

Appendix 1: Influencing factors for Atopic Dermatitis, Asthma, Rhinoconjunctivitis and Food Allergy

The search was done in December 2021 in PubMed. Only Meta-Analyses were included. The terms were (atopic rhinitis) AND (children) AND ((determinants) OR (influencing factors)), (136 articles), (asthma) AND (children) AND ((determinants) OR (influencing factors)) (860 articles), (atopic dermatitis) AND (children) AND ((determinants) OR (influencing factors)) (120 articles) and (food allergy) AND (children) AND ((determinants) OR (influencing factors)) (129 articles). When necessary, more recent studies were supplemented. (D: Dermatitis, A: Asthma, R: Rhinoconjunctivitis, F: Food Allergy)

Factor	D	A	R	F	Reference
Psychological Aspects					
Prenatal mental disorders		x			(1)
Stress or depression of the mother		x			(2)
Mental disorders of parents		x			(3)
Attention deficit hyperactivity disorder		x	x		(4)
Air pollution					
Passive smoking	x	x			(2)
Air pollution in the household (e.g. from stoves)		x			(5)
Cooking with gas stove		x			(6)
Nanoparticles		x			(7)
Fine dust			x		(8)
Air pollution in general		x			(9)
Microbial aerosols			x		(10)
Household Allergens					
Household Allergens		x			(2)
Cats and dogs	x	x	x		(11)
Indoor fungi (Penicillium, Aspergillus, Cladosporium)		x			(12)
Dampness and mold in the house			x		(13)
Staphylococcus aureus		x	x		(14)
Household microbes		x			(2)
Medical conditions					
Hypertension during pregnancy		x			(15)
Atopic disease of parents		x			(16)
Asthma			x	x	(17)(18)
Food Allergy		x			(18)
Simultaneous occurrence of other atopic diseases	x	x	x		(19)
Diabetes mellitus of the mother	x	x			(20)
Type 1 diabetes of the child		x			(21)
Sleep-related breathing disorder/sleep apnea			x		(22)
Rhinovirus infection in the first 3 years of life		x			(23)
Vitiligo	x				(24)
Otitis media			x		(25)

Medication					
Contraceptive pill		x	x		(26)
Paracetamol during pregnancy		x			(27)
Acid suppressants in pregnancy		x			(28)
Acid suppressants in early life				x	(29)
Antibiotics during pregnancy	x	x		x	(30)
Antibiotics in the first 3 years of life		x		x	(31,32)
Measles and pertussis infection		x			(33)
Diet/Weight					
Overweight of the child		x			(34)
Overweight of the mother during pregnancy/ severe weight gain of the mother during pregnancy	x	x			(35,36)
Rapid weight gain as infant		x			(37)
Low birth weight		x			(37)
Underweight of the mother during pregnancy	x				(38)
Vitamin D		x			(39)
Vitamin D during pregnancy		x		x	(40,41)
Vitamin A, D, E, zinc, selenium deficiency		x			(42,43)
Folate intake during pregnancy		x			(44)
Soft drinks		x			(45)
Breastfeeding	x	x	x		(46)
Raw cow's milk		x			(47)
Probiotics	x			x	(48–50)
Fruit and vegetables intake		x			(51)
Mediterranean diet		x			(52)
Fish	x	x	x	x	(53)
Omega-3 supplementation during pregnancy		x			(54)
Early introduction of egg and peanut				x	(55)
Pesticides		x			(56)
Other					
Second generation immigrants compared with first		x			(57)
Ethnic affiliation		x			(58)
Rural residential area		x			(59)
Autumn/winter birth	x				(60)
Cesarean section and female sex		x			(61)
Cesarean section		x			(62)
Birth in the 34 th -36 th week of pregnancy		x			(63)
Preterm birth		x			(37)
Male gender		x	x		(64)
Social disadvantage		x			(65)
Physical activity		x			(66)
Daycare attendance	x	x	x		(67)

