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PEDIATRIC ASTHMA

The effect of early child care attendance on childhood asthma and wheezing: A meta-analysis

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ABSTRACT

Objective: Research evidence offers mixed results regarding the relationship between early child care attendance and childhood asthma and wheezing. A meta-analysis was conducted to synthesize the current research evidence of the association between early child care attendance and the risk of childhood asthma and wheezing. *Method*: Peer reviewed studies published from 1964–January 2017 were identified in MEDLINE, CINAL, and EMBASE using MeSH headings relevant to child care and asthma. Two investigators independently reviewed the selected articles from this search. All relevant articles that met our inclusion criteria were selected for further analysis. Data were extracted from studies that had sufficient data to analyze the odds of asthma or wheezing among children who attended child care. *Results*: The meta-analysis of 32 studies found that (1) early child care attendance is protective against asthma in children 3–5 years of age but not for children with asthma 6 years of age or older. (2) Early child care attendance increases the risk of wheezing among children 2 years of age or younger, but not the risk of wheezing for children over 2 years of age. *Conclusions*: This meta-analysis shows that early child care attendance is not significantly associated with the risk of asthma or wheeze in children 6 years of age or older.

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Introduction

Asthma is a leading respiratory disorder among children worldwide (1). When poorly controlled, childhood asthma can result in significant health care costs and have a negative impact on the quality of life of affected children and their families (1,2). Research studies suggests that asthma may develop in response to complex interactions between genetic variants and environmental exposures (3,4), which may include early life exposure to child care outside the home.

Increased utilization of child care outside the home has coincided with greater maternal participation in the workforce in both the United States and abroad (5). For example, 52% of children in the United States attended child care in 1993 (6) and by 2011, 61% of children under the age of 5 years attended child care for an average of 36 hours per week (7). Although child care can provide a safe, nuturing environment outside the home for children with working parents, attending child care may increase young children's incidence of upper and lower respiratory tract infections (8–11), which is a potential risk factor for the development of asthma in childhood (12,13). In a longitudinal study of respiratory infections among children 2 to 24 months of age, attending child care was associated with an increased risk of bronchial obstruction in the first 2 years of life, but not asthma at 4 years of age (14). However, there are consistent findings in several studies (15–18) demonstrating an increased risk of asthma among children who attend child care compared to those who did not attend child care. For instance, one case-control study found that children who attended child care within the first 4 months of life were 1.6 times more likely to develop asthma later in childhood (19), and one longitudinal study reported that children who attended child care before 6 months of age were 3.1 times more likely to have asthma at 7 years of age (17). Alternatively, other studies suggest that child care attendance before 12 months of age is protective against asthma later in childhood (20–22).

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In summary, studies of child care attendance and asthma offer conflicting results. Previous studies have not consistently offered comparitive analyses of the effect of the child's age at the time of exposure or attendance in child care on the risk of asthma or wheeze. Therefore, we conducted a meta-analysis to evaluate the strength of the relationship between the age of entry into child care and the age of diagnosis of asthma or the age of onset of wheeze in children. A more refined understanding of this relationship may be salient for both health care providers and parents, given that family decisions regarding child care arrangements not only focus on location, cost, and type of child care, but also on health concerns, including the potential risk of infectious diseases and asthma.

Methods

Study design

We conducted a meta-analysis of studies evaluating the association between child care attendance and childhood asthma or wheeze. We describe the methodology below, using guidelines based on PRISMA, a standard reporting system for meta-analyses (23). The literature search was conducted through the following databases: PubMed (MEDLINE), CINAL, and EMBASE using MeSH headings relevant to child care attendance and asthma; *asthma* was combined with *child care, child preschool, child day care centers*, and *schools nursery*. The search yielded original studies published in English from the inception of PubMed (1964) to January 9, 2017.

Definition of child care and child care exposure

There are a variety of terms used to refer to child care settings internationally, including child care, day care, nursery school, preschool, and pre-kindergarten. Child care can be provided in a variety of settings, including center-based and home-based (i.e., family child care homes). These programs can be publicly-funded by local, state, or federal agencies, or they can be privately operated (either for-profit or non-profit). Additionally, there are differences in the quality of care and amount of time children spend in child care. Some programs offer part-day or full-day and part-year or full-year. The programs also differ in the number of children present in each age group. We defined "child care" as programs that offer early care and education for young children in out-of-home settings before kindergarten entry. Henceforth in this paper, these programs will be referred to as *child care*.

