



Assessment of formaldehyde levels in relation to respiratory and allergic symptoms in children from Alba County schools, Romania

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Abstract Our study assessed the exposure to formaldehyde of Romanian school children in relation to the classroom indoor environment characteristics and respiratory and allergic symptoms reported in a questionnaire survey, using the data collected in the SINPHONIE

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(Schools Indoor Pollution and Health: Observatory Network in Europe) project. Measurements of formaldehyde and microclimate parameters were conducted in three classrooms per school, in five schools, together with one outdoor measurement at each school. Questionnaires were used to collect information on classroom characteristics and health effects among children. The indoor formaldehyde levels for a school week varied between 15.5 and 66.2 $\mu\text{g}/\text{m}^3$, with a median value of 34.8 $\mu\text{g}/\text{m}^3$. The adjusted odds ratios for allergy-like, asthma-like, and flu-like symptoms were 3.23 (95% CI 1.31–8.00), 2.69 (95% CI 1.04–6.97), and 2.39 (95% CI 1.04–5.50), respectively, when exposed to higher formaldehyde levels ($\geq 35 \mu\text{g}/\text{m}^3$) during a school week, compared to lower formaldehyde level exposure ($< 35 \mu\text{g}/\text{m}^3$). Higher levels of indoor formaldehyde were significantly associated with health symptoms in children. The high indoor formaldehyde levels were related to the use of water-resistant paint for ceiling coverings, moisture damage signs, and lower classroom natural ventilation rates.

Keywords Exposure · Formaldehyde levels · Indoor air quality · Respiratory and allergic symptoms · School children

Introduction

In modern life, we spend much of our time in the indoor environment, which becomes a significant contributor to our exposure to air contaminants.

Indoor air quality (IAQ) has been found to be related to a variety of health effects, such as allergic diseases and asthma (Annesi-Maesano et al. 2012), thus, becoming a major concern in Europe, especially for the school environment, considering that children are a susceptible subpopulation, as their defense mechanisms are developing, and the volume of air inhaled per their body weight is higher than in adults (Annesi-Maesano et al. 2003).

Along the years, a series of studies have been conducted in Europe, such as the Indoor Air Pollution in Schools, Health Effects of School Environment (HESE), School Environment and Respiratory Health of Children (SEARCH), and Schools Indoor Pollution and Health: Observatory Network in Europe (SINPHONIE), to collect data on the IAQ in European schools, in order to provide recommendations and guidelines for a healthy environment inside schools (European Commission 2006; Csobod et al. 2010; Csobod et al. 2014).

Formaldehyde is a highly reactive aldehyde, known for its preservative and anti-bacterial properties, but it is also widely used in construction materials and furniture production, and, thus, formaldehyde has come to act as a ubiquitous air pollutant in the indoor environment from homes and schools (IARC 2012). Epidemiologic studies in the last 10 years have shown associations between formaldehyde exposure and an increased risk of health effects, such as sensory irritation, allergy, and respiratory diseases, especially in children. Thus, children's exposure to formaldehyde in the household indoor environment has been linked to a higher risk of allergic sensitization to ordinary aeroallergens. Also, an increased frequency of respiratory symptoms was found in children exposed to higher indoor levels of formaldehyde (Garrett et al. 1999). A body of evidences has indicated an association between exposure to formaldehyde and asthma in children (McGwin et al. 2010). In addition, a study by Dannemiller et al. showed that children with poorly controlled asthma tended to be exposed to higher formaldehyde concentrations in their home indoor environments as compared to other asthmatic children (Dannemiller et al. 2013). Considering the risk for adverse health effects, the World Health Organization (WHO) established a guideline value for formaldehyde exposure in the indoor environment of 0.1 mg/m^3 ($100 \text{ }\mu\text{g/m}^3$ or

0.08 ppm), to be protective for the overall population (WHO 2002; Nielsen and Wolkoff 2010; Wolkoff and Nielsen 2010; Nielsen et al. 2013). However, few studies have examined the health impacts of relatively low levels of formaldehyde exposure among children, especially in school settings. This study's aim was to use the Romanian dataset from the SINPHONIE project to evaluate formaldehyde levels inside classrooms in Romanian schools and assess school children's exposure to levels of formaldehyde lower than the WHO guideline, in relation to the classroom indoor environment characteristics and health effects reported in a questionnaire survey.

