

Cost of acute cough in Italian children

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Objectives: Acute cough is the most common symptom among children in primary care, but the economic impact of cough episodes has never been investigated in Italian families.

Materials and methods: A cross-sectional telephone survey was conducted on a representative sample of Italian families, randomly selected from general population. Collected data were analyzed to evaluate the economic impact of cough episodes according to, first, Italian Family Perspective and, second, National Health System Perspective (NHS-P). The costs considered in the analysis were the cost of drugs used (antibiotics, corticosteroids, antitussive drugs, and aerosol therapy) and the cost of child care during nursery/school absenteeism.

Results: Six hundred four valid questionnaires were analyzed: mean age of children is 7 years (SD=3.3) and that of parents is 40 years (SD=6.2). Mean rate of cough episodes was 3.15/year, and in general, they were short lasting (94.6%, <2 weeks). Nursery/school absenteeism was mostly <7 days (63.2%), but almost 30% of respondents declared 7–15 days. The respondents' willingness to spend out-of-pocket for an "effective remedy" against cough was an average of €20 (>€30 in 19.7% of cases). The overall economic impact on Italian families was estimated as €1,204 (SD=€88); it resulted in a cost per cough episode equal to €337, mainly due to nursery/school absenteeism (94.6%), whereas pharmaceutical expenditure was marginal (5.4%).

Conclusion: Cough episodes are acute (lasting <1 week, mainly) but frequent, causing a considerable socioeconomic impact. The pharmaceutical costs are in line with parents' willingness to pay but these costs result negligible when compared to those related to school absenteeism, generally not perceived by parents.

Keywords: acute cough, acute cough in children, cough impact, cost of acute cough

Introduction

Cough is defined as a physiological mechanism that allows protection from inhalation of airborne irritant materials and clearing secretions from the airways.¹ It also represents a very common respiratory symptom, a nonspecific clinical sign possibly due to a number of diseases (bronchial asthma, allergic disorders, postnasal drip, upper airway infections (UAIs), neoplastic diseases, tracheomalacia, gastroesophageal reflux, environmental pollution, and psychological disturbances) and some drugs (ie, ACE inhibitors and β -blockers).

Cough can be either acute or chronic, when it lasts for at least 8 weeks. Among children, acute cough is the most common symptom in primary care, and it is mainly due to seasonal respiratory infectious events.^{2–6}

If cough episodes are due to simple cold, they usually tend to resolve spontaneously within 4–5 days in the vast majority of cases, but when they are the consequence of influenza or other UAIs, they can be more severe.^{7–9} High rates of vaccination coverage

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are in fact promoted every year in order to minimize both the morbidity and the societal impact of at least airway tract infections due to influenza.¹⁰

In addition to causing a large number of general practitioners' (GPs) and pediatricians' visits every year, these cough episodes also cause substantial school absenteeism, which in turn can affect parents' working activities.¹¹ Even if the epidemiology of cough was episodically investigated among Italian children,¹² the true burden of cough was never calculated in Italian families to our knowledge.

The aim of the study was to assess the different cost components of cough episodes in Italian children and factors contributing to the impact on their families.

Materials and methods

This retrospective study was conducted by the National Centre for Respiratory Pharmacoeconomics and Pharmacoeconomics (CESFAR), Research & Clinical Governance, and AdRes Health Economics and Outcome Research. The study design was approved by the CESFAR Ethical Committee on October 26, 2016, and it was carried out between March 5 and 21, 2017. A cross-sectional telephone survey was conducted on a sample of Italian families with children, randomly selected from the general population. The minimum sample size required for achieving the quantity of the sample in terms of children's age, gender, and geographical distribution was previously estimated to be 600 respondent families (3% mean effect size; 5% significance level, and 80% statistical power).

All interviews with the parents of the children (or with their care-givers) were made according to the Computer-Assisted Telephone Interview methodology¹³ by experts and professional interviewers. The interviewer was provided with a "work station" consisting of a personal computer connected to a central processing unit. The central processing unit was also equipped with a specific software for the random selection of individuals (eg, the telephone numbers) to contact. All interviews were preceded by a short explanation of the aim of the survey and had a mean duration of 10 minutes.

