



CORRESPONDENCE

Chlorinated pool exposure, allergic sensitization, and risk of age 5-year asthma

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Bronchiolitis is an infection of small airways causing breathing difficulties in young children. This infection is also the leading cause of US infant hospitalization (severe bronchiolitis)¹ and a major risk factor for childhood asthma. Many factors contribute to the development of childhood asthma, within this high-risk previously hospitalized group as well as the general population, including environmental factors.^{2,3} These environmental factors include, but are not limited to, passive smoke exposure, inhaled chemical byproducts, and air pollution. The “pool chlorine hypothesis” suggests that increased exposure of children to toxic gases and aerosols around indoor chlorinated pools, mainly trichloramine, may contribute to the rise in childhood asthma.² Mean trichloramine levels are around 0.5 mg/m³, making this gas one of the most concentrated air pollutants that children in industrialized countries are regularly exposed to.²

This “pool chlorine hypothesis” has been examined by several researchers; however, there is no clear consensus about the association between early-life chlorinated pool exposure and the development of childhood asthma, even when stratifying by indoor vs outdoor pools^{2–9}—and especially within a high-risk group of infants hospitalized with bronchiolitis. Some studies have proposed a stronger link between swimming pool exposure and asthma among children with allergic sensitization.^{3,7,10} One case–control study of 337 adolescents with asthma and 633 controls reported that swimming pool exposure in early life was associated with a significantly higher risk of pre-school asthma onset, and children who were both sensitized and exposed were at even higher risk.³

Our objective was to investigate the association between chlorinated pool exposure in early life (birth until age 2 years) and the development of age 5-year asthma within a severe bronchiolitis cohort. We examined whether this association was modified by allergic sensitization.

The 35th Multicenter Airway Research Collaboration (MARC-35) is a multicenter, prospective cohort study of 921 infants hospitalized for bronchiolitis across three consecutive fall/winter seasons from 2011 to 2014 from 17 hospitals across 14 U.S. states (Appendix 1). Evaluation and treatment of patients was done at the discretion of the healthcare providers at each site. In each month of enrollment, investigators enrolled patients within 24 h of admission using a standardized protocol. Inclusion criteria for the study included an attending physician’s diagnosis of bronchiolitis and age <1 year. Exclusion criteria included transfer to a participating hospital >48 h after original admission, a time >24 h since having transferred to a participating hospital, certain chronic conditions (e.g., immunodeficiency, known heart-lung disease), or gestational age <32 weeks. Parents/guardians of all children provided informed consent and all participating hospitals had local approval of their institutional review board.

Follow-up was conducted via biannual parent interviews including questions about cumulative pool attendance (CPA) as well as other characteristics (Table 1). Early-life chlorinated pool exposure was defined as total hours from birth until age 2 years. Exposure duration was categorized as 0 h CPA, >0–20 h CPA, and >20 h CPA. Parents were asked about indoor and outdoor chlorinated pools separately during the enrolled child’s 2.5-year follow-up interview. If the families were unreachable at this follow-up call, they were asked about CPA from birth until age 2 years during the enrolled child’s 3.5-year follow-up interview. We defined age 5-year asthma as a parent report of clinician-diagnosed asthma by age 5 years and either asthma medication use or symptoms during age 4–4.9 years.¹¹ We defined infant allergic sensitization as a total IgE of >100 IU/L or any positive serum-specific IgE to food or aeroallergens during infancy.

We estimated odds ratios (ORs) with 95% confidence intervals (95% CIs) using logistic regression models to test the association between CPA and incident asthma, adjusting for other covariates selected a priori. In sensitivity analyses, indoor pool and outdoor pool exposures were individually tested using logistic regression models, adjusting for the same covariates as the primary model. To test effect modification, we used a likelihood ratio test to compare the multivariate models with and without an interaction term between CPA and allergic sensitization. A two-sided $P < 0.05$ was considered statistically significant.