Materials and methods

Study population and data collection

This study analyzed the Romanian dataset collected in the SINPHONIE project, a multicenter research project funded by the European Parliament, which included 38 environment and health institutions across 25 European countries, and was conducted between 2010 and 2012 (Csobod et al. 2014; Kephelopoulos et al. 2014).

In Romania, five public primary schools from both rural and urban areas of Alba County (two schools in rural area, in the localities of Unirea and Vintu de Jos, and three schools in urban areas, in the localities of Aiud, Alba Iulia, and Sebes) were selected to be included in the study. In a total of 15 classrooms (three classrooms per school), microclimate parameters (temperature, relative humidity (RH), ventilation rates) and formaldehyde levels were measured during an entire school week (five days). A more detailed description of the selection criteria for the schools and classrooms was provided in our previous work (Lin et al. 2017). Fifteen indoor measurements and five outdoor measurements were conducted in five schools. A total of 280 questionnaires were collected from 139 male students and 141 female students, and 15 questionnaires about the characteristics of each monitored classroom (such as number of occupants, surface, volume), were answered by teachers. This particular study used some of the data collected from two SINPHONIE questionnaires—the *questionnaire for students* and the *classroom questionnaire*. From the *questionnaire for students*, we

abstracted information on students' respiratory symptoms and allergic health conditions (symptoms in the past week), and, from the *classroom questionnaire*, we abstracted information on the characteristics of the classroom, cleaning and ventilation procedures, furnishings, perceptions of IAQ, microclimate conditions in the classroom during the cold season, and the presence of moisture damage and mold. The participants in the study provided written informed consent prior to study participation (given by the parents in the case of children).

A more detailed description of the SINPHONIE questionnaire content was given in our previous work (Lin et al. 2017; Palumbo et al. 2018). All data we used in this manuscript were collected in the autumn–winter season of 2011 (from late October to December).

Exposure measurements and outcome definition

The measurements of microclimate parameters and carbon dioxide (CO₂) indoor and outdoor concentrations were performed for five days using a calibrated IAQ-CALC 7545-type multimeter device (TSI Inc., Shoreview, USA) and reported as average concentrations for the school week. Indoor and outdoor formaldehyde concentrations from air samples were analyzed using high-performance liquid chromatography (HPLC) coupled with a UV–Vis detector. The air samples were collected on Radiello passive samplers exposed for five days inside the three investigated classrooms and in one outside location, in each school.

Our study included variables from the *questionnaire for students* to define the outcomes of allergy-like symptoms, asthma-like symptoms, and flu-like symptoms, as described in our previous work (Palumbo et al. 2018). In brief, allergy-like symptoms were characterized by any symptoms/diagnoses in the past week of skin conditions, such as rash, itch, eczema, eye disorders, such as red, dry, swollen, itching, or burning eyes, or sensation of “sand in the eyes,” and symptoms related to rhinitis, such as itching nose, sneezes, and/or stuffy or blocked nose. Asthma-like symptoms included the following symptoms: difficult breathing, dry cough, and wheezing in the past week. Flu-like symptoms included symptoms/diagnoses like runny, bleeding nose, dry throat, sore throat, feeling like getting a cold, headache, malaise, fatigue, having a cold, influenza or fever, and muscle pain, in the past week.

