Risk Factors and Treatment Outcomes for Oral Immunotherapy–Induced Gastrointestinal Symptoms and Eosinophilic Responses (OITIGER)
Goldberg et al

What is already known about this topic? Recurrent non–IgE-mediated gastrointestinal symptoms occur during the course of oral immunotherapy.

What does this article add to our knowledge? These non–IgE-mediated gastrointestinal symptoms may be reversible or transient in most patients with dose modification. Their occurrence is related to oral immunotherapy starting dose, its rate of increase, and baseline absolute eosinophil count.

How does this study impact current management guidelines? Risk stratification based on baseline blood absolute eosinophil count may identify patients who would benefit from a slower oral immunotherapy dosing regimen and decrease the occurrence of oral immunotherapy–induced gastrointestinal and eosinophilic responses.

Association Between Folate Metabolites and the Development of Food Allergy in Children
McGowan et al

What is already known about this topic? Folate exposure has been proposed as a risk factor for the development of allergic disease. Unmetabolized folic acid (UMFA) is uniquely derived from synthetic folic acid exposure, and 5-methyltetrahydrofolate (5-MTHF) is the principal folate form involved in DNA methylation.

What does this article add to our knowledge? This is the first study to examine the association between UMFA/5-MTHF and the development of food allergy. We found that higher concentrations of UMFA at birth were associated with the development of food allergy.

How does this study impact current management guidelines? Our findings suggest that there may be unintended consequences from widespread folic acid fortification and supplementation in recent decades. However, whether this is due to increased exposure to folic acid or underlying genetic differences remains unknown.

Skin Prick Test Predictive Values for the Outcome of Cashew Challenges in Children
McWilliam et al

What is already known about this topic? Skin prick test (SPT) cut-offs with 95% positive predictive value (PPV) for food allergy are used commonly in clinical practice, but to date are limited to only a few food allergens.

What does this article add to our knowledge? This article is the first to report the SPT wheal size that correlates to 95% PPV for a positive food challenge for cashew in both a population and a clinic-based cohort of children, at 10mm and 14mm respectively.

How does this study impact current management guidelines? It is known that 95% PPVs can vary depending on the population they are generated from and this study has highlighted considerable variation between clinic and population based cohorts for the 95% PPV for cashew SPT and the generic SPT cut-off of 8mm used commonly in clinical practice may be too conservative for cashew.
Oral Food Challenge Implementation: The First Mixed-Methods Study Exploring Barriers and Solutions
Hsu et al

What is already known about this topic? Because of inaccuracies in commonly used food allergy testing including skin prick tests and specific IgE tests, oral food challenges (OFCs) are the criterion standard in diagnosis. However, despite this, clinician and patient barriers result in suboptimal OFC implementation.

What does this article add to our knowledge? Using data from multiple sources, we looked at barriers that are influential among both clinicians (allergists and pediatricians) and parents, and suggested solutions to mitigate those barriers.

How does this study impact current management guidelines? OFCs could be more accessible if standardized guidelines are created including which patients need in-hospital versus community OFCs, and family-centric information (including psychosocial resources) is provided. Parents and clinicians should be consulted in the creation of guidelines.

Clinical and Molecular Characterization of Walnut and Pecan Allergy (NUT CRACKER Study)
Elizur et al

What is already known about this topic? We previously showed that although all pecan-allergic patients are allergic to walnut, one-third of walnut-allergic subjects tolerate pecan. We also demonstrated that all walnut-pecan—allergic patients were desensitized to pecan after walnut oral immunotherapy.

What does this article add to our knowledge? Sensitization pattern to walnut components improved diagnosis of walnut allergy and distinction of dual walnut-pecan—allergic from single walnut-allergic patients. Competitive ELISA indicates that pecan comprises a subset of the allergenic determinants of walnut.

How does this study impact current management guidelines? The use of walnut components might reduce the need for oral food challenges when assessing patients with suspected walnut-pecan allergy. The molecular basis for walnut oral immunotherapy in desensitizing walnut and pecan allergies is provided.

