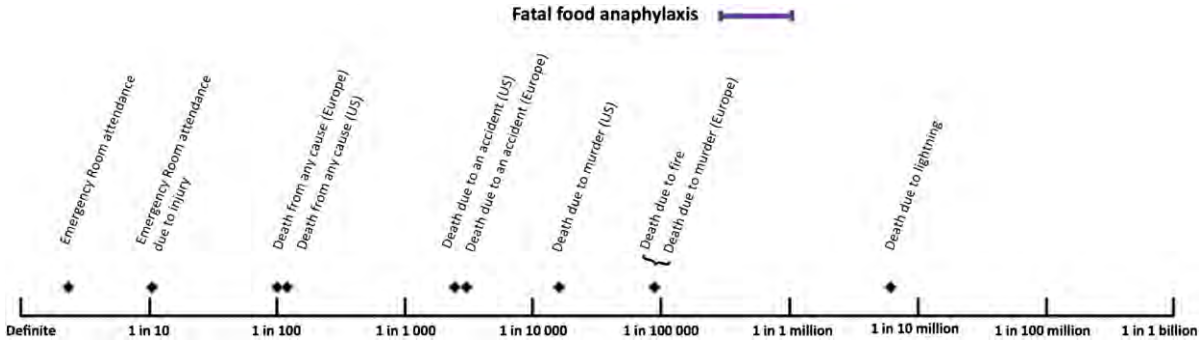
Many Different Foods Cause Anaphylaxis



FAIR Health, nonprofit organization that oversees the nation's largest collection of health care claims data, including more than 23 billion billed medical and dental claims from more than 150 million privately insured individuals.

7

Rate of Fatal Food Anaphylaxis

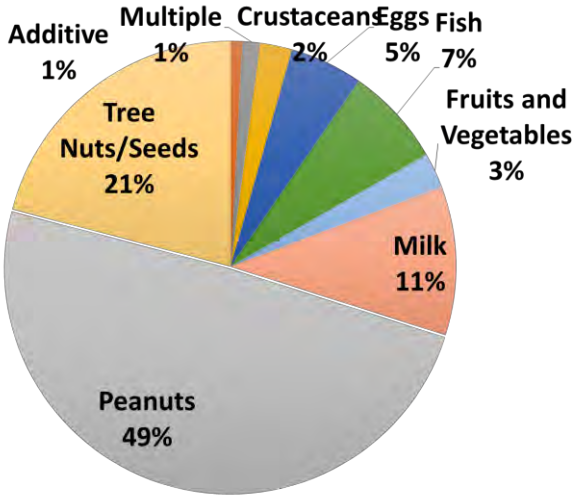


Turner et al. J Allergy Clin Immunol Pract. 2017; 5(5):1169–1178

8

Causes of Pediatric Anaphylaxis with ICU Admission

Peanut allergy is the largest identified food trigger of mortality
from anaphylaxis



Ramsey NB, Guffey D, Coleman NE, Davis CM. Journal of Allergy and Clinical Immunology. 2018 Feb; 141(2), AB148.

9

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Peanut Oral Immunotherapy (OIT)

- Peanut OIT has been demonstrated to increase the threshold of reactivity to peanut protein.
- Early studies desensitized to doses up to 4000 mg[1-3], and recent studies use lower doses, typically 300-2000 mg as a target dose[4-8]
- Double blind placebo controlled food challenge (DBPCFC) is considered the gold standard method to determine OIT treatment effect
- In OIT, end of treatment DBPCFC top cumulative doses of peanut protein are typically ≤ 5-10 grams

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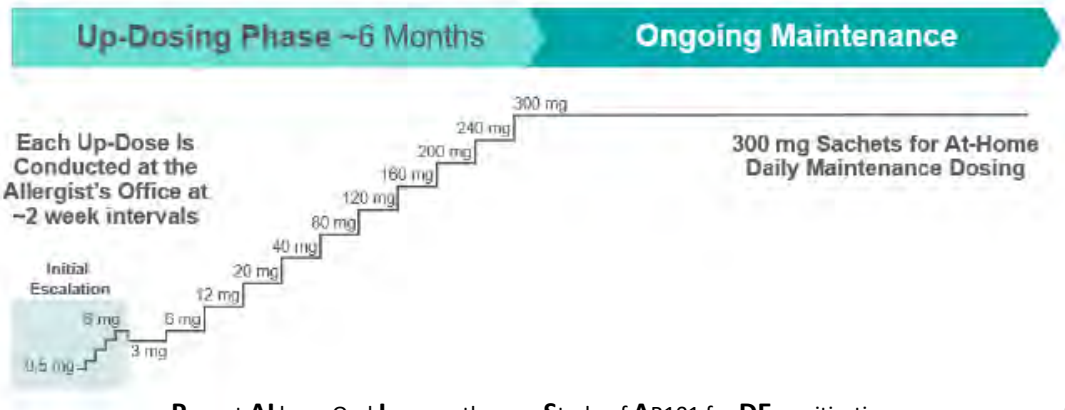
[1]Jones et al. 2009, [2]Varshney et al. 2011, [3]Vickery et al. 2014, [4]Syed et al. 2014
[5]Anagnostou et al. 2014, [6]Tang et al. 2015, [7]Fleischer et al. 2013,[8]Narisety et al. 2015

11

PALISADE Study Design



Peanut **AL**lergy Oral **I**mmunotherapy **S**tudy of **A**R101 for **DE**sensitization in Children and Adults

PALISADE Group of Clinical Investigators et al. N Engl J Med. 2018 Nov 22;379(21):1991-2001.

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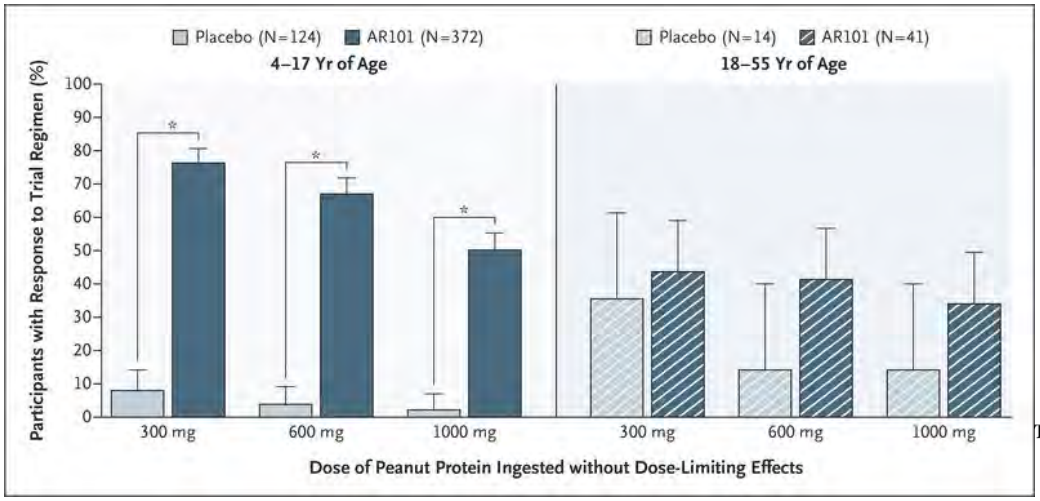
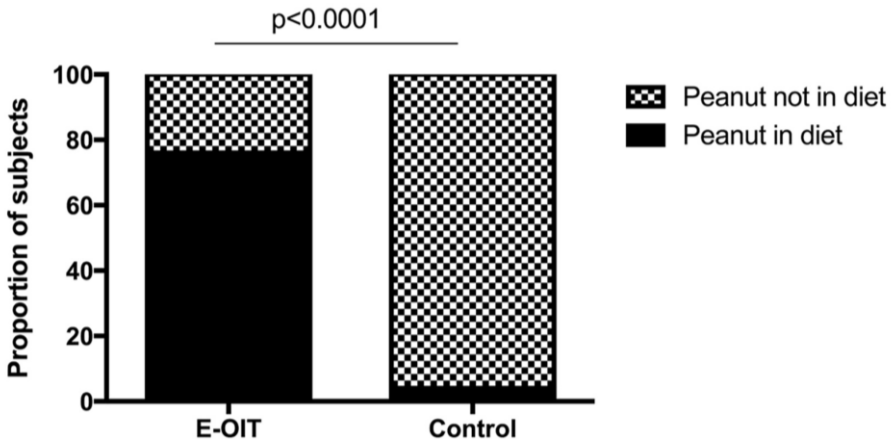
Response to Peanut Oral Immunotherapy Treated Patients



PALISADE Group of Clinical Investigators et al. N Engl J Med. 2018 Nov 22;379(21):1991-2001.

13

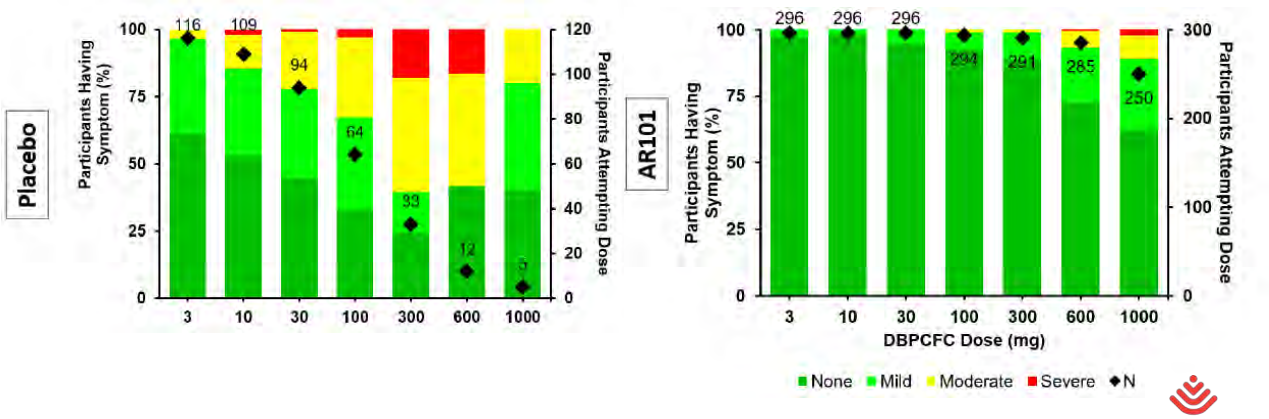
Early Oral Immunotherapy (E-OIT) in 9 mo– 3 yr olds



Vickery BP et al. J Allergy Clin Immunol. 2017 Jan;139(1):173-181.e8.

14

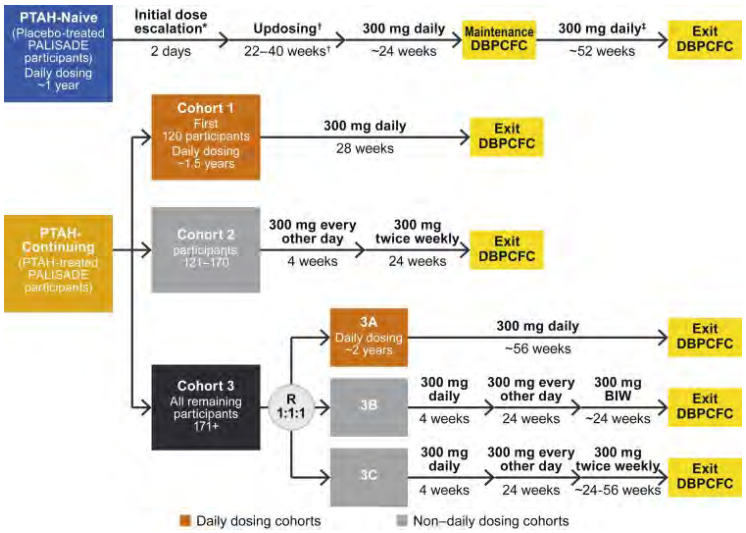
Maximum Symptoms at End of Study Challenge



PALISADE Group of Clinical Investigators et al. N Engl J Med. 2018 Nov 22;379(21):1991-2001.

15

Follow-On Study from PALISADE

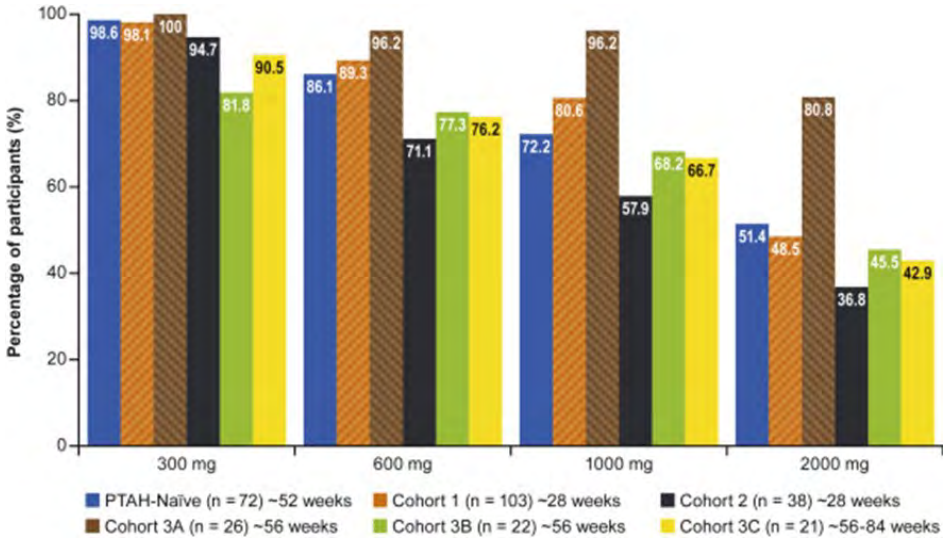


Vickery BP…Adelman DC. Continuous and Daily Oral Immunotherapy for Peanut Allergy: Results from a 2-Year Open-Label Follow-On Study. J Allergy Clin Immunol Pract. 2021 May;9(5):1879-1889.e14.

16

Desensitization rates based on the single highest tolerated dose at the exit DBPCFC

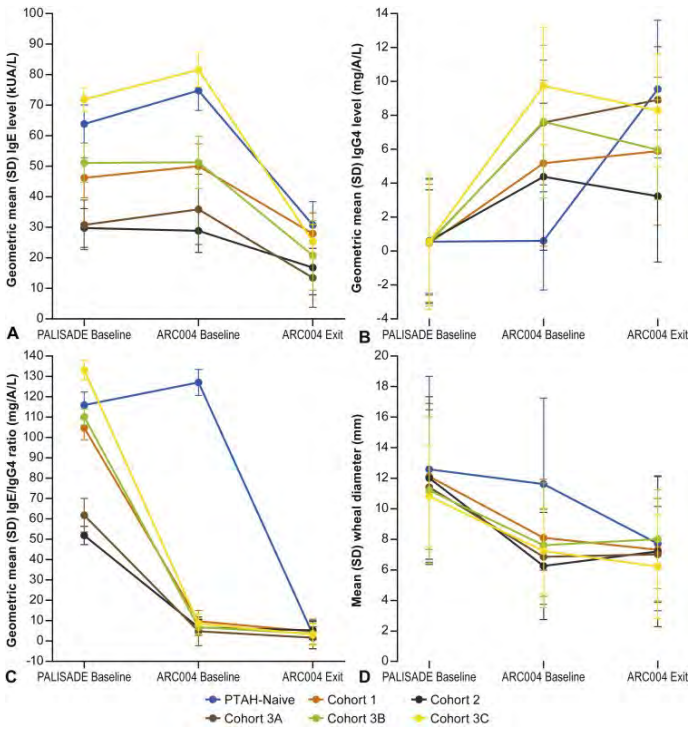
1- Daily
2- Every other day, then twice weekly
3A- Daily
3B- Daily, Every other day, biweekly
3C- Daily, Every other day, twice weekly



Vickery BP…Adelman DC. Continuous and Daily Oral Immunotherapy for Peanut Allergy: Results from a 2-Year Open-Label Follow-On Study. J Allergy Clin Immunol Pract. 2021 May;9(5):1879-1889.e14.

17

Specific IgE and IgG4 levels and SPT wheal size



Vickery BP…Adelman DC. Continuous and Daily Oral Immunotherapy for Peanut Allergy: Results from a 2-Year Open-Label Follow-On Study. J Allergy Clin Immunol Pract. 2021 May;9(5):1879-1889.e14.

18

Peanut Oral Immunotherapy: "Real-World" Experience

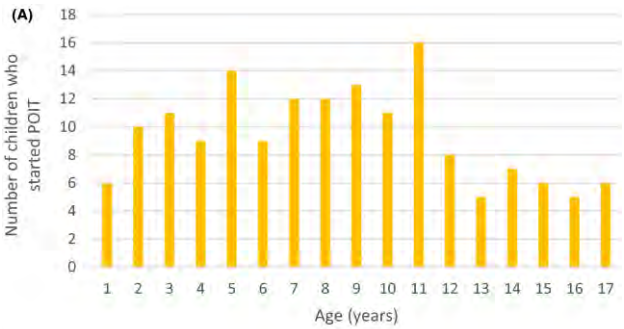
Treatment regimen characteristics	Protocol June 1, 2016
Starting dose	2 µg
Doses to reach the day 1 target	10 doses
Day 1 target dose	2.05 mg
Daily dosing frequency during escalation	Twice a day
Post-dose observation time	45 min
Doses to complete escalation	21 after day 1
Target dose	12 peanuts (3 g protein) then pass 24-peanut challenge
Maintenance dosing frequency	Once a day

~80% reached the target dose

Wasserman RL et al. J Allergy Clin Immunol Pract. 2019 Feb;7(2):418-426.e4.

19

Discontinuation occurs more frequently in older children

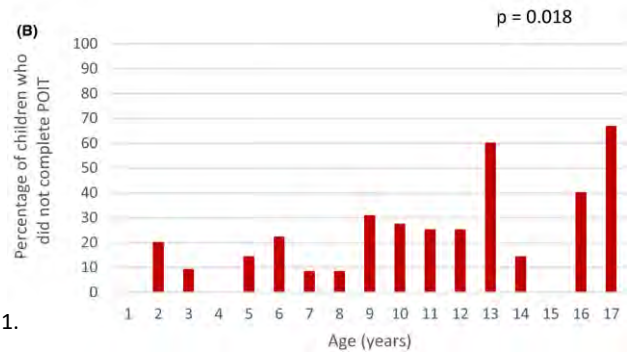


80% completed POIT (n=129/160)

Only 3% required Epinephrine during up-dosing

Younger age was associated with completion

Side effects of GI symptoms most common reason for stopping



Zhu et al. Pediatric Allergy and Immunology. 2021.

20

Peanut Sublingual Immunotherapy (SLIT)

Dose No.	Weeks on IT	SLIT Dose (ug)	SLIT Increase from last dose (%)	OIT Comparison Dose (mg)	OIT Increase from last dose (%)
1	2	0.000165		0.1	
10	4	0.165	150	12	100
12	6	0.66	100	24	100
14	8	3.3	100	48	100
16	10	16.5	150	75	56
19	13	165	150	255	50
21	15	660	100	2000	54
23	17	1386	67		
24	18	3696	60		

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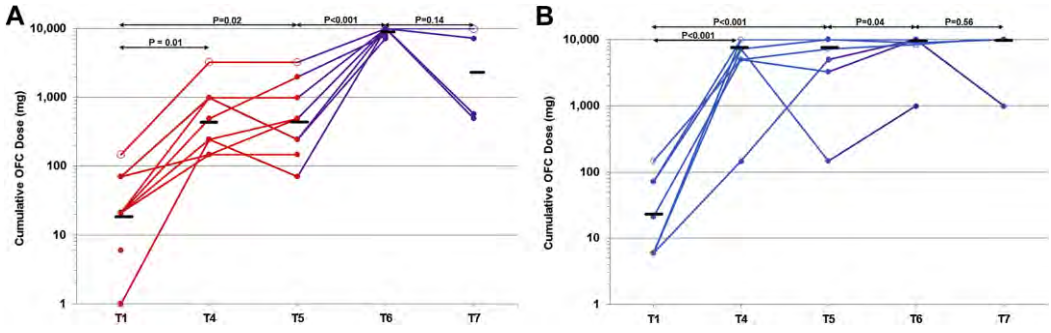
Narisety SD et al. J Allergy Clin Immunol. 2015 May;135(5):1275-82.e1-6.

21

Sublingual Immunotherapy vs. Oral Immunotherapy



Change in cumulative OFC dose after SLIT **(A)** and OIT **(B)**. *Red lines* indicate active SLIT, *blue lines* indicate active OIT, and *purple lines* represent combined SLIT and OIT after unblinding.

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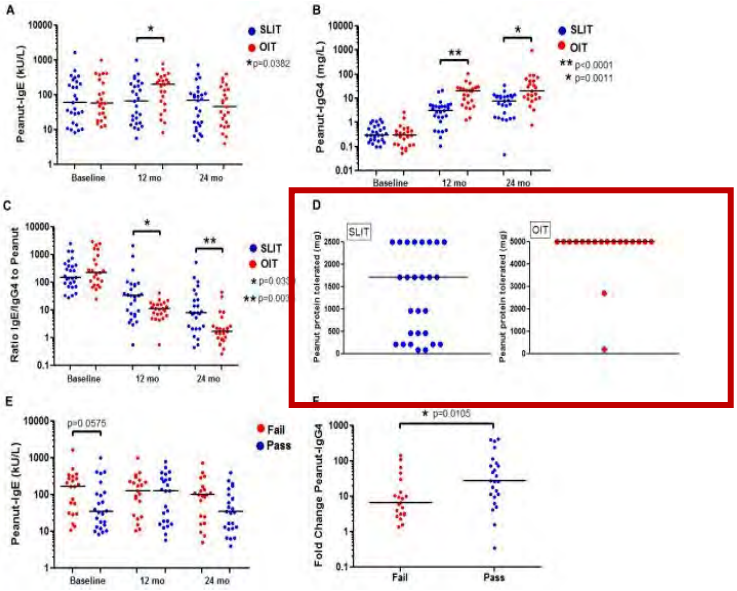
Narisety SD et al. J Allergy Clin Immunol. 2015 May;135(5):1275-82.e1-6.

22

Oral IT vs. Sublingual IT



Chin S et al. J Allergy Clin Immunol. 2013 Aug;132(2):476-8.e2.

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Peanut Powder

Oral Immunotherapy 300 mg

Peanut Patch

Epicutaneous Immunotherapy 250 ug

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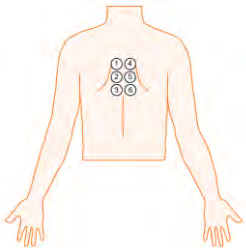
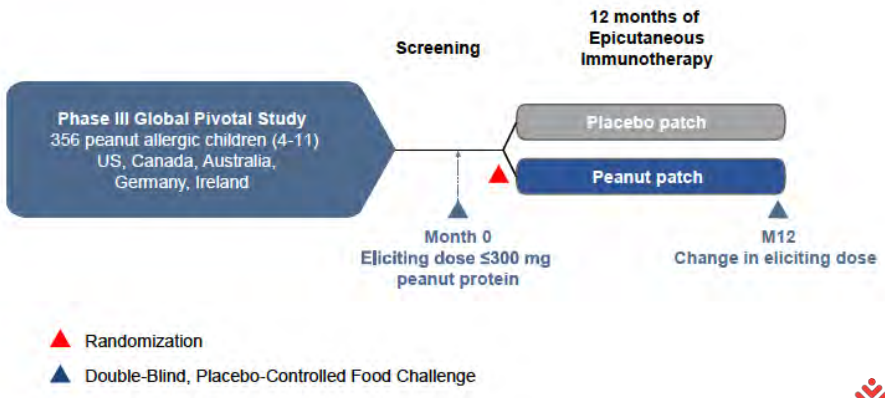
PEPITES Study Design





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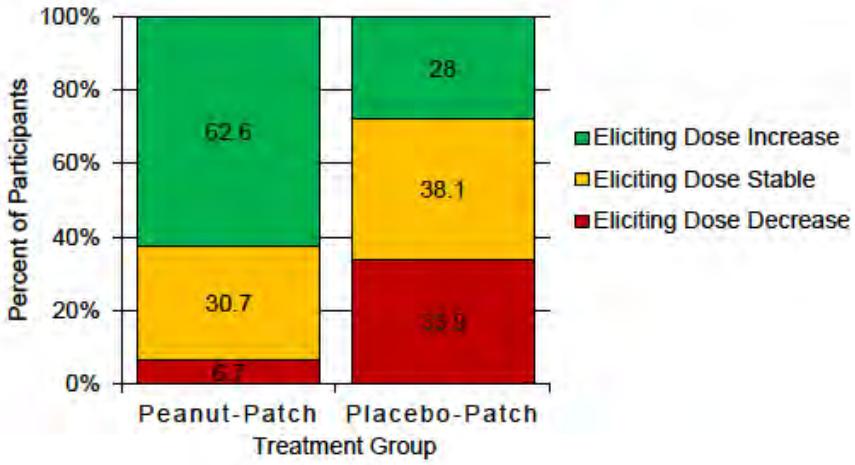
Fleischer DM et al. The PEPITES Randomized Clinical Trial. JAMA. 2019 Mar 12;321(10):946-955.

25

Response for Peanut Patch Treated Patients



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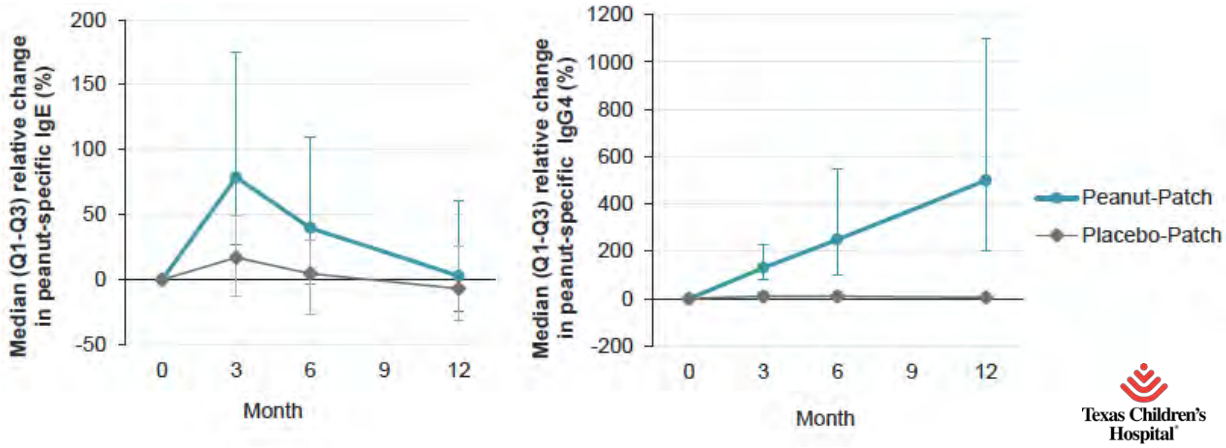
Fleischer DM et al. The PEPITES Randomized Clinical Trial. JAMA. 2019 Mar 12;321(10):946-955.

26

Peanut Specific IgE and IgG4



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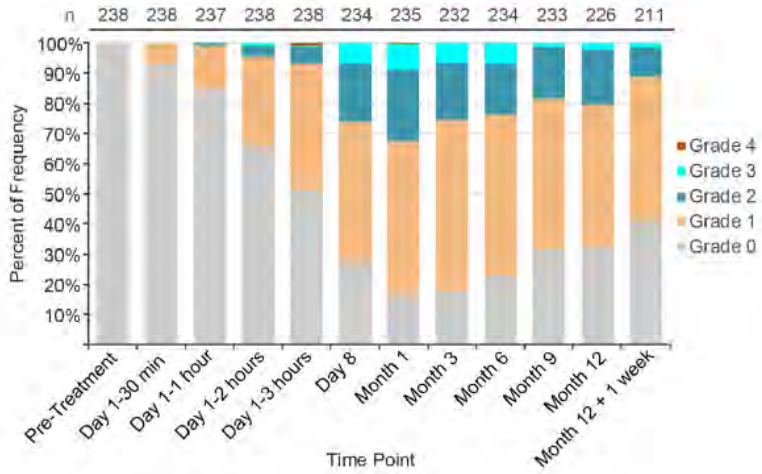
Fleischer DM et al. The PEPITES Randomized Clinical Trial. JAMA. 2019 Mar 12;321(10):946-955.

27

Skin Reactions with Peanut Patch Treatment



Participants are still receiving treatment at month 12 + 1 week.
Reaction definitions: Grade 0: negative; Grade 1: only erythema, or erythema + infiltration; Grade 2: erythema, few papules; Grade 3: erythema, many or spreading papules; Grade 4: erythema, vesicles.

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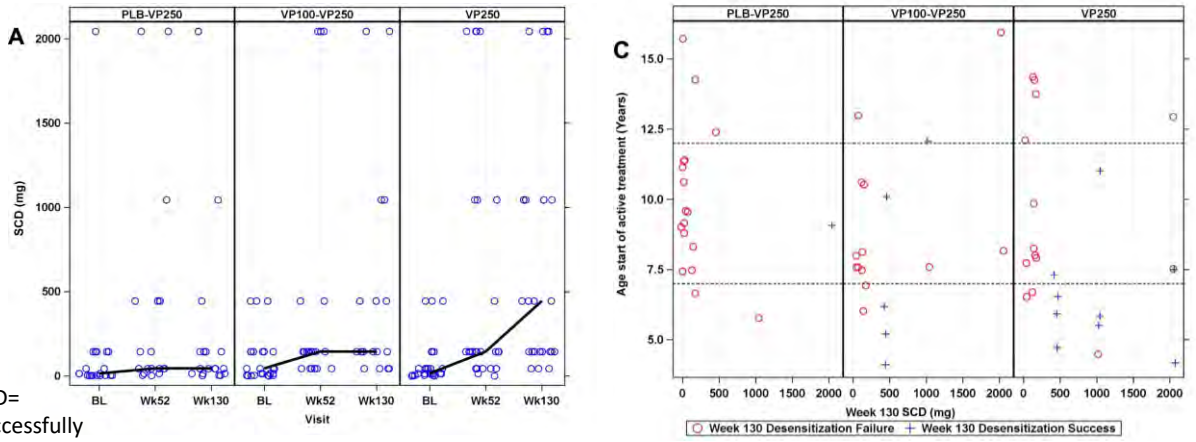
Epicutaneous immunotherapy for treatment of peanut allergy: Follow-up from the Consortium for Food Allergy Research



SCD= successfully consumed dose

Scurlock AM et al. J Allergy Clin Immunol. 2021 Mar;147(3):992-1003.e5.

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Phase 3 trial EPITOPE (EPIT in TOddlers with PEanut Allergy) Study

- Safety and efficacy of Viaskin™ Peanut 250 µg for the treatment of peanut-allergic toddlers ages 1 to 3
- Response was defined as
  - a subject with a baseline ED ≤10 mg who reached an ED ≥300 mg of peanut protein at month 12
  - a subject with a baseline ED >10 mg who reached an ED ≥1,000 mg of peanut protein at month 12.
- 67.0% of treated subjects responded, compared to 33.5% of subjects in the placebo arm ($p<0.001$)
- Safety results were generally consistent with treatment in subjects ≥4 years in prior clinical trials

https://www.globenewswire.com/news-release/2022/06/07/2458239/0/en/DBV-Technologies-Announces-Positive-Topline-Results-from-Phase-3-EPITOPE-Trial-of-Viaskin-Peanut-in-Peanut-Allergic-Toddlers.html

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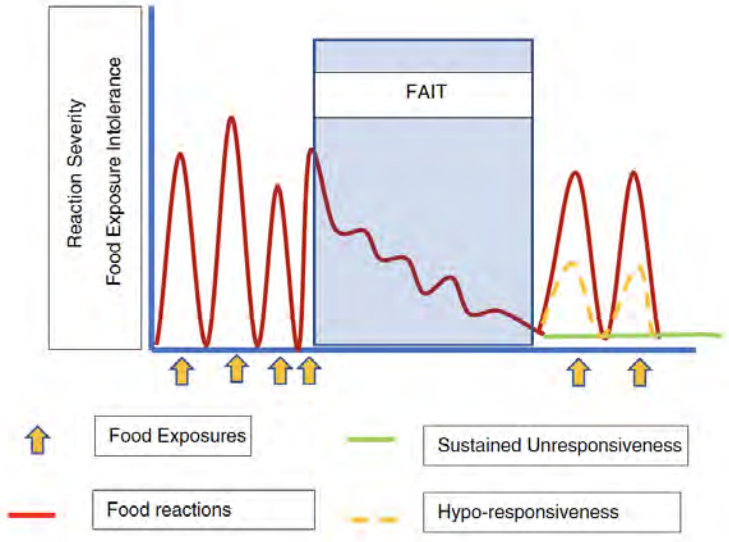
Effect of Food Allergen Immunotherapy (FAIT) on Responses



Spergel et al. Curr Allergy and Asthma Reports. 2018

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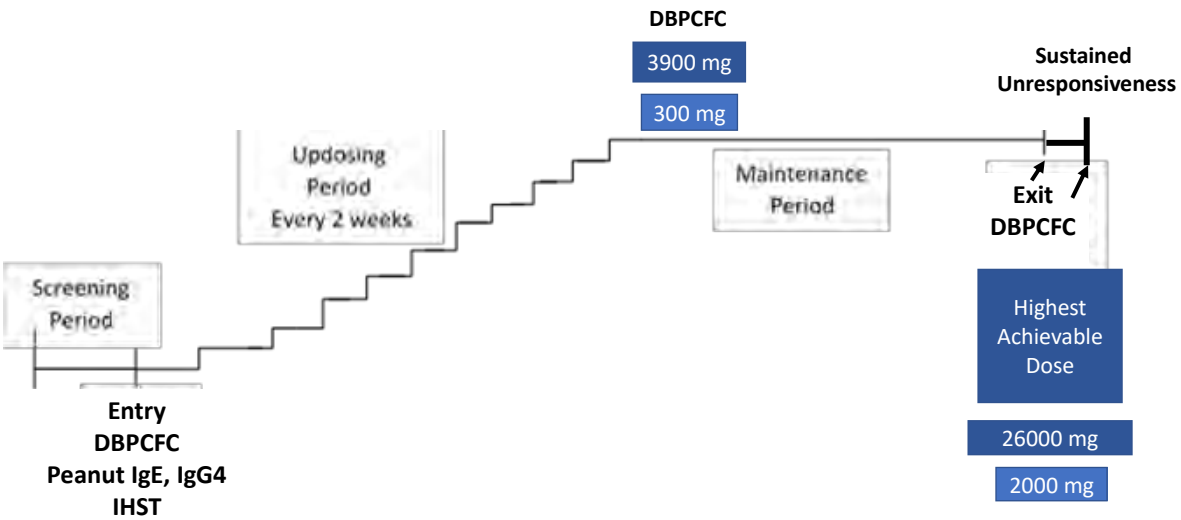
POIT Maximum Dose (POIMD) Food Immunotherapy Study



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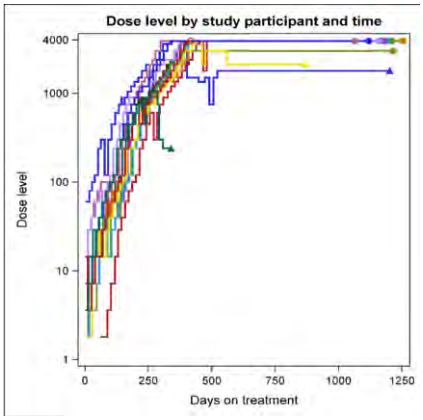
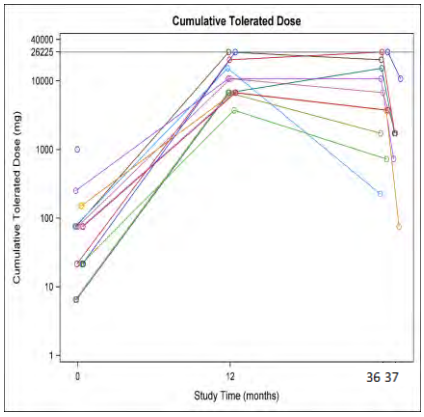
Peanut Oral Immunotherapy Maximum Dose (POIMD) Study





Baseline - 73.4 mg (1/4 peanut)
36 months- 9,407 mg (30 peanuts)
1 month avoidance – 2,783 (9 peanuts)

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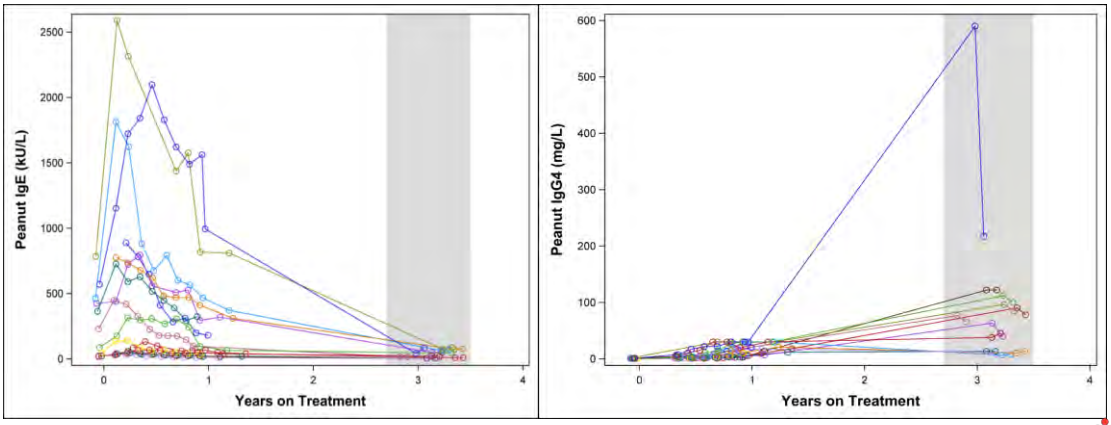
Blood Testing



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Comparison and Limitations of Food IT

	Oral Immunotherapy	Sublingual Immunotherapy	Epicutaneous Immunotherapy
Route of Administration	Oral (mouth)	Under the tongue	On the skin
Foods Evaluated	Cow's milk, hen's egg, peanut, tree nuts, fruits, vegetables	Cow's milk, peanut, hazelnut, kiwi	Cow's milk, peanut
Daily Doses (Food Protein)	300–4000 mg	2–7 mg	250 μg
Efficacy *	Large	Small-to-Moderate	Small, but variable
Side Effects	Common: local (oral or gastrointestinal including EoE)	Common: local (oral or pharyngeal)	Common: local (skin)
	Less common: systemic (3-4%)	Rare: systemic	Not yet reported: systemic

*Refers to desensitization effect, not sustained unresponsiveness (SU).

