

Prevalence of childhood cough in epidemiological studies depends on the question used: findings from two population-based studies

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Summary

BACKGROUND: Epidemiological studies use different questions to assess recurrent cough in children. In two independent population-based studies, we assessed how prevalence estimates of cough vary depending on the questions parents are asked about their child's cough and how answers to the different questions overlap.

METHODS: We analysed cross-sectional data from two population-based studies on respiratory health: *LuftiBus in the School* (LUIS), conducted in 2013–2016 among 6- to 17-year-school children in the Canton of Zurich, Switzerland, and the 1998 *Leicester Respiratory Cohort* (LRC) study, UK where we used data from 6- to 8-year-old children from the 2003 follow-up survey. Both studies used parental questionnaires that included the same three questions on the child's cough, namely cough without a cold, dry cough at night and coughing more than others. We assessed how the prevalence of cough varied depending on the question and how answers to the different questions on cough overlapped. We also assessed how results were influenced by age, sex, presence of wheeze and parental education.

RESULTS: We included 3457 children aged 6–17 years from LUIS and 2100 children aged 6–8 years from LRC. All respiratory outcomes – cough, wheeze and physician-diagnosed asthma – were reported twice as often in the LRC as in LUIS. We found large differences in the prevalence of parent-reported cough between the three cough questions. In LUIS, 880 (25%) parents reported cough without a cold, 394 (11%) dry night cough, and 159 (5%) reported that their child coughed more than other children. In the LRC, these numbers were 1003 (48%), 527 (25%) and 227 (11%). There was only partial overlap of answers, with 89 (3%) answering yes to all questions in LUIS and 168 (8%) in LRC. Prevalence of all types of cough and overlap between the cough questions was higher in children with current wheeze.

CONCLUSION: In both population-based studies prevalence estimates of cough depended strongly on the question used to assess cough with only partial overlap of responses to different questions. Epidemiological studies on cough can only be compared if they used exactly the same questions for cough.

Introduction

Epidemiological studies often estimate prevalence of cough in children through parental questionnaires [1–5]. Cough is common in children and occurs as a physiological response during respiratory tract infections, but frequent cough in the absence of a respiratory tract infection is typical for chronic respiratory diseases and is often present in children with asthma [6]. Different research networks have developed specific questions to identify children with cough that exceeds the expected physiological occurrence. The American Thoracic Society (ATS) questionnaire asks if the child has “a cough even without having a cold” [7]. The International Study of Asthma and Allergies in Childhood (ISAAC) asks for “a dry cough at night, apart from a cough associated with a cold or a chest infection” [8] and a questionnaire developed in Southampton and used in several studies inquires if the child “coughs more than other children” [9].

Most epidemiological studies conducted in the field of child respiratory health have included only one of these cough questions, basing estimates on the prevalence of cough on this single question [10–12]. This has made it impossible to distinguish whether differences in prevalence of cough between studies reflect regional variations, differences in study populations, varying exposure to environmental risk factors or if they merely result from differences in the wording of the question. We used data from two large population-based studies that included all three questions on cough in the same questionnaire. We aimed to assess how prevalence of parent-reported cough in children

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varies depending on the question used and how answers to the different cough questions overlap.

Methods

Study design and population

We used cross-sectional data from two population-based studies on respiratory health in children. *LuftiBus in the School* (LUIS) was a population-based study conducted in 2013–2016 among school children aged 6–17 years in the canton of Zurich, Switzerland [13]. The heads of the 490 schools in the canton were approached and their schools invited to participate in the study. Whole classes were recruited and parents completed a questionnaire on their child's respiratory symptoms after informed consent had been obtained. Trained field workers measured lung function of participating children in a specially equipped bus that visited the schools. Further information on questionnaires and measurements have been published [13]. The LUIS study was approved by the ethics committee of the canton of Zurich (KEK-ZH-Nr: 2014-0491). For this analysis, we included all participants who returned a parental questionnaire.

To externally validate our findings, we also analysed data from the 1998 *Leicester Respiratory Cohort* (LRC), a population-based cohort study conducted in children in Leicestershire, UK [14]. The LRC study was approved by the Leicestershire Health Authority Research Ethics Committee. In order to have a group of children matched for age and the same questions on cough as in LUIS, we analysed answers from the LRC questionnaires obtained in 2003 when the children were aged 6–8 years.

