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Strategic Consensus on a Proposed Vaccination Schedule for Adults in Portugal

Consenso Estratégico sobre uma Proposta de Calendário de Vacinação para Adultos em Portugal

Laura MOURA [1], Catarina HERMENEGILDO [1], Maria Teresa ROSA [1], Mariana CASTRO [1], Diogo FRANCO [1], João DIOGO[1], Adalberto CAMPOS FERNANDES [2], Céu MATEUS [3], Filipe FROES [4,5], Francisco GEORGE [6], Henrique LOPES [1]
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Keywords: Adult; Immunization Programs; Immunization Schedule; Portugal; Vaccination
Palavras-chave: Adulto; Calendário de Imunização; Portugal; Programas de Imunização; Vacinação

Vaccination as a tool for preventing disease across lifespan

The current and projected demographic context, characterized by an increase in average life expectancy,[1] highlights the growing necessity for a collective reflection on strategies to enhance the quality of life of the population. One of the most effective strategies for achieving this goal is investing in health technologies proven to reduce mortality and morbidity—vaccination being among the most prominent examples.[2]

Vaccination is one of the most powerful innovations in human history. Nowadays, vaccines protect individuals from over 20 diseases throughout their lives, preventing 3.5 to 5 million deaths worldwide each year.[3]

With vaccination coverage falling worldwide and anti-vaccine rhetoric gaining more visibility,[4] the scientific community remains firm in its stance that vaccination should be reinforced and treated as a lifelong responsibility for everyone.

An expanding body of published literature highlights adult and lifelong vaccination,[5] with data indicating that the epidemiological burden of vaccine-preventable diseases among adults remains substantial. For instance, influenza is responsible for approximately 72 000 deaths annually in Europe, predominantly affecting individuals over 65 years old.[6] The incidence of herpes zoster reaches up to 10.9 cases per 1000 adults, with a lifetime risk of 50% in individuals over the age of 80.[7] These data highlight the critical need for targeted adult vaccination strategies to reduce disease incidence, hospitalization, and mortality.

Adult vaccination not only prevents infections but also reduces their severity and may help prevent conditions like dementia.[8,9] Therefore, it is crucial to prioritize the ongoing integration of new vaccines into immunization programs while actively combating the infodemic of misinformation. In Portugal, the success of the National Vaccination Program, active since 1965, underscores the importance of vaccination and the health gains it has provided; however, the program continues to primarily focus on the pediatric population, and to some extent, the elderly.[10]

Between April and May 2024, a think tank initiative was carried out by a research team from NOVA Information Management School (IMS) at NOVA University of Lisbon, in support of the "+Longevity" project. This think tank brought together valuable insights from prominent Portuguese healthcare stakeholders and key opinion leaders (KOLs) on lifelong vaccination, collectively referred to as 'participants'. The initiative benefited from the guidance of a steering committee, all recognized subject-matter experts in the domains examined in the project, who collaborated with the NOVA IMS research team in conducting the study.

The "+Longevity Think Tank" was conducted in person at NOVA IMS and consisted of three structured sessions, each lasting approximately three hours, which included a discussion phase followed by a convergence of ideas phase, both facilitated by a member of the research team. Participation varied across sessions, with experts selected based on their specific areas of expertise relevant to the session topic. The first session focused on "The Future of Vaccine-Preventable Diseases in Adults", the second addressed "The Economic and Social Impact of Vaccine-Preventable Diseases in Adults", and the third explored "A Future Path for Adult Vaccination in Portugal". Before each session, a brief presentation was delivered summarizing the available evidence related to the session's specific topic. Following each session, a short summary was prepared and made available to the participants. The method used to reach consensus on the results throughout the process was majority

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agreement. Following the three sessions, participants were invited to complete a survey in which they rated the level of impact and priority of each recommendation that emerged from the initiative, using a 1-to-10 scale. A final consolidated technical report was subsequently drafted by the research team, reviewed by the Steering Committee, and then circulated to all participants for final review and feedback. This report was developed based on participants' insights and the available scientific literature.

The "+Longevity Think Tank" recommendations focus on three strategic priorities: investing in prevention and healthy aging, strengthening the health system's capacity and resilience, and securing the adult population's commitment to vaccination (Table 1).

Among other targeted recommendations, the think tank participants offered valuable insights into an optimal adult vaccination schedule for Portugal, aimed at advancing lifelong vaccination coverage. The goal was to inspire changes to the existing National Vaccination Program, reinforcing a societal commitment to lifelong vaccination and recognizing prevention as a vital component at every stage of life. Rather than developing a separate schedule, the emphasis should be on advancing a unified approach that reshapes the narrative—positioning vaccination as a cornerstone of disease prevention and a key driver of improved quality of life.

A proposed vaccination schedule for adults in Portugal

The think tank panel, composed of 19 experts, collaboratively contributed insights toward a proposed adult vaccination schedule for Portugal, which was subsequently refined and consolidated by the research team. This proposal represents what participants view as the ideal vaccination schedule, while remaining aligned with current epidemiological trends, vaccine efficacy and effectiveness, and economic considerations (Table 2).[5]

Lifelong vaccination awareness narrative

The think tank participants share a common vision: shifting the vaccination narrative to emphasize a lifelong approach is essential. Incorporating a dedicated segment for the adult population within the National Vaccination Program offers a top-down implementation strategy that facilitates faster adoption. At the same time, think tank participants emphasized the importance of raising awareness among healthcare professionals and the general public about the benefits of lifelong vaccination. As noted—and in line with practices in several European countries—the

Table 1 – Recommendations of the "+Longevity Think Tank"

Area	Recommendation
Investment in prevention and healthy aging	Adult vaccination program
	Literacy narrative for adult vaccination and longevity
	Integration of mechanisms in the preventive approach
	Evaluate the impact of vaccination in addressing Global Health challenges
	Redefining management indicators to strengthen the vaccination strategy
	Personalization in data collection and management
	Models to incentivize community prevention
Health system capacity and resilience, along with community synergies	Strengthening the role of long-term care and personalized healthcare units in intervention efforts
	Strengthening existing capacity and fostering synergies to enhance surveillance efforts
	Assessment study on barriers to adult vaccination access
	Innovative funding models for vaccination
	Multiannual planning in vaccine procurement
	A platform for sharing best practices in vaccination strategy and coverage management
	Co-funding of complementary interventions in vaccination coverage
Ensuring the adult population's commitment to vaccination	Transparency and quality in communication and evidence dissemination
	Population segmentation of narratives and lines of action
	Simulation study and impact assessment of vaccination strategies in real life
	Multisectoral collaboration to advance literacy promotion
	Strategic alignment with the Action Plan for Active and Healthy Ageing
	Investment in strategies for infodemiological management
	Interventions supported by behavioral science algorithms

Table 2 – Proposed vaccination schedule for adults in Portugal

Infectious disease	Vaccination coverage assumptions
Influenza (seasonal flu)	Universal for people **aged 60 and over**
Influenza (high dose)	Long-term care home residents and Individuals aged 75 and older—ideally extending to those 65 and above—and/or those with comorbidities that place them in a high-risk group
COVID-19	Universal (annual)
Pneumococcal disease	Universal for individuals aged 65 and older, or those with comorbidities that place them in a high-risk group
Respiratory Syncytial Virus	Applicable to all individuals aged 65 and over, as well as those with comorbidities that place them in a high-risk group
Tetanus-Diphtheria-Pertussis	Universal **every 25 years until the age of 65** and Universal **every 10 years from the age of 65**
Herpes Zoster	Universal **from the age of 50** or from the age of 18 in high-risk groups
Human Papilloma Virus	**Up to the age of 46 years**, for both men and women

use of targeted communication tools to support awareness campaigns aimed at the adult population is regarded as essential. Moreover, the importance of tailoring communication strategies to specific sub-populations within the adult group—such as different age cohorts, risk groups, migrant communities, and others with potential disparities in vaccination coverage—has been emphasized as a means to maximize protection and enhance quality of life.

Implementation

As emphasized by the Think Tank participants, implementing the concept of lifelong vaccination requires that management, governance, scientific validation, budgeting, and logistical frameworks align with those already established in the National Vaccination Program. To strengthen the vaccination policy agenda, it is recommended to introduce additional indicators—such as quality-of-life metrics—that capture broader dimensions of health and well-being alongside coverage rates. This approach offers a more accurate measure of success and reinforces the effectiveness of the proposed strategy.

Synergies with other social actors

To effectively raise awareness and support implementation, participants proposed establishing synergies—among others—with the Ministry of Social Security, local municipalities, and the occupational health network. These collaborations would foster a multidisciplinary and multisectoral approach, improving vaccination coverage by leveraging every healthcare interaction as an opportunity for immunization. This novel vaccination paradigm seeks to systematically translate evidence into comprehensive strategies that actively promote lifelong well-being and a culture of health consciousness.

Call for action

The public health challenges we face today, particularly regarding vaccination, call for decisive action from political and executive leaders to establish a compelling narrative and vision highlighting the benefits and need for lifelong vaccination. The agreement among national experts on this issue reflects a clear intent to move forward with its implementation.

PREVIOUS AWARDS AND PRESENTATIONS

The results of the study were publicly presented at two events: the first at the Portuguese Parliament on September 24th, 2024, and the second at the IMPRESA building (Portugal) on November 18th, 2024. Although the results were publicly presented, they have not been presented in a scientific context or submitted/published in any journal.

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The authors have declared that no AI tools were used during the preparation of this work.

AUTHOR CONTRIBUTIONS

LM, MC: Original draft, review & editing.
CH: Investigation, review & editing.
MTR: Review & editing.

DF: Project administration, review & editing.

JD: Conceptualization, methodology, formal analysis, investigation, visualization, project administration, funding acquisition, review & editing.

ACF: Supervision, review & editing.

CM, FF, FG, HL: Investigation, supervision, review & editing.

All authors approved the final version to be published.

CONFLICTS OF INTEREST

FF declares that, over the past 36 months (reporting to January 2025) he has received funding research and/or clinical trials from Merck, Sharp & Dohme (MSD). Additionally, he has served as lecturer for MSD, GSK, AstraZeneca, Sanofi, Novavax, Gilead, Bial, Hipra, and Roche; has also been a member of the scientific advisory boards of MSD, GSK, AstraZeneca, Sanofi, and Hipra.

All other authors have no conflicts of interest to declare.

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Admission of Children from Portuguese-Speaking African Countries to a Portuguese Early Childhood Medical Unit

Internamentos de Crianças dos Países Africanos de Língua Oficial Portuguesa numa Unidade Médica de Primeira Infância em Portugal

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ABSTRACT

Introduction: Medical assistance provided in Portugal to patients from Portuguese-Speaking African Countries (PALOP) is regulated by political evacuation protocols, although many patients come by their own means (OM). The aim of this study was to characterize PALOP patients admitted to a Portuguese early childhood medical unit (ECMU), comparing those evacuated under official protocols with those who arrived by OM, and reflect on their medical complexity and associated challenges.

Methods: We conducted an observational study, with a retrospective chart review of all PALOP patients (<18 years old) admitted to an ECMU of a tertiary hospital in Lisbon, Portugal, between January 2018 and December 2022. Demographic and clinical data were extracted from patients' medical records. Patients were grouped into evacuated patients (EP) and OM patients.

Results: A total of 71 patients were included, with 76.1% in the EP group and 23.9% in the OM group. Admissions increased throughout the study period, peaking in 2022. Most patients were male (62%), with a median age of 16 months. Own means patients were significantly older than EP patients (31 months *vs* 16 months, $p = 0.026$). Most EP patients originated from São Tomé and Príncipe and Cape Verde, whereas most OM patients came from Angola. The EP group had a higher prevalence of surgical, cardiac, and neurosurgical conditions, whereas the OM group showed a predominance of neurological and hematological diagnoses. Surgical intervention was required in 74.6% of cases, more frequent in EP patients ($p = 0.008$). Follow-up appointments were necessary for 95.8% of patients and 84.5% required social services support. The mortality rate was 84.5/1000, higher in the OM group (117.6/1000). Only 9.9% of patients returned to their country of origin.

Conclusion: Admissions of children from PALOP had an upward trend from 2018 to 2022, with most patients presenting complex comorbidities in both groups, and requiring highly specialized healthcare resources, prolonged hospitalizations, and readmissions. Mortality rate was considerable, and only a few returned to their country. These findings emphasize the need for improved coordination between countries to provide sustainable healthcare from both patient/families and healthcare system perspectives.

Keywords: Africa; Child; Chronic Disease; Global Health; Hospitalization; International Cooperation; Portugal

RESUMO

Introdução: A assistência médica a doentes evacuados de Países Africanos de Língua Oficial Portuguesa (PALOP) em Portugal é prestada ao abrigo de protocolos políticos de evacuação, embora muitos cheguem por meios próprios (MP). O estudo visa caracterizar os doentes PALOP internados numa Unidade de Pediatria de Primeira Infância (UPPI), comparando os doentes evacuados ao abrigo destes protocolos oficiais com os doentes que chegam por MP, e refletir sobre a complexidade médica e os desafios associados.

Métodos: Realizou-se um estudo observacional e retrospetivo de todos os doentes PALOP (< 18 anos) admitidos numa UPPI de um hospital terciário em Portugal, Lisboa, entre janeiro de 2018 e dezembro de 2022. Foram recolhidos dados demográficos e clínicos dos registos clínicos. Os participantes foram divididos em doentes evacuados (DE) e MP.

Resultados: Foram incluídos 71 doentes, 76,1% no grupo DE e 23,9% no grupo MP. As admissões aumentaram ao longo dos anos, com máximo em 2022. A maioria era do sexo masculino (62%), com mediana de idade de 16 meses. A idade foi estatisticamente superior no grupo MP comparativamente ao DE (31 meses *vs* 16 meses, $p = 0,026$). A maior parte dos DE era oriunda de São Tomé e Príncipe e de Cabo Verde, enquanto a maioria do grupo MP era de Angola. O grupo DE apresentou maior prevalência de doenças cirúrgicas, cardíacas e neurocirúrgicas, enquanto o grupo MP apresentou diagnósticos neurológicos e hematológicos. A intervenção cirúrgica foi necessária em 74,6% dos casos, sendo mais frequente no grupo DE ($p = 0,008$). Foi necessário seguimento em consultas em 95,8% dos casos e 84,5% necessitaram de apoio social. A taxa de mortalidade foi de 84,5/1000, superior no grupo MP (117,6/1000). Apenas 9,9% dos doentes regressaram ao país de origem.

Conclusão: As admissões de crianças dos PALOP aumentaram entre 2018 e 2022, a maioria com doenças complexas em ambos os grupos, com necessidade de cuidados médicos diferenciados, internamentos prolongados e reinternamentos. A taxa de mortalidade foi considerável, e poucos retornaram ao seu país. Esses achados salientam a necessidade de uma melhor coordenação entre os países para oferecer uma assistência médica sustentável, tanto do ponto de vista dos pacientes/famílias quanto do sistema de saúde.

Palavras-chave: Africa; Cooperação Internacional; Criança; Doença Crónica; Hospitalização; Portugal; Saúde Global

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KEY MESSAGES

- The first pediatric study addressing inpatient PALOP children coming to Portugal under international cooperation protocols reports a high burden of complex chronic diseases.
- Inpatient PALOP children have a much higher mortality rate (84.5/1000) comparing to a previous study including complex pediatric patients in Portugal (23.7/1000).
- Social issues within this population are a significant factor contributing to extended hospital stays.
- When comparing PALOP evacuated patients and PALOP patients arriving by their own means, both groups have similar clinical severity and prognosis.
- It is urgent to reflect on and revise the cooperation protocols to prevent healthcare system overload, ensure that countries of origin are held accountable, and facilitate the timely evacuation of seriously ill children.

INTRODUCTION

Medical care for evacuated patients (EP) from Portuguese-speaking African Countries (PALOP) is provided through international cooperation protocols established between healthcare systems, following the independence of the former Portuguese colonies (1977 - 1992).[1] Patient evacuation involves institutionalized circuits in both the country of origin and Portugal, with a variable response time.[2] Each country's agreement stipulates an annual patient quota, with a recommended range of 50 - 300 patients per country per year.[1,2] According to the Annual Report on Access to Healthcare in Establishments of the National Health System and Conventional Entities of 2019, the number of evacuees has largely exceeded these quotas, with 8305 patients evacuated between 2016 and 2019, when the stipulated number was 1050.[3] This discrepancy was especially pronounced for Guinea-Bissau and Cape Verde.[3]

In addition to patients who are officially evacuated, many others seek medical assistance on their own (OM) due to healthcare system limitations or delayed responses in their own countries.