Sara Anvari, Aikaterini.Anagnostou. Children. 2018 Apr 4;5(4).

35

Limitations of Food Allergen IT

- Side effects are common, with GI symptoms being frequent
- Discontinuation occurs in older children compared to younger
- Hyporesponsiveness is achieved, but sustained unresponsiveness has been elusive
- Daily dosing is necessary to maintain response

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Promise for the Future of Immunotherapy

- OIT with probiotics, herbal formulations and other adjuvants
- Omalizumab and dupilumab as monotherapies or in combination with allergen-specific therapies to improving safety and achieve SU
- OIT for non-peanut, egg and milk allergens and multiple foods
- Identification of best candidates for food allergen IT

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Food Allergy Program
at Texas Children's Hospital®

TCH Food Allergy Program Team:

Carla M. Davis, MD
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Katherine Anagnostou, MD, PhD
Meera Gupta, MD
Chivon McMullen-Jackson, RN
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Andrea Amarante
Supriya Parikh
Nelly Hernandez
Amanda Vega
Brenda Bin Su, PhD
Harold Ames, MS
Warren Blackmon

TCH Center for Human Immunobiology

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Food Allergy Patients and Families

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Funding and Community Support

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QUALITY MAT COMPANY

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Cooking Up A CURE

TEXAS Department of State Health Services

Allergy & Asthma NETWORK

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STU College of Pharmacy and Health Sciences

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Food Allergy Program
at Texas Children's Hospital®

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Carla M. Davis, MD
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Presentations for Saturday, June 25, 2022

Operationalizing an Allergy Framework for COVID-19 Vaccinations
Paige Wickner, MD, MPH

PAERF 2021 Grant Presentation
Investigating epidemiologic and immunologic relationships between systemic and gastrointestinal food allergies
Stan Gabryszewski, MD, PhD

Recognizing Health Disparities in Food Allergy
Carla Davis, MD

AERD - Diagnosis and Treatment
Tanya Laidlaw, MD

Quality/Safety in the Allergy Practice
Paige Wickner, MD, MPH

Disparities in Asthma
Torie Grant, MD, MHS

WORKSHOP: Aspirin and NSAID Challenges
Tanya Laidlaw, MD

PAAA
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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Operationalizing an Allergy Framework for COVID-19 Vaccinations

Presented by:
Paige Wickner, MD, MPH

Saturday, June 25, 2022
8:00 a.m. – 8:45 a.m.

PAAA does not have permission to share slides.

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

PAERF 2021 Grant Presentation

Investigating epidemiologic and immunologic relationships between systemic and gastrointestinal food allergies

Presented by:

Stanislaw Gabryszewski, MD, PhD

Saturday, June 25, 2022

8:45 a.m. - 8:55 p.m.

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Determination of National and Regional Patterns of Pediatric Allergy Using Electronic Health Record Data

Stanislaw J. Gabryszewski, MD, PhD[a], Jesse Dudley, MS[b], Di Shu, PhD[c,d], Robert W. Grundmeier, MD[b], Alexander G. Fiks, MD, MSCE[b], David A. Hill, MD, PhD[a,e]

Affiliations: [a]Division of Allergy and Immunology, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; [b]Center for Pediatric Clinical Effectiveness, Department of Biomedical and Health Informatics, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; [c]Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; [d]Center for Pediatric Clinical Effectiveness, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; [e]Institute for Immunology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Rationale: Analyses of electronic health record (EHR)-based clinical cohorts overcome limitations of survey-based methodologies, such as reporting bias. To date, EHR-based analyses have not been applied to the study of national allergic disease patterns.

Methods: We defined a cohort of 219,397 children aged 0-18 years using the United States (US) multi-state Comparative Effectiveness Research Through Collaborative Electronic Reporting (CER2) EHR database, which spans 27 states. Diagnosis codes and medication prescriptions were used to identify subjects with atopic dermatitis (AD), IgE-mediated food allergy (IgE-FA), asthma, allergic rhinitis (AR), and eosinophilic esophagitis (EoE). We determined cumulative incidence and peak age of incidence, regional variations in cumulative incidence, and the most common food allergens for IgE-FA.

Results: The cumulative incidence (and peak age of incidence) for allergic manifestations were 10.2% (0.3 years) for AD, 4.0% (1.1 years) for IgE-FA, 20.0% (1.1 years) for asthma, 19.7% (2.1 years) for AR, and 0.11% (2.9 years) for EoE. Cumulative incidences varied by geographical region. 13.3% of children had 2 or more allergic conditions, and respiratory allergies (asthma, AR) shared marked comorbidity with each other and with other manifestations. The most common documented food allergens overall were peanut (1.9%), egg (0.8%), and shellfish (0.6%).

Conclusion: Our EHR-based analysis of a multi-state cohort expands on previous regional analyses to detail US pediatric allergy rates on a national scale. Incidence patterns support the classical allergic march sequence and the variable natural histories of food allergies. We detected notably lower rates of IgE-FA and milk allergy as compared with prior studies. The ability to accurate describe trends in pediatric allergic disease patterns is important from the perspectives of clinical medicine, public health, and scientific inquiry.

PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Recognizing Health Disparities in Food Allergy

Presented by:
Carla Davis, MD

Saturday, June 25, 2022
9:00 a.m. – 9:45 a.m.

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Recognizing Health Disparities in Food Allergy

Pennsylvania Allergy and Asthma Association

Carla M. Davis, MD
Professor of Pediatrics
Chief, Immunology, Allergy, and Retrovirology Section
Director, Food Allergy Program
Texas Children's Hospital
Baylor College of Medicine

June 25, 2022

Texas Children's Hospital

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Disclosures

- **In relation to this presentation, I declare the following, real or perceived conflicts of interest:**
  - Research Grants: National Institute of Allergy and Infectious Disease, DBV Technologies, Aimmune Therapeutics, Food Allergy Research and Education, Allergenis, Regeneron Pharmaceuticals, Pfizer, The Scurlock Foundation
  - Consultant/Advisory Board: Moonlight Therapeutics

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Objectives

- Describe current evidence regarding health disparities within food allergy in racial and ethnic underserved populations
- Know what interventions to mitigate disparities that can be implemented
- Share what you can do in the future to address disparities in food allergy

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Outline

Definition of Health Disparity and Health Equity
Disparities in Food Allergy Prevalence
Disparities in Food Allergy Management
Disparities in Food Allergy Reaction Preparedness
Disparities in Food Allergy Eczema and Asthma
Socioeconomic Variables Impacting Clinical Outcomes
What You Can Do

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CROSSING THE QUALITY CHASM:
A NEW HEALTH SYSTEM FOR THE 21ST CENTURY

The U.S. health care delivery system does not provide consistent, high-quality medical care to all people. Americans should be able to count on receiving care that meets their needs and is based on the best scientific knowledge--yet there is strong evidence that this frequently is not the case. Health care harms patients too frequently and routinely fails to deliver its potential benefits. Indeed, between the health care that we now have and the health care that we could have lies not just a gap, but a chasm.

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AAAAI Work Group Report

American Academy of Allergy Asthma & Immunology

Health disparities in allergic and immunologic conditions in racial and ethnic underserved populations: A Work Group Report of the AAAAI Committee on the Underserved

Check for updates

Carla M. Davis, MD, FAAAAI,[a,b] Andrea J. Apter, MD, MA, MSc, FAAAAI,[c] Adrian Casillas, MD, FAAAAI,[d] Michael B. Foggs, MD, FAAAAI,[e] Margee Louisias, MD,[f] Elsie C. Morris, MD,[g] Anil Nanda, MD, FAAAAI,[h,i,j] Michael R. Nelson, MD, PhD, FAAAAI,[k] Princess U. Ogbogu, MD, FAAAAI,[l] Cheryl Lynn Walker-McGill, MD, MBA, FAAAAI,[m,n] Julie Wang, MD, FAAAAI,[o] and Tamara T. Perry, MD[p,q]

Houston, El Paso, Lewisville, Flower Mound, and Dallas, Tex; Philadelphia, Pa; Chicago, Ill; Boston, Mass; Tucker, Ga; Bethesda, Md; Cleveland Ohio; Charlotte, NC; New York, NY; and Little Rock, Ark

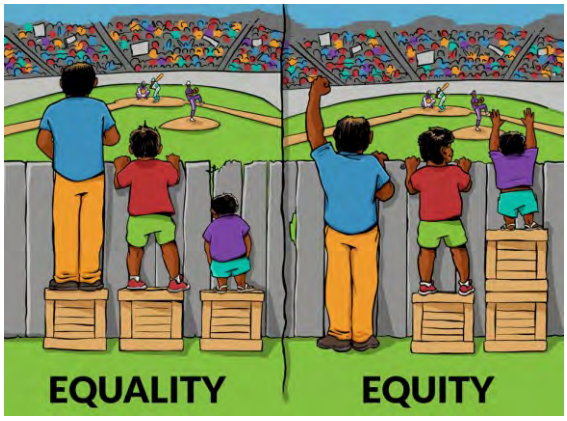
Davis CM et al. J Allergy Clin Immunol. 2021 May;147(5):1579-1593.

6

What are Healthcare Disparities?

- **Health disparity:** Health difference linked with economic, social and environmental disadvantage
  - Adversely affects groups that have systematically experienced greater social or economic obstacles to health based on their race, ethnicity, religion, SES status, gender, age, disability, sexual orientation, and/or geographic location

- **Health Equity:** Principle underlying the commitment to reduce disparity and its determinants



"Interaction Institute for Social Change | Artist: Angus Maguire."

Braveman, What Are Health Disparities and Health Equity? We Need to Be Clear, Public Health Rep 2014

7

Davis et al. JACI. 2021.

8

Social Determinants of Health

Davis et al. JACI. 2021.

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Disparities in Food Allergy Prevalence

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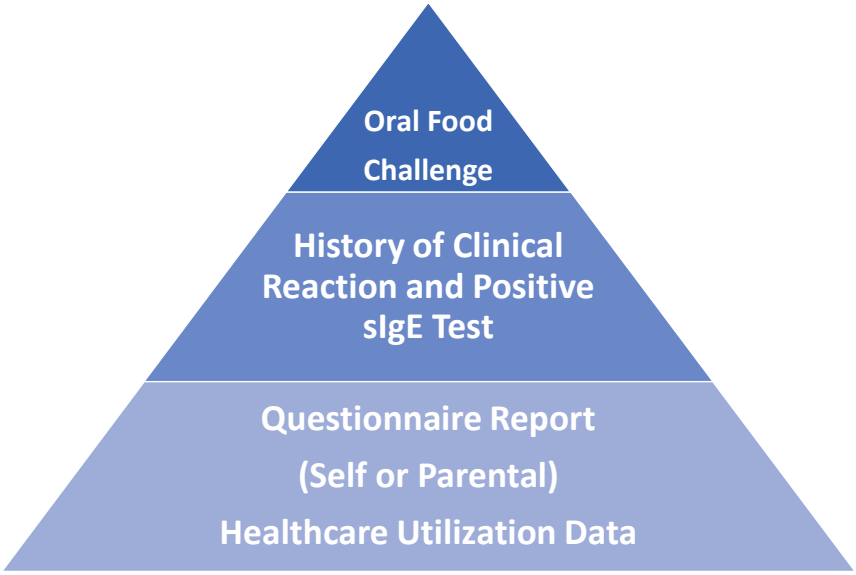
Prevalence is Influenced by the Criteria Used for the Definition of Food Allergy



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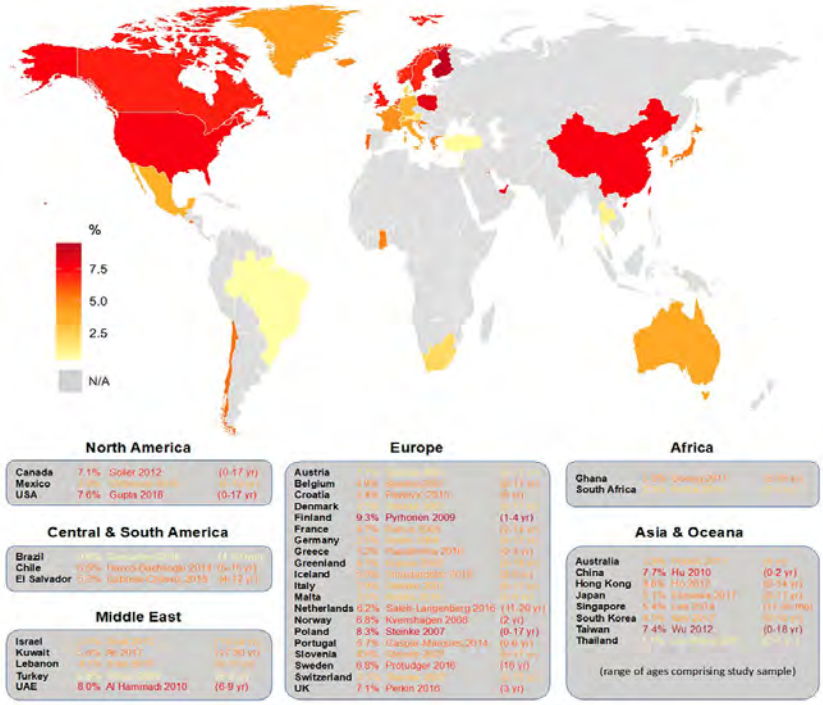
Data suggest increasing prevalence, with rates up to 8-10% depending on age, geography, and criteria used for definition



Warren CM, Jiang J, Gupta RS. Curr Allergy Asthma Rep. 2020 Feb 14;20(2):6. doi: 10.1007/s11882-020-0898-7.

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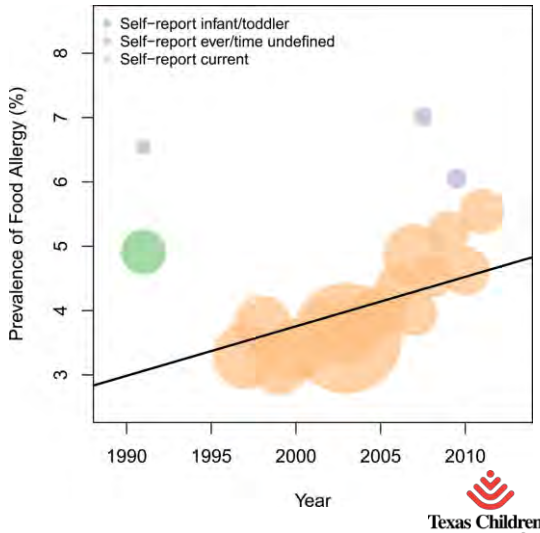
Disparities in Prevalence of Food Allergy

Self-report of food allergy among US children has sharply increased in the past 2 decades with the greatest increase among non-Hispanic black children

Retrospective cohort study of children compared with non-Hispanic white children:

- African American children had
  - more asthma and eczema (P < .01)
  - significantly higher odds of allergy to wheat, soy, corn, fish, and shellfish (P < .01)
- Hispanic children had
  - significantly higher odds of allergy to corn, fish, and shellfish (P < .01)
  - Hispanic children higher odds of eczema (P < .01)



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Keet CA et al. Ann Allergy Asthma Immunol. 2014 Mar;112(3):222-229.e3.; Mahdavinia M et al. JACI in Practice, 2017

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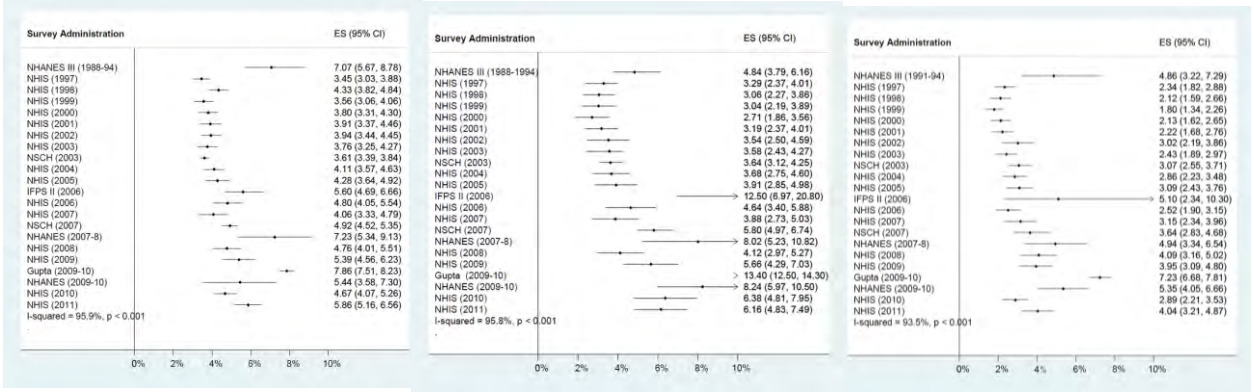
Self-report of current food allergy by ethnicity increased from 1991 to 2011

White **Black** **Hispanic**



1.0 % increase **2.1 % increase** **1.2 % increase**

Keet CA et al. Ann Allergy Asthma Immunol. 2014 Mar;112(3):222-229.e3

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Table 1. Estimated Current FA Prevalence Rates Among US Adults

Variable	Prevalence of Current FA, % (95% CI)	*P* Value	Prevalence of Adult-Onset Current FA, % (95% CI)	*P* Value
Overall	10.8 (10.4-11.1)	NA	5.2 (4.9-5.4)	NA
Race/ethnicity				
Asian, non-Hispanic	11.4 (9.8-13.3)	<.001	4.8 (3.8-6.1)	<.001
Black, non-Hispanic	11.2 (10.2-12.3)		5.1 (4.4-5.9)	
White, non-Hispanic	10.1 (9.7-10.6)		5.2 (4.9-5.5)	
Hispanic	11.6 (10.5-12.8)		4.6 (3.9-5.4)	
Multiple or other	15.9 (13.6-18.6)		7.2 (5.8-9.0)	
Sex				
Male	7.5 (7.0-7.9)	<.001	3.0 (2.7-3.3)	<.001
Female	13.8 (13.3-14.4)		7.2 (6.8-7.7)	

Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. JAMA Netw Open 2019; 2:e185630.

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Caregiver reported FA significantly lower among children in household incomes <$50 000 vs ≥$50 000

TABLE 4 Multiple Logistic Regression Models: Adjusted Odds of Food Allergy, Diagnosis of Food Allergy, and Severe Food Allergy

Variable	Food Allergy vs No Food Allergy	Confirmed vs Convincing Food Allergy	Severe vs Mild-to-Moderate Food Allergy
Race/ethnicity vs white, non-Hispanic			
Asian, non-Hispanic	1.4 (1.2–1.7)	0.7 (0.4–0.9)	0.7 (0.4–1.0)
Black, non-Hispanic	1.8 (1.6–2.1)	0.8 (0.6–1.0)	1.1 (0.8–1.4)
Hispanic	0.9 (0.8–1.1)	0.8 (0.6–1.0)	0.9 (0.7–1.2)
Multiple/other, non-Hispanic	1.1 (0.9–1.4)	1.2 (0.8–1.8)	1.1 (0.7–1.7)
Gender			
Male vs female	0.9 (0.9–1.1)	1.1 (0.9–1.3)	1.3 (1.0–1.5)
Age vs 0–2 y			
3–5	1.5 (1.3–1.8)	1.4 (1.0–1.9)	1.6 (1.1–2.4)
6–10	1.2 (1.1–1.4)	1.2 (0.9–1.)	1.6 (1.2–2.3)
11–13	1.3 (1.1–1.5)	1.1 (0.8–1.6)	1.9 (1.4–2.8)
14–17	1.4 (1.2–1.6)	1.2 (0.9–1.7)	2.1 (1.5–3.0)
Household income, $			
<50 000 vs ≥50 000	0.5 (0.4–0.7)	0.5 (0.4–0.6)	0.8 (0.6–0.9)
Geographic region vs Midwest			
Northeast	1.3 (1.2–1.5)	1.3 (1.0–1.7)	1.1 (0.9–1.5)
South	1.5 (1.3–1.7)	1.1 (0.9–1.4)	1.1 (0.8–1.4)
West	1.3 (1.1–1.5)	1.0 (0.7–1.3)	1.0 (0.7–1.3)
Report of multiple food allergies			
Yes vs no	—	3.1 (2.6–3.8)	3.2 (2.7–4.0)

Each estimate is adjusted for all variables listed in the table.

Gupta RS et al. Pediatrics. 2011 Jul;128(1):e9-17.

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Exploring racial differences in IgE-mediated food allergy in the WHEALS birth cohort

Christine L.M. Joseph, PhD [*,†]; Edward M. Zoratti, MD [‡,†]; Dennis R. Ownby, MD [‡,§]; Suzanne Havstad, MA [*,†]; Charlotte Nicholas, MPH [†]; Christian Nageotte, MD [‡,†]; Rana Misiak, MD [‡,†]; Robert Enberg, MD [‡]; Jerel Ezell, MPH [¶]; Christine Cole Johnson, PhD [*,†]

[*] Department of Public Health Sciences, Henry Ford Hospital, Detroit, Michigan
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[§] Division of Allergy and Immunology, Department of Pediatrics, Georgia Regents University, Augusta, Georgia
[¶] School of Nursing, University of Michigan, Ann Arbor, Michigan

- Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (590 infants)
- Sensitization (serum specific IgE >0.35 IU/mL) to the food allergens was significantly higher for African American children compared with non-African American children
- A higher proportion of African American children were designated as having peanut allergy
  - % African American children with sIgE level >95% predictive decision points for peanut was 1.7% vs 0.5% for non-African American children.
- After logistic regression, race/ethnicity was associated with sensitization to >1 of the food allergens (aOR, 1.80; 95% CI, 1.22-2.65; P = .003).

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The prevalence and characteristics of food allergy in urban minority children

Sarah Taylor-Black, MD; and Julie Wang, MD

The Elliot and Roslyn Jaffe Food Allergy Institute, Division of Allergy and Immunology, Department of Pediatrics, Mount Sinai School of Medicine, New York, New York

Ann Allergy Asthma Immunol 109 (2012) 431–437

- A retrospective review of EMR from children seen in the hospital-based general pediatric clinic at Mount Sinai Hospital serving East Harlem, NY, between July 1, 2008 and July 1, 2010
- Of 9,184 children seen in this low-income, minority clinic, 3.4% (313) had a physician-documented food allergy
- Significantly more black children (4.7%) were affected than children of other races (2.7%, P < .0001)

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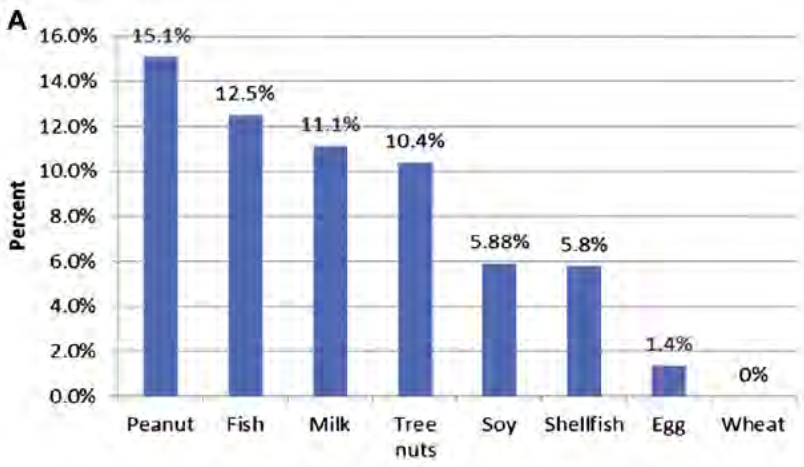
Taylor-Black S, Wang J. The prevalence and characteristics of food allergy in urban minority children. Ann Allergy Asthma Immunol. 2012 Dec;109(6):431-7.



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Higher prevalence of food allergy in Black and Hispanic NYC school children

Results of questionnaire by school type

	Private schools (n = 495 students)	Public charter schools (n = 437 students)	*P* value
Response rate, n (%)	263 (60)	135 (27)	<.0001
Age (y), median (range)	8 (4–12)	6 (6–10)	<.001
Girls, n (%)	126 (48)	65 (48)	.8
Race, n (%)			
White	196 (74.5)	8 (5.9)	<.0001
Black	12 (4.6)	67 (49.6)	<.0001
Asian	19 (7.2)	0 (0)	.0006
Hispanic	18 (6.8)	74 (54.8)	.0001
Median annual income (US$)	>150,000	25,000–49,000	<.0001
Has a doctor ever told you that your child has a food allergy? n (%)			
Yes	46 (17.5)	11 (7.4)	.006
Unsure	5 (1.9)	5 (4.4)	.19
Parental report of food allergy by food, n (%)			
Egg	3 (1.1)	2 (1.5)	1
Milk	3 (1.1)	1 (0.7)	1
Peanut	15 (5.7)	5 (3.7)	.5
Tree nuts	16 (6.1)	1 (0.7)	.02

Taylor-Black SA, Mehta H, Weiderpass E, Boffetta P, Sicherer SH, Wang J. Ann Allergy Asthma Immunol. 2014 Jun;112(6):554-556.e1.

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FORWARD (Food allergy Outcomes Related to White and African-American Racial Differences)

- Objective was to compare clinical and psychosocial outcomes, phenotypes and endotypes, and management practices among a large, socioeconomically and geographically diverse sample of food allergic African American and White children.
- African Americans had higher adjusted odds of allergy to finfish (OR: 2.54, P < .01) and shellfish (OR: 3.10, P < .001) than Whites.
- African Americans also had higher adjusted odds of asthma than Whites (asthma prevalence of 60.5% in African Americans and 27.2% in Whites; OR: 2.70, P < .001).
- In addition, shellfish allergy was associated with asthma, after controlling for race.

Mahdavinia M…Gupta RS. J Allergy Clin Immunol Pract. 2021 Jul;9(7):2867-2873.e1.
Davis CM. J Allergy Clin Immunol Pract. 2021 Jul;9(7):2874-2875.

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Disparities in Food Allergy Management

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FA Physician Documentation, Testing, and Anticipatory Guidance is Lower in Minority Patients

- In low income, urban minority patients with a physician-documented food allergy, fewer than half had confirmatory testing or evaluation by an allergy specialist.
- Although most had epinephrine autoinjectors prescribed, most were not given food allergy action plans.
  - Significantly more blacks were affected than children of other races.
- Black and Hispanics have higher rates of FA-related anaphylaxis and emergency department visits (P < .01).

Taylor-Black S et al. Ann Allergy Asthma Immunol. 2012;109(6):431-7
Bilaver LA et al. Pediatrics. 2016;137(5)
Mahdavinia M et al. JACI in Practice, 2017;5(2):352-357.e1.

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Food Allergy Diagnosis and Follow Up

- Formal food allergy diagnosis is lower among black children despite higher sensitization rates and higher odds of reported severe reactions due to food allergy
- Black and Hispanic children have a shorter duration of follow-up for FA with an allergy specialist (~ 2 years vs. 3 years in White children)

Greenhawt, et al. J Allergy Clin Immunol: In Practice. 2013;1:378-86
Mahdavinia M et al. J Allergy Clin Immunol: In Practice. 2017
Gupta et al. Pediatrics. 2011;128:e9-e17

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Medicaid insurance status is associated with decreased duration of follow up

TABLE E2. Impact of insurance status on food allergy-related outcomes

Insurance group	No Medicaid	Medicaid
Percent of cases with anaphylaxis to foods	21.4	32.4
Odds ratios (95% CI)*	ref	1.17 (0.80-1.70) $P = .423$
Percent of cases with ED visit for food allergy	23.1	38.0
Odds ratios (95% CI)	ref	1.33 (0.92-1.92) $P = .128$
Age in years at first allergist visit (mean ± standard deviation)	4.35 ± 3.70	4.66 ± 3.73
Regression coefficients (95% CI)†	ref	0.17 (−0.13 to 0.46) $P = .263$
Duration of follow-up (y) (mean ± standard deviation)	3.20 ± 2.12	2.32 ± 2.38
Regression coefficients (95% CI)	ref	−0.54 (−0.90 to −0.19) $P = .002$

Mahdavinia M et al. J Allergy Clin Immunol Pract. 2017;5(2):352-357.e1.

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Disparities in Food Allergy Parental Knowledge

- Black, Hispanic, and Asian parents were:
  - Less likely to correctly identify signs of a FA reaction
  - Less likely to identify triggers
  - More likely to recognize the need to avoid food allergens

Characteristic	Able to identify 2 signs of a milk allergy reaction	Able to identify 3 triggers of food allergy	Recognize necessity of allergenic food avoidance	Aware that daily medicine cannot treat food allergy
Aged ≥65 y	0.81 (0.69–0.96)[b]	0.72 (0.52–0.99)[b]	1.28 (1.14–1.43)[b]	1.16 (0.95–1.42)
Female sex	1.26 (1.14–1.39)[b]	1.02 (0.86–1.22)	1.07 (0.99–1.16)	1.14 (1.00–1.31)[b]
Race				
Black	0.83 (0.73–0.95)[b]	0.64 (0.48–0.84)[b]	1.13 (1.02–1.25)[b]	1.02 (0.85–1.22)
Hispanic	0.80 (0.71–0.91)[b]	0.68 (0.53–0.89)[b]	1.15 (1.04–1.26)[b]	1.01 (0.85–1.21)
Asian	0.84 (0.72–0.97)[b]	0.97 (0.76–1.25)	1.06 (0.94–1.20)	1.04 (0.86–1.26)
College graduate	0.96 (0.86–1.07)	1.05 (0.86–1.28)	0.99 (0.90–1.09)	1.23 (1.06–1.42)[b]
Annual income <$75,000	1.03 (0.94–1.12)	0.86 (0.72–1.02)	1.09 (1.00–1.18)	0.92 (0.81–1.05)
Parent of child <18 y	1.03 (0.94–1.13)	1.01 (0.85–1.21)	1.11 (1.02–1.20)[b]	1.07 (0.93–1.23)
Prior training in food allergy	1.12 (1.00–1.25)[b]	1.42 (1.15–1.74)[b]	1.04 (0.93–1.15)	1.11 (0.94–1.31)
Food-allergic acquaintance	1.22 (1.11–1.35)[b]	1.03 (0.86–1.30)	0.93 (0.86–1.01)	1.03 (0.90–1.18)

[a] Data are given as relative risk ratio (95% confidence interval).
[b] $P < .05$.

Gupta et al. Ann Allergy Asthma Immunol. 2009;103:43-50

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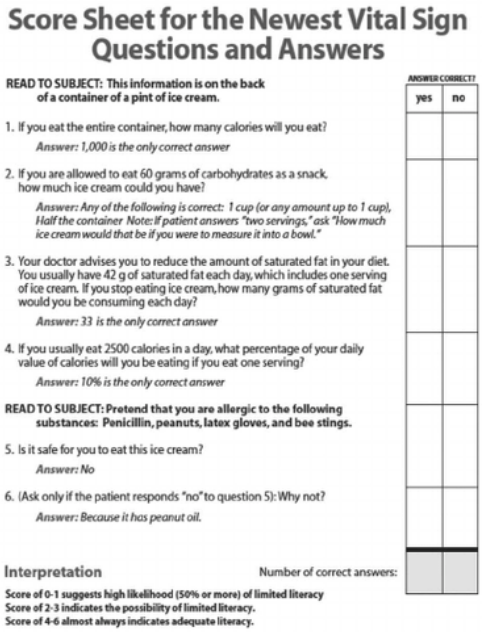
Health Literacy and Food Allergy Management Knowledge

- Health literacy was assessed using the Newest Vital Sign (NVS), a validated index consisting of 6 questions regarding an individual's ability to read an ice cream label
- Higher scores = better health literacy

Nutrition Facts	
Serving Size	½ cup
Servings per container	4
Amount per serving	
Calories 250	Fat Cal 120
	%DV
Total Fat 13g	20%
Sat Fat 9g	40%
Cholesterol 28mg	12%
Sodium 55mg	2%
Total Carbohydrate 30g	12%
Dietary Fiber 2g	
Sugars 23g	
Protein 4g	8%

*Percentage Daily Values (DV) are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

Ingredients: Cream, Skim Milk, Liquid Sugar, Water, Egg Yolks, Brown Sugar, Milkfat, Peanut Oil, Sugar, Butter, Salt, Carrageenan, Vanilla Extract.



Score Sheet for the Newest Vital Sign Questions and Answers

	ANSWER CORRECT? yes	no
READ TO SUBJECT: This information is on the back of a container of a pint of ice cream.		
1. If you eat the entire container, how many calories will you eat? *Answer: 1,000 is the only correct answer*		
2. If you are allowed to eat 60 grams of carbohydrates as a snack, how much ice cream could you have? *Answer: Any of the following is correct: 1 cup (or any amount up to 1 cup), Half the container Note: If patient answers "two servings," ask "How much ice cream would that be if you were to measure it into a bowl."*		
3. Your doctor advises you to reduce the amount of saturated fat in your diet. You usually have 42 g of saturated fat each day, which includes one serving of ice cream. If you stop eating ice cream, how many grams of saturated fat would you be consuming each day? *Answer: 33 is the only correct answer*		
4. If you usually eat 2500 calories in a day, what percentage of your daily value of calories will you be eating if you eat one serving? *Answer: 10% is the only correct answer*		
READ TO SUBJECT: Pretend that you are allergic to the following substances: Penicillin, peanuts, latex gloves, and bee stings.		
5. Is it safe for you to eat this ice cream? *Answer: No*		
6. (Ask only if the patient responds "no" to question 5): Why not? *Answer: Because it has peanut oil.*		
Interpretation Number of correct answers:		

Score of 0-1 suggests high likelihood (50% or more) of limited literacy
Score of 2-3 indicates the possibility of limited literacy.
Score of 4-6 almost always indicates adequate literacy.

Egan M, Yin HS, Greenhawt M, Wang J. J Allergy Clin Immunol Pract. 2019 Feb;7(2):655-658.

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Lower health literacy in caregivers is associated with deficiencies in management

Outcome assessed	Health literacy association
Demonstrated correct use of EA (caregiver), mean ± SD	- Every 1-point increase in the EA score was associated with a 0.3 increase in the NVS score ($P = .002$)
Unexpired EA present at visit*	- Device being present was associated with a 1.5-point increase in the NVS score ($P = .001$)
Food allergy reaction rates (no. of events in the past 12 mo), mean ± SD	- The NVS score decreased by 0.46 for every additional allergic reaction ($P = .002$)
History of anaphylaxis	- Those with a higher NVS score were less likely to have a history of anaphylaxis (OR, 0.76; 95% CI, 0.61-0.94)
Health care utilization (no. of events in the past 12 mo), median (IQR)	- No association with calls to pediatrician - No association with ED visits - For every additional allergy call, the NVS score increased by 0.46 ($P = .002$)
Clinical vignette: Treatment of mild hives† (participants able to select multiple answers)	- The mean NVS score was lower among patients reporting taking child to the ED ($P = .003$) or calling 911 for hives ($P = .008$)
Clinical vignette: Treatment of anaphylaxis‡ (participants able to select multiple answers)	- The NVS score was lower in patients who would take child to the ED for anaphylaxis ($P = .05$)

1) Demonstrating correct use of an epinephrine autoinjector
2) Increased reactions to foods in the past 12 months
3) Knowledge gaps on treatment of allergic reactions.

Egan M, Yin HS, Greenhawt M, Wang J. J Allergy Clin Immunol Pract. 2019 Feb;7(2):655-658.

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Disparities in Food Allergy Reaction Preparedness

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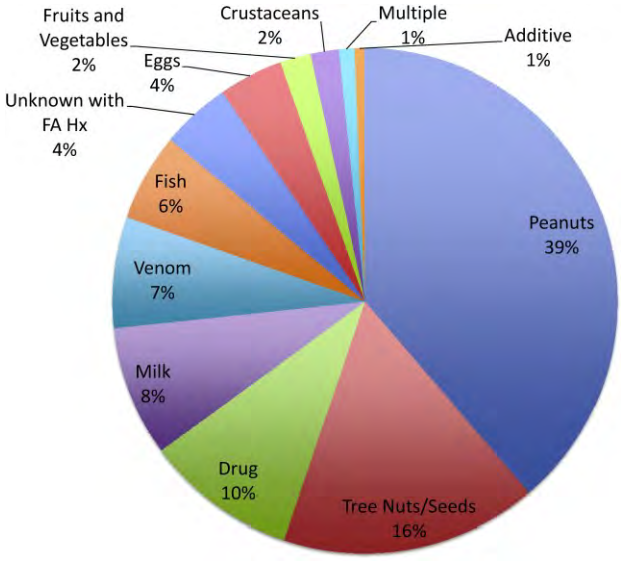
Food-Induced PICU Anaphylaxis

Children in 131 North American (US and Canada) PICUs prospectively enrolled in the Virtual Pediatric Systems database from 2010 to 2015



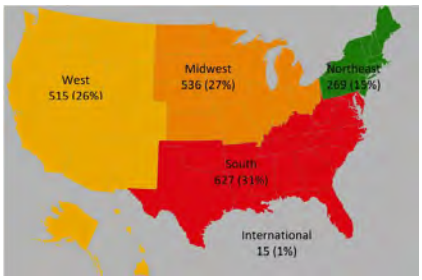
Ramsey NB, Guffey D, Anagnostou K, Coleman NE, Davis CM. J Allergy Clin Immunol Pract. 2019 Sep-Oct;7(7):2241-2249.

30

Population Specific Triggers

- There were differences among children with different race/ethnicities ($P < .001$)
  - In Black children, fish (60%) and shellfish (67%) were the most common triggers
  - In White children, tree nuts (59%) and milk (64%)
  - In Asian children, eggs (10%) and tree nuts/seeds (9%)
  - In Hispanic children, crustaceans (22%), eggs (20%), and fish (20%).

