

Epidemiology of Frequently Occurring Skin Diseases in Italian Children from 2006 to 2012: A Retrospective, Population-Based Study

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Abstract

Background: Recent estimates indicate an increase in the prevalence of skin diseases in children. Few large epidemiologic studies have examined prevalence trends in Europe. This study evaluated the incidence and prevalence of frequently occurring pediatric skin diseases (PSDs) in Italy as seen by family pediatricians (FPs).

Methods: Data were retrospectively extracted from the Pedianet database (2006–2012) in children ages 0 to 14 years presenting with a skin disease at their FP. The incidence and prevalence estimates were calculated per year and stratified according to sex, age, and geographic area.

Results: A mean of 145,233 children (52.1% male) across five Italian regions were registered with their participating FP for a total of 913,253 person-years of follow-up. The majority of patients were from the northeast (44.6%) and 37.7% were ages 5–9 years. Incidence estimates (new cases/1,000 person-years) for most PSDs increased from 2006 to 2012, the highest being for atopic dermatitis (AD) (14.1 vs 16.5), acute urticaria (10.1 vs 11.6), and contact dermatitis (9.3 vs 10.8), whereas psoriasis remained unchanged over the 7 years (0.61 vs 0.57). In contrast, prevalence estimates (cases/100 patients) increased two to three times for several PSDs, including AD (2.7% vs 8.5%), seborrheic dermatitis (0.5% vs 1.6%), chronic urticaria (0.4% vs 0.8%), and psoriasis (0.09% vs 0.22%). Differences in prevalence according to age range and geographic area were observed for psoriasis, AD, and urticaria.

Conclusion: This study provides comprehensive evidence of the increasing prevalence and incidence of PSDs across Italy. Additional causality studies to address this important clinical and psychosocial problem are recommended.

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Skin diseases are a common reason for children to visit pediatric clinics and emergency departments (1–3). The severity of pediatric skin diseases (PSDs) is variable (2), but the burden that they impose on children, their families, and health care resources should not be underestimated (4). It has also been shown that skin diseases, in particular chronic diseases such as atopic dermatitis (AD), negatively affect quality of life (QoL) (5). Patients with chronic PSDs show high impairment in their QoL, with AD (being one of the most common PSDs) having a greater effect on QoL than other, more severe clinical conditions (6). Because recent epidemiologic data indicate that specific PSDs are increasing in children in developed countries (7–9), a more precise map of the incidence is needed to improve management of these diseases.

Although several studies have estimated the incidence or prevalence of chronic PSDs in different European countries (1–3,7–19), the majority of these have focused on a single condition, such as AD, urticaria, or psoriasis, over a period of 1 to 3 years or on hospitalized children. Several studies have compared two time points (or historical records) (7,8,10,11,14), but few have reported data on trends over several years. Some of the most important prevalence and trend data on AD have emerged from the International Study of Asthma and Allergies in Childhood (ISAAC) (20), but because the prevalence of PSDs tends to change over time and is different in different countries, direct comparison of prevalence or incidence rates of specific PSDs is difficult because of variations in the years when different studies were performed. Although these epidemiologic studies provide important insights into incidence or prevalence trends for specific PSDs, particularly AD, they lack data on many other frequently occurring PSDs. In Italy, four studies have assessed the prevalence of AD in children (12,14,16,18), and one of these studies also examined the prevalence of psoriasis (16). Although a number of studies strongly suggest an increase in the prevalence of AD in recent years (7,8,11,14), trends in the incidence and prevalence of other frequently occurring PSDs (as well as AD) are not yet available. To address some of these issues, we used data from a large cohort of patients registered in a nationwide network of family pediatricians (FPs) (Pedianet) (21) already used to conduct similar epidemiologic studies (22). The incidence and prevalence of the most frequently occurring PSDs in different regions of Italy from 2006 to 2012 were estimated.

METHODS

Patients

The study population consisted of 145,233 children ages 0 to 14 years, resident in Italy, and registered with 137 pediatricians providing data to the Pedianet database (21).

Study Design

This retrospective cohort study was based on clinical data registered on the Pedianet database (<http://www.pedianet.it>) from January 2006 to December 2012. After written informed consent was received from parents, FPs submitted anonymous individual patient medical records to a central database. Data generated during routine patient care were collected and handled anonymously, in compliance with Italian regulations, and stored under a unique numerical identifier. Each numerical code provided access to different files containing information specific to each child: the identification file contained demographic data and eligibility status, the prescription file contained information on all medications and vaccinations prescribed by the assigned FP, and the medical file contained diagnostic information and anthropometric measurements. This study was conducted in accordance with the Declaration of Helsinki and the Guidelines of Good Epidemiology Practices.

For the purpose of this study, we defined PSDs according to the International Classification of Diseases, Ninth Revision (ICD-9) (23).

