

Discussion | Use of legal performance-enhancing substances among young adult men (aged 18-26 years) was significantly prospectively associated with anabolic-androgenic steroid use at 7-year follow-up (aged 24-32 years). To our knowledge, this is the first longitudinal investigation of this association among a nationally representative sample. Results suggest that legal performance-enhancing substance use may serve as a gateway to anabolic-androgenic steroid use. This has significant implications for regulation of legal performance-enhancing substances, which are relatively common among the adolescent and young adult population,^{1,2} accessible over the counter, and unregulated by the US Food and Drug Administration.⁴ The notion that use of legal performance-enhancing substances may lead to a 3-fold increased risk for future use of illicit anabolic-androgenic steroids provides support for increasing state and federal regulation of these products. Limitations to this study include self-reported data, lifetime (as opposed to 12-month) assessment of anabolic-androgenic steroids use, inability to distinguish between prescription or nonprescription anabolic-androgenic steroid use, and inability to analyze associations between specific substances (ie, creatine monohydrate or androstenedione) and anabolic-androgenic steroid use.

Conclusions | The current study suggests that use of performance-enhancing substances among young men may increase vulnerability for anabolic-androgenic steroid use in young adulthood. Health care professionals should monitor and screen for anabolic-androgenic steroid use among adult men who have previously used legal performance-enhancing substances and refer patients to mental health and substance abuse treatment when appropriate.

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Allergen Specificity in Specific IgE Cutoff

The specific IgE (sIgE) cutoff of 0.35 kU_A/L used to confirm allergic sensitization originates from the detection limit of the first assays available. This has been shown to have limited clinical relevance and little concordance with the skin prick test,¹ which may be partially explained by the uniform use of this cutoff value for all tested allergens. There are substantial differences between the individual allergens as to molecular structure, affinity, and classes and newer assays have a lower detection limit of 0.1 kU_A/L.

Methods | In this cohort study, we investigated the distribution of sIgE levels to 5 common aeroallergens in 835 children age 6 years from the at-risk Copenhagen Prospective Study on Asthma in Childhood₂₀₀₀ (COPSAC₂₀₀₀) and the population-based COPSAC₂₀₁₀ mother-child cohorts.² We also investigated the distribution of sIgE levels among the children with symptoms of allergic rhinitis (AR) to the allergen in question.

The sIgE levels were assessed for *Dermatophagoides pteronyssinus* (HDM), cat, dog, grass, and birch using ImmunoCAP (Thermo Fisher Scientific) in 296 of the 411 children from COPSAC₂₀₀₀ (72%) and 539 of the 700 children from COPSAC₂₀₁₀ (77%). The diagnosis of AR was made by the COPSAC pediatricians through structured parental interviews requiring congruence between symptoms and relevant allergen exposure.

Figure. Distribution of Specific IgE (sIgE) Levels to 5 Common Aeroallergens

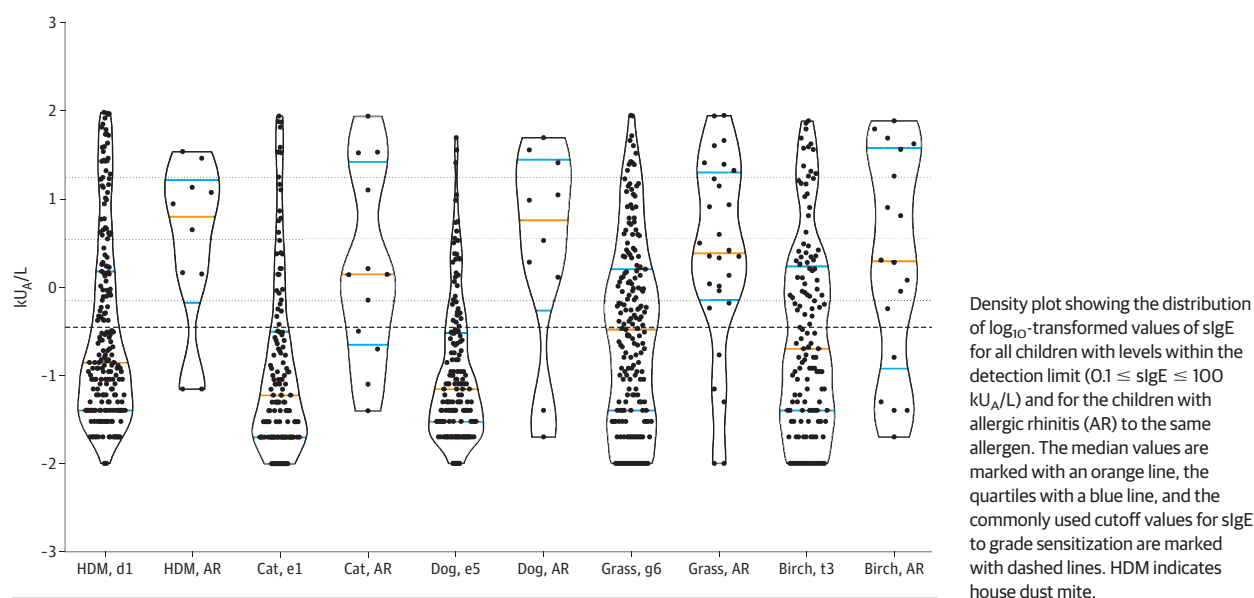


Table. Median Values of Specific IgE and the 25% and 75% Percentiles Among All Children With Measurable Levels and Among Children With AR to the Same Allergen

Participants	HDM	HDM, AR	Cat	Cat, AR	Dog	Dog, AR	Grass	Grass, AR	Birch	Birch, AR
No.	207	10	133	12	158	10	191	28	133	18
Median (IQR), kU _A /L	0.14 (0.04-1.51)	6.29 (0.67-16.4)	0.06 (0.02-0.31)	1.41 (0.22-26.5)	0.07 (0.03-0.30)	5.73 (0.54-28.1)	0.33 (0.04-1.60)	2.43 (0.72-20.0)	0.20 (0.04-1.72)	1.97 (0.12-37.9)

Abbreviations: AR, allergic rhinitis; HDM, house dust mite; IQR, interquartile range.