Formaldehyde sampling and chemical analysis

The air samples were collected by passive sampling on Radiello cartridges (Sigma-Aldrich, Hamburg, Germany) impregnated with 2,4-dinitrophenylhydrazine (2,4-DNPH). The samplers were installed in three classrooms and in an outdoor location in each of the five schools participating in the project, according to ISO 16000-2 protocol (ISO 16000-2 2004). In brief, the Radiello passive samplers were installed in the same location in each classroom, at 2 m away from the walls and 1.5 m height from the ground. The passive samplers were exposed for five school days (Monday to Friday). At the end of the five days of exposure, the passive samplers were collected and transported to the lab, where they were analyzed within 48 h from collection. The method used for formaldehyde analysis from the air samples was a validated method described in detail and published by the Joint Research Centre (JRC), the European Commission's science and knowledge service (JRC 2011). In brief, the method is based on the derivatization of formaldehyde with 2,4-DNPH from the passive sampler and the chemical analysis using the HPLC technique coupled with UV–Vis detection. In our laboratory, the formaldehyde analysis was performed using a HPLC Shimadzu SPD-10A with a UV–Vis detector (Shimadzu Corporation, Kyoto, Japan). All the chemicals used for analysis were of high purity grade. Also, the water needed for analysis was purified using a Milli-Q Ultrapure water purification system (Millipore, USA). The chromatographic separation was performed with a reverse-phase (RP) column Nova-Pak C18 (60 Å, 300 mm × 3.9 mm, with a particle size of 4 µm) (Waters, USA) by isocratic elution with a mixture of acetonitrile (Sigma-Aldrich, Germany) and water 62:38 (v:v). The samples were manually injected using a valve with a volume of 5 µL loop. The separations were performed with a constant flow rate of 1 mL/min, and the column temperature was maintained at ambient temperature. The detection was performed at 360 nm wavelength. The calibration linearity was evaluated using the following concentrations: 0.5, 1, 5, 15, 25, 50, and 70 µg/mL. RP-HPLC procedure had a good linearity as the correlation coefficients were over 0.999, for the whole range of concentrations. The method detection limit was 0.1 µg/m³. Formaldehyde concentration determination in the air was based on the absolute amount of free formaldehyde detected, the exposure time of five days (108 h and 6480 min,

respectively), and the sampling rate for free formaldehyde, of 99 mL/min.

Statistical analysis

Descriptive statistics was conducted for the indoor and outdoor measured formaldehyde and CO₂ concentrations and other microclimate parameters. Differences in formaldehyde exposure, temperature, RH, and ventilation rate for various classroom characteristics were tested by univariate analysis. For the multivariate analysis, formaldehyde was categorized as “higher level ($> 35 \mu\text{g}/\text{m}^3$)” and “lower level ($\leq 35 \mu\text{g}/\text{m}^3$)” based on the median concentration of measured values. Health outcomes were divided into the following 3 categories: asthma-like symptoms, flu-like symptoms, and allergy-like symptoms. Each category had been labeled as “yes” if any of the symptoms in the category occurred in children, or it had been labeled as “no” and used as reference group for each category, when no symptoms occurred (the entire category of symptoms including asthma-like symptoms, flu-like symptoms, and allergy-like symptoms together was categorized as “1” if any of the above-mentioned symptoms showed up among children, and “0” if no symptoms occurred). Backward model selection was used to check whether

respiratory symptoms could be associated with other parameters (e.g., CO₂, microclimate parameters, asthma attack, and exposure to tobacco smoke in the past week) and select potential confounders. Multivariate logistic regression was applied to analyze associations between outcomes (children’s respiratory health symptoms) and exposure (indoor formaldehyde and other selected chemical parameters), controlling for potential confounders, including age, gender, asthma attack, and exposure to tobacco smoke in the past week, and microclimate parameters. Asthma-like symptoms, flu-like symptoms, and allergy-like symptoms were all considered as dependent variables and fitted in each regression model separately. All statistical analysis was conducted using SAS V9.4 (SAS Institute Inc., Cary, NC).

Results

Table 1 shows the characteristics of the classrooms where the environmental measurements were performed. Each classroom had an average of 23 students (ranging from 15 to 32). Among these classrooms, room surface (floor space) per student ranged from 1.3 to 3.9 m², and room volume per student ranged between 4.6 and 12.8 m³.

