



Immigrant Respiratory Health: a Diverse Perspective in Environmental Influences on Respiratory Health

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Abstract

Purpose of Review The aim of this review is to examine the prevalence of and impact of environmental exposures in the workplace and home on immigrant respiratory health in the USA.

Recent Findings Few studies report levels of workplace and home environmental exposures for immigrant children and adults, and documenting these findings is an important first step to addressing their respiratory health concerns. Rates of respiratory disease are lowest upon first arrival and increase with duration of residency in the USA. Community Health Workers may be an efficacious intervention to reducing exposures and improving lung health among immigrant populations.

Summary Immigrant children and adults have a high risk of occupational and home environmental exposures that can negatively affect their respiratory health. While limited studies exist, more documentation of these exposures and their impact on immigrant person's respiratory health are needed to begin to tackle these disparities.

Keywords Adult allergy · Allergy · Asthma · Allergen exposure · Immigrant allergy · Immigration and allergy · Occupational asthma · Pediatric allergy

Introduction

Asthma affects approximately 24.6 million adults and children in the USA [1]. With the growing immigrant population in the USA, and their increased vulnerability to environmental exposures that can lead to respiratory diseases, this is an

important underserved population that demands attention and resources.

Between 2000 and 2007, the immigrant population in the USA increased by almost 35%, from about 28.3 million to 38.1 million [2, 3]. Their legal status, education level, socio-economic status, ethnicity, and language barriers [4–9] make them vulnerable to a lack of knowledge of their rights to demand better working and living conditions and to poor access to occupational health services and housing advocacy agencies [8, 10]. In turn, these work and home environmental exposures may increase the rate and impact of respiratory disease in their communities. The aim of this review was to assess the prevalence of respiratory disease and impact of environmental exposures in the workplace and home in adult and pediatric immigrant populations in the USA.

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Methods

This article represents a review of the recent literature (2010 to present) on respiratory disease, specifically asthma, in the immigrant population. This search was not limited by country of origin, sex, age, type of study, nor occupation. The initial search took place using the MEDLINE-OVID search engine.

Search terms from previous systematic reviews were modified [11•], and the search initially included all allergic disease states including asthma, allergic rhinitis, allergic rhinoconjunctivitis, food allergy, food hypersensitivity, atopic dermatitis or eczema and urticaria and allergy. The search was then limited to the English language, human studies, and studies performed in the USA. Three-hundred and fifteen articles were originally identified after duplicates were removed, but after removal of those articles that were published prior to 2010, were not on the correct topic, and/or were performed outside of the USA, 34 articles remained. Because there were minimal articles on allergic diseases other than asthma, the authors decided to focus this article on immigrant health as it relates to asthma or allergic respiratory disease. Of the remaining 18 articles, three were excluded because they were related to asthma, but focused on another unrelated disease, and the final 15 articles were included in this review.

Results

All studies included in this review can be found highlighted in the accompanying table (Table 1) in alphabetical order of the published first author's last name.

Adult

Prevalence

In a study of over 16,000 Latino adults across the USA, called the Hispanic Community Health Study/Study of Latinos (SOL), the greatest prevalence of asthma was seen in the Puerto Rican population (36.5%, 95% CI, 33.6–39.5%) [12•]. Prevalence in all populations of Latinos significantly increased ($p < 0.001$) if the individual was US-born (19.6%) and a long-term US resident (19.4%) compared to a recent immigrant (14.1%) [12•]. The reported prevalence are higher than the US baseline prevalence of asthma in Whites [13]. While the Mexican Immigration to California: Agricultural Safety and Acculturation (MICASA) population-based study that interviewed Mexican-American adults in their homes in Spanish found an overall prevalence of asthma of 6.0%, 12.9% of participants reported having a respiratory symptom seen in asthma [14]. Agricultural work was associated with asthma (OR 1.04; 95% CI 1.00 to 1.09) and medium to highly acculturated women were six times more likely to have asthma (95% CI = 1.40 to 26.29) [14] and seven times more likely to have chronic bronchitis (OR 3.60; 95% CI 1.16 to 11.16) [14]. Men did not demonstrate the same association [14].