We also defined child care exposure as the onset of attendance in child care, measured by the age of attendance in child care. Given that children under 12 months of age who attend child care have a higher risk of respiratory infections, (11,24), which may subsequently increase their risk of asthma (25,26), we used 12 months as the comparison age to determine if the risk of asthma in young children was different for children under or over 12 months of age. Therefore, child care exposure was categorized as *any* child care attendance, *early* child care attendance (entering child care before 12 months of age), and *late* child care attendance (entering child care between 1 to 5 years of age).

Definition of outcomes

The outcomes evaluated in the study are parent report of asthma and/or wheeze (see Tables 1 and 2). Medical provider report or pulmonary function testing was not uniformly required in the studies to confirm the diagnosis. We stratified these outcomes by age. To be consistent with studies that report stronger evidence of confirmed asthma among children older than 5 years of age (27), we compared children diagnosed with asthma between the ages 3–5 years to those diagnosed between the ages of 6 to 18 years. Similarly, the outcome of wheezing was categorized by diagnosis between the ages 0–2 years, 3– 5 years, and 6–18 years.

Study selection

Studies were included if they met the following inclusion criteria. Studies must include a sample of children 18 years of age or younger. In addition, the articles reported the age of child care attendance, the diagnosis or identification of asthma on or after 3 years of age, and the diagnosis or identification of wheeze on or after 1 year of age. All studies must provide the crude odds ratio (OR) measuring the association between child care attendance and childhood asthma or wheeze, and/or provide enough data to calculate the crude OR. Studies were excluded if they were review articles, non-English language articles, or if they did not provide enough information to calculate an OR.

Two independent reviewers conducted the study selection in three phases using the inclusion criteria. First, each full bibliographic reference identified in the database search was reviewed. After narrowing down the articles, the abstracts from these references were reviewed. Finally, the full text of the selected articles was reviewed to determine, which assessed the association between child care attendance and asthma or wheeze in children. A kappa score was calculated during each step of the article selection process to determine the degree of agreement between the two reviewers. Inter-rater reliability was valid for kappa scores indicating greater than 80% agreement.

Table 1. Child care attendance and asthma – table of studies.

				Exposure: Parent report of child care attendance age		
Reference Number	Study Design	Study Location	Sample Size	Type of child care	Age of attendance	Outcome: Parent report of asthma diagnosis or Identification age
(21)	Cross-sectional	United States	996	Day care	<6 months 7–12 months 12 months–3 years	Physician diagnosed asthma at age 6–13 years
(51)	Cross-sectional case-control	Chile	482	Day care	<12 months	Physician diagnosed asthma at age 6–15 years
(21)	Prospective cohort	United States	461	Day care	<12 months	Physician diagnosed asthma at age 4 years
(22)	Prospective cohort	United States	453	Day care	<12 months	Physician diagnosed asthma at age 6 years
(44)	Cross-sectional	Canada	48,921	Child care	Age not specified	Asthma at age 6–14 years
(18)	Cross-sectional nested case-control	Taiwan	5804	Day care	<2 years 2–3 years >3 years	Asthma at age 6–14 years
(17)	Prospective cohort	United States	589	Day care center	<12 months	Asthma 7 years
(32)	Prospective cohort	United States	815	Child care center	<15 months 16–36 months	asthma by 15 years
(52)	Cross-sectional	Sweden	10,851	Daycare	<12 months 1–2 years >2 years	Asthma diagnosed by doctor at 1–6years
(46)	Prospective cohort	United States	6900	Center based care	Age not specified	Asthma at Kindergarten age
(20)	Cross-sectional case-control	Canada	914	Day care	<12 months <3–4 years	Physician diagnosed asthma at 3–4 years
(47)	Cross-sectional	United States	8257	Day care	>10 h/wk	Asthma <6 years
(48)	Cross-sectional case-control	Canada	109746	Day care	Birth to index date	Asthma at 10 years, or index date
(49)	Prospective cohort	Canada	8486	Daycare	<2 years	Physician diagnosed asthma at age 2–5 years
(50)	Cross-sectional	Norway	3749	Day care center	<2 years 2–3 years	Asthma at age 4–5 years
(56)	Prospective cohort	Norway	2540	Child care	<12 months	(1) Ever diagnosed asthma by age 10 years (2) Diagnosed current asthma symptoms at age 10 years
(30)	Prospective cohort	United States	984	Daycare	7–12 months 13–24 months	Late onset asthma at >54 months of age
(53)	Cross-sectional	Finland	8387	Day care centre	1–3 years	(1) Ever diagnosed asthma by age 13–14 years (2) Current diagnosis asthma at age 13–14 years
(19)	Cross-sectional case-control	United States	691	Day care center	<4 months	Parental report of physician-diagnosed asthma at age 3–5 years
(16)	Cross-sectional	Canada	6657	Child care	Age not specified	Asthma at <11 years of age
(15)	Cross-sectional	United States	2819	Daycare center	<12 months	Diagnosed asthma at age 1–6 years
(54)	Cross-sectional case-control	New Zealand	474	Day care	<12 months	Asthma at age 7–9 years

