Respiratory and allergic multi-trajectories between 1 to 5.5 years old and their association with early life sleep characteristics

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INTRODUCTION

- Sleep troubles such as short sleep, difficulty falling asleep and frequent nocturnal awakenings affect 20-30% of children before the age of 3 and are likely to become chronic and persist into adolescence or even adulthood (Silvertsen et al, 2017).
- Associations between sleep disorders, respiratory and allergic health problems have been recently suggested (Krouse et al, 2008; Zhang et al, 2011; Koinis-Mitchell et al, 2012; Hu et al, 2020). However, the time line of their association is overlooked and data in children are lacking.

OBJECTIVES

- Identify clusters of sleep characteristics at 1 and at 5.5 years.
- Identify multi-trajectories of respiratory and allergic symptoms between 1 and 5.5 years.
- Examine the associations between sleep patterns at age 1 year and respiratory and allergic multi-trajectories between 1 and 5.5 years and the associations between those multi-trajectories and sleep patterns at age 5.5 years.

STUDY POPULATION : ELFE BIRTH COHORT

- The ELFE cohort recruited 18,300 newborns in metropolitan France in 2011.
- Data were collected from medical records and face-to-face interviews at the maternity ward and by telephone interviews at 2 months, 1, 2, 3.5 and 5.5 years.
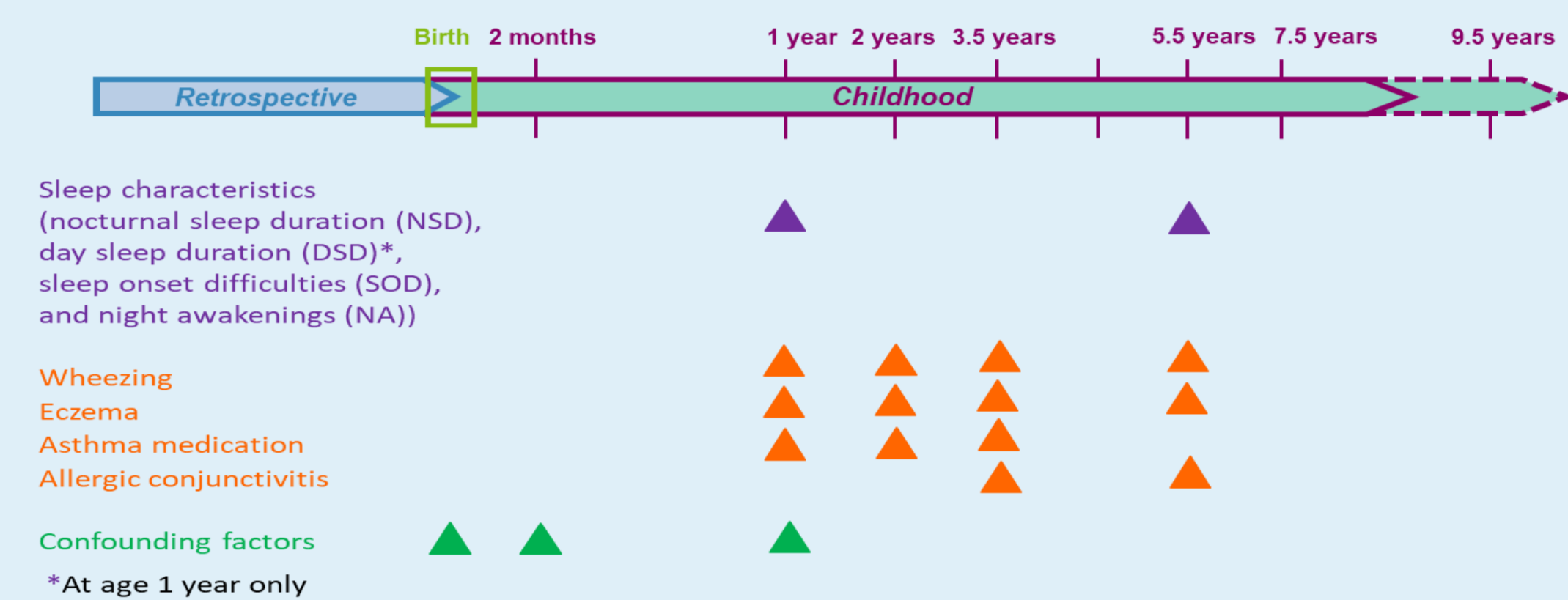
- Confounding factors were identified from the literature:
  - **Socio-demographic factors:** Mother's level of education, household income
  - **Mother characteristics:** age at conception, born abroad, single mother, body mass index (BMI) before pregnancy, parity, depressive symptoms and smoking during pregnancy, activity status at 1 year
  - **Child characteristics and perinatal factors**: sex, gestational age, birth weight, breastfeeding duration, exposure to passive smoking between 2 months and 1 year, mode of care at 1 year