Data Collection

Data were extracted from digital medical records registered in the Pedianet database. Patients diagnosed with PSDs were identified by performing database searches with ICD-9 diagnosis codes or skin disorder names (“atopic dermatitis,” “contact dermatitis,” “diaper rash,” “seborrheic dermatitis,” “dermatophytosis,” “dermatomycosis,” “erythema nodosum,” “ichthyosis,” “urticaria,” and “psoriasis”) (22,23). From each medical record, demographic characteristics (age and sex), medical information (consultations, referrals, hospitalizations, examinations, and tests related to PSDs), and information on PSD clinical symptoms, diagnoses subsequent to PSD, and drug prescriptions were collected. Incidence was estimated by censoring at the time of the first diagnosis.

Data Analysis

Statistical analysis was performed in this epidemiologic study and data are presented as incidence or prevalence estimates or proportions. Incidence was calculated as the number of new cases from 1,000 patients per year. Prevalence was calculated by dividing the number of individuals identified with a PSD during the follow-up period by the number of patients in the study population and expressed as a percentage. The 95% confidence intervals around the rates were based on Poisson or binomial distribution. For chronic conditions (ichthyosis, AD, psoriasis, seborrheic dermatitis, chronic urticaria), a patient presenting with the diagnosis was considered to be a “case” and was included in the numerator once. For acute conditions (acute urticaria, contact dermatitis, mycosis, or nodular erythema), subjects were considered prevalent cases only if they presented at the FP during the year. Incidence and prevalence estimates were also stratified according to sex, age, and area.

RESULTS

Patient Demographic and Clinical Characteristics

Over the 7-year period, 137 FPs registered a mean of 145,233 children (52.1% male) in all five areas of Italy. Patients were followed up for a total of 913,253 person-years.

There was an equal distribution of boys and girls across the five geographic areas. The majority of patients were registered from the northeastern (Veneto) region (44.6%), and 37.7% were ages 5 to 9 years (Fig. 1A). Although the total number of patients registered for each year did not change markedly over the 7-year period (127,316 patients in 2006 vs 153,642 in 2012), the number of patients in various age ranges differed slightly over the study period (Fig. 1B). This age-related difference was observed to a similar extent according to sex and between the five geographic areas (data not shown).

Number of Incident Cases of Frequently Occurring PSDs

The number of incident cases of each PSD is presented in Table 1. A total of 37,083 cases were reported over the entire study period, predominantly in children ages 1 to 4 years. The highest number of cases was for AD (12,588), accounting for 33.9% of

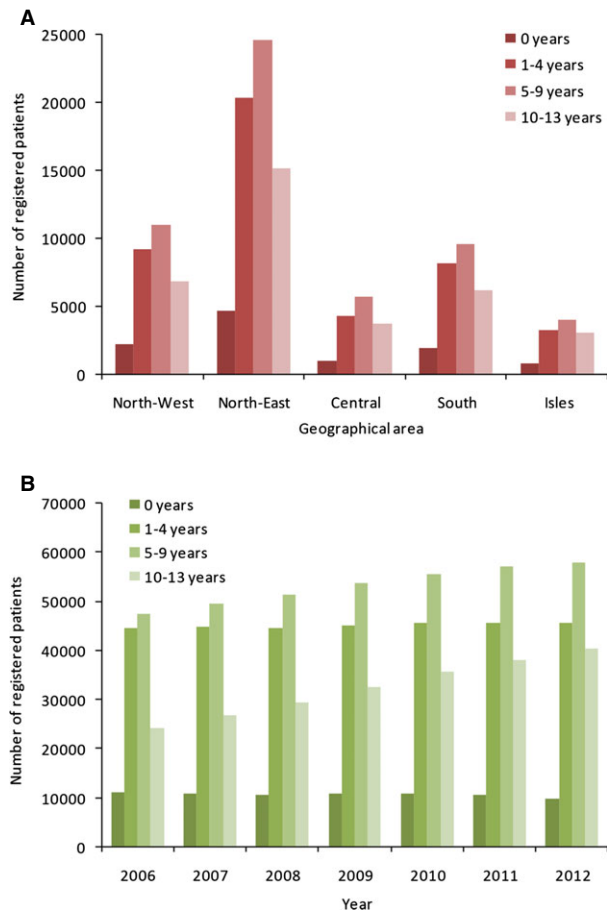


Figure 1. Distribution of patients according to geographic area and age range. (A) Proportion of patients according to age range for the five geographic areas. (B) Number of registered patients over the 7-year study period according to age range.