Table 1 Selected classroom characteristics

School	Classroom	Occupancy (number of students) (N)	Room surface (floor space) (m ²)	Ceiling height (m)	Room volume (m ³)	Floor space per student (m ² per student)	Room volume per student (m ³ per student)
1	1	24	68.0	3.50	238.0	2.83	9.92
	2	20	32.0	3.50	112.0	1.60	5.60
	3	20	52.0	3.50	182.0	2.60	9.10
2	1	26	55.0	3.20	176.0	2.12	6.77
	2	28	55.0	3.20	176.0	1.96	6.29
	3	26	37.6	3.20	120.3	1.45	4.63
3	1	20	27.0	3.80	102.6	1.35	5.13
	2	22	39.0	3.80	148.2	1.77	6.74
	3	24	42.0	3.80	159.6	1.75	6.65
4	1	27	63.6	3.25	206.7	2.36	7.66
	2	15	59.0	3.25	191.8	3.93	12.78
	3	27	49.5	3.80	188.1	1.83	6.97
5	1	15	40.0	3.20	128.0	2.67	8.53
	2	32	48.6	3.80	184.7	1.52	5.77
	3	23	48.6	3.80	184.7	2.11	8.03

Table 2 summarizes the results of the environmental measurements performed in schools, during the cold season. The indoor formaldehyde level had a median value of $34.8 \mu\text{g}/\text{m}^3$ (ranging from 15.5 to $66.2 \mu\text{g}/\text{m}^3$), while the median outdoor level was $10.1 \mu\text{g}/\text{m}^3$ (ranging from 6 to $12.9 \mu\text{g}/\text{m}^3$). The average indoor temperature was 20.3°C (ranging from 16 to 23.9°C), while the average outdoor temperature was 1.9°C (ranging from -4.1 to 5.6°C). Among all the classrooms, the average RH of the classrooms was $45.1 \pm 10.0\%$ indoor and $81 \pm 7.7\%$ outdoor. The ventilation rate in the classrooms was on average $0.08 \pm 0.03 \text{ h}^{-1}$, and the average CO_2 level indoor was 1569.9 ppm (ranging between 311.1 and 2767.7 ppm).

Within the limited range of indoor environment in school classroom measurements, formaldehyde concentration had a tendency to increase with the decline of the ventilation rate and with the rise of temperature and RH, but no significant correlation was found.

Table 3 describes the classroom characteristics reported in the questionnaires and their relationship with the levels of formaldehyde and microclimate factors measured indoors. Among all the characteristics, the water-resistant paint used for ceiling coverings in some of the classrooms was significantly associated with higher levels of indoor formaldehyde ($p = 0.042$). The orientation of classrooms was found to be significantly associated with ventilation rate, with higher recorded ventilation rates when classrooms faced the yard or garden as compared with when classrooms faced the streets ($p = 0.019$). Visible signs of moisture damage reported in some of the classrooms were significantly associated with higher levels of RH ($p = 0.016$) and lower ventilation rates ($p = 0.037$). Formaldehyde concentration was also

found to be related to visible signs of moisture damage, but less significant ($p = 0.053$). In addition, an association was seen between the RH and the moldy odor, with higher humidity recorded in classrooms where it has ever been noticed a moldy odor ($p = 0.028$). In the heating period, classrooms with windows opened every inter-class break had lower indoor formaldehyde than those with windows opened only 2 to 3 times or once a day, but the relationship was less significant ($p = 0.091$).

Logistic regression was conducted to calculate the odds ratios (OR) for the association between formaldehyde exposure and respiratory symptoms. An adjusted OR of 3.2 (95% CI 1.31–8.00) for allergy-like symptoms with higher indoor levels of formaldehyde was found, when controlling for age, gender, temperature, RH, and ventilation rate. Similarly, the odds for flu-like symptoms in children exposed to higher indoor formaldehyde levels ($> 35 \mu\text{g}/\text{m}^3$) were 2.4 (95% CI 1.04–5.50) times higher than the odds in children with lower level indoor formaldehyde exposure. Also, the odds for asthma-like symptoms were 2.7 (95% CI 1.04–6.97) times higher for children exposed to higher levels of indoor formaldehyde than for those exposed to lower indoor formaldehyde concentrations (Table 4).