Timing of Introduction, Sensitization, and Allergy to Highly Allergenic Foods at Age 3 Years in a General-Population Canadian Cohort
Simons et al

What is already known about this topic? Early dietary introduction of highly allergenic foods has been associated with decreased risk of food allergy in high-risk infants. Further information is needed regarding the importance of early introduction to highly allergenic foods in population-based cohorts.

What does this article add to our knowledge? This study examined associations between age of dietary introduction of peanut, egg, and cow’s milk in general-population infants and sensitization and possible or probable clinical IgE-mediated allergy to the specific highly allergenic food being introduced.

How does this study impact current management guidelines? General-population infants introduced to peanut before age 12 months showed lower peanut sensitization and allergy, even after exclusion of high-risk infants. Introduction of egg and cow’s milk before 12 months showed no increased risk.

A Pragmatic Trial of Symptom-Based Inhaled Corticosteroid Use in African-American Children with Mild Asthma
Sumino et al

What is already known about this topic? Symptom-based, as-needed use of inhaled corticosteroids (ICS) has been shown to provide asthma control and event rates comparable to daily ICS in rigorous controlled trials and has been recently added to the global asthma guideline.

What does this article add to our knowledge? To our knowledge, our study is the first real-world, open-label pragmatic study assessing the effectiveness of intermittent symptom-based use of ICS in children with mild asthma implemented by community primary care pediatricians.

How does this study impact current management guidelines? Intermittent, symptom-based use of ICS can be considered as an alternative patient-centered strategy in mild asthma in the primary care setting, especially in those who have difficulty in adhering to daily therapy.
Risk of Acute Myocardial Infarction and Ischemic Stroke in Patients with Asthma Exacerbation: A Population-Based, Self-Controlled Case Series Study
Raita et al 188

What is already known about this topic? Patients with asthma have a higher incidence of cardiovascular diseases (eg, acute myocardial infarction and ischemic stroke) through chronic activation of proinflammatory cytokines with resultant systemic and vascular inflammation.

What does this article add to our knowledge? By applying self-controlled case series design to population-based data, we identified that asthma exacerbation was associated with a significantly increased incidence of these cardiovascular outcomes—particularly in the first 1-week period after acute exacerbation.

How does this research impact current management guidelines? Our findings provide the opportunities for applying cardiovascular prevention measures to patients with severe asthma exacerbation during hospitalization and transition to outpatient care.

The Relationship of Psychological Factors and Asthma Control to Health-Related Quality of Life
González-Freire et al 197

What is already known about this topic? Anxiety, depression, avoidant coping, and asthma control (estimated by the patient or by the physician) affect quality of life; however, these factors have not been concurrently evaluated to determine their independent contribution to asthma quality of life.

What does this study add to our knowledge? Anxiety, depression, and patient-rated asthma control are important independent contributors to asthma quality of life and they are associated with almost all dimensions. The impact of physician-rated control and avoidant coping on quality of life is lower.

How does this study impact current management guidelines? Anxiety, depression, and control of asthma (preferably estimated by the patient) should be routinely screened in asthmatic patients, and interventions focused on these potentially modifiable factors should be implemented to improve quality of life in asthmatic patients.

Allergy Development in Adulthood: An Occupational Cohort Study of the Manufacturing of Industrial Enzymes
Larsen et al 210

What is already known about this topic? In the 1960s massive occupational exposure to industrial enzymes caused frequent sensitization and inhalation allergies. Problems were quantitatively diminished during the following decades but the literature is scarce, and no reliable incidence figures are available.

What does this article add to our knowledge? Studying 5000+ employees (50,000 person-years) we found solid evidence of a dose-response relationship between exposure to industrial enzymes and risk of developing IgE-mediated allergy. Importantly we also identified smoking as a major risk factor.

How does this study impact current management guidelines? Enduring exposure control can minimize the risk of occupational allergy, and surveillance of IgE sensitizations can be an indicator for exposure control.

How Maternal BMI Modifies the Impact of Personalized Asthma Management in Pregnancy
Murphy et al 219

What is already known about this topic? Fractional exhaled nitric oxide—based asthma management reduces exacerbations in pregnancy and infant bronchiolitis.