TABLE 1. Number of Incident Cases of Frequently Occurring Pediatric Skin Diseases According to Age Range for the Entire Study Period

Skin disease	0	1–4	5–9	10–13	Total
Atopic dermatitis	4,170	5,328	2,369	721	12,588
Acute urticaria	570	4,916	2,873	1,082	9,441
Contact dermatitis	1,165	4,027	2,516	1,046	8,754
Seborrheic dermatitis	1,702	348	261	240	2,551
Dermatomycoses	193	663	662	462	1,980
Chronic urticaria	111	702	327	77	1,217
Psoriasis	19	81	222	145	467
Erythema nodosum	2	17	29	5	53
Ichthyosis	7	15	9	1	32
Total	7,939	16,097	9,268	3,779	37,083

all incident cases (Table 1). The total number of incident cases for erythema nodosum and ichthyosis was 53 and 32, respectively. The number of incident cases was equally represented for male and female patients (data not shown).

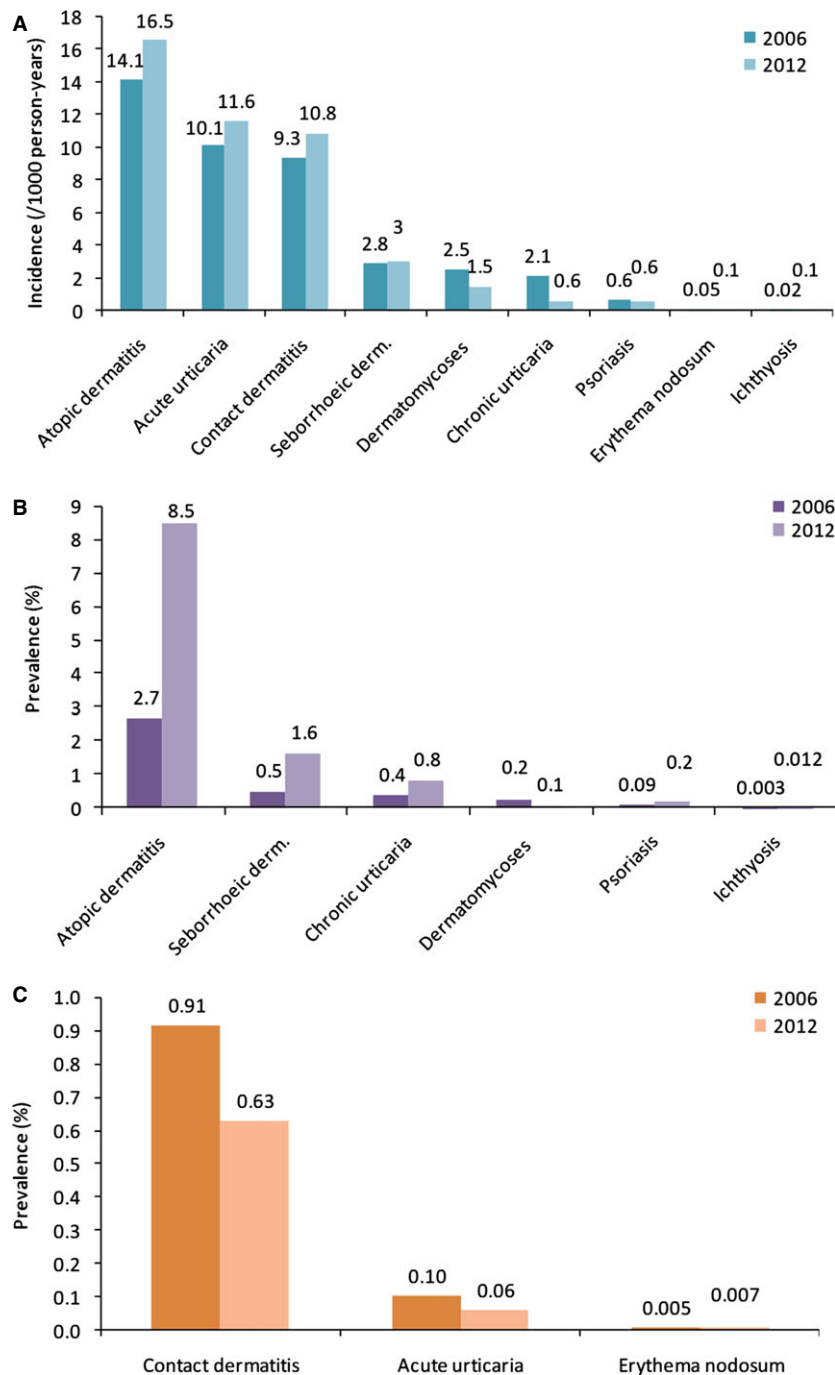


Figure 2. Incidence and prevalence estimates of the most frequently occurring pediatric skin diseases in 2006 and 2012. (A) Incidence estimates of frequently occurring pediatric skin diseases in 2006 and 2012. (B) Prevalence estimates of chronic pediatric skin diseases in 2006 and 2012. (C) Prevalence estimates of acute pediatric skin diseases in 2006 and 2012. Incidence and prevalence values for individual skin diseases are shown.