Among 817 (89%) children with complete exposure and outcome data, 539 (66%) reported going to a chlorinated pool by age 2 years; 278 (34%) were unexposed to chlorinated pools (Table 1). Of those with chlorine exposure, 413 (77%) had a CPA of >0–20 h, and 126 (23%) had a CPA of >20 h. Overall, 228 (28%) children developed asthma by age 5 years. By CPA exposure categories (0 h, >0–20 h, and >20 h), asthma developed in 32%, 25%, and 28% of children, respectively ($P = 0.20$). We compared children with complete exposure and outcome data vs those without and found no material difference in baseline characteristics. These participants are missing subsequent information because they could not be reached during an interview period. In multivariable models, there was no significant association between total CPA during early life and asthma ($P > 0.30$ for both CPA exposure groups; Table 2). Sensitivity analyses found those with >20 h of indoor CPA had non-significantly higher odds of developing asthma (adjusted OR 2.27; 95% CI 0.90–5.74; $P = 0.08$; Table 2). There was no significant effect modification by allergic sensitization of the CPA exposure–asthma association (all P values ≥ 0.20).

In a large cohort at higher risk of childhood asthma due to their infant bronchiolitis hospitalization, we found no association between total CPA and asthma diagnosis by age 5 years. This concurs with a meta-analysis of seven general population cohorts (total $n = 5851$) that found no significant difference in asthma development between children with chlorinated pool exposure and those without.⁴ The sensitivity analysis in our current study

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Table 1. Cohort characteristics by pool exposure status from birth until 2 years.

Characteristics	0 h CPA (<i>n</i> = 278, 34%) <i>n</i> (%)	>0–20 h CPA (<i>n</i> = 413, 51%)	>20 h CPA (<i>n</i> = 126, 15%)	<i>P</i> value*
Age at enrollment, months				0.27
<2	80 (29)	128 (31)	47 (37)	
2–5.9	129 (46)	179 (43)	57 (45)	
6–11.9	69 (25)	106 (26)	22 (17)	
Female sex	111 (40)	170 (41)	55 (44)	0.78
Race/ethnicity				<0.001
Non-Hispanic white	73 (26)	212 (51)	87 (69)	
Non-Hispanic black	77 (28)	81 (20)	15 (12)	
Hispanic	119 (43)	100 (24)	20 (16)	
Non-Hispanic other	9 (3)	20 (5)	3 (2)	
Median household income by ZIP code				<0.001
<\$40,000	140 (50)	113 (27)	18 (14)	
\$40,000–\$79,999	125 (45)	234 (57)	86 (68)	
≥\$80,000	13 (5)	66 (16)	22 (17)	
Premature birth (≤37 weeks)	57 (21)	75 (18)	18 (14)	0.32
Child history of eczema (≤2 years)	119 (43)	189 (46)	62 (49)	0.47
Number of siblings				<0.001
No sibling	48 (17)	97 (23)	26 (21)	
1 sibling	90 (32)	175 (42)	53 (42)	
2 siblings	69 (25)	80 (19)	36 (29)	
>2 siblings	71 (26)	61 (15)	11 (9)	
Passive smoke exposure during early life (≤2 years)	76 (27)	104 (25)	27 (21)	0.45
Child ever breastfed	179 (64)	295 (71)	92 (73)	0.045
Daycare attendance during early life (≤2 years)	109 (39)	226 (55)	72 (57)	<0.001
<i>Parental factors</i>				
Parental history of allergic disease	134 (48)	240 (58)	71 (56)	0.11
Maternal smoking during pregnancy	48 (17)	44 (11)	19 (15)	0.06
<i>Laboratory results at index hospitalization</i>				
Total IgE				0.34
>100 kIU/L	9 (3)	10 (2)	1 (1)	
≤100 kIU/L	269 (97)	403 (98)	125 (99)	
Any positive food or aeroallergen sIgE	58 (21)	78 (19)	20 (16)	0.49
Virus				0.91
RSV only	162 (58)	240 (58)	79 (63)	
Rhinovirus only	14 (5)	23 (6)	7 (6)	
RSV and Rhinovirus	31 (11)	53 (13)	15 (12)	
Other	71 (26)	97 (23)	25 (20)	

CPA cumulative pool attendance, IgE immunoglobulin E, sIgE specific immunoglobulin E, RSV respiratory syncytial virus.