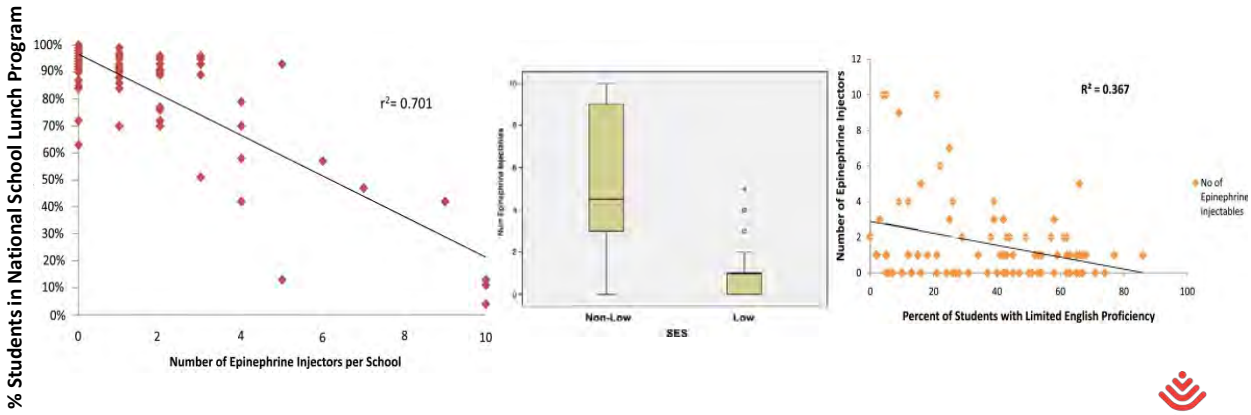
- There were also significant differences among children in different US regions ($P = .044$).
  - In Midwestern children, milk (46%) or shellfish (45%) were the most common triggers
  - In Northeastern children, eggs (25%) and milk (22%)
  - In Southern children, shellfish (45%)
  - In Western children, tree nuts/seeds (30%) or peanuts (31%).



31

Disparities in Emergency Preparedness

- Epinephrine has shown to be less available in schools when needed in low income, low English proficiency and rural populations.



Shah SS et al. J Allergy Clin Immunol Pract. 2014;2:288-93.e1.

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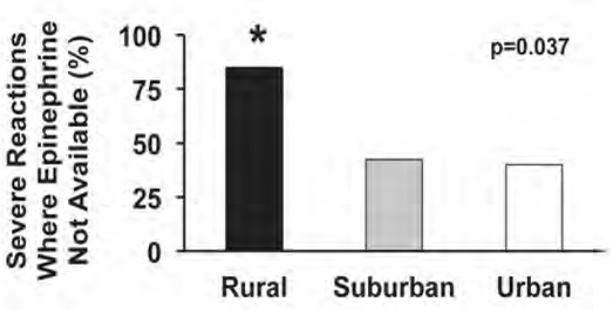
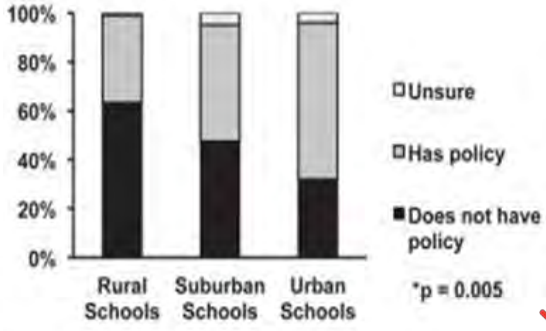
Rural communities reported less epinephrine availability than urban and suburban communities



Nurses from rural schools were least likely to report a policy for undesignated epinephrine



Szychlinski C et al. J Allergy Clin Immunol Pract. 2015;3(5):805-7.e8.

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Socioeconomic Variables Impacting Food Allergy

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Socioeconomic Disparities in the Economic Impact of Childhood Food Allergy

Lucy A. Bilaver, PhD,[a] Kristen M. Kester, MD, MPH,[b] Bridget M. Smith, PhD,[c,d,e] Ruchi S. Gupta, MD, MPH[c,d]

- Cross-sectional survey data (November 2011 and January 2012) from 1,643 US caregivers with a food-allergic child.
- 2-part regression model to estimate mean costs and identified differences by levels of household income and race or ethnicity.
- Children in the lowest income stratum incurred 2.5 times the amount of emergency department and hospitalization costs as a result of their food allergy than higher-income children.
- Costs incurred for specialist visits were lower in the lowest income group ($228) compared with the highest income group ($311; P < .01) as was spending on out-of-pocket medication costs ($117, lowest income; $366, highest income; P < .001).
- Conclusion: Affordable access to specialty care, medications, and allergen-free foods are critical to keep all food-allergic children safe, regardless of income and race.

Bilaver LA, Kester KM, Smith BM, Gupta RS. Pediatrics. 2016 May;137(5):e20153678.

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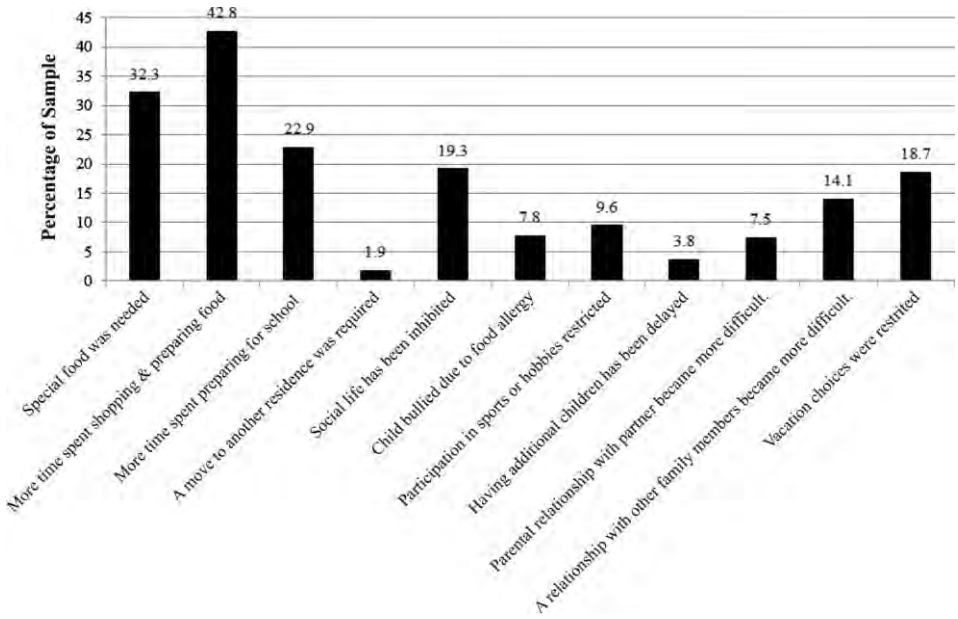


Bilaver LA, Kester KM, Smith BM, Gupta RS. Pediatrics. 2016 May;137(5):e20153678.

36

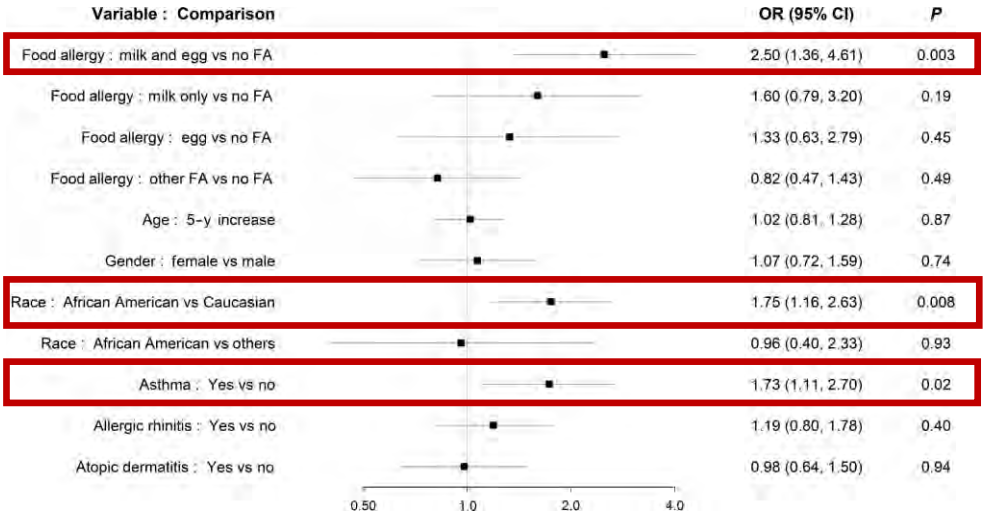
Food allergy-related bullying and associated peer dynamics among Black and White children

- FORWARD - prospective multicenter cohort study, initiated to evaluate racial differences in the natural history of food allergy among Black and White children.
- No significant racial differences in FA-related bullying prevalence were identified overall (20.0% of White vs 15.6% of Black; *P* = .50)
- In those ≥11 years old, the rates were higher among White (44.8% vs 18.2% of Black), *P* = .046
- In contrast, bullying unrelated to FA was higher among Black (38.6%), vs. White children (17.7%), *P* = .002

Brown D…Warren C. Ann Allergy Asthma Immunol. 2021 Mar;126(3):255-263.e1.

37

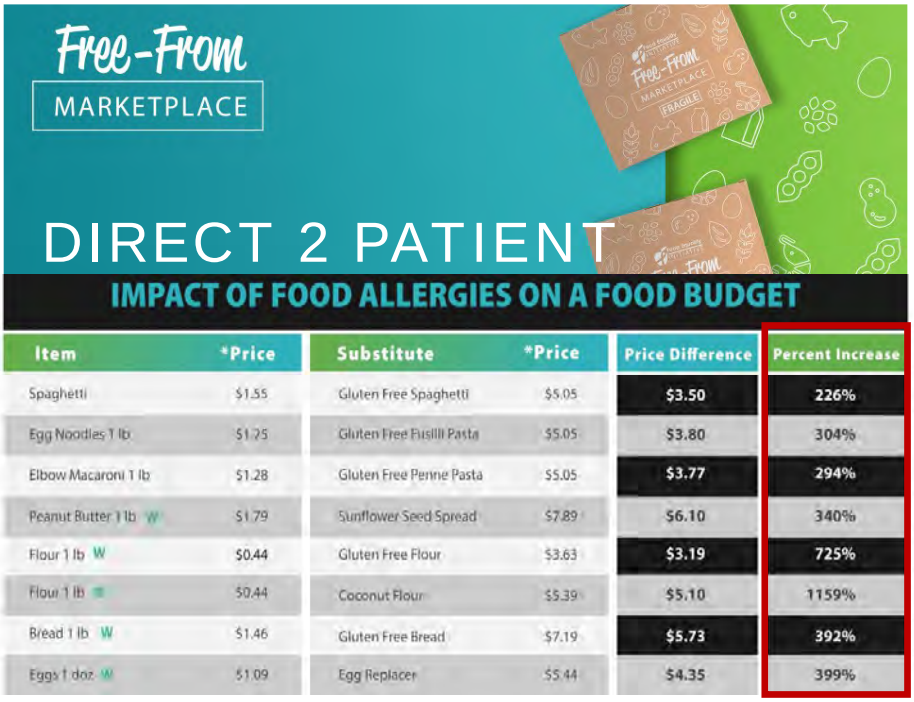
Food Insecurity Risk Factors



Food insecurity is associated with poorer quality of life.

Dilley MA et al. Pediatr Allergy Immunol. 2019 May;30(3):363-369.

38



Item	*Price	Substitute	*Price	Price Difference	Percent Increase
Spaghetti	$1.55	Gluten Free Spaghetti	$5.05	$3.50	226%
Egg Noodles 1 lb	$1.25	Gluten Free Fusilli Pasta	$5.05	$3.80	304%
Elbow Macaroni 1 lb	$1.28	Gluten Free Penne Pasta	$5.05	$3.77	294%
Peanut Butter 1 lb W	$1.79	Sunflower Seed Spread	$7.89	$6.10	340%
Flour 1 lb W	$0.44	Gluten Free Flour	$3.63	$3.19	725%
Flour 1 lb	$0.44	Coconut Flour	$5.39	$5.10	1159%
Bread 1 lb W	$1.46	Gluten Free Bread	$7.19	$5.73	392%
Eggs 1 doz W	$1.09	Egg Replacer	$5.44	$4.35	399%

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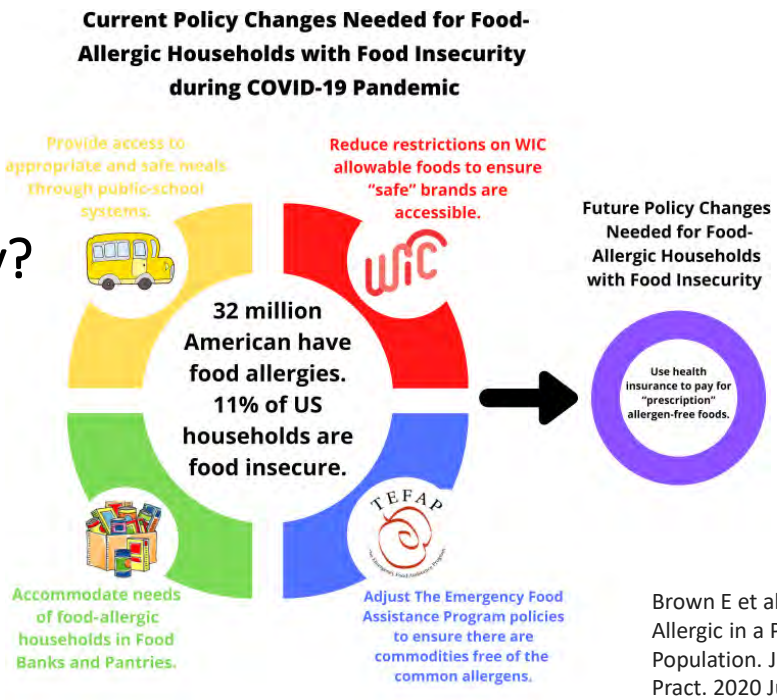
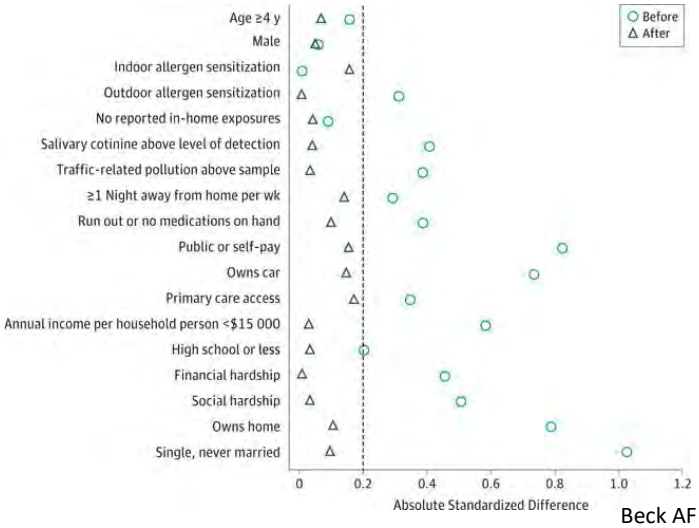
How to Address Food Insecurity?



Brown E et al. Food Insecure and Allergic in a Pandemic: A Vulnerable Population. J Allergy Clin Immunol Pract. 2020 Jul-Aug;8(7):2149-2151.

40

Asthma readmission disparity explained after statistically balancing SES variables



Socioeconomic hardship variables explained 53% of the observed disparity

Beck AF et al. JAMA Pediatr. 2016 Jul 1;170(7):695-703.

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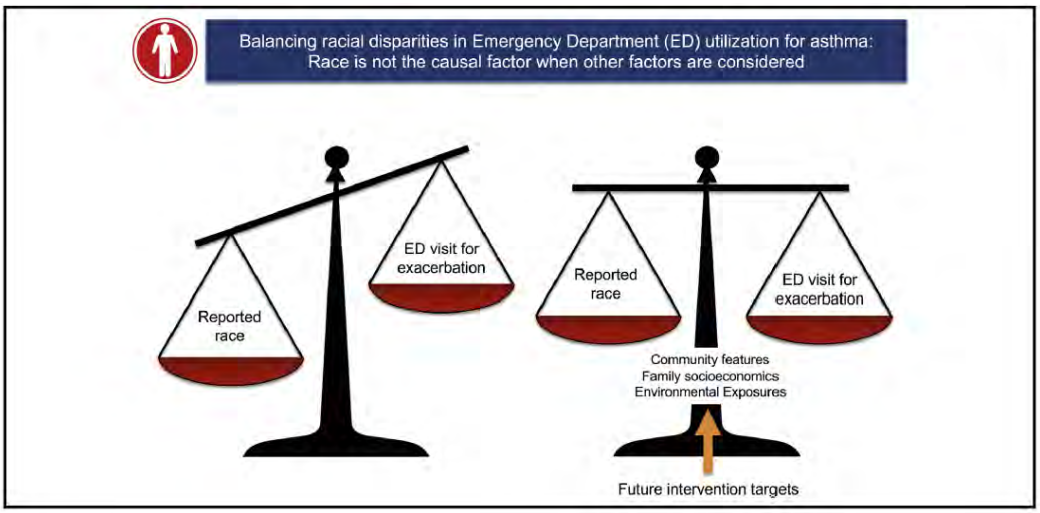
Racial disparities in asthma-related ED use are evident between black and white patients with asthma but can be eliminated when socioeconomic and environmental variables are equally balanced between groups.



Fitzpatrick et al. JACI 2019

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Social Determinants of Health

Davis et al. JACI. 2021.

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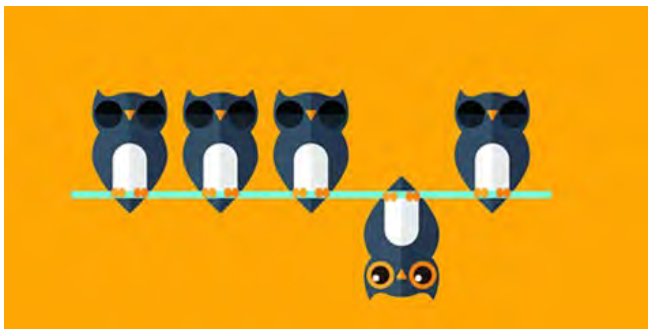
Implicit Bias is……

- A bias that results from the tendency to process information based on ***unconscious associations and feelings***, even when these are contrary to one's conscious or declared beliefs



The bias blind spot is the cognitive bias of recognizing the impact of biases on the judgment of others, while failing to see the impact of biases on one's own judgment.

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We're Not Bad, We're Human.

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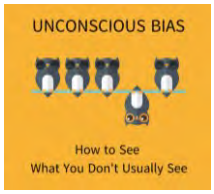

Healthcare Quality and Implicit (Unconscious) Bias

- **Healthcare professionals have implicit biases - No one is immune.**
  - We resist the unfamiliar, and our processes can reflect or reinforce bias.
  - Studies show a significant positive correlation between level of implicit bias and lower quality of health care.

- **Implicit bias affects clinical judgement and behavior**
  - Bias is evident either in the diagnosis, the treatment recommendations, the number of questions asked of the patient, the number of tests ordered, or other responses.

- **There are specific determinants of bias**
  - Socio-demographic characteristics of physicians and nurses (e.g. gender, race, type of healthcare setting, years of experience, country where medical training received) are correlated with level of bias.

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FitzGerald C, Hurst S. Implicit bias in healthcare professionals: a systematic review. BMC Med Ethics. 2017 Mar 1;18(1):19. https://www.boyden.com/media/checking-your-blind-spot-ways-to-find-and-fix-unconscious-bias-7627148/index.htm

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What You Can Do

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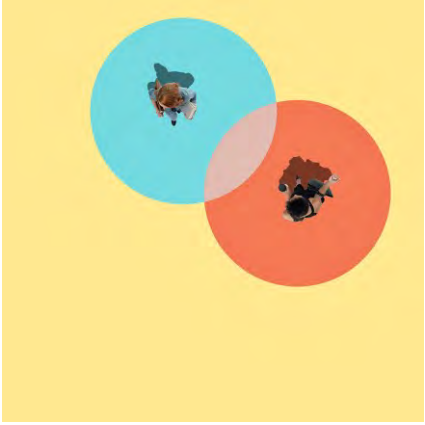
What Can You Do to Minimize Your Implicit Bias?

Project Implicit®
Harvard Implicit Association Test - Harvard University
implicit.harvard.edu

- **Introspection:** Explore and identify your own prejudices
- **Mindfulness:** Since you're more likely to give in to your biases when you're under pressure, practice ways to reduce stress
- **Perspective-taking:** Consider experiences from the point of view of the other person
- **Learn to slow down:** Before interacting with people from certain groups, pause and reflect to reduce reflexive actions
- **Individuation:** Evaluate people based on their personal characteristics rather than those affiliated with their group



"You can't eliminate bias but you can 'learn how to dance with it' to minimize its effect." Howard Ross

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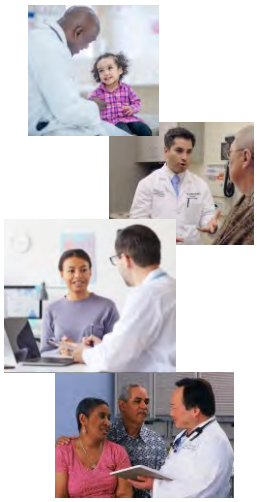
Strategies to Help Reduce Food Allergy Health Disparities



- Require medical provider training with cross-cultural education to reduce implicit/unconscious bias.
- Recruit and hire diverse patient-facing faculty and staff, who can help educate non-English speaking patients or patients with low health literacy.
- Identify systemic and other barriers to care for underserved populations in your practice/institution and develop strategies to address them.

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Ali A et al. Can Respir J. 2019: 5165189. Apter AJ et al. J Allergy Clin Immunol. 2019;144(3):846-853.e11.
George M et al. J Adv Nurs. 2019;75(4):876-887. Delaigue S et al. Frontiers in Public Health 2014; 2: 1-9.

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Strategies to Help Reduce Food Allergy Health Disparities

- Implement more culturally sensitive patient education efforts and collaborative patient-clinician decision-making processes.
- Improve access to specialty care in underserved communities.
  - Develop relationships with community primary care physicians and other healthcare providers or organizations
  - Commit resources to have a proportion of patients in a practice who have public insurance
- Increase research studies addressing diagnosis, management and outcomes for underserved populations.

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Ali A et al. Can Respir J. 2019: 5165189. Apter AJ et al. J Allergy Clin Immunol. 2019;144(3):846-853.e11.
George M et al. J Adv Nurs. 2019;75(4):876-887. Delaigue S et al. Frontiers in Public Health 2014; 2: 1-9.

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Strategies to Help Reduce Food Allergy Health Disparities

- Screen for social determinants of health (SDOH) with a non-biased approach and address in office visits.
  - https://www.aafp.org/journals/fpm/blogs/inpractice/entry/social_determinants.html
- Give patient education about SDOH and provide clinical care resources to address them
  - Social service resources like auntbertha (www.findhelp.org) and 211 (www.211.org)
  - Dietary resources like Food Equality Initiative
- Join and advocate through medical societies and lay organizations for policy change in insurance coverage for underserved communities.
- Engage trainees from minority communities for training and mentoring opportunities.

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Ali A et al. Can Respir J. 2019: 5165189. Apter AJ et al. J Allergy Clin Immunol. 2019;144(3):846-853.e11. George M et al. J Adv Nurs. 2019;75(4):876-887. Delaigue S et al. Frontiers in Public Health 2014; 2: 1-9.; Wear Det al. AcadMed. 2017;92(3):312-317.

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Conclusions

- Health disparities are significant in populations with food allergies.
- Socioeconomic factors and other social determinants of health contribute to these disparities.
- Health disparities include increased risks for anaphylaxis and ER visits and lack of access to subspecialty care.
- Understanding the key features to recognize the presentation and concerns of patients from underserved communities with food allergies can target early, specific and meaningful prevention strategies and interventions.

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Food Allergy Program
at Texas Children's Hospital®

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Annual Business Meeting

Saturday, June 25, 2022

9:45 a.m. – 10:15 a.m.

PAAA

Pennsylvania Allergy & Asthma Association

1

AGENDA

A. Call to Order (*Sigrid DaVeiga, MD*)

B. Approval of Minutes of June 26, 2021, Annual Business Meeting (*Sigrid DaVeiga, MD*)

C. President's Report (*Sigrid DaVeiga, MD*)

D. Treasurer's Report/Finance Committee (*Gisoo Ghaffari, MD*)

E. Committee/Representative Reports
1) Membership (*Janet Beausoleil*)
2) Nominating (*Allyson Larkin, MD*)
3) PAERF (*Sarah Henrickson, MD*)

F. New/Old Business (Sigrid DaVeiga, MD)
1) Bylaws Amendment – DEI Standing Committee

G. Recognition of Long-Standing Attendees (Janet Beausoleil, MD)

H. Recognition of Outgoing President and Remarks (Sigrid DaVeiga, MD and Janet Beausoleil, MD)

I. Remarks of Incoming President's Remarks *(Robert Zemble, MD)*

J. Adjournment

PAAA
Pennsylvania Allergy & Asthma Association

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APPROVAL OF THE MINUTES
June 26, 2021

- **I. Call to Order** – Dr. Allyson Larkin, PAAA President, called the meeting to order at 10:00 am.

- **II. Approval of Minutes of June 27, 2020, Annual Business Meeting** – On a motion made and seconded, those present voted unanimously via a Zoom Poll to approve the minutes of the 2020 Annual Business Meeting.

- **III. President's Report** – Dr. Larkin thanked everyone for coming to the virtual annual business meeting. Dr. Larkin expressed her appreciation and thanks to Planning Committee, recognized the excellent programming and speakers the committee had assembled for this year's annual meeting, and stated that she looked forward to meeting in person next year.

3

- **IV. Treasurer's Report/Finance Committee** – Dr. Robert Zemble reported on the financial statement as of December 2020. He commented on PAAA's total assets and total liabilities. On a motion made and seconded, those present voted unanimously via a Zoom Poll to accept the financial statement.

- **V. Report of the Membership Committee** – Dr. Janet Beausoleil reported on the membership statistics. She reported that PAAA gained one new member and three new fellows in training over the last year. The current membership stands at 177 dues-paying members. The Board has agreed to conduct an outreach drive to recoup these nonrenewing members.

- **VI. Report of the Nominating Committee** - In the absence of Dr. Fisher, Dr. Larkin presented the Nominating Committee slate and called for any nominations from the floor. Hearing none, on a motion made and seconded, those present voted unanimously via a Zoom Poll to accept the slate as presented.

4

- **VII. PAERF** – Dr. Sarah Henrickson reviewed the financial report as of May 31, 2021, the PAERF list of donors, PAERF Research Grant recipients for 2021, winning abstract and digital poster presenters and the PAERF mentee/mentor program for 2021.

- **VIII. Recognition of Long-Standing Attendees -** PAAA Historian Janet Beausoleil recognized Drs. Effat Mahmoud and Mary Fontana-Penn.

- **IX. New/Old Business** – There was no new or old business.

- **X. President Awards** - Dr. Janet Beausoleil thanked Dr. Larkin for her outstanding leadership as PAAA president and presented the president's award virtually.

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- **XI. Passing of the Gavel** – Dr. Larkin passed the mantle of leadership to Dr. Sigrid DaVeiga and expressed complete confidence in her ability to lead PAAA going forward.

- **XII. Remarks of Incoming President** – Dr. DaVeiga thanked Dr. Larkin for her leadership.

- There being no further business, the meeting adjourned at 10:17 a.m.

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PRESIDENT'S REPORT

Sigrid DaVeiga, MD

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TREASURER'S REPORT

Gisoo Ghaffari, MD

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TREASURER'S REPORT

Pennsylvania Allergy and Asthma Association
Statement of Financial Position
December 31, 2021

	YEAR TO DATE	PRIOR YEAR TO DATE
ASSETS		
Cash - Checking	$0.00	$500.00
Cash Management - Fulton	70,046.56	13,114.56
Long Term Investment	497,440.92	475,221.99
Total Cash	567,487.48	488,836.55
Accounts Receivable	150.00	3,300.00
Prepaid Expenses	0.00	0.00
TOTAL ASSETS	567,637.48	492,136.55
LIABILITIES AND NET ASSETS		
Accounts Payable - General	$2,291.90	5,988.48
Accounts Payable - PAMED	6,561.38	6,248.93
Unearned Revenue	49,950.00	9,950.00
Total Liabilities	57,803.28	22,187.41
Net Assets, January 1	469,949.14	448,313.26
Change in Net Assets	39,885.06	21,635.88
Net Assets, Year to Date	509,834.20	469,949.14
TOTAL LIAB AND NET ASSETS	567,637.48	492,136.55

Prepared by the Foundation of the PA Medical Society

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MEMBERSHIP REPORT

Janet Beausoleil, MD

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MEMBERSHIP COMMITTEE REPORT

Current Membership	
Active	158
Associate	2
Corresponding	10
Emeritus	50
In-training	11
Total Members	231

New Members Since June 2021

Active
Taha Al-Shaikhly, MD
David Anmuth, MD
Stanislaw Gabryszewski, MD
Sujal Ghelani, MD
Marc Goldstein, MD
Maria Paula Henao, MD
Lauren Kaminsky, MD

Active
Jennifer Kannan, MD
John Kim, MD
Mosopefoluwa Lanlokun, MD
Archana Mehata, MD
Sunjay Modi, MD
Matthew Norris, MD
Mary Lee Wong, MD, MS

Corresponding
Victoria Durf, MSN
Matthew D. Stryker, Pharm D

In Training
Hannah Harrison, MD
Kim Nguyen, MD
Sunjay Modi, MD
Marvi Rizwan, MD
Elizabeth Hodara, MD

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NOMINATING COMMITTEE REPORT

Ally Larkin, MD

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NOMINATING COMMITTEE REPORT

2021-2022 Board of Regents Nominees

Name	Position
Antonella Cianferoni, MD, PhD, Philadelphia, PA	Member-At-Large (4-year term)
Desha M, Jordan, MD, Pittsburgh, PA	Member-At-Large (4-year term)
Mosopefoluwa Lanlokuna, MD Pittsburgh, PA	Member –At-Large (1-year term)
Matthew Norris, MD, Hershey, PA	FIT (1-year term)

Appointments	
Magee DeFelice, MD	Program Chair 2023
Sarah Henrickson, MD, PhD	Assistant Program Chair 2023

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PAERF REPORT

Sarah Henrickson, MD, PhD

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PAERF DONORS

Platinum

Corinna Bowser, MD
Kara E. Coffey, MD
Robert E. Coifman, MD
Magee L. DeFelice, MD
Denise DiPrimio-Kalman, DO
Joel M. Fiedler, MD
Laura H. Fisher, MD
Mary E. Fontana- Penn, MD
Richard L. Green, MD
Gretchen A. Harmon, MD
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Michael J. Prematta, MD
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Gold

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Melanie A. Ruffner, MD
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Thank you PAERF Donors!

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Bronze

Janet L. Beausoleil, MD
Soheil Chegini, MD
Hey Chong, MD
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Tom Ferro, MD
Sandra M. Gawchik, DO
Prakash Kaur, MD
Kristen Lutzkanin, MD
David Lee Miller, MD
Thekkemadom Ramakrishnan,MD
Karen Flynn-Rodden, MD

Thank you PAERF Donors!

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PAERF RESEARCH GRANT RECIPIENTS

2022 Grant Recipient

- $10,000 grant to Dr. Linda Nguyen - Impact of anaphylaxis plans in multiple languages in an outpatient pediatric allergy clinic setting

2021 Grant Recipients

- $10,000 grant to Dr. Stanislaw Gabryszewski - Investigating epidemiologic and immunologic relationships between systemic and gastrointestinal food allergies
- $2,500 mini-grant to Dr. Patrick Gleason – Utilization of biologics for persistent asthma
- $2,500 mini-grant to Dr. Amandeep Sandhu – Systemic immune dysregulation in patients who have undergone Fontan procedure

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PAERF POSTERS

Ramin Beheshti, MD
Hannah Harrison, MD
Elisabeth Hodara, MD
Lauren Kaminsky, MD, PhD
Anthony LaCava, MD
Sunjay Modi, MD
Kim Nguyen, MD
Catherine Popadiuk, MD
Colleen Shannon, MD, MPH
Sebastian Sylvestre, MD
Paulina Tran, DO

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NEW/OLD BUSINESS – BYLAWS AMENDMENT

Sigrid DaVeiga, MD

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NEW/OLD BUSINESS

Proposed Bylaws Amendment – Creates a new PAAA Standing Committee on Diversity, Equity, and Inclusion. The language would add new paragraph i in Section 2.

ARTICLE VI – COMMITTEES

- Section 2. The Standing Committee chairs shall be members of the Board of Regents. The committees are:
  - i. Diversity, Equity, and Inclusion Committee - This committee is responsible for maintaining a repository of resources and model programs that serve to reduce barriers to entry into the medical profession and the A/I specialty for the historically underrepresented. Additionally, this committee is available as a resource, for example, to assist the Planning Committee for the Annual Meeting and other educational programs provided by PAAA to support consideration of diverse expert speakers and topics.

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RECOGNITION OF LONG-STANDING ATTENDEES

Janet Beausoleil, MD

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2022 ANNUAL MEETING LONG-STANDING ATTENDEES

- Janet Beausoleil, MD
- Neil Feldman, DO
- Robert Rabinowitz, DO

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RECOGNITION OF OUTGOING PRESIDENT AND REMARKS

Janet Beausoleil, MD
Sigrid DaVeiga, MD

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REMARKS OF INCOMING PRESIDENT

Robert Zemble, MD

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Quality/Safety in the Allergy Practice

Presented by:

Paige Wickner, MD, MPH

Saturday, June 25, 2022

11:30 a.m. – 12:15 p.m.

PAAA does not have permission to share slides.

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Disparities in Asthma

Presented by:
Torie Grant, MD, MHS

Saturday, June 25, 2022
12:15 p.m. – 1:00 p.m.

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Pennsylvania Allergy & Asthma Association

Disparities in Asthma: A Focus on the Social Determinants of Health

Torie Grant, MD, MHS
Assistant Professor of Medicine and Pediatrics
Johns Hopkins University School of Medicine

1

Disclosures

- Current Funding
  - National Institutes of Health K23 Mentored Patient-Oriented Research Career Development Award
  - American Academy of Allergy, Asthma, and Immunology Foundation Faculty Development Award

2

Objectives

1. Discuss asthma disparities through the lens of social determinants of health (SDoH)
2. Highlight how disparities in socioeconomic status, physical environment, and health care influence racial and ethnic asthma disparities

3

What are Social Determinants of Health (SDoH?

"The social determinants of health are the **non-medical factors that influence health outcomes.** They are the conditions in which people are **born, grow, work, live, and age**, and the **wider set of forces and systems shaping the conditions of daily life**. These forces and systems include *economic policies and systems, development agendas, social norms, social policies and political systems*."

https://www.who.int/health-topics/social-determinants-of-health

4

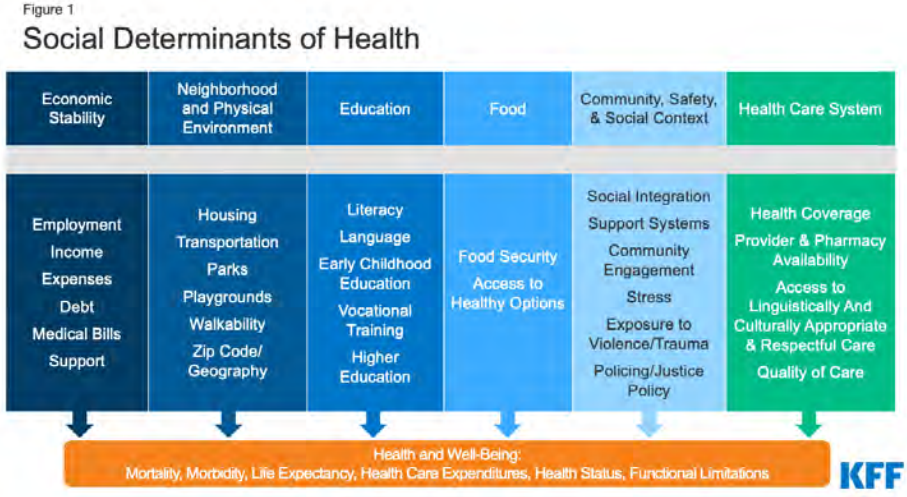
What are Social Determinants of Health (SDoH)?

- Income and social protection
- Education
- Unemployment and job insecurity
- Working life conditions
- Food insecurity
- Housing, basic amenities and the environment
- Early childhood development
- Social inclusion and non-discrimination
- Structural conflict
- Access to affordable health services of decent quality.

https://www.who.int/health-topics/social-determinants-of-health

5

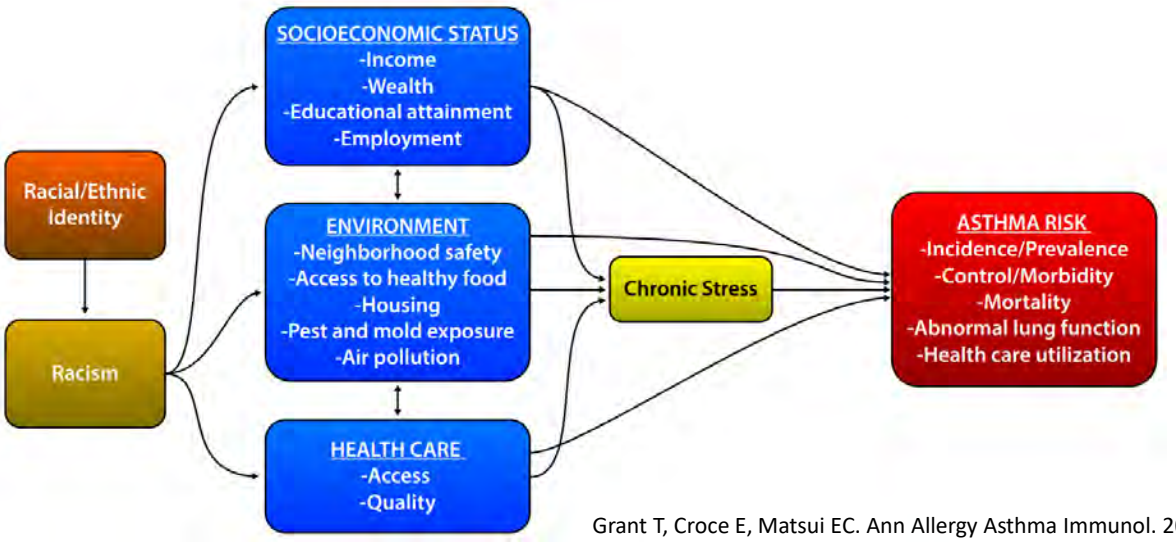
What are Social Determinants of Health (SDoH)?



https://www.kff.org/coronavirus-covid-19/issue-brief/tracking-social-determinants-of-health-during-the-covid-19-pandemic/

6

The relationship between racism, SDoH, and asthma disparities



Grant T, Croce E, Matsui EC. Ann Allergy Asthma Immunol. 2022

7

Why talk about race and racism when we are discussing asthma disparities?