Incidence Estimates for Frequently Occurring PSD

Incidence estimates in 2006 and 2012 for nine PSDs are shown in Fig. 2A. Incidence values for one-third of PSDs increased from 2006 to 2012. The highest

incidence was observed for AD, which increased over time (14.1 in 2006 vs 16.5 in 2012), followed by acute urticaria (10.1 vs 11.6) and contact dermatitis (9.3 vs 10.8). Other PSDs had lower incidence values, ranging from 0.02 to 3 cases/1,000 person-years, and only

marginally increased or were unchanged during the study period. Incidence estimates and 95% confidence intervals for all nine PSDs for each year are presented in Table 2.

Prevalence Estimates for Frequently Occurring PSD

For chronic diseases (ichthyosis, AD, psoriasis, seborrheic dermatitis, chronic urticaria), prevalence estimates (number of cases/100 patients) increased from 2006 to 2012 by two to three times for several PSDs, including AD (2.7% vs 8.5%), seborrheic dermatitis (0.5% vs 1.6%), chronic urticaria (0.4% vs 0.8%), and psoriasis (0.09% vs 0.22%) (Fig. 2B). In contrast, prevalence values for acute dermatitis such as acute urticaria and contact dermatitis remained low (0.1–0.9%), whereas their incidence estimates were higher (9.3–11.6) (Fig. 2C). Prevalence estimates and 95% confidence intervals for all nine PSDs for each year are presented in Table 3.

Incidence and Prevalence Estimates for Psoriasis, AD, and Chronic Urticaria Stratified According to Sex, Age, and Geographic Area

Because chronic skin diseases such as psoriasis, AD, and chronic urticaria cause significant psychological and social burden, directly affecting quality of life (6), they were further analyzed for incidence and prevalence estimates stratified according to sex, age range, and geographic area from 2006 to 2012.

Incidence and prevalence estimates for psoriasis are shown in Fig. 3. Although the incidence of psoriasis was similar for male and female patients and remained fairly stable over the 7-year period (with a slight increase from 2011 to 2012) (Fig. 3A), prevalence values increased (approximately doubling) in a time-dependent manner (Fig. 3B). Incidence estimates were also higher for patients ages 5 to 9 years and 10 to 13 years than for newborns and babies (age <4 yrs) from 2006 to 2011, with a sharp increase in incidence in patients younger than 1 year from 2011 to 2012 (Fig. 3C). This age-related difference was also noted for prevalence estimates (Fig. 3D). Although no marked geographic differences were noted for incidence (Fig. 3E), a clearly defined difference was observed for prevalence estimates, which were lower in the northern areas and higher in the south, central area, and islands (Fig. 3F).

Similar to psoriasis, no difference was observed in incidence or prevalence estimates for AD according to sex. Although incidence values (Fig. 4A) remained relatively stable over the 7 years, prevalence estimates

TABLE 2. Incidence Estimates of Frequently Occurring Pediatric Skin Diseases from 2006 to 2012

	2006	2007	2008	2009	2010	2011	2012
New cases/1,000 person-years (95% confidence interval)							
Skin disease							
Atopic dermatitis	14.05 (13.4–14.7)	13.24 (12.6–13.9)	13.45 (12.8–14.1)	13 (12.4–13.6)	14.31 (13.7–14.9)	13.16 (12.6–13.8)	16.52 (15.6–17.5)
Acute urticaria	10.06 (9.5–10.6)	10.38 (9.8–10.9)	10.46 (9.9–11)	9.91 (9.4–10.4)	10.48 (9.9–11)	10.07 (9.6–10.6)	11.55 (10.8–12.3)
Contact dermatitis	9.32 (8.8–9.9)	9.89 (9.4–10.5)	10.03 (9.5–10.6)	9.37 (8.9–9.9)	9.69 (9.2–10.2)	8.6 (8.1–9.1)	10.84 (10.1–11.6)
Seborrheic dermatitis	2.83 (2.5–3.1)	2.83 (2.6–3.1)	3.04 (2.8–3.3)	2.71 (2.5–3)	2.67 (2.4–2.9)	2.64 (2.4–2.9)	2.95 (2.6–3.4)
Dermatomycoses	2.5 (2.2–2.8)	2.39 (2.1–2.7)	1.98 (1.8–2.2)	2.14 (1.9–2.4)	2.07 (1.9–2.3)	2.34 (2.1–2.6)	1.48 (1.2–1.8)
Chronic urticaria	2.1 (1.9–2.4)	2.1 (1.9–2.4)	1.7 (1.5–1.9)	1.33 (1.2–1.5)	1.05 (0.9–1.2)	0.59 (0.5–0.7)	*
Psoriasis	0.61 (0.5–0.8)	0.45 (0.3–0.6)	0.54 (0.4–0.7)	0.53 (0.4–0.7)	0.53 (0.4–0.7)	0.4 (0.3–0.5)	0.57 (0.4–0.8)
Erythema nodosum	0.05 (0.02–0.1)	0.05 (0.02–0.1)	0.1 (0.05–0.16)	0.01 (0.00–0.05)	0.05 (0.02–0.1)	0.05 (0.02–0.1)	0.13 (0.06–0.24)
Lichenoid dermatitis	0.02 (0.00–0.06)	0.05 (0.02–0.1)	0.02 (0.00–0.06)	0.01 (0.00–0.05)	0.01 (0.00–0.05)	0.04 (0.01–0.09)	0.14 (0.07–0.26)

*In the database, there is no distinction between chronic and acute urticaria, because the family pediatrician reported only generic "urticaria." We defined cases of chronic urticaria as patients who were diagnosed again at least 6 weeks after the incidence date. Given this definition, there was insufficient time to record subsequent visits for children with a first diagnosis in early 2012, so only data up to 2011 are presented.