Study outcomes

We analysed responses to three different questions about recurrent cough: “Does your child have a cough even without having a cold?” (cough without a cold) from the ATS questionnaire [7], “In the last 12 months has your child had a dry cough at night, apart from a cough associated with a cold or a chest infection?” (dry night cough) from the ISAAC questionnaire [8] and “Do you think your child coughs more than other children?” (cough more than others) from the Southampton study [9]. In the Swiss-based study, the questions were asked in German and in the UK-based study, the questions were asked in English.

Statistical analysis

We compared the prevalence of cough as assessed using the three questions and constructed a Venn diagram to describe the degree of overlap between answers to the three questions. We stratified the analyses for factors that could affect the prevalence of cough: current wheeze (as a proxy for asthma), sex, age-group (6–9, 10–13 and 14–17 years; only in LUIS) and parental education level. In the LUIS study, we also assessed how the responses to two questions on cough duration (cough continuing for >3 weeks and >2 months) differed across the responses to the three cough questions. These questions had not been asked in the LRC 2003 questionnaire. We summarised categorical data as proportions with 95% confidence intervals (95% CIs) and continuous data as medians with interquartile range

(IQR), and range. We used chi-square or Fisher's exact tests for associations between categorical variables (e.g., difference in proportion of cough without a cold among children with and without current wheeze). To compare results between LUIS and LRC in children of similar age, we did a subgroup analysis including only 6- to 8-year-olds in LUIS. Missing data for the questions on respiratory symptoms was ≤5% in both populations (supplementary table S1 in the appendix). We recoded these missing data as “no”, as we expected symptoms to be absent or borderline when parents had not answered with “yes”. We used STATA (Version 15.1, StataCorp) for statistical analysis. Venn diagrams were plotted with STATA using the `pvenn` command.

Results

In LUIS, 3457 participants from 37 schools returned both the parental questionnaire and informed consent and were included in the analysis. Median age was 13 years (IQR 10–14, range 6–17) and 1736 (50%) were girls. Most had been born in Switzerland and almost half lived in large urban areas. In the LRC, 2100 children (62% of the initial population of 3401 children) returned the 2003 follow-up questionnaire. Median age was 7 years (IQR 6–7, range 6–8) and 994 (47%) were girls.

Prevalence of cough based on the three questions

Respiratory outcomes were reported approximately half as often in the Swiss LUIS study as in the UK-based LRC study. This was the case for all three cough questions, but also for current wheeze and physician-diagnosed asthma (table 1).

Both studies revealed large differences in prevalence of cough, depending on the question used. In LUIS, parents of 880 children (25%, 95% CI 24–27%) reported cough without a cold, 394 (11%, 95% CI 10–13%) reported dry night cough and 159 (5%, 95% CI 4–5%) reported cough more than others. In the LRC, these numbers were 1003 (48%, 95% CI 46–50%) for cough without a cold, 527 (25%, 95% CI 23–27%) for dry cough at night and 227 (11%, 95% CI 10–12%) for coughing more than other children. We found a modest overlap of answers (fig. 1A and B): in LUIS only 89 (3%) parents answered yes to all three cough questions and in the LRC 168 (8%) answered yes to all three questions. Among parents who did not report cough without a cold or dry night cough in their child, hardly any (13 (<1%) in LUIS and 12 (1%) in LRC) reported that their child coughed more than others.

Prevalence of cough in children with and without current wheeze

In children who had also wheezed in the last 12 months, the three questions about coughing were answered in the affirmative much more often than in children who had not wheezed. ($p < 0.001$, table 2). In LUIS, cough without a cold was reported for 160 (57%) children with wheeze and for 720 (23%) of those without (i.e., two-fold), night cough was reported for 100 (36%) children with and 294 (9%) children without wheeze (four-fold) and coughing more than others for 59 (21%) and 100 (3%) respectively (seven-fold; table 2). Similar differences between children with

and without current wheeze were seen in the LRC study (table 2).

There was a larger overlap between the responses to the three questions about cough in children with reported wheeze, but still some remarkable difference between the LUIS and LRC populations (figs 2A–2D): 42 (15%) of children with current wheeze in LUIS and 92 (31%) in LRC said yes to all three cough questions. This overlap was very small in children without reported wheeze (47 (1%) and 76 (4%) in LUIS and LRC, respectively). In contrast to wheeze, prevalence of cough differed little by sex, age-group and parental education (table 2), with some exceptions such as a higher prevalence of night cough and coughing more than others in the 6- to 9-year-olds and a

higher prevalence of cough without a cold and night cough in children whose parents have a lower education level.