Table 2. Child care attendance and wheezing – table of studies.

Reference Number	Study Design	Study Location	Sample Size	Exposure: Parent report of child care attendance age		Outcome: Parent report of wheezing diagnosis or identification age
				Type of child care	Age of attendance	
(57)	Cross-sectional	Spain	958	Child care	<12 months	Recurrent wheezing at 12–15 months of age
(33)	Prospective cohort	United States	498	Day care	<12 months	Any wheeze at age 1 year 2+ episodes of wheeze at age 1 year
(31)	Prospective cohort	United States	461	Day care	<12 months	Recurrent wheeze at age 4 years
(22)	Prospective cohort	United States	453	Day care	<12 months	Recurrent wheeze at age 6 years
(58)	Cross-sectional	Brazil	3003	Day care	<12 months	Recurrent wheeze in the first 12 months of age
(52)	Cross-sectional	Sweden	10,851	Daycare	<12 months 1–2 years >2 years	Wheeze (in the past 12months) at age 1–6 years
(59)	Cross-sectional	Ukraine	2127	Kindergarten	<3 years	Wheeze in past 12 months at age 6–7years
(60)	Cross-sectional	Jamaica	2017	Day care	Age not specified	Current wheeze (age not specified)
(40)	Prospective cohort	Portugal	308	Kindergarten	<12 months	Recurrent wheeze (>3 episodes in the last year) at age 6 years
(55)	Prospective cohort	United Kingdom	845	Nursery School	<6 months 6–12 months >12 months	Current wheeze at age 5 years
(61)	Cross-sectional	Turkey	109	Day care		Ever wheeze at age 2–4 years
(62)	Cross-sectional	Italy	16,333	Day care center	<2 years	Transient wheeze at age 6–7 years Persistent wheeze at age 6–7 years Late-onset wheeze at age 6–7 years
(63)	Cross-sectional	Netherlands	1,115	Day care	<12 months	Wheeze ever in the first 12 months of age Recurrent wheeze in the first 12 months of age Severe wheeze in the first 12 months of age

Differences were resolved by informal consensus among all participating reviewers. Retrieved full text articles were cross-referenced and manually screened for any potentially missed articles. Lastly, study authors were contacted to review our list of selected articles.

Data extraction and analysis

The following data were extracted from the selected studies by two lead investigators: authors' names, publication year, country of study, study design, sample size, study population type, mean or age range, gender of participants, age when child care attendance was assessed, age when asthma and/or wheeze was assessed, type of risk factors or confounders adjusted for in the models, and the statistic reported on the outcome variable of interest (asthma or wheeze) including: odds ratio, adjusted odds ratio, or relative risks, and 95% confidence intervals.

Data were pooled using a meta-analysis model. Random-effects was applied to each meta-analysis model with high heterogeneity as indicated by statistical tests. Heterogeneity was measured using the I-squared statistic. The pooled results were graphed using a forest plot for each association measured between child care attendance and asthma or wheeze. Because unique samples are needed for pooled analysis, only the most recent publication was included when duplicate samples were found among our selected studies. We examined the potential for weighted influence of any given study by looking at the percentage of total weight to the final pooled results for each study. Publication bias was assessed using funnel plots (28). All analyses were performed using Stata 13.1 (29).