References

1. Chen S, Chen S. Are prenatal anxiety or depression symptoms associated with asthma or atopic diseases throughout the offspring's childhood? An updated systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2021 Jun 22;21(1):435.
2. Bacharier LB, Beigelman A, Calatroni A, Jackson DJ, Gergen PJ, O'Connor GT, et al. Longitudinal Phenotypes of Respiratory Health in a High-Risk Urban Birth Cohort. *Am J Respir Crit Care Med*. 2019 Jan 1;199(1):71–82.
3. Pierce M, Hope HF, Kolade A, Gellatly J, Osam CS, Perchard R, et al. Effects of parental mental illness on children's physical health: systematic review and meta-analysis. *Br J Psychiatry J Ment Sci*. 2020 Jul;217(1):354–63.
4. Cortese S, Sun S, Zhang J, Sharma E, Chang Z, Kuja-Halkola R, et al. Association between attention deficit hyperactivity disorder and asthma: a systematic review and meta-analysis and a Swedish population-based study. *Lancet Psychiatry*. 2018 Sep;5(9):717–26.
5. Lee KK, Bing R, Kiang J, Bashir S, Spath N, Stelzle D, et al. Adverse health effects associated with household air pollution: a systematic review, meta-analysis, and burden estimation study. *Lancet Glob Health*. 2020 Nov;8(11):e1427–34.
6. Lin W, Brunekreef B, Gehring U. Meta-analysis of the effects of indoor nitrogen dioxide and gas cooking on asthma and wheeze in children. *Int J Epidemiol*. 2013 Dec;42(6):1724–37.
7. Li Q, Yi Q, Tang L, Luo S, Tang Y, Zhang G, et al. Influence of Ultrafine Particles Exposure on Asthma Exacerbation in Children: A Meta-Analysis. *Curr Drug Targets*. 2019;20(4):412–20.
8. Lin L, Li T, Sun M, Liang Q, Ma Y, Wang F, et al. Effect of particulate matter exposure on the prevalence of allergic rhinitis in children: A systematic review and meta-analysis. *Chemosphere*. 2021 Apr;268:128841.
9. Zheng X yan, Ding H, Jiang L na, Chen S wei, Zheng J ping, Qiu M, et al. Association between Air Pollutants and Asthma Emergency Room Visits and Hospital Admissions in Time Series Studies: A Systematic Review and Meta-Analysis. *PloS One*. 2015;10(9):e0138146.
10. Fakunle AG, Jafta N, Naidoo RN, Smit LAM. Association of indoor microbial aerosols with respiratory symptoms among under-five children: a systematic review and meta-analysis. *Environ Health Glob Access Sci Source*. 2021 Jul 1;20(1):77.
11. Gao X, Yin M, Yang P, Li X, Di L, Wang W, et al. Effect of Exposure to Cats and Dogs on the Risk of Asthma and Allergic Rhinitis: A Systematic Review and Meta-analysis. *Am J Rhinol Allergy*. 2020 Sep;34(5):703–14.
12. Sharpe RA, Bearman N, Thornton CR, Husk K, Osborne NJ. Indoor fungal diversity and asthma: a meta-analysis and systematic review of risk factors. *J Allergy Clin Immunol*. 2015 Jan;135(1):110–22.
13. Jaakkola MS, Quansah R, Hugg TT, Heikkinen SAM, Jaakkola JJK. Association of indoor dampness and molds with rhinitis risk: a systematic review and meta-analysis. *J Allergy Clin Immunol*. 2013 Nov;132(5):1099–1110.e18.
14. Pastacaldi C, Lewis P, Howarth P. Staphylococci and staphylococcal superantigens in asthma and rhinitis: a systematic review and meta-analysis. *Allergy*. 2011 Apr;66(4):549–55.
15. Li P, Xiong T, Hu Y. Hypertensive disorders in pregnancy and risk of asthma in offspring: a systematic review and meta-analysis. *BMJ Open*. 2021 Sep 2;11(9):e046769.
16. Ravn NH, Halling AS, Berkowitz AG, Rinnov MR, Silverberg JI, Egeberg A, et al. How does parental history of atopic disease predict the risk of atopic dermatitis in a child?