METHODS

Identification of clusters of sleep characteristics
- Among children at age 1 year with information on nocturnal sleep duration (NSD), day sleep duration (DSD), sleep onset difficulties (SOD), and night waking (NW) (n=13,064); and at age 5.5 years with information on NSD, SOD, and NA (n=10,504).
- Using latent class analysis (LCA), an unsupervised modelling method.
- The child was assigned to the class for which he/she had the highest probability of belonging to.

Identification of respiratory and allergic multi-trajectories between 1 and 5.5 years
- Among children with data on wheezing, asthma medication (bronchodilators and/or inhaled corticosteroids), eczema, and allergic conjunctivitis between 1 and 5.5 years of age with at least 2 of 4 collection points (n= 10,524).
- Using group-based multi-trajectory modeling (GBMTM) method.
- Children were assigned to the multi-trajectory group for which they had the highest probability of belonging to.

Association analyses
- Among children with data on clusters of sleep characteristics at age 1 and 5.5 years and respiratory and allergic multi-trajectories (n=9,577).
- Using multinomial regression adjusted for confounding factors.
- After imputation of missing data for confounding factors (1.1%).

RESULTS

1. Characteristics of the study population

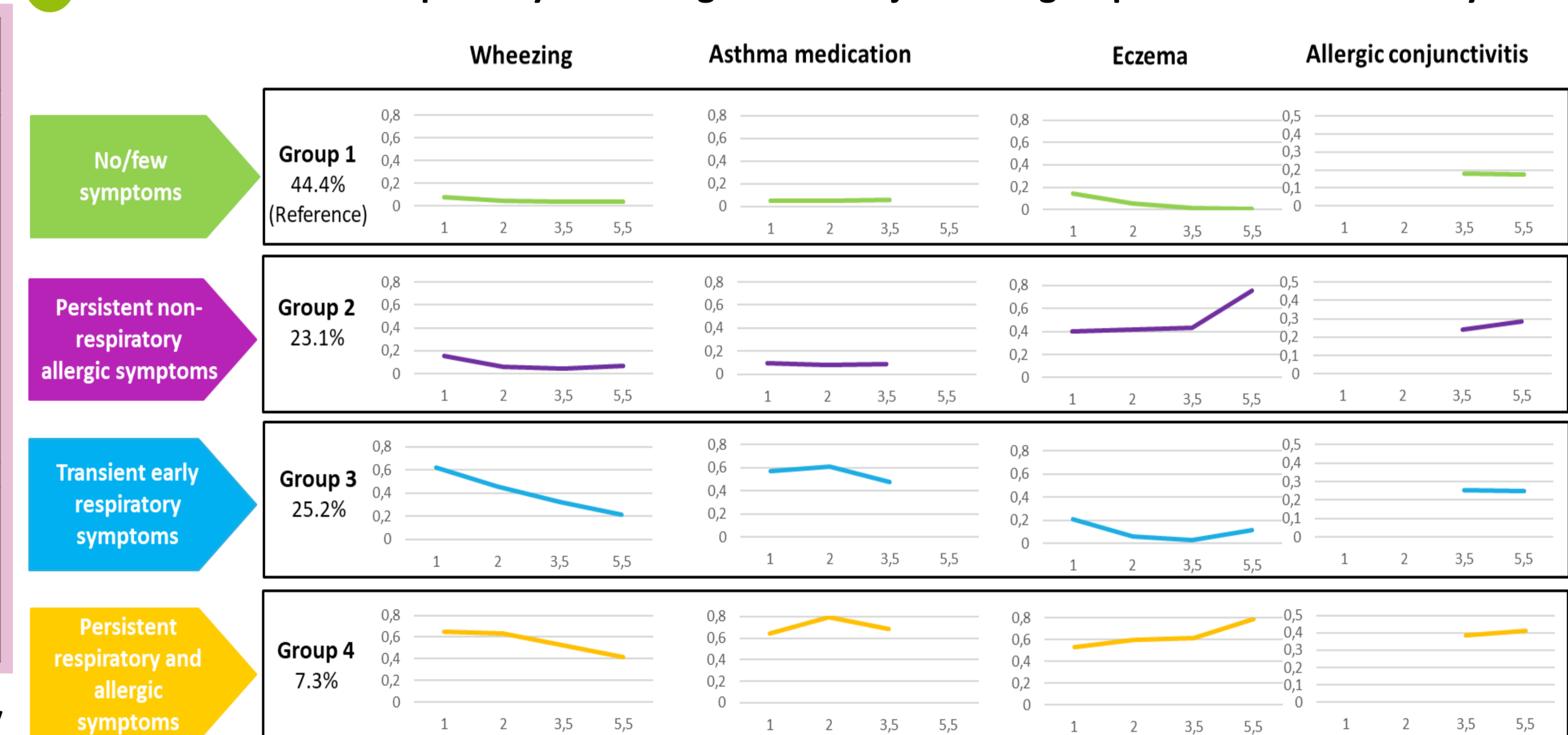|		Excluded population %(n) or mean(SD) (n=7,046)	Included population %(n) or mean(SD) (n=9,577)	p-value
Socio-demographics and maternal characteristics				
Maternal education level	< High school	61.4(3557)	30.0(2869)	<.0001
	High school	17.7(1023)	24.1(2312)	
	> High school	21.0(1214)	45.9(4396)	
Household monthly income (€/Consumption Unit)	≤ 1000	33.9(1684)	12.5(1154)	<.0001
	]1000 − 1385]	22.7(1128)	18.2(1676)	
	]1385 − 1662]	14.6(724)	18.1(1665)	
	]1662 − 2078]	16.7(833)	26.4(2436)	
	2078	12.2(605)	24.8(2285)	
Maternal age at conception (years)		29.5(5.5)	31.4(4.5)	<.0001
Mother born abroad	Yes	19.3(1352)	8.8(844)	<.0001
Maternal smoking during pregnancy	Yes	25.9(1795)	15.7(1496)	<.0001
Maternal pre-pregnancy BMI (kg/m²)		23.8(5.1)	23.3(4.5)	<.0001
Multiparous mother	Yes	67.9(4761)	65.6(6264)	0.0016
Maternal depressive symptoms during pregnancy	Yes	12.8(893)	11.8(1119)	0.0438
Children characteristics				
Sex	Boy	51.6(3637)	50.9(4879)	0.3859
Gestational age (weeks)		39.4(1.1)	39.5(1.1)	<.0001
Breastfeeding duration (month)		1.9(4.2)	4.1(5.7)	<.0001
Passive smoking exposure up to 1-year-old	Yes	8.2(260)	3.5(328)	<.0001
Main day-care arrangement at 1-year-old	Collective care	12.5(448)	17.6(1668)	<.0001
	Cared by employed person	30.4(1093)	46.7(4439)	
	Cared by family members	57.1(2051)	35.7(3392)	