Of the studies that provided sufficient data, we stratified the models to compare the effects of the age of entry into child care (any child care attendance, early child care attendance, or late child care attendance). We also categorized the outcomes (either asthma or wheeze) into different diagnostic age groups (ever/any diagnosis or identification, 0 to 2 years, 3 to 5 years, and 6 to 18 years).

Results

Descriptive results

Our search used broad MeSH headings to cast a wide net, which resulted in identifying 16,749 citations. Application of our inclusion/exclusion criteria produced 43 studies of the relationship between child care attendance and childhood asthma or wheeze. Thirty-two studies included results that met the criteria to be included in the meta-analysis (Figure 1). Of the 32 included studies, 22 studies reported the odds of asthma among children who attended child care (Table 1) and 13 studies reported the odds of wheeze among children who attended child care (Table 2). Three studies reported the odds of both outcomes. Based on the funnel plot analyses, there was no evidence of publication bias among the selected studies.

Among the pooled studies that evaluated the relationship between child care attendance and asthma ($n = 20$), the participants (mean = 12,156 participants, range = 453–109,746) were recruited from pediatric clinical settings from 9 countries, with the majority from either the United States ($n = 10$) or Canada ($n = 5$). Two studies (30,31) could not be included in this model due to the inclusion of duplicate samples from other studies (22,32). The pooled results from these studies are summarized in Table 3. Similar to the studies that evaluated asthma, the participants (mean = 3465 participants; range 109–16,333) from the studies that evaluated the relationship between child care attendance and wheeze ($n = 11$) were recruited from pediatric clinical settings from 11 countries. Two studies (31,33) could not be included in this model due to the inclusion of a duplicate sample from another study (22). The pooled results of this group of studies are summarized in Table 4.

Pooled results: Child care attendance and asthma

The pooled analysis showed that children who attend child care at any age have increased odds of asthma between ages 0 to 18 years compared to children who did not attend child care (OR = 1.17 [95% CI, 1.01–1.35]; I^2 statistic = 80.4%) (Table 3). The stratified analysis based on the age of entry into child care showed that there was no association between asthma among children and adolescents (0 to 18 years of age) who attended early child care compared to those who did not attend child care (OR = 0.94 [95% CI, 0.70–1.27]; I^2 statistic = 64.4%) (Table 3). In contrast, the odds of asthma among children and adolescents (0 to 18 years of age) who attended late child care was increased, compared to children who did not attend child care (OR = 1.19 [95% CI, 1.01–1.41]; I^2 statistic = 32.5%) (Table 3).

We found no association between asthma at ages 3 to 5 years among children who attend child care at any age compared to children who did not attend child care (OR = 1.11 [95% CI, 0.92–1.35]; I^2 statistic = 0.0%) (Table 3). The stratified analysis based on the age of entry showed that children who attended early child care had a reduced odds of asthma at 3 to 5 years of age compared to children who did not attend child care (OR = 0.66 [95% CI, 0.50–0.87]; I^2 statistic = 0.0%) (Table 3). No