What does this article add to our knowledge? Effects are attenuated among obese mothers and those with excess gestational weight gain.

How does this study impact current management guidelines? Weight management is important for contributing to improved asthma management in pregnancy.
Small Airway Dysfunction by Impulse Oscillometry in Symptomatic Patients with Preserved Pulmonary Function
Chiu et al 229

**What is already known about this topic?** Compared with forced expiratory flow between 25% and 75%, impulse oscillometry (IOS) is an effort-independent utility to detect small airway dysfunction.

**What does this article add to our knowledge?** This study provides reference values of IOS parameters, and the IOS parameter resonant frequency is more sensitive than forced expiratory flow between 25% and 75% to detect small airway dysfunction.

**How does this study impact current management guidelines?** Patients with respiratory symptoms and preserved pulmonary function may have small airway dysfunction that can be diagnosed with IOS in addition to spirometry.

Atopic Dermatitis Endotypes Based on Allergen Sensitization, Reactivity to *Staphylococcus aureus* Antigens, and Underlying Systemic Inflammation
Leonard et al 236

**What is already known about this topic?** Atopic dermatitis is a chronic inflammatory skin disease characterized by significant barrier disruption that permits allergen penetration and microbial invasion.

**What does this article add to our knowledge?** Stratification of patients with atopic dermatitis on the basis of allergen sensitization profiles reveals differential systemic inflammation profiles and anti-*Staphylococcus aureus* toxin antibody levels.

**How does this study impact current management guidelines?** This study highlights the need to further characterize the allergen-specific responses in patients with atopic dermatitis because more personalized approaches to therapeutic intervention may be needed to effectively treat the differential systemic inflammation and microbial responses.

Atopic Eczema in Adulthood and Risk of Depression and Anxiety: A Population-Based Cohort Study
Schonmann et al 248

**What is already known about this topic?** Atopic eczema is a common debilitating skin condition. An association between atopic eczema and common mental disorders is well documented, but its nature and temporal direction remain unclear.

**What does this article add to our knowledge?** Individuals affected with atopic eczema are more likely to develop new depression (14% increased incidence) and anxiety (17% increased incidence). The observed dose-response relationship between atopic eczema severity and depression supports a causal mechanism for the association.

**How does this study impact current management guidelines?** Recent atopic eczema guidelines comment briefly on the influence of psychological and emotional factors on the clinical course of atopic eczema. Our findings suggest that depression and anxiety should be addressed explicitly in updated guidelines.

Multiple Drug Hypersensitivity Syndrome in a Large Database
Landry et al 258

**What is already known about this topic?** Multiple drug hypersensitivity syndrome is defined as confirmed drug hypersensitivity to at least 2 chemically and pharmacologically unrelated drugs. It is a very rare condition often overestimated because of lack of proper allergy testing.

**What does this article add to our knowledge?** On the basis of our experience in drug allergy practice, we confirmed that the prevalence of multiple drug hypersensitivity syndrome is very low (0.5%). Among patients with confirmed drug hypersensitivity, the prevalence is 2.5%.

**How does this study impact current management guidelines?** Further studies should associate in vivo and in vitro testing to better characterize these patients.
Validation of the Prescreening Intradermal Skin Test for Predicting Hypersensitivity to Iodinated Contrast Media: A Prospective Study with ICM Challenge
Lee et al

What is already known about this topic? The role of intradermal skin test for predicting hypersensitivity reaction to iodinated contrast media has not been fully evaluated due to limited data of positive predictive value.

What does this article add to our knowledge? Skin testing before a computed tomography scan does not predict the occurrence of hypersensitivity reactions to iodinated contrast media because of its extremely low sensitivity and positive predictive value.

How does this study impact current management guidelines? Intradermal skin test before performing computed tomography has no clinical value for prediction of a hypersensitivity reaction and should not be performed routinely.

Rituximab Unveils Hypogammaglobulinemia and Immunodeficiency in Children with Autoimmune Cytopenia
Ottaviano et al

What is already known about this topic? Postrituximab hypogammaglobulinemia can occur, but the prevalence in children with autoimmune cytopenia is unknown.