Only interviews obtained after having recorded the respondents' informed consent to the interview and to the possible use of information for scientific purposes were considered for the present study.

The questionnaire

The study was based on the use of a specific, validated, anonymous questionnaire consisting in 29 closed and 5 open questions ([Supplementary materials](#)). According to

consolidated validation procedures, the original version of the questionnaire was previously submitted to a sample of 25 individuals (the usual sample size for a pilot test of different educational levels and randomly chosen) in order to check the comprehension of the questions included. Items where linguistic errors and/or misunderstandings had occurred were reworded up to their full comprehension.¹⁴ The questionnaire was planned to cover several domains:

- demographic characteristics of children (age, gender) and their families (job, smoking habit, geographical distribution)
- frequency of cough episodes in the last 12 months
- clinical presentation of cough
- duration of cough episodes
- cough impact on families: nursery or school absenteeism, taking care of children, infectious involvement of other family members
- home management of cough episodes: medical consultations, home remedies, prescription, and use of drugs

Summary statistics

Response to all questions were analyzed and summarized using proper statistical measures: for categorical outcomes (eg, sex, smoking status, cough type) or mean and SD for continuous data (eg, age). Furthermore, for continuous variables that were not normally distributed, the median and interquartile range were reported. With regard to categorical answers, the mean value of each category was considered in order to compute the weighted mean; for example, for the annual number of cough episodes, patients had to choose 1–2, 3–5, or >5 episodes, the mean values for each level (1.5, 4, and 6, respectively) were weighted according to the correspondent frequency to estimate the annual number of cough episodes; it was assumed no more than seven episode per year (see the section "Economic evaluation" for details). All analyses were performed using computer software R 3.1.2.¹⁵

Economic evaluation

In general, as the vast majority of drugs prescribed in these cases are not reimbursed by the National Health Service (NHS), the cough impact in the National Health System Perspective (NHS-P) was presumed to be lower than that in the Italian Family Perspective (IF-P).

Methods used for calculating each component of resource consumption are described analytically. The cost of cough episode has been multiplied for the number of episodes occurred over the last 12 months. A maximum value of seven

episodes was estimated by fitting a Poisson distribution on data recorded from the questionnaires. This distribution was used to represent the number of events occurring in a fixed interval of time or space (1 year, in this analysis) assuming that these events occur with a constant rate and independently of the time since the last event.¹⁶

Cost of child care during nursery/school absenteeism

This cost was calculated by multiplying the daily cost of the care-giver for the number of days of nursery/school absenteeism. The absenteeism duration was estimated from the answers to question # 1f of the questionnaire (such as <7, 7–15, 16–30, >30 days). When duration was claimed >30 days, it was supposed as a maximum duration of 45 days. Care-giver could be either a parent or a baby-sitter or a grandparent.

In the case of one parent caring for his/her child at home, the corresponding cost was derived from the Italian National Institute of Statistics (ISTAT) officially published mean wage by age in 2010;¹⁷ they provide figures related to professional and personal characteristics of employees, their salary structure, and their working time (Table S1). In particular, the cost of the parent remaining at home caring for his/her child was calculated according to two methods:

- cost by sex and age: age and sex of respondents were valued
- cost by sex and job

Assuming that

- when one of the two parents was unemployed, he or she was supposed to take care of the child at home; thus, the corresponding cost was valued equal to zero.
- when parents were both active workers, it was supposed that the parent with lower salary would take care of the child at home.

As the ISTAT job categories did not correspond exactly to those reported during the interviews, the following correspondences were assumed:

- Intellectual and scientific jobs – entrepreneur category
- technical jobs – freelance category
- office employees – clerks/employee category
- workers in commercial activities and services – self-employment and traders category
- artisans and specialized workers – craftsman and specialized workers
- unqualified job – precarious work category

In the base case scenario, the hourly caring-cost per family was calculated as the mean of the values obtained according to the two methods described above. This cost was then multiplied for the mean working time per day, which is 5.38 hours.¹⁸

The baby-sitter cost was estimated from the minimum wage/year 2016, to be €5.36/hour.¹⁹ This cost was then multiplied for the mean working time/day.