Discussion

Indoor and outdoor formaldehyde levels

We found higher average levels and wider variations of formaldehyde concentrations inside the classrooms during a school week, compared to the levels outdoors, as

Table 2 Descriptive statistics on formaldehyde and CO_2 concentrations and microclimate parameter values measured indoor and outdoor in the Romanian schools

Variable	Mean	SD	Min.	25th percentile	Median	75th percentile	90th percentile	Max.
Indoor								
Formaldehyde ($\mu\text{g}/\text{m}^3$)	34.16	15.07	15.50	19.85	34.83	44.83	50.28	66.19
CO_2 (ppm)	1569.89	834.38	311.11	716.46	1828.95	2090.96	2562.89	2767.67
RH (%)	45.06	10.00	29.22	38.03	45.49	52.53	55.50	64.19
Temperature ($^\circ\text{C}$)	20.32	2.48	16.03	19.70	20.19	21.72	23.71	23.86
Ventilation rate (h^{-1})	0.08	0.03	0.03	0.06	0.08	0.11	0.11	0.12
Outdoor								
Formaldehyde ($\mu\text{g}/\text{m}^3$)	9.50	3.23	6.03	6.28	10.06	12.21	12.90	12.90
RH (%)	81.03	7.75	70.81	77.27	79.83	87.08	90.16	90.16
Temperature ($^\circ\text{C}$)	1.94	4.18	-4.07	-0.76	4.14	4.73	5.64	5.64

Table 3 Association between classroom characteristics and environment measurements

Classroom characteristics	Formaldehyde ($\mu\text{g}/\text{m}^3$)	<i>p</i>	Relative humidity (%)	<i>p</i>	Temperature ($^{\circ}\text{C}$)	<i>p</i>	Ventilation rate (h^{-1})	<i>p</i>
Orientation of the classroom								
Facing street	34.6	0.924	42.7	0.416	20.4	0.926	0.062	0.019**
Facing yard or garden	33.8		47.1		20.3		0.094	
Ceiling covering								
Water-resistant paint	38.8	0.042**	48.1	0.049**	20.2	0.789	0.082	0.514
Other materials	21.4		36.8		20.6		0.071	
Ever visible signs of moisture damage								
No	30.5	0.053*	42.1	0.016**	20.1	0.450	0.086	0.037**
Yes	48.9		56.8		21.3		0.050	
Ever noticed moldy odor								
No	33.2	0.138	42.9	0.028**	20.1	0.336	0.082	0.347
Yes	40.3		59.0		22.0		0.062	
Windows opened in heating period								
Every inter-class break	25.3	0.091*	44.0	0.939	19.8	0.777	0.081	0.225
2 to 3 times a day	35.3		46.3		20.3		0.064	
Once a day	46.1		45.0		21.1		0.095	

Only characteristics with *p* values less than 1.0 were shown in the table

**p* < 0.10

***p* < 0.05

shown also in another recent study (Lee et al. 2018). Comparing the indoor (34.2 ± 15.1) and outdoor (9.5 ± 3.2) average formaldehyde levels in our study, we showed that the outdoor formaldehyde levels are significantly lower, as previously reported in other studies (JRC 2005) (average of $7.2 \mu\text{g}/\text{m}^3$). Consequently, we can state that formaldehyde is, par excellence, a specific contaminant for the indoor environment. The wider variations of indoor formaldehyde concentrations might be due to the presence of multiple and different indoor formaldehyde sources with emissions that vary over time, in a larger range. We also report higher average formaldehyde levels inside the classrooms during a school week, in rural area compared to urban area, probably due to lower ventilation rate in the classrooms in rural area (in the attempt to conserve the heat inside)

and indoor sources with higher emission (e.g., building materials of poor quality) compared to urban schools. We calculated the ratios of indoor/outdoor (I/O) average formaldehyde concentrations in urban and rural areas, showing a higher I/O ratio in the rural area (4.8) compared to urban area (2.8), which is consistent with results reported in a previous study conducted in Korea (Yoon et al. 2011). Among the schools, the highest average formaldehyde level inside the classrooms was measured in the school in Unirea, located towards a heavy traffic road and having only natural ventilation, and is probably due to the higher emissions from the sources inside (laminated flooring and particleboard furniture that may release formaldehyde due to the degradation process of the formaldehyde-based resins used in these wood composite products (Roffael 1993)).

