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Regional disparities in access to epinephrine auto-injectors for children and adults in Italy

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KEY WORDS

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To the Editor,

anaphylaxis is a potentially life-threatening systemic reaction that requires rapid recognition and treatment, with adrenaline representing the first-line (1, 2). In a 2024 study, the overall incidence of anaphylaxis in France was estimated at 1.34 per 100,000 people per year, with a hospital admission rate for severe reactions of 0.08 per 100,000 per year (2). Globally, in the pediatric population, the incidence of anaphylaxis is estimated to range from 1 to 761 episodes per 100,000 people per year (3), with most cases

occurring before six years of age and being influenced by the presence of atopic comorbidities. The most common triggers in children are foods, including milk, eggs, and tree nuts, whereas drug- and insect venom-induced anaphylaxis occurs more frequently in adults (4). Risk factors for severe reactions include pulmonary diseases, including asthma, and mastocytosis. Diagnosis is clinical, with no single sign or symptom being pathognomonic. However, serum tryptase levels measured in the acute phase may support the diagnosis. Reaction patterns may differ by trigger, with the skin being the most frequently affected. Most

reactions occur within 30 min of exposure, although a delay of 4 h can be seen for specific triggers, and biphasic anaphylaxis has also been described (5). Epinephrine autoinjectors (EAI) are prescribed for at-risk individuals to facilitate prompt epinephrine administration during anaphylaxis in the community (6). In Italy, EAI are available and dispensed by the National Health System. Epinephrine halts and reverses reactions in a manner that other treatments cannot. Different EAI brands are available as doses of 150 µg, 300 µg, or 500 µg (7); however, there is limited global availability of the 500-µg dose, contributing to disparities in access at both national and international level. The European Medicines Agency (EMA) recommends patients at risk of anaphylaxis should always be prescribed two EAI and should carry both at all times (8).

Currently, there is insufficient data on the availability and reimbursement of autoinjectors across different states for both children and adults. The Italian Society of Pediatric Allergy and Immunology (SIAIP) and the Association of Italian Territorial

and Hospital Allergists and Immunologists (AAIITO) have analyzed the availability of EAI for children and adults, respectively. To investigate potential regional differences, data were collected from junior and senior SIAIP and AAIITO regional representatives between June and September 2024.

EAI availability and reimbursement in Italy demonstrated marked regional disparities, affecting both pediatric and adult populations. A key issue is the absence of updated regional regulations for supply and reimbursement. Consequently, several regions still rely on heterogeneous policies, leading pharmacies to dispense whichever device is available. Most regions provide two injectors per year for children. Exceptions include Sardinia and Trentino-Alto Adige (Bolzano province), which reimburse only one injector annually. Additionally, in Piedmont, Veneto, and Aosta Valley one injector is reimbursed by default, and a second provided only in specific circumstances. Reimbursement policies for adults show greater variability. Two injectors per year are reimbursed in Basilicata, Calabria, Emilia-Romagna, Lazio,

Table I - Number of reimbursed autoinjectors in Italian regions in the pediatric and adult populations.

Italian regions	Number of reimbursed autoinjectors	
	Children	Adults
Abruzzo	2/year	1-2/year
Basilicata	2/year	2/year
Calabria	2/year	2/year
Campania	2/year	1-2/year
Emilia Romagna	2/year	2/year
Friuli Venezia Giulia	2/year	1-2/year
Lazio	2/year	2/year
Liguria	2/year	1-2/year
Lombardy	2/year	1-2/year
Marche	2/year	1-2/year
Molise	2/year	1-2/year
Piedmont	1-2/year	1-2/year
Puglia	2/year	1-2/year
Sardinia	1/year	1/year
Sicily	2/year	1-2/year
Tuscany	2/year	2/year
Trentino Alto Adige – Bolzano province	1/year	1/year
Trentino Alto Adige – Trento province	2/year	1-2/year
Umbria	2/year	1-2/year
Veneto	1-2/year	2/year
Aosta Valley	1-2/year	1-2/year

Tuscany and Veneto. In Sardinia and Trentino-Alto Adige (Bolzano province), only one injector per year is reimbursed. In several regions, including Abruzzo, Campania, Friuli Venezia Giulia, Liguria, Lombardy, Marche, Molise, Piedmont, Puglia, Sicily, Trentino-Alto Adige (Trento province), Umbria, and Aosta Valley, the reimbursement for two injectors is restricted to specific circumstances, such as systemic mastocytosis, biphasic anaphylaxis, near-fatal anaphylaxis, severe anaphylaxis, severe obesity, or remote residence (**table 1** and **figure 1**).