According to a recent paper concerning social costs in Italy,²⁰ it was decided to attribute an economic value to grandparents' time spent caring for their grandchildren when not at school. The annual cost estimated for over-65s is €6.531 for males and €14.491 for females; these two values were balanced for the over-65s gender distribution in Italy (43% male, 57% female) and converted into a corresponding cost per day.

When “Others” was the answer to the question #2 of the questionnaire (“Who is usually caring for your child when he/she is not at school?”), the cost was considered equal to zero, because specific information for a realistic calculation of cost is missing.

Cost of drugs

In a recent survey carried out on a sample of 773,492 Italian children with regard to antibiotic prescriptions,²¹ it was reported that almost 60% of prescriptions consists of amoxicillin (24%) and amoxicillin+clavulanic acid (33%). These results were also confirmed by the OsMed Report,²² which calculated that the mean antibiotic consumption of amoxicillin and amoxicillin+clavulanic acid (measured in DDD/1,000 inhabitants/day) corresponds to 56% of the overall 2015 antibiotic consumption in Italy.

As antibiotics are in Class A,²³ the cost for families is zero in case of generic drugs or equal to the difference between the public price and the reference price in the case of originator drugs. Table S2 reports that all antibiotics available in Italy contains amoxicillin. In the case of dose limitations by age, median growth curves for males and females in the range 2–20 years of age were used.²⁴ In order to calculate the mean cost, it was first assumed that generic drugs cover 24% of total antibiotic requirement, and then the cost was calculated as the ratio between the DDD value/1,000 inhabitants/day for equivalent antibiotics (5.4) and the value of total DDD (22.8) recorded in Italy at 2015.²² As results proved to be corresponding to those of a recent analysis concerning the consumption of equivalent drugs in Italy and in other countries,²⁵ data from the OsMed Report²² were also used for calculating the cost of corticosteroids.

When “sometimes” was the answer to question #8 of the questionnaire (such as that one concerning the frequency of the pediatrician’s antibiotic prescription), it was assumed that antibiotic prescription has occurred in 50% of cases. Furthermore, two antibiotic courses were assumed when the duration of cough episodes was longer than 2 weeks.

The widely used corticosteroids in childhood were beclomethasone and betamethasone, which were positioned at the 2nd and 11th position in the ranking of the first 30 drugs in 2015.²² All steroids valued in the present investigation are reported in [Table S3](#). As in the case of antibiotics, the cost of steroids was differently calculated for generic drugs and originators, and a mean duration of treatment was assumed to be 1 week.

After the exclusion of drugs not indicated for children, all remaining drugs indicated in case of cough were grouped in the four categories and has been reported in the questions #10 and 12 of the questionnaire, that is, mucolytics, cough suppressants, anti-inflammatory, and compounds for aerosol delivery ([Tables S4–S7](#)); only public prices are reported since these drugs are not reimbursed by NHS. In order to simplify calculations, treatment duration was presumed equal to cough duration. Finally, in the case of aerosol treatments, only the cost of drug(s) used was considered; the cost of the equipment for aerosol delivery assumed equal to zero as it was already available at home or it was temporarily provided by relatives or friends in most of the cases.

Scenario analysis

A deterministic sensitivity analysis was also conducted, and the most relevant parameters were stressed by a minimal–maximal variation in order to check the unreferenced hypotheses. In particular, four parameters were investigated:

- Number of cough episodes
 - Min/max scenario: according to the responses collected, min/max value associated to each category reported in question #1a
- Duration of episodes
 - Min/max scenario: according to the responses collected, min/max value associated to each category reported in question #1b
- Parents’ hourly cost
 - Min/max scenario: min/max value estimated according to method 1 (cost by age and sex) and method 2 (cost by job and sex) described in “Cost of child care during nursery/school absenteeism” section
- Duration of treatment with steroids
 - Min. scenario: 5 days of treatment

- Max. scenario: 10 days of treatment
- When cough episodes lasted more than 2 weeks, the duration of treatments was doubled

Results

The number of complete interviews was 604. Demographics and general characteristics of the sample are reported in [Table 1](#). In particular, mean age of respondent parents was 40 years, while that of their children was 7 years. Children’s distribution was: males 53%, and females 47%. Mothers responded to the interview in 80% of cases. In 60% of families, at least one parent was an active smoker. The geographic distribution of respondents was homogeneous all over the country.