Duration of cough

In LUIS, we had information about duration of cough. We found that approximately half of parents who reported that their child coughs more than others also reported episodes of cough lasting >3 weeks (n = 81, 51%) and one in 10 reported cough for >2 months (n = 17, 11%). These proportions were much lower among parents who reported cough without a cold or dry night cough (Supplementary table S2).

Table 1:

Characteristics of children from the LuftiBus in the School study and Leicester Respiratory Cohort included in this analysis.

| | | LuftiBus in the School (n = 3457) | Leicester Respiratory Cohort 3 (n = 2100) |
|--|---------------------------------|-----------------------------------|---|
| | | n (%) | n (%) |
| Sociodemographic factors | | | |
| Female sex | | 1736 (50) | 997 (47) |
| Age group (years) | 6–9 | 958 (28) | – |
| | 10–13 | 1555 (45) | – |
| | 14–17 | 944 (27) | – |
| Living in large urban area | | 1674 (48) | 910 (43) |
| Swiss socioeconomic position index median (IQR) ¹ | | 69.7 (62.2–76.6) | – |
| Townsend score median (IQR) ² | | – | –0.9 (–2.8–2.0) |
| Highest parental education ³ | Lower | 108 (4) | 710 (38) |
| | Middle | 875 (35) | 707 (37) |
| | Upper | 1512 (61) | 469 (25) |
| Symptoms/comorbidities | Cough without a cold | 880 (25) | 1003 (48) |
| | Dry night cough | 394 (11) | 527 (25) |
| | Cough more than others | 159 (5) | 227 (11) |
| | Wheeze past 12 months | 281 (8) | 299 (14) |
| | Physician diagnosed asthma ever | 293 (8) | 465 (22) |

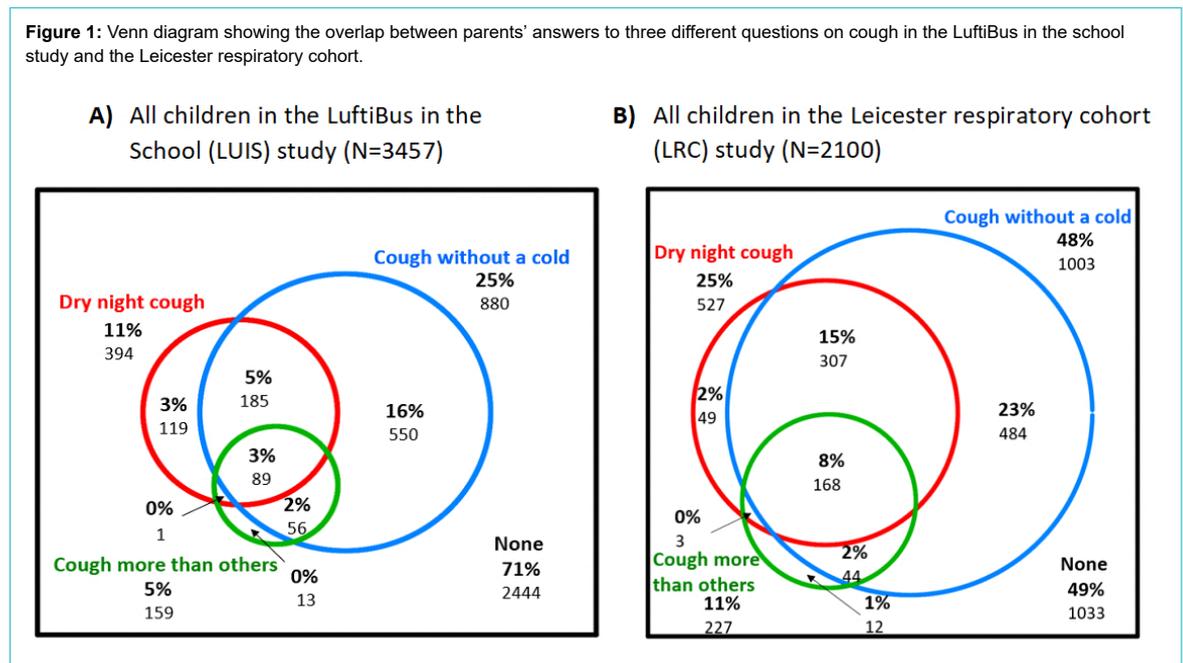
IQR: Interquartile range

¹ Swiss socioeconomic position index ranges from 0-lowest (worse) to 100-highest (better)