TABLE 3. Prevalence Estimates of Frequently Occurring Pediatric Skin Diseases from 2006 to 2012

	2006	2007	2008	2009	2010	2011	2012
Skin disease	Number of cases/100 participants (95% confidence interval)						
Atopic dermatitis	2.66 (2.6–2.8)	3.75 (3.7–3.9)	4.78 (4.7–4.9)	5.73 (5.6–5.9)	6.82 (6.7–6.9)	7.78 (7.7–7.9)	8.45 (8.3–8.6)
Acute urticaria	0.1 (0.09–1)	0.1 (0.09–1.1)	0.11 (0.09–1.1)	0.09 (0.09–1.1)	0.11 (0.1–1.1)	0.1 (0.1–1.1)	0.06 (0.05–0.06)
Contact dermatitis	0.91 (0.86–0.96)	1.01 (0.96–1.06)	1.05 (1–1.1)	1.01 (0.96–1.06)	1.07 (1.02–1.1)	0.97 (0.93–1.02)	0.63 (0.59–0.67)
Seborrheic dermatitis	0.5 (0.46–0.54)	0.72 (0.68–0.7)	0.95 (0.9–1)	1.15 (1.09–1.2)	1.34 (1.28–1.4)	1.53 (1.47–1.59)	1.64 (1.58–1.7)
Dermatomycoses	0.24 (0.22–0.27)	0.24 (0.21–0.26)	0.2 (0.18–0.22)	0.22 (0.2–0.25)	0.22 (0.19–0.24)	0.25 (0.22–0.27)	0.08 (0.07–0.1)
Chronic urticaria	0.38 (0.35–0.4)	0.56 (0.5–0.6)	0.68 (0.64–0.7)	0.76 (0.7–0.8)	0.83 (0.8–0.9)	0.84 (0.8–0.9)	0.84 (0.8–0.9)
Psoriasis	0.09 (0.08–0.11)	0.13 (0.11–0.15)	0.16 (0.14–0.19)	0.19 (0.17–0.22)	0.21 (0.19–0.24)	0.21 (0.19–0.24)	0.22 (0.2–0.25)
Erythema nodosum	0.005 (0.003–0.01)	0.004 (0.002–0.01)	0.009 (0.005–0.016)	0.001 (0.00–0.005)	0.005 (0.002–0.01)	0.005 (0.003–0.01)	0.007 (0.004–0.01)
Ichthyosis	0.003 (0.001–0.008)	0.007 (0.004–0.014)	0.009 (0.005–0.016)	0.01 (0.006–0.17)	0.011 (0.007–0.018)	0.015 (0.01–0.02)	0.012 (0.015–0.03)

approximately tripled in a time-dependent manner from 2006 to 2012 (Fig. 4B). This increase was mainly attributed to patients ages 1 to 4 years and 5 to 9 years (Fig. 4C), whereas new cases of AD (Fig. 4D) were strongly represented in the first year of life. Although no marked geographic differences were noted for incidence estimates, the prevalence of AD increased in a time-dependent manner for all five areas (Fig. 4E).

In contrast to psoriasis and AD, incidence estimates for chronic urticaria decreased sharply in males and females over the 7-year period (Fig. 5A). Prevalence doubled in boys and girls from 2006 to 2012 (Fig. 5B). Similar to psoriasis and AD, age-related differences were also observed for incidence and prevalence estimates. Although patients ages 1 to 4 years had the highest incidence in 2006 (Fig. 5C), these values decreased (as did prevalence estimates; Fig. 5D) over the study period. Although incidence estimates generally decreased for all geographic areas, a higher incidence was noted for patients from the islands (Fig. 5E). Likewise, the prevalence of urticaria from the islands was higher than other areas and continued to increase and diverge from the other areas over the 7-year period (Fig. 5F).

DISCUSSION

This large retrospective epidemiologic study provides comprehensive evidence of the high burden of skin diseases occurring in Italian children. Age-related and geographic differences have also emerged for chronic skin diseases (e.g., psoriasis, AD, chronic urticaria) that suggest future trends and warrant further studies.