Table 4 Logistic regression for the relationship between formaldehyde exposure and reported health outcomes

Formaldehyde concentration	Adjusted OR		
	Allergy-like symptoms	Flu-like symptoms	Asthma-like symptoms
Higher ($> 35 \mu\text{g}/\text{m}^3$)	3.23 (1.31–8.00)	2.39 (1.04–5.50)	2.69 (1.04–6.97)
Lower ($\leq 35 \mu\text{g}/\text{m}^3$)	Ref	Ref	Ref

Adjusted for age, gender, NO_2 , CO, CO_2 , temperature, relative humidity, ventilation rate, and tobacco smoke exposure for the past week

Comparison of the indoor formaldehyde levels with formaldehyde levels measured in previous studies

The levels of formaldehyde exposure in schools have wide variations across countries. However, sometimes, the comparisons of formaldehyde levels across studies may be problematic due to the differences in the sampling methods, measurement, and analysis. At the European level, in the SINPHONIE project, the overall (for all participating countries) median of average weekly formaldehyde levels inside the classrooms in the investigated European schools was $12 \mu\text{g}/\text{m}^3$, with variations between 1 and $66 \mu\text{g}/\text{m}^3$, lower than the concentration we report (median of $34.8 \mu\text{g}/\text{m}^3$, ranging between 15.5 and $66.2 \mu\text{g}/\text{m}^3$). The maximum indoor formaldehyde level during a school week, and also the highest median value at the country level, was reported in our county, Romania, closely followed by Poland (WHO 2015), but none of the formaldehyde concentrations measured inside the classrooms in our study exceeded the current WHO guideline of $0.1 \text{ mg}/\text{m}^3$ ($100 \mu\text{g}/\text{m}^3$) for indoor formaldehyde (WHO 2002). In another European project, the SEARCH project, the indoor formaldehyde levels measured during one school week (the same sampling period as in our study) had wide variations among the participating countries, ranging from very low average values ($1.7 \mu\text{g}/\text{m}^3$ in Serbia, $2.4 \mu\text{g}/\text{m}^3$ in Hungary) to high average values ($33.1 \mu\text{g}/\text{m}^3$ in Italy) (Csobod et al. 2010), close to the average weekly concentration that we report in our study. A WHO Schools Survey carried out between 2012 and 2014, in five European countries, with monitoring conducted during a school week (as in our study), reported a median indoor formaldehyde concentration of 6.6, 8.5, and $10.7 \mu\text{g}/\text{m}^3$ for the schools in Albania, Croatia, and Estonia, respectively, much lower than the median of weekly levels we report in our study, and a median outdoor formaldehyde concentration of 3.3, 2.2, and $1.7 \mu\text{g}/\text{m}^3$ in Albania, Croatia, and Estonia, respectively, also, much lower than the outdoor formaldehyde level we report here (WHO 2015). A study conducted within the frame of the ISAAC project, in 1999, in 108 schools and 401 classrooms, in 6 cities from France (Annesi-Maesano et al. 2001), reported formaldehyde concentrations in the range 4– $100 \mu\text{g}/\text{m}^3$, with a mean value of $27 \mu\text{g}/\text{m}^3$, lower than the mean of weekly levels measured in our study (of $34.2 \mu\text{g}/\text{m}^3$). An evaluation of the IAQ performed during the cold (heating) and hot (non-heating) seasons, in 2004–2005, in 167 classrooms from

schools in Germany (Fromme et al. 2008), reported indoor formaldehyde concentrations, between 3.1 and $46.1 \mu\text{g}/\text{m}^3$, lower than the minimum and maximum weekly concentrations that we measured.