This study characterizes PALOP patients admitted to an early childhood medical unit (ECMU) in Portugal between January 2018 and December 2022. It also compares evacuated patients (EP) with those seeking assistance by their OM, and describes the severity and complexity of their medical conditions, providing insights into the clinical challenges and specific healthcare needs of this population.

METHODS

Study design and patient selection

This study is an observational study, with retrospective chart review of all pediatric patients (< 18 years old) from PALOP admitted to a tertiary hospital ECMU in Lisbon, Portugal, between January 2018 and December 2022. It was approved by the Ethics Committee of Unidade Local de Saúde de São José (ref. 1724/2025).

Data collection

Patient data was collected on May 2023, from clinical records (SClinico®) and comprised demographic and clinical variables: sex, age, country of origin, year of admission, mode of arrival, hospital subunit where patients were initially admitted, reason for hospitalization, main comorbidities, diagnostic tests, surgical interventions, final diagnosis, length of hospital stay, number of hospitalizations, follow-up appointments, readmissions, return to the country of origin, mortality and need for social services' support.

The patients were divided into two groups: the group who arrived by their OM and the group of EP. The EP group included children who had been assessed by a medical board in their country of origin and were transferred following coordination with Portugal's Directorate-General of Health, sometimes bringing some documentation or medical reports. The OM group included those who, due to health reasons and without being evacuated through a medical board, were brought by their families, independently and at their own expense, in search of healthcare.

Data analysis

Statistical analysis was conducted using the Statistical Package for Social the Sciences (SPSS) version 29.0®, with the significance level set at 0.05. Descriptive statistics were presented as absolute frequencies and percentages for categorical variables, and as summary statistics for continuous variables. Percentages within variables were calculated excluding missing information. The groups were compared using chi-square test or Fisher's exact test (categorical variables) and Mann-Whitney test (continuous variables).

RESULTS

Demographic data

Between January 2018 and December 2022, 71 patients from PALOP countries were admitted to the ECMU, 54 (76.1%) were EP and 17 (23.9%) belonged to the OM

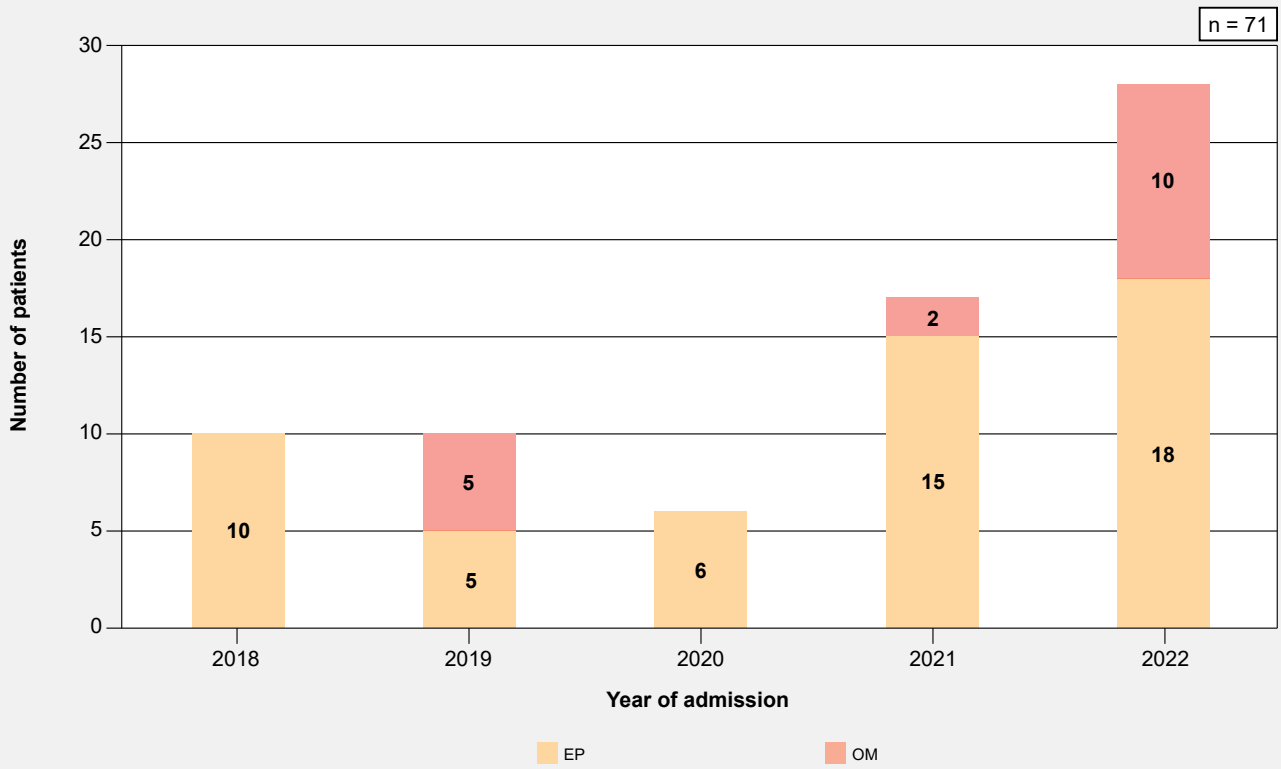

Figure 1 – Temporal evolution of patient admissions
EP: evacuated patients' group; OM: arriving by own means group

Table 1 – Demographic data of admitted children

		EP		OM		Total		*p*-value	
		n	%	n	%	n	%		
Sex	Male	32	59.3	12	70.6	44	62.0	0.400	
	Female	22	40.7	5	29.4	27	38.0		
Age	Minimum, days	30		27		27		**0.026**	
	Maximum, years	7		10		10			
	Median, months	14		31		16			
Country of origin	São Tomé and Príncipe	24	44.4	4	23.5	28	39.4	< 0.001	0.160*
	Cape Verde	16	29.6	1	5.9	17	23.9		0.054*
	Angola	3	5.6	10	58.8	13	18.3		**< 0.001***
	Guinea-Bissau	10	18.5	1	5.9	11	15.5		0.277*
	Mozambique	1	1.9	1	5.9	2	2.8		0.424*
Subunit of admission	Emergency service	36	66.7	14	82.4	50	70.4	0.220	
	Hospital appointment	18	33.3	3	17.6	21	29.6		

EP: evacuated patients' group; OM: arriving by own means group
*: *p*-values calculated for each country *versus* other countries (exact Fisher test)

group. The number of patients arriving increased progressively every year, except for a reduction in 2020, with less than 10% arriving in that year (Fig. 1). The peak of admissions was in 2022, with 28 (39.4%) patients admitted, with 10 (37.7%) of the OM group.

Of the 71 patients, 44 (62.0%) were male, and the median age was 16 months (Table 1). Own means patients had a median age of 31 months (min-max: 27 days-10 years),

and were older than EP patients (median age of 16 months, min-max: 30 days-7 years; $p = 0.026$).

The distribution of the country of origin was statistically significantly different between EP and OM patients ($p < 0.001$). The majority of EP were from São Tomé and Príncipe (n = 24; 44.4%), followed by Cape Verde (n = 16; 29.6%). In the OM group, Angola was the main country of origin (n = 10; 58.8%), followed by São Tomé and Príncipe (n = 4; 23.5%).

Regarding the evacuation process and its duration, we only had access to data from São Tomé and Príncipe, where the median time for patients' evacuation was 162 days, with a maximum of 758 days. The longest delay was of a patient diagnosed in Portugal with a severe polymalformative syndrome. Data regarding the evacuation process from other PALOP countries was unavailable.

Admission characteristics

In 50 (70.4%) cases, patients were admitted through the emergency department, while the remaining were admitted from scheduled hospital appointments. Admission in the emergency department was more frequent in OM group (Table 1).

The main admission purposes were related to Neurology (26.8%), followed by General Surgery (18.3%), Cardiology (16.9%) and Neurosurgery (16.9%) (Table 2). In the EP group, the most frequent conditions were surgical (24.1%, $p = 0.029$), cardiac (22.2%, $p = 0.057$) and neurosurgical (20.4%, $p = 0.270$), compared to the OM group, with a higher prevalence of medical conditions, particularly neurological (47.1%, $p = 0.056$) and hematological (23.5%, $p = 0.002$).

Among comorbidities at arrival, psychomotor developmental delay was observed in 40 (56.3%) patients, with a higher incidence among OM group patients (64.7% *vs* 53.7% in the EP group), although not statistically significant ($p = 0.577$). In 30 (43.7%) cases, the weight on admission was below the 3rd percentile (Fig. 2). Among the EP group this proportion was higher (48.1% *vs* 29.4% in the OM group), although no statistically significant difference was observed ($p = 0.263$). Absence of feeding autonomy was observed in 23 (32.4%) patients, more frequently in the OM group, accounting for 41.2% of patients ($p = 0.389$). The main conditions identified in these patients were global developmental delay, severe/refractory epilepsy, polymalformative syndromes, hydrocephalus and hypoxic-ischemic encephalopathy.

Clinical evolution

The median length of hospital stay was 10 days, ranging from 1 day to 270 days, with no statistically significant difference between the groups ($p = 0.559$). The longest hospitalization was of a previously evacuated patient readmitted at 14 months due to a Fournier's gangrene and severe malnutrition. This hospitalization was extended due to social factors that prevented the patient's discharge, and it ended with institutionalization.

Notable cases included a patient with multiple human bite injuries in the face, chest and genitals, requiring tracheostomy, nasogastric tube feeding and several reconstructive surgeries (EP group, 204 days); a patient with recessive type 6 heterotaxy syndrome needing multiple surgeries and complicated with several infections (EP group, 194 days); a patient with Krabbe disease, presenting gait regression (OM group,185 days), and a patient with esophageal atresia, microcephaly and developmental delay requiring multiple surgeries and nutritional rehabilitation (EP group, 154 days).

Regarding the number of hospitalizations per patient, 18 (25.4%) patients experienced at least one readmission, with similar findings observed in both groups ($p = 0.751$). The maximum number of hospitalizations was nine, in a patient with esophageal atresia (EP group), whose readmissions were mainly motivated by the need for several esophageal dilations and nutritional rehabilitation. Other patients also had multiple readmissions, including a Krabbe disease

Table 2 – Diagnosis reported at the time of patients' arrival

Organ/ system	EP		OM		Global		*p*-value
	n	%	n	%	n	%	
Neurological	11	20.4	8	47.1	19	26.8	0.056
Surgical	13	24.1	0	0.0	13	18.3	**0.029**
Cardiac	12	22.2	0	0.0	12	16.9	0.057
Neurosurgical	11	20.4	1	5.9	12	16.9	0.270
Oncological	5	9.3	1	5.9	6	8.5	0.662
Hematological	1	1.9	4	23.5	5	7.0	**0.002**
Gastrointestinal	1	1.9	1	5.9	2	2.8	0.381
Others	7	13.0	2	11.8	9	12.7	1.000

EP: evacuated patients' group; OM: arriving by own means group

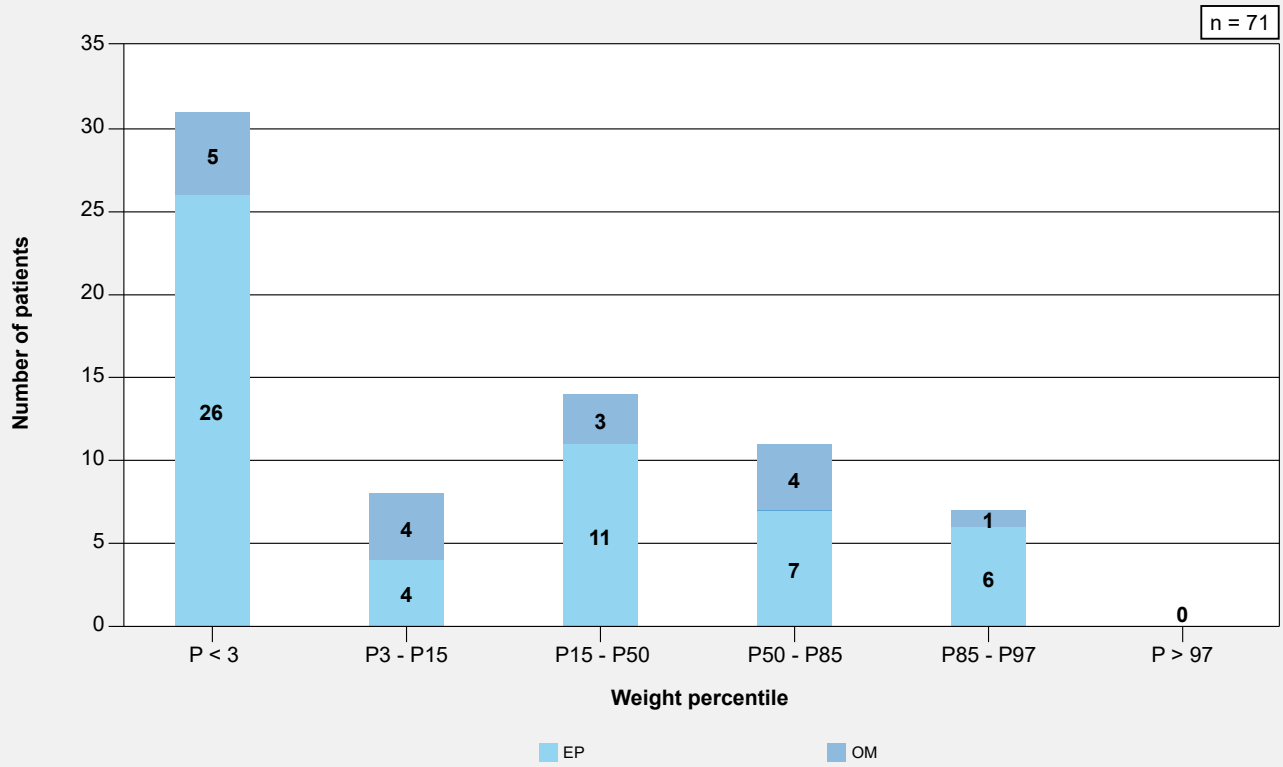

Figure 2 – Admission weight percentiles
EP: evacuated patients' group; OM: arriving by own means group

case from the OM group, requiring symptomatic management and treatment of infectious complications, and two patients from the EP group – one with stage 5D chronic kidney disease and another with neurogenic bladder. Readmissions in the latter two cases were primarily due to recurrent urinary tract infections, including some caused by multidrug-resistant organisms.

A significant proportion of patients underwent a variety of specialized diagnostic exams, as detailed in Table 3.

Genetic studies established the diagnosis of various rare disorders, such as progressive familial intrahepatic cholestasis type 1 (PFIC1), Townes-Brocks syndrome, visceral heterotaxy syndrome type 6, spinal muscular atrophy, contiguous gene deletion syndrome and osteogenesis imperfecta in the EP group, as well as Alagille syndrome, neuronal ceroid lipofuscinosis and metachromatic leukodystrophy in the OM group.

Metabolic studies yielded conclusive results for three patients, identifying two cases of mitochondrial disease, one in each group, and one case of phenylketonuria in the

Table 3 – Diagnostic tests performed

Exams	EP		OM		Global		*p*-value
	n	%	n	%	n	%	
Magnetic resonance imaging	24	44.4	8	47.1	32	45.1	1.000
Genetic study	16	29.6	7	41.2	23	32.4	0.389
Metabolic study	11	20.4	7	41.2	18	25.4	0.112
Videofluoroscopic swallowing study	10	18.5	4	23.5	14	19.7	0.730
Esophageal transit	12	22.2	2	11.8	14	19.7	0.493
Retrograde cystourethroscopy	9	16.7	0	0.0	9	12.7	0.102
Others	12	22.2	1	5.9	13	18.3	0.140

EP: evacuated patients' group; OM: arriving by own means group

EP group.