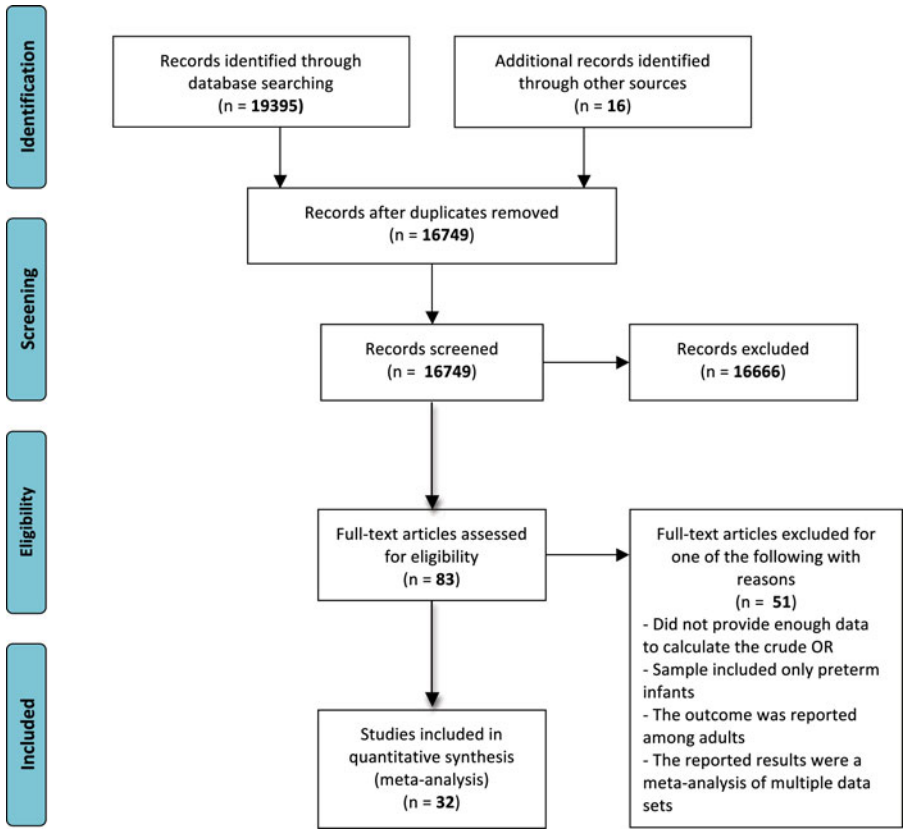

Figure 1. Search results.

association was found between children who attended late child care and their odds of asthma at 3 to 5 years of age, compared to children who did not attend child care (OR = 1.12 [95% CI, 0.90–1.38]; I^2 statistic = 0.0%) (Table 3).

No association was found between asthma diagnosed at 6 to 18 years of age among children who attended child care at any age compared to children who did not attend child care (OR = 1.08 [95% CI, 0.88–1.33]; I^2 statistic = 57.2%) (Table 3). Additionally, there was no association between asthma at 6 to 18 years of age and early child care attendance compared to no child care attendance (OR = 0.98 [95% CI, 0.66–1.47]; I^2 statistic = 63.4%) (Table 3) or late child care attendance compared to no child care attendance (OR = 1.47 [95% CI, 0.73–2.97]; I^2 statistic = 71.1%) (Table 3).

Pooled results: Child care attendance and wheeze

The pooled analysis showed that there was no association between children who attended child care at any age compared to children who did not attend child care, and the odds of wheeze between 0 to 18 years of age (OR = 1.07 [95% CI, 0.83–1.39]; I^2 statistic = 86.8%) (Table 4). These studies are highly heterogeneous. Stratification of these studies by the age of entry into child care suggests that there is no association between the odds of wheezing among children under 18 years of age who attended early child care (OR = 0.98 [95% CI, 0.55–1.75]; I^2 statistic = 91.5%) or late child care (OR = 0.91 [95% CI, 0.54–1.52]; I^2 statistic = 85.0%) when compared to those children who did not attend child care (Table 4).

Table 3. Summary of pooled results: child care attendance and asthma.

	Exposure: Child Care Attendance*		
Outcome: Asthma diagnosis or identification age	**Attendance at any age**	**Early Attendance** Attendance starting younger than 12 months of age	**Late Attendance** Attendance starting at 12 months of age or older
0–18 years	OR = 1.17 (1.01, 1.35)	OR = 0.94 (0.70, 1.27)	OR = 1.19 (1.01, 1.41)
0–2 years	*No Data*	*No Data*	*No Data*
3–5 years	OR = 1.11 (0.92, 1.35)	OR = 0.66 (0.50, 0.87)	OR = 1.12, (0.90, 1.38)
6–18 years	OR = 1.08 (0.88, 1.33)	OR = 0.98 (0.66, 1.47)	OR = 1.47 (0.73, 2.97)

When appropriate meta-analysis models were conducted using log scaled odds ratios and random effects.
*Compared to no child care attendance.

Table 4. Summary of pooled results: child care attendance and wheezing.