CO₂ levels inside the classrooms

We also detected high CO₂ levels inside all the investigated classrooms in the participating schools. The average value of the indoor CO₂ weekly concentrations was 1569.9 ppm, exceeding the UK guideline value and the reference value in Germany, of 1000 ppm (Coley and Beisteiner 2002; WHO 2015), and, also, the Netherlands guideline value of 1200 ppm (Health Council of The Netherlands 2010), indicating poor ventilation rate inside the classrooms. However, CO₂ should also be looked at as an air contaminant, since the indoor exposure to high levels (> 1000 ppm) has been shown to affect human decision-making performance (Satish et al. 2012). As compared to the average indoor CO₂ values reported in the HESE study conducted in schools from five European countries (Italy, Norway, Sweden, Denmark, and France), our results showed an average indoor CO₂ value higher than the average values reported in some of the HESE study schools, in the six participating cities (Siena: 1954 ppm; Udine: 1818 ppm; Oslo: 1158 ppm; Uppsala: 681 ppm; Aarhus: 1568 ppm; Reims: 1660 ppm) (European Commission 2006).

Microclimate parameters and floor space measurement

For the microclimate parameters measured inside the classrooms, we report lower minimum and maximum temperature values and higher RH maximum values as compared to the reference values in Germany (WHO 2015) (our values at 16–24 °C as compared to 20–26 °C in Germany and our maximum RH value at 64% as compared to 50% in Germany, respectively). The higher RH value can explain the “steamy window glasses” reported in the questionnaire survey, and it may support mold growth which can explain the moldy odor inside the classroom, also reported in the questionnaire survey. Moreover, our study results showed a significant association between RH and moldy odor, with higher humidity recorded in classrooms where it has ever been noticed a moldy odor ($p = 0.028$).

As regards the floor space per student in the classroom, we report an overall average value of 2 m^2 per student (for the 15 investigated classrooms), but we had

two classrooms in two different schools for which the floor space per student was less than 1.5 m², pointing out that those classrooms were overcrowded. Overcrowding of the classrooms (less than 1.5 m² per student) was previously linked to increased indoor levels of contaminants, such as CO₂, formaldehyde, volatile organic compounds (VOCs), and PM₁₀, and a significantly higher number of children in these classrooms developed respiratory symptoms compared to the children in classrooms with more floor space (WHO 2015).

Indoor environment factors in relation to formaldehyde levels

In this study, we showed that formaldehyde concentration tended to increase with the decline of the ventilation rate and the rise of temperature and RH, but no significant correlation was found. Previous studies have shown that indoor formaldehyde levels are influenced by a few factors, such as the age of the building (Raw et al. 2004), temperature and RH (Haghighat and De Bellis 1998), ventilation rate (Raw et al. 2004; Gilbert et al. 2006), the season (Raw et al. 2004), and smoking in the room (Marchand et al. 2006). The levels of contaminant concentrations, such as formaldehyde and CO₂, in the indoor environment can be decreased by controlling the main factor that causes their release into the air, in the first place, namely, the specific sources. Thus, the use of low-emission materials and products, an adequate choosing of the heating system, the fuel used, a proper venting system for the combustion products, and adapting the number of occupants to the size of the classroom are few simple measures that can highly contribute to the decrease of the pollutant levels indoors, positively influencing the IAQ.

Another factor that has a significant impact on the IAQ is the ventilation of the indoor space. During our investigation in the heating season, we measured higher indoor formaldehyde levels in the classrooms with lower natural ventilation rates (windows opening during inter-class breaks less frequent and for shorter time), as compared to those with higher natural ventilation rates (windows opening every inter-class break and for longer time). Thus, ensuring an adequate ventilation inside the classrooms will considerably improve the quality of the air the children are breathing (WHO 2000).

Water-resistant paint used for ceiling coverings in some of the classrooms was significantly associated with higher indoor formaldehyde levels, probably due

to a greater release of formaldehyde from the recently applied paint, as it is a current practice in Romania to paint the classroom walls and ceiling at the beginning of the school year. We can speculate that the paint may have had formaldehyde-releasing compounds that were used as biocides in the paint (Salthammer et al. 2010), thus explaining the association that we found with higher indoor formaldehyde levels. Also, this finding is consistent with results reported in a recent study conducted in Korea (Lee et al. 2018). Moreover, we showed that indoor formaldehyde levels were also related to visible signs of moisture damage, although less significant ($p = 0.053$), suggesting that the higher RH inside the classrooms that may produce moisture damage, may also influence the indoor formaldehyde levels.