- A systematic review and meta-analysis. *J Allergy Clin Immunol*. 2020 Apr;145(4):1182–93.
17. Kou W, Li X, Yao H, Wei P. Meta-analysis of the comorbidity rate of allergic rhinitis and asthma in Chinese children. *Int J Pediatr Otorhinolaryngol*. 2018 Apr;107:131–4.
 18. Zhou H, Dai C, Pan J. Pediatric Asthma and Food Allergy. *Indian J Pediatr*. 2017 Aug;84(8):585–90.
 19. Pols DHJ, Wartna JB, van Alphen EI, Moed H, Rasenberg N, Bindels PJE, et al. Interrelationships between Atopic Disorders in Children: A Meta-Analysis Based on ISAAC Questionnaires. *PLoS One*. 2015;10(7):e0131869.
 20. Li Z, Yu M, Wang P, Qian H, Fan Y, Li X, et al. Association between maternal diabetes mellitus and allergic diseases in children - A systematic review and meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Jul;32(5):880–91.
 21. Cardwell CR, Shields MD, Carson DJ, Patterson CC. A meta-analysis of the association between childhood type 1 diabetes and atopic disease. *Diabetes Care*. 2003 Sep;26(9):2568–74.
 22. Cao Y, Wu S, Zhang L, Yang Y, Cao S, Li Q. Association of allergic rhinitis with obstructive sleep apnea: A meta-analysis. *Medicine (Baltimore)*. 2018 Dec;97(51):e13783.
 23. Liu L, Pan Y, Zhu Y, Song Y, Su X, Yang L, et al. Association between rhinovirus wheezing illness and the development of childhood asthma: a meta-analysis. *BMJ Open*. 2017 Apr 3;7(4):e013034.
 24. Acharya P, Mathur M. Association of atopic dermatitis with vitiligo: A systematic review and meta-analysis. *J Cosmet Dermatol*. 2020 Aug;19(8):2016–20.
 25. De Corso E, Cantone E, Galli J, Seccia V, Lucidi D, Di Cesare T, et al. Otitis media in children: Which phenotypes are most linked to allergy? A systematic review. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Apr;32(3):524–34.
 26. Bai XF, Wu ZX, Zhao CH, Wu Y, Fei CS, Zhang LQ, et al. Maternal oral contraceptive pill use and the risk of atopic diseases in the offspring: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2020 Apr;99(16):e19607.
 27. Fan G, Wang B, Liu C, Li D. Prenatal paracetamol use and asthma in childhood: A systematic review and meta-analysis. *Allergol Immunopathol (Madr)*. 2017;45(6):528–33.
 28. Lai T, Wu M, Liu J, Luo M, He L, Wang X, et al. Acid-Suppressive Drug Use During Pregnancy and the Risk of Childhood Asthma: A Meta-analysis. *Pediatrics*. 2018 Feb;141(2):e20170889.
 29. Muhammad Danial Song HJJ, Min Lee CT, Ci Ng FY, Jyn Tan BK, Ho Siah KT, Tham EH. Childhood Acid Suppressants May Increase Allergy Risk-A Systematic Review and Meta-Analysis. *J Allergy Clin Immunol Pract*. 2023 Jan;11(1):228-237.e8.
 30. Zhong Y, Zhang Y, Wang Y, Huang R. Maternal antibiotic exposure during pregnancy and the risk of allergic diseases in childhood: A meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Apr;32(3):445–56.
 31. Ahmadizar F, Vijverberg SJH, Arets HGM, de Boer A, Turner S, Devereux G, et al. Early life antibiotic use and the risk of asthma and asthma exacerbations in children. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2017 Aug;28(5):430–7.
 32. Ahmadizar F, Vijverberg SJH, Arets HGM, de Boer A, Lang JE, Garssen J, et al. Early-life antibiotic exposure increases the risk of developing allergic symptoms later in life: A meta-analysis. *Allergy*. 2018 May;73(5):971–86.
 33. Nagel G, Weinmayr G, Flohr C, Kleiner A, Strachan DP, ISAAC Phase Two Study Group. Association of pertussis and measles infections and immunizations with asthma and allergic sensitization in ISAAC Phase Two. *Pediatr Allergy Immunol*. 2012 Dec;23(8):736–45.
 34. Malden S, Gillespie J, Hughes A, Gibson AM, Farooq A, Martin A, et al. Obesity in