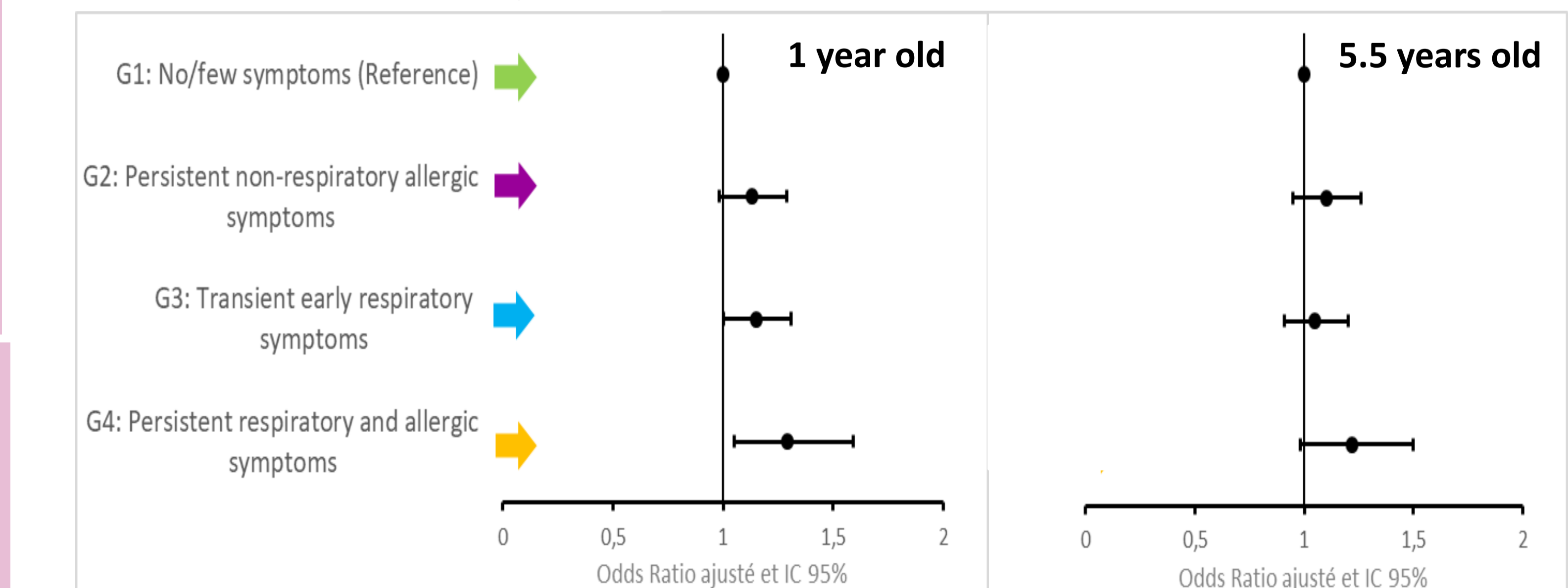### 2. Identification of 2 sleep characteristics clusters at age 1 and age 5.5 years respectively

- C1a (adequate sleep, 79.9% of children): NSD and DSD adequate for age with few SOD and NW;
- C2a (sleep troubles, 20.1% of children): Short night and day sleep duration with high prevalence of SOD and NW.

- C1b (adequate sleep, 83.1% of children): Sleep duration consistent with recommendations for age with low SOD and NW;
- C2b (sleep troubles, 16.9% of children): Short night sleep duration with high prevalence of SOD and NW.

3. Identification of 4 respiratory and allergic multi-trajectories groups between 1 and 5.5 years

- Group 1 — No/few symptoms — 44.4% (Reference)
- Group 2 — Persistent non-respiratory allergic symptoms — 23.1%
- Group 3 — Transient early respiratory symptoms — 25.2%
- Group 4 — Persistent respiratory and allergic symptoms — 7.3%

4. Associations between cluster C2a at 1 year (sleep troubles) and respiratory and allergic multi-trajectories (left panel) and between respiratory and allergic multi-trajectories and cluster C2b at 5.5 years (sleep troubles) (right panel)

- G1: No/few symptoms (Reference)
- G2: Persistent non-respiratory allergic symptoms
- G3: Transient early respiratory symptoms
- G4: Persistent respiratory and allergic symptoms

Belonging to cluster C2a was associated with an increased odds of belonging to G3 (adjusted odds ratio [95% interval confidence]; 1.14 [0.99-1.31]) and G4 (1.29 [1.05-1.59]).

After accounting for sleep clusters at age 1 year, belonging to G4 was associated with an increased odds of belonging to cluster C2b (1.21 [0.98-1.5]).

CONCLUSION

- This study evaluated sleep characteristics and the respiratory and allergic health evolution among preschoolers by using novel modelling methods.
- Sleep disturbances at 1 year were associated with poorer respiratory and allergic health between 1 and 5.5 years and respiratory and allergic problems between age 1 and 5.5 years were associated with sleep troubles at 5.5 years suggesting a certain bidirectional association between sleep and respiratory and allergic problems from an early age.
- Therefore, sleep could be a potential target for interventions to alleviate allergic and respiratory symptoms in preschoolers.

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