At admission, the patients were screened for infectious diseases, namely 63.4% (n = 45) for human immunodeficiency virus infection, 60.6% (n = 43) for hepatitis B and C, 42.3% (n = 30) for tuberculosis and 11.3% (n = 8) for syphilis. Among patients who were not screened upon admission, eight (26.8%) had previously been tested. Additionally, colonization screening for extended-spectrum beta-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* (ESBL) and methicillin-resistant *Staphylococcus aureus* (MRSA) was performed in 70.4% (n = 50) cases, with ESBL positivity detected in 49.3% (n = 35) and MRSA positivity in 9.9% (n = 7).

Concerning patients with absence of feeding autonomy (n = 23; 32.4%), 11 (47.8%) required gastrostomy procedures, with a higher frequency in the OM group (n = 5; 29.4%) compared to the EP group (n = 6; 11.1%); however, this difference was not statistically significant (p = 0.389).

Surgical interventions were necessary in 53 (74.6%) cases, more frequently in the EP group, with a statistically significant value (p = 0.008). The main interventions included Nissen fundoplication, ventriculoperitoneal shunt placement, brain space-occupying lesion resection, correction of atrial and ventricular communications, and posterior urethral valve resection.

Final diagnoses are described in Table 4, with the most frequent being neurological. The frequency of hematological pathology was higher among OM group (p = 0.01). No significant difference was identified in the remaining diagnoses.

In 53 (74.6%) cases, the medical diagnosis suspicion at the country of origin matched the final diagnosis. Despite this, most cases involved much more complex or systemic diseases, and many patients also presented several comorbidities.

Follow-up and outcomes

The median observational period of the patients during the study was 11 months (min - max: 1 month - 5 years). Follow-up appointments were necessary in 68 (95.8%) cases, with a median of five specialty appointments per patient. The maximum number of appointments per patient was 11, referring to a patient with osteogenesis imperfecta.

Only seven (9.9%) patients returned to their country of origin until December 2022. The clinical conditions of these patients were congenital heart diseases and nephroblastoma.

Do-not-resuscitate decisions were implemented in five (7.0%) cases, as part of a palliative care plan. Overall, six (8.4%) deaths were observed, four in the OM group and two in the EP group. The mortality rate was 84.5/1000, higher in the OM group (117.6/1000), with no statistical significance (p = 0.625). Half of the deceased patients had signed do-not-resuscitate declarations.

Social service support was needed by 56 (78.9%) patients, with four (5.6%) requiring institutionalization. Among patients who did not require social services' support, three (4.2%) died during the hospitalization period.

DISCUSSION

Our results underline several noteworthy aspects that warrant discussion and reflection.

Table 4 – Final diagnoses of the patients

Medical area	EP		OM		Global		*p*-value
	n	%	n	%	n	%	
Neurological	15	27.8	7	41.2	22	31	0.370
Genetic/Congenital	14	25.9	7	41.2	21	29.6	0.240
Cardiovascular	15	27.8	2	11.8	17	23.9	0.213
Surgical	16	29.6	1	5.9	17	23.9	0.054
Hematological	4	7.4	6	35.3	10	14.1	**0.010**
Neurosurgical	8	14.8	1	5.9	9	12.7	0.677
Oncological	6	11.1	1	5.9	7	9.9	1.000
Gastrointestinal	4	7.4	1	5.9	5	7.0	0.830
Respiratory	2	3.7	1	5.9	3	4.2	0.697
Endocrinological	1	1.9	1	5.9	2	2.8	0.381
Ophthalmological	2	3.7	0	0.0	2	2.8	0.421
Nephrological	1	1.9	0	0.0	1	1.4	0.572
Infectious	0	0.0	1	5.9	1	1.4	0.730
Others	3	5.6	0	0.0	3	4.2	0.321

EP: evacuated patients' group; OM: arriving by own means group

Trends in admissions and clinical complexity

The increase in the admissions observed throughout the study period aligns with the Annual Report on Access to Healthcare in Establishments of the National Health System and Conventional Entities of 2019.[3] This coincides with an increase in both the severity and complexity of patients' medical conditions, evidenced by higher mortality rates, extended lengths of stay, frequent readmissions and the need for specialized procedures, such as gastrostomy or ventriculoperitoneal shunts, as seen in a previous study.[4]

Also, several studies report an increase in hospitalizations of children with complex chronic conditions across various countries[4,5] namely neuromuscular, congenital/genetic, and cardiovascular conditions,[4,6] with the first two also representing the most common in our sample (Table 2). This association of comorbidities likely contributed to longer hospital stays.[6] Indeed, the length of stay in our cohort was longer than that reported in a national study of pediatric complex cases.[7]

Our sample had a mortality rate of 84.5/1000 patients, which was significantly higher than the 23.7/1000 reported in a previous Portuguese study of complex pediatric patients,[7] further underscoring the severity of our cases. Advances in diagnostic capacities and multidisciplinary teams, even in low-income countries, may be contributing to more accurate and timely diagnoses of complex conditions. However, we speculate that the COVID-19 pandemic, which strained healthcare systems and delayed care for non-COVID patients, worsened clinical conditions at presentation and increased comorbidities, manifesting as malnutrition, developmental delay and absence of feeding autonomy. The pandemic may also explain the decrease in numbers in 2020 and the subsequent peak in admissions in 2022.

Contrary to the possible initial assumption that OM patients might present with less severe conditions, which could explain why they were not evacuated, our results indicate otherwise: a greater number of complex diseases were diagnosed, and gastrostomy procedures were more frequent, aligning with the higher prevalence of neurological conditions associated with impaired autonomous feeding in this group. In addition, OM patients had a higher mortality rate (117.6/1000) and older median age (31 months *versus* 16 months in the EP group), possibly reflecting delayed diagnosis and treatment with poorer outcomes. There were no statistically significant differences in hospital stay.

However, surgical procedures were more common in the EP group, likely due to the possibility that surgical diseases are more easily and accurately diagnosed, prompting earlier initiation of evacuation procedures. Also, malnutrition was extremely high in the EP group, with almost half of the patients with low weight (48.1%). Malnutrition is a known issue in African hospitals[8] and, while not statistically significant, this is concerning, given that EP patients came from healthcare facilities. Furthermore, approximately one-third of patients were referred with a diagnosis that differed from the final one, possibly reflecting the limited diagnostic resources in these countries.

Admission planning

The inadequate planning here demonstrated by the delay in patient evacuation, the unpredictability in arrival, with two thirds of patients admitted in the emergency department, and diagnostic inaccuracies must be addressed, and better coordination is mandatory. This could begin with the creation of special teams for pre-evacuation assessments, more accurate diagnoses and criteria for evacuation, as well as predictable patient entry. The widespread use of telemedicine could facilitate patient care and clinical discussion before their arrival in Portugal, minimizing possible comorbidities and optimizing timely diagnosis and intervention approaches.

It is worth mentioning that, from our practice, most patients lacked clinical reports, even those transferred directly from a hospital, so their medical histories were mainly obtained from parents/caregivers' information. When clinical reports were available, they had sparse information, contributing to the overload of the emergency department resources.

In order to control hospital infections from multidrug-resistant organisms, we screened PALOP patients for colonization: MRSA colonization was lower (n = 7; 9.8%) than reported in the African continent (33%),[9] while ESBL colonization was higher (n = 35; 49.2%), compared to a previous study in children under five years of age in Guinea-Bissau (32.6%).[10] Despite limited literature, the available data emphasizes the potential dissemination risk of these resistant strains from PALOP patients,[11] with urgent need for standardized screening procedures, either on arrival or before patients are evacuated.

Sociocultural and socioeconomic factors

The family's financial capacity for self-transportation, less bureaucracy in border control, and more flights from these countries to Portugal may have contributed to the rise in OM admissions.

Furthermore, the fact that 13.6% of the migrant community in Portugal comes from PALOP countries[12] likely increases the chances of OM patients having established support networks in our country. Unfortunately, once they arrive, and given that they are not covered by any established international protocol, these families do not receive any social or economic support from their home countries. Accordingly, this worsens the emergency overload, as most patients lack accommodation outside the hospital.

The case described above involving a child admitted with Fournier's gangrene in the context of severe malnutrition illustrates the living conditions endured by these families in Portugal and the inadequacy of available social support systems. In fact, a previous study showed that 81.8% of the immigrant African pediatric population admitted to a Portuguese pediatric unit faced social challenges, particularly poverty.[13] Although 60 (84.5%) patients received social support, this remains inadequate given the complexity and bureaucratic demands. Post-discharge, families often require ongoing assistance with food, clothing, medication, and emergency housing. According to international cooperation protocols, these outpatient needs should be addressed by the patient's home country,[1,2] but this is not consistently fulfilled. Some children in our sample (n = 4; 5.6%) required institutionalization.

Additionally, the low rate of return to the country of origin (n = 7; 9.9%) due to clinical or social reasons highlights the chronic burden on Portugal's healthcare system.

The social needs of these patients prolong and complicate the hospital discharge process, leading to healthcare system overload, increased risk of infectious complications, and worsened quality of life for both children and their families. Additionally, the relocation of patients and caregivers away from their home countries causes feelings of alienation and places them in a socially vulnerable position, especially for those with poor prognoses. Moreover, these patients often require full-time caregivers, which limits parental employment and children's social integration, leading to isolation and a higher social and economic burden that must be addressed.

Although most patients in our sample were evacuated, the time-consuming nature of this process often leads many parents to bring their children to Portugal by their own means. This decision places them in an even more complex and vulnerable social situation upon arrival. This requires immediate attention, as the proportion of such patients may continue to rise.

In a time of health system crisis with lack of resources, it is crucial to reflect on established protocols with PALOP countries and invest in timely pre-evacuation patient assessments and planning, scheduling patient admissions to avoid overburdening emergency teams. Political intervention is necessary to hold countries of origin accountable for timely evacuation and post-discharge social support.

Limitations

This study presents some limitations. The retrospective design relied on clinical records, with limited information available from the patients' countries of origin, namely the lack of systematic data regarding the evacuation process in certain countries (e.g., time for evacuation). We also recognize the small sample size from a single medical unit which can limit the generalizability of the findings. Nevertheless, this unit is one of the largest pediatric hospitals in the country, receiving a significant proportion of evacuated patients from PALOP (between 2009 and 2019, received 717 children).[14] On the other hand, inclusion was limited to hospitalized patients, potentially introducing selection bias toward more severe clinical cases and limiting applicability to other populations and healthcare settings. Lastly, no objective measures or scales were used to classify the clinical complexity of patients or their social support needs, preventing determination of the overall burden of care.

CONCLUSION

To the best of our knowledge, this is the first pediatric study addressing inpatient PALOP children coming to Portugal under International Cooperation Protocols.

Our results showed that the number of patients doubled during the study period, and that these patients have complex and multisystem conditions requiring highly specialized care, posing significant challenges for medical teams and the healthcare system, and imposing political and social reflections on this topic. Because some patients arrive in life-threatening condition, more effective operationalization of protocols is warranted.

PREVIOUS AWARDS AND PRESENTATIONS

This work was presented as a poster at the "*23.º Congresso Nacional de Pediatria"* in Lisbon, on October 26th, 2023.

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The authors have declared that no AI tools were used during the preparation of this work.

AUTHOR CONTRIBUTIONS

NB, RN, MA: Study design, data collection and analysis, writing and critical review of the manuscript.

RP: Study design and critical review of the manuscript.

PR: Study design, data analysis, writing and critical review of the manuscript.

SS, MA, AIC, SF, DA, BC, RM: Critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki

Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Childhood Circumstances and Alcohol Consumption in Portuguese People Aged 50 and Over: An Analysis of the "Survey of Health, Ageing and Retirement in Europe" Project

Circunstâncias da Infância e Adolescência e Consumo de Álcool nos Portugueses com 50 ou Mais Anos: Análise no Âmbito do Projeto "Survey of Health, Ageing and Retirement in Europe"

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ABSTRACT

Introduction: The aim of this study was to estimate the association between childhood and adolescence circumstances and alcohol consumption in Portuguese adults aged 50 and over, particularly focusing on socioeconomic conditions, physical abuse, family and social integration during childhood and adolescence, and alcohol consumption in adulthood.

Methods: We conducted an observational, cross-sectional, and analytical epidemiological study using self-reported data collected face-to-face through computer-assisted interviews in waves 7 (2017) and 9 (2022) of the Survey of Health, Ageing, and Retirement in Europe in Portugal. Participants included all Portuguese individuals who responded to the "Childhood and Adolescence Circumstances" module (wave 7) and "Behavioural Risks" module (wave 9). Associations were assessed using chi-squared or Student's *t*-tests. Odds ratios (OR) with 95% confidence intervals (95% CI) were estimated through binary and multinomial logistic regressions models.

Results: A total of 903 participants were included; 378 (41.9%) were male and 770 (85.3%) were over 65 years old. Higher-risk drinking was identified in 220 participants (50.0%). The optimized binary logistic regression model for the current drinkers revealed significant positive associations between higher-risk alcohol consumption and male sex (OR = 6.444; 95% CI 4.329 – 11.111; $\rho < 0.001$), and having been a victim of physical abuse in childhood and adolescence (OR 2.063; 95% CI 1.119 – 3.803; $\rho = 0.020$). Living in a house with better conditions (OR = 0.767; CI 0.608 – 0.968; $\rho = 0.025$) revealed a significant negative association with higher-risk alcohol consumption. The optimized multinomial logistic regression model considering the non and current drinkers supported that being male (low-risk OR = 2.312; 95% CI: 1.567 – 0.3409; $\rho < 0.001$ higher-risk OR = 15.682; 95% CI: 10.041 – 24.491; $\rho < 0.001$) and physical abuse in the childhood and adolescence (higher-risk OR = 2.049; 95% CI: 1.200 – 3.497; $\rho = 0.008$) were risk factors for higher-risk alcohol consumption.

Conclusion: Physical abuse in childhood was associated with higher-risk alcohol consumption, while living in better housing conditions during these periods showed a protective association. Being male was strongly associated with both low- and higher-risk drinking patterns. Further studies, especially longitudinal ones, are needed to clarify the role of early-life circumstances in alcohol consumption.

Keywords: Adult Survivors of Child Adverse Events; Adverse Childhood Experiences; Alcohol Drinking

RESUMO

Introdução: Este estudo teve como objetivo estimar a associação entre as circunstâncias da infância e adolescência e o consumo de álcool em adultos portugueses com 50 ou mais anos, particularmente considerando as condições socioeconómicas, o abuso físico, a integração familiar e social durante a infância e adolescência e o consumo de álcool na idade adulta.

Métodos: Realizou-se um estudo epidemiológico observacional, transversal e analítico, utilizando dados recolhidos presencialmente através de entrevistas assistidas por computador nas vagas 7 (2017) e 9 (2022) do *Survey of Health, Ageing, and Retirement in Europe* em Portugal. Foram incluídos todos os participantes portugueses que responderam ao módulo "Circunstâncias da infância" (vaga 7) e "Comportamentos de risco" (vaga 9). As associações foram avaliadas com os testes do qui-quadrado ou *t* de Student. As razões de *odds* (OR) com intervalos de confiança a 95% (IC 95%) foram estimadas por modelos de regressão logística binária e multinominal.

Resultados: Foram incluídos 903 participantes; 378 (41,9%) do sexo masculino e 770 (85,3%) com mais de 65 anos. O consumo de maior risco foi identificado em 220 (50,0%). No modelo de regressão logística binária otimizado foram encontradas associações positivas significativas entre o consumo de álcool de maior risco e o sexo masculino (OR = 6,444; IC 95% 4,329 - 11,111; $\rho < 0,001$) e ter sido vítima de abuso físico na infância e adolescência (OR = 2,063; IC 95% 1,119 - 3,803; $\rho = 0,020$). Melhores condições habitacionais durante a infância (OR = 0,767; IC 95% 0,608 - 0,968; $\rho = 0,025$) revelaram uma associação negativa significativa com o consumo de álcool de maior risco. O modelo de regressão logística multinominal otimizado indicou que ser do sexo masculino (OR baixo risco = 2,312; IC 95% 1,567 - 3,409; $\rho < 0,001$; OR de maior risco = 15,682; IC 95% 10,041 - 24,491; $\rho < 0,001$) e ter sofrido abuso físico na infância e adolescência (OR de maior risco = 2,049; IC 95% 1,200 - 3,497; $\rho = 0,008$) constituem fatores de risco para o consumo de álcool de maior risco.