- young children and its relationship with diagnosis of asthma, vitamin D deficiency, iron deficiency, specific allergies and flat-footedness: A systematic review and meta-analysis. *Obes Rev Off J Int Assoc Study Obes*. 2021 Mar;22(3):e13129.
35. Forno E, Young OM, Kumar R, Simhan H, Celedón JC. Maternal obesity in pregnancy, gestational weight gain, and risk of childhood asthma. *Pediatrics*. 2014 Aug;134(2):e535-546.
36. Miceli Sopo S, Sinatti D, Gelsomino M. Retrospective analysis of 222 oral food challenges with a single dose in acute food protein-induced enterocolitis syndrome. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Jul;32(5):1066-72.
37. den Dekker HT, Sonnenschein-van der Voort AMM, de Jongste JC, Anessi-Maesano I, Arshad SH, Barros H, et al. Early growth characteristics and the risk of reduced lung function and asthma: A meta-analysis of 25,000 children. *J Allergy Clin Immunol*. 2016 Apr;137(4):1026-35.
38. Chen W, Wang L, Yao H, Dai H, Zheng R, Zhang W. Prepregnancy BMI, gestational weight gain and risk of childhood atopic dermatitis: A systematic review and meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Jul;32(5):892-904.
39. Venter C, Agostoni C, Arshad SH, Ben-Abdallah M, Du Toit G, Fleischer DM, et al. Dietary factors during pregnancy and atopic outcomes in childhood: A systematic review from the European Academy of Allergy and Clinical Immunology. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2020 Nov;31(8):889-912.
40. Vahdaninia M, Mackenzie H, Helps S, Dean T. Prenatal Intake of Vitamins and Allergic Outcomes in the Offspring: A Systematic Review and Meta-Analysis. *J Allergy Clin Immunol Pract*. 2017;5(3):771-778.e5.
41. Shi D, Wang D, Meng Y, Chen J, Mu G, Chen W. Maternal vitamin D intake during pregnancy and risk of asthma and wheeze in children: a systematic review and meta-analysis of observational studies. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet*. 2021 Feb;34(4):653-9.
42. Chen M, Sun Y, Wu Y. Lower circulating zinc and selenium levels are associated with an increased risk of asthma: evidence from a meta-analysis. *Public Health Nutr*. 2020 Jun;23(9):1555-62.
43. Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. *J Allergy Clin Immunol*. 2011 Mar;127(3):724-733.e1-30.
44. Li W, Xu B, Cao Y, Shao Y, Wu W, Zhou J, et al. Association of maternal folate intake during pregnancy with infant asthma risk. *Sci Rep*. 2019 Jun 6;9(1):8347.
45. Al-Zalabani AH, Noor Elahi I, Katib A, Alamri AG, Halawani A, Alsindi NM, et al. Association between soft drinks consumption and asthma: a systematic review and meta-analysis. *BMJ Open*. 2019 Oct 14;9(10):e029046.
46. Lodge CJ, Tan DJ, Lau MXZ, Dai X, Tham R, Lowe AJ, et al. Breastfeeding and asthma and allergies: a systematic review and meta-analysis. *Acta Paediatr Oslo Nor 1992*. 2015 Dec;104(467):38-53.
47. Brick T, Hettinga K, Kirchner B, Pfaffl MW, Ege MJ. The Beneficial Effect of Farm Milk Consumption on Asthma, Allergies, and Infections: From Meta-Analysis of Evidence to Clinical Trial. *J Allergy Clin Immunol Pract*. 2020 Mar;8(3):878-889.e3.
48. Zuccotti G, Meneghin F, Aceti A, Barone G, Callegari ML, Di Mauro A, et al. Probiotics for prevention of atopic diseases in infants: systematic review and meta-analysis. *Allergy*. 2015 Nov;70(11):1356-71.
49. Tan-Lim CSC, Esteban-Ipac NAR, Recto MST, Castor MAR, Casis-Hao RJ, Nano ALM. Comparative effectiveness of probiotic strains on the prevention of pediatric atopic