The majority of prevalence studies performed in Europe in children have focused on a single skin disease such as AD, psoriasis, or urticaria, whereas the current report presents a global picture of incidence and prevalence estimates for a range of skin diseases over 7 years. The unique strengths of the present study therefore lie in the quantity of data obtained in a primary care setting: the large sample size (approximate mean of 145,000 per year) over a 7-year period, encompassing five geographic areas (northwest, northeast, central, the islands, south), with a large age range (0–14 yrs). Furthermore, FPs diagnosed skin diseases rather than using a self-reported questionnaire as in previous large population cohorts (14,20). Because virtually all children younger than 14 years are assigned an FP in Italy, our estimates should provide a more accurate measure of the presence of a specific disease that is representative of the general population. Prevalence values

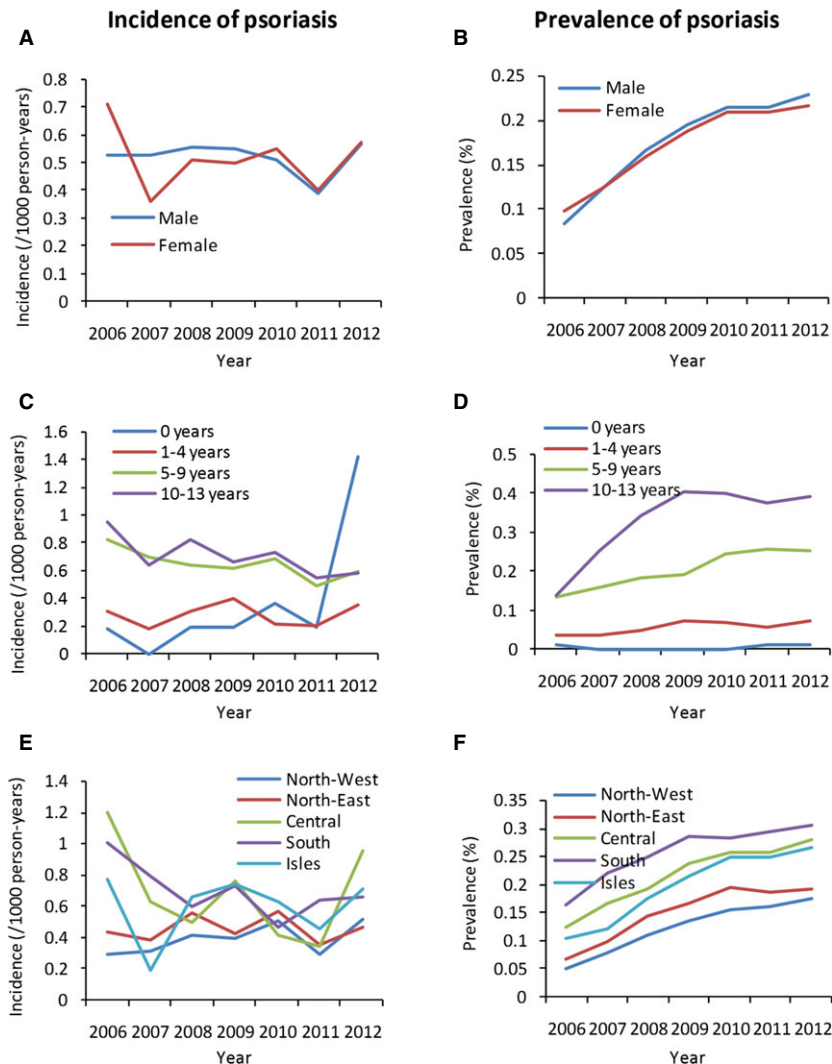


Figure 3. Incidence and prevalence estimates for psoriasis, stratified according to sex, age, and geographic area, from 2006 to 2012.

obtained in the present study (2.7% in 2006 to 8.5% in 2012) confirm previous Italian epidemiologic studies for AD that ranged from 5.8% to 10.4% (12,14,16,18). An incidence of 10% was estimated from a questionnaire-based survey by Ruggiero et al (18), which was marginally lower than that observed in our analysis (14.1 per 1,000 person-years in 2006 and 16.5 in 2012); since ours was based on a clinical diagnosis, it should be more sensitive. The most recent epidemiologic study performed in Italian children by Galassi et al (14) used ISAAC questionnaires to compare the prevalence of AD in 6- to 7-year-old children and 13- to 14-year-old adolescents in 1994–1995 with that in 2002. This study noted an increase from 6% in 1994–1995 to 10.4% in 2002 in 6- to 7-year-old children and an increase from 6.5%

to 8.5% for 13- to 14-year-old adolescents. Although in the present study we observed a five times increase (approximately 2% to 10%) in 5- to 9-year-old children, the prevalence of AD in adolescents (ages 10–13 yrs) did not increase at the same rate or to the same extent (reaching 4.7% in 2012). Nevertheless, the number of new cases was identical across different age ranges (independent of patient age) in a study performed in The Netherlands in 2001 (7), in which infants (age <1 yr) had the highest incidence of AD (90.9%). Incidence values for other age ranges closely matched estimates in the present report. In this same study, incidence estimates for urticaria closely matched estimates observed in the present study, in which the highest incidence values were observed in children ages 1 to 4 years in 2006. We observed an