Conclusão: O abuso físico está associado ao consumo de álcool de maior risco, enquanto viver em melhores condições habitacionais apresenta uma associação protetora. Ser do sexo masculino está fortemente associado a padrões de consumo de álcool de baixo risco e de maior risco. Estudos longitudinais são necessários para esclarecer o papel das circunstâncias precoces no consumo de álcool.

Palavras-chave: Adultos Sobreviventes de Eventos Adversos na Infância; Consumo de Álcool; Experiências Adversas da Infância

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KEY MESSAGES

- This is the first study in Portugal to examine the long-term influence of childhood and adolescence circumstances on alcohol consumption in older adults.
- By adopting a life-course perspective, the study addresses a current public health problem and generates relevant insights for targeted prevention and intervention strategies.
- The use of nationally representative SHARE data and robust analytical methods ensures high scientific validity and reliability.
- The cross-sectional design precludes causal inference.
- Self-reported data may be subject to recall and social desirability biases.

INTRODUCTION

Alcohol consumption imposes a substantial global burden on mortality and disability.[1]

Despite its toxic, psychoactive, and addictive properties, alcohol remains widely consumed and deeply ingrained in the culture of many countries, often leading to an underestimation of its health and social consequences.

Alcohol has significant toxic effects on the central nervous, digestive and cardiovascular systems, and contributes to a wide range of health problems such as liver disease, oncological diseases, particularly cancer of the oral cavity, pharynx, larynx, esophagus, liver, colorectal and breast, and cardiovascular diseases.[2-5] Due to its immunosuppressive effects, it also increases the risk of communicable diseases such as tuberculosis and human immunodeficiency virus (HIV).[6] In addition, alcohol consumption is one of the main causes of road traffic accidents, injuries and trauma.[1,7]

Harmful alcohol consumption, which is detrimental to both physical and mental health, imposes a substantial social and economic burden, accounting for 132.6 million disability-adjusted life years (DALYs) in 2016.[6] In 2019, 2.6 million deaths were attributed to alcohol consumption, representing 4.7% of all deaths worldwide in that year.[8]

According to the World Health Organization (WHO), Portugal has one of the highest alcohol consumption rates *per capita* in the world: among the Portuguese who drink, 16.9% drink excessively and 2.1% are alcohol dependent.[9] In 2014, 5% of the Portuguese population reported harmful alcohol consumption, while the European Union average was 3%.[10] Among the Portuguese population, hazardous alcohol consumption was seven times higher among men (8.3%) than among women (1.2%), and three times higher among people with a lower level of education. It was found that 7.1% of people living in rural areas reported harmful alcohol consumption, which is more than double the rate found in urban areas (3.4%). Similarly, harmful alcohol consumption was almost twice as much in those with the lowest income (5%) compared with those with the highest income (3%).[10]

When seeking solutions to address this public health issue, it is essential to take multiple factors into account, including early-life factors that underlie consumption patterns. The family environment, the socio-economic status of the family, the quality of education, access to health services, the cultural and social context and the presence of traumatic experiences are key aspects that shape the individuals and their health behavior (Fig. 1).[11]

In this regard, childhood and adolescence represent crucial periods of life, as experiences during these years may shape behavioral patterns that persist in adulthood. Socioeconomic conditions, exposure to adverse childhood experiences, and the family environment can strongly influence health trajectories, including the risk of alcohol misuse later in life.[16-22]

This study aimed to explore the relationship between childhood circumstances (socioeconomic status, adverse experiences, and family and social integration) and alcohol consumption in Portuguese people aged 50 and over, in order to support the development of targeted policies and interventions.

METHODS

SHARE project

This study is based on information collected as part of the Survey of Health, Ageing and Retirement in Europe (SHARE) project. It is a longitudinal, multinational survey providing data on the health, socioeconomic status, and social and family networks of more than 140 000 individuals aged 50 and over from 28 European countries (including Israel).[23]

The first data collection process (first wave) started in 2004, and the last wave took place in 2022. Portugal first participated in SHARE in wave 4 (2010 - 2011) and subsequently in waves 6 (2015), 7 (2017-2018), Corona 1 (2020), Corona 2 (2021), and 9 (2022).

Participant selection

The sampling frame was the National Health Service User Register. The basic sample was established in the first wave in which Portugal participated (2010 - 2011) and was extended in wave 9 (2022) to maintain the representativeness

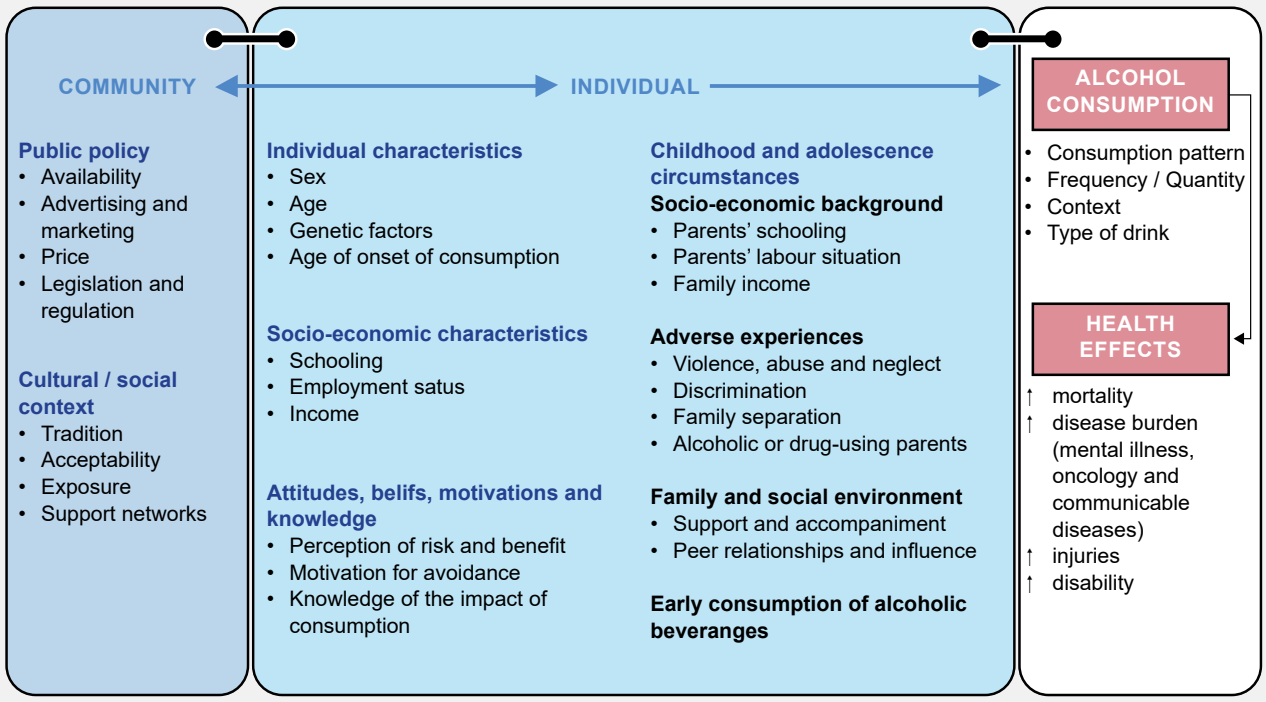

Figure 1 – Conceptual map of the social, cultural, and environmental determinants of alcohol consumption. Adapted from Freisthler *et al*[12]; Gruenewald *et al*[13]; Roche *et al*[14] and Sudhinaraset *et al*.[15]

of the 50 - 59 age group and to be able to analyze less frequent phenomena. In this latest wave, 1686 people participated, 577 of them for the first time.[24]

Stratified sampling was used and consisted of five consecutive stages: (1) selection of four postcode digits; (2) selection of municipalities; (3) selection of seven postcode digits; (4) selection of addresses; and (5) verification of eligibility by age.

In stage one, Portugal was stratified into 22 sub-regions based on a combination of geographical criteria and the size of the population aged 50 and over. In each sub-region, a four-digit postal code was randomly selected.

In stage two, for each of these codes, a random sample of municipalities was selected with probability proportional to the number of seven-digit postcodes. In stage three, for each municipality, a sample of seven-digit postcodes was selected by simple random sampling.

In stage four, a sample of addresses was selected for each seven-digit postcode using systematic sampling with random selection of the first unit.

Stage five consisted of the random selection of eligible persons by age, which was carried out by interviewers in the field.

All SHARE respondents interviewed in any wave are part of the longitudinal sample. Age-eligible respondents are traced and interviewed even if they move within the country.

This study included Portuguese individuals aged 50 and over in 2022 who participated in waves 7[25] and 9[26] of SHARE and completed the "Childhood and Adolescence Circumstances" module in wave seven and the "Risk Behaviours" module in wave 9. The final sample comprised 903 individuals (525 women and 378 men) with an average age of 73.07 years.

Data collection

Participants were assessed using a computer-assisted personal interview (CAPI). The interview was organized into several thematic modules covering aspects of physical health, mental health, employment and pensions, childhood and adolescent circumstances, risk behaviors, cognitive functioning, social networks, family, and children. The various dimensions assessed in the SHARE project questionnaires can be found in Appendix 1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/24100/15875).

Interviewers are trained before fieldwork. Their participation is voluntary and confidential. In wave nine there were 68 interviewers in Portugal, more than half of whom were aged between 19 and 39 years old.[26]

Answers were allowed to be given by someone other than the participant (the respondent's proxy) in cases of physical or mental illness that prevented direct participation. However, questions about relationships with parents and friends were answered only by the participant.

In wave seven, in addition to the regular panel questionnaire, SHARE includes a section called "SHARELIFE", which looks at the life stories of the respondents. This section brings together detailed demographic, economic and sociological information, and allows us to improve our understanding of the influence of childhood and adolescent experiences and events.

Wave nine is the most recent and includes modules on various topics, one of which is of particular interest for this specific study, called "Risk Behaviours", from which information on alcohol consumption was obtained.

This study used data from the "Childhood and Adolescence Circumstances" module in wave seven and the "Sociodemographic" and "Risk Behaviours" modules in wave nine.

"Sociodemographic" module

The "Sociodemographic" module contains basic sociodemographic information, such as sex, year of birth, marital status, level of education, job situation, ability to meet monthly expenses, and area of residence.

The participants' age was calculated by considering their year of birth and the year in which the questionnaire was administered (2022). This was then divided into two categories: (1) 50 - 64 years old and (2) ≥ 65 years old.

The level of education is standardized across countries as the SHARE project uses the International Standard Classification of Education (ISCED). This variable was coded as: (0) none or still studying, (1) low level of education, (2) medium level of education and (3) high level of education. Low level of education corresponds to primary education; medium level of education corresponds to secondary and post-secondary non-tertiary education and high level of education corresponds to tertiary education.

Marital status was categorized as: (1) single, (2) married or in a civil partnership, (3) divorced and (4) widowed.

Job situation was categorized as: (1) retired, (2) employed, (3) unemployed, (4) permanently sick or disabled, (5) homemaker and (6) other.

The ability to meet monthly expenses, (1) with difficulty and (2) easily, was used to characterize household income.

Area of residence was coded as (1) urban area and (2) rural area. 'Urban area' refers to a large city, suburbs or outskirts of a large city or a large town. 'Rural area' refers to a small town, rural area or village.

"Risk Behaviours" module

The "Risk Behaviours" module contains information on health behaviors such as smoking, alcohol consumption, and physical activity. For this study, only data on alcohol consumption was used: consumption of at least one alcoholic drink in the last seven days and total number of units of alcoholic drinks consumed per week.

Participants who had consumed at least one alcoholic drink in the past seven days (yes/no) were considered current drinkers; the remaining participants were considered non-drinkers.

For participants who were considered current drinkers, the level of risk of alcohol consumption was calculated based on the number of units of alcohol consumed in the last seven days. This value was calculated at the time of the interview by the interviewer together with the respondent, using the card with standard units of alcoholic drinks [Appendix 2 (Appendix 2: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/24100/15876)]. The result was rounded up to the nearest whole number.

The level of risk of alcohol consumption was categorized as (1) low-risk and (2) higher-risk and was determined by the number of units of alcohol consumed in the previous seven days. Participants were categorized as having low-risk consumption if they had consumed up to seven units of a standard drink in the previous seven days, and as having higher-risk if they had consumed more than seven units. This classification was made considering the recommended maximum daily intake for people over 65 years of age [one standard drink or ten grams (g) of pure alcohol].[27,28] This is a population group that is more vulnerable to the effects of alcohol, predisposing to a higher concentration and consequent toxicity of this substance.[28]

"Childhood and Adolescence Circumstances" module

The information from the "Childhood and Adolescence Circumstances" module has been grouped into three dimensions: (a) socioeconomic status, (b) adverse experiences, and (c) family and social integration.

Socioeconomic status

This dimension includes variables that represent the individual's health and position on the socioeconomic scale, such as the family's financial situation, the provider's occupation, the quality of housing and the family's level of literacy.

Child health was categorized as (1) excellent, (2) very good, (3) good, (4) fair and (5) poor. The financial situation of the family, considering the period between birth and age 16, was categorized as (1) very favorable, (2) average, (3) poor and (4) variable. The occupation of the person supporting the household (providing most of the household income) was coded according to the International Standard Classification of Occupations as: (1) high-skilled occupation, (2)

medium-skilled occupation and (3) low-skilled occupation. High-skilled occupations refer to managers, professionals and technicians; medium-skilled occupations correspond to administrative support workers, service and sales workers, agricultural, forestry and fishery workers, and craft and similar workers; low-skilled occupations refer to factory workers, machine operators, and elementary occupations.

Housing quality was assessed based on the following characteristics of the dwelling in which the respondent lived at the age of ten (yes/no): the presence of a bath, the presence of a piped cold-water supply and the presence of overcrowding.

The presence of a bath was assigned one point, while its absence was scored as zero points; the presence of a piped cold water supply was assigned one point and its absence was scored as zero points; and overcrowding was calculated by dividing the 'number of people living in the household at age ten' by the 'number of rooms, including bedrooms but excluding kitchen, bathrooms and hallways'. A house was considered overcrowded if this ratio was greater than two and these cases were given a score of zero. Housing without overcrowding was scored as one point. The final housing quality score was obtained by adding the scores for the three aforementioned characteristics, resulting in a scale of zero to three points, with the lowest score representing the worst housing conditions.

Family literacy was estimated by the number of books available in the home at age ten: (1) none or very few (0 - 10 books), (2) enough to fill one shelf (11 - 25 books), (3) enough to fill one bookshelf (26 - 100 books), (4) enough to fill two bookshelves (101 - 200 books) and (5) enough to fill two or more bookshelves (more than 200 books).

Adverse experiences

The adverse experiences dimension included variables reporting hostile situations that may have occurred before the age of 17 in which individuals were physically harmed, either by being pushed, grabbed, slapped, hit or having something thrown at them. These situations of physical harm were characterized by the frequency with which the harm was inflicted by the mother, the father, and someone other than the parents. Four categories of frequency were considered: (1) often, (2) sometimes, (3) seldom, (4) never.

The participants who often suffered harm caused by their mother, father or someone else were classified as victims of physical abuse.

Family and social integration

This dimension includes variables characterizing the quality of relationships with parents and friends. The quality of the relationship with the mother and the quality of the relationship with the father before the age of 17 were classified in the following categories: (1) excellent, (2) very good, (3) good, (4) fair and (5) poor.

The frequency with which they felt lonely and the frequency with which they had a group of friends with whom they felt comfortable socializing between the ages of six and 16 both were classified as: (1) often, (2) sometimes, (3) rarely and (4) never.

Statistical analysis

Microsoft Excel® was used to optimize the cleaning and preparation of the database. The statistical analysis tool used to analyze the data was the Software Package for Social Science (SPSS) 29.0.0.0®.

The association between each of the independent variables and the variable level of risk of alcohol consumption was assessed using the chi-squared hypothesis test or the Student *t*-test, with a significance level of 5%.