This is the first nationwide analysis addressing the availability and reimbursement of EAI in Italy, covering the pediatric and adult populations. Our work was limited by several factors, including intra-regional variability (so we described the prevailing regional trend), the reliance on data reported by regional representatives, the absence of formally published updated regional regulations in some areas, and the lack of quantitative data on prescription volumes. These issues reflect broader trends observed in low- and middle-income countries, as detailed in the World Allergy Organization survey (9). Emerging adrenaline delivery systems, such as intranasal formulations, may improve ease and readiness of use, even if knowledge gaps remain.

The role of patient associations should also be considered, as these organizations substantially contribute in improving awareness of anaphylaxis management and in promoting equitable

access to EAIs. Their inclusion in national strategies together with other relevant stakeholders may facilitate policy harmonization and strengthen educational initiatives aimed at reducing regional disparities.

Without standardized policies, access to EAIs appears unreliable, potentially representing a risk for patients in emergencies. Harmonizing reimbursement policies and procurement frameworks across Italian regions is essential to ensure egalitarian and prompt access to EAI, aligning national practice with international recommendations.

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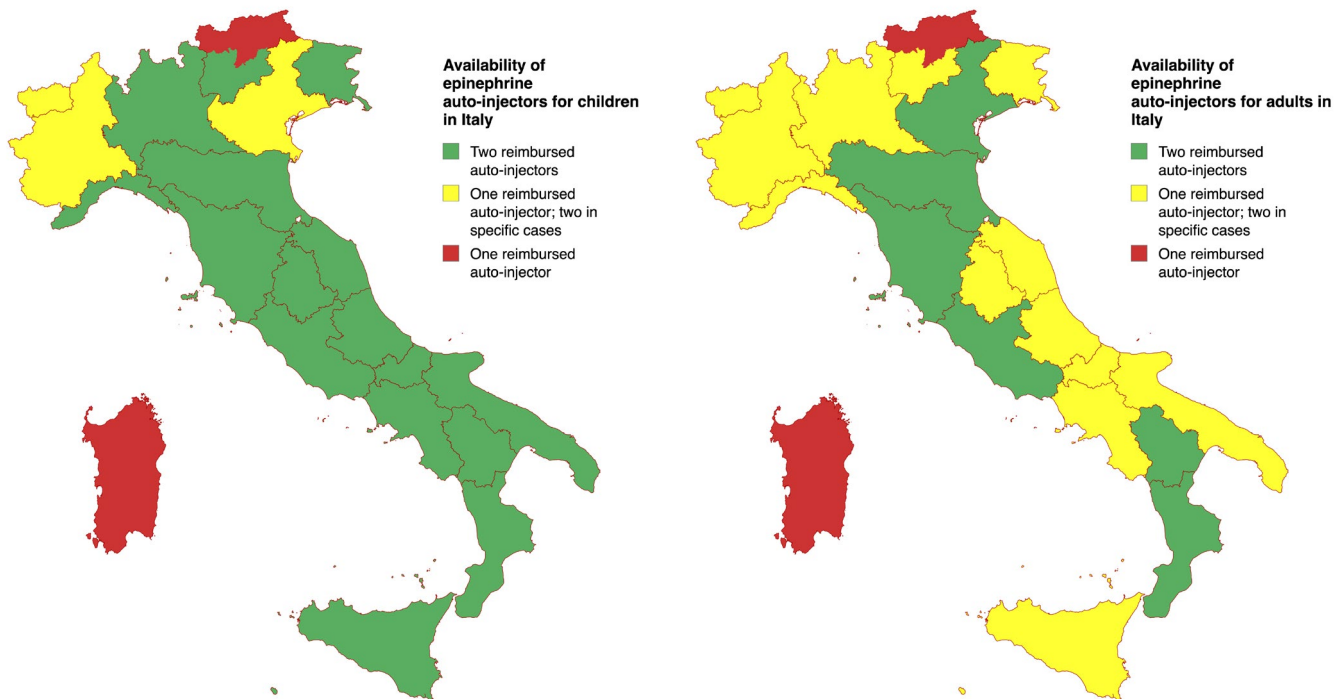
Contributions

AK, MG: conceptualization. AK, BY: writing - original draft. LC, MDF, MG, AMM, MM, GLM, MMdG, FM: writing - review & editing, investigation, formal analysis.

Conflict of interests

MG reports personal fees from Sanofi, Thermo Fisher Scientific. Other authors declare no conflict of interests.

Figure 1 - Disparities in access to epinephrine auto-injectors for children and adults in Italy.



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