**P* values calculated using χ^2 test.

focused on indoor vs outdoor pools and found support for the pool chlorine hypothesis. While we did not observe a statistically significant association ($P = 0.08$), we believe this is due to small numbers, with only 26 (3%) reporting >20 h of indoor CPA during early life. Indoor pools may be poorly ventilated leading to increased concentration of potentially toxic aerosols. In the current study, effect modification by allergic sensitization was not observed. This observation differs from other studies that found the opposite result, albeit in difference in the study population and measurements for CPA.^{3,7,10}

A potential limitation of our study is the retrospective reporting of CPA so parents may not recall the occurrence or duration of

CPA accurately. Other measures for measuring CPA include documented evidence and/or quantitative assessment of swimming, and direct observation of swimming exposure in experimental conditions. While self-report may introduce bias when measuring the exposure, it seems to be the most practical and commonly used data source in similar studies.⁴ In addition, the way we obtained CPA is categorical rather than continuous, so we may have lost some information. Given the small number of children that had higher categorical levels of CPA, especially within indoor pools, having a continuous variable may not have changed our results significantly. We were also unable to account for any differences in chlorine concentrations between different

Table 2. Multivariable logistic regression models for the association between chlorinated pool exposure from birth until age 2 years and age 5-year asthma.

Models for pool exposure ^a	Number of participants	Number of cases (%)	Age 5-year asthma		
			aOR	95% CI	P value
Primary analysis					
Model 1—total CPA					
0 h CPA	278	88 (32)	1.00	Reference	
>0–20 h CPA	413	105 (25)	0.81	(0.53–1.24)	0.34
>20 h CPA	126	35 (28)	1.24	(0.70–2.20)	0.46
Sensitivity analyses					
Model 2—indoor CPA					
0 h CPA	561	153 (27)	1.00	Reference	
>0–20 h CPA	230	65 (28)	1.05	(0.69–1.60)	0.81
>20 h CPA	26	10 (38)	2.28	(0.90–5.76)	0.08
Model 3—outdoor CPA					
0 h CPA	323	100 (31)	1.00	Reference	
>0–20 h CPA	394	100 (25)	0.88	(0.59–1.32)	0.55
>20 h CPA	100	28 (28)	1.23	(0.68–2.24)	0.50

aOR adjusted odds ratio, CI confidence interval, CPA cumulative pool attendance.

^aModels adjusted for age at enrollment, sex, premature birth, race/ethnicity, virus at index hospitalization, median household income by ZIP code, child history of eczema, child allergic sensitization, parental history of allergic disease, passive smoking exposure, maternal smoking during pregnancy, breastfeeding, daycare attendance, and number of siblings.

pools.³ Furthermore, statistical power was limited for testing effect modification by allergic sensitization—even when using a more inclusive definition of infant allergic sensitization including those who had total IgE of >100 IU/L or any positive serum-specific IgE to food or aeroallergens. It will be difficult for individual cohorts to enroll enough participants with >20 h of indoor CPA exposure, allergic sensitization, and childhood asthma, highlighting the importance of individual participant data meta-analyses.

In summary, total chlorinated pool exposure during early life was not associated with childhood asthma in a severe bronchiolitis cohort. Although there were fewer participants with indoor pool CPA, we did observe a possible two-fold increased odds of asthma with this specific exposure. We encourage future studies where this topic is a main aim to examine CPA exposure by differentiating pool types or chlorine concentrations. While this may be impractical in some settings due to the variability of chlorine concentrations in private pools, there may be opportunities where this may be more standardized on a community level.

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DATA AVAILABILITY

The data presented in this study are available upon reasonable request, from the corresponding author, if the proposed research investigates severe bronchiolitis, recurrent wheezing, asthma, and related concepts. The data are not publicly available to be compliant with the informed consent forms of the MARC-35 study and the data sharing plan.

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AUTHOR CONTRIBUTIONS

E.J.M. and S.F. conceived the study. E.J.M. and V.C. assisted in data collection. J.A.E. and J.G. conducted statistical analysis. J.A.E., J.G., C.A.C., K.H., and G.M. assisted in the interpretation of data. E.J.M. drafted the manuscript and all authors contributed substantially to its revision. All authors approved the final version for publication.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Parents/guardians of all children provided informed consent and all participating hospitals had local approval of their institutional review board.

ADDITIONAL INFORMATION

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