² Townsend score: deprived = ≤0, not deprived >0

³ Highest parental education: lower: completed education at ≤16 years old; middle: completed education at ≤20 years old but >16 years old; upper: completed education after 20 years old

Figure 1: Venn diagram showing the overlap between parents' answers to three different questions on cough in the LuftiBus in the school study and the Leicester respiratory cohort.



Subgroup analysis in 6- to 8-year-olds

When repeating the analyses for LUIS in the age-group that was closely comparable to the LRC sample (LUIS: 423 children aged 6 to 8 years; median 7; IQR 7–8 years and LRC: 2100 children aged 6 to 8 years; median 7; IQR 6–7 years), findings on prevalence and degree of overlap between answers to the three cough questions were comparable to the whole LUIS study population (Supplementary table S3).

Discussion

We studied the answers to three different questions about cough in two cross-sectional population-based studies which differed by geographical location (Switzerland, UK), year of survey (2013–16; 2003), age distribution and prevalence of wheeze (twice as high in the UK study). Both studies demonstrated how strongly reported prevalence of excessive cough (cough exceeding the normal physiological occurrence) depends on how the question to parents is asked. Prevalence varied up to five-fold between questions, and the overlap between answers to different questions was small. This suggests that when comparing prevalence of cough in children between different studies, the exact wording of the questions is fundamental.

Few population-based studies reporting on cough have used more than one question [15–17]. In a study conducted among 6–12-year-olds in the Netherlands, Brunekreef et al. used two other questionnaires (World Health Organization and Child Health Care questionnaire), which included several questions on cough [17]. Even though the ques-

tions used (e.g., morning cough, day/night cough, chronic cough, cough usually, cough 3 months) differed from ours and we cannot make a direct comparison, the prevalence of cough differed strongly between questions. However, the authors did not assess overlap of answers to different questions.

We previously used the LRC dataset to analyse differences in prevalence of cough by age, but we did not assess overlap between answers to different questions on cough [16]. In our current analysis, we found that compared to the Swiss LUIS study, all three cough questions had been affirmed about twice as often in Leicestershire. This remained true when we validated the same age-group to 6- to 8-year-olds (supplementary table S3). We hypothesise that the explanation might be the higher prevalence of asthma, severe asthma and respiratory problems in general in the UK compared with many other European countries, which was found in many international comparisons and remains largely unexplained [18–20]. Higher exposure to indoor allergens such as house dust mites and moulds might contribute [21–24]. In addition, the two studies were conducted 10 years apart. Air quality has improved considerably during this period, which resulted in a lower prevalence of cough in children [25–28]. The fact that, despite absolute differences in prevalence of cough between the two countries, the relative difference in affirmative answers to the three questions and the narrow overlap was comparable adds robustness and generalisability to our findings.

Our findings have implications for epidemiological studies on cough in children. The most important implication is that comparison of prevalence of cough in children be-

Table 2:

Prevalence of cough in school children from the LuftiBus in the school (LUIS) study and Leicester Respiratory Cohort (LRC) based on parents' answers to differently worded questions stratified by presence of wheeze, sex, age group and parental education level (row percentage).