Corlin et al. used data from the Community Assessment of Freeway Exposure and Health Study to examine the prevalence of chronic disease in Chinese immigrants in comparison to US-born Whites [15]. Chinese immigrants were found to be less likely than their US-born White counterparts to have asthma (OR 0.20, 95% CI = 0.09–0.48) [15]. They also reported less tobacco use, less perceived stress, better diet, and higher levels of exercise than the US-born whites. The study did not assess whether asthma prevalence rates changed over time in the USA [15]. An analysis of Asian immigrants from the National Latino and Asian American Study found that individuals of Chinese origin were more likely to have hay fever and allergies compared to Filipinos [16]. On the other hand, Filipinos reported the highest rate of asthma among Asian groups [16]. While Vietnamese-American men had the highest rate of both current (29.4%) and past tobacco (27.4%) use, Filipino-American men had the highest rate of marijuana use (46.1%) [16]. No correlations were made between rates of tobacco or marijuana use and prevalence of asthma [16]. A New York City-based analysis of the Community Health Survey also found asthma to be less prevalent in those who were foreign-born vs US-born (OR 0.43, $p < 0.001$) and found that this discrepancy was even higher in immigrants from countries with low gross national income [17].

Occupational Exposures

In a cross-sectional analysis of predominantly Latino (98%) young migrant farm workers living in employer housing, only 3.8% of the sample reported asthma, yet 60% experienced a wheezing sound outside of illness [18]. Specific exposures were associated with certain asthma-related symptoms, including pesticides and chest tightness ($p = 0.0001$) [18] and mold with productive cough ($p = 0.0262$) [18]. Of note, in this population where 42% were living in barracks, they reported elevated rates of nasal (16.5%) and skin (22.4%) allergies [18].

A survey administered by the Oregon Health and Sciences University and the Asian Health and Services Center to a population of predominantly female nail salon workers of Vietnamese descent found a discrepancy between the prevalence of symptoms individuals admitted to experiencing themselves vs what they reported observing in their colleagues [19•]. Specifically, they reported lower rates of skin irritation (11%), cough (9%), and difficulty breathing (3%) in themselves compared to their co-workers (in skin irritation (26.2%), cough (10.8%), and difficulty breathing (4.6%)) [19•]. Proper use of ventilation was inconsistent and application of acrylic nails was associated with worse health ($p = 0.004$) [19•]. Material safety data sheet (MSDS) sheets of the chemicals used were only reportedly available in 26.1% of the salons [19•].

Table 1 Relevant articles in immigrant respiratory health

Reference	Population (N)	Intervention	Control	Outcomes/results	Timeframe	Setting
Balcazar 2015	n = 1568 caregivers of children of Hispanic origin, 4th to 5th graders in the El Paso Independent School District	Cross-sectional analysis of primary survey data sent to 6295 households looking at generational effect on immigrant children's health status	General population of El Paso, TX	30.2% response rate. Sample characteristics: current asthma 8%, bronchitis 9%, and 50% with allergies overall. Findings: asthma—the 4th generation vs 2nd ($p < 0.10$), 2.5 ($p < 0.10$), 3rd ($p > 0.10$) generation children were more likely to have current asthma. Allergies: 3rd and 4th generations were more likely to have allergies ($p < 0.10$) than the 1st generation. Findings: physician-diagnosed asthma prevalence greater in Puerto Ricans (36.5%, 95% CI, 33.6–39.5%). Increased asthma prevalence in US-born or long-time residents of USA vs those who came to USA as adults (19.6, 19.4 and 14.1%, $p < 0.001$).	Year 2012	Hispanic, urban, El Paso, TX, on Mexico-USA border
Barr 2016	n = 16,415 Hispanics/Latinos, ages 18–74 years old	Hispanic Community Health Study/Study of Latinos	No control group	Findings: foreign-born had lower odds of asthma vs US-born (OR 0.43, $p < 0.001$), gross national income (GNI) was seen associated with asthma specifically lower GNI in country of birth less likely to have asthma than a high GNI country (OR 0.26, $p = 0.014$). Chinese immigrants had less tobacco use (OR = 0.31, 95% CI = 0.16–0.60) and exposure (OR = 0.34, 95% CI = 0.18–0.66) than US Whites, had a more favorable diet and exercise behaviors, less perceived stress ($t = 5.65$, $p < 0.001$), and are less likely to have asthma (OR 0.20, 95% CI = 0.09–0.48). Length of time in USA did not associate with asthma.	Years 2008–2011	New York, Chicago, Miami, and San Diego
Chang 2014	n = 9860, age > 18 years old	Cross-sectional analysis of the Community Health Survey	No control group	Findings: Chinese origin had a higher rate of allergies/hay fever where Filipinos had the highest rate of asthma. Vietnamese men had highest rate of current smokers (29.4%) and past smokers (27.4%).	Year 2009	New York City
Corlin 2014	n = 147 Chinese immigrants and US-born Whites n = 167, mean age 62.5 years (total subset, not used in this analysis was 704 participants)	Cross-sectional analysis of health conditions found in the Community Assessment of Freeway Exposure and Health study	US-born Whites	Findings: Chinese origin had a higher rate of allergies/hay fever where Filipinos had the highest rate of asthma. Vietnamese men had highest rate of current smokers (29.4%) and past smokers (27.4%).	Years 2009–2012	Chinese participants lived primarily in Chinatown while US-born Whites lived in Somerville, Dorchester and Malden, Boston, Massachusetts
Huang 2013	n = 998 (> 18 years of age, mean age 41)	National Latino and Asian American Study epidemiologic survey	No control group	Findings: Chinese origin had a higher rate of allergies/hay fever where Filipinos had the highest rate of asthma. Vietnamese men had highest rate of current smokers (29.4%) and past smokers (27.4%).	Years 2002–2003	National sample of Latino and Asian American population
Johnson 2010	n = 600 for analysis		No control group		Years 2001 to 2002	Urban, Detroit, Michigan