- Asthma prevalence varies by race/ethnicity
  - Non-Latinx (NL) Blacks - 10.8%
  - Native American/Alaska Native - 10.8%
  - NL Whites - 7.6%
  - Latinx - 6.7%
  - NL Asians - 3.5%
  - NL Multiracial - 11.5%

https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm

8

Why talk about race and racism when we are discussing asthma disparities?

- Asthma morbidity and mortality varies by race/ethnicity
  - Black Americans have higher rates ER visits and hospitalizations due to asthma[1]
  - Black Americans have higher asthma mortality[1]
  - Puerto Ricans and Dominican Americans have higher asthma prevalence, more exacerbations and ER visits due to asthma[1-3]

1. Moorman JE et al. *MMWR Surveill Summ*. 2007
2. Rosser FJ, et al. *Am J Respir Crit Care Med*. 2014
3. Dumanovsky T, et al. *Journal of Asthma*. 2007

9

What are race and ethnicity?

- Race and ethnicity are *self-identified social constructs*
- American Sociological Association
  - Race = "physical differences that groups and cultures consider socially significant"
  - Hispanic or Latinx Ethnicity = "shared culture, such as language, ancestry, practices, and beliefs"

https://www.asanet.org/topics/race-and-ethnicity

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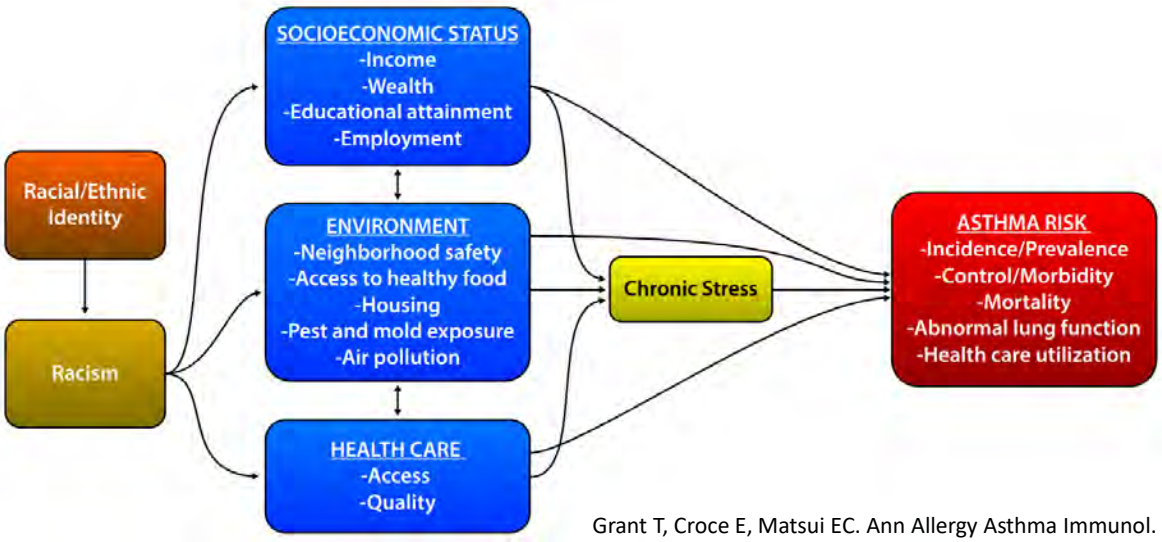
The relationship between racism, SDoH, and asthma disparities



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What is racism?

- Racism occurs at the **individual and population level**
- **Prejudicial treatment** of individuals and communities based on the belief that **one race or ethnic group is superior or inferior to another**
- Racism **structures and affords opportunities and assigns value** and worth based on an individual's self-identified race or ethnicity
- Structural racism, which is population-level racism, exists in our **social, legal, economic, medical, housing, criminal justice, and political systems** and unfairly denies opportunity and disadvantages racial and ethnic minority populations

Bailey ZD, et al. *The Lancet*. 2017

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What is racism?

America: Equity and Equality in Health 3

Structural racism and health inequities in the USA: evidence and interventions

Zinzi D Bailey, Nancy Krieger, Madina Agénor, Jasmine Graves, Natalia Linos, Mary T Bassett

Despite growing interest in understanding how social factors drive poor health outcomes, many academics, policy makers, scientists, elected officials, journalists, and others responsible for defining and responding to the public discourse remain reluctant to identify racism as a root cause of racial health inequities. In this conceptual report, the third in a Series on equity and equality in health in the USA, we use a contemporary and historical perspective to discuss research and interventions that grapple with the implications of what is known as structural racism on population health and health inequities. Structural racism refers to the totality of ways in which societies foster racial discrimination through mutually reinforcing systems of housing, education, employment, earnings, benefits, credit, media, health care, and criminal justice. These patterns and practices in turn reinforce discriminatory beliefs, values, and distribution of resources. We argue that a focus on structural racism offers a concrete, feasible, and promising approach towards advancing health equity and improving population health.

Lancet 2017; 389: 1453–63

See Editorial page 1369

See Comment pages 1376 and 1378

This is the third in a Series of five papers about equity and equality in health in the USA

New York City Department of Health and Mental Hygiene, Long Island City, NY, USA (Z D Bailey ScD, N Linos ScD, M T Bassett MD); Department

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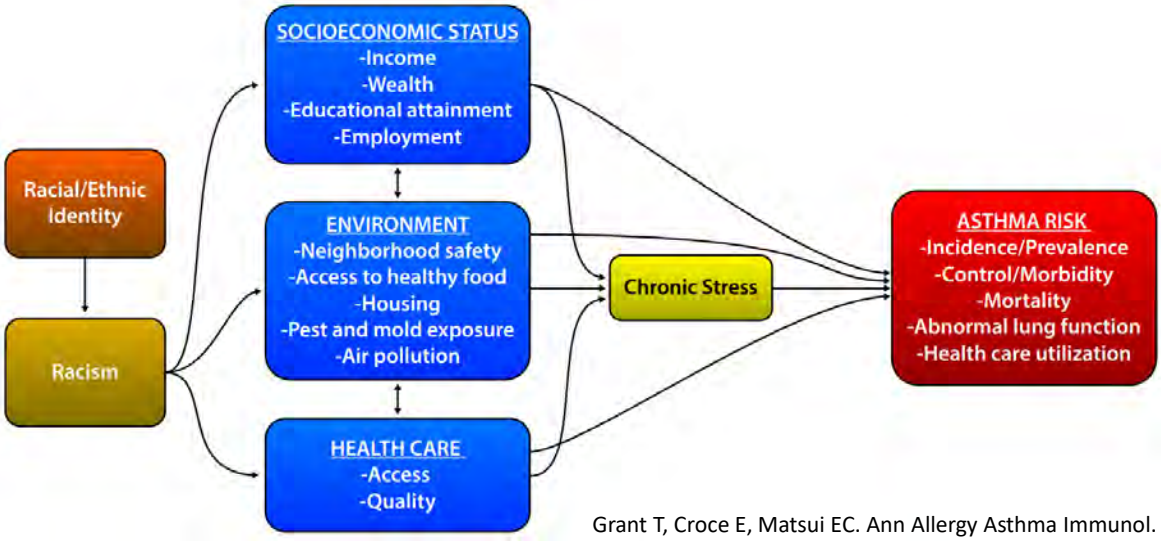
The relationship between racism, SDoH, and asthma disparities



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Socioeconomic status (SES)

- Broad marker of social standing
- Affects basic needs such as housing, food, and education
- Affects upward mobility in society

- Often income, highest educational degree obtained, occupation, type of health insurance, or zip code are used as a surrogate for SES in medicine
- Income, wealth, education, and employment

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Socioeconomic status (SES) – Income

- Low income has been repeatedly linked to increased asthma prevalence, exacerbations, hospitalizations and ICU admission
- In 2019, CDC[1] reports a dose-response relationship between poverty level and asthma prevalence:
  - 11.8% - family income <100% of the poverty threshold
  - 8.5% - family income 100% to <250% of the poverty threshold
  - 7.3% - family income 250% to <450% of the poverty threshold
  - 5.9% - family income ≥450% of the poverty threshold

- 7% increase in the odds of prevalent asthma for each one-unit decrease in the household income to poverty ratio[2]

[1]https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm
[2]Keet CA, et al. *JACI* 2015

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Socioeconomic status (SES) – Income

- Adults with a household income of <$50,000[1]
  - 1.6-fold higher rate of asthma treatment failure
  - 2.0-fold higher rate of asthma exacerbations
- Children living in extreme poverty (household income <$10,000)[2]
  - 125% higher odds of having a prior ICU admission for asthma
- Home ownership is associated with a 38% decreased in odds of ER visit for asthma in children[3]

[1]Cardet JC, et al. *JACI* 2018 [2]Bollinger ME, et al. *Ann. Allergy Asthma Immunol* 2019 [3] Hughes HK, et al. Acad Pediatr. 2017

17

SES – Education

- Lower educational attainment contributes to limited health literacy
- CDC defines individual health literacy as:
  - "the degree to which individuals have the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others."[1]
- Low health literacy[2]
  - Decreased asthma understanding and the perceived increased need for asthma medications
  - Inability to follow an asthma action plan
  - Lower likelihood of being treated by an asthma specialist
  - Poorer asthma control
  - More missed days of school
  - Increased ER visits and hospitalizations for asthma

[1] https://www.cdc.gov/healthliteracy/learn/index.html
[2] Morrison AK, et al. Pediatrics in Review 2019

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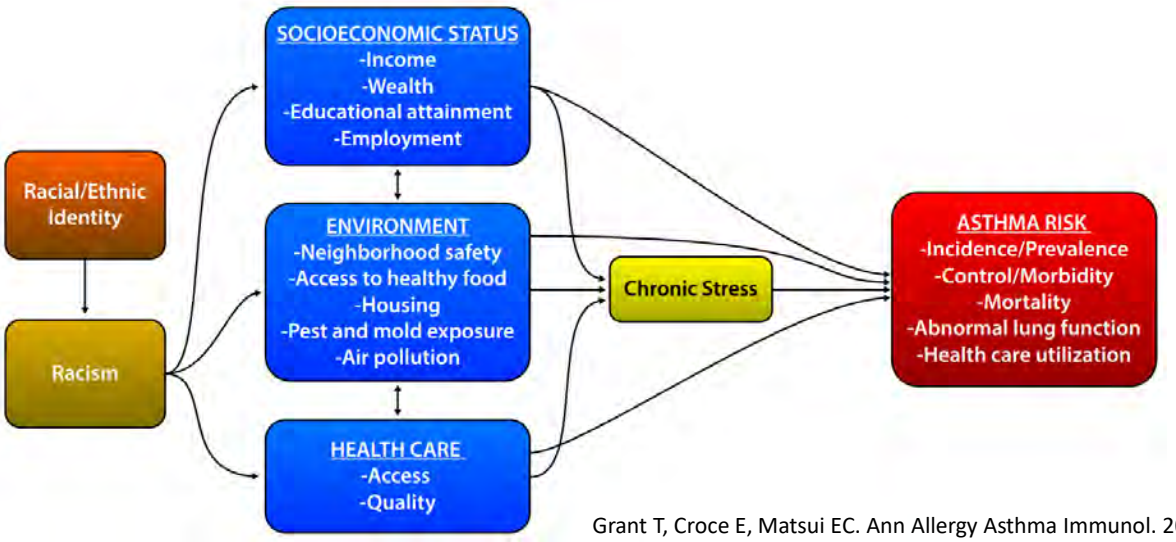
The relationship between racism, SDoH, and asthma disparities



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Environment

- Neighborhood Safety
- Access to Affordable, Healthy Food
- Housing and Exposure to Pest, Mold, and Pollution

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Environment – Neighborhood Safety

- Children in low-income and disadvantaged communities are frequently exposed to violence
- In a study out of Boston, maternal report of increased community violence during pregnancy was associated with increased risk of wheeze at age 2 in the offspring[1]
- In a study out of Chicago, neighborhoods with a high incidence of violent crime having a 27% increased odds of prevalent neighborhood asthma[2]
- In a study out of Chicago, living in a neighborhood with increased property and violent crimes, children had increased odds of parent-reported wheezing, lifetime asthma, and ER use and hospitalization due to asthma [3]

[1]Chiu Y-HM, et al. *JACI* 2014 [2]Gupta RS, et al. *Ann. Allergy Asthma Immunol* 2010 [3]Eldeirawi K, et al. *Ann. Allergy Asthma Immunol* 2016

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Environment – Access to Affordable, Healthy Food

- Low-income communities have fewer healthy food options and poorer quality produce
- Healthy food is more expensive
- Low-income Black families are less likely to live in neighborhood with access to affordable healthy food[1]
- Healthier foods, such as diets rich in fruits and vegetables, have been associated with fewer asthma symptoms and higher lung function[2]
- Lack of affordable healthy food has also been linked to obesity, which is associated with asthma incidence and asthma morbidity[3]
- Proposed mechanisms for healthier diets effects on asthma include anti-inflammatory effects, changes in the intestinal microbiome, and reduced risk of obesity[2]

[1]Bower KM, et al. *Prev Med* 2014 [2]Grant T, et al. *J Allergy Clin Immunol Pract.* 2020 [3]Khalid F, et al. *J Asthma*. 2018

22

Environment – Housing, Indoor Exposures

- Poor housing quality and home disrepair have been associated with risk of childhood asthma and asthma morbidity[1]
- Poor housing repair is associated with pest (mouse, cockroach) allergen and mold exposure
- Pest allergen exposure has been repeatedly linked to risk of asthma, asthma prevalence, morbidity and abnormal lung function
- Exposure to mold is associated with childhood wheeze, asthma prevalence, and asthma morbidity

[1]Hughes HK, et al. Acad Pediatr. 2017

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Environment – Pollution

- Racial and ethnic minority urban communities are exposed to higher levels of indoor air pollution, which is associated with asthma symptoms[1]
- Outdoor air pollution is associated with incident asthma, asthma morbidity, and lung function decline
- Black residents, persons living in poverty, and persons with lower education are more likely to be exposed to higher levels of outdoor air pollution[2]
- A study of eight California cities found higher diesel particle emissions in historically redlined communities[3]
  - 2.4 fold increase in age-adjusted ER visits for asthma

[1]Matsui EC, *Allergy* 2014 [2] https://www.lung.org/clean-air/outdoors/who-is-at-risk/disparities
[3]Nardone A, et al. *The Lancet Planetary Health*. 2020

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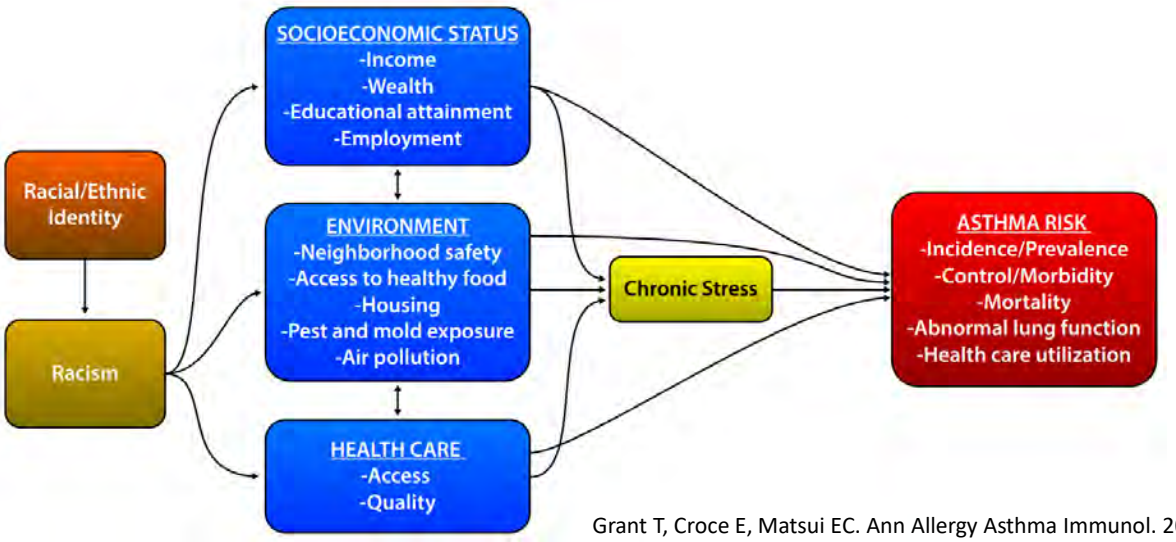
The relationship between racism, SDoH, and asthma disparities



Grant T, Croce E, Matsui EC. Ann Allergy Asthma Immunol. 2022

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Health Care Access and Quality

- Black and Latinx patients are more likely to be uninsured than White patients[1]
- Black and Latinx families are more likely to live in zip codes with primary care physician shortages[2]
- Black and Latinx children with the same insurance were less likely to see a specialist for asthma than White children[3]

- Lack of health insurance, access to primary care, and fewer referrals to asthma specialists all result in higher ER utilization for asthma, increased school and work absences, decreased provider consistency, uncontrolled asthma, and overall worse asthma care

[1]https://www.census.gov/content/dam/Census/library/publications/2019/demo/p60-267.pdf [2] Gaskin DJ, et al. *Health Serv Res*. 2012 [3]Stewart KA, et al. *Arch Pediatr Adolesc Med*. 2010

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Health Care Quality

- Underuse of asthma biologics in Black and Latinx patients

- 2021 study found patients with public insurance were less like to be prescribed a biologic for asthma treatment[1]
- Among patients with public insurance, racial and ethnic minority patients were less likely to be prescribed an asthma biologic compared with White patients[1]

[1]Akenroye AT, et al. *J Allergy Clin Immunol Pract* 2021

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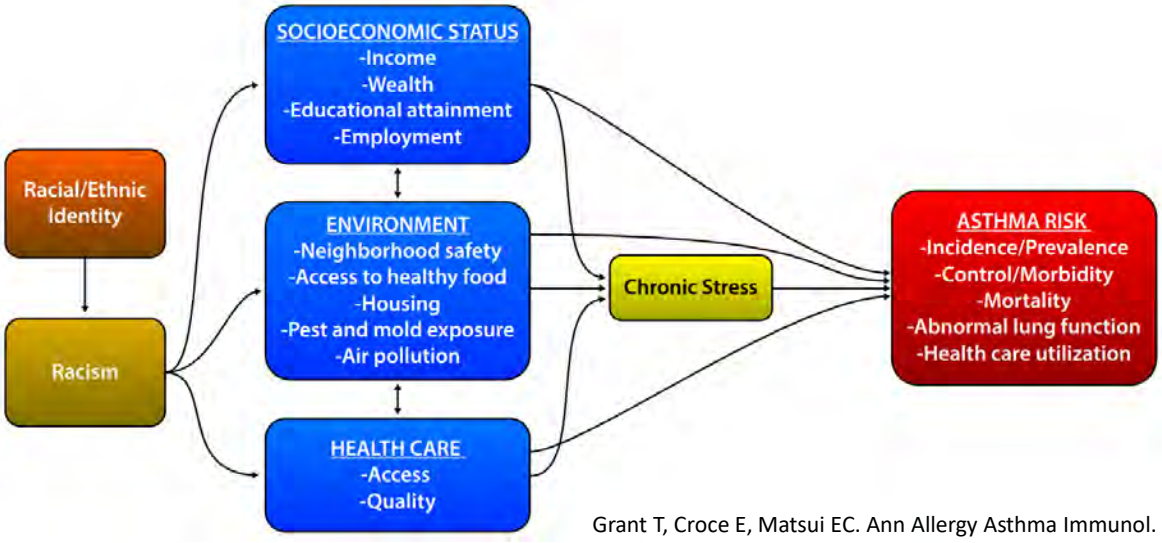
The relationship between racism, SDoH, and asthma disparities



Grant T, Croce E, Matsui EC. Ann Allergy Asthma Immunol. 2022

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Chronic Stress

- Families living in poverty and racial and ethnic minority populations experience higher levels of stress from many sources:[1]
  - income instability
  - lower education
  - fewer assets
  - barriers to employment
  - food insecurity
  - higher rates of incarceration
  - social disadvantage
  - exposure to violence
- High levels of chronic stress in children and adults have been associated with increased asthma exacerbations, decreased asthma control, increased hospitalizations, decreased quality of life, and decreased lung function

[1]https://www.apa.org/pi/health-equity/resources/stress-report.pdf

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Chronic Stress

- Effects of chronic stress on asthma include chronic hypothalamic-pituitary-adrenocortical activation[1] leading to:
  - ↓β2 adrenergic and glucocorticoid receptors
  - ↓Responsiveness to asthma medications
  - ↑Asthma symptoms
- Maternal prenatal stress[2] leading to:
  - ↑IL-13 response , ↓IFN-γ response to allergen/mitogen stimulation in cord blood mononuclear cells
- Early life (<3yrs) exposure to environmental stressors and maternal depression, anxiety has been associated with asthma diagnosis[3]

[1]Landeo-Gutierrez J, et al. *Ann. Allergy Asthma Immunol* 2020 [2]Wright RJ, et al. *Am J Respir Crit Care Med*. 2010 [3] Rosa M, et al. *Curr Opin Allergy Clin Immunol*. 2018

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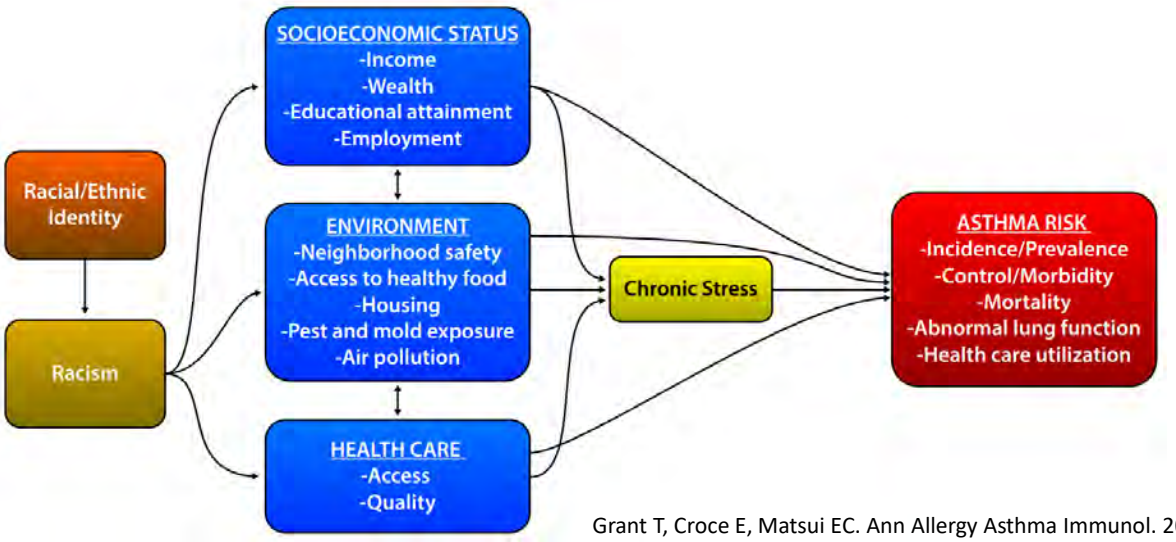
The relationship between racism, SDoH, and asthma disparities



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Final Thoughts

- SDoH such as poverty, inequities in education and employment, poor housing quality, greater risk of exposure to pests, mold, and pollution, unequal health care access and quality, and high levels of chronic stress

- SDoH have been associated with asthma prevalence/incidence, morbidity, exacerbations, and abnormal lung function, which suggests that they are also likely a major cause of asthma disparities

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Knowledge Gaps

- Degree to which SDoH contribute to asthma disparities
- Which SDoH contribute most to asthma disparities
- Mechanisms by which SDoH cause asthma disparities
- What are the most impactful approaches to mitigating economic barriers to asthma care and self-management
- Which environmental exposures should be prioritized for targeting to reduce asthma disparities
- What are the most impactful approaches to improving health care access and quality for racial and ethnic minority populations
- Which individual-level and systems-level interventions are most effective at reducing racial and ethnic asthma disparities

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References

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Aspirin Desensitization Protocols (Inpatient and/or Outpatient)

Recommended Protocols:

History of Urticaria/Angioedema with Aspirin

Time	Dose of aspirin
0	5 mg
½ hr	10 mg
1 hr	20 mg
1½ hr	40 mg
2 hr	81 mg
2½ hr	162 mg
3 hr	325 mg

No premedication recommended

History of Respiratory Symptoms with Aspirin

Time	Dose of aspirin
0 hour	40 mg
1 ½ hours	81 mg
3 hours	162 mg
4 ½ hours	325 mg
6 hours	650 mg (optional)

Consider premedication with leukotriene antagonist (montelukast, zileuton) to decrease lower respiratory symptoms

Safety of Outpatient Aspirin/NSAID Challenges in Non-AERD Patients

	No Reaction	Immediate Reaction	Delayed Reaction	Total
Aspirin	114	15	3	132
Ibuprofen	52	6	2	60
Naproxen	8	1	1	10
Other NSAID*	2	1	0	3
Total	176 (85.9%)	23 (11.2%)	6 (2.9%)	205 (100%)

>85% with no reaction and allergy removed
Of those that reacted, 62.5% occurred at >60 minutes

Li L et al, J Allergy Clin Immunol Pract 2021.

Presentations for Sunday, June 26, 2022

Rheumatology in the AI Clinic
Megan Cooper, MD, PhD

Patient Education in the Office
David Stukus, MD

Immune Dysregulation
Megan Cooper, MD, PhD

Oral Food Challenges in Infants and Toddlers
David Stukus, MD

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Rheumatology in the AI Clinic

Presented by:

Megan Cooper, MD, PhD

Sunday, June 26, 2022

7:45 a.m. – 8:30 a.m.

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Pennsylvania Allergy & Asthma Association

Rheumatology in the AI Clinic

PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION
73RD PAAA ANNUAL MEETING
JUNE 24-26, 2022 | THE HOTEL HERSHEY, HERSHEY, PA

Megan A. Cooper, MD, PhD
Professor of Pediatrics, Division of Rheumatology/Immunology
Director, Clinical Immunology
Washington University in St. Louis
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BJC HealthCare

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School of Medicine

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Disclosures

- Dr. Cooper has the following disclosures to declare:
- Consultant: Enzyvant
- No products related to this disclosure will be discussed
- All therapies discussed are off-label

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Learning Objectives

1. Identify how rheumatologic disease can present to the allergist/immunologist

2. Identify overlap between immune deficiency and rheumatologic disease

Case 1: 13 yo girl with urticaria

- Widespread urticaria ~2 months, with itching
- Initial CBC, ESR, CRP – normal
- ANA 1:160
- Responded to anti-histamines and steroids
- 2 years later, recurrence of urticaria, now with oral ulcers
  - Positive lupus anti-coagulant & other abnormalities

Spadoni et al, Lupus, 2011.

Urticaria in Lupus

- Pediatric SLE:
  - Multicenter study of 852 pts in Brazil showed 1% incidence (10 pts) of chronic urticaria ***(Ferriani et al, Int Arch Allergy Immunol, 2015)***
  - Median duration 190 days
- Review of 12,778 patients with chronic urticaria in Israel ***(Confino-Cohen, JACI, 2012)***
  - 0.4% had Systemic lupus erythematosus (SLE)
    - 15% had urticaria before a diagnosis of SLE
  - More common where hypothyroidism (~10%), hyperthyroidism (~2.6%), RA (1.5%), T1DM (1.3%), Sjogren syndrome (0.5%), Celiac (0.5%)

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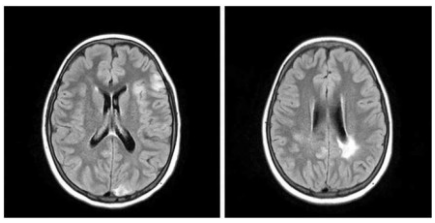
Case 2: 3 year old with arthritis

- 3 yo girl with polyarticular arthritis involving knees and ankles
- Continued disease for several years despite therapies (MTX, etanercept)
- Age 6: fevers, splenomegaly, AIHA, AIN
  - Concern for macrophage activation syndrome
  - Refractory cytopenias (rituximab, IVIG, cyclosporine, splenectomy)
- Age 9: autoimmune enteritis & CNS white matter lesions



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Oz & Tesher, Pediatric Rheumatology, 17: 82 (2019)

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Case 2: 3 year old with arthritis

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- LRBA deficiency diagnosed (compound heterozygous variants in LRBA)
- Age 15: started abatacept (CTLA4-Ig) with improvement, sirolimus later added
- Age 18: hematopoietic stem cell transplant

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Oz & Tesher, Pediatric Rheumatology, 17: 82 (2019)

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Rheumatology in the AI clinic

Outline

- Allergy/Immunology manifestations of common rheumatologic disease, with a focus on pediatric rheumatology

- Rheumatologic disease seen in Inborn Errors of Immunity (IEI)

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Rheumatology in the AI clinic

Outline

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Systemic Lupus Erythematosus (SLE)

ACR Rheumatology Image Library

Systemic Lupus Erythematosus (SLE)

- Prevalence in the US is 20-50/100,000
- Increased prevalence in Asian, black, and Hispanic individuals
- F>M, 7:1 – 15:1 overall
  - For patients <9 yo, F:M is 4:3
- 20% of patients present <16 years of age
- Very rare before age 5 (look for an immune deficiency!)

ACR Rheumatology Image Library

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Clincial symptoms

Physical exam findings/symptoms:
- Malar rash
- Oral hard palate or nasal mucocutaneous ulcers
- Vasculitic rashes
- Photosensitivity
- Nonerosive arthritis
- Encephalopathy: szs, psychosis

Organ damage:
- Nephritis
- Pleuritis or pericarditis
- Other organ involvement: liver, pancreas, lungs, GI

Laboratory studies:
- Cytopenias, immune mediated:
  - Hemolytic anemia; WBC <4k 2+ times; ALC <1.5k 2+ times; or Plt <100k.
- High-positive ANA
- Other positive immunoserology:
  - dsDNA; anti-Smith; Antiphospholipid ab

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1997 revised ACR

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Most common clinical features of childhood SLE

- Review of 256 Pediatric SLE pts in Toronto, 4.7:1 F:M from 1982-2005.

Symptom	At diagnosis %	Ever %
Arthritis	61	67
Malar rash	61	66
Headache	58	62
Nephritis	37	55
Fatigue	50	55

Hiraki et al, J Pediatr, 2008.
Tucker et al, Lupus, 2008

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Rashes in SLE

Small vessel vasculitis, non-blanching

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Rashes in SLE

Discoid lupus

Photosensitive malar rash

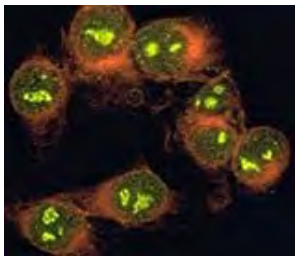
ACR Rheumatology Image Library

Rashes in SLE

ACR Rheumatology Image Library

Initial evaluation of suspected lupus in AI clinic

- Laboratory studies:
  - CBC
  - ANA (if high → dsDNA & other antibodies)
  - ESR (CRP rarely elevated)
  - Urinalysis for nephritis (protein/blood)
  - IgG typically *elevated*
- Other diagnostic tests:
  - Chest x-ray for chest pain/effusion
  - EKG/echocardiogram if there is concern for pericardial effusion



ANA

ANA in healthy populations

- Low titer ANAs (<1:320) are common in healthy individuals and don't always require follow-up

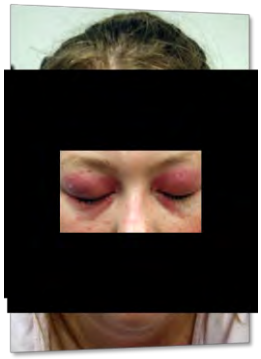
ANA titer	699 children Canada[1]	125 adults International[2]	304 adults Mexico[3]
1:20-1:40	17%	32%	35%
1:80	10%	13%	13%
1:160	9%	5%	3%
1:320	5%	3%	1%

- Patients with titer ≥ 1:160-1:320 warrant further evaluation

[1] Malleson et al, Arch Dis Child, 1997
[2] Tan et al, Arthritis Rheum, 1997
[3] Marin et al, J Clin Rheumatol, 2009

Juvenile Dermatomyositis (JDM)

- Inflammatory disease of the skin, muscle, and blood vessels.



  - Rare, incidence is ~1:100,000 kids
  - Prior to corticosteroids 1/3 of children died
  - Proximal muscle weakness
  - Characteristic rash:
    - Eyelids
    - Hands (gottron's papules)
    - Papules on extensor surfaces (elbows/knees)

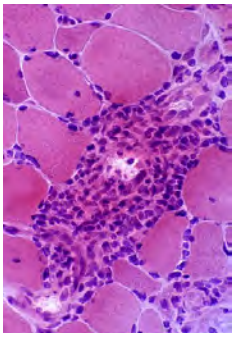
Clinical signs of JDM

World J Dermatol. May 2, 2015; 4(2): 80-94

ACR Rheumatology Image Library

Initial Evaluation of JDM in the AI Clinic

- Muscle enzymes
  - CK, aldolase, AST, ALT, LDH
- Acute phase reactants may or may not be elevated
- Consider imaging of affected muscle:
  - MRI
  - Ultrasound



http://www.neuro.wustl.edu/neuromuscular

Raynaud Phenomenon

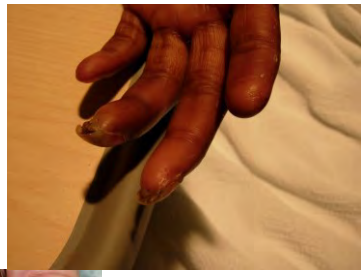
- Transient arterial vasospasm
- Can be 3-color phase:
  - Pallor → Cyanosis → Erythema/pain
- Dark skin tends to have pallor
- Frequently sharply demarcated
- Often associated with cold

https://www.nhs.uk/conditions/raynauds/

ACR Rheumatology Image Library

Primary vs. Secondary

- Primary Raynaud is a benign exaggerated vasoconstriction response
  - 5-20% of women; 5-15% of men
- Secondary Raynaud:
  - Associated with systemic disease
    - Scleroderma
    - Lupus
    - Overlap syndromes
  - Risk of ulceration
  - Requires treatment



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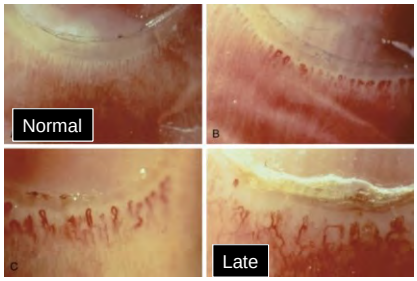
Evaluation of Raynaud Phenomenon

- Primary:
  - Triggers apparent to patient
  - No systemic symptoms
  - Normal nailbed capillaries
  - No further testing necessary
- Secondary:
  - Other systemic symptoms
  - Can see dilated nailbed capillaries
  - Initial lab studies:
    - CBC, ESR, renal function, ANA, antiphospholipid antibodies



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Other rheumatic skin disease: Erythema Nodosum

www.Blackandbrownskin.co.uk

- Post-strep
- Inflammatory bowel disease
- Sarcoidosis
- Idiopathic/infection-associated

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Other rheumatic skin disease: Anti-phospholipid antibody syndrome

Livedo reticularis

DIL: https://med.unc.edu/dil

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Rheumatology in the AI clinic

Outline

- AI manifestations of common rheumatologic disease, with a focus on pediatric rheumatology

- **Rheumatologic disease seen in Inborn Errors of Immunity (IEI)**

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Inborn Errors of Immunity (**IEI**)

- Inborn Errors of Immunity (**IEI**) are inherited disorder of the immune system, also known Primary immunodeficiencies (**PID**)
- There are more than 470+ single-gene inborn errors of immunity
  - Diverse range of clinical symptoms
  - Infectious susceptibility, **autoimmunity**, autoinflammation, lymphoproliferation, bone marrow failure, cancers

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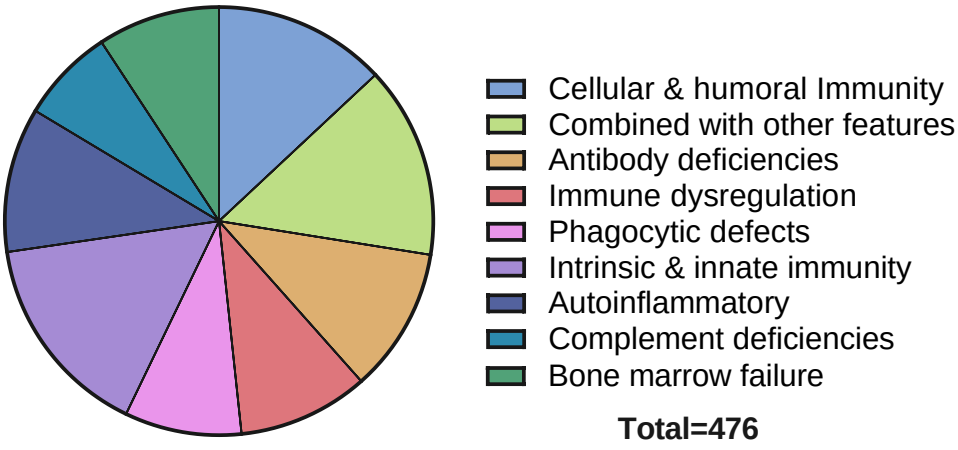
The spectrum of IEI



Data from: IUIS Reports: Tangye et al, J Clin Immunol, 2020; Tangye et al, J Clin Immunol 2021; and https://iuis.org/committees/iei/

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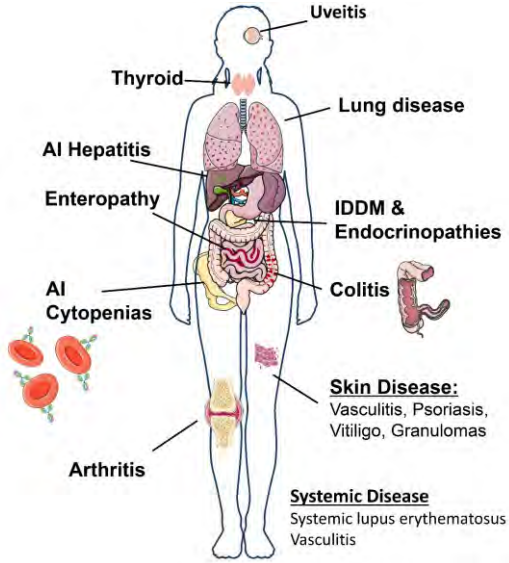
Autoimmunity in IEI



Kitcharoensakkul & Cooper, Curr Opin Allergy Immunol, 2019

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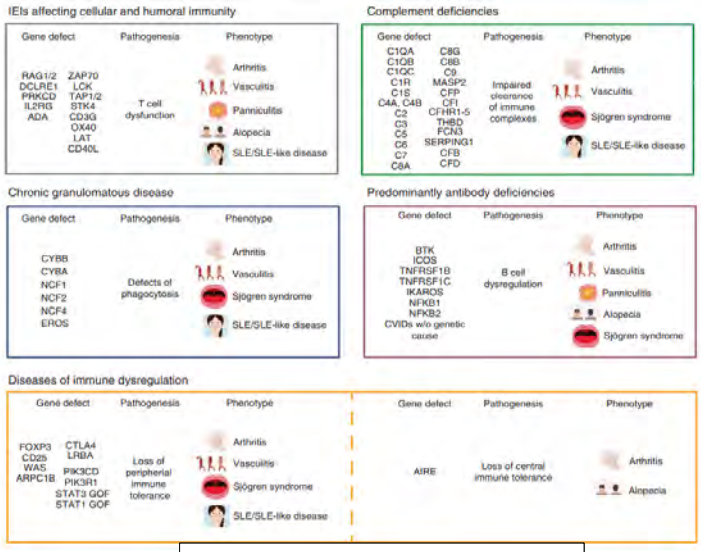
Rheumatologic disease and IEI



Bal et al, Pediatric Research, 2020, 87:293-9

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Skin disease in IEI

Autoinflammatory diseases

- Often neonatal but can be adult-onset
- Urticaria, urticarial-like rashes
- Pustulosis
- Psoriasis
- Vasculopathy

NLRC4 Moghaddas et al, JACI, 2018.