- dermatitis: A systematic review and network meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2021 Aug;32(6):1255–70.
50. Qamer S, Deshmukh M, Patole S. Probiotics for cow's milk protein allergy: a systematic review of randomized controlled trials. *Eur J Pediatr*. 2019 Aug;178(8):1139–49.
51. Hosseini B, Berthon BS, Wark P, Wood LG. Effects of Fruit and Vegetable Consumption on Risk of Asthma, Wheezing and Immune Responses: A Systematic Review and Meta-Analysis. *Nutrients*. 2017 Mar 29;9(4):341.
52. Garcia-Marcos L, Castro-Rodriguez JA, Weinmayr G, Panagiotakos DB, Priftis KN, Nagel G. Influence of Mediterranean diet on asthma in children: a systematic review and meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2013 Jun;24(4):330–8.
53. Zhang GQ, Liu B, Li J, Luo CQ, Zhang Q, Chen JL, et al. Fish intake during pregnancy or infancy and allergic outcomes in children: A systematic review and meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2017 Mar;28(2):152–61.
54. Lin J, Zhang Y, Zhu X, Wang D, Dai J. Effects of supplementation with omega-3 fatty acids during pregnancy on asthma or wheeze of children: a systematic review and meta-analysis. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet*. 2020 May;33(10):1792–801.
55. Al-Saud B, Sigurdardóttir ST. Early Introduction of Egg and the Development of Egg Allergy in Children: A Systematic Review and Meta-Analysis. *Int Arch Allergy Immunol*. 2018;177(4):350–9.
56. Rodrigues M de B, Carvalho DS de, Chong-Silva DC, Urrutia-Pereira M, Albuquerque GSC de, Cieslak F, et al. Association between exposure to pesticides and allergic diseases in children and adolescents: a systematic review with meta-analysis. *J Pediatr (Rio J)*. 2022;98(6):551–64.
57. Cabieses B, Uphoff E, Pinart M, Antó JM, Wright J. A systematic review on the development of asthma and allergic diseases in relation to international immigration: the leading role of the environment confirmed. *PLoS One*. 2014;9(8):e105347.
58. Netuveli G, Hurwitz B, Levy M, Fletcher M, Barnes G, Durham SR, et al. Ethnic variations in UK asthma frequency, morbidity, and health-service use: a systematic review and meta-analysis. *Lancet Lond Engl*. 2005 Jan 22;365(9456):312–7.
59. Genuneit J. Exposure to farming environments in childhood and asthma and wheeze in rural populations: a systematic review with meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2012 Sep;23(6):509–18.
60. Calov M, Alinaghi F, Hamann CR, Silverberg J, Egeberg A, Thyssen JP. The Association Between Season of Birth and Atopic Dermatitis in the Northern Hemisphere: A Systematic Review and Meta-Analysis. *J Allergy Clin Immunol Pract*. 2020 Feb;8(2):674–680.e5.
61. Pennington AF, Strickland MJ, Klein M, Drews-Botsch C, Hansen C, Darrow LA. Caesarean delivery, childhood asthma, and effect modification by sex: An observational study and meta-analysis. *Paediatr Perinat Epidemiol*. 2018 Nov;32(6):495–503.
62. Słabuszewska-Jóźwiak A, Szymański JK, Ciebiera M, Sarecka-Hujar B, Jakiel G. Pediatrics Consequences of Caesarean Section-A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2020 Oct 31;17(21):8031.
63. Isayama T, Lewis-Mikhael AM, O'Reilly D, Beyene J, McDonald SD. Health Services Use by Late Preterm and Term Infants From Infancy to Adulthood: A Meta-analysis. *Pediatrics*. 2017 Jul;140(1):e20170266.
64. Bao Y, Chen Z, Liu E, Xiang L, Zhao D, Hong J. Risk Factors in Preschool Children for Predicting Asthma During the Preschool Age and the Early School Age: a Systematic Review

and Meta-Analysis. *Curr Allergy Asthma Rep*. 2017 Nov 18;17(12):85.

65. Spencer NJ, Blackburn CM, Read JM. Disabling chronic conditions in childhood and socioeconomic disadvantage: a systematic review and meta-analyses of observational studies. *BMJ Open*. 2015 Sep 3;5(9):e007062.

66. Eijkemans M, Mommers M, Draaisma JMT, Thijs C, Prins MH. Physical activity and asthma: a systematic review and meta-analysis. *PLoS One*. 2012;7(12):e50775.

67. Nagasaki T, Tabuchi T, Matsumoto H, Horimukai K. Age-specific associations of early daycare, older siblings, severe airway infection, and preterm birth with subsequent atopic diseases. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol*. 2022 Apr;33(4):e13771.

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