A binary logistic regression model was constructed to estimate the magnitude of the associations between the level of risk of alcohol consumption among current drinkers and sociodemographic variables and childhood and adolescence circumstances. Additionally, a multinomial logistic regression model including all participants (both non-drinkers and current drinkers) was developed to study these associations. The results were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Ethical considerations

The SHARE project is subject to ongoing ethical review.

Waves seven and nine were reviewed and approved by the Ethics Committee of the Max Planck Society [Appendix 3 (Appendix 3: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/24100/15877)], and the SHARE application at the national level was approved by the Ethics Committee of each country. The numerous reviews covered all aspects, including the sub-projects, and confirmed that the project complied with the relevant legislation and that the procedures were in line with international ethical standards.

All data provided to the scientific community is anonymized.

The SHARE data was requested by the principal investigator who signed a declaration of commitment to use it exclusively for its intended purpose.

RESULTS

From the 903 participants included in this study, 378 (41.9%) were male, 770 (85.3%) belonged to the over-65 age group, 656 (72.7%) had a low level of education, 695 (77.0%) were married or living in a civil partnership, 692 (77.8%) were retired, 317 (56.0%) said that the money available to the household lasted until the end of the month

with difficulty and 466 (54.1%) lived in a rural area.

Regarding alcohol consumption, 440 (48.7%) had consumed at least one alcoholic drink in the last seven days. The median number of units of alcohol consumed per week was 7.50. Within this group of current drinkers, 220 (50.0%) practiced higher-risk alcohol consumption.

About childhood and adolescence circumstances, 47 (5.2%) reported poor health, 341 (39.3%) considered their

Table 1 – Prevalence of low-risk and higher-risk alcohol drinking patterns, according to sociodemographic variables

	Low-risk	Higher-risk
n (%)	n = 220 (50.0%)	n = 220 (50.0%)
Sex		
Men	89 (32.8%)	182 (67.2%)
Women	131 (77.5%)	38 (22.5%)
p-value	0.001	
Age (years)		
50 - 64	44 (65.7%)	23 (34.3%)
≥ 65	176 (47.2%)	197 (52.8%)
p-value	0.008	
Education level*		
None or still studying	13 (48.1%)	14 (51.9%)
Low	144 (47.2%)	161 (52.8%)
Medium	28 (54.9%)	23 (45.1%)
High	34 (60.7%)	22 (39.3%)
p-value	0.258	
Marital status		
Single	5 (33.3%)	10 (66.7%)
Married or registered partnership	169 (46.8%)	192 (53.2%)
Divorced	22 (78.6%)	6 (21.4%)
Widowed	24 (66.7%)	12 (33.3%)
p-value	< 0.001	
Job situation**		
Retired	163 (46.8%)	185 (53.2%)
Employed	24 (53.3%)	21 (46.7%)
Unemployed	9 (90.0%)	1 (10.0%)
Permanently sick or disabled	5 (62.5%)	3 (37.5%)
Homemaker	13 (76.5%)	4 (23.5%)
Other	6 (60.0%)	4 (40.0%)
p-value	0.014	
To make ends meet***		
With difficulty	79 (58.5%)	56 (41.5%)
Easily	71 (56.3%)	55 (43.7%)
p-value	0.802	
Area of residence†**		
Urban area	100 (49.5%)	102 (50.5%)
Rural area	109 (49.8%)	110 (50.2%)
p-value	1.000	

*: 1 missing value; **: 13 missing values; ***: 337 missing values; †: 41 missing values.
p-values calculated by chi-square test and Fisher-Freeman-Halton's exact test.

financial situation to be bad, 147 (19.7%) described the profession of the person who supported their household as being low-skilled, 693 (78.8%) had between zero and ten books at home. The median quality of housing was 1.00.

In terms of adverse experiences, 505 (57.2%) suffered physical abuse from their mother, 382 (46.3%) from their father and 158 (18.7%) from someone else and 130 (15.5%) were victims of physical abuse on a regular basis. In addition, 96 (11.4%) said they did not have a good relationship with their mother and 146 (17.7%) with their father.

Concerning the field of sociability, 407 (47.6%) said they felt lonely and 300 (35.4%) did not often have a group of friends with whom they felt comfortable socializing.

Table 1 shows the bivariate analysis comparing sociodemographic variables and the consumption risk level. There were statistically significant differences between the proportion of participants with higher-risk alcohol consumption when comparing male and female participants (67.2% *vs* 22.5%, r < 0.001). There were also statistically significant differences between the two groups in terms of age group (34.3% *vs* 52.8%, r = 0.008), marital status (r < 0.001) and job situation (r = 0.014).

Table 2 shows the bivariate analysis, which compares the variables of childhood and adolescence circumstances and the alcohol consumption risk level. There were statistically significant differences in housing quality (r = 0.002), family literacy (r = 0.026), physical abuse (r = 0.008), quality of relationship with the father (r = 0.035) and frequency of feeling lonely (r = 0.009).

Table 3 presents binary logistic regression analysis to estimate the associations between current drinkers and sociodemographic characteristics and childhood and adolescence circumstances after model optimization. The analysis revealed that sex, physical abuse and quality of housing in childhood were independently associated with higher-risk alcohol consumption. Male sex seems to be a risk factor for higher-risk alcohol consumption (OR 6.444; 95% CI 4.329 - 11.111; $p < 0.001$). Suffering physical abuse in childhood (OR = 2.063; 95% CI 1.119 - 3.803) was significantly and positively associated with higher-risk alcohol consumption and better housing conditions in childhood were associated with lower odds of higher-risk alcohol consumption (OR = 0.767; 95% CI 0.608 - 0.968).

Comparing participants with low-risk and higher-risk levels of alcohol consumption to non-drinkers (considered as reference category within the multinomial regression model) (Table 4), we found that, after model optimization: the low-risk drinkers showed a significant positive association with male sex (OR = 2.312; 95% CI: 1.567 - 3.409), being divorced (OR = 2.988; 95% CI: 1.324 - 6.744), and better housing conditions in childhood (OR = 1.292; 95% CI: 1.077 - 1.550); and the higher-risk drinkers presented a significant positive association with male sex (OR = 15.682; 95% CI: 10.041 - 24.491) and had a higher probability of having been victims of physical abuse in childhood (OR = 2.049; 95% CI: 1.200 - 3.497).

DISCUSSION

Comparison with other data/studies

In this study, 48.9% of participants reported currently consuming alcoholic beverages, with a higher prevalence among men (61.7%). The 2019 National Health Survey[29] or the 2022 Fifth National Survey on the Substances in Portugal[30] provide useful context for understanding alcohol use in older adults; however, they rely on different consumption indicators and temporal reference periods. While the present study measures weekly consumption, the national surveys mentioned rely on a 30-day or a 12-month period, which limit the ability to interpret and compare. Our findings offer a broader perspective on alcohol use patterns across varying definitions of consumption.

Both regression models showed that male sex and experiencing physical harm during childhood increased the odds of engaging in risky alcohol consumption behavior. Male sex emerged as a robust determinant of alcohol use across both low-risk and higher-risk drinking patterns. This finding is consistent with previous literature demonstrating that biological and psychosocial factors contribute to men's greater propensity for excessive alcohol use.[11,31] It should be noted that we have tried a stratified analysis by sex with no relevant results for a discussion about this eventual effect modifier. Being a victim of physical abuse in childhood was associated with significantly higher odds of higher-risk alcohol consumption, which is consistent with prior research indicating that individuals who endured household abuse throughout childhood were more likely to engage in alcohol consumption practices.[20]

Regarding the circumstances of childhood and adolescence examined in this study, the quality of childhood housing – used as a proxy for socioeconomic status – appears to be an important determinant of alcohol consumption risk among current drinkers. This suggests that individuals from lower socioeconomic backgrounds were more likely to engage in higher-risk drinking. This finding is consistent with evidence that links poorer living conditions to high-risk drinking.[32] However, the association between childhood housing quality and alcohol consumption risk level was not consistent across analyses, with opposite directions of effect observed when comparing the low-risk drinkers with non-drinkers. This may reflect the limited sensitivity of the housing quality variable to assess socioeconomic factors. Considering the country's economic development during the period in which the study participants were children and adolescents, additional indicators – like parental income

Table 2 – Prevalence of low-risk and higher-risk alcohol drinking patterns, according to childhood and adolescence circumstances (section 1 of 2)

	Low-risk	Higher-risk
n (%)	n = 220 (50.0%)	n = 220 (50.0%)
Health status*		
Excellent	50 (45.5%)	60 (54.5%)
Very good	44 (51.8%)	41 (48.2%)
Good	93 (52.0%)	86 (48.0%)
Fair	19 (51.4%)	18 (48.6%)
Poor	8 (47.1%)	9 (52.9%)
p-value	0.852	
Family financial situation**		
Pretty well off financially	19 (67.9%)	9 (32.1%)
About average	111 (50.0%)	111 (50.0%)
Poor	75 (45.2%)	91 (54.8%)
It varied	7 (53.8%)	6 (46.2%)
p-value	0.161	
Main earner's occupational grade***		
High-skilled	33 (62.3%)	20 (37.7%)
Mid- skilled	115 (47.7%)	126 (52.3%)
Low-skilled	30 (42.9%)	40 (57.1%)
p-value	0.085	
Housing quality		
Mean (IQR)	1.42 (1)	1.11 (0)
Minimum; maximum	0;3	0;3
p-value	0.002	
Family literacy†		
0 – 10 books	149 (45.7%)	177 (54.3%)
11 – 25 books	25 (59.5%)	17 (40.5%)
26 – 100 books	17 (53.1%)	15 (46.9%)
101 – 200 books	11 (73.3%)	4 (26.7%)
> 200 books	13 (72.2%)	5 (27.8%)
p-value	0.026	
Mother physical harm††		
Often	16 (35.6%)	29 (64.4%)
Sometimes	50 (47.2%)	56 (52.8%)
Rarely	44 (51.8%)	41 (48.2%)
Never	95 (54.6%)	79 (45.4%)
p-value	0.13	
Father physical harm†††		
Often	7 (30.4%)	16 (69.6%)
Sometimes	35 (49.3%)	36 (50.7%)
Rarely	57 (49.6%)	58 (50.4%)
Never	104 (52.5%)	94 (47.5%)
p-value	0.258	

*: 28 missing values; **: 36 missing values; ***: 157 missing values; †: 24 missing values; ††: 67 missing values; †††: 78 missing values; ‡: 56 missing values; ‡‡: 63 missing values; ‡‡‡: 76 missing values; §: 55 missing values; §§: 55 missing values.
p-values were calculated using the chi-squared test and the Student's *t*-test for the numerical variable housing quality.

Table 2 – Prevalence of low-risk and higher-risk alcohol drinking patterns, according to childhood and adolescence circumstances (section 2 of 2)

	Low-risk	Higher-risk
Anybody else physical harm‡		
Often	10 (55.6%)	8 (44.4%)
Sometimes	12 (46.2%)	14 (53.8%)
Rarely	21 (53.8%)	18 (46.2%)
Never	165 (49.4%)	169 (50.6%)
p-value	0.888	
Physical abuse		
Yes	24 (34.8%)	45 (65.2%)
No	182 (52.9%)	162 (47.1%)
p-value	0.008	
Relationship with the mother‡‡		
Excellent	72 (51.4%)	68 (48.6%)
Very good	47 (49.0%)	49 (51.0%)
Good	66 (48.5%)	70 (51.5%)
Fair	17 (56.7%)	13 (43.3%)
Poor	6 (50.0%)	6 (50.0%)
p-value	0.938	
Relationship with the father‡‡‡		
Excellent	50 (43.9%)	64 (56.1%)
Very good	56 (65.1%)	30 (34.9%)
Good	63 (47.0%)	71 (53.0%)
Fair	24 (47.1%)	27 (52.9%)
Poor	10 (47.6%)	11 (52.4%)
p-value	0.035	
Frequency of feeling lonely§		
Often	22 (68.8%)	10 (31.3%)
Sometimes	19 (35.8%)	16 (64.2%)
Rarely	63 (56.8%)	48 (43.2%)
Never	103 (47.0%)	116 (53.0%)
p-value	0.009	
Frequency of feeling comfortable in friendships§§		
Often	141 (50.0%)	141 (50.0%)
Sometimes	44 (50.0%)	44 (50.0%)
Rarely	13 (40.6%)	19 (59.4%)
Never	9 (64.3%)	5 (35.7%)
p-value	0.535	

*: 28 missing values; **: 36 missing values; ***: 157 missing values; †: 24 missing values; ††: 67 missing values; †††: 78 missing values; ‡: 56 missing values; ‡‡: 63 missing values; ‡‡‡: 76 missing values; §: 55 missing values; §§: 55 missing values.
p-values were calculated using the chi-squared test and the Student's *t*-test for the numerical variable housing quality.

and education – would provide a more accurate assessment of early-life conditions. Marital status, particularly being divorced, also seems to be an important determinant within the low-risk drinkers, supporting evidence that changes in family structure or processes of marital transition may influence alcohol-related behaviors.[33] There appears to be

Table 3 – Binary logistic regression model: Associations between current drinkers (low-risk *versus* higher-risk) and sociodemographic characteristics and childhood and adolescence circumstances

	OR (95% IC)	*p*-value
Sex		
Men	6.444 (4.329-11.111)	< 0.001
Women	1	
Physical abuse		
No	1	
Yes	2.063 (1.119-3.803)	0.02
Housing quality	0.767 (0.608-0.968)	0.025

95% CI, 95% confidence interval. The logistic regression model was statistically significant ($p < 0.001$) and the Hosmer-Lemeshow test indicated a good model fit ($p = 0.946$). The model correctly predicted 71.4% of cases. The initial model included the following variables: sex, age group, marital status, job situation, family literacy, frequency of feeling lonely, physical abuse, housing quality and area of residence. The area under the ROC curve was 0.757.

a suggestion that being single is associated with higher-risk alcohol consumption. This aligns with current evidence indicating that single individuals are approximately two to four times more likely to engage in excessive drinking compared with those living with a partner.[34]

This research also found a statistically significant association between sociodemographic characteristics (age, job situation), childhood and adolescence circumstances (family literacy, relationship with the father, frequency of feeling lonely), and the level of risk of alcohol consumption, which aligns with prior research.[35-40]

Limitations, methodological considerations and future research

Other methodological issues deserve to be discussed. One of the main limitations of this study is that it is a cross-sectional study and, as such, it does not allow us to infer a causal relationship, but only to estimate whether there is an association between the variables. However, it should be noted that there is a clear temporal sequence to the data, as two distinct moments in the individual's life cycle are considered (childhood and adulthood).

Moreover, relying on secondary data imposes limitations on the scope of aspects that can be addressed, both in characterizing childhood and adolescent circumstances and in assessing alcohol consumption risk levels.

The variables that characterize the circumstances of childhood and adolescence are subjective and depend entirely on the respondent's perspective of that period of their life and do not include questions that allow us to ascertain the existence of a family history of alcohol dependence. This omission is salient considering the numerous studies that underscore the substantial impact of environmental and social contexts on alcohol-use behaviors, including proximity to alcohol outlets.[11] Concurrently, the analysis also lacked data on age of alcohol-use initiation, co-use of other substances, and participants' attitudes, social interactions, and risk perceptions – factors that shape drinking patterns.[11] Additionally, life events such as health problems, bereavement, emotional distress, social isolation, retirement, or loss of independence were not considered, despite their potential influence on alcohol-use behaviors through maladaptive coping. Furthermore, the age range of the subjects in the present study is predominantly composed of individuals aged 65 years and older, thereby constraining the extent to which the findings can be generalized.

Collecting accurate retrospective data can be affected by memory bias, particularly if recall differs between low- and higher-risk drinkers. Individuals with higher-risk alcohol consumption may not be able to recall or remember their childhood and adolescent circumstances in greater detail than individuals with lower risk alcohol consumption. This challenge has been overcome using a life history calendar that has been designed to help recall past events. Through SHARE studies, this framework has been shown to reliably capture older adults' reports of health and living conditions from ages 0 to 15, supporting its use for retrospective research.[41]

The question "How many units of alcoholic beverages have you consumed in the last seven days?" was used as a proxy for determining the risk level of alcohol consumption, which may not be representative of the usual pattern of consumption. The database also lacks variables that characterize attitudes, sociability, and perceptions of risk, which can affect the intensity, context, and motivations for alcohol consumption. In this sense, future studies should consider using a validated questionnaire, such as the Alcohol Use Disorders Identification Test (AUDIT), to assess the risk of excessive drinking.