Table 1 (continued)

Reference	Population (N)	Intervention	Control	Outcomes/results	Timeframe	Setting
Kearney 2014	<i>n</i> = 352, average age: 33 years	Arab-American Health Project (AAEHP), survey to Arab-American homes in Detroit, Michigan. They created an environmental risk index for 17 risk and protective factors called the Environmental Risk Index (ERI).	No control group	Findings: health care access was associated with asthma ($p = 0.025$), ERI was associated with asthma ($p = 0.034$) and odds of asthma greater with the higher the risk factors. Hypertension was also associated with asthma ($p = 0.0006$) as well and seems to also be related to ERI ($p = 0.015$). Findings: 95.2% were Mexican in origin, 98% Latino with 42% living in barracks, and 36% never smoked. Wheezing in 11.4%, wheezing/whistling sound without a cold in 60%, chest tightness at night 16.8%, shortness of breath 14.0%, coughing episodes 97.4%, asthma 3.4%, nasal allergy in 16.5%, skin allergy in 22.4%. Spirometry was mostly normal in almost all participants. Pesticides used in the home was associated with chest tightness ($p = 0.0001$), coughing up phlegm associated with mold in the home $p = 0.0262$.	Unknown	16 counties in Eastern North Carolina
Kim 2014	<i>n</i> = 1322, children	Cross-sectional analysis from a English/Spanish survey that was mailed to caregivers of 4th/5th grade students in the El Paso Independent School District investigating with 3 models: model 1—“determinants of current wheeze are modeled with only individual level,” model 2—“neighborhood-level percent foreign-born variable is included,” and model 3—“cross-level interaction model that includes interactions between the individual level and percent foreign-born influences”	No control group	Primary outcome: increased wheezing the longer a child was in El Paso and if caregiver was from the USA. Being born in another country is negatively associated with wheezing (OR = 0.983). Poverty reduced odds of wheezing as immigrant density increased, foreign-born primary caregivers reduced wheezing when immigrant density was higher ($p = 0.065$). “Foreign-born density significantly predicts asthma diagnosis at the $p < 0.05$ level and maintains the same directionality as current wheeze.”	Year 2012	El Paso, TX
Koimis-Mitchell 2011	<i>n</i> = 232 Latino children, mean age 10.6 years with Dominican and Puerto Rican caregivers	Rhode Island-Puerto Rico Asthma Center (RIPRAC)	No control group	Findings: asthma severity and functional limitation was not significantly different in immigrant	Unknown	Urban Rhode Island

Table 1 (continued)