Effects of formaldehyde exposure on respiratory health

Our study results showed that higher formaldehyde levels inside the classrooms were associated with a higher risk for the children to develop health symptoms, such as allergy-like, flu-like, and asthma-like symptoms.

Several potential mechanisms through which formaldehyde exposure may affect the respiratory system have been described. Thus, formaldehyde is an irritant pollutant which is readily absorbed into the respiratory tract tissue, where it may produce a T helper-2 mediated inflammatory response of the respiratory mucosa, possibly leading to cytokine mediator release. As a small molecule, formaldehyde may bind to the amino group in proteins acquiring antigenic capacities, so, the exposure may lead to an immune response with the formation of specific antibodies, triggering a local mast cell response (Elias et al. 2003). Also, it has been shown that formaldehyde may react with the thiol group thus interfering with the functions of *S*-nitrosoglutathione (a bronchodilator produced in the body), leading to an airway response (Thompson et al. 2008).

Exposures to a complex mixture of chemical and biological contaminants in the school environment, where children spend a lot of their time, may be higher than in homes due to the high density of occupants and may negatively impact children's health, well-being, learning, and academic performance. In this regard, the development and implementation of environmental health programs in schools to promote children's health is a comprehensive and cost-effective approach, in order to achieve public health benefits.

Strengths and limitations

Among the strengths of our study, we enumerate the following: the use of the complex Romanian dataset within the SINPHONIE study, comprising data collected by pursuing standardized work protocols for all the participating countries, to secure comparable databases at the European level; the use of two different questionnaires in this survey, to attain a multiple perspective insight of the classroom and school; the easy access to the population groups with high susceptibility to develop respiratory health effects when exposed to air pollutants, with a high response rate in the questionnaire survey (89.7% for the questionnaire applied to the school children, and 100% for the classroom questionnaire filled in by the teachers), and the high-quality formaldehyde measurement data, as the sample collection, and the formaldehyde chemical analysis was performed following the JRC standardized operating procedures, with quality control at the JRC laboratories. Also, another strength of our study is that we have performed the measurements during the heating season when the natural ventilation is provided for much shorter periods of time compared to the warm and hot seasons, and when there is no natural ventilation after the school hours; so, our measurements reflect very well the level of exposure inside the classrooms, due to all sources of pollution, a fact confirmed by the wide variation between the indoor and outdoor formaldehyde levels, in all the investigated schools. As far as we know, we are one of the first who used the Romanian dataset from the SINPHONIE study to assess school children's exposure to formaldehyde in relation to the classroom indoor environment characteristics and respiratory health symptoms reported in a questionnaire survey.

As limitations of our study, we quote the following: the possibility of an altered perception of the study participants on their symptoms and recall bias as regards the health symptoms, but we believe that the bias was reduced by using questions standardized and validated in the previous studies, and by including exposure frequency and duration questions, not only yes/no type questions. Selection bias is also of concern. Nevertheless, we included schools from both rural and urban areas, and within each school, we insured variability as regards the location and the orientation of the classroom. Also, the analysis that we have performed here did not include other indoor pollutants that we measured inside the classrooms in our study (such as PM₁₀, NO₂,

VOCs), as we plan to perform a complex multi-pollutant model analysis, to assess the exposure to these pollutants in relation to the children's spirometry test results, and present those results in a future manuscript.

Conclusions

In the SINPHONIE project, among all the European participating countries, Romania had the highest indoor formaldehyde maximum concentration during a school week and, also, the highest median value at the country level. Our study indicated that the classroom indoor formaldehyde concentrations measured during the heating season tend to increase with the decline of the ventilation rate and the rise of temperature and RH. The use of water-resistant paint for ceiling coverings in the classroom was found to be significantly associated with higher indoor formaldehyde levels, while moisture damage signs and lower natural ventilation rates (windows open less time) were also associated with higher indoor formaldehyde, but less significant. Also, we showed an association between higher indoor formaldehyde level and the risk for health symptoms (allergy-like, flu-like, and asthma-like symptoms) in children exposed during the school hours.

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Compliance with ethical standards

Conflict of interest The authors report that there are no other conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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