Immune dysregulation syndromes

- Typically neonatal onset
- Eczema, dermatitis
- Psoriasis, scleroderma
- Pigmentation changes

STAT3 GOF
Khoury et al, Clin Therap, 2017

IPEX syndrome
Halabi-Tawil et al, 2008 BJD

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Skin disease in IEI: Inflammatory lesions

Midline granulomas

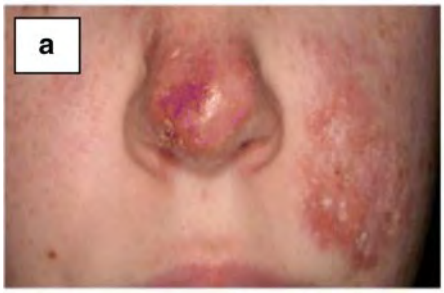
Hypomorphic *RAG1* variants
De Ravin et al, Blood 2010

Pyoderma gangrenosum

Leukocyte adhesion deficiency

Consider infectious causes

Vaccine-strain Rubella virus



Combined T/B Immunodeficiency
Buchbinder et al, J Clin Immunol, 2019

Atypical EBV lymphoproliferative cutaneous disease

Magnesium transporter deficiency X-linked
Klinken et al, J of Clin Immunology, 2019.

Case: Arthritis and IEI

- 3 yo girl with polyarticular arthritis involving knees and ankles
- Continued disease for several years despite therapies (MTX, etanercept)
- Age 6: fevers, splenomegaly, AIHA, AIN
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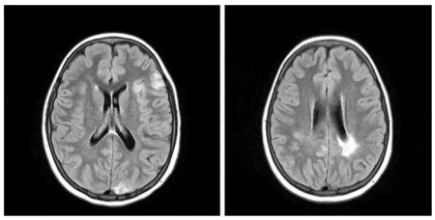

Oz & Tesher, Pediatric Rheumatology, 17: 82 (2019)

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Arthritis and IEI

- 3 yo girl with polyarticular arthritis involving knees and ankles
- Continued disease for several years despite therapies (MTX, etanercept)
- Age 6: fevers, splenomegaly, AIHA, AIN
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- Age 15: started abatacept with improvement, sirolimus later added
- Age 18: hematopoietic stem cell transplant

Oz & Tesher, Pediatric Rheumatology, 17: 82 (2019)

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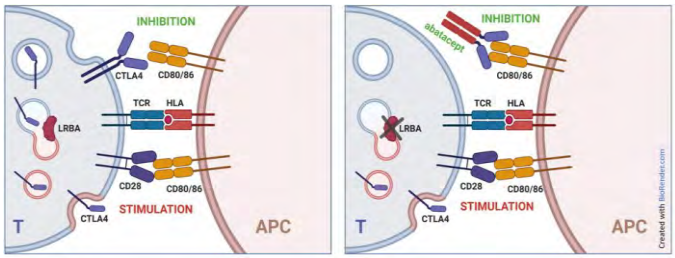
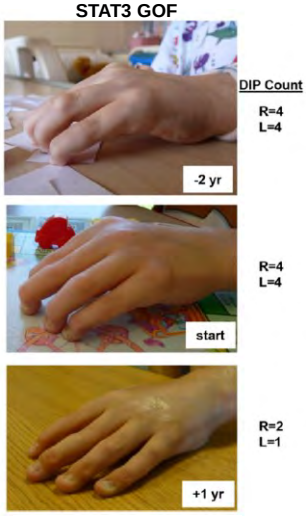
Arthritis and IEI

- Typically polyarticular
- May respond to steroids and therapies for JIA
- Consider how diagnosis may alter therapy



Boz et al, Front Immunol 2021

STAT3 GOF



Milner et al, Blood 2015

Key points for treating rheumatologic disease in IEI

- Treat the rheumatologic disease:
  - May require immune 'suppression', which for monogenic disease is really more 'modulation', *e.g.*, JAK inhibitor in STAT3 GOF or STAT1 GOF, sirolimus in IPEX syndrome or P13K gain of function disease
- Your expertise can help rheumatologists feel comfortable with treating disease and choose the right agent
  - Should disease monitoring and/or prophylaxis change?
  - Drugs to avoid – anti-TNF-alpha in patients with infectious susceptibility

Summary

- Rheumatologic disease can present to the AI clinic, often due to skin disease
- Patients with inborn errors of immunity can present with a wide range of rheumatologic disease, the AI physician can help guide immune modulation
- Early recognition and multi-disciplinary care is important for these complex patients

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Patient Education in the Office

Presented by:
David Stukus, MD

Sunday, June 26, 2022
8:30 a.m. – 9:15 a.m.

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Pennsylvania Allergy & Asthma Association

Patient Education in the Office

David Stukus, MD, FAAAAI, FACAAI, FAAP

Professor of Clinical Pediatrics
Director, Food Allergy Treatment Center
Division of Allergy and Immunology
Nationwide Children's Hospital
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@AllergyKidsDoc

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1

Disclosures

- Social Media Medical Editor – American Academy of Allergy, Asthma and Immunology
- Associate Editor – Annals of Allergy, Asthma and Immunology
- Consultant – Before Brands, Integrity CE, Kaleo, Novartis
- Honoraria – ACAAI, AAP, AAAAI
- Royalties – Springer Publishing
- Non-financial:
  - Member – Joint Task Force on Practice Parameters
  - Member - Board of Regents, ACAAI

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

2

Objectives

- Appreciate the various ways in which patients are influenced by outside sources of information
- Understand the origins surrounding misconceptions specific to allergic conditions
- Anticipate confusion and misinformation from patients and actively address this during clinical encounters

3

Did You Ever Think THIS Would Cause Such an Uproar?

4

COVID-19: An 'Infodemic'

https://theconversation.com/controls-to-manage-fake-news-in-africa-are-affecting-freedom-of-expression-137808

5

Mis-in-fer-mey-shuhn

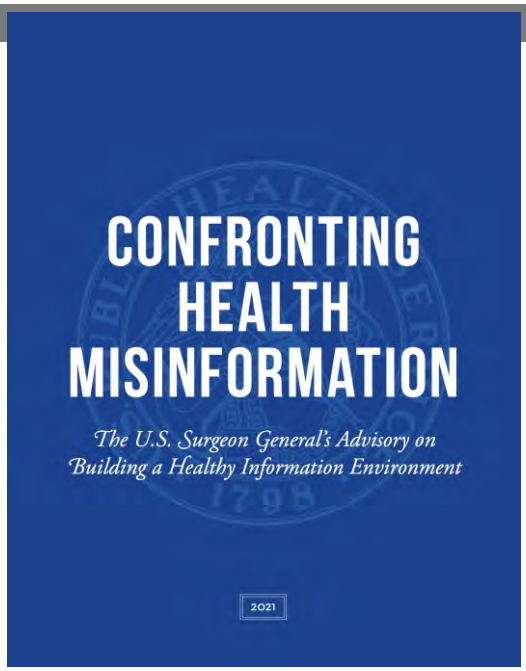
noun

1. false information that is spread, regardless of whether there is intent to mislead

Dictionary.com 'Word of the Year'

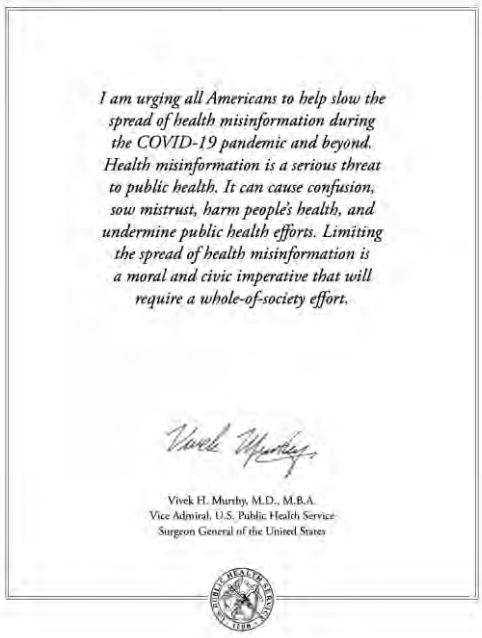
https://apnews.com/article/entertainment-north-america-ap-top-news-religion-fake-news-e4b3b7b395644d019d1a0a0ed5868b10

6



https://www.hhs.gov/sites/default/files/surgeon-general-misinformation-advisory.pdf

7



https://www.hhs.gov/sites/default/files/surgeon-general-misinformation-advisory.pdf

8

https://medium.com/@viriatovb/what-is-the-cnn-effect-and-how-relevant-is-it-today-a78b15b18f05

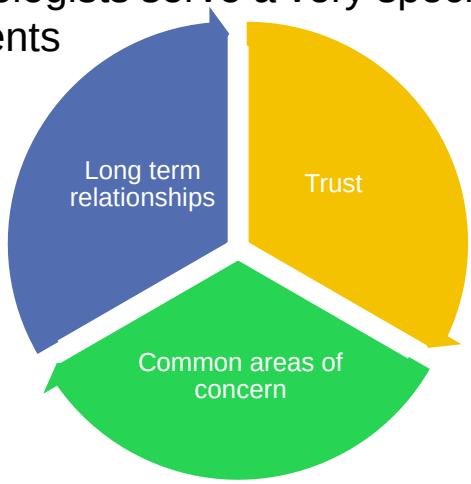
9

10

11

Initial Thoughts…

- Allergist/Immunologists serve a very special role in the lives of our patients



12

WE Have an Advantage

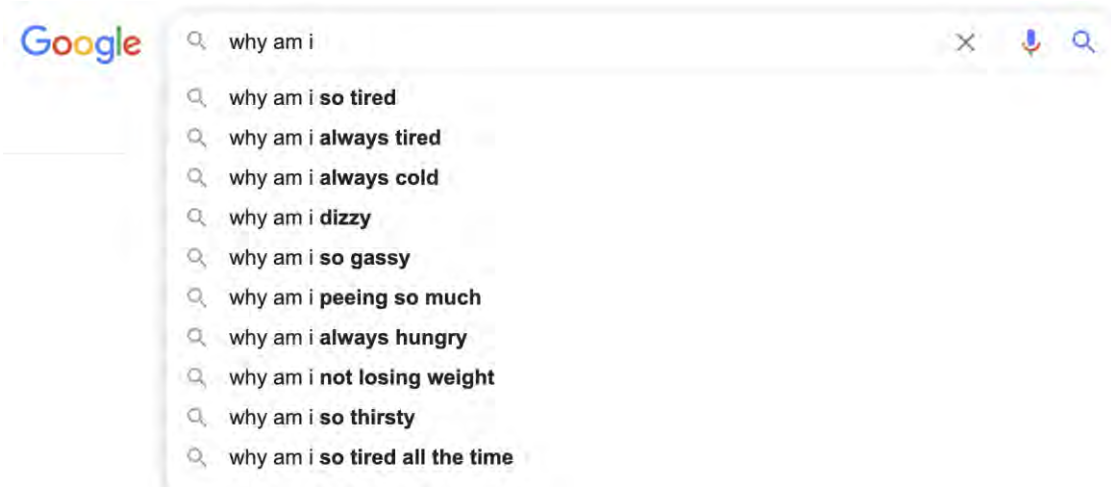
- Can ask questions
- Monitor body language
- Dive into nuance surrounding complex topics
- Most importantly…we need to:

- **Listen**
- **Give our time**
- **Show empathy**
- **Be non-judgmental**
- **Be available for follow up discussion**

13

There MUST Be Something Wrong…

14

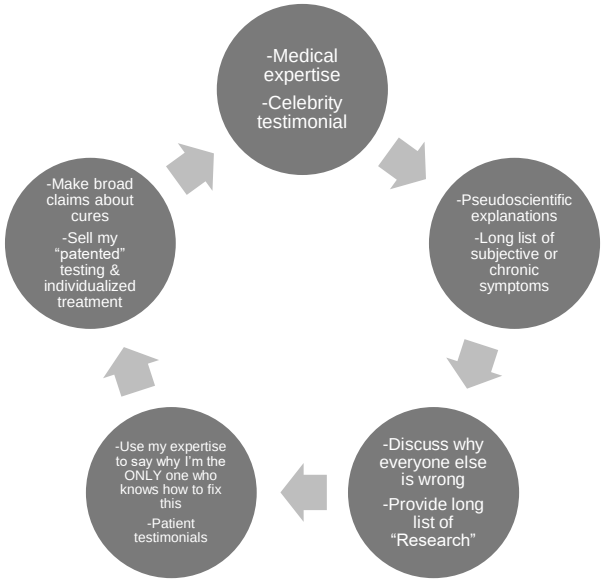

Google
why am i
why am i so tired
why am i always tired
why am i always cold
why am i dizzy
why am i so gassy
why am i peeing so much
why am i always hungry
why am i not losing weight
why am i so thirsty
why am i so tired all the time

15

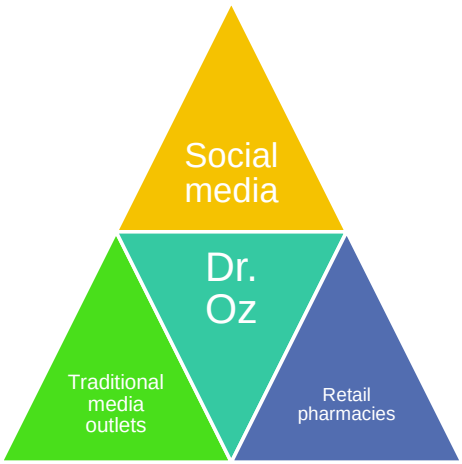
V. LAURENT
CLARK
SNAKE OIL
LINIMENT
A GUARANTEED CURE
FOR ALL ACHES AND PAINS

16

If I Lacked a Conscience…

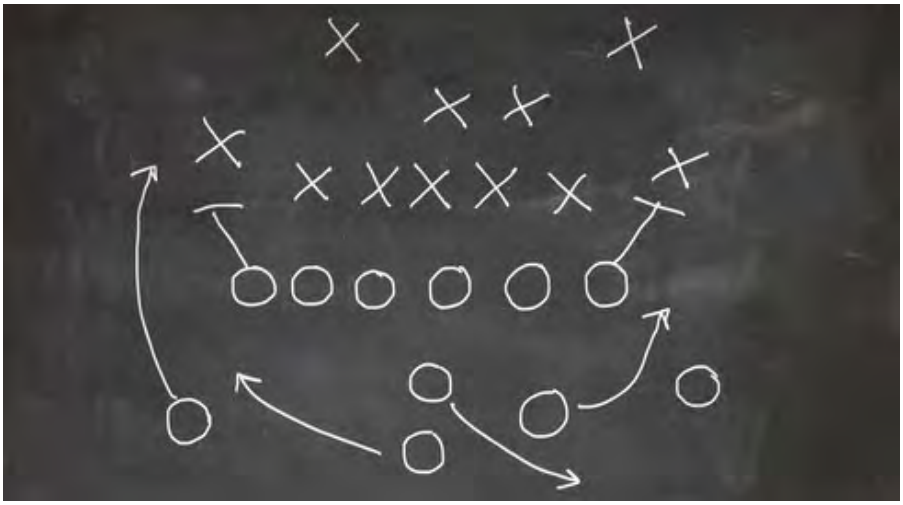


Normalize through saturation



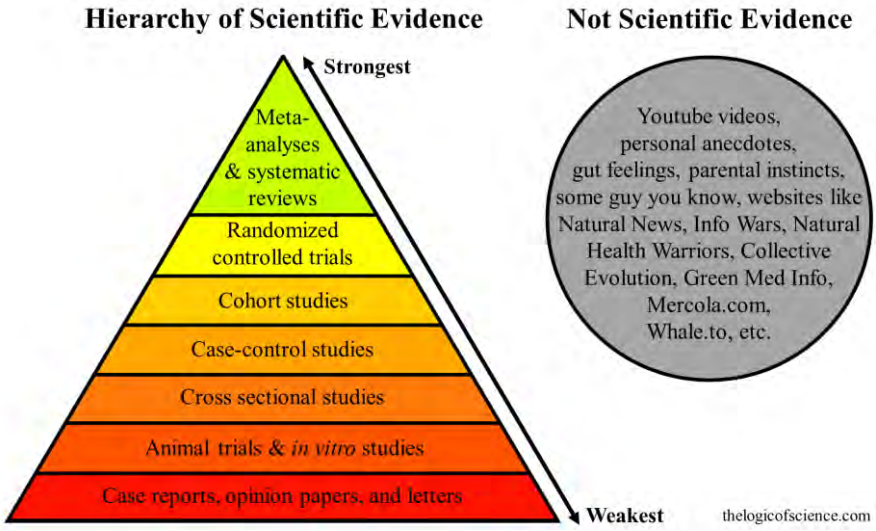
17

The Best Defense…is a Good Offense



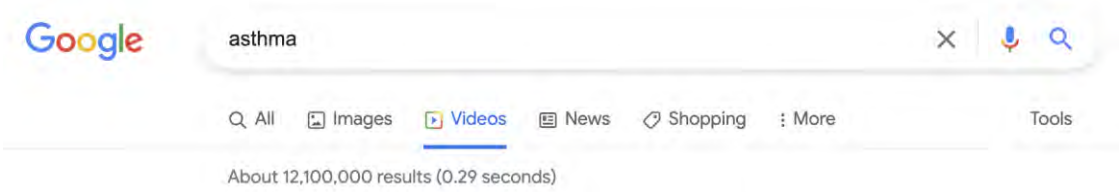
18

What Constitutes Evidence?



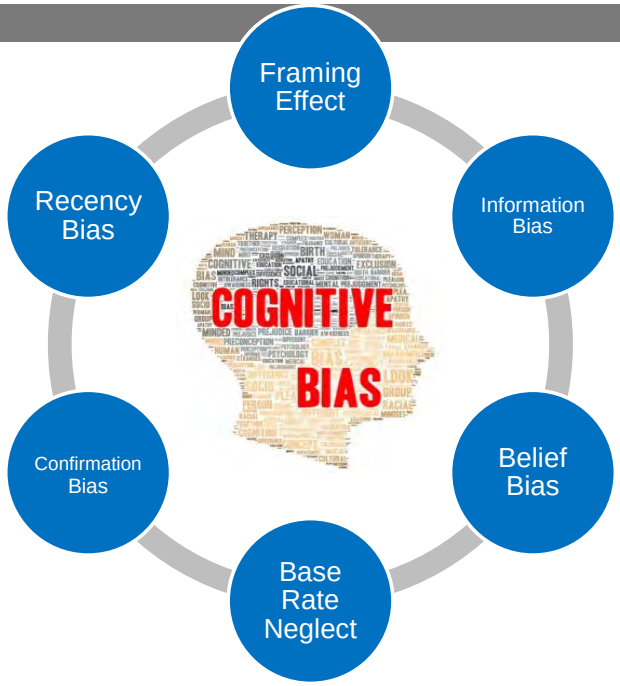
19

Quality Matters

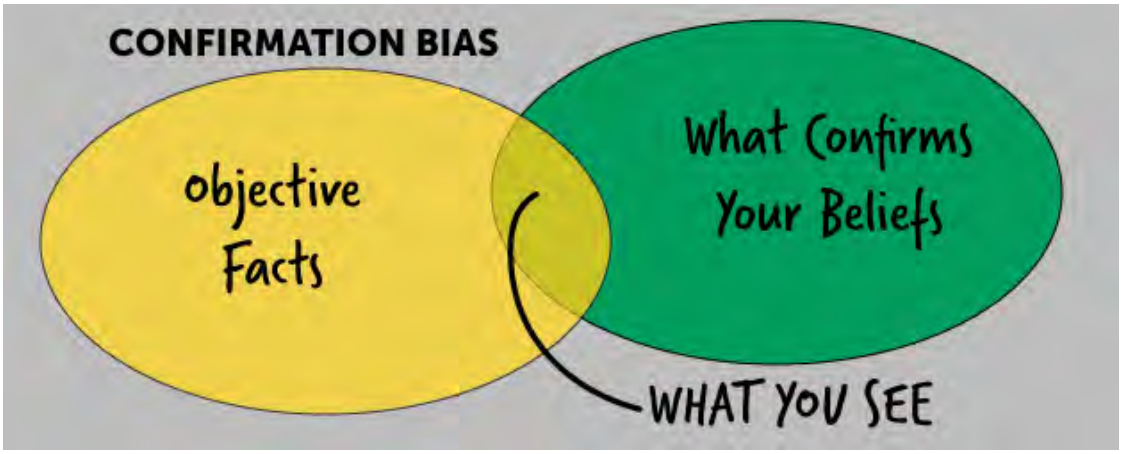


1. Kaul V, et al. J Asthma. 2022 Feb;59(2):325-332.
2. Wu AC, et al. J Allergy Clin Immunol Pract. 2022 Feb 22:S2213-2198(22)00142-8.
3. Kornafeld A, Gonzalez-Estrada A, Dimov V. 'Googling' anaphylaxis. Curr Opin Allergy Clin Immunol. 2019 Oct;19(5):432-438.

20

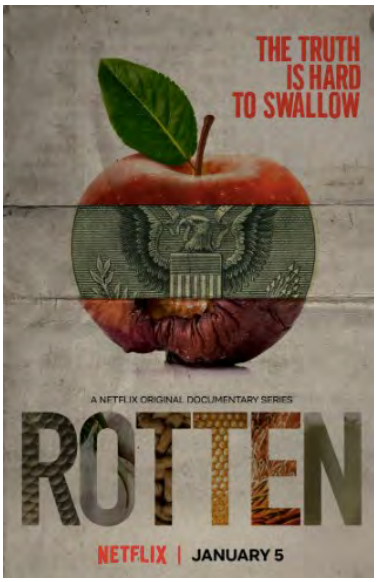

Framing Effect
Information Bias
Belief Bias
Base Rate Neglect
Confirmation Bias
Recency Bias
COGNITIVE
BIAS

21


CONFIRMATION BIAS
objective Facts
What Confirms Your Beliefs
WHAT YOU SEE

22

23


THE TRUTH
IS HARD
TO SWALLOW
A NETFLIX ORIGINAL DOCUMENTARY SERIES
ROTTEN
NETFLIX | JANUARY 5

24

2 at Takeout Restaurant in U.K. Are Convicted of Manslaughter in Nut Allergy Death

By Palko Karasz • Oct. 27, 2018

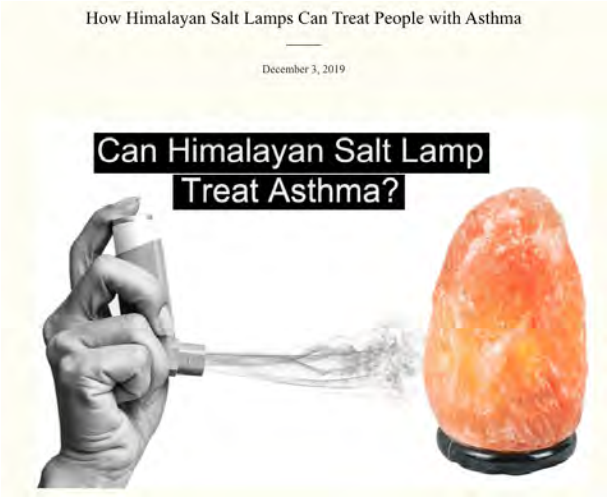
https://www.nytimes.com/2018/10/27/world/europe/uk-takeaway-allergy-death.html

25

Pseudoscience Bingo!!!

Inflammation	**Free radicals**	**Detox**	**Celebrity endorsement**	**Energy**
Cleanse	**Fatigue**	**Crystals**	**Naturopathic**	**All natural**
Chemical free	**Ancient Wisdom**	**FREE SPACE**	**Instinctively know best**	**Organic**
Conspiracy	**Molecules**	**Toxins**	**Cure**	**'Western' Medicine**
Pharma shills	**"Science doesn't know everything"**	**Government/ mind control**	**Miracle**	**Magnetic**

26



…are actually rock crystals…
…release negative ions into the air…
…we are surrounded by ions, some from outer space…
…some people claim to feel refreshed after a storm…probably due to the negative ions emitted…

The main culprit of asthma lies in the water vapors that dance around and are filled with allergens…and viruses.
…Himalayan salt lamps attract water molecules and cause them to evaporate, eliminating the air of any allergen or pollutant.

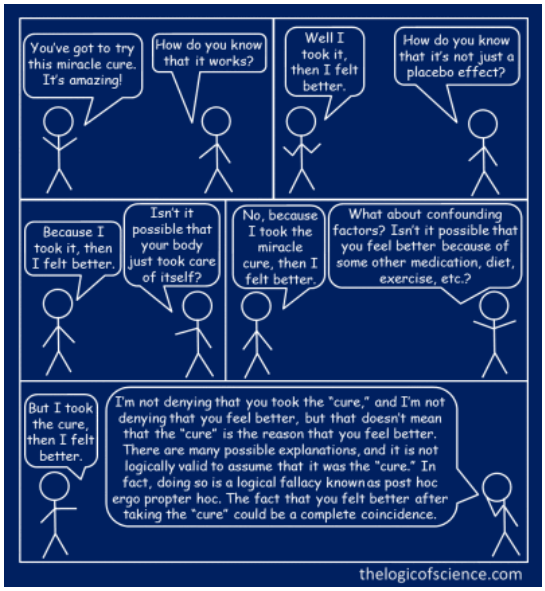
- **Improves blood flow/circulation**
- **Increases energy levels**
- **Helps us sleep better**

https://ambientsaltlamp.com/blogs/news/how-himalayan-salt-lamps-can-treat-people-with-asthma

27

The Plural of Anecdote…is NOT Data

- Logical fallacy
  - *Post hoc ergo propter hoc* = "after this, therefore because of this"
  - X happened before Y…therefore, X caused Y
- True representation is lacking
  - How many others tried and failed?
- No control → placebo effect
- Small sample size
- Not collected systematically



https://thelogicofscience.com/2016/02/10/5-reasons-why-anecdotes-are-totally-worthless/

28

Lack of Context From Celebrities and Influencers

https://people.com/health/mark-wahlberg-allergic-to-almost-everything/

29

APRIL 15, 2019, 12:21 AM ET

Bethenny Frankel's Fish Allergy Is So Severe, This Is What Happened When a Friend Who Ate Lox Kissed Her Face

The Real Housewives of New York City mogul Bethenny Frankel's fish allergy has almost killed her.

BY ALESANDRA DUBIN

https://www.bravotv.com/the-real-housewives-of-new-york-city/the-feast/bethenny-frankel-fish-allergy-reaction-instagram-pictures

30

5 Signs A Hidden Food Sensitivity Is Sabotaging Your Health

23 Signs Of A Hidden Food Intolerance

By William Cole, D.C., IFMCP
Functional Medicine Practitioner

ASK DrSEARS
The Trusted Resource for Parents

Pregnancy & Childbirth ▾ Feeding & Eating ▾ Parenting & Behavic

Topics / Feeding & Eating / Feeding Infants & Toddlers / Food Allergies / Tracking Down

Tracking Down Hidden Food Allergies

31

BUSINESS

A 'Shark Tank'-funded test for food sensitivity is medically dubious, experts say

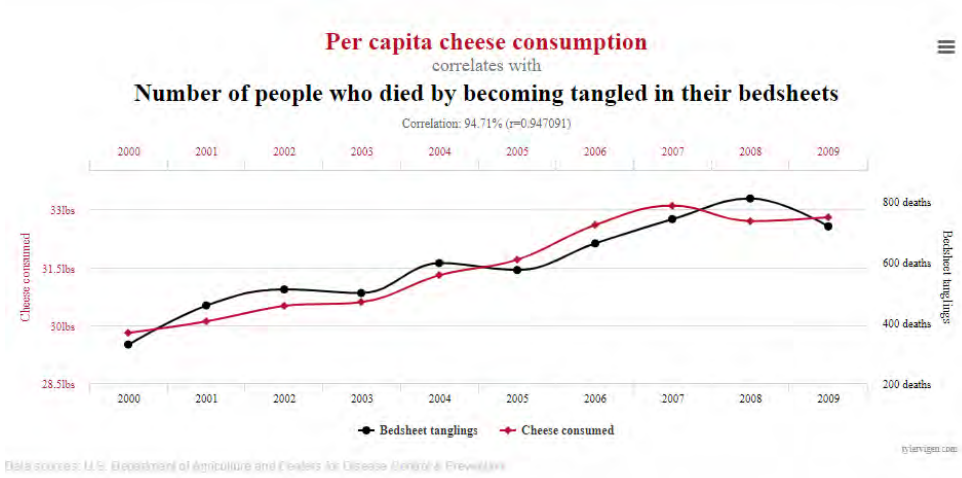
By ALLISON BOND / JANUARY 23, 2018

Julia Cheek, CEO of EverlyWell, on a November 2017 episode of "Shark Tank."
SCREEN CAPTURE

https://www.statnews.com/2018/01/23/everlywell-food-sensitivity-test/

32

Correlation ≠ Causation



https://www.tylervigen.com/spurious-correlations

33

The Vaccine Reaction

An enlightened conversation about vaccination, health and autonomy

https://thevaccinereaction.org/2015/11/mercks-peanut-oil-adjuvant/

34

NEWS

Teen dies of allergic reaction after classmate throws cheese at him

By Yaron Steinbuch

May 2, 2019 | 2:26pm | Updated

[WEBMD HEALTH NEWS]

Alabama Boy's Death Worries Food Allergy Parents

By Jennifer Clopton

35

https://www.deadlyfoodallergies.com/#why-food-allergies-matter

36

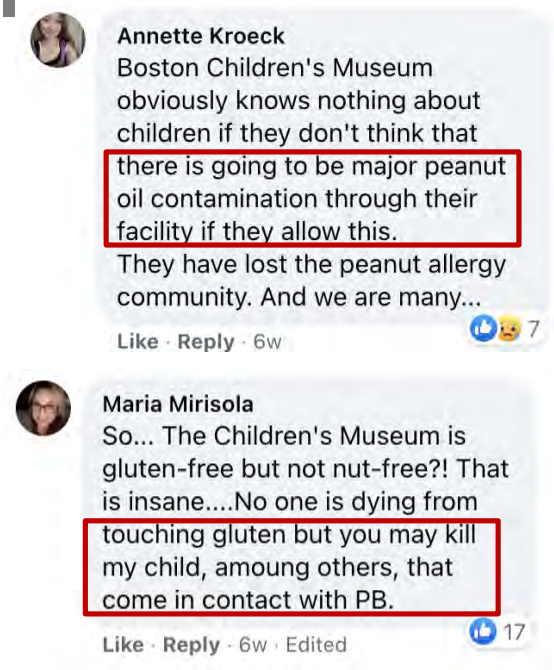
PB&J Cafe next to Boston Children's Museum sparks outrage by allergy-conscious parents

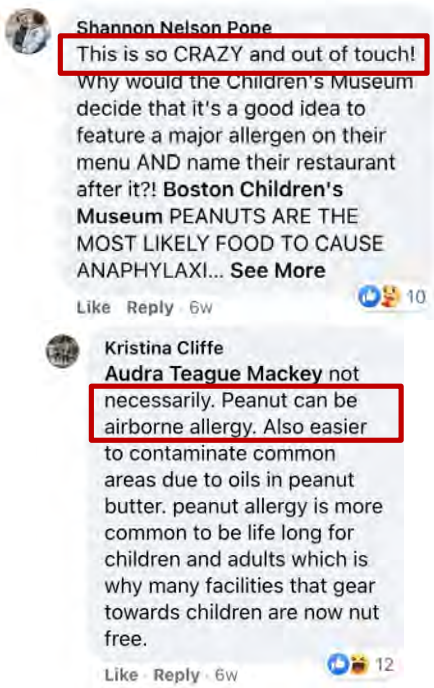
One concerned parent said the fear of contamination from kids' fingers would keep her away from the museum.

For some people with a peanut allergy, even tiny amounts of peanuts can cause anaphylaxis, a serious reaction that can even be life-threatening. Maren Caruso / Getty Images

https://www.today.com/food/pb-j-cafe-next-boston-children-s-museum-sparks-outrage-t203515

37





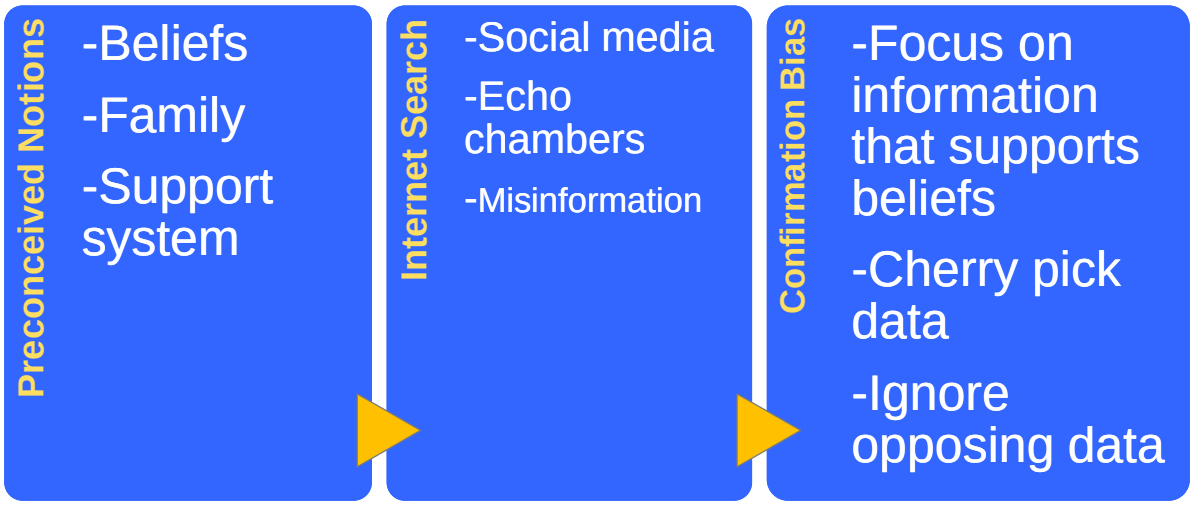
38

39

“Research”

40

"Research" in 2022



41

What's the Harm?