Reference	Population (N)	Intervention	Control	Outcomes/results	Timeframe	Setting
Litt 2010	n = 473, recently immigrated Mexican families, primary language Spanish, children lived in home < 18 years, one parent must be foreign-born and in the USA < 10 years.	Population-based descriptive study using promotoras de salud	No control group	<p>populations. Acculturative stress was higher in island PR born caregivers vs US-born caregivers ($F(2,219) = 3.57, p < 0.05$), family cohesion highest in those PR- and DR- born ($F(2,232) = 0.16; p < 0.001$), mediational analysis showed that caregiver nativity and cultural stress seem to be independent of each other.</p> <p>Findings: 28% with "adequate ventilation potential," dampness in homes. Basement used for living in 20%. Wheezing increased with decreased "Ventilation Potential Score (VPS)," $p = 0.02$. Children with pests in home likely to have current wheezing ($p = 0.02$), two times as likely to have atopic symptoms ($p = 0.05$). 1.8% prevalence of "ever had asthma."</p>	Years 2005–2007	Urban, industrial area north of Denver, Colorado
Martin 2011	n = 11, community health workers	Community-based participatory Community Health Worker training evaluation, pre/post	No control group	<p>Findings: asthma knowledge improved after training ($p < 0.01$), 70% pre-training and 90% post-training could identify controllers ($p = 0.50$). The higher acculturation, the better the asthma knowledge improved ($p = 0.04$). Ten percent could identify an inhaled steroid prior to the course and after 91% could ($p < 0.01$). Inhaler technique also improved with 25% at baseline and 69% post-training ($p < 0.01$), positively correlated with acculturation score $p < 0.01$ for both MDI alone and MDI with spacer</p>	Year 2009	Low-income, urban Mexican-American population on the South Side of Chicago
Postma 2011	N = 866, children, mean age 5.6 years (4.6 SD), n = 312 used in analysis	The Childhood Asthma Project through the Yakima Valley Farm Workers Clinic's (YVFWC), home-visitation program with CHWs to reduce environmental triggers for children with asthma. Pre-/post-design, retrospective study	No control group	<p>Primary: there was a statistically significant difference in Emergency Room (0.46 (9) vs 0.22 (5) z score - 4.76 $p < 0.0005$) and hospital admissions (0.15 (3) vs 0.01 (3) z score - 5.567 $p < 0.0005$) after the CHW intervention. Secondary outcomes: statistically significant improvement seen in medication</p>	Years 2002 to 2006	Rural, 100% migrant population

Table 1 (continued)

Reference	Population (N)	Intervention	Control	Outcomes/results	Timeframe	Setting
Singh 2013	n = 91,532 children of immigrant and US-born parents < 18 years	Cross-sectional analysis of primary survey data from the 2007 National Survey of Children's Health	No control group	and device management ($z = -9.803$, $p < 0.0005$ ($n = 253$)), environmental trigger reduction measures in child's bedroom ($z = -12.628$, $p < 0.0005$, $n = 259$), indoor asthma triggers ($z = -9.162$, $p < 0.0005$, $n = 236$), and cleaning throughout the home ($z = -7.432$, $p < 0.0005$, $n = 239$), but not in outdoor asthma triggers. Response rate 46.7%, 12,539 children with immigrant parents were 42.8% Hispanic, 30.1% non-Hispanic White, 12.4% Asian, 5.9% non-Hispanic Black, and 8.8% other. Findings: immigrant children were less likely to have asthma ($p < 0.001$) than native-born children and less likely to have respiratory allergy ($p < 0.001$). If immigrant non-Hispanic White, non-Hispanic Black, and Hispanic children had health insurance, they had a 31, 40, and 56% lower odds of asthma vs native-born non-Hispanic White ($p < 0.01$). Asthma increased as time in USA increased. Exposure to tobacco smoke was less likely in children of immigrant children ($p < 0.001$), and children of immigrant parents were more likely to be inactive ($p < 0.001$).	Years 2007 to 2008	US survey, represents approximately 1800 children/state
Stoecklin-Marois 2015	n = 702, adults, mean age 37.7 years (10.0)	Mexican Immigration to California: Agricultural Safety and Acculturation (MICASA) population-based study using home interviews by Spanish speakers	No control group	Findings: prevalence—asthma (6.0%), chronic cough (5.0%), chronic bronchitis (3.1%), and persistent wheeze (6.7%) with 12.9% having 1 or more respiratory symptoms. Current smokers demonstrated a higher prevalence of chronic cough ($p = 0.01$), but not significant for asthma. Men had more exposure to dust in their work environment. Long-standing agricultural work was associated with asthma (OR 1.04; 95% CI 1.00 to 1.09), medium/high acculturated women	Years 2006 to 2007	California's Central Valley