More than 90% of children suffered at least one cough episode during the previous 12 months ([Table 2](#)), but more than 12% of them suffered more than five cough episodes in the same period, being nearly three of the average number of episodes/year. In general, cough episodes were short lasting (about a week), with duration longer than 2 weeks only in 5% of cases.

Main characteristics of cough episodes and their consequences on children’s care are summarized in [Table 3](#).

Table 1 Demographics of the overall sample (children and respondents)

Variable	n=604
Children’s age (years)	6.93 (3.28)
Respondent parents’ age (years)	40.39 (6.19)
Children’s sex (% male)	53.0%
Respondent parents’ sex (% male)	19.5%
Smoke at home (% at least one parent)	57.6%
Families’ geographical distribution	
North-West	25.2%
North-East	25.2%
Center	21.5%
South and Isles	28.1%

Note: Continuous data are expressed as mean±SD while dichotomous data as percentages.

Table 2 Main characteristics of cough episodes

Variable	n=604
% children suffering cough episodes	91.1%
Mean cough episodes	3.15 per year
1–2 episodes	40.9%
3–5 episodes	37.9%
>5 episodes	12.2%
Mean duration (days)	8.42 per episode
<7 days	40.9%
7–15 days	53.7%
15–30 days	4.7%
>30 days	0.7%

Table 3 Cough characteristics and consequence on children's management

Cough type	Cough occurrence	Absenteeism ^a	Home caring	Pediatrician intervention
Dry	14.7% Day only	11.8% <7 days	63.2% Parent(s)	<7 days 87.8%
Dry followed by secretions	74.7% Day and night	82.4% 7–15 days	28.6% Grandparents	7–15 days 9.0%
Initially with secretions	10.6% Night only	5.3% 16–30 days	3.7% Baby-sitter	16–30 days 2.4%
	Exertional only	0.5% >30 days	4.6% Other	>30 days 0.8%

Note: ^aFrom nursery or school.

Cough episodes were characterized by dry cough followed by production of secretions in 74% of cases, and their occurrence was both diurnal and nocturnal in 82% of cases. Cough episodes were related to infectious events (namely influenza or UAIs) in 53% of cases. Maximum school absenteeism was shorter than 1 week in 63% of cases; in these circumstances, the child was mostly cared by one of his or her parents (70%) or by his or her grandparents (29%). In the vast majority of cases (86%), parents refer to their pediatrician almost immediately during the first week of cough, and in 72% of cases, they use first-line domestic remedies for managing cough while waiting for the pediatric consultation.

Parents were willing to spend an average of €20 for an effective remedy against their children's cough (range €14–26), and a nonnegligible proportion of them (one out of five) were willing to spend >€30 (Table 4).

Calculated mean cost for an antibiotic course was lower than €2 according to the family perspective, while it increased up to €6 in the NHS perspective (Table 5). Costs for one corticosteroid course are reported in Figure 1 (around €2.00 in the IF-P, linearly increasing by age up to €8.00 in the NHS-P), while the daily cost for antitussive and aerosol drugs by age is reported in Figure 2, where the cost in the NHS perspective is not reported since these drugs are not reimbursed by the NHS.

The cost calculated for managing cough resulted in about €1,200 per year according to the family's perspective. The main component of this cost was that related to school absenteeism (€1,122), whereas the cost for drugs corresponded to 7% of total cost (€82) and 90% due to antitussive and aerosols treatments (Table 6). On the contrary, the cost of cough proved quite marginal (<€14) from NHS perspective: in particular, it was mainly due to antibiotic (67%) and steroid (33%) use.