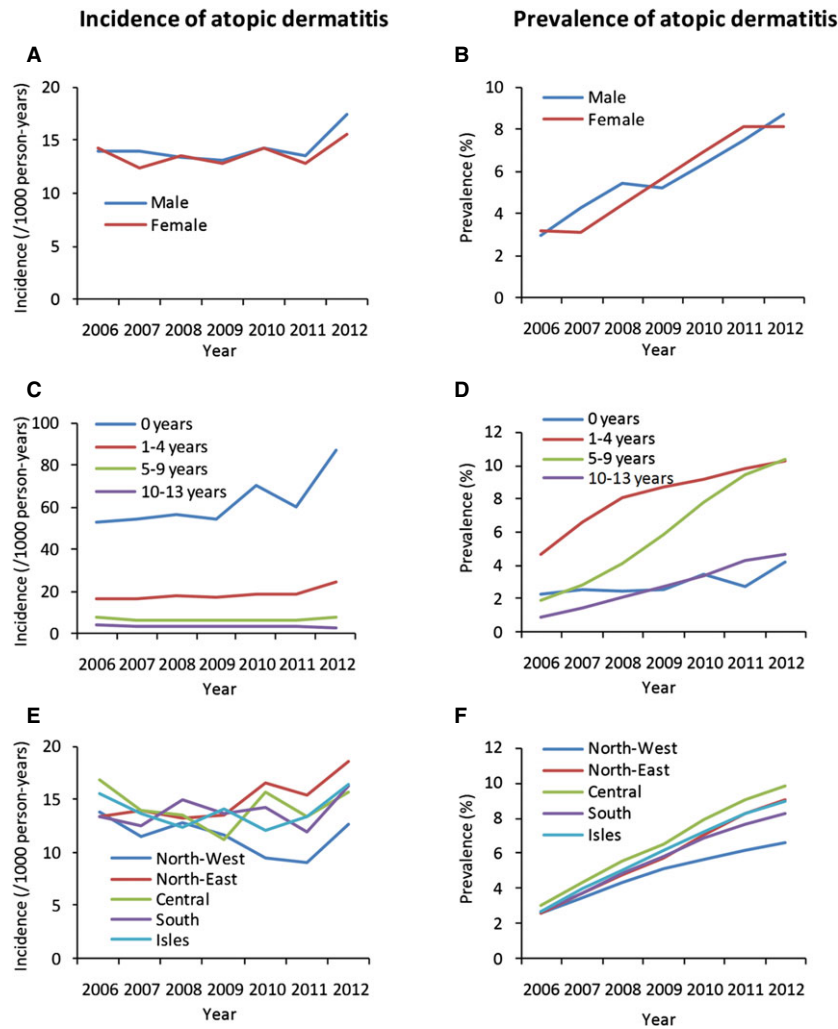


Figure 4. Incidence and prevalence estimates for atopic dermatitis, stratified according to sex, age, and geographic area, from 2006 to 2012.

increase in the incidence of acute urticaria (10.1 per 1,000 person-years in 2006 to 11.6 in 2012) and a reduction in the chronic form (from 2.1 to 0.6), whereas a slight increase was noted in the Dutch study (7.4% in 1987 to 8.2% in 2001), in which both forms were included together. Further studies are needed to explain our finding. We observed a small increase in the incidence of seborrheic dermatitis (from 2.8 in 2006 to 3 in 2012), as Mohammedamin et al (7), who observed an increase from 3.4% in 1987 to 5.1% in 2001, also noted. Schafer et al (11) also saw an increase in the number of newly diagnosed AD cases in children younger than 6 years of age in eastern Germany, from 16% in 1991 to 23.4% in 1997. Likewise, the prevalence of psoriasis reported in the present study ranged from 0.09% in 2006 to 0.2% in 2012, similar to a study in 2005 in Germany in which a point prevalence of 0.71% was estimated, but this was

3-fold lower (2.1%) than another Italian study performed in 1997 (16).

In addition to age-related differences in prevalence and incidence estimates, the prevalence of psoriasis and chronic urticaria increased in a time-dependent manner for all five Italian areas, with a higher prevalence being observed in the south and islands than in the northern areas. Although climate differences such as ultraviolet exposure, temperature, precipitation, and humidity affect the prevalence of skin diseases, particularly AD (24), and may differ substantially from the north to the south of Italy, their precise role and effect on prevalence differences remains to be determined.