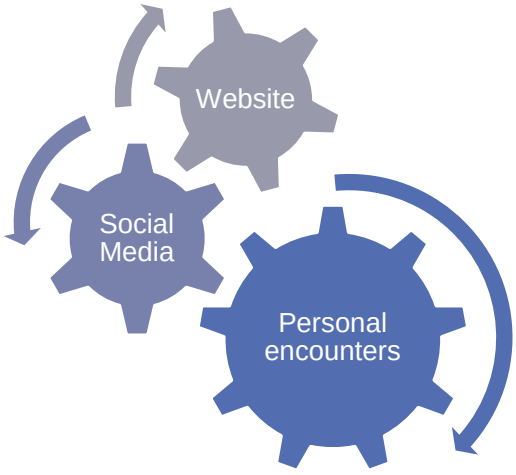
People don't know who to trust anymore

42

Practical Tools You Can Start Using Today

43

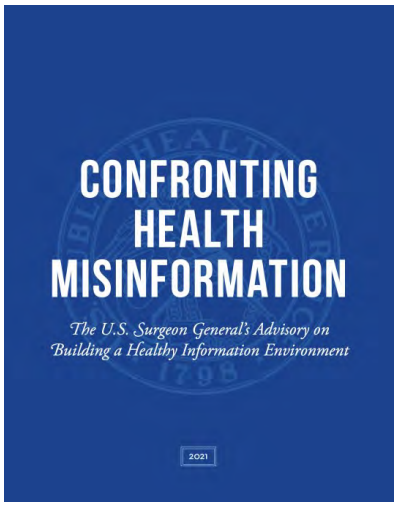
Multipronged Approach



44

What Health Professionals Can Do

- Proactively engage with patients and the public
- Use technology and media platforms to share evidence based information
- Partner with community groups and local organizations



https://www.hhs.gov/sites/default/files/surgeon-general-misinformation-advisory.pdf

45

It's Time To Reclaim Our Expertise and Role as Educators

- This requires
  - Time
  - Effort
  - Dedication
  - Respect
- Let's become better
  - Listeners
  - Communicators

46

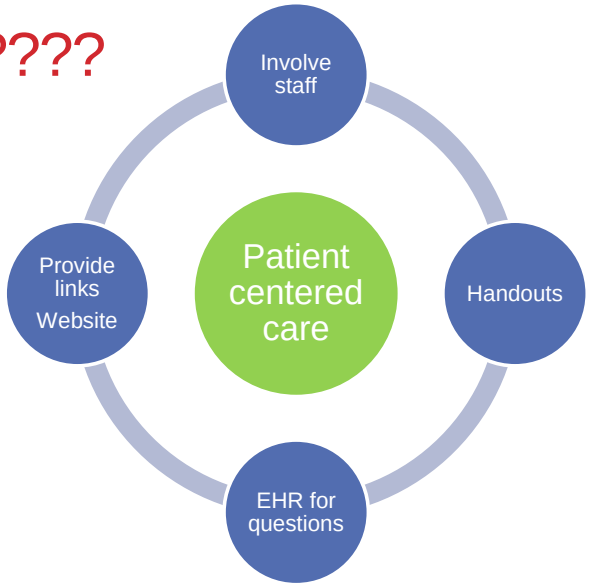
Steps YOU Can Take Now

- Try to ‘think like a patient’ to understand how and where they are receiving information
- Discuss internet searches, social media, and misinformation with patients
- Increase your awareness regarding the amount and types of misinformation surrounding various conditions
- Get involved!!!

47

Who Has the Time????

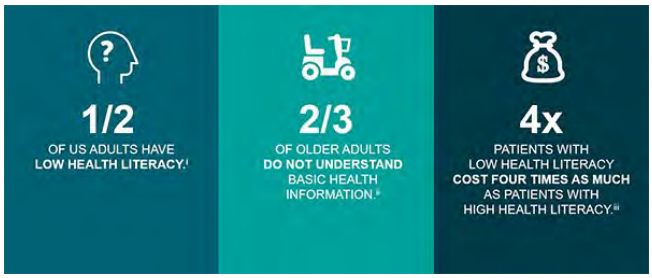
WE need to match the education we provide to the preferred learning style of each patient



48

Many of Our Patients Have Low Health Literacy

- "The degree to which individuals have the capacity to obtain, process, and understand basic health information needed to make appropriate health decisions."



https://www.healthypeople.gov/2020/topics-objectives/topic/social-determinants-health/interventions-resources/health-literacy

49

Red Flags for Low Literacy

- ✓ Frequently missed appointments
- ✓ Incomplete registration forms
- ✓ Non-compliance with medication
- ✓ Unable to name medications, explain purpose or dosing
- ✓ Identifies pills by looking at them, not reading label
- ✓ Unable to give coherent, sequential history
- ✓ Ask fewer questions
- ✓ Lack of follow-through on tests or referrals

https://www.ahrq.gov/health-literacy/improve/precautions/1stedition/tool3.html

50

Keep it Simple…But Don't Dumb it Down

51

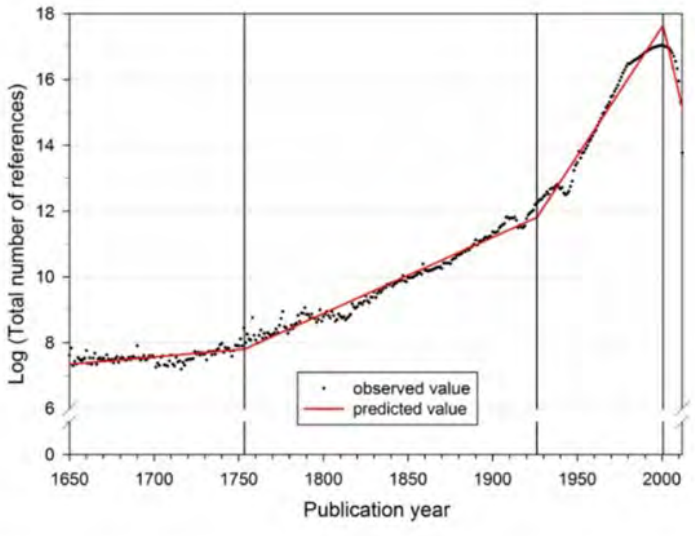
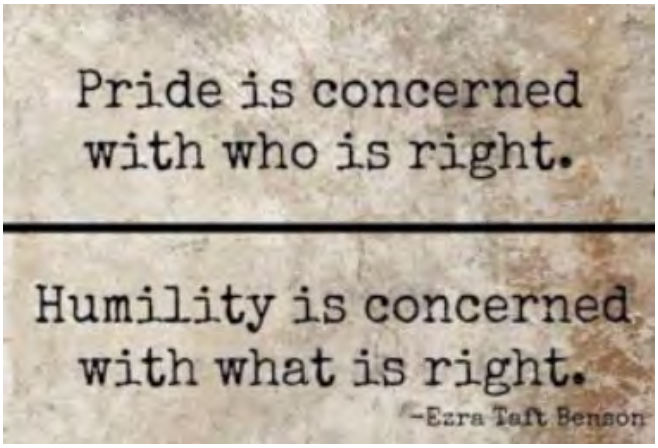


Figure 2. Segmented growth of the annual number of cited references from 1650 to 2012 (citing publications from 1980 to 2012)

Bornmann L, et al. J Assoc Info Sci Tech: arxiv.org/abs/1402.4578

52

#ScienceIsHard



53

We Can't Reach Everyone

Nurse uses key, hairpin to try to prove she is magnetic from vaccine during Ohio House hearing (video)

Joanna Overholt (Source: Ohio Channel)

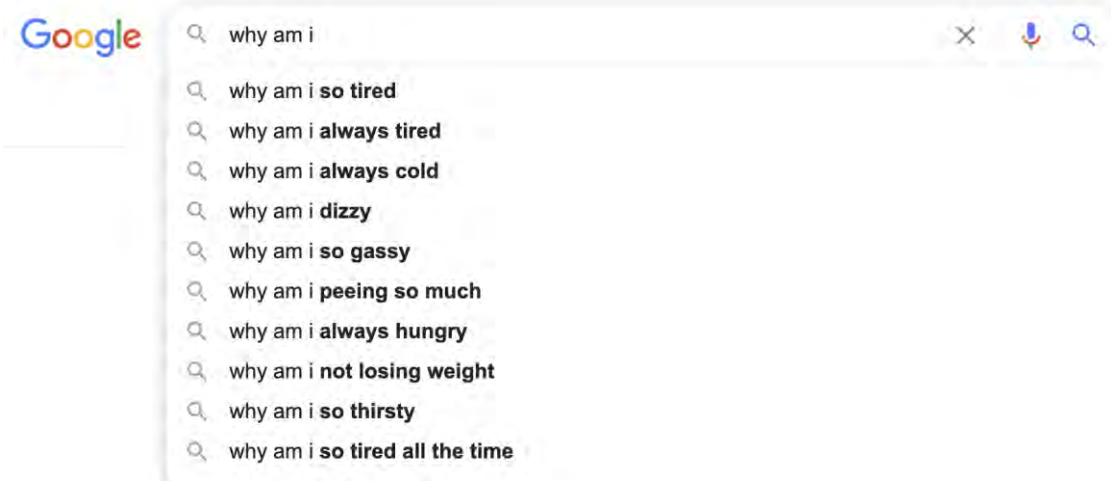
https://www.kbtx.com/2021/06/10/nurse-uses-key-hairpin-try-prove-she-is-magnetic-vaccine-during-ohio-house-hearing-video/

54

Just wanted you to know that your excellent simplified share of info on the delta variant finally convinced my hubby to get his vaccine! I just scheduled jt for today- he's been SO hesitant...and I haven't wanted to be the nagging wife 😬🤦‍♀️

55

The Number 1 Thing YOU Can Do to Help Your Patients…



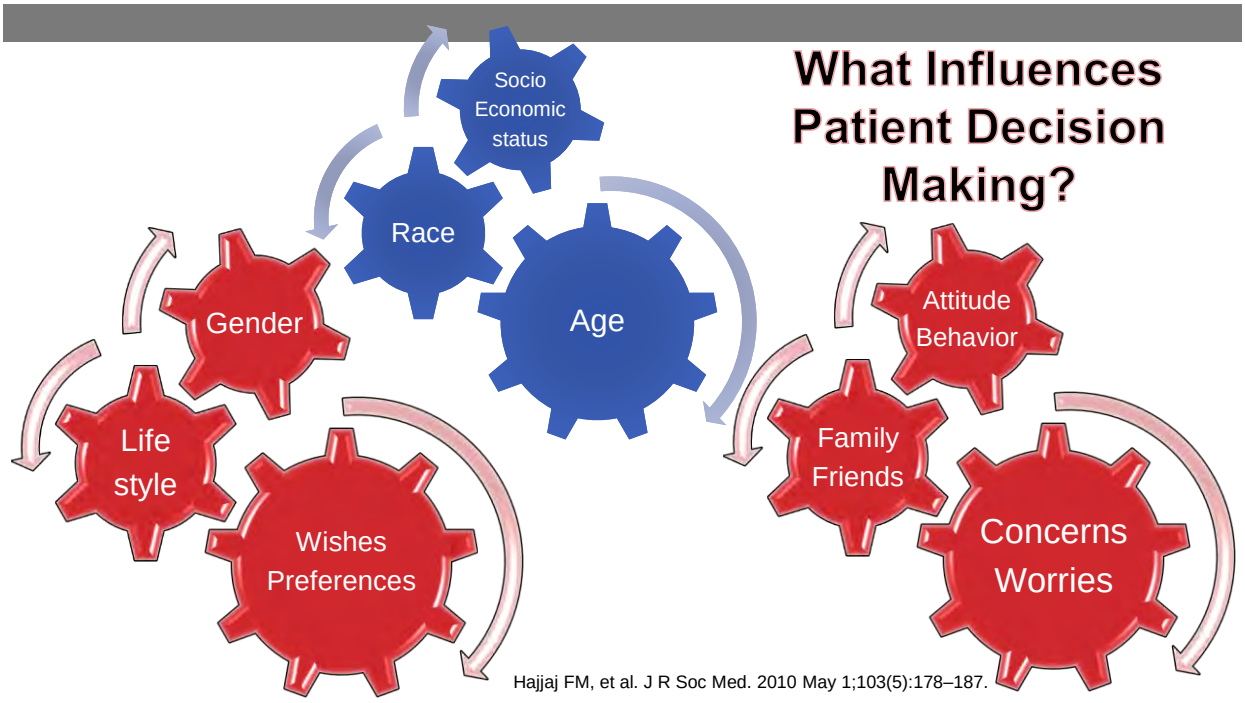
56

Learn, Anticipate, Address

- Provide anticipatory guidance at every visit
- Ask permission to discuss
- Make it a normal part of every encounter…especially the hard topics

- If you don't understand how your patients are being influenced, you won't be able to help them

57



Hajjaj FM, et al. J R Soc Med. 2010 May 1;103(5):178–187.

58

Word Choices Matter

59

Shared Decision Making

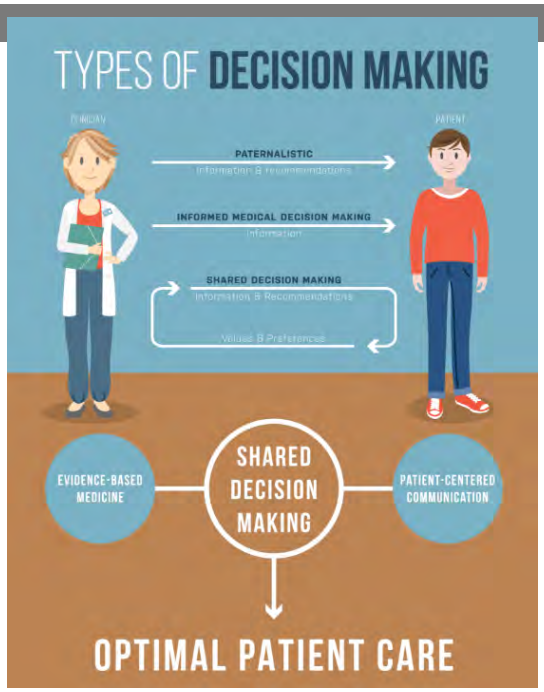
WE discuss evidence, options, risks

+

PATIENTS discuss preferences & values

+

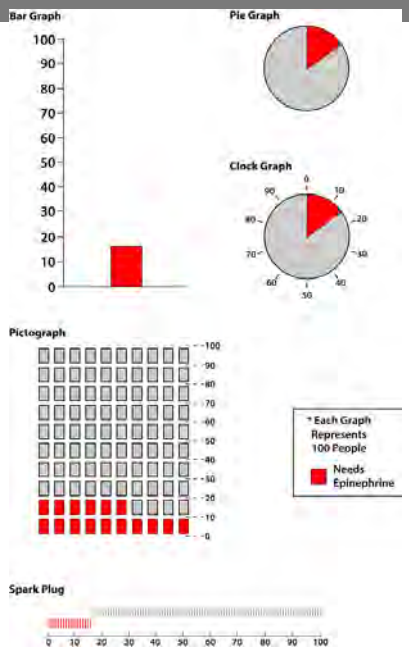
WE help PATIENTS make decisions based upon “what matters most”



60

Discuss Risk with Patients

- Provide numeric likelihoods of risks and benefits
- Provide absolute risks, not just relative risks
- Keep denominators consistent
- Keep time frames constant
- Use pictograms and other visual aids when possible
- Reduce superfluous information (cognitive overload)
- Provide positive and negative frames
- Keep risk in perspective of everyday hazards



Shaker M, et al. Ann Allergy Asthma Immunol. 2020;125(3):252-261.

61

The Simplest Way to Spot Coronavirus Misinformation on Social Media

A digital literacy expert shares his method

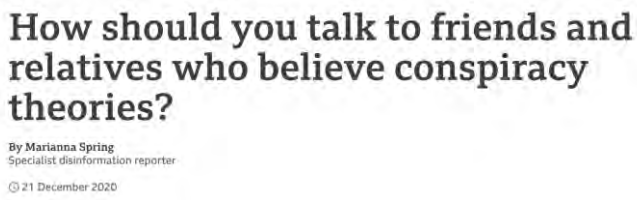
Will Oremus Follow
Mar 4 · 8 min read ★

He sums it up with the acronym SIFT:

1. Stop.
2. Investigate the source.
3. Find better coverage.
4. Trace claims, quotes, and media to the original context.

https://onezero.medium.com/the-simplest-way-to-spot-coronavirus-misinformation-on-social-media-4b7995448071

62



How should you talk to friends and relatives who believe conspiracy theories?

By Marianna Spring
Specialist disinformation reporter

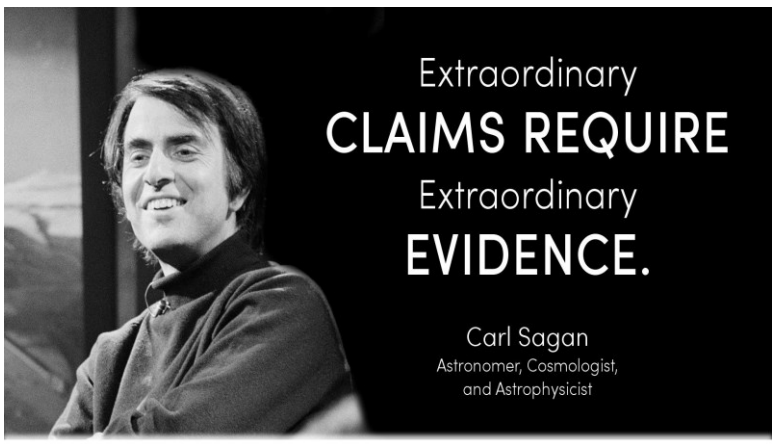
21 December 2020

- Keep calm
- Don't dismiss
- Encourage critical thinking
- Ask questions
- Don't expect immediate results
- You can't reach everyone

https://www.bbc.com/news/blogs-trending-55350794

63

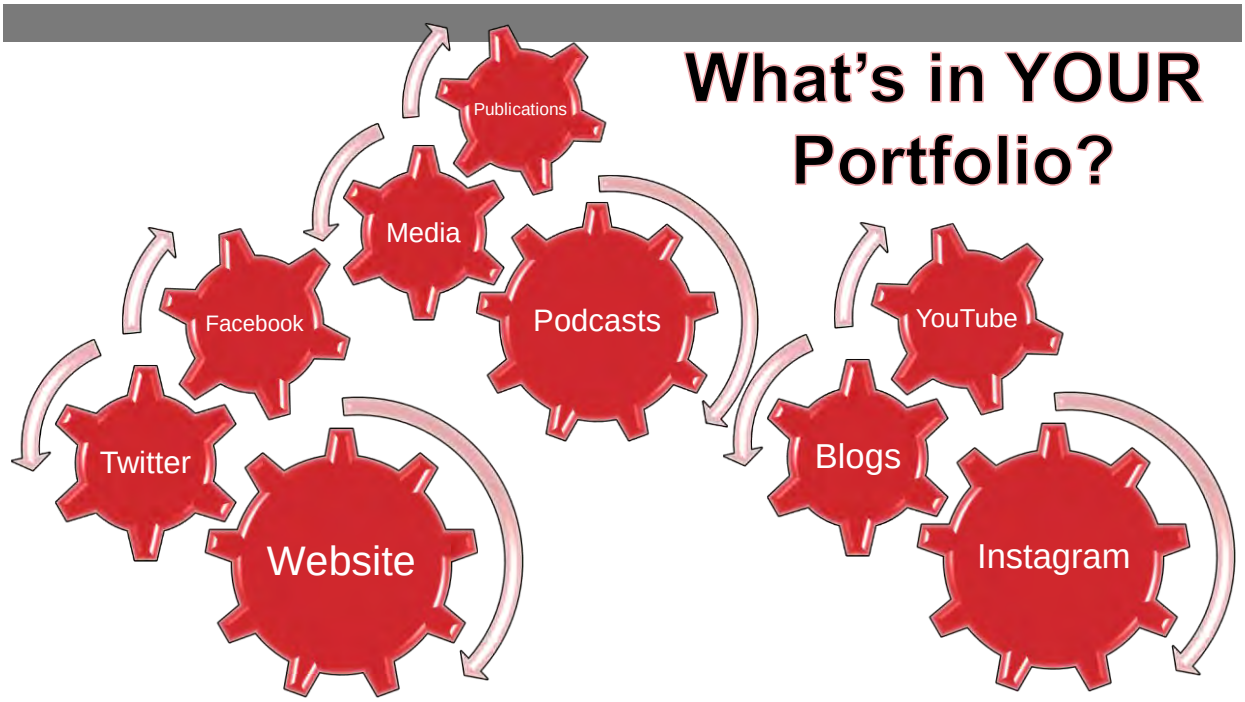
- Encourage questions
- Listen to replies
- Offer logical explanations
- Admit when you don't know the answer
- Make yourself available for follow up questions



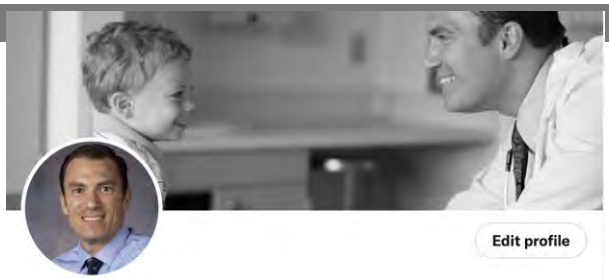
64

Addressing Misinformation Beyond Your Office Doors

65



66



Edit profile

Dr. Dave Stukus
@AllergyKidsDoc

Professor of Pediatrics & Director, Food Allergy Center @nationwidekids
Social media editor @aaaai_org /Board member @acaai
Science is cool. Evidence matters.

Medical & Health · Columbus, OH
nationwidechildrens.org/david-r-stukus · Joined April 2013

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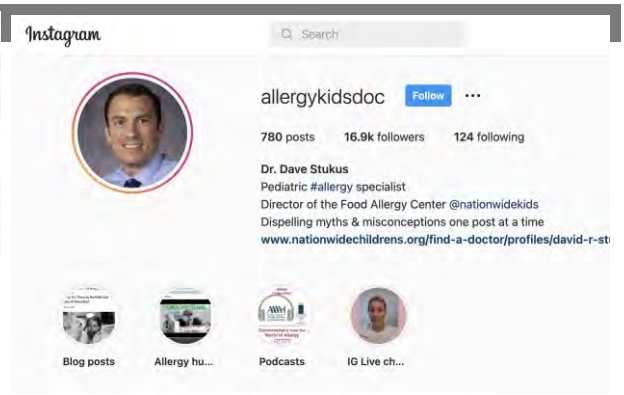

67

We Are All Living in the Matrix

68

Meta

The metaverse is the next evolution of social connection. Our company's vision is to help bring the metaverse to life, so we are changing our name to reflect our commitment to this future.

Augmented reality

Through photo and video, AR lets you enhance shared experiences with playful virtual effects at swipe of a screen, letting you express yourself with the people who matter most.

A future made by all of us

The metaverse will be a collective project that goes beyond a single company. It will be created by people all over the world, and open to everyone.

https://about.facebook.com/meta/

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This is What Keeps Me Up at Night

70

Steps YOU Can Take Now

- Try to ‘think like a patient’ to understand how and where they are receiving information
- Proactively ask patients about common areas of misinformation
- Provide resources and ENCOURAGE open communication

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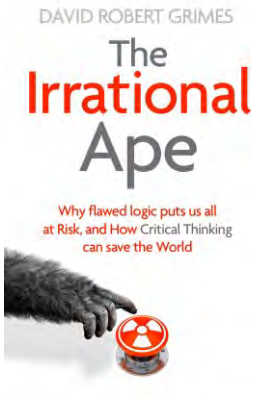
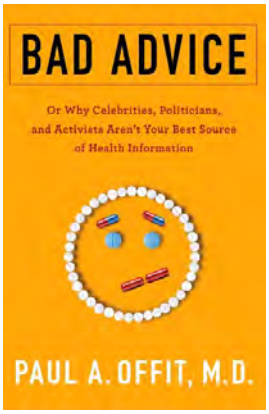
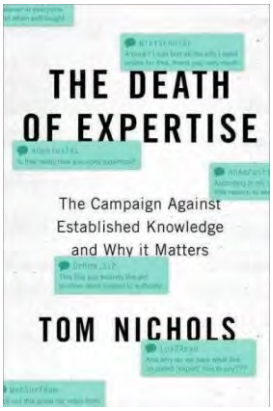
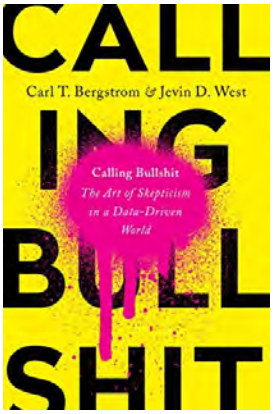
Thank You


DAVID ROBERT GRIMES
The Irrational Ape
Why flawed logic puts us all at Risk, and How Critical Thinking can save the World


BAD ADVICE
Or Why Celebrities, Politicians, and Activists Aren't Your Best Source of Health Information
PAUL A. OFFIT, M.D.


THE DEATH OF EXPERTISE
The Campaign Against Established Knowledge and Why it Matters
TOM NICHOLS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Carl T. Bergstrom & Jevin D. West
Calling Bullshit
The Art of Skepticism in a Data-Driven World
BULL
SHIT

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Immune Dysregulation

Presented by:

Megan Cooper, MD, PhD

Sunday, June 26, 2022

9:30 a.m. - 10:15 a.m.

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Pennsylvania Allergy & Asthma Association

Immune Dysregulation

PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION
73RD PAAA ANNUAL MEETING
JUNE 24-26, 2022 | THE HOTEL HERSHEY, HERSHEY, PA

Megan A. Cooper, MD, PhD
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Children's HOSPITAL • ST. LOUIS
BJC HealthCare

Washington University in St. Louis
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Disclosures

- Dr. Cooper has the following disclosures to declare:
- Consultant: Enzyvant
- No products related to this disclosure will be discussed
- All therapies discussed are off-label

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Learning Objectives

- Identify signs of immune dysregulation in patients seen in the allergy/immunology clinic
- Demonstrate knowledge of genetic testing and interpretation for immune dysregulation syndromes
- Describe potential therapies for patients with immune dysregulation

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Outline

- Case-based discussion of the spectrum of and treatment for immune dysregulation disorders
- Expanding spectrum of immune dysregulation in Primary Immunodeficiencies
- Genetic diagnosis of immune dysregulation

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Outline

- Case-based discussion of the spectrum of and treatment for immune dysregulation disorders
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Case: 3 yo with anemia & infections

- 3 yo boy with refractory autoimmune hemolytic anemia (*AIHA*)
- Infection history:
  + viral URIs and sinusitis
- Otherwise well grown and developing normally.

Case: 3 yo with anemia & infections

- 3 yo boy with refractory autoimmune hemolytic anemia (*AIHA*)
- Infection history:
  + viral URIs and sinusitis
- Otherwise well grown and developing normally.

- Immune evaluation:
  – Normal CBC and IgG
  – Normal T cell numbers
  – Elevated B cells
  – Non-protective responses to tetanus and streptococcus pneumoniae (Prevnar) vaccination
    - Absent memory B cells

Diagnosis: 3 yo with AIHA & infections

- Clinical exome sequencing:
  – Heterozygous *de novo* variant in:
    - *PIK3CD* - pE1021K
- Leads to gain-of-function (GOF) in p110δ subunit of PI3K with increased mTOR activity
- Autosomal dominant primary immune dysregulation disorder

Lymphoid hyperplasia on bronchoscopy

Angulo et al Science 2013; Lucas et al Nat Immunol 2014; Kracker et al, JACI 2014; Hartman et al, J Clin Immunol 2015; Coulter et al JACI 2017

Diagnosis: 3 yo with AIHA & infections

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- Leads to gain-of-function (GOF) in p110δ subunit of PI3K with increased mTOR activity
- Autosomal dominant primary immune dysregulation disorder
- *Treatment: mTOR inhibitor (sirolimus) for modulation of the immune response*

Lymphoid hyperplasia on bronchoscopy

Angulo et al Science 2013; Lucas et al Nat Immunol 2014; Kracker et al JACI 2014; Hartman et al, J Clin Immunol 2015; Coulter et al JACI 2017

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Inborn Errors of Immunity (**IEI**)

- Inborn Errors of Immunity (**IEI**) are inherited disorder of the immune system, also known Primary immunodeficiencies (**PID**)
- There are more than 470+ single-gene inborn errors of immunity
  - Diverse range of clinical symptoms
  - Infectious susceptibility, autoimmunity, autoinflammation, lymphoproliferation, bone marrow failure, cancers

Genomic discovery advances our understanding of the immune system and can provide targeted therapies for patients

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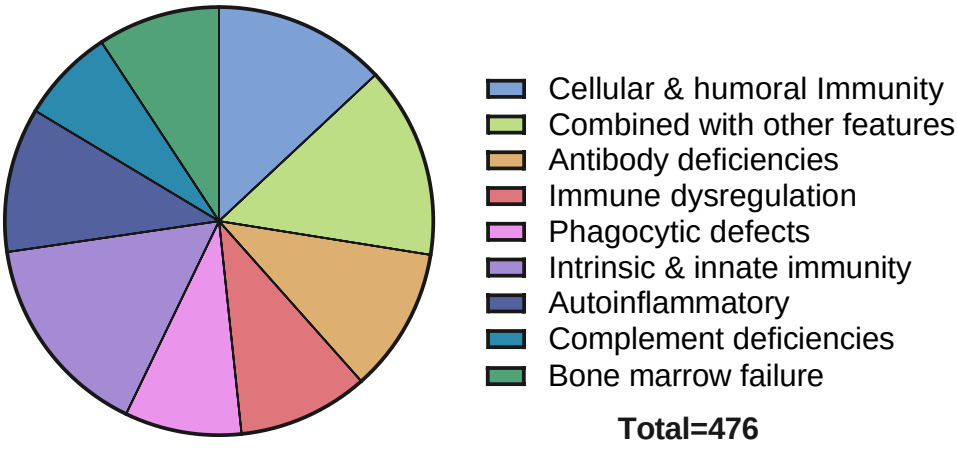
The Spectrum of IEI



Data from: IUIS Reports: Tangye et al, J Clin Immunol, 2020; Tangye et al, J Clin Immunol 2021; and https://iuis.org/committees/iei/

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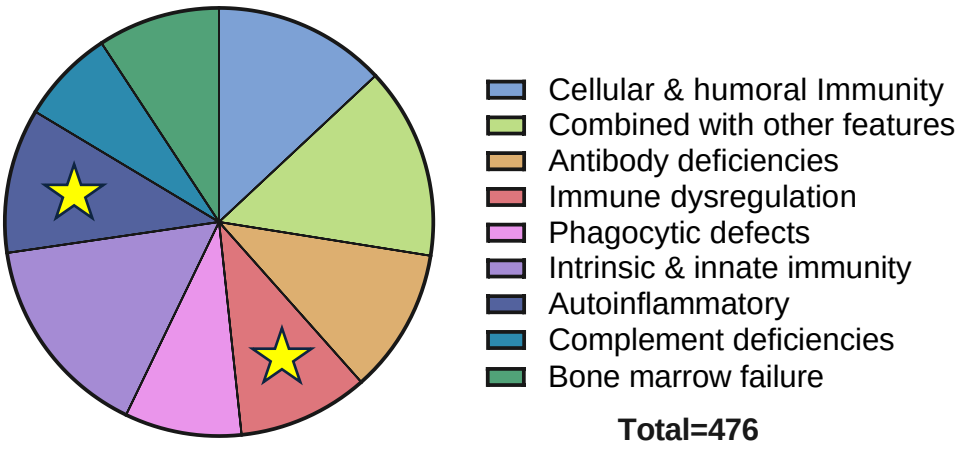
The Spectrum of IEI



Data from: IUIS Reports: Tangye et al, J Clin Immunol, 2020; Tangye et al, J Clin Immunol 2021; and https://iuis.org/committees/iei/

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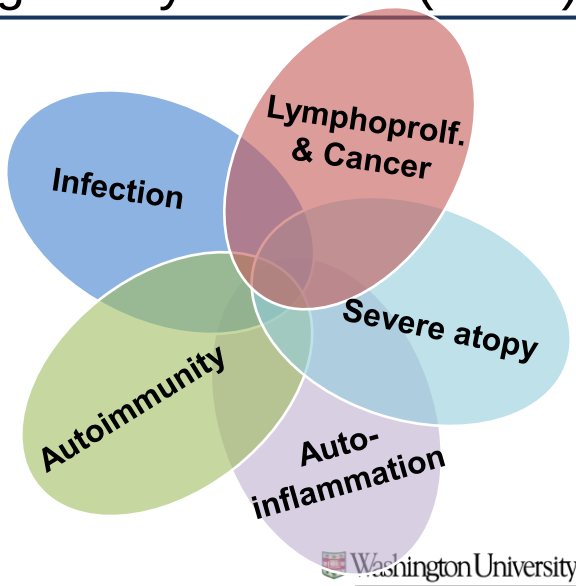
Primary Immune Regulatory Disorder (PIRD)

- A subset of Inborn Errors of Immunity (IEI)
- Abroad category of inborn errors characterized by altered regulation of the immune response



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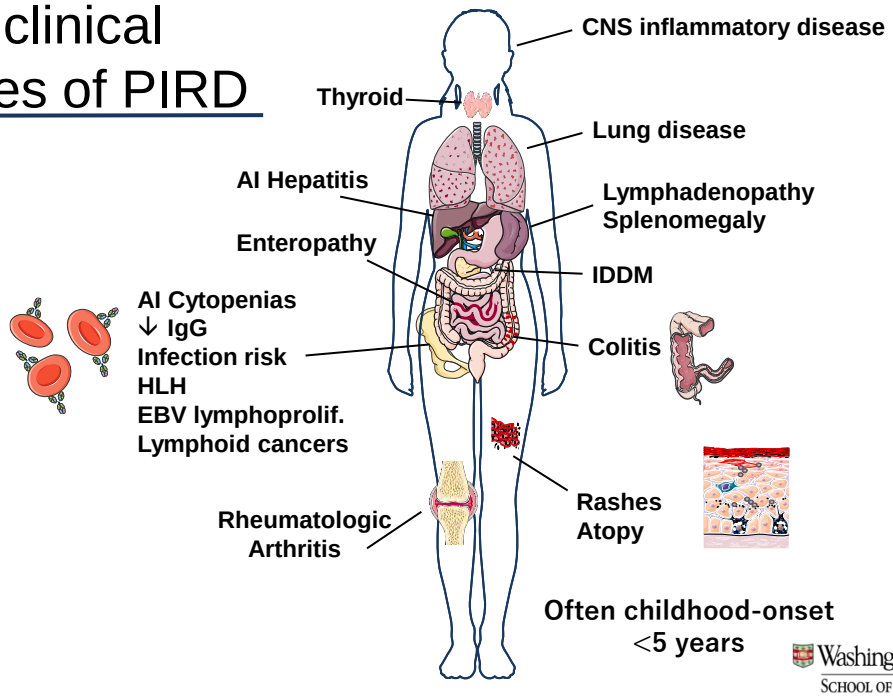
Major clinical features of PIRD



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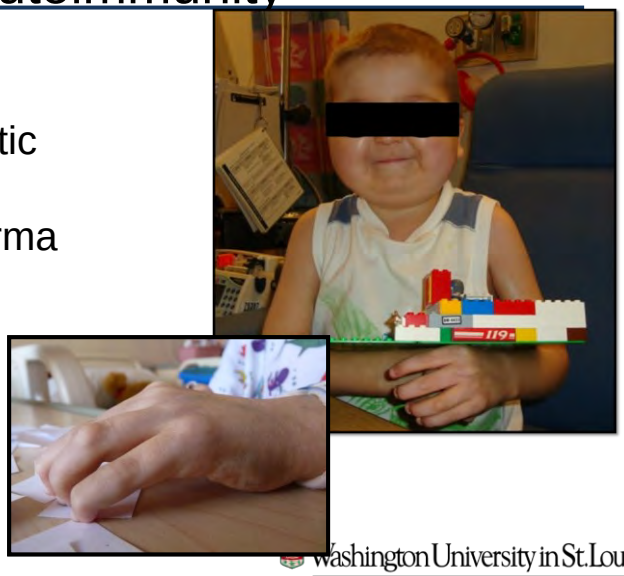
Case 2: 4 year old with autoimmune hepatitis and poly-autoimmunity

- Autoimmune hepatitis
- Severe autoimmune hemolytic anemia (Hgb 2.6)
- Overlap syndrome scleroderma and arthritis
- Short stature (<2 SD)
- No significant family history
- *No infections*



Patient photos used with permission

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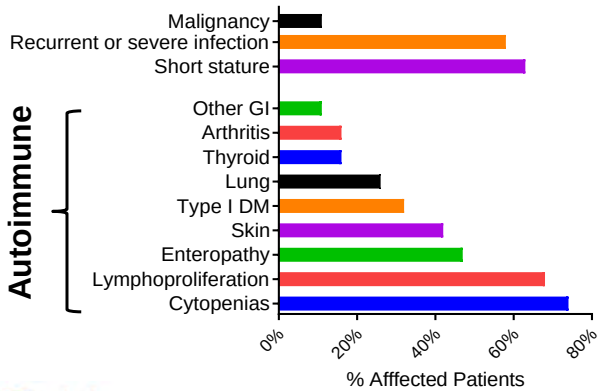
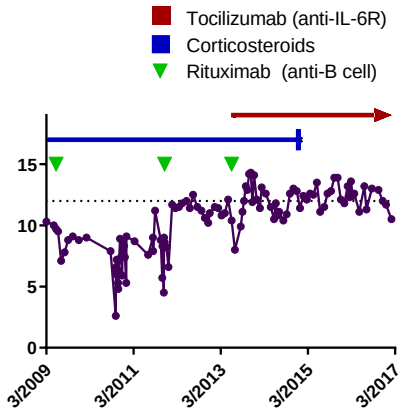
Case 2 Dx: 4yo boy with AI hepatitis, anemia, arthritis

- **STAT3 gain-of-function syndrome**: early-onset poly-autoimmunity & infections with prominent cytopenias and enteropathy





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Case 3: 20 mo with anemia & rash

- 20 mo male infant with developmental delays presents with a year of intermittent fevers, rash, and anemia with new sternal and ankle pain
- Mother with history of recurrent oral and genital ulcers
- Exam: nodular skin rash
- CBC:
  - **Hgb – 6.5 g/dL** (11.5-13.5)
  - Plt – 483 cells/μL (150-400)
  - WBC – 8.6 cells/μL (6-17.5)
- ESR 77 (ref <20)
- CRP 69 (ref <10)

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Inpatient evaluation

- **Immunology/Rheumatology:**
  - **IgG 1581**, **IgA 185.5**, IgM 111.9
  - Normal immune subsets
  - Serum cytokines: elevated

    TNF 21.5 [<10], **IL-6 258** [<5], **MCP-1 769** [<198], **IL-1β 22.1** [<20], **sIL2Rα >4000** [<9]
  - MRI of foot and chest – **osteomyelitis**
- **Neurology**:
  - Differential including Aicardi-Goutières
  - Brain MRI – normal; EEG normal; LP normal
- **Hematology**:
  - Coombs negative → anemia of chronic disease
  - Low concern for malignancy
- **Orthopedics**:
  - Bone biopsy – non-specific inflammation, no infection
- **Infectious diseases:**
  - Extensive evaluation negative for infection
- **Dermatology**:
  - Skin biopsy - Neutrophilic panniculitis
- **Genetic testing → 2-4 weeks**

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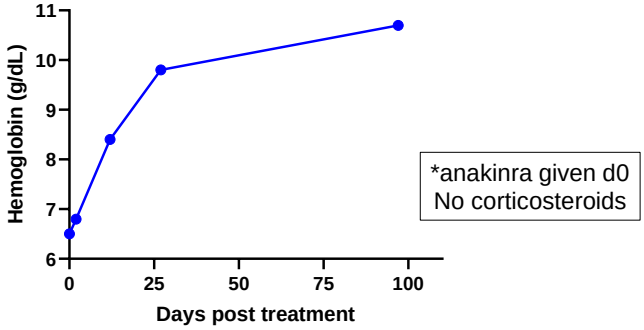
Case 3 Dx: 1yo with anemia & rash

- Started anakinra (2mg/kg) → rapid improvement of rash and anemia.