Outcome: Wheezing diagnosis or identification age	Exposure: Child Care Attendance*		
	Attendance at any age	**Early attendance** Attendance starting younger than 12 months of age	**Late Attendance** Attendance starting at 12 months of age or older
0–18 years	OR = 1.07 (0.83, 1.39)	OR = 0.98 (0.55, 1.75)	OR = 0.91 (0.54, 1.52)
0–2 years	OR = 1.80 (1.38, 2.36)	OR = 1.80 (1.38, 2.36)	*No Data*
3–5 years	OR = 0.66 (0.49, 0.90)	OR = 0.59 (0.31, 1.12)	OR = 0.43 (0.24, 0.77)**
6–18 years	OR = 0.68 (0.44, 1.05)	OR = 0.43 (0.27, 0.68)	*No Data*

When appropriate meta-analysis models were conducted using log scaled odds ratios and random effects.
*Compared to no child care attendance.
**This category includes data from 1 study.

The relationship between child care exposure and risk of wheeze differs by the age of wheeze diagnosis. There are increased odds of wheeze among children 2 years of age or younger who attended early child care compared to those who did not attend child care (OR = 1.80 [95% CI, 1.38–2.36]; I^2 statistic = 63.9%) (Table 4). In contrast, there was no association between the odds of wheeze for 3 to 5 year olds among children who attended early child care compared to those who did not attend child care (OR = 0.59 [95% CI, 0.31–1.12]; I^2 statistic = 55.0%) (Table 4). There are decreased odds of wheeze among children 6 to 18 years of age who attended early child care compared to those who did not attend child care (OR = 0.43 [95% CI, 0.27–0.68]; I^2 statistic = 0.0%) (Table 4).

We were not able to conduct a stratified analysis on the effect of late child care attendance on wheeze in the different age categories. There was only one study that evaluated the effect of late child care attendance on wheeze between 3 to 5 years of age, which reported reduced odds of wheeze (OR = 0.43 [95% CI, 0.24–0.77]). There were no studies that evaluated the effect of late child care attendance on wheeze among children 6 years of age or older.

Discussion

This meta-analysis of 32 studies found an overall small increased risk of childhood asthma among children who attended child care compared to children who did not attend child care. However, we found that this outcome depends on the age of asthma diagnosis and the timing of child care exposure. When the findings are stratified by early (before 12 months) and late (after 12 months) child care attendance, our results suggest that early child care attendance has a *protective* effect against asthma in children 3 to 5 years of age; however, the effect is not sustained for children with a diagnosis of asthma after 5 years of age. Additionally, we found that that early child care attendance increases the risk of wheeze among children two years of age or younger, but not the risk of wheeze in children older than 5 years of age.

A protective effect of early child care attendance on asthma is consistent with the hygiene hypothesis (34) which suggests that the lack of exposure to infectious diseases (commonly found in child care settings) may increase the risk of allergic diseases, such as asthma (35), in childhood. However, in our analysis, we found that the protective effect of child care, if any, seems to be transient. We did not note long term protection after 5 years of age when the diagnosis of asthma is more conclusive. Specifically, no association was found between 6 to 18 years of age, which may be due to the amount of heterogeneity observed among those studies.

Wheeze is a common presentation of viral infections frequently observed in infants who attend child care (26). Therefore, the increased risk of early/transient wheeze among children two years of age or younger who attend child care could be driven by the studies that measured wheeze at 1 year of age. The increase in wheeze is likely representative of the increased risk of viral infections in this age group. These results also suggest the importance of analysis stratified by age of diagnosis. By stratifying our models, we found that if the diagnosis is at an early age (two years or younger), there is an increased risk of wheeze for children who attend child care. However, there is a protective effect of early child care against wheeze in the older age group.

The studies included in this meta-analysis vary in quality and design, include both longitudinal and cross-sectional designs, and represent heterogeneous data from several different countries around the world, spanning more than two decades. This heterogeneity might affect the internal validity of the findings. Although the use of a random-effects meta-analysis model produces a more conservative estimate of the pooled statistic of heterogeneous data, it does not fully account for the heterogeneity observed in our data. Despite the differences in population demographics, location and the timing of the studies, the main source of heterogeneity is likely attributed to the variation in the amount or type of each child's exposure to child care (e.g. duration of time spent in child care per week, type of child care setting, quality of child care, or number of other children in attendance).