Table 1 (continued)

Reference	Population (N)	Intervention	Control	Outcomes/results	Timeframe	Setting
White 2017	n = 65, 94% female	Cross-sectional analysis of a survey of nail salon workers of Vietnamese descent from the Oregon Health and Sciences University and Asian Health and Services Center	Previous study completed in California with an n = 73 by the California Health Nail Salon Collaborative	<p>were 6 times more likely to have asthma (95% CI= 1.40 to 26.29) and 7 times to have chronic bronchitis (OR 3.60; 95% CI 1.16 to 11.16). Men did not have same association.</p> <p>Findings: 23% reported nasal irritation, 21.5% allergy symptoms, 11% skin irritation, 9% cough, 3% difficulty breathing, and 1.5% asthma in themselves but reported a higher percentage in allergies (40%), skin irritation (26.2%), cough (10.8%), and difficulty breathing (4.6%) when reporting for a co-worker.</p> <p>Knowledge of what an MSDS sheet was at 54.7% and MSDS information reportedly available in 26.1% of the salons. Application of acrylic nails reported fair or poor general health more often 83.3 vs 48.5%, p = 0.004.</p>	Unknown	Portland, Oregon

Home Exposures

The Arab-American Health Project (AAEHP) reviewed both protective and adverse environmental risk factors, to create an environmental risk index (ERI) to evaluate for exposures and their association with chronic disease in Arab-American adults in Detroit, Michigan [20]. Low health care access ($p = 0.025$) [20] and high ERI ($p = 0.034$) [20] were associated with asthma, and the odds of asthma increased with a higher number of risk factors [20]. Interestingly, this study showed hypertension also being related to both asthma and a high ERI [20].

Pediatric

Environmental Exposure and Prevalence

Investigators in El Paso, Texas, surveyed parents of fourth and fifth graders to identify who had asthma, and if the duration of residence in the USA was associated with asthma prevalence [21]. Specifically, rates of current wheeze increased the longer a child resided in El Paso, Texas (OR 0.983 [21]). Being foreign-born was negatively associated with wheeze ($p < 0.05$) [21]. Lastly, exposure to indoor mold was also found to be associated with wheeze ($p < 0.10$) [21]. An additional study conducted in the same patient population demonstrated a clear generational effect on asthma prevalence rates [22•]. While the overall prevalence of asthma among students was 8%, the fourth generation had the highest, the third generation had the second highest, and the first generation had the lowest prevalence of asthma [22•].

Looking further into environmental exposures in Mexican-American families, a group in Colorado created a ventilation potential score (VPS) to assess participants indoor air quality [23]. While dampness was found in 44% [23], adequate ventilation was reported in only 28% of the homes [23]. Wheezing symptoms were found to be associated with worse VPS ($p = 0.02$) [23]. Although families reported an asthma prevalence of only 1.8% [23], children with pests in the home were more likely to have wheezing symptoms ($p = 0.02$) [23] and twice as likely to have other atopic symptoms ($p = 0.05$) [23].

Koinis-Mitchell and colleagues investigated children of Puerto Rican and Dominican descent in Rhode Island [24]. They did not find a difference in asthma severity between Puerto Rican and Dominican populations in Rhode Island [24]. Island-born Puerto Ricans were found to have increased prevalence of asthma ($p = 0.05$) [24] and acculturative stress ($p < 0.05$) [24]. This finding is similar to what others have found regarding Puerto Rican children, specifically that compared to US children, Puerto Rican children are more likely to

have asthma and their asthma is also more likely to be more severe [25•, 26•].

Singh et al. conducted a telephone survey of a diverse group of caregivers (42.1% Hispanic, 30.1% non-Hispanic White, 12.4% Asian, 5.9% non-Hispanic Black, and 9.9% other) of over 90,000 children across the USA [27]. Similar to what was seen in the adult studies, immigrant children were less likely to have asthma ($p < 0.001$) vs US-born White children [27] and increased asthma prevalence was associated with increased duration of residence in the USA [27].