- Genetic testing demonstrated a novel heterozygous truncation variant in **TNFAIP3 (A20)** causing haploinsufficiency of A20 ***(anti-TNF-a would have been another therapy to try given this)***

Case 4: 5yo girl with autoimmune hepatitis

- 5 year old girl with 2 months of abdominal pain and weight loss
- Liver biopsy → autoimmune hepatitis
- Low calcium → hypoparathyroidism
- No family history of autoimmune disease
- Normal growth & development
- *No infections*

Patient photo provided by family and used with permission

Case 4 Dx: 5yo girl with AI hepatitis

- Genetic testing demonstrated homozygous inherited pathogenic variants in *AIRE*, abnormal thymic selection of T cells
  - Autoimmune polyendocrinopathy, candidiasis & ectodermal dysplasia = **APECED** (or APS1).
- Change in clinical care including monitoring and treatment.

Mycophenolate mofetil
Rituximab
Discontinue steroids

Patient photos provided by family and used with permission

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Outline

- Case-based discussion of the spectrum of and treatment for immune dysregulation disorders
- Expanding spectrum of immune dysregulation in Primary Immunodeficiencies
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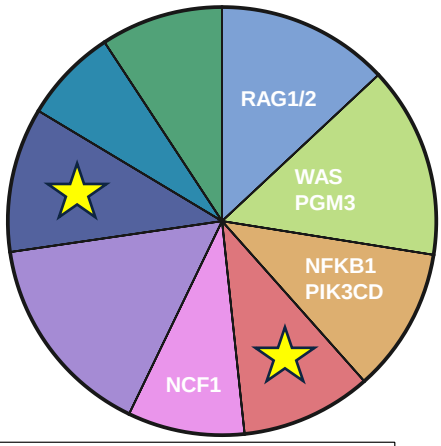
Expanding spectrum of PIRD



- Cellular & humoral Immunity
- Combined with other features
- Antibody deficiencies
- Immune dysregulation
- Phagocytic defects
- Intrinsic & innate immunity
- Autoinflammatory
- Complement deficiencies
- Bone marrow failure

Total=476

See: Chan & Torgerson, Curr Opin Allergy Clin Immunol, 2020

Data from: IUIS Reports: Tangye et al, J Clin Immunol, 2020; Tangye et al, J Clin Immunol 2021; and https://iuis.org/committees/iei/

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'Immunodeficienies' with immune dysregulation

Table 1. Autoimmune clinical manifestations by organ system of select primary immunodeficiency syndromes*

Gene	Disease name	AI Cyto-penias	Skin disease	Enter-opathy	Lung	Endocrin-opathy	Arthritis	Other
Severe Combined Immunodeficiency								
RAG1, RAG2	Omenn	++	++++	+++	-	+	-	++
PNP	SCID	+++	-	-	-	-	-	-
Combined Immune Deficiencies								
CD40L	XL HIgM	+++	++	++	-	++	++	++
ICOS	ICOS	+	++	+++	+	-	++	++
PI3KCD, PI3KR1	APDS	++	+	++	+++	++	++	++
22q11.2	DiGeorge	++	++	+	-	++	+	+
WAS	WAS	+++	++++	+	-	-	++	++
STIM1	STIM1 def	++++	-	+	-	-	-	-
STK4	MST1 def	+++	-	-	-	-	-	-

SCID = Severe combined immunodeficiency, defect in T cell numbers and/or function
CID = Combined immune deficiency, defects in T and B cell function and/or development

Kitcharoensakkul & Cooper, Textbook of Autoimmunity, 2020

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RAG Deficiency

SCID	OMENN	CID with G/AI
Infections	Infections	Normal T/B #
T/B deficiency	+/-T/B Cells	Hyperinflammation
➢ Transplant	Restricted repertoire	Autoimmunity
	Rash, GI disease	➢ Immune modulators
	➢ Transplant	

Notarangelo lab

CID with G/AI = combined immunodeficiency with granulomatosus and autoimmunity

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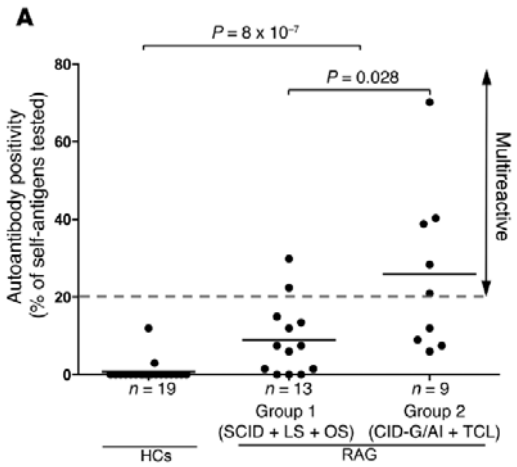
Autoimmunity in RAG deficiency



- 22 patients with RAG-deficiency
- High rate of autoantibodies in the serum of patients
- Multiple anti-cytokine antibodies

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Walter et al, JCI, 2015

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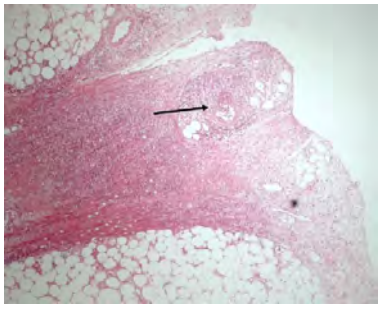
Autoimmunity with RAG1/2 deficiency

- AI cytopenias: anemia, thrombocytopenia, neutropenia
  - 10/13 CID patients

Case reports:

- Granulomatous disease (GPA mimic)
- Crohn's disease
- Vasculitis, lupus
- Juvenile arthritis
- Myasthenia Gravis
- Psoriasis
- Vitiligo

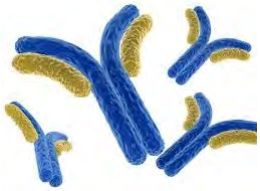


Hypomorphic RAG1 defect in a child presented with pulmonary hemorrhage and digital necrosis. Taskiran et al, Clin Immunol, 2018.

Antibody deficiencies & immune dysregulation

Gene	Disease name	AI Cyto-penias	Skin disease	Enter-opathy	Lung	Endocrin-opathy	Arthritis	Other
Predominantly Antibody Deficiencies								
BTK	XLA	++	+	++	-	-	++	-
Multiple/ unknown	CVID	++	++	++	++	++	++	++

XLA= **X linked agammaglobulinemia**, absence of B cells
CVID= **Common variable immunodeficiency**, antibody deficiency characterized by low immunoglobulin and abnormal response to vaccination



Kitcharoensakkul & Cooper, Textbook of Autoimmunity, 2020

CVID

Table 2. Selected complications from a large cohort ($n=473$) of common variable immune deficiency patients followed at one medical center over four decades

Associated condition	Number ($n=473$)	Percentage of cohort (%)
Infections only (no complications)	151	31.9
Chronic lung disease (functional/structural)	135	28.5
Bronchiectasis	53	11.2
Autoimmunity	134	28.6
Immune thrombocytopenic purpura (ITP)	67	14.2
Autoimmune hemolytic anemia (AIHA)	33	7
Gastrointestinal disease	73	15.4
Malabsorption	28	5.9
Inflammatory Bowel Disease (Crohn's disease, ulcerative colitis, ulcerative proctitis)	20	4.2
Liver disease/hepatitis	43	9.1
Granulomatous disease	46	9.7
Lymphoma	39	8.2
Cancer	33	7
Splenectomy	39	8.2

Resnick & Cunningham-Rundles,Curr Opin Allergy Clin Immunol, 2012

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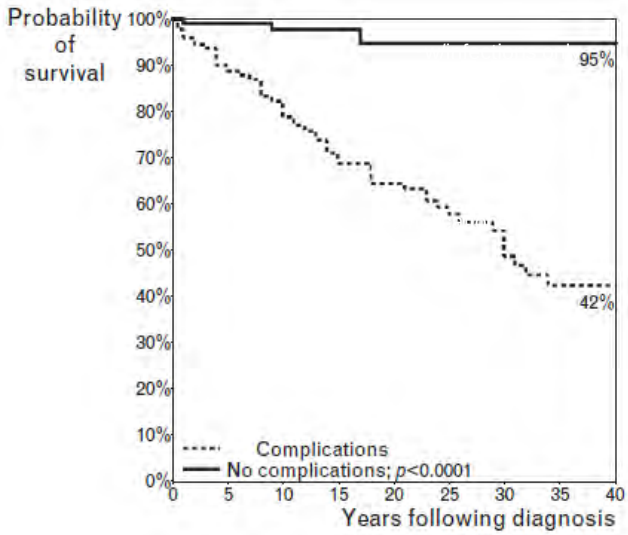
CVID



Resnick & Cunningham-Rundles,Curr Opin Allergy Clin Immunol, 2012

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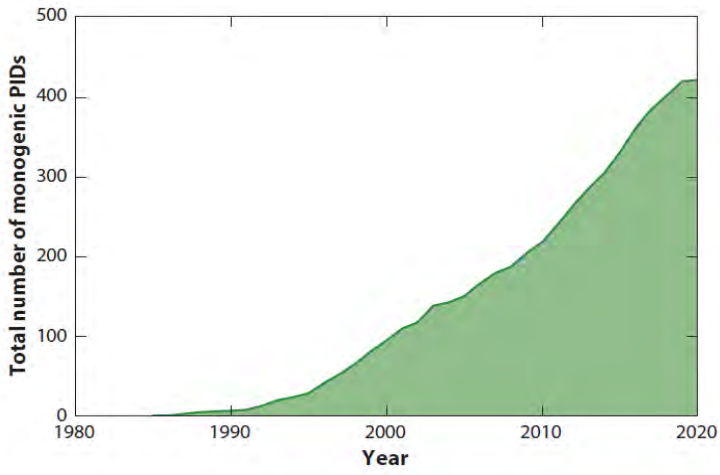
Cytopenias in CVID

- Autoimmune cytopenias can precede the diagnosis of CVID
- These patients are more likely to have other non-infectious complications (OR 2.9, Feuille et al, J Clin Immunol, 2018)
  - Enteropathy, interstitial lung disease, liver, lymphoproliferation, granulomatous disease)
  - May reflect an increased rate of monogenic (or digenic) cause for their CVID
- Treatments:
  - Can consider B cell depletion therapy for refractory cytopenias
  - Avoid splenectomy

Outline

- Case-based discussion of the spectrum of and treatment for immune dysregulation disorders
- Expanding spectrum of immune dysregulation in Primary Immunodeficiencies
- Genetic diagnosis of immune dysregulation

Genetic discovery of Inborn Errors of Immunity



Schmitt & Cooper, Ann Rev Immunol, 2021

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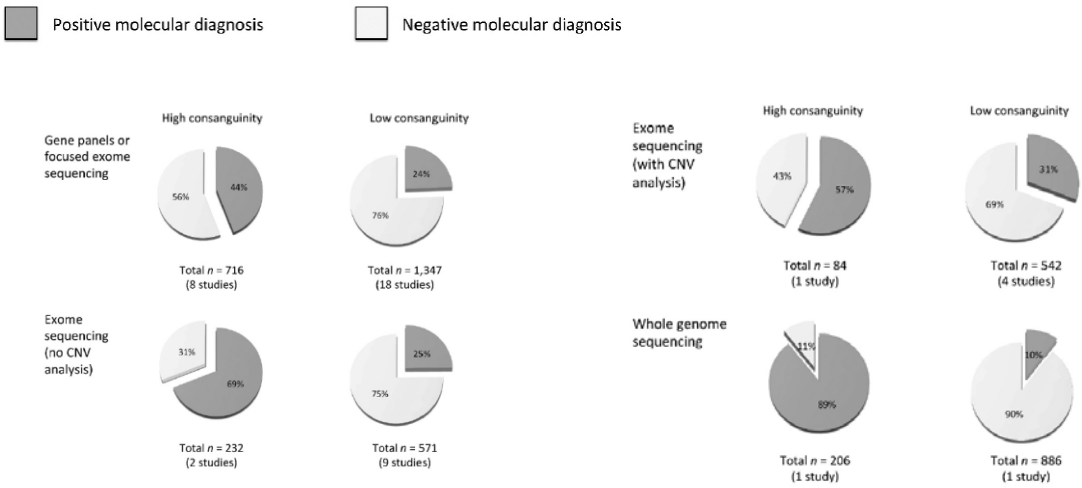
Molecular diagnosis rates for IEI



Chinn & Orange, Expert Review of Clin Immunol, 2020

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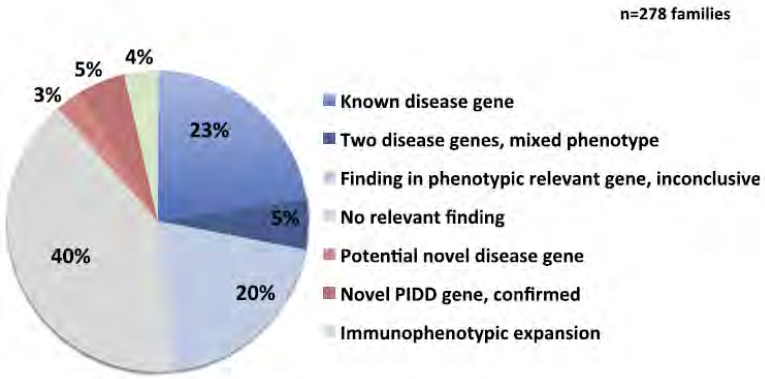
Molecular diagnosis rates of IEI

- Exome sequencing of 278 patients/families with IEI
- A genetic diagnosis was identified in ~40%



Stray-Pedersen et al, JACI, 2016

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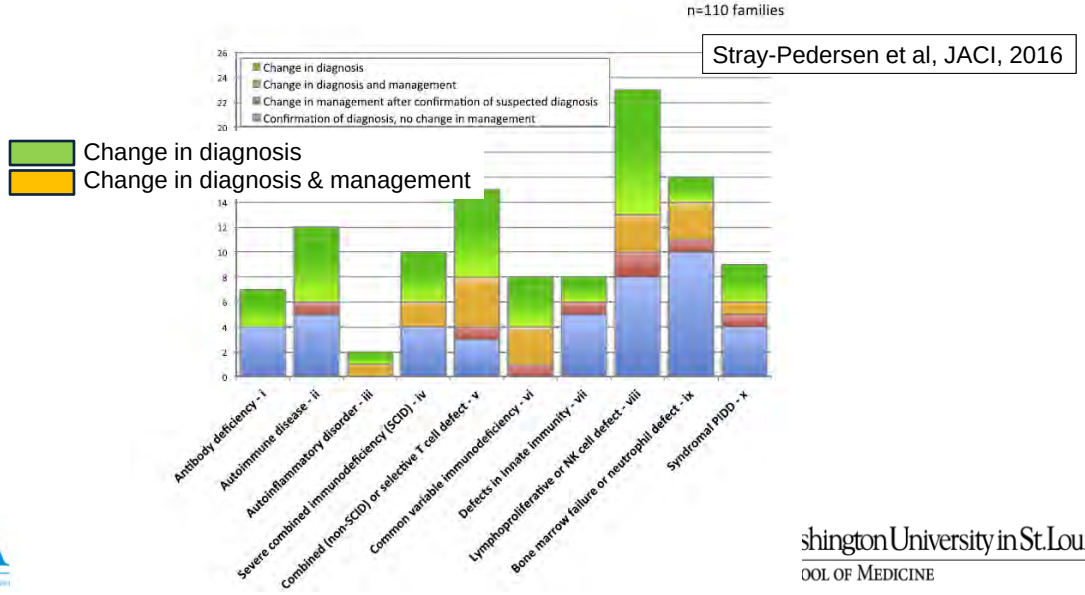
Molecular diagnosis: changes in diagnosis and treatment



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What genetic test to order?

- Single gene testing:
  - Do you know with certainty what they have? Strong family history
- Panel-based testing:
  - Readily available, 2-3 week turnaround, test for ~500 genes associated with known disease
  - Cost: frequently low out-of-pocket or free testing through several programs
- Exome or genome sequencing:
  - Has the patient been through a diagnostic odyssey or does their phenotype not fit a clear syndrome?
  - Consider referral to genetic counselor, there may be secondary findings
  - Exome doesn't pick up everything
    - Hard to sequence by exome: NCF1, NEMO, TBX1…
    - intronic variants – ATM, BTK, JAK3, LRBA…
    - UTR and poly A variants – IL2RG, FOXP3, WAS…
- Chromosomal microarray:
  - Detect large insertions deletions, e.g., Chr22q11.2 microdeletion syndrome

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Summary

- Inborn errors of immunity can present predominantly with immune dysregulation rather than infectious susceptibility
- Variation in genetic changes can lead to immune dysregulation in diseases typically associated with severe immunodeficiency
- Genetic testing can change diagnosis and treatment of patients

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PENNSYLVANIA ALLERGY & ASTHMA ASSOCIATION

73RD PAAA ANNUAL MEETING

Oral Food Challenges in Infants and Toddlers

Presented by:
David Stukus, MD

Sunday, June 26, 2022
10:15 a.m. – 11:00 a.m.

PAAA
Pennsylvania Allergy & Asthma Association

Oral Food Challenges in Infants and Toddlers

David Stukus, MD, FAAAAI, FACAAI, FAAP

Professor of Clinical Pediatrics
Director, Food Allergy Treatment Center
Division of Allergy and Immunology
Nationwide Children's Hospital
Columbus, Ohio

@AllergyKidsDoc

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  - Member – Joint Task Force on Practice Parameters
  - Member - Board of Regents, ACAAI

Nationwide Children's — When your child needs a hospital, everything matters.
The Ohio State University College of Medicine

2

Objectives

- Identify optimal patients for oral food challenges
- Interpret food allergy test results in the proper context
- Incorporate information learned from oral food challenges into standard practice

3

Here is THE Reference

AAAAI Work Group Report

American Academy of Allergy Asthma & Immunology

Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report

J. Andrew Bird, MD[b], Stephanie Leonard, MD[b,c], Marion Groetch, MS, RDN[d], Amal Assa'ad, MD[e], Antonella Cianferoni, MD, PhD[f], April Clark, RDN, LD[g], Maria Crain, APRN, CPNP[g], Tracy Fausnight, MD[h], David Fleischer, MD[i,j], Todd Green, MD[k], Matthew Greenhawt, MD, MBA, MSc[l,j], Linda Herbert, PhD[j,m], Bruce J. Lanser, MD[n], Irene Mikhail, MD[o], Shahzad Mustafa, MD[p,q], Sally Noone, RN[d], Christopher Parrish, MD[g], Pooja Varshney, MD[r,s], Berber Vlieg-Boerstra, RD, PhD[t,u], Michael C. Young, MD[v], Scott Sicherer, MD[d], and Anna Nowak-Wegrzyn, MD, PhD[w] *Dallas and Austin, Texas; San Diego, Calif; New York and Rochester, NY; Cincinnati and Columbus, Ohio; Philadelphia, Hershey, and Pittsburgh, Pa; Denver and Aurora, Colo; Washington, DC; Amsterdam and Groningen, The Netherlands; and Boston, Mass*

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

4

Additional References for Infant OFCs

Oral Food Challenges in Infants and Toddlers

Justin Greiwe, MD[a,b,*]

KEYWORDS

• Food allergy • Oral food challenge • Anaphylaxis • Infants • Epinephrine

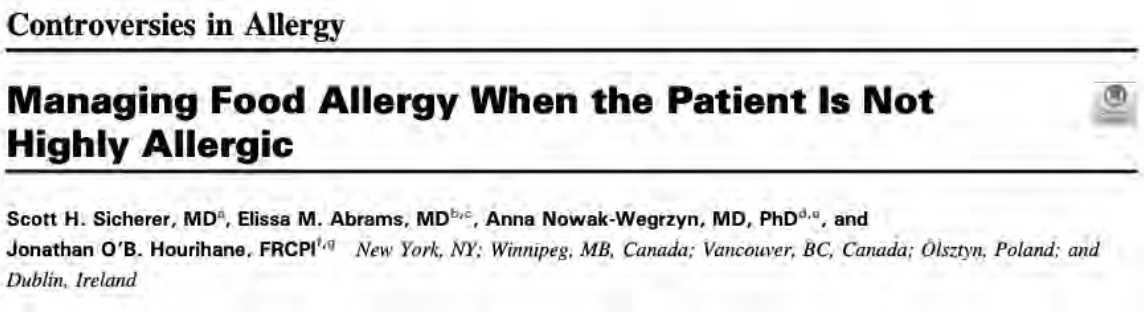
KEY POINTS

- Oral food challenges are a critical procedure to identify patients with IgE-mediated food allergy when the history and testing are not specific enough to confirm a diagnosis.
- Food challenges in infants and toddlers are both safe and practical in a clinical setting.
- Comprehensive past medical history is critical in the diagnosis of food allergy and should be used to determine subsequent testing and interpretation of results.
- Food allergies are associated with significant social and psychological consequences that often are overlooked by health care professionals.
- More emphasis needs to be placed on food challenge education and hands-on experience during fellowship training.

1. Greiwe J. Immunol Allergy Clin North Am. 2019 Nov;39(4):481-493.
2. Greenhawt M. Allergy Asthma Proc. 2019 Jan 1;40(1):62-69.

5

Here is My New FAVORITE Reference



Controversies in Allergy

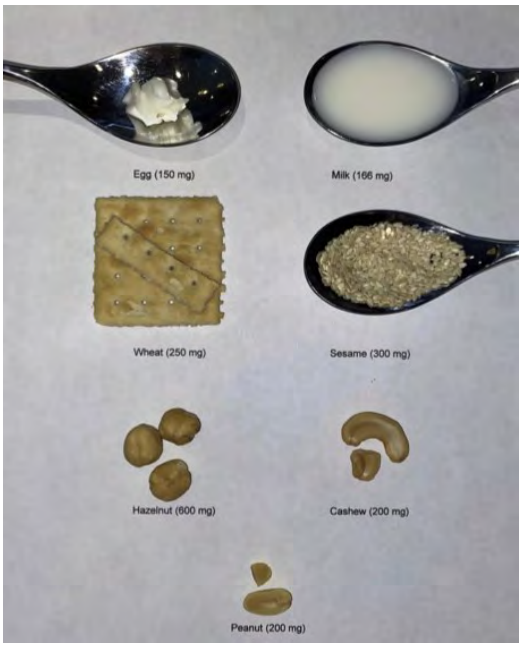
Managing Food Allergy When the Patient Is Not Highly Allergic

Scott H. Sicherer, MD[a], Elissa M. Abrams, MD[b,c], Anna Nowak-Wegrzyn, MD, PhD[d,a], and Jonathan O'B. Hourihane, FRCPI[f,g] *New York, NY; Winnipeg, MB, Canada; Vancouver, BC, Canada; Olsztyn, Poland; and Dublin, Ireland*

J Allergy Clin Immunol Pract 2022;10:46-55

6

Eliciting Dose for 50% of the population with each food allergy



J Allergy Clin Immunol Pract 2022;10:46-55

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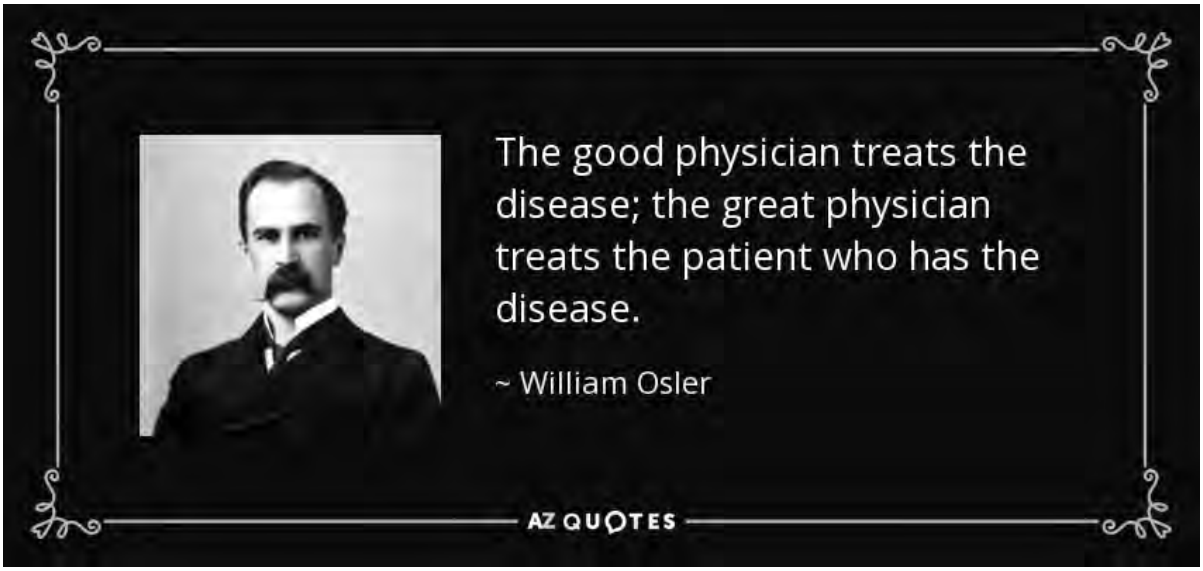

8

“Treat the patient, not the numbers”

9

Initial Thoughts…

- Food allergies are grossly over diagnosed and misdiagnosed
- WE have the expertise to understand pathophysiology and clinical features of food allergy
- Testing does not diagnose food allergy – WE DO

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Case 1

- 6 year old boy with peanut allergy
- Diagnosed 13 months of age
  - Facial hives after eating peanut butter, resolved with antihistamines
- Followed by multiple allergists
  - Repeat skin tests ~8 mm wheal
  - Serum levels:
    - 2012 = 2.64 kU/L
    - 2013 = 9.96 kU/L
    - 2015 = 5.39 kU/L
    - 2016 = 2.90 kU/L
    - 2017 = 5.60 kU/L

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They said we have to treat all of his allergies at once to reduce the risk of severe reactions. I agree with you that it seems like it would overwhelm his system. They also want to skin test him for 110 allergens including foods he is eating without problems. This is our 5th allergist. Can I seriously fax or email you our records? We will drive to you to perform the oral challenge if you think he stands a chance of passing it. It'll be a 10 hour drive so we can't really do preliminary appointments. I have all of his blood work and a recent skin test tho. He starts kindergarten in august so I feel like we are running out of time and options. Thank you for your time.

12

Leaving his first Kindergarten field trip... never would've happened without you. Keep doing what your doing. It's changing lives.

First real Halloween! Had to share 😃

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An Ideal Food Allergy Test

Noninvasive
- Readily available
- Easy to use and interpret

Reliable
- High positive predictive value
- Low false positives

Clinically relevant
- Threshold dose
- Severity of reaction

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Current Food Allergy Tests

Noninvasive
- Readily available
- Easy to use and interpret

Reliable
- LOW positive predictive value
- HIGH false positives

Clinically relevant
- Threshold dose
- Severity of reaction

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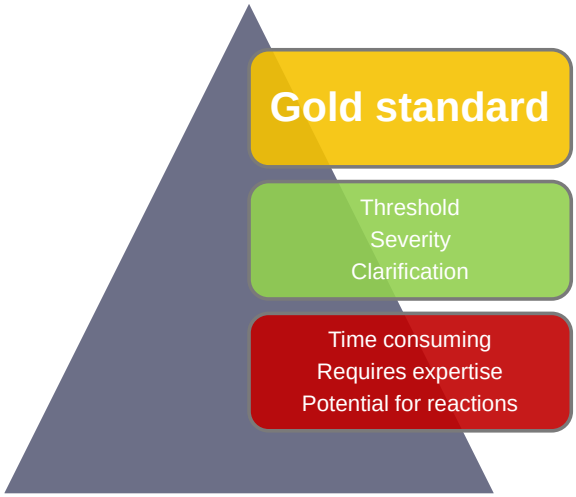
Oral Food Challenges



Upton JE, Bird JD. Ann Allergy Asthma Immunol. 2020;124(5):451-458.

16

OFCs in Clinical Practice

TABLE I. Reported number of oral food challenges performed during fellowship and in practice

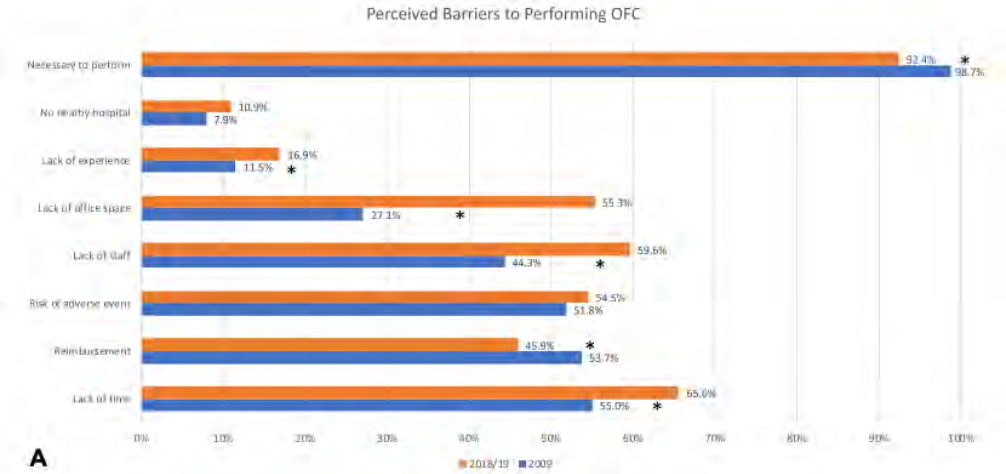
OFC performed in fellowship (per fellowship duration), total number	Percent reporting (535 answered)
0	28.97% (155)
1-10	26.92% (144)
11-20	15.70% (84)
21-30	9.72% (52)
31-40	3.93% (21)
41 or more	14.77% (79)
OFC performed in practice (per month), total number	**Percent reporting (513 answered)**
0	5.46% (28)
1-5	58.09% (298)
6-10	19.30% (99)
11-15	7.21% (37)
16-20	9.94% (51)

OFC, Oral food challenge.

Greiwe J, et al. J Allergy Clin Immunol Pract. 2020;8(10):3348-3355.

17

Barriers to Oral Food Challenges in Practice



Greiwe J, et al. J Allergy Clin Immunol Pract. 2020;8(10):3348-3355.

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Oral Food Challenge

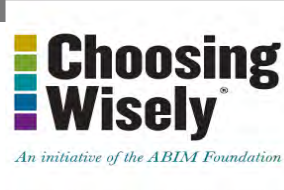
- Gold standard diagnostic procedure to establish a diagnosis of food allergy
- Can be utilized in **any** age group
- Can help determine:
  - If allergy is present when history/testing indeterminate
  - If tolerance has developed
  - If individual can tolerate other tree nuts not involved in suspected reaction

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

19

The ONLY Absolute Contraindication…

20



American Academy of Allergy, Asthma & Immunology

Five Things Physicians and Patients Should Question

Don't perform unproven diagnostic tests, such as immunoglobulin G (IgG) testing or an indiscriminate battery of immunoglobulin E (IgE) tests, in the evaluation of allergy.

Don't perform food IgE testing without a history consistent with potential IgE-mediated food allergy.

https://www.choosingwisely.org/societies/american-academy-of-allergy-asthma-immunology/

21

What Makes a Good Screening Test?

Important Characteristics	Food IgE Skin and Serum Tests
Is asymptomatic disease prevalent?	No
Does the disease cause significant morbidity or mortality?	Potentially
Is treatment available to prevent disease through early detection?	No
Does the test accurately identify those with disease? (True positives)	No
Does the test inaccurately identify those without disease? (False positives)	Yes
Will inaccurate screening lead to unnecessary additional testing or treatment?	Absolutely

Inhal Toxicol. 2014 Nov; 26(13): 811–828.

22

Proper Interpretation of IgE Testing

- Use test results to determine sensitization vs no sensitization
- Size of sensitization helps determine likelihood of allergy being present
- All testing can help determine is the best approach to eating the food again
  - Home
  - Office
  - Avoidance

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Case 2

- 2 year old boy diagnosed with milk, egg, peanut, soy, tree nut allergies
- No prior ingestion or immediate onset reactions
- Severe eczema as infant
- PCP obtained a food allergy panel at 9 months of age to 'find the cause'
  - Milk = 1.91 kU/L
  - Egg = 7.21 kU/L
  - Peanut = 5.63 kU/L
  - Soy = 0.67 kU/L

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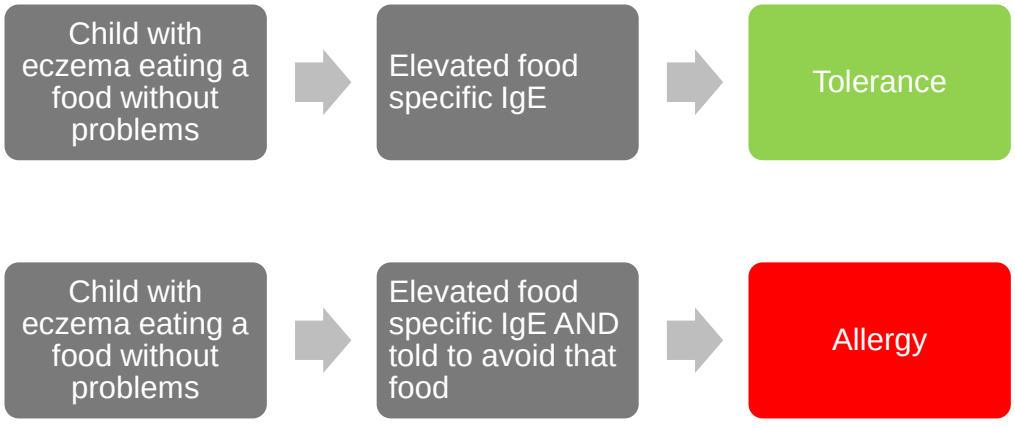
Case 2

- Family told to strictly avoid milk, egg, peanut, soy, tree nuts
- Mother told to remove from her diet while breast feeding
- Eczema gradually improved
- Tolerating fruits, vegetables, meats and also now soy products
- Sought evaluation by allergist at 2 years of age
- Repeat testing

Milk = 1.91 kU/L → 21.4 kU/L
Egg = 7.21 kU/L → 3.27 kU/L
Peanut = 5.63 kU/L → 12.4 kU/L

25

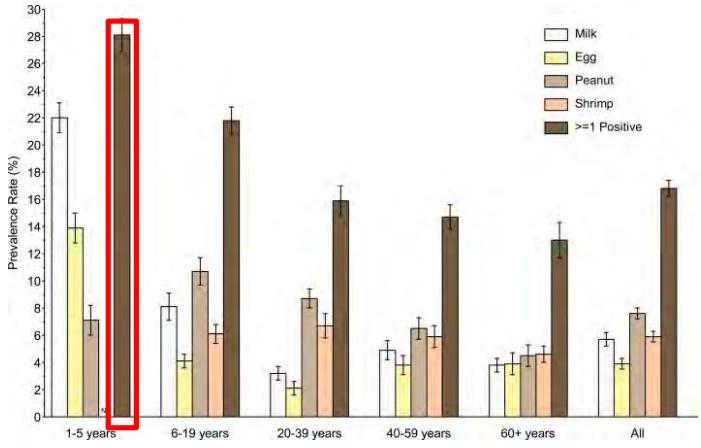
Primum non nocere
(First, do no harm)



Spergel J, et al. Pediatrics 2015;136(6):e1530-e1538

26

Rates of Sensitization > Clinical Allergy



- NHANES data reveal 28% of children with specific IgE > 0.35 kU/L
- Clinical allergy rates 2-6%

Liu AH et al. JACI. 2010;126(4):798-806.

27

We Should NOT Diagnose Food Allergy Based Upon:

- Testing alone
  - Especially if they are eating the food without problems!!!
- Eczema
- Chronic urticaria
- Parental concern
- Chronic GI symptoms
- Family history

28

Food Elimination is NOT a Benign Intervention

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Rare Causes of IgE Mediated Allergy

Table 5. Contact Urticaria

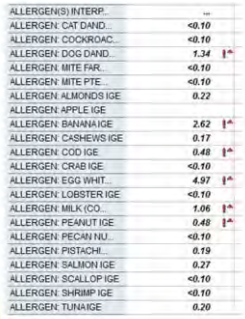
Meats, fruits, vegetables, and other foodstuffs		Spices	Additives
Apple	Liver	Caraway seed	Acetic acid
Apricot	Lupin seed	Cayenne pepper	Amarith
Almond	Maize	Cinnamon	Benzic acid
Artichoke	Malt	Coriander	Butyric acid
Arugula	Mango	Curry	Cinnamic acid
Asparagus	Melon	Dill	Cinnamic aldehyde
Banana	Milk	Garlic	Cellulase
Barley	Mushroom	Mustard	Caraway
Beans	Oatmeal	Onion	Benzaldehyde
Beef	Onion	Paprika	Balsam of Peru
Beer	Orange	Parsley	Ethyl, butyl, isopropyl, acetyl alcohol
Brazil nut	Parsnip	Thyme	Methanol
Buckwheat	Peach		Neocaocine
Cabbage	Peanut		Sorbic acid
Carrot	Pear		Sodium benzate
Cauliflower	Pickles		Sunset Yellow
Celery	Pineapple		Tartrazine (FD & C no. 5)
Chamomile	Plum		
Cheese	Pomegranate		
Chicory	Pork		
Chicken	Potato		
Chives	Rice		
Coffee bean (Green)	Rutabaga		
Corn	Seaweed		
Cucumber	Sesame seeds		
Egg	Shallots		
Endive	Shellfish		
Fennel	Soybean		
Fig	Spinach		
Fish	Strawberry		
Flour	Sesame seeds		
Frog's legs	Sunflower seeds		
Garlic	Tofu		
Grapefruit	Tomato		
Green pepper	Turkey		
Honey	Venison		
Kiwi lamb	Watercress		
Leek	Watermelon		
Lemon	Wheat		
Lettuce	Wheat bran		
Lime	Winged bean		
Litchi			

Brancaccio RR. Dermatol Ther. 2004;17(4):302-13.