As with other studies conducted using health care records, this study had some limitations associated with a retrospective cohort that could affect the interpretation of results. Data were collected during routine

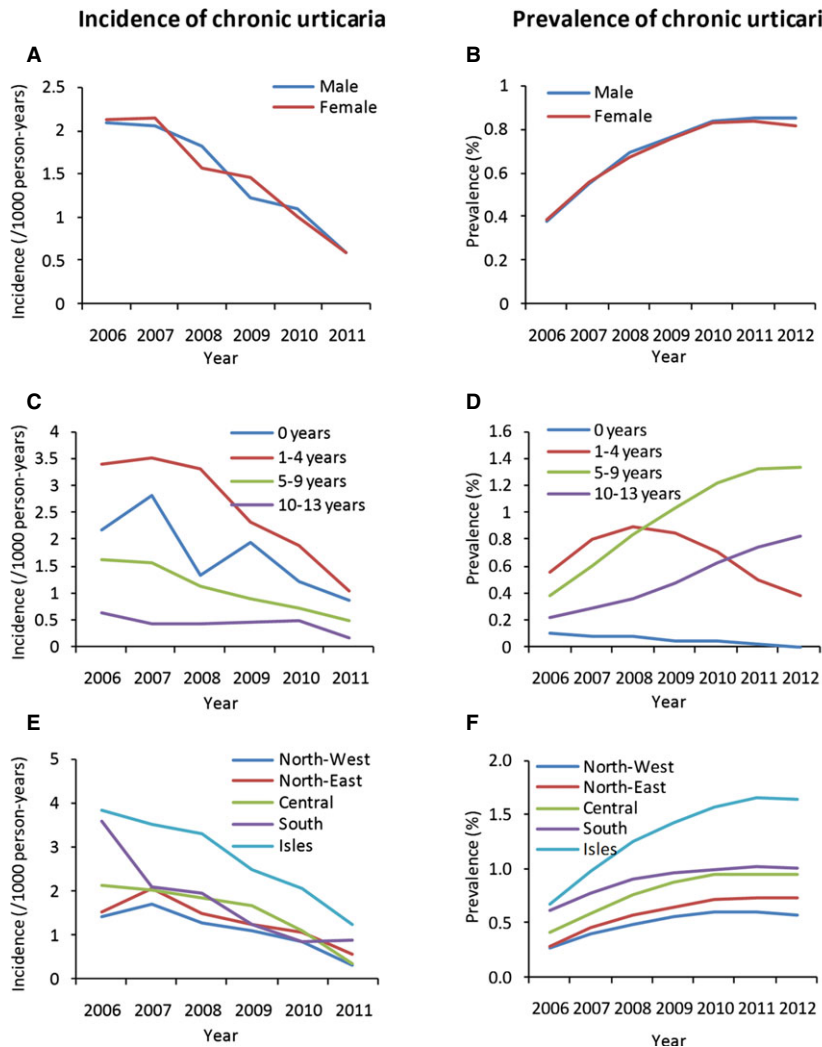


Figure 5. Incidence and prevalence estimates for chronic urticaria, stratified according to sex, age, and geographic area, from 2006 to 2011. In the database, there is no distinction between chronic and acute urticaria, because the family pediatrician reported only generic “urticaria.” We defined cases of chronic urticaria as patients who were diagnosed again at least 6 weeks after the incidence date. Given this definition, there was insufficient time to record subsequent visits for children with a first diagnosis in early 2012, so only data up to 2011 are presented.

patient care, and only visits in the clinic were recorded, so information from telephone consultations (which can be common for patients with PSD) with patients whose skin diseases were not considered severe could have been missing. Although the 7-year follow-up provided sufficient data to indicate the recent past and potential future prevalence trends in Italy, a longer period (e.g., ≥ 10 years) might have reinforced these findings. A follow-up analysis will allow confirmation of these trends. The diagnosis of PSD was clinical, and not all participating FPs would have used the same criteria to diagnose patients. Nevertheless, FPs (not a specialist or dermatologist) care for the vast majority of individuals with PSDs, and it is unlikely that potential

diagnostic biases would change over time. Therefore, retrieving data from primary care settings is likely to be the most accurate way to evaluate trends in PSDs over different periods. Last, recent evidence indicates that the incidence of infectious skin diseases (e.g., viral warts) is also increasing in children, and although not specifically assessed in the present study, they warrant strict monitoring in future longitudinal epidemiologic studies (8,15,25).

CONCLUSIONS

The main findings that have emerged from the present study indicate that although the incidence of certain

skin diseases (AD, contact dermatitis, seborrheic dermatitis) appears to have increased over the past 7 years, the incidence of most diseases (particularly chronic skin diseases) has remained unchanged. In contrast, trends in prevalence estimates appear to have continuously increased for several skin diseases, particularly for the chronic skin diseases such as AD, psoriasis, and urticaria. Marked differences in incidence and prevalence estimates were noted for different age ranges for AD, psoriasis, and urticaria, an important indicator of future trends.

Despite these differences, the overall burden of skin disease in children in Italy is high, with a major effect on quality of life and health care costs, further studies are needed to evaluate these factors.

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