Community Health Workers

Two studies highlighted the potential role of the community health worker (CHW) in the context of immigrant asthma and environmental exposure reduction, and to help enhance asthma-related knowledge. In the first study, investigators in California assessed the exposures children of farm workers experienced and how that affected their respiratory health [28]. The Childhood Asthma Project, through the Yakima Valley Farm Workers Clinic's home visitation program, utilized CHWs to reduce environmental triggers [28]. Several indoor environmental exposures were reduced significantly ($p < 0.0005$) [28], especially within the child's bedroom ($p < 0.0005$) [28]. They found a statistically significant reduction in emergency department visits ($p < 0.0005$) [28], hospital admissions ($p < 0.0005$) [28], and indoor environmental trigger exposures ($p < 0.0005$) [28]. Additionally, the children's asthma self-management skills improved in the areas of medication and device management ($p < 0.0005$) [28].

An intervention to promote asthma education and self-management skills for low-income Mexican-American CHWs in Chicago demonstrated successful CHW training methods that could be further utilized in the immigrant population [29]. Martin et al. reported that after successful CHW training, the CHW's asthma knowledge ($p < 0.01$), inhaler technique (25 to 69%, $p < 0.01$), and identification of an inhaled steroid medication (10 to 91%, $p < 0.01$) improved [29]. Of note, inhaler technique improvement also positively correlated with higher acculturation score of the CHW ($p < 0.01$) [29].

Discussion

This review aimed to assess the impact of environmental influences on respiratory health in diverse adult and pediatric immigrant populations in the USA [12•, 14–24, 27–29]. Across studies, the prevalence of respiratory disease in immigrant populations is consistently lowest upon arrival [12•, 14, 17, 21, 22•, 27] and increases with duration of residency in the USA [12•, 14, 21, 27] and in future generations [22•]. This

trend is seen regardless of the person's country of origin or age [17, 27]. Further study of this phenomenon, and the underlying causative factors, may help us to better understand why the prevalence of allergic respiratory diseases is higher in the USA than that in other countries [30, 31].

While alarming occupational exposures in immigrant populations are well documented, resources to address workplace conditions are lacking [14, 18, 19]. It is necessary to fervently protect vulnerable immigrant workers from occupational exposures that may affect their health, as well as their children's health, as they may feel that they have no choice but to accept these work conditions. In addition, they may not have the knowledge or resources to know how to advocate for themselves or contact agencies to monitor and ensure a safe workplace.

As demonstrated in the study by Martin et al., CHWs offer promise as an efficacious intervention to improve asthma outcomes for immigrant populations [29]. Historically, CHW interventions have demonstrated improvements in clinical outcomes and reductions in exposures to respiratory triggers in the home [32, 33, 34, 35]. As health workers who are also trusted members of the communities they serve, they can function as bridges between immigrant individuals and health care systems, increasing the quality of and access to services [36].

This review has several limitations. Although articles were researched methodically similar to that of a systematic review, this review was neither a meta-analysis nor a systematic review that was true to PRISMA guidelines [37]. Furthermore, in order to limit the review to the most recent literature, important studies in this area conducted prior to 2010 were not included. Finally, because there are few studies on immigrant respiratory health, and the existing studies often focused on only one group (e.g., only Chinese vs only Hispanics), it is not possible to generalize findings across immigrant populations. Strengths of this review include that it encompasses both adult and pediatric populations as well as environmental exposures within the workplace and home. In addition, both authors have research and clinical expertise in caring for underserved, largely immigrant, populations.

Conclusion

In conclusion, immigrant populations suffer a disproportionate burden of respiratory disease prevalence and morbidity that may be largely attributed to occupational and home environmental exposures [12, 14–24, 27–29]. As clinicians caring for this vulnerable population, it is important to advocate for additional protection in their workplace and residence, as well as be sensitive to these unique environmental exposures in order to provide optimal treatment of their respiratory conditions.

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Compliance with Ethical Standards

This review is in compliant with ethical standards.

Conflict of Interest Giselle Mosnaim receives research grant support from GlaxoSmithKline and Propeller Health, owns stock options in Electrocore, and serves as a consultant and/or member of a scientific advisory board for Electrocore, GlaxoSmithKline, Teva, Novartis, Astra Zeneca, Boehringer Ingelheim, and Propeller Health. Andrea Pappalardo served on the Speaker's Bureau for Boehringer Ingelheim in 2017.

Human and Animal Rights Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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- Of major importance

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