The overall economic impact of each cough episode on Italian families resulted in about €350, mainly due to nursery/school absenteeism (Figure 3). Pharmaceutical expenditure was €19.30, such figure is absolutely in line with the parents' claim on their willingness to spend (Table 4).

Table 4 Parents' willingness to spend for an effective remedy against their children's cough

Mean cost per episode (range)	€19.95 (14.04–25.86)
Nothing	0.35%
<€10	11.15%
€10–€20	57.15%
€20–€30	11.50%
>€30	19.65%

Table 5 Mean cost per antibiotic course according to family and NHS perspective

Age	Family	NHS
<11 years	€0.80	€5.55
11 years	€0.93	€5.61
>11 years	€1.35	€5.72

Abbreviation: NHS, National Health Service.

Finally, results of the sensitivity analysis are reported in Figure 4. Data confirm the strong correlations between annual cost of cough and both the number of days of school absenteeism (range: €733–1.717) and the annual rate of cough episodes (range: €916–1.492). On the other hand, the annual cost of cough does not seem to be affected by the cost of drugs and treatment duration.

Discussion

The incidence of cough episodes reported in the present survey proved very high indeed, as more than 90% of Italian children suffered from these events over the year, though at different rates, severity, and duration. These data are in concordance with consolidated specific literature.^{2–6,8,9}

Usually, cough episodes occur mostly due to upper respiratory tract infections of viral origin and frequently lead to transient limitations in the daily activities of sick children. The involvement of other members of the family is frequent in these cases and, when it happens, the overall impact of these events is magnified.

Even if each single episode is generally short lasting, the overall duration of the entire annual events (an average of three per year) can cause a considerable socioeconomic

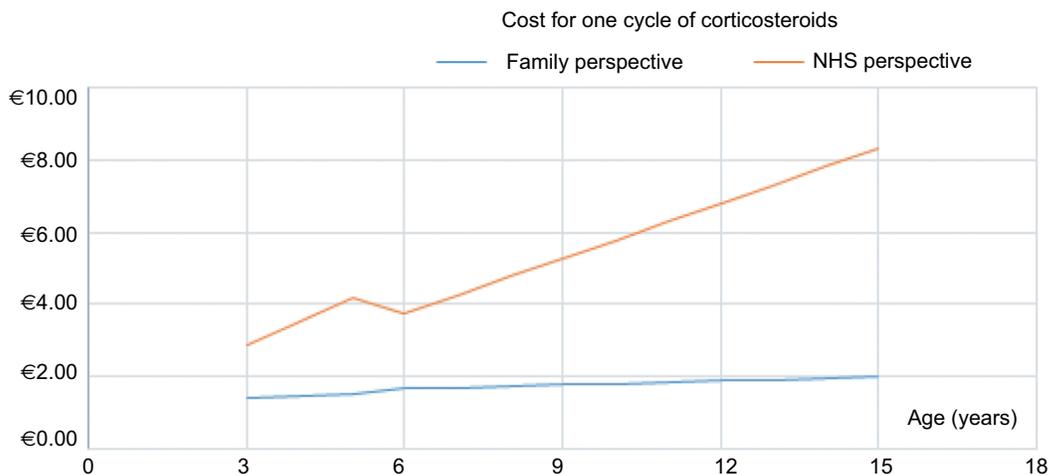


Figure 1 Cost of corticosteroids by age according to societal and NHS perspective. **Abbreviation:** NHS, National Health Service.