30

Why Are There So Many False Positives?

- Eczema
- Allergic rhinitis
- Cross reactive allergens
- IgG binding
- Dermatographism



ALLERGEN(S) INTERP...	...	
ALLERGEN: CAT DAND...	<0.10	
ALLERGEN: COCKROAC...	<0.10	
ALLERGEN: DOG DAND...	1.34	H
ALLERGEN: MITE FAR...	<0.10	
ALLERGEN: MITE PTE...	<0.10	
ALLERGEN: ALMONDS IGE	0.22	
ALLERGEN: APPLE IGE		
ALLERGEN: BANANA IGE	2.62	H
ALLERGEN: CASHEWS IGE	0.17	
ALLERGEN: COD IGE	0.48	H
ALLERGEN: CRAB IGE	<0.10	
ALLERGEN: EGG WHIT...	4.97	H
ALLERGEN: LOBSTER IGE	<0.10	
ALLERGEN: MILK (CO...	1.06	H
ALLERGEN: PEANUT IGE	0.48	H
ALLERGEN: PECAN NU...	<0.10	
ALLERGEN: PISTACHI...	0.19	
ALLERGEN: SALMON IGE	0.27	
ALLERGEN: SCALLOP IGE	<0.10	
ALLERGEN: SHRIMP IGE	<0.10	
ALLERGEN: TUNA IGE	0.20	

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Cross-Reactivity: Clinical vs Testing

Foods	Clinical Reactions	Testing
Peanut + Tree nuts	Low/none	Moderate
Tree nuts + Other tree nuts	Pecan + walnut Cashew + pistachio	High
Fish + Shellfish	Low/none	Low/none
Fish + Other fish	High	High
Shellfish + Other shellfish	High	High
Peanut + soy	Low/none	High
Wheat + grains	Low/none	High
Cow's milk + goat/sheep's milk	High	High

Sampson HA, et al. JACI. 2014;134(5).

32

Aeroallergen Cross Reactivity

Aeroallergen	Food
Dust mite Cockroach	Shellfish
Birch tree pollen	Peanut Fruits Soy
Grass pollen	Wheat
Tree pollen	Tree nuts

Sampson HA, et al. JACI. 2014;134(5).

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Testing Does Not Predict Severity of Reactions

- 19 year old college sophomore
- Seeking 2nd opinion as previous allergist retired
- Seeking OIT for peanut
- “I’m deathly allergic to peanuts”

34

Peanut/Tree Nut Component Testing

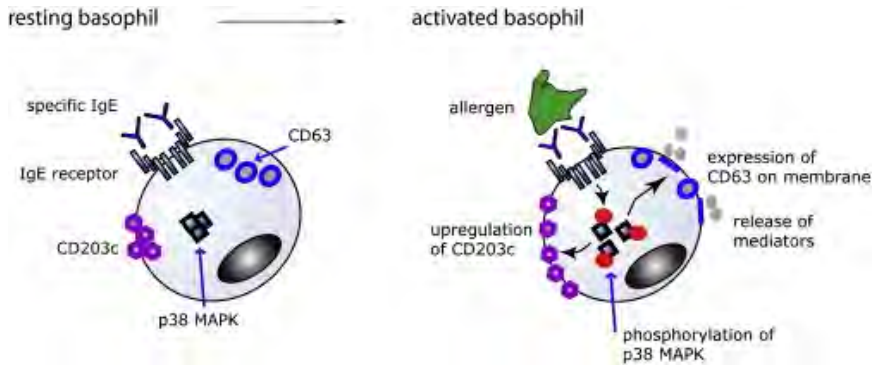
- Predictive capabilities vary according to population background

Nut	Antigens Associated with Clinical Allergy
Peanut	Ara h 1, 2, 3
Hazelnut	Cor a 9, Cor a 14
Cashew	Ana o 3
Walnut	Jug r 1
Pecan	Car I 1, Car I 2
Pistachio	Pis v 1, Pis v 2

BSACI guideline for the diagnosis and management of peanut and tree nut allergy. Clin & Exp Allergy. 2017;47:719-39.

35

Basophil Activation Testing



Hausmann OV, et al. Immunology and Allergy Clinics. 2009;29(3):555-566.

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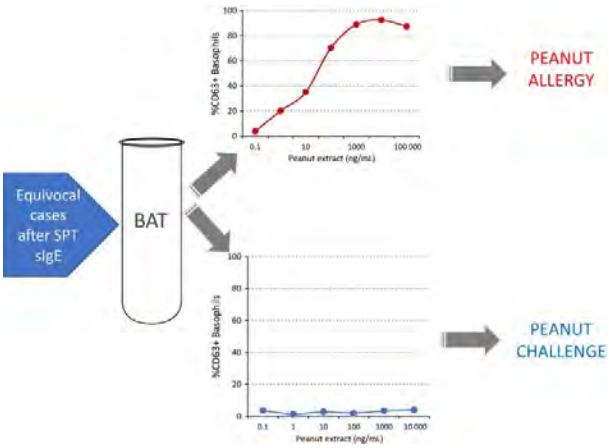
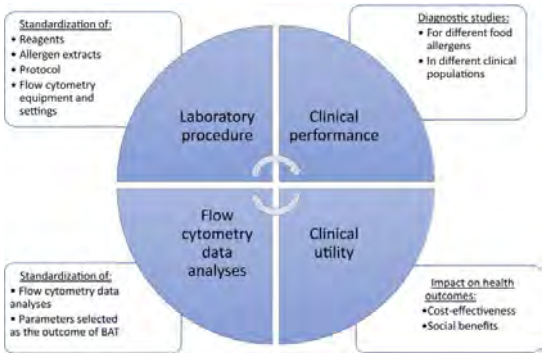
BAT as 2nd Line Test





Santos AF, Shreffler WG. Clin Exp Allergy. 2017 Sep; 47(9): 1115–1124.

37

Epitope Mapping for Peanut Allergy

Results: In the validation using CoFAR2 and POISED cohorts, the peanut BBEA diagnostic test correctly diagnosed 93% of the subjects, with a sensitivity of 92%, specificity of 94%, a positive predictive value of 91%, and negative predictive value of 95%.

Conclusions: In validation of the peanut BBEA diagnostic test, the overall accuracy was found to be superior to existing diagnostic tests for peanut allergy including skin prick testing, peanut sIgE, and peanut component sIgE testing.

Suárez-Fariñas M, et al. Allergy. 2021 May 15. doi: 10.1111/all.14905. Epub ahead of print.

38

It Always Comes Back to Ingestion

Upton JE, Bird JD. Ann Allergy Asthma Immunol. 2020;124(5):451-458.

39

Safety of Oral Food Challenges

- Akuete et al determined OFCs are much safer than previously thought[1]
  - 6,377 OFCs from 2008-2013
  - **86% patients challenged w/o reaction**
  - **Only 2% required epinephrine**
  - **98% of OFCs completed without anaphylaxis**
- Stark contrast to previous studies
  - Epinephrine use during OFC 6-33%[1-6]
- Late-phase & biphasic reactions after OFCs are rare
  - 1.5-4% in previously published studies[7,8]
- 2 known fatalities since description of modern OFC procedure published in 1976

1. Akuete K, Guffey D, Israelsen RB, et al. Multicenter prevalence of anaphylaxis in clinic-based oral food challenges. Ann Allergy Asthma Immunol. 2017 Oct;119(4):339-348.e1.
2. Fleischer DM, Bock SA, Spears GC, Wilson CG, Miyazawa NK, Gleason MC, et al. Oral food challenges in children with a diagnosis of food allergy. J Pediatr 2011;158:578-83.
3. Noone S, Ross J, Sampson HA, Wang J. Epinephrine use in positive oral food challenges performed as a screening test for food allergy therapy trials. J Allergy Clin Immunol Pract. 2015;3:424e428.
4. Lieberman JA, Cox AL, Vitale M, Sampson HA. Outcomes of office-based, open food challenges in the management of food allergy. J Allergy Clin Immunol. 2011;128:1120e1122.
5. Perry TT, Matsui EC, Conover-Walker MK, Wood RA. Risk of oral food challenges. J Allergy Clin Immunol. 2004;114:1164e1168.
6. Ram G, Cianferoni A, Spergel JM. Food allergy to uncommonly challenged foods is rare based on oral food challenge. J Allergy Clin Immunol Pract. 2016;4:156e157.e5.
7. Järvinen, K.M., Amalanayagam, S., Shreffler, W.G. et al. Epinephrine treatment is infrequent and biphasic reactions are rare in food-induced reactions during oral food challenges in children. J Allergy Clin Immunol. 2009; 124: 1267–1272
8. Lee, J., Garrett, J.P., Brown-Whitehorn, T., and Spergel, J.M. Biphasic reactions in children undergoing oral food challenges. Allergy Asthma Proc. 2013; 34: 220–226

40

Safety with Infants/Toddlers

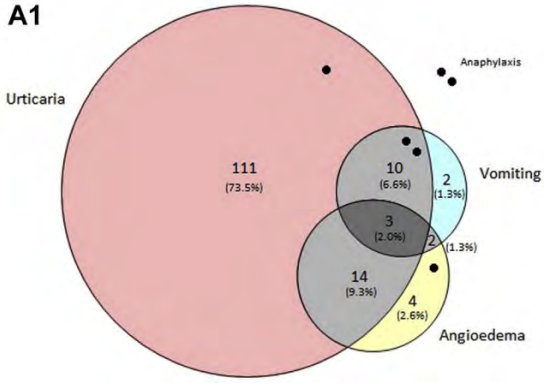
- Body of evidence demonstrates safety and efficacy in children <18 months
- Most reactions are mild and cutaneous
  - Low rate of anaphylaxis
  - Epinephrine rarely needed

1. Osborne NJ, Koplin JJ, Martin PE, et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. J Allergy Clin Immunol 2011;127:668-76 e1-2.
2. Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015;372:803-13.
3. Perkin MR, Logan K, Tseng A, et al. Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants. N Engl J Med 2016;374:1733-43.
4. Wei-Liang Tan J, Valerio C, Barnes EH, et al. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. J Allergy Clin Immunol 2017;139:1621-8 e8.
5. Palmer DJ, Sullivan TR, Gold MS, Prescott SL, Makrides M. Randomized controlled trial of early regular egg intake to prevent egg allergy. J Allergy Clin Immunol 2017;139:1600-7 e2.
6. Bellach J, Schwarz V, Ahrens B, et al. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants. J A

41

HealthNuts Food Challenges

- 598 peanut challenges at 1 year of age



Chan JC, et al. J Allergy Clin Immunol Pract. 2017;5(2):398-409.

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Which Infants Should We Challenge?

- Anyone with a ~50% chance of not having symptoms
- OR…any family that wishes to better understand their child's allergic potential

TABLE II. Tests to assess the likelihood of obtaining a positive or negative OFC in children

	Serum food-IgE (kIU/L)*		SPT wheal (mm)*	
Food	~95% Positive	~50% Negative†	~95% Positive	~50% Negative†
Cow's milk	≥15[16] ≥5 if younger than 1 year[132]	≤2[23]	≥8[21]	
Egg white	≥7[16] ≥2 if younger than 2 years[133]	≤2[23]	≥7[21]	≤3[22]
Peanut	≥14[16]	≤2 with and ≤5 without history of peanut reaction[24]	≥8[17,21]	≤3[17]
Fish	≥20[16]			

Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, et al. Work Group report: oral food challenge testing. J Allergy Clin Immunol 2009;123:S365-83.

43

Risk Assessment for OFCs

Low Risk of Reaction	**1. Recent accidental ingestion to small amount of food without clinical symptoms** **2. Favorable test results**
High Risk of Reaction	**1. Recent reaction to the food in the past 6-12 mo** **2. Diagnostic or high-positive test results**
Low Risk of Severe Reaction	**1. No past severe reactions** **2. Food not usually implicated in severe food-induced anaphylaxis (eg, meat, fruit, vegetable)** **3. No asthma**
High Risk of Severe Reaction	**1. Past severe reaction** **2. Severe reaction to trace amounts of food** **3. Food frequently implicated in fatal and near-fatal food-induced anaphylaxis (eg, peanut, tree nuts, fish, shellfish, seeds)** **4. Asthma (regardless of severity)** **5. Conditions that may affect the resuscitation: cardiovascular disease, difficult vascular access or intubation, β-blocker medication**

Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, et al. Work Group report: oral food challenge testing. J Allergy Clin Immunol 2009;123:S365-83.

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Day of: Reasons to Reschedule

TABLE I. Reasons to reschedule or delay an OFC

Consider postponing the OFC if the patient has any of the following:

- Concurrent illness, fever, or active respiratory symptoms (ie, wheeze or cough)
- Used a short-acting β-agonist within the preceding 48 h for cough or wheeze
- Poorly controlled asthma, AD, or allergic rhinitis
- Unstable cardiovascular disease
- Pregnancy
- Beta-blocker therapy
- Patient has not discontinued medications as outlined in Tables II and III

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

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Conversations with the Family

- Why pursue the oral challenge?
- Risks
- Benefits
- Likely outcome
- Possible outcome
- Are they willing to keep in the diet after the challenge?
  - 25% do NOT

Eigenmann PA, et al. Pediatr Allergy Immunol. 2006 Dec;17(8):601-5.

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Risks of Unsuccessful Challenge

- Acute allergic reaction
- Anaphylaxis
- Emotional distress
- Anxiety

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

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Benefits of Unsuccessful Challenge

- Demonstration of signs/symptoms of allergic reaction
- Demonstration of possible threshold/reactive dose
- Demonstration of rapid response to therapy
  - Have the parents administer epinephrine
- Decreased anxiety
- Decreased dietary restrictions
  - Precautionary labeling
  - Dining out
  - Particularly powerful when families have imposed severe restrictions

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

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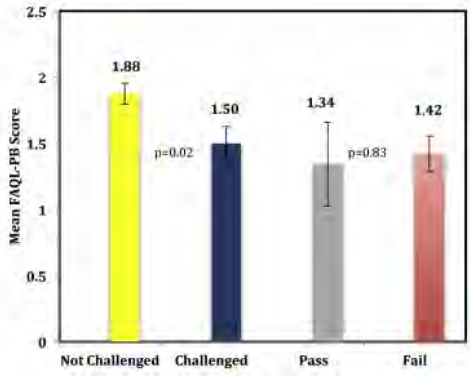
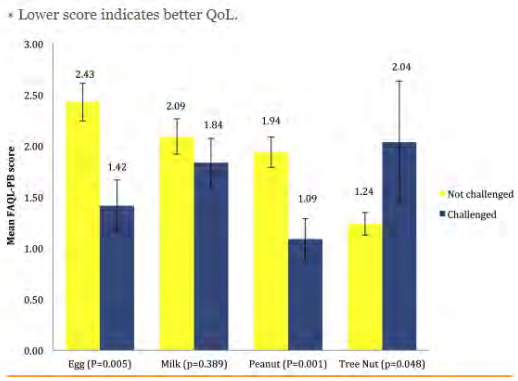
Benefits of Unsuccessful Challenge

- Quality of life improves after a challenge





Franxman TJ, et al. J Allergy Clin Immunol Pract. 2015 Jan-Feb;3(1):50-6

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Benefits of a Successful Challenge

- Life altering
- Improved quality of life

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Tips for a Successful Day

- Discuss and REPEAT what day entails
- Address anxiety and potential scenarios before feeding
- Distraction, distraction, distraction
- Have families bring food, snacks, utensils, sippy cups
- Stock vehicles and masking agents in your office

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Rate Limiting Step is ALWAYS Desire to Eat

- Offer choices
- Limit stress, act casual when refusal occurs
- Toddlers are always in charge
- Be prepared to not achieve desired amount of protein
- There is no absolute protocol to follow

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

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TABLE V. Age-appropriate portion sizes for open OFC

Allergen	Food	Protein content per serving size	Age				
			4-11 mo	1-3 y	4-8 y	9-18 y	19+ y
Egg	French toast (1 egg per 1 slice of bread)*	6 g if made with 1 large egg	½-1 slice	½-1 slice	1 slice	1-2 slices	1-2 slices
	Hard-boiled or scrambled egg	6 g/1 large egg	½-1 egg	½-1 egg	1 egg	1-2 eggs	1-2 eggs
Fish	Cooked fish†	6 g/1 oz	½-1 oz	1 oz	1 oz	2-3 oz	3-4 oz
Grains	Cooked cereal	5 g per 1/4 cup dry (oatmeal or Cream of Wheat)	¼ cup	¼ cup	½-½ cup	½-1 cup	½-1 cup
	Cooked pasta*/rice	3 g per 1/2 cup	¼ cup	¼ cup	½-½ cup	½-1 cup	½-1 cup
	Infant cereal	1-2 g per 1/4 cup	¼-½ cup	¼-½ cup			
	Muffin or roll bread‡	4-6 g/muffin or roll	¼-½ piece	½ piece	½-1 piece	1 piece	1 piece
	Ready-to-eat cereal	2-6 g/1 cup	¼-½ cup	¼-½ cup	½-¾ cup	¾-1 cup	¾-1 cup
	Slice bread	2-4 g/slice	¼-½ slice	½ slice	½-1 slice	1-2 slices	2 slices
Milk	Infant formula	2-3 g/5 oz	4-8 oz				
	Milk	8 g/8 oz		4-8 oz	4-8 oz	8 oz	8 oz
	Cottage cheese	10-14 g/4 oz	¼-½ cup	¼-½ cup	½-1 cup	½-1 cup	1 cup
	Hard cheese	6-8 g/1 oz	¼-½ oz	½ oz	1 oz	1 oz	1½ oz
	Yogurt (NOT Greek style)	8 g/8 oz	¼-½ cup	¼-½ cup	½-1 cup	½-1 cup	½-1 cup
Peanut	Peanut (whole)	2 g/~8 peanuts			16 pieces	16 pieces	16 pieces
	Peanut butter	8 g/1 tbsp	1 rounded tbsp‖	1-2 tbsp	1-2 tbsp	2 tbsp	2 tbsp
	Peanut flour or peanut butter powder	3 g/1 tbsp original or 2.25 g/1 tbsp chocolate flavor	1 rounded tbsp‖	1-2 tbsp	1-2 tbsp	2 tbsp	2 tbsp
	Peanut/chocolate candy cups (full-size)	0.875 g/1 cup		1-2 candy cups	1-2 candy cups	2-3 candy cups	2-3 candy cups
Shellfish	Shellfish§	5 g/1 oz	½-1 oz	1 oz	1 oz	2-3 oz	3-4 oz
Soy/legumes	Infant formula	2-3.1 g/5 oz	4-8 oz				
	Soy beverage	7 g/8 oz		4-8 oz	4-8 oz	8 oz	8 oz
	Cooked beans (kidney, black, chickpeas, lentils)	7-9 g per 1/2 cup	⅛-¼ cup	¼ cup	½-½ cup	½-1 cup	1 cup
	Tofu	8 g/3 oz Firm tofu	½-1 oz	1 oz	1 oz	2-3 oz	3-4 oz
	Yogurt	5 g/6 oz	¼-½ cup	¼-½ cup	½-1 cup	1 cup	1 cup
Tree nut	Almond	3 g/11 whole nuts			11 pieces	11 pieces	11 pieces
	Almond butter (Barney butter brand)	3 g/1 tbsp	1 tbsp ‖	1-2 tbsp	1-2 tbsp	1-2 tbsp	1-2 tbsp
	Brazil nut	3 g/4.5 nuts			4½ pieces	4½ pieces	4½ pieces
	Cashew	3 g/10 whole nuts			10 pieces	10 pieces	10 pieces
	Coconut flour	3 g/1 tbsp	1 tbsp	1-2 tbsp	1-2 tbsp	2-3 tbsp	2-3 tbsp
	Coconut milk‖	3 g/3 oz		3 oz	3 oz	4-8 oz	4-8 oz
	Hazelnut	3 g/3 tbsp hazelnuts or hazelnut meal			3 tbsp	3 tbsp	3 tbsp
	Pecan (halves)	3 g/25 halves			10-25 halves	25 halves	25 halves
	Pine nuts	3.5 g/3 tbsp pine nuts			3 tbsp	3-4 tbsp	4 tbsp
	Pistachio	3 g/20 whole nuts			20 pieces	20 pieces	20 pieces
	Walnut (halves)	3 g/10 halves			10 halves	10 halves	10 halves

Bird JA, et al. Conducting an Oral Food Challenge: An Update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020 Jan;8(1):75-90.e17.

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Multiple Tree Nut Challenges

- "Tree Nut allergy" is not a diagnosis

- Peanut + tree nuts (any) = no clinical cross reactivity
- Cashew + pistachio = HIGH cross reactivity
- Walnut + pecan + hazelnut = HIGH cross reactivity

Andorf S, et al. JACI: IP. 2017;5(5):1325-1334.

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At Home Challenges

- Can consider when risk is low
  - Age
  - Prior history
  - Recent IgE results
  - Type of food
- Telemedicine visits???

MacGinnitie, Andrew J. et al. Journal of Allergy and Clinical Immunology: In Practice, Volume 6, Issue 2, 353 – 360
Mack DP, et al. J Allergy Clin Immunol Pract. 2020 Oct;8(9):2851-2857.

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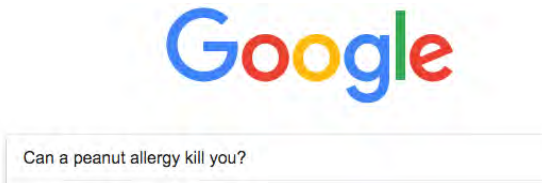
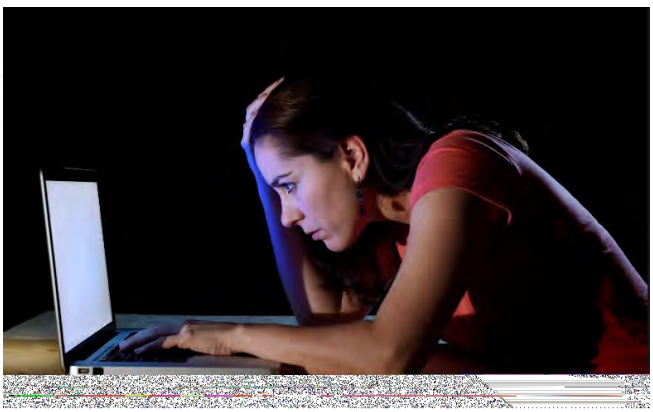
High Risk Challenges, aka “Exposure Therapy”





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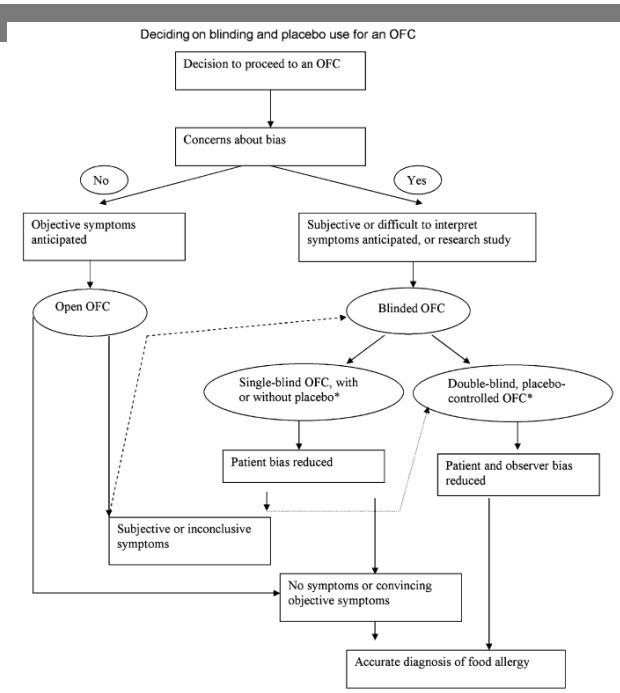
To Blind, Or Not To Blind?



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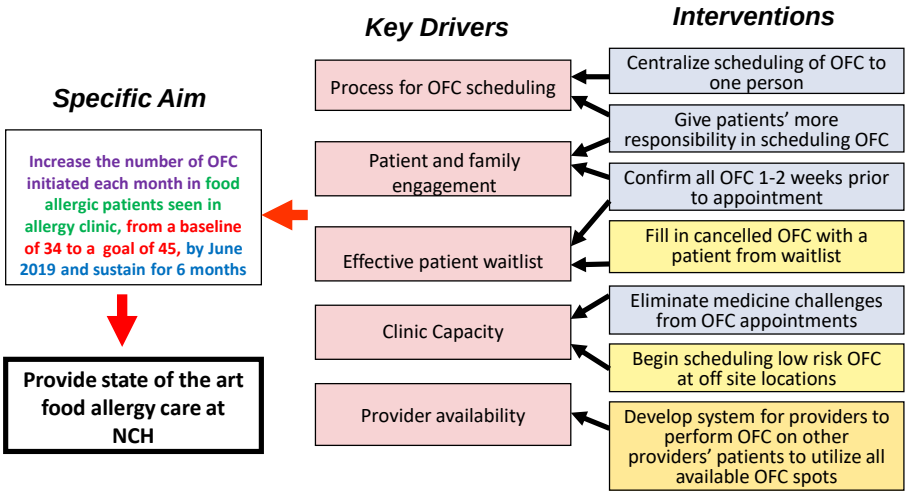
Increasing the number of Oral Food Challenges in Allergy Clinic



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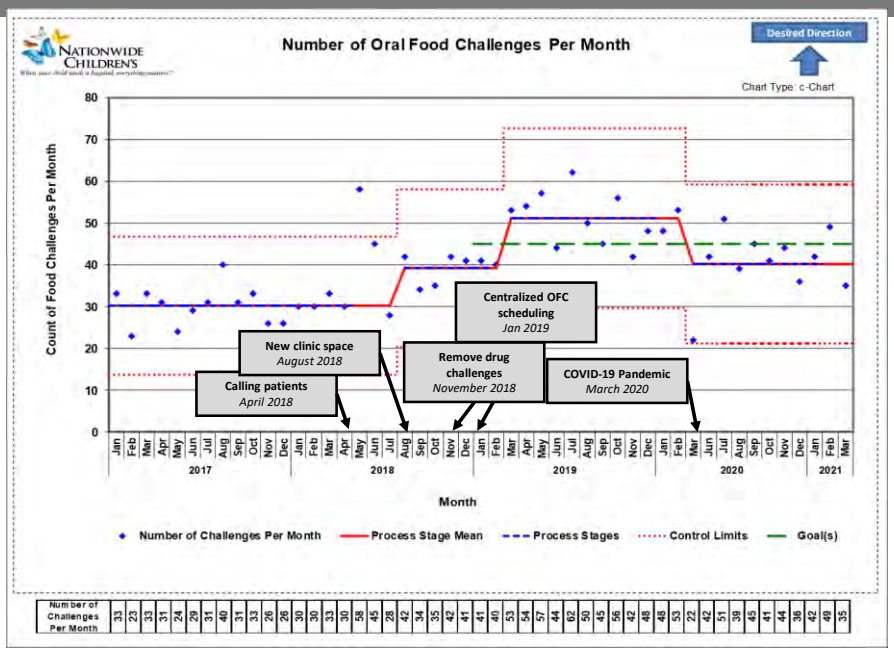
Nationwide Children's
Number of Oral Food Challenges Per Month
Desired Direction
Chart Type: c-Chart
Count of Food Challenges Per Month
Centralized OFC scheduling
Jan 2019
New clinic space
August 2018
Remove drug challenges
November 2018
COVID-19 Pandemic
March 2020
Calling patients
April 2018
Month
Number of Challenges Per Month
Process Stage Mean
Process Stages
Control Limits
Goal(s)

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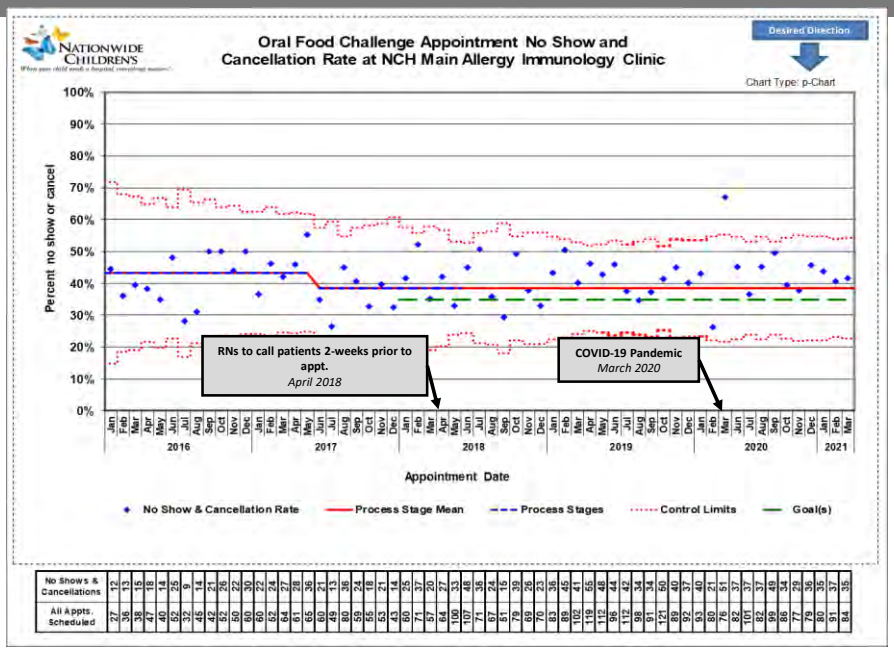
Nationwide Children's
Oral Food Challenge Appointment No Show and Cancellation Rate at NCH Main Allergy Immunology Clinic
Desired Direction
Chart Type: p-Chart
Percent no show or cancel
RNs to call patients 2-weeks prior to appt.
April 2018
COVID-19 Pandemic
March 2020
Appointment Date
No Show & Cancellation Rate
Process Stage Mean
Process Stages
Control Limits
Goal(s)

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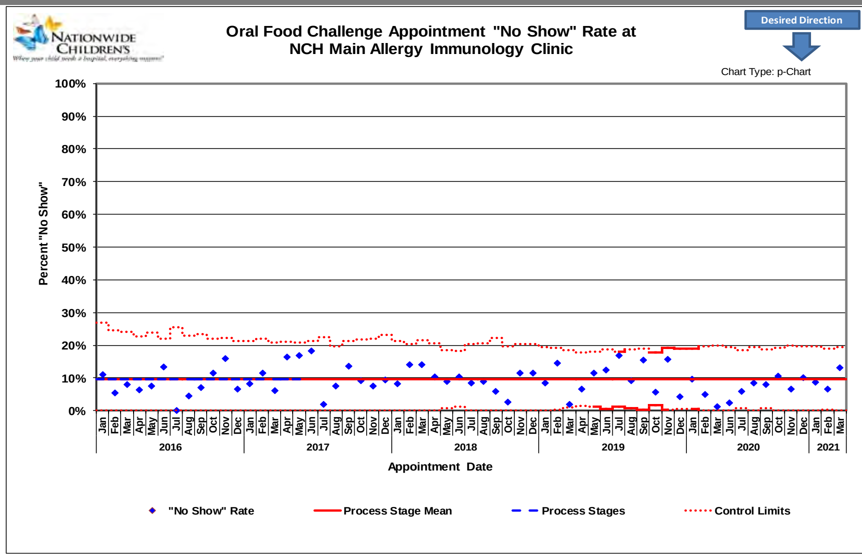

"No Shows"	3	2	3	3	3	7	0	2	3	6	8	4	5	6	4	10	11	11	1	6	8	5	4	4	5	10	8	7	9	11
All Appts. Scheduled	27	36	38	47	40	52	32	45	42	52	50	60	60	52	64	61	65	60	49	80	59	55	53	43	60	71	57	67	100	107

"No Shows"	6	6	3	2	8	8	7	13	2	8	13	12	19	9	14	7	14	4	9	4	1	2	6	7	8	9	5	8	7	6	11
All Appts. Scheduled	71	67	51	79	69	70	83	89	102	119	112	96	112	98	91	121	89	92	93	80	76	82	101	82	99	86	77	79	80	91	84

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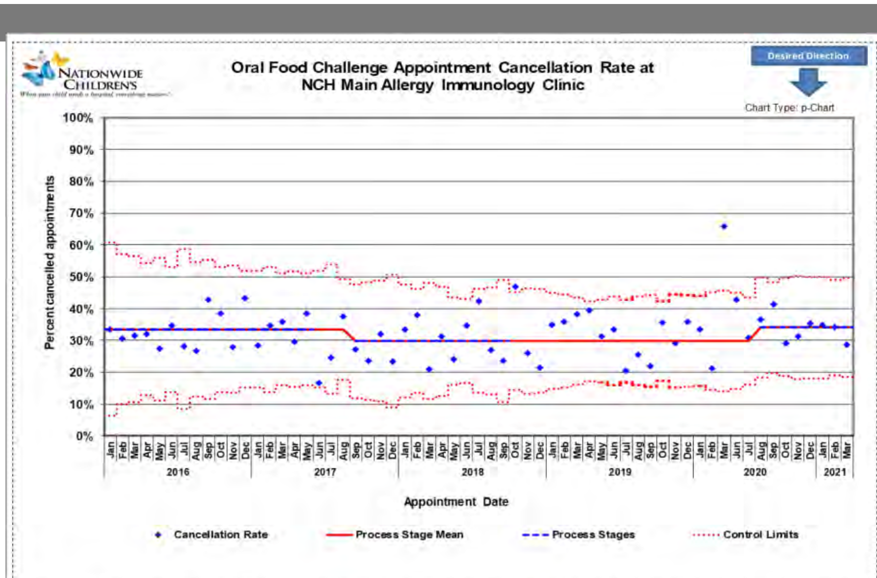

Cancellations	9	11	12	15	11	18	9	12	18	20	14	26	17	18	23	18	25	10	12	30	16	13	17	10	20	27	12	20	24	37
All Appts. Scheduled	27	36	38	47	40	52	32	45	42	52	50	60	60	52	64	61	65	60	49	80	59	55	53	43	60	71	57	64	100	107

Cancellations	30	18	12	37	18	15	29	32	39	47	35	32	23	25	20	43	26	33	31	17	50	35	31	30	41	25	24	28	28	31	24
All Appts. Scheduled	71	67	51	79	69	70	83	89	102	119	112	96	112	98	91	121	89	92	93	80	76	82	101	82	99	86	77	79	80	91	84

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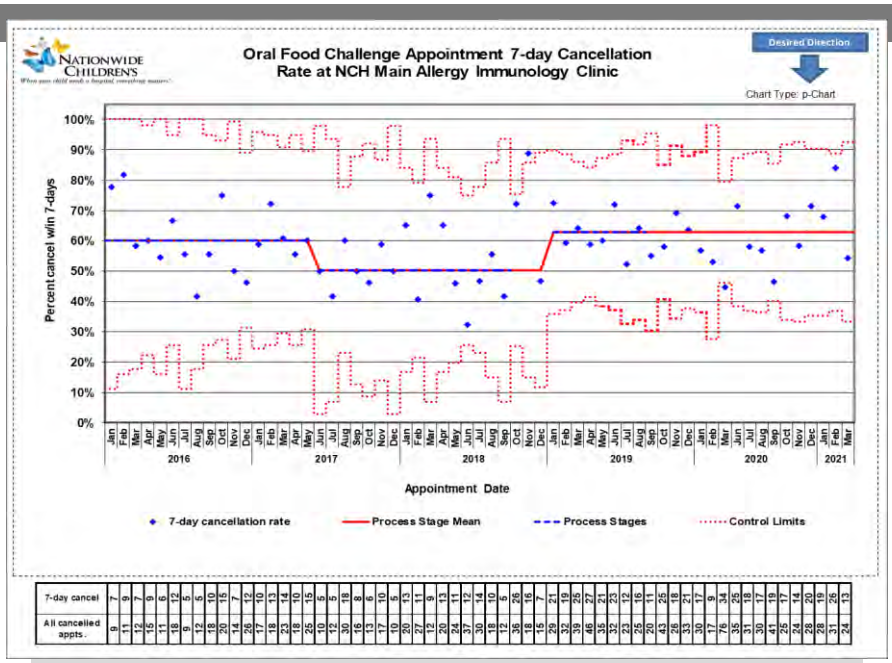

Patients who cancel within 7-days (including same day) of scheduled oral food challenge

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Food Allergy Treatment Center

Nationwide Children's
When your child needs a hospital, everything matters.

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Our Mission

Provide a comprehensive center dedicated to evidence based and personalized food allergy management for individual families, our community, and beyond.

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Hi - would you mind if one of our media folks from the hospital reached out to you? Please let me know if it's ever too much!!! Thanks - hope all is well

May 8, 2019, 10:04 AM ✓

Of course not! It'll never be too much. My hope is that more doctors will perform oral challenges and more parents will feel comfortable doing them. 😁

Thanks for all you do!

May 8, 2019, 10:16 AM

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Final Thoughts

- Oral food challenges offer a mechanism for families and patients to gain any semblance of control over a condition that is filled with uncertainty
- The information obtained is VALUABLE
- We can help our patients by giving them information, confidence, and experience

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Thank You

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