What does this article add to our knowledge? Persistent hypogammaglobulinemia after rituximab is associated with delayed B-cell recovery. Risk factors for persistent hypogammaglobulinemia included younger age, better overall response to treatment, and a diagnosis of autoimmune hemolytic anemia or Evans syndrome; an underlying primary immune deficiency was identified more frequently in these children.

How does this study impact current management guidelines? Persistent hypogammaglobulinemia after rituximab in children with autoimmune cytopenia should not always be interpreted as iatrogenic immunologic impairment because it may unveil a diagnosis of primary immune deficiency and should prompt further diagnostic tests.

Serum B-Cell Maturation Antigen (BCMA) Levels Differentiate Primary Antibody Deficiencies
Maglione et al

What is already known about this topic? Diagnosis of primary antibody deficiency requiring immunoglobulin replacement often necessitates laborious testing that can be impeded by medications.

What does this article add to our knowledge? Patients with common variable immunodeficiency and X-linked agammaglobulinemia have markedly reduced serum B-cell maturation antigen levels and its measurement may improve evaluation of primary antibody deficiency.

How does this study impact current management guidelines? Low levels of serum B-cell maturation antigen can identify severe primary antibody deficiency, without requiring stoppage of immunoglobulin replacement or protracted functional antibody evaluation.

Skewed Lymphocyte Subpopulations and Associated Phenotypes in Patients with Mastocytosis
Kulinski et al

What is already known about this topic? Mast cell mediators affect lymphocyte differentiation and function, but lymphocyte subpopulations have not been thoroughly examined in patients with mastocytosis who exhibit expansion of mast cells and increase in mediator release.

What does this article add to our knowledge? Adult patients with indolent systemic mastocytosis exhibit immunologic phenotypic alterations compared with the normal adult population including lower absolute counts of peripheral CD8+ T cells and circulating natural killer cells.

How does this study impact current management guidelines? Skewed lymphocyte subsets are a feature of mastocytosis, suggesting the need for determining the lymphocyte immunophenotypic profile in patients with indolent systemic mastocytosis and associated infectious complications and/or autoimmune findings.
Asthma Is the Dominant Factor for Recurrence in Chronic Rhinosinusitis  
Sella et al

What is already known about this topic? Patients with chronic rhinosinusitis may present different clinical outcomes, according to different phenotypes.

What does this article add to our knowledge? In this long-term study, we evaluated which clinical factors could be related to a higher chance of recurrence after endoscopic sinus surgery in a group of patients with chronic rhinosinusitis, both with and without nasal polyps.

How does this study impact current management guidelines? The presence of nasal polyps and asthma was strongly related to a higher chance for additional surgical procedure. Patients with these 2 conditions should be carefully followed after surgery.

Development of the Hereditary Angioedema Rapid Triage Tool  
Betschel et al

What is already known about this topic? Patients with hereditary angioedema (HAE) experience delays in diagnosis because they exhibit overlapping symptoms that are commonly associated with allergic or gastrointestinal conditions, leading to emergency department (ED) visits.

What does this article add to our knowledge? Currently, there are no tools that can quickly diagnose and appropriately manage patients with undiagnosed HAE who present to the ED.

How does this study impact current management guidelines? We developed a prototype tool that has the potential to facilitate the rapid triage of undiagnosed patients with HAE who present in the ED.

Eosinopenia, in Chronic Spontaneous Urticaria, Is Associated with High Disease Activity, Autoimmunity, and Poor Response to Treatment  
Kolkhir et al

What is already known about this topic? While blood basopenia has been linked to severe, antihistamine-resistant, and autoimmune urticaria, the role of eosinophils in chronic spontaneous urticaria is largely unknown.

What does this article add to our knowledge? Low blood eosinophil counts in patients with chronic spontaneous urticaria can point to severe disease and poor response to treatment.

How does this study impact current management guidelines? Eosinophil count is a cost-effective and easy-to-perform parameter approved by current urticaria guidelines. It may help physicians to identify the right patients for choosing the next step in the chronic urticaria algorithm.