| | | Cough without a cold | | Night cough | | Cough more than others | | Overlap of the three cough questions ² |
|-------------------------------------|-------------------|----------------------|----------------------|-------------|----------------------|------------------------|----------------------|---|
| | | n (%) | p-value ¹ | n (%) | p-value ¹ | n (%) | p-value ¹ | |
| LuftiBus in the school study | | | | | | | | |
| Total (all aged 6–17 years) | | 880 (25) | – | 394 (11) | – | 159 (5) | – | 89 (3) |
| Presence of wheeze | Current wheeze | 160 (57) | <0.001 | 100 (36) | <0.001 | 59 (21) | <0.001 | 42 (15) |
| | No current wheeze | 720 (23) | | 294 (9) | | 100 (3) | | 47 (1) |
| Sex | Male | 470 (27) | 0.011 | 188 (11) | 0.390 | 87 (5) | 0.200 | 45 (3) |
| | Female | 409 (24) | | 206 (12) | | 72 (4) | | 44 (3) |
| Age group (years) | 6–9 | 250 (26) | 0.806 | 142 (15) | <0.001 | 64 (7) | 0.001 | 38 (4) |
| | 10–13 | 388 (25) | | 154 (10) | | 58 (4) | | 30 (2) |
| | 14–17 | 242 (26) | | 98 (10) | | 37 (4) | | 21 (2) |
| Parental education ³ | Lower | 34 (31) | 0.256 | 11 (10) | 0.834 | 2 (2) | 0.157 | 1 (0) |
| | Middle | 225 (26) | | 99 (11) | | 37 (4) | | 26 (3) |
| | Upper | 371 (25) | | 179 (12) | | 81 (5) | | 46 (3) |
| Leicester Respiratory Cohort | | | | | | | | |
| Total (all aged 6–8 years) | | 1003 (48) | | 527 (25) | | 227 (11) | | 168 (8) |
| Presence of wheeze | Current wheeze | 224 (75) | <0.001 | 159 (53) | <0.001 | 122 (41) | <0.001 | 92 (31) |
| | No current wheeze | 779 (43) | | 368 (20) | | 105 (6) | | 76 (4) |
| Sex | Male | 529 (48) | 0.848 | 269 (24) | 0.432 | 137 (12) | 0.012 | 98 (9) |
| | Female | 474 (48) | | 258 (26) | | 90 (9) | | 70 (7) |
| Parental education ³ | Lower | 382 (54) | <0.001 | 195 (27) | 0.025 | 86 (12) | 0.066 | 63 (9) |
| | Middle | 322 (46) | | 176 (25) | | 75 (11) | | 56 (8) |
| | Upper | 191 (41) | | 93 (20) | | 36 (8) | | 26 (6) |

¹ p-value of the difference in frequency of the different cough questions for presence of wheeze, sex, age group and parental education; p-value calculated using chi-square test

² percentage who answer yes to all three cough questions

³ Highest parental education: lower: completed education at ≤16 years old; middle: completed education at ≤20 years old but >16 years old; upper: completed education after 20 years old

tween regions or time periods should be considered only when exactly the same question is used for cough. The three- to five-fold differences we found between answers to different cough questions (i.e., 5% vs 25% in LUIS and 11% vs 48% in the LRC) are much higher than any differences we would expect to find between regions based on environmental exposures or social gradients, where usually odds ratios between 1 and 2 are reported (less than doubled prevalence). Second, the three questions on cough seem to identify different subgroups of children, as illustrated by the partial overlap. This might reflect differences in underlying pathophysiology of cough. Thus, researchers working on risk factors and causes of excessive cough in children need to carefully consider which questions they want to ask. The choice of questions might also depend on whether a study puts more emphasis on sensitivity or specificity. If high sensitivity is needed, the question on cough without a cold [7] is particularly useful since it also captures most children who additionally report dry night cough or coughing more than others. If a study aims to

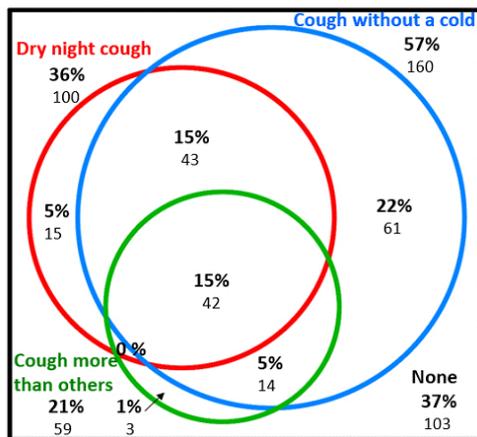
identify children with more severe cough caused by airway diseases such as asthma, the question on whether the child coughs more than other children [9] may be better. This question was least often answered in the affirmative, and then usually in combination with cough without a cold, dry night cough and longer duration of cough episodes.