Although people living in institutions are included in the SHARE sampling frame, they are not included in the survey database. As a result, this study does not cover the whole population. Since the group of people without a home of their own has a high preponderance in the study population. In wave 9 of SHARE in Portugal, 1103 households were contacted, and the overall response rate was 65.45%.[24] To date, no information is available to characterize the non-respondents.

Given the nature of the variables being studied, there may also be a social desirability bias. Knowing which behaviors are socially unacceptable can be a challenge in a CAPI data collection process. Respondents may tend to answer what they consider to be socially acceptable, influenced by the culture and social norms of the country, thus distorting the reality of alcohol consumption patterns and circumstances during childhood and adolescence.

Despite its limitations, this study is strengthened by a

Table 4 – Multinomial logistic regression model: Associations between the level of risk of alcohol consumption (non-drinkers versus low-risk and non-drinkers *versus* higher-risk) and sociodemographic characteristics and childhood and adolescence circumstances

Risk level[a]		**OR** (95% IC)	***p*-value**
Low-risk	**Sex**		
	Men	2.312 (1.567 - 3.409)	< 0.001
	Women	1	
	Marital status		
	Single	1.218 (0.376 - 3.943)	0.742
	Married or in a civil partnership	1.576 (0.914 - 2.715)	0.102
	Divorced	2.988 (1.324 - 6.744)	0.008
	Widowed	1	
	Physical abuse		
	No	1	
	Yes	0.956 (0.561 - 1.629)	0.868
	Housing quality	1.292 (1.077 - 1.550)	< 0.001
Higher-risk	**Sex**		
	Men	15.682 (10.041 - 24.491)	< 0.001
	Women	1	
	Marital status		
	Single	3.077 (0.906 - 10.452)	0.072
	Married or in a civil partnership	1.644 (0.798 - 3.385)	0.178
	Divorced	0.915 (0.257 - 3.252)	0.890
	Widowed	1	
	Physical abuse		
	No	1	
	Yes	2.049 (1.200 - 3.497)	0.008
	Housing quality	1.020 (0.821 - 1.267)	0.858

[a]: The reference category is non-drinkers (absence of risk). 95% CI: 95% confidence interval. The Hosmer-Lemeshow test indicated a good model fit ($p = 0.224$). The model correctly predicted 61.1% of cases. The initial model included the variables that were statistically significant in the bivariate analysis, when the alcohol consumption risk level variable was operationalized into three categories (non-drinkers, low-risk, higher-risk): sex ($p < 0.001$), age group ($p = 0.01$), educational level ($p = 0.028$), marital status ($p < 0.001$), job situation ($p = 0.026$), housing quality ($p = 0.002$), family literacy ($p = 0.006$), father physical harm ($p = 0.035$), physical abuse ($p = 0.015$) and frequency of feeling lonely ($p = 0.038$).

large, representative sample and the inclusion of multiple sociodemographic and socioeconomic characteristics. The use of a comprehensive set of health determinants and SHARE data enhances the robustness and reliability of the findings. Its originality provides a foundation for future research, highlighting the need for comparative studies using diverse methodologies.

This study adds to the knowledge of the subject studied and also has important applications in the field of public health, in that it can help in the design of programs and projects aimed at at-risk groups and supports a personalized and precise approach to combating excessive alcohol consumption.

In order to reduce the incidence of alcohol-related health harm, we need to continue to understand which early life factors may underlie drinking patterns, which drinking patterns emerge over the life cycle, and which trajectories lead to poorer health outcomes.

It is important that the circumstances of childhood and adolescence continue to be taken into account in the study of risk behaviors, in order to draw conclusions about their real impact on the adoption of these behaviors and to design policies and interventions targeted at disadvantaged and particularly vulnerable populations.

CONCLUSION

The present study found a positive association between physical abuse in childhood and higher-risk alcohol consumption, whereas living in better housing conditions during this developmental stage showed a protective association. Being male was strongly associated with both low- and higher-risk drinking patterns.

DATA AVAILABILITY

Access to the data collected by SHARE is free to all individuals who can prove that they are part of a scientific institution. This can be requested from http://www.share-project.org/dataaccess.html.

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This paper uses data from SHARE Waves 7 and 9 (DOIs: 10.6103/SHARE.w7.900, 10.6103/SHARE.w9.900).

The authors have declared that no AI tools were used during the preparation of this work.

AUTHOR CONTRIBUTIONS

CMM: Conceptualization, methodology, statistical analysis, writing - original draft preparation.

PA: Conceptualization, methodology, statistical analysis support, supervision, writing – review.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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ACTA MÉDICA PORTUGUESA
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Skin Prick Testing in a Portuguese Pediatric Population: A Multicenter Cross-Sectional Study of Clinical and Allergen Sensitization Profiles

Testes Cutâneos por Picada numa População Pediátrica Portuguesa: Estudo Transversal Multicêntrico de Perfis Clínicos e de Sensibilização Alérgica

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ABSTRACT

Introduction: Allergic diseases, particularly allergic rhinitis and asthma are highly prevalent among children and adolescents and frequently associated with sensitization to inhalant allergens. However, recent data on sensitization profiles in the Portuguese pediatric population are scarce, especially regarding regional and demographic variability. In this context, we aimed to characterize the clinical and allergen sensitization profiles of children and adolescents with allergic diseases in Portugal, through a multicenter approach.

Methods: We conducted a retrospective, cross-sectional study across 14 Portuguese hospitals between January 2021 and June 2023. Children and adolescents (< 18 years) with a clinical diagnosis of allergic diseases and at least one positive skin prick test to inhalant allergens were included. Demographic, clinical, and environmental data were collected from electronic medical records. Skin prick tests followed European Academy of Allergy & Clinical Immunology recommendations. Statistical analysis was performed using IBM® SPSS® Statistics version 29.

Results: A total of 3456 patients were included (60.5% male; median age 10 years). Allergic rhinitis (78.1%) and asthma (54.5%) were the most common diagnoses and 43.1% presented with both conditions. Sensitization was most frequent to *Dermatophagoides pteronyssinus* (84.3%) and *Dermatophagoides farinae* (74.3%), followed by *Lepidoglyphus destructor* (57.8%), grass pollens (60.4%), and *Blomia tropicalis* (23.5%). Polysensitization occurred in 58.4% of patients. Sensitization patterns varied with age. Geographic differences were noted: house dust mites sensitization predominated in coastal regions, whereas sensitization to pollens, molds, and animal epithelia was more frequent inland. Migrant children (14.2%) showed lower sensitization rates to most allergens, despite a comparable disease burden.

Conclusion: To the best of our knowledge, this is the first multicenter study to describe pediatric allergen sensitization patterns in Portugal. The high rates of polysensitization and the regional variability underscore the importance of tailored diagnostic strategies. Skin prick test remains a key tool in the initial assessment of allergic diseases.

Keywords: Allergens; Child; Hypersensitivity; Portugal; Skin Tests

RESUMO

Introdução: As doenças alérgicas, em particular a rinite alérgica e a asma, são frequentes em idade pediátrica e estão muitas vezes associadas a sensibilização a alergénios inalantes. Apesar disso, dados sobre os perfis de sensibilização na população pediátrica portuguesa são escassos, sobretudo no que diz respeito à variabilidade regional e demográfica. Neste contexto, propusemo-nos caracterizar os perfis clínicos e de sensibilização a alergénios numa população pediátrica com doenças alérgicas em Portugal, através de uma abordagem multicêntrica.

Métodos: Realizou-se um estudo retrospetivo, transversal, em 14 hospitais portugueses, entre janeiro de 2021 e junho de 2023. Foram incluídas crianças e adolescentes (< 18 anos) com diagnóstico clínico de doenças alérgicas e pelo menos um teste cutâneo por picada positivo para alergénios inalantes. Os dados demográficos, clínicos e ambientais foram obtidos através dos processos clínicos eletrónicos. Os testes cutâneos por picada seguiram as recomendações da European Academy of Allergy & Clinical Immunology. A análise estatística foi efetuada através do *software* IBM® SPSS® *Statistics*, versão 29.

Resultados: Foram incluídos 3456 doentes (60,5% do sexo masculino; mediana de idade de 10 anos). As patologias mais frequentes foram a rinite alérgica (78,1%) e a asma (54,5%), com coexistência de ambas em 43,1%. A sensibilização mais frequente foi a *Dermatophagoides pteronyssinus*

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(84,3%) e *Dermatophagoides farinae* (74,3%), seguida de *Lepidoglyphus destructor* (57,8%), pólenes de gramíneas (60,4%) e *Blomia tropicalis* (23,5%). A polissensibilização foi observada em 58,4% dos casos, variando com a idade. Identificaram-se diferenças geográficas: a sensibilização a ácaros foi mais prevalente em zonas costeiras, enquanto a sensibilização a pólenes, fungos e epitélio de animais foi mais frequente em regiões do interior. As crianças imigrantes (14,2%) apresentaram taxas inferiores de sensibilização, apesar de prevalência clínica semelhante.
Conclusão: Tanto quanto é do nosso conhecimento, este é o primeiro estudo multicêntrico a descrever os perfis de sensibilização a alergénios na população pediátrica em Portugal. As elevadas taxas de polissensibilização e a variabilidade geográfica reforçam a importância de estratégias diagnósticas dirigidas. Os testes cutâneos por picada mantêm-se fundamentais na abordagem inicial das doenças alérgicas.
Palavras-chave: Alergénios; Criança; Hipersensibilidade; Portugal; Testes Cutâneos

KEY MESSAGES

- This is the first multicenter study on allergen sensitization profiles in the Portuguese pediatric population.
- Allergic rhinitis and asthma are the most common allergic diseases in this sample and frequently co-occur.
- House dust mites and grass pollens are the most common sensitizing allergens identified through skin prick testing.
- Significant geographic and demographic variations in sensitization patterns were observed.
- Skin prick testing remains a key tool in the initial assessment of allergic diseases.

INTRODUCTION

The prevalence of allergic diseases (AD) has substantially increased in recent decades, which can be associated with more sedentary lifestyles, regular practice of indoor activities, urban air pollution, tobacco consumption and exposure, and the escalating global epidemic of overweight and obesity.[1]

Among children, the most common AD are rhinitis and asthma. According to data from the International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of rhinitis and asthma in children aged 6 - 7 years is 8.5% and 11.7%, respectively, increasing to 14.6% and 14.1% in adolescents aged 13 - 14 years.[2] In Portugal, the estimated prevalence of rhinitis in pre-school children is 43.4% and the prevalence of asthma in the pediatric population is 8.4% [Cost of Asthma in Children (CASCA) study].[3,4]

Although rarely life-threatening, allergic rhinitis and asthma are associated with significant morbidity, as symptoms interfere with patients' social and academic life (usually decreasing school performance), and the economic costs are not negligible.[1,3] Therefore, the identification of specific sensitization profiles and accurate diagnosis are essential for effective management, enabling both environmental control strategies and the selection of appropriate immunotherapy, if clinically relevant.

Skin prick tests (SPT) are considered the first-line investigation for allergic sensitization. They are widely available, low-cost, and applicable to all ages.[5] These demonstrate high sensitivity and specificity (over 80% - 97% and 70% - 95%, respectively), with a good safety profile (systemic reactions occur in less than 0.1% in pediatric cases).[5] Additionally, they provide rapid results, with few contraindications, namely acute urticaria and exacerbated atopic eczema.[5,6] The main disadvantages include the limited range of available extracts and the potential interference of certain medications, as antihistamines may suppress wheal responses and topical corticosteroids applied to the test area for more than one week may reduce local skin reactivity, leading to false-negative results.[5] Therefore, SPT interpretation should be grounded in a robust understanding of diagnostic limitations and allergic pathophysiology, as described in pediatric allergology guidelines.[6]

Geographic variation in sensitization profiles is well documented and attributed to differences in climate, vegetation, and urban versus rural environments, highlighting the need for individualized avoidance measures tailored to each patient's environmental context and specific sensitization profile.[7,8] In Portugal, the last acarological map was published in 2009 and included data from both children and adults.[8] However, in recent years, Portugal has witnessed a steady rise in migrant pediatric populations, many of whom may have sensitization profiles that differ from native residents due to environmental and genetic factors. This highlights the need for updated region-specific and demographically inclusive data on allergen sensitization. Migration has been increasingly recognized as an important determinant of AD risk. A recent systematic review and meta-analysis showed that migrants often have a lower initial prevalence of asthma, rhinitis and atopic dermatitis than host populations, but this apparent protection decreases over time, with allergy prevalence converging towards that of the host country as environmental exposures change.[9] In addition, population-based data from Germany indicate that children and adolescents with a two-sided migrant background are less frequently sensitized to the most common aeroallergens than their non-migrant peers, suggesting a complex interaction between early-life environment, migration history and allergen exposure.[10]

A previous study investigated allergen sensitization patterns in a pediatric population attending a Portuguese hospital located in northern mainland Portugal.[11] Recent

multicenter and regional studies have highlighted substantial heterogeneity in aeroallergen sensitization profiles and clinical phenotypes among children across different climatic and geographical settings, particularly in Southern Europe.[12,13] The aim of the present study was to expand the previous Portuguese perspective through a multicenter approach, offering a comprehensive view of allergic sensitization profiles in different regions of the mainland in a Portuguese population.

This represents a crucial step toward improving clinical decision-making and optimizing therapeutic strategies in pediatric allergy care. It also provides an important update to the existing knowledge of the most prevalent allergen sensitizations in the pediatric population.

Specifically, this multicenter study seeks to characterize the clinical profiles and allergen sensitization patterns of children and adolescents with AD in Portugal.

METHODS

A multicenter, retrospective cross-sectional study was conducted in 14 Portuguese hospitals, which were selected by convenience. The institutions were geographically categorized according to two criteria:

1. By geographic region, based on the *Nomenclatura das Unidades Territoriais para Fins Estatísticos* (NUTS) II: 11 hospitals in the North, 1 in the Centre, 1 in Oeste e Vale do Tejo and 1 in the Alentejo.
2. By location type: 11 coastal and 3 inland hospitals.

Participants

The inclusion criteria were: (1) children and adolescents under 18 years of age; (2) follow-up in the pediatric allergology or pediatric pulmonology clinic; (3) clinical diagnosis of an AD (asthma, allergic rhinitis, atopic dermatitis and/or conjunctivitis), based on a compatible medical history and physical examination; (4) positive SPT performed between January 2021 and June 2023.

To avoid duplicate entries, each patient was included only once in the dataset. In cases where a participant underwent more than one SPT during the study period, the most recent test was considered for analysis.

Operational definitions and group definitions

Clinical diagnoses were retrieved from the electronic medical records as recorded by the attending pediatrician and were considered to be in line with contemporaneous guideline-based practice. Asthma was defined according to the international Global Initiative for Asthma (GINA) guidelines, requiring a compatible clinical history (episodic respiratory symptoms such as wheeze, dyspnea or cough), objective evidence of variable airflow limitation when available, and/or a prior physician diagnosis of asthma. Allergic rhinitis was defined according to Allergic Rhinitis and Its Impact on Asthma (ARIA) criteria, requiring nasal symptoms (rhinorrhea, nasal obstruction, sneezing or nasal pruritus) for more than one hour on most days, with or without ocular symptoms, together with a prior diagnosis by an allergist or pediatrician. Atopic dermatitis was defined according to the United Kingdom Working Party refinement of the Hanifin & Rajka criteria, requiring chronic or relapsing eczema with typical age-dependent distribution and pruritus. For the purposes of analysis, patients were classified into mutually exclusive groups according to the diagnoses documented in their electronic medical records.

Ethical considerations

The study was approved by the Ethics Committee of Unidade Local de Saúde Santo António/Instituto de Ciências Biomédicas Abel Salazar [reference 2023.168(140-DEFI/132-CE)].