The Copenhagen Ethics Committee (HKF 01-289/96) and the Danish Data Protection Agency (2008-41-2434) approved the study. Oral and written informed consent was obtained from all parents. Prism 8 (GraphPad) was used to calculate values in the **Figure** and the interquartiles ranges (IQRs).

Results | The $\log_{10}$ -transformed levels of sIgE against the 5 individual allergens for children with values within the detection limit of 0.1 to 100 kU_A/L and for children with AR to the same allergen are shown in a density plot in the **Figure**. The median values and the 25% and 75% values of sIgE levels are listed in the **Table**.

The median (IQR) value of sIgE in all children varied among the 5 allergens: HDM, 0.14 kU_A/L (0.04-1.51); cat, 0.06 kU_A/L (0.02-0.31); dog, 0.07 kU_A/L (0.03-0.30); grass, 0.33 kU_A/L (0.04-1.60); and birch, 0.20 kU_A/L (0.04-1.72). In the children with AR to the same allergen, the median (IQR) values of sIgE were higher and had great variation: HDM, 6.29 kU_A/L (0.67-16.4); cat, 1.41 kU_A/L (0.22-26.5); dog, 5.73 kU_A/L (0.54-28.1); grass, 2.43 kU_A/L (0.72-20.0); and birch, 1.97 kU_A/L (0.12-37.9). An overlap existed in levels between symptomatic and asymptomatic children, with many asymptomatic children demonstrating very high levels.

Discussion | These findings highlight the problem of using the same sIgE cutoff for all allergens. Our results align with pre-

vious studies that have attempted to define new sIgE sensitization thresholds for food allergens by using double-blinded placebo-controlled food challenges.³ They report a much higher cutoff value for predicting clinical reactivity than the current sensitization threshold of 0.35 kU_A/L and great variation in cutoffs between allergens. For aeroallergens, to our knowledge only few studies have tried to define the levels of sIgE separating symptomatic and asymptomatic individuals. One cross-sectional study of children and adults also showed results in agreement with ours; however, they grouped the aeroallergens in seasonal and perennial allergens, not showing results for the individual allergens.⁴

Furthermore, there is a potential importance of low levels of sIgE. A Swedish study of 268 children showed that sIgE levels between 0.1 to 0.7 kU_A/L to egg and/or cow's milk early in life increased the risk of sensitization and eczema later in childhood.⁵ Additionally, newer studies of wasp venom allergy and drug allergies indicate the importance of low levels of sIgE in terms of clinical reactivity.⁶ Therefore, we cannot rule out that even low levels of sIgE may be of biological importance (eg, for predicting later symptomatic allergic disease).

Conclusions | We find that a uniform sIgE cutoff value across allergens does not exist. We advocate that updated cutoffs should be made to correctly predict clinically relevant sensitization.

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Cumulative Incidence of Child Protection Services Involvement Before Age 5 Years in 153 670 Australian Children

Child maltreatment has immediate and lifelong consequences for health and well-being and is costly for governments.¹ Historically, reporting of child protection services (CPS) contacts has offered a system view of child protection based on point incidence. Because CPS data have become increasingly available for research, the scale of the child maltreatment problem across the life span has begun to emerge. In the US, maltreatment is investigated in 37% of children,² confirmed in 13% of children,³ and results in the placement of 6% of children in out-of-home care (OOHC) at least once by the time the child is 18 years of age. In New Zealand, 24% of children born in 1998 had 1 or more CPS notifications, 10% had experienced substantiated maltreatment, and 3% had 1 or more OOHC placements by 17 years of age.⁴ More than one-third of New Zealand children reported to CPS by adulthood were first reported by age 5 years.⁴ This study used cross-sectoral data linkage to quantify the cumulative incidence of CPS involvement before 5 years of age among children in their first year of school in New South Wales, Australia.

Methods | We used linked birth registrations, perinatal records, and CPS data for 153 670 Australian children who started school in New South Wales in 2009 or 2012 and had a birth record in New South Wales. Ethical approval was obtained from the New South Wales Population Health Services and Research Ethics Committee, the New South Wales Aboriginal Health and Medical Research Council Ethics Committee, and the Australian National University Human Research Ethics Committee, which included a waiver of consent to obtain the deidentified, population-level data for this record linkage cohort study. Data on CPS outcomes included notifications that were screened in after meeting the statutory threshold for risk of significant harm, investigations, incidents of substantiated maltreatment, and OOHC placements.

We estimated children's ages at the first of each CPS outcome using date of birth and the outcome. The numerator for age-specific cumulative incidence was the cumulative number of children with 1 or more CPS outcomes at each age. Because the cohort was defined as children who started school in 2009 or 2012, the denominator was 153 670 children for all incidence estimates from 0 to 5 years. We report the cumulative incidence of primary substantiated neglect and physical,