This study has limitations. First, the symptoms are parent-reported, and several studies have shown discrepancies between reported and recorded symptoms, especially for nocturnal ones [29, 30]. Studies have also shown that parents wrongly understand the term wheeze [31, 32]. However, as most epidemiological studies continue to work with questionnaires rather than with 24-hour cough recordings, our recommendations for future research remain valid. Second, we included children from one region of Switzerland and one region in the UK, and the absolute prevalence may not be generalisable to other regions. However, the magnitude of the difference and degree of overlap between children with positive answers to different cough questions is likely

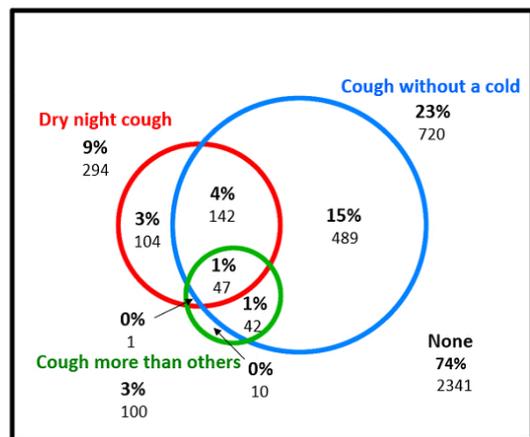
Figure 2: Venn diagram showing the overlap between parents' answers to three different questions on cough in the LuftiBus in the school study and the Leicester Respiratory Cohort.

(i) LuftiBus in the School study (N=3457)

A) Children with current wheeze (N=281)

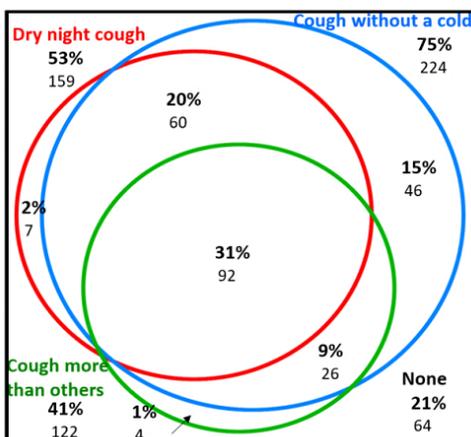


B) Children without current wheeze (N=3176)

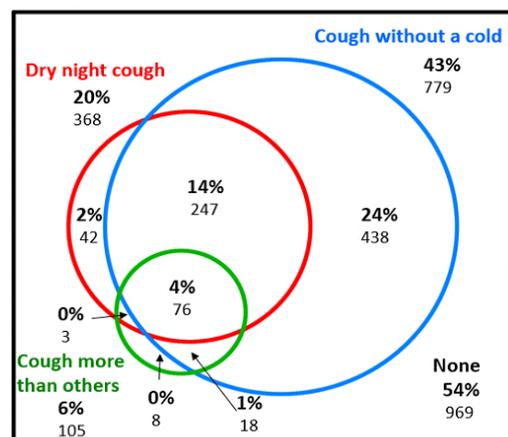


(ii) Leicester respiratory cohort (N=2100)

C) Children with current wheeze (N=299)



D) Children without current wheeze (N=1801)



to be typical, supported by similar findings from two independent studies conducted in different countries and time periods.

We conclude that the wording of the question used to assess cough strongly affects prevalence estimates. The three- to five-fold differences in prevalence we found between questions is much more than the expected effects of environmental exposures such as air pollution or tobacco smoke and makes comparison between studies impossible unless the wording of the cough question is exactly the same.

Availability of data and material

For LUIS, researchers can obtain datasets for analysis if a detailed concept sheet is presented for the planned analyses and approved by the principal investigators (Alexander Moeller, Philipp Latzin and Claudia Kuehni).

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Potential conflicts of interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Latzin P reports personal fees from OM pharma, Polyphor, Santhera, Vertex, Vifor, Sanofi Aventis and grants from Vertex, all outside the submitted work. Moeller A reports personal fees from Vertex outside the submitted work. Erol A Gaillard reports consultancy work for Boehringer Ingelheim with money paid to the institution (University of Leicester), investigator led research grant from Circassia Group, Gilead Sciences, Chiesi Limited and Propeller Health, research collaboration with AstraZeneca and Adherium (NZ) Limited, speaker fees from Circassia Group and travel grant from Sanofi all outside the submitted work. No other potential conflict of interest was disclosed.