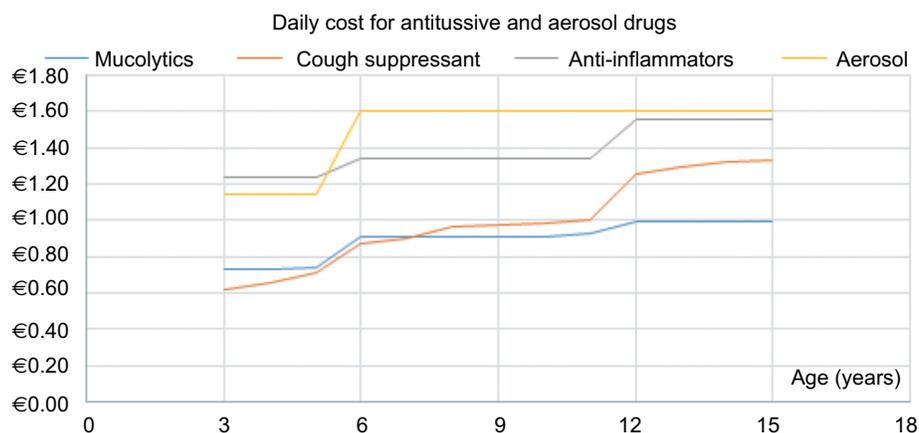


Figure 2 Daily cost of antitussive drugs in the societal perspective.

Table 6 Annual cost of cough: comparison between the family's and the NHS' perspectives

Variable	Family	NHS
Total cost	€1,203.71±87.78	€13.74±0.48
School day off	€1,122.11±83.02	NA
Drugs	€81.60±5.24	€13.74±0.48
Antibiotics	€1.45±0.05	€9.21±0.31
Corticosteroids	€1.67±0.09	€4.52±0.26
Antitussive drugs	€41.48±3.14	NA
Aerosol (only drug cost)	€37.00±2.89	NA

Note: Data are expressed as mean±SD.

Abbreviation: NHS, National Health Service; NA, not applicable.

impact. It is presumable in fact that the net effect of cough episodes on both the family organization and its annual income would largely depend on parents' occupations (ie, white collars, blue collars, unemployed, housewives, students) and on the number of children in the family.

Data of the present study show that the burden of cough episodes usually impacts more on families rather than on NHS, with substantial economic consequences on their annual income.

The study highlighted that families tend to seek medical advice immediately. As suggested in other studies, rather than to the severity of the episodes, which are short lasting in the vast majority of cases, this attitude is likely to be related to the presumed difficulty of managing children at home for some days by parents who both are actively occupied and who try to safeguard their job and their economic position.^{26,27} In addition, other factors can further contribute to parents' concern and the decision in favor of a rapid medical consultation, such as the anxiety of one or both parents and the disruption of their daily organization; their inexperience with the situation (particularly if at their first experience); the role of other family members (namely grandparents) who most of

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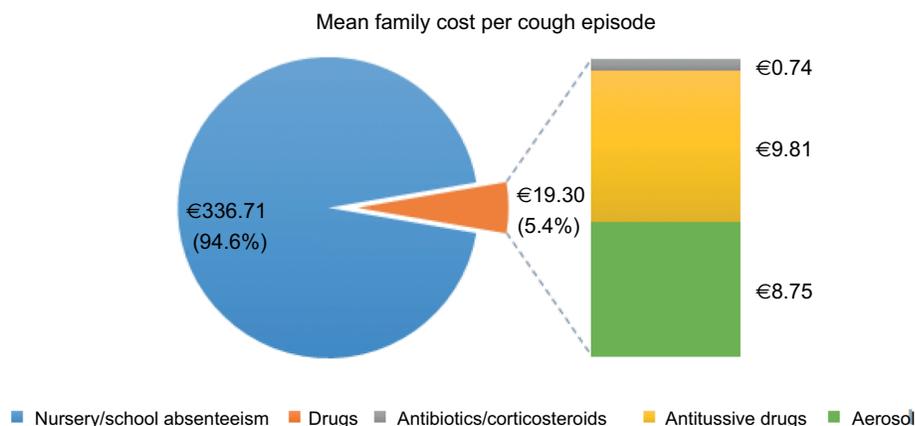


Figure 3 Cost per cough episode: the impact of absenteeism and drugs on the Italian families.