Additionally, variations in child care settings (e.g. centers or family child care homes) can lead to misclassification bias when comparing one type of child care arrangement to another. For example, the included studies did not differentiate between the amount of exposure of a child who attends a large child care center with 20 other children 37 hours per week from that of a child who attends a small family child care home with 2 other children 6 hours per week. The measurement of child care attendance in the reviewed studies was not specific enough to accurately group the children by exposure. As a result, it is difficult to identify a dose–response relationship beyond the effect of the age of child care attendance on asthma or wheeze. The rate of each child's exposure to child care (hours per week), and the number of other children attending child care would need to be measured to standardize comparisons across child care programs.

Other potential variables that may play a role in increasing the heterogeneity between studies include differences in sample-specific potential confounding factors in each study, such as maternal history of asthma (22), maternal smoking (36), breastfeeding status during the first year of life (37), and the number of siblings present in the home (21). Our analysis pooled the crude odds of either asthma or wheeze among children without accounting for these potential confounding factors.

Additionally, the selected studies had the potential for selection bias regarding sociodemographic characteristics. For example, most studies had families with "high" socioeconomic status (SES), which may limit the generalizability of our findings. Since high SES families tend to send their children to high quality child care programs that are more likely to adhere to quality standards for health and safety (38), children's rate of exposure to health and safety hazards (i.e.; infectious diseases) in high quality child care may differ from children attending lower quality child care.

The variables of interest in this study (child care attendance, asthma, and/or wheeze) were all identified by parent report, which introduces potential reporting and recall bias, especially for the age of entry into child care and age of asthma diagnosis or wheeze. However, many of the studies stated that parents were able to recall if their child attended child care before 12 months of age. Additionally, the parent's report of a diagnosis of asthma among children ages 3–5 years of age can be problematic, as it can be difficult to confirm a diagnosis of asthma for a child under 6 years of age (39). To determine if there was any difference in the results between stratifying the outcome of asthma diagnosis before or after 6 years of age compared to asthma diagnosed before or after 5 years of age, we conducted a sensitivity analysis and found no difference in our results.

Most studies included in our meta-analysis were cross-sectional, limiting our ability to establish a causal relationship between early child care attendance and later diagnosis of asthma or wheeze in childhood. Of the longitudinal studies included in our model of the association between child care attendance and asthma, one found that early child care attendance was associated with an approximate two-fold increased risk of asthma at 7 years of age (17), which is not consistent with our findings.

Our findings of the association between child care attendance and wheezing were consistent with the longitudinal studies (22,31,33,40) identified in our search. Specifically, one longitudinal study (33) found that early child care attendance increased the risk of wheezing at 1 year of age, but not at 4 or 6 years of age (22,31). Another longitudinal study (40) found that early child care attendance was protective for wheezing at 6 years of age.

Finally, the studies included in our meta-analysis were limited to those published in English peer-reviewed journals entered into three medical journal databases (EMBASE, MEDLINE, and CINAHL) from the earliest entries in these databases (1946) to January 9, 2017. Therefore, some relevant studies may not have been included in our final analysis, which could bias our results. Although our funnel plot analysis demonstrated no potential publication bias, there is a remaining possibility of missing a study published in non-peer reviewed journals or outside of the search timeframe.

Conclusion

We found that early child care attendance increases the risk of wheeze among children 2 years of age or younger, but decreases the risks of asthma among children 3 to 5 years and wheeze among children 6 years and older. However, early child care attendance was not significantly associated with reduced risk of asthma after 6 years of age. The effect of late child care attendance (after 1 year of age) on asthma and wheeze remains inconclusive.

Clinically, the results of this analysis are useful for primary care providers who care for young children. The most common health concerns for parents of children less than 5 years of age include acute infections, allergies, and asthma (41). Parents can be reassured that despite the increase in respiratory infections observed in the first year of life among children who attend early child care, child care attendance before 1 year of age is not significantly associated with asthma or wheeze later in childhood.

For clinical investigators, the variation among studies in this review highlights the need for standardized definitions of child care exposure and asthma diagnosis in children. We recommendations that future studies evaluating potential health risks associated with child

care attendance include standardized measures of child care environmental quality, such as environmental rating scales (42) and national health and safety performance standards (43) to provide a more in depth and comparable description of child care facilities. Additionally, standardized definitions of children's time spent in child care could increase the validity and reliability of the findings to determine the dose-response relationship between child care exposure and health outcomes.

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