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Appendix: Supplementary tables

Table S1:

Wording of questions and frequency of missing values in the LuftiBus in the School (LUIS) study and Leicester Respiratory Cohort (LRC).

| Variable | Question | Missing, n (%) |
|------------------------|--|-----------------------------|
| Cough without a cold | Does your child have a cough even without having a cold? | LUIS: 46 (1)LRC: 20 (1) |
| Dry night cough | In the last 12 months has your child had a dry cough at night, apart from a cough associated with a cold or a chest infection? | LUIS: 46 (1)LRC: 17 (1) |
| Cough more than others | Do you think your child coughs more than other children? | LUIS: 43 (1)LRC: 24 (1) |
| Current wheeze | Did your child have wheezing or whistling in the chest in the past 12 months? | LUIS: 33 (1)LRC: 8 (0) |
| Cough >3 weeks | In the past 12 months, has your child had a cough that lasted more than three weeks at a time? | LUIS: 54 (2) |
| Cough >2 months | In the past 12 months, has your child had a cough that lasted more than two months at a time? | LUIS: 158 (5) |
| Level of education | Parental highest level of education | LUIS: 962 (28)LRC: 214 (10) |

Table S2:

Comparison of cough duration among children with parent-reported cough apart from colds, dry night cough and cough more than others in the LuftiBus in the School study.

| | Total population (n = 3457) | Cough without a cold (n = 880) | Dry night cough (n = 394) | Cough more than others (n = 159) |
|-----------------|-----------------------------|--------------------------------|---------------------------|----------------------------------|
| | n (%) | n (%) | n (%) | n (%) |
| Cough >3 weeks | 336 (10) | 193 (22) | 116 (29) | 81 (51) |
| Cough >2 months | 37 (1) | 30 (3) | 18 (5) | 17 (11) |

Table S3:

Prevalence of cough based on parents' answers to differently worded questions and stratified by presence of wheeze, sex, and parental education in a subgroup of school children aged 6–8 years (n = 423) from the LuftiBus in the school (LUIS) study compared to school children aged 6–8 years from the Leicester Respiratory Cohort (LRC) (n = 2100) (row percentage).

| | | Cough without a cold | Night cough | Cough more than others | Overlap of three cough questions ¹ |
|-------------------------------------|------------------------------|----------------------|-------------|------------------------|---|
| | | n (%) | n (%) | n (%) | n (%) |
| LuftiBus in the school study | | | | | |
| Total (n = 423) | | 96 (23) | 66 (16) | 25 (6) | 14 (3) |
| Presence of wheeze | Current wheeze (n = 30) | 14 (47) | 14 (47) | 8 (27) | 7 (23) |
| | No current wheeze (n = 393) | 82 (21) | 52 (13) | 17 (4) | 7 (2) |
| Sex | Male (n = 195) | 49 (25) | 29 (15) | 12 (6) | 7 (3) |
| | Female (n = 228) | 47 (21) | 37 (16) | 13 (6) | 7 (4) |
| Parental education ² | Lower (n = 0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | Middle (n = 62) | 17 (27) | 6 (10) | 3 (5) | 7 (2) |
| | Upper (n = 258) | 57 (22) | 46 (18) | 16 (6) | 11 (4) |
| Leicester Respiratory Cohort | | | | | |
| Total (n = 2100) | | 1003 (48) | 527 (25) | 227 (11) | 168 (8) |
| Presence of wheeze | Current wheeze (n = 299) | 224 (75) | 159 (53) | 122 (41) | 92 (31) |
| | No current wheeze (n = 1801) | 779 (43) | 368 (20) | 105 (6) | 76 (4) |
| Sex | Male (n = 1103) | 529 (48) | 269 (24) | 137 (12) | 98 (9) |
| | Female (n = 997) | 474 (48) | 258 (26) | 90 (9) | 70 (7) |
| Parental education ² | Lower (n = 710) | 382 (54) | 195 (27) | 86 (12) | 63 (9) |
| | Middle (n = 707) | 322 (46) | 176 (25) | 75 (11) | 56 (8) |
| | Upper (n = 683) | 191 (41) | 93 (20) | 36 (8) | 26 (6) |

¹ Percentage who answer yes to all three cough questions² Highest parental education: lower: completed education at ≤16 years old; middle: completed education at ≤20 years old but >16 years old; upper: completed education after 20 years old