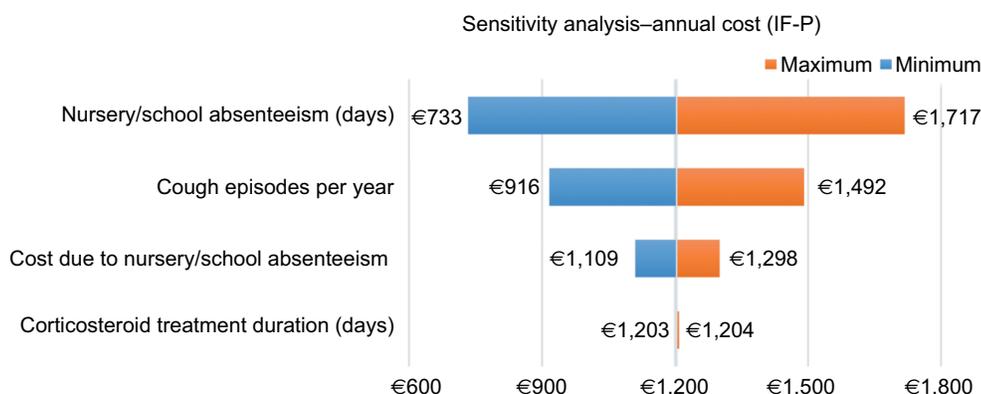


Figure 4 Sensitivity analysis results: annual cost of cough management in the societal perspective.
Abbreviation: IF-P, Italian family perspective.

the times push for a quick therapeutic intervention in favor of their beloved grandson(s)/granddaughter(s).^{21,22}

Concerning the therapeutic approach, in agreement with data from previous studies,^{28–30} the majority of pediatricians’ home prescriptions consist of antibiotics, followed by corticosteroid (mostly via the inhalation route), mucolytics, antitussive drugs, and nonsteroidal anti-inflammatory agents. The reported characteristics of cough episodes would have suggested the occurrence of an upper airway viral infection in the majority of cases, and the immediate prescription of antibiotics and/or oral steroids should then have been regarded as an inappropriate first-line therapeutic choice. However, from the strict point of view of the overall economic burden of cough episodes, the expenses due to the resource consumption due to all these drugs prove quite marginal, even though slightly higher from the family’s perspective.

When comparing data reported in Table 4 with those in Figure 3 of the present study, the pharmaceutical cost are in line with the elicited willingness to spend €19.95 versus €19.30. This cost appears negligible when compared to that

related to school absenteeism (more than €300 per episode), which, on the other hand, is generally not perceived by parents, even if it has a substantial societal impact due to the cost of parents’ work permits.

Limitations and strength of the study

The study was conducted according to a cross-sectional, retrospective design, not aimed to the precise definition of cough etiology and to the assessment of prospective outcomes. Moreover, as the problem of cough was being faced in childhood, information was collected by using a questionnaire also usable by care-givers different from the children’s parents, who were sometimes recalled. Finally, information on therapeutic prescriptions were derived from parents (or care-givers), and not directly obtained from pediatricians or GPs. This could lead to risk of recall bias, that is, a systematic error caused by differences in the accuracy or completeness of the recollection retrieved by study participants regarding events or experiences from the past. However, the main causes

of recall bias are personal questions about embarrassing or social unacceptable arguments (eg, sexually transmitted disease or intravenous drug use), life-threatening disease or life-changing disease (eg, cancer or Parkinson's), preexisting belief about the subject of the study (eg, relationship between cell phone and brain cancer), or questions related to arguments far from the present. Our study did not involve any of these conditions; hence, we are quite confident that the risk of recall bias would be minimum.

On the other hand, a point of strength is that the study was conducted on a representative sample of Italian families evenly distributed across regions, and the corresponding redemption was pretty good.

At present, further calculations are still in progress aimed to investigate more precisely the factors leading to the economic burden of cough episodes among children and their families.

Other methods can be used for assessing the socio-economic impact of acute cough. Studies based on self-administered postal questionnaires might also be conducted, even if time-consuming, biased usually by a much lower redemption rate, and characterized by a different target of responders. However, a comparison between data from the present study and a national survey carried out via self-administered questionnaires is already in advanced progress and ready for submission in near future. Finally, study protocols conducted in cooperation with the pharmacists or with the pediatricians and GPs are also possible, even if stemming from a different point of view, such as not solely from the patients' or the family's perspective.

Disclosure

The authors report no conflicts of interest in this work.

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