Data collection

Clinical and demographic data were obtained from clinical records through a retrospective review of electronic medical records by the Pediatric Allergology or Pediatric Pulmonology clinic team of each hospital, including age at testing, sex, place of residence, migratory status, AD profile, environmental exposures (presence of humidity, tobacco smoke exposure, and domestic animals), and family history of atopy (with specification when available). All data were anonymized to ensure full patient confidentiality and privacy, in compliance with applicable ethical standards and data protection regulations applicable to each hospital involved in the study.

Skin prick tests

Skin prick tests were commercialized by two pharmaceutical companies (LETI® and Roxall®) and the results were analyzed together, with no specification of the pharmaceutical company at the time of data collection. The tests were performed according to the European Academy of Allergy & Clinical Immunology (EAACI) recommendations, considering a mean papule diameter ≥ 3 mm compared to the negative control, assessed after 15 minutes, as a positive SPT. The panel of allergens tested included house dust and storage mites, animal epithelia, pollens (grasses, trees and other plants), and molds. Monosensitization was defined as a positive SPT to aeroallergens from a single allergen family, whereas polysensitization was defined as positive SPT to aeroallergens from two or more different allergen families.

Statistical analysis

Descriptive, univariate and multivariable analysis were

conducted using IBM® SPSS® Statistics, version 29. Categorical variables were summarized as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were summarized as means and standard deviations or medians and interquartile ranges. Multivariable associations between covariates and the study outcomes were examined using logistic regression models. A *p*-value < 0.05 was considered statistically significant.

RESULTS

General sample characteristics

A total of 3456 children and adolescents with positive SPT, performed between January 2021 and June 2023, were included in the analysis. Of these, 60.5% were male and 39.5% were female. The median age at the time of testing was 10 years [interquartile range (IQR) = 6], with the majority (66.6%) falling within the 6 - 9 and 10 - 13-year age groups. Other sample characteristics are summarized in Table 1.

Regarding geographical distribution based on the NUTS II division, 85.4% of patients were from the North, 8.1% from Oeste e Vale do Tejo, 4.9% from the Centre, and 1.6% from the Alentejo. In terms of hospital location, 87.2% were followed in coastal institutions. A total of 14.2% were migrants, most commonly from Brazil and Switzerland. These patients were predominantly followed in coastal hospitals ($p < 0.001$).

Exposure to potential environmental risk factors was frequently reported: 55.0% had domestic animals, 33.3% had documented exposure to tobacco smoke, and 28.1% were exposed to household dampness. A family history of atopy was reported in 63.4% of cases, most commonly involving the mother (30.0%) or both parents (24.4%).

Clinical profile

The most frequent AD identified among participants were allergic rhinitis (78.1%) and asthma (54.5%), followed by allergic conjunctivitis (21.2%) and atopic dermatitis (18.6%). Notably, 43.1% presented with coexisting asthma and rhinitis, 19.0% and 9.3% had isolated rhinitis and isolated asthma, respectively (Table 1). Rhinitis was the most prevalent allergic condition across all age groups, showing a progressive increase with age, followed by asthma. Isolated asthma showed a decreasing trend after the age of 10 years (Fig. 1).

Allergen sensitization profile

The overall sensitization profile is summarized in Fig. 2. Sensitization to house dust mites was almost universal, with 90.5% of patients sensitized to at least one mite species. The most frequent sensitizations were to *Dermatophagoides pteronyssinus* (84.3%) and *Dermatophagoides farinae* (74.3%), followed by *Lepidoglyphus destructor* (57.8%) and *Blomia tropicalis* (23.5%). Sensitization to *Acarus siro* was less frequent (1.3%). Overall, 74.3% were sensitized to two or more mite species.

Among pollens, the most prevalent sensitizations were to grass pollens (60.4%), including wild (51.2%) and cultivated species (34.6%), as well as *Olea europaea* (16.8%), *Platanus acerifolia* (9.2%) and *Parietaria judaica* (7.7%).

Regarding animal epithelia, sensitization was observed in 35.5% of patients, with 28.3% sensitized to cat epithelia and 21.2% to dog epithelia. Concerning fungal allergens, sensitization to *Alternaria alternata* and *Aspergillus fumigatus* were reported in 8.9% and 2.7%, respectively.

Overall, 58.4% of the sample presented polysensitization. Among monosensitized patients (41.6%), the most common pattern was sensitization to house dust mites (84.8%), followed by grass pollen (11.8%). Monosensitized patients were significantly younger than polysensitized patients ($p < 0.001$).

The mean number of sensitizations per patient was 3.52 (standard deviation = 1.87), with a median of 3.0 (IQR = 3). The four most frequent allergen sensitization combinations were: (1) *Dermatophagoides pteronyssinus* + *Dermatophagoides farinae* + *Lepidoglyphus destructor* (12.4%); (2) *Dermatophagoides pteronyssinus* + *Dermatophagoides farinae* (9.9%); (3) *Dermatophagoides pteronyssinus* + *Lepidoglyphus destructor* (3.2%); (4) *Dermatophagoides pteronyssinus* + *Dermatophagoides farinae* + *Lepidoglyphus destructor* + wild grass pollen (3.15%). All remaining combinations occurred in less than 3% of the patients.

A positive SPT to only one allergen was observed in 12.3% of the patients. Among these, the most common sensitizing allergen was *Dermatophagoides pteronyssinus* (44.5%), followed by wild grass pollen (17.4%), and *Lepidoglyphus destructor* (14.6%).

Sensitization profiles varied across age groups, with younger children showing a predominance of indoor allergen sensitization such as house dust mites, while older children and adolescents exhibited broader sensitization patterns, with a progressive increase in sensitization to other allergen sources. Patients with isolated rhinitis showed higher rates of sensitization to cultivated grass pollens ($p = 0.013$) and *Olea europaea* ($p = 0.04$). Regarding isolated asthma, these patients had higher rates of sensitization to *Acarus siro* ($p = 0.004$), and less sensitization to wild and cultivated grass pollen ($p < 0.001$).

Regional distribution and geographic patterns

Distinct patterns emerged when comparing AD prevalence and sensitization profiles between coastal and inland regions (Table 2), as well as between migrant and

Table 1 – Summary of demographic, environmental and clinical characteristics of the study population, n = 3456*

Variable	n (%)**
Sex	
Male	2091 (60.5)
Female	1365 (39.5)
Age, years (median, IQR)	10 (6)
Age category	
0 - 5 years	486 (14.1)
6 - 9 years	1221 (35.3)
10 - 13 years	1082 (31.3)
14 - 18 years	667 (19.3)
Region	
North	2950 (85.4)
Center	170 (4.9)
Oeste e Vale do Tejo	281 (8.1)
Alentejo	55 (1.6)
Location	
Coastal	3015 (87.2)
Inland	441 (12.8)
Migratory status (n = 2958)	
Migrants	421 (14.2)
Brazil	124 (29.5)
Switzerland	27 (6.4)
France	17 (4.0)
Angola	11 (2.6)
Venezuela	11 (2.6)
Spain	7 (1.7)
United Kingdom	5 (1.2)
Luxembourg	5 (1.2)
Other countries	214 (50.8)
Exposure status	
Domestic animals (n = 2674)	1472 (55.0)
Tobacco smoke (n = 2595)	865 (33.3)
Household dampness (n = 2355)	662 (28.1)
Family history of atopy	2191 (63.4)
Family history of atopy – specification (n = 2191)	
Mother	657 (30.0)
Father	461 (21.0)
Both parents	535 (24.4)
Siblings	288 (13.1)
Not specified	250 (7.2)
Allergic diseases	
Rhinitis (n = 3413)	2666 (78.1)
Asthma (n = 3357)	1831 (54.5)
Conjunctivitis (n = 3329)	705 (21.2)
Atopic dermatitis (n = 3416)	635 (18.6)
Asthma + rhinitis (n = 3343)	1441 (43.1)
Isolated asthma (n = 3296)	305 (9.3)
Isolated rhinitis (n = 3296)	626 (19.0)

IQR: interquartile range
*: Sample size n = 3456 unless otherwise specified
**: Results n (%) unless otherwise specified

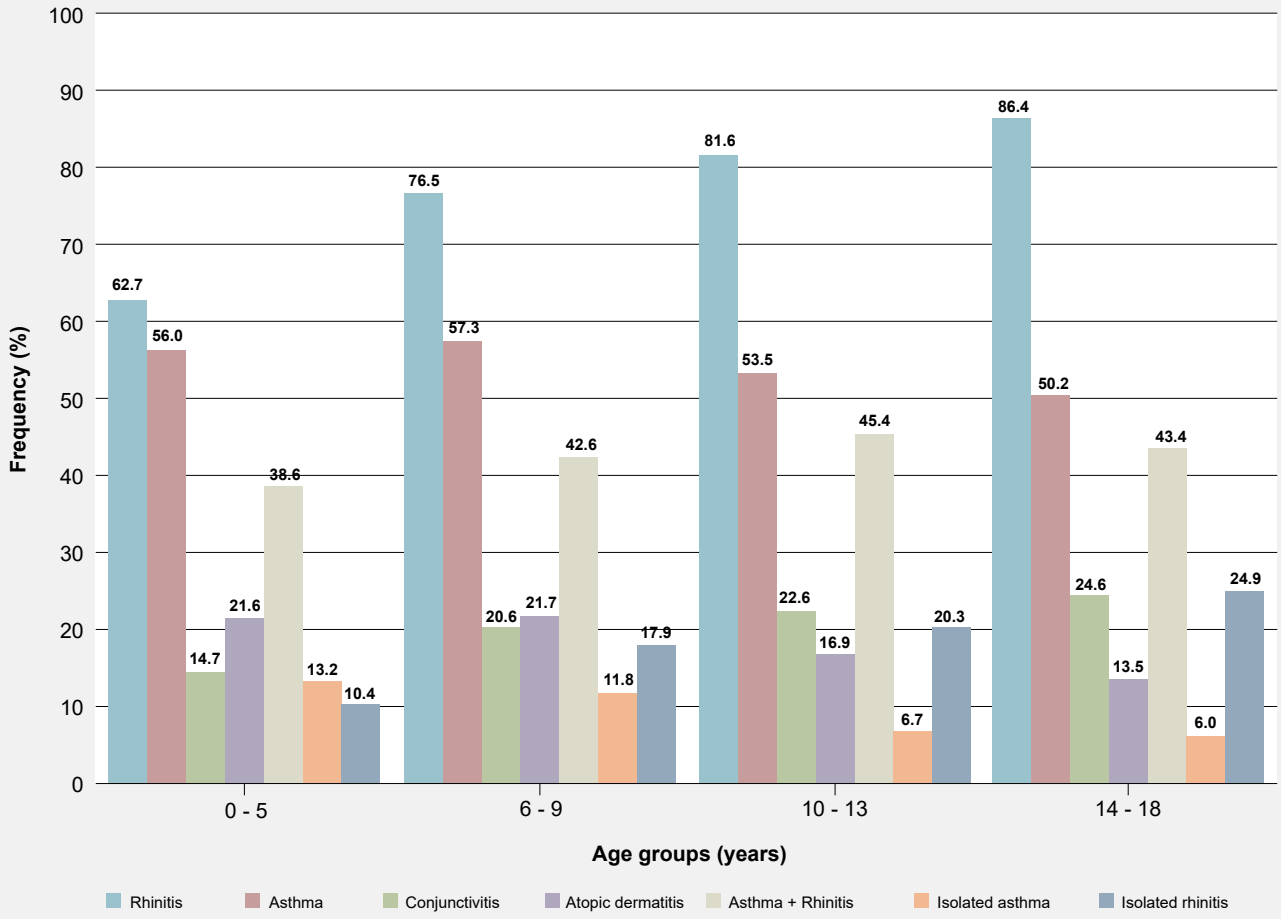

Figure 1 – Distribution of allergic diseases by age group, expressed as relative frequencies

non-migrant patients (Table 3).

Patients from coastal regions presented a higher prevalence of isolated asthma ($p = 0.002$) and combined asthma and rhinitis diagnoses ($p < 0.001$), while those from inland regions showed comparatively higher frequencies of isolated rhinitis ($p = 0.030$).

Sensitization to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* was more common in patients followed in coastal hospitals ($p < 0.001$), whereas unadjusted comparisons regarding sensitization to grass pollen, *Parietaria judaica*, *Platanus acerifolia*, *Olea europaea*, animal epithelia and molds occurred more frequently in the inland group ($p < 0.001$). Sensitization to *Lepidoglyphus destructor* and *Blomia tropicalis* did not vary between these regions.

Regarding migratory status, migrant patients exhibited lower sensitization rates to several allergens in unadjusted comparisons, namely less sensitization to *Dermatophagoides farinae*, *Blomia tropicalis,* animal epithelia, grass pollen, *Parietaria judaica, Platanus acerifolia, Olea europaea* and molds ($p < 0.001$). The distribution of AD was similar, except for isolated asthma ($p = 0.027$), more common in non-migrant patients.

Multivariable analysis

To examine independent predictors of sensitization patterns, as well as asthma diagnosis, four logistic regression models (A, B, C and D) were estimated (Table 4). All models showed statistically significant improvement over the null model ($\Delta\chi^2$, $p < 0.001$), with Nagelkerke R^2 ranging from 0.031 to 0.092.

In Model A (sensitization to at least one house dust mite species), only a few variables remained significant after adjustment. Children followed in inland hospitals had markedly lower odds of house dust mite sensitization than those in coastal hospitals [OR (95% CI) = 0.26 (0.18 - 0.37), $p < 0.001$]. Other sociodemographic and environmental variables did not show independent associations.

Model B (monosensitization *versus* polysensitization)

showed that each additional year of age decreased the odds of being monosensitized by about 7% [OR (95% CI) = 0.93 (0.91 - 0.96), $p < 0.001$]. Monosensitization was less frequent among children followed in inland hospitals [OR (95% CI) = 0.70 (0.53 - 0.93), $p = 0.013$], indicating that polysensitization was relatively more common in the inland group.

In Model C (grass pollen sensitization), older age was independently associated with higher odds of sensitization [OR (95% CI) = 1.06 (1.03 - 1.09) per year, $p < 0.001$]. Grass pollen sensitization was also more likely in non-migrant children [OR (95% CI) = 1.78 (1.26 - 2.54), $p = 0.001$].

Model D examined factors associated with asthma diagnosis and included sensitization variables. Children followed in inland hospitals had roughly half the odds of having asthma compared with those from coastal hospitals [OR (95% CI) = 0.44 (0.30 - 0.65), $p < 0.001$]. No exposure to tobacco smoke was associated with lower odds of asthma [OR (95% CI) = 0.64 (0.48 - 0.84), $p = 0.002$]. Sensitization to house dust mites and animal epithelia were both independently associated with higher odds of asthma [OR (95% CI) = 1.81 (1.22 - 2.68), p = 0.003, and OR (95% CI) = 1.44 (1.08 - 1.92), $p = 0.012$, respectively]. Age was not independently associated with asthma after adjustment for other variables.

DISCUSSION

To our knowledge, this is the first multicenter study conducted in Portugal to comprehensively characterize allergen sensitization profiles in the pediatric population across different geographic and demographic contexts. The large sample size and broad territorial coverage provide an updated overview of the current patterns of AD and sensitization, which are essential for clinical management and public health strategies.

The high prevalence of allergic rhinitis (78.1%) and asthma (54.5%) observed in our cohort aligns with international findings and confirms the significant burden of AD in Portuguese children and adolescents.[2] The results also corroborate national data, which had already identified high rates of rhinitis and asthma in this population.[3,4] The higher estimates observed in our sample are likely due to its clinical nature, as it comprised children and adolescents followed in a hospital setting for AD.

The frequency of coexisting asthma and rhinitis (43.1%) in our sample highlights the clinical relevance of the atopic march, whereby initial sensitization, typically to indoor allergens, may precede the development of more complex allergic phenotypes.[14]

The age-related trends observed, namely, the increase in rhinitis prevalence with age and the decline in isolated

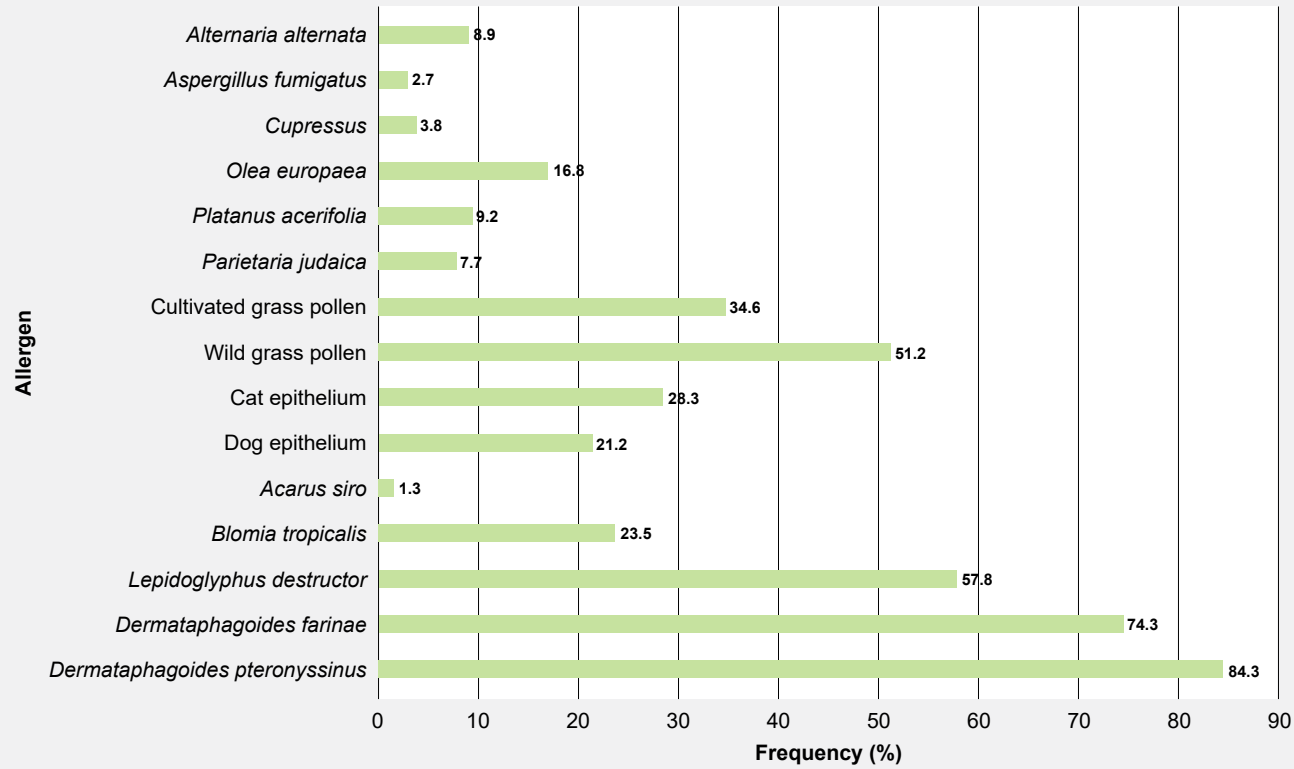

Figure 2 – Distribution of sensitization to individual allergens, expressed as relative frequencies

Table 2 – Distribution of allergic diseases and sensitization profile according to geographic location

Variable	Coastal (%)	Inland (%)	*p*-value
Allergic diseases			
Rhinitis (n = 3413)	76.6	88.4	**< 0.001**
Asthma (n = 3357)	56.3	42.7	**< 0.001**
Conjunctivitis (n = 3329)	18.3	39.8	**< 0.001**
Atopic dermatitis (n = 3416)	17.5	26.2	**< 0.001**
Asthma + rhinitis (n = 3343)	44.4	34.8	**< 0.001**
Isolated asthma (n = 3296)	9.9	5.2	**0.002**
Isolated rhinitis (n = 3296)	18.4	22.8	**0.030**
Sensitization profile			
Dermatophagoides pteronyssinus (n = 3304)	85.6	74.1	**< 0.001**
Dermatophagoides farinae (n = 3164)	75.3	67.2	**< 0.001**
Lepidoglyphus destructor (n = 3105)	58.3	53.7	0.114
Blomia tropicalis (n = 852)	23.5	21.4	0.795
Acarus siro (n = 523)	1.0	1.4	**0.013**
Dog epithelia (n = 2879)	19.0	39.8	**< 0.001**
Cat epithelia (n = 2887)	27.7	33.7	**0.030**
Wild grass pollen (n = 3001)	48.6	71.3	**< 0.001**
Cultivated grass pollen (n = 2122)	29.7	63.5	**< 0.001**
Parietaria judaica (n = 2431)	6.6	18.0	**< 0.001**
Platanus acerifolia (n = 2026)	7.4	31.0	**< 0.001**
Olea europaea (n = 2611)	13.0	48.4	**< 0.001**
Cupressus (n = 1585)	3.9	2.2	0.577
Aspergillus fumigatus (n = 1768)	2.4	5.1	**0.029**
Alternaria alternata (n = 2652)	7.6	21.0	**< 0.001**

asthma after 10 years, support the hypothesis that allergic manifestations evolve over time, reinforcing the need for longitudinal monitoring. Given that allergic rhinitis is a known risk factor for the later development or persistence of asthma, early identification of sensitization and symptom control is vital to prevent progression. This is further supported by evidence of a bidirectional interaction between upper and lower airway inflammation.[15]

Regarding allergen sensitization, house dust mites remain the dominant sensitizers in this population. *Dermatophagoides pteronyssinus* (84.3%) and *Dermatophagoides farinae* (74.3%) led the sensitization profile, supporting their central role in routine diagnostic panels. Sensitization to storage mites was also frequent, with *Lepidoglyphus destructor* identified in 57.8% of patients. This may reflect environmental changes or improved detection and highlights the need to include storage mites in routine panels. The proportion of patients sensitized to *Dermatophagoides farinae* was higher than that of *Lepidoglyphus destructor*, in accordance with previous regional reports.[16] *Blomia tropicalis*, although more prevalent in tropical and subtropical regions, was also detected in nearly one-quarter of the sample, confirming its emerging relevance in southern Europe.[17] Considering that our study was conducted mainly in the northern part of the country, these findings may also be influenced by changing climatic conditions.

The observed sensitization to pollens reflects the diversity of Portuguese flora and aligns with previous aerobiological studies demonstrating regional differences in pollen prevalence across the country.[17] Sensitization to grass pollens, both wild and cultivated, was particularly prevalent, especially among older children, which may mirror increased outdoor exposure and seasonal allergen load. Sensitization to tree pollens such as *Olea europaea*, *Platanus acerifolia*, and *Parietaria judaica* also varied regionally, highlighting the influence of local vegetation and climatic conditions.[17-19]

A geographic gradient was observed in our study, with patients from coastal areas presenting higher rates of sensitization to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, and those from inland regions showing greater sensitization to pollens, animal epithelia, and molds, although the latter findings are based on unadjusted observations. These patterns are likely influenced by environmental and housing differences, levels of humidity, and biodiversity, and reinforce the need for region-specific diagnostic strategies.[17,19]

Table 3 – Distribution of allergic diseases and sensitization profile according to migratory status

Variable	Migrants (%)	Non-migrants (%)	*p*-value
Allergic diseases			
Rhinitis (n = 2915)	82.5	83.2	0.718
Asthma (n = 2859)	57.1	55.7	0.607
Conjunctivitis (n = 2831)	27.2	24.5	0.277
Atopic dermatitis (n = 2918)	21.9	19.8	0.351
Asthma + rhinitis (n = 2845)	48.2	42.4	0.069
Isolated asthma (n = 2798)	7.0	10.9	**0.027**
Isolated rhinitis (n = 2798)	18.5	22.6	0.090
Sensitization profile			
Dermatophagoides pteronyssinus (n = 2806)	86.5	85.0	0.421
Dermatophagoides farinae (n = 2667)	60.2	76.5	**< 0.001**
Lepidoglyphus destructor (n = 2610)	54.0	58.9	0.071
Blomia tropicalis (n = 852)	11.6	29.2	**< 0.001**
Acarus siro (n = 523)	0.9	1.7	0.704
Dog epithelia (n = 2391)	13.5	23.0	**< 0.001**
Cat epithelia (n = 2398)	18.5	29.1	**< 0.001**
Wild grass pollen (n = 2504)	32.9	54.1	**< 0.001**
Cultivated grass pollen (n = 1842)	22.7	38.2	**< 0.001**
Parietaria judaica (n = 1940)	2.8	8.1	**< 0.001**
Platanus acerifolia (n = 1545)	2.7	10.3	**< 0.001**
Olea europaea (n = 2122)	7.4	19.3	**< 0.001**
Cupressus (n = 1102)	0.4	3.3	**0.007**
Aspergillus fumigatus (n = 1278)	0.0	2.3	**0.001**
Alternaria alternata (n = 2160)	2.8	9.6	**< 0.001**

The analysis of sensitization profiles in migrant children is particularly relevant given the rising migration flows into Portugal, and our study encompassed migrant patients from diverse countries of origin. In unadjusted comparisons, while the clinical prevalence of AD was similar between migrants and non-migrants, sensitization profiles differed, with migrant children showing lower sensitization rates to several common Portuguese allergens. However, in adjusted analyses, migratory status was not an independent predictor of sensitization to at least one house dust mite (Model A), not supporting a generally lower house dust mite sensitization rate among migrant children. These patterns may reflect prior exposures in their countries of origin, genetic background, or mismatches in testing panels. Moreover, previous international cohort studies demonstrate that sensitization rates and allergen patterns vary with migrant origin.[10,20] This underlines the importance of considering migratory history in allergology assessment, as current SPT panels may not fully capture relevant sensitizations in this population.

Given the high rates of polysensitization (58.4%), identifying specific allergens is critical to guide environmental control and allergen-specific immunotherapy (AIT). In pediatric patients, AIT has been shown to reduce symptom severity, improve quality of life, and potentially modify the course of AD.[21,22] Although molecular diagnostic tools are increasingly available and may provide more precise identification of clinically relevant components, their accessibility may be limited. In this context, SPT continues to be a first-line, cost-effective, rapid, and informative approach in daily clinical practice.[5,6]

Importantly, our multivariable analysis that included both sensitization patterns and asthma diagnosis corroborated these clinical associations. In the asthma diagnosis model, sensitization to house dust mites and to animal epithelia remained independently associated with asthma after adjustment for age, sex, location, migratory status, environmental exposures, and other allergen families. These findings confirm the central role of indoor allergen sensitization in pediatric asthma. Additionally, exposure to tobacco smoke emerged as an independent factor associated with asthma in our study. This aligns with the established epidemiological evidence linking secondhand smoke exposure to pediatric asthma risk and supports reinforcing smoking avoidance policies in households of allergic children.[23,24]

Table 3 – Multivariable logistic regression models for sensitization patterns and asthma diagnosis.

Predictor	Model A		Model B		Model C		Model D	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age (years)	0.994 (0.95 - 1.04)	0.779	0.932 (0.91 - 0.96)	< 0.001	1.057 (1.03 - 1.09)	< 0.001	0.969 (0.93 - 1.00)	0.095
Inland hospital	0.255 (0.18 - 0.37)	< 0.001	0.697 (0.53 - 0.93)	0.013	1.184 (0.86 - 1.63)	0.302	0.444 (0.30 - 0.65)	< 0.001
Female sex	1.122 (0.81 - 1.55)	0.486	1.092 (0.91 - 1.32)	0.354	0.830 (0.66 - 1.04)	0.103	0.822 (0.63 - 1.07)	0.142
Non-migrant	0.535 (0.28 - 1.04)	0.066	0.908 (0.68 - 1.22)	0.518	1.784 (1.26 - 2.54)	0.001	0.686 (0.44 - 1.07)	0.097
No tobacco smoke	0.613 (0.42 - 0.90)	0.012	0.995 (0.81 - 1.22)	0.958	1.185 (0.93 - 1.51)	0.166	0.637 (0.48 - 0.84)	0.002
No household dampness	0.722 (0.49 - 1.06)	0.098	1.073 (0.87 - 1.33)	0.510	1.152 (0.90 - 1.48)	0.267	1.034 (0.77 - 1.38)	0.820
No domestic animals	1.224 (0.89 - 1.69)	0.218	1.031 (0.86 - 1.24)	0.751	1.428 (1.14 - 1.79)	0.002	1.116 (0.86 - 1.45)	0.414
No family history of atopy	1.033 (0.73 - 1.46)	0.855	1.274 (1.05 - 1.55)	0.016	0.811 (0.64 - 1.03)	0.086	0.803 (0.61 - 1.07)	0.128
Sensitized to grass pollens							0.746 (0.57 - 0.98)	0.038
Sensitized to ≥ 1 house dust mite species							1.808 (1.22 - 2.68)	0.003
Sensitized to animal epithelia							1.441 (1.08 - 1.92)	0.012
Sensitized to molds							0.684 (0.42 - 1.12)	0.131
Sensitized to other plants							0.798 (0.50 - 1.26)	0.334
Sensitized to tree pollens							1.433 (0.95 - 2.15)	0.084

OR: odds ratio; CI: confidence interval
All models showed statistically significant improvement over the null model ($\Delta\chi^2$, $p < 0.001$), with Nagelkerke R^2 ranging from 0.031 to 0.092.
Model A outcome: sensitization to at least one house dust mite species.
Model B outcome: monosensitization.
Model C outcome: sensitization to grass pollens.
Model D outcome: asthma diagnosis.

This study has some limitations, which should be carefully considered when interpreting the findings. First, its retrospective design may have led to missing or incomplete data in clinical records, particularly regarding environmental exposures and family history. Second, several comparisons were based on unadjusted analyses and should be interpreted as descriptive, since residual confounding cannot be excluded. Third, there was no standardization of all allergen extracts used across hospitals, and some (e.g., *Blomia tropicalis*, *Aspergillus fumigatus*, *Acarus siro*, and cultivated grass pollen) may present higher prevalence rates. Fourth, most of the participating hospitals were in coastal (87.2%) and northern (85.4%) regions of Portugal, which may reduce the generalizability of the findings. Fifth, information regarding the manufacturer of the SPT extracts was not consistently recorded in electronic medical records, and in many cases the company was not specified. Therefore, this information could not be systematically collected, and it was not possible to reliably stratify the results according to the commercial brand. Sixth, the study included only patients with positive SPT, which introduces selection bias. As a result, our findings are not generalizable to the general pediatric population. Seventh, molecular diagnostic techniques were not analyzed in this study, limiting our ability to distinguish genuine primary sensitization from cross-reactive patterns.

Future studies should include longitudinal follow-up of sensitized children, and integration of molecular diagnostic techniques to refine allergen profiles. They should also be designed with standardized, prospective data collection that allows robust multivariable statistical modelling. It is also necessary to expand the scope of investigation to other regions of Portugal, particularly the South and inland areas. Comparative studies with other Mediterranean countries may also help contextualize our findings and improve cross-border allergy management strategies.

CONCLUSION

This multicenter study provides a comprehensive overview of allergen sensitization profiles in a large pediatric population across Portugal, highlighting significant regional and demographic variations. The predominance of sensitization to house dust mites and grass pollens, the high frequency of polysensitization, and the distinct profiles observed in migrant children emphasize the importance of tailored diagnostic and therapeutic strategies in pediatric allergy care. Given the progressive nature of AD and the role of early sensitization in disease development, SPT remains a fundamental tool in guiding clinical decisions, including the timely initiation of AIT. These findings underscore the need for continued surveillance of allergen exposure patterns, particularly in the context of changing environments and population dynamics. Future research should address prospective data collection and molecular confirmation of sensitization and explore longitudinal outcomes to better understand the natural history and modifiability of AD in childhood.

PREVIOUS AWARDS AND PRESENTATIONS

"Skin prick testing in a Portuguese paediatric population – a multicentric study" – Poster viewing and discussion on EAACI PAAM Hybrid 2023, Porto, Portugal.

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The authors have declared that no AI tools were used during the preparation of this work.

AUTHOR CONTRIBUTIONS

MLF: Study conceptualization and design, data collection, interpretation and statistical analysis, drafting and critical review of the manuscript.

MM: Study conceptualization and design, data collection, interpretation and statistical analysis, critical review of the manuscript.

ARA, ST: Study conceptualization and design, data collection, critical review of the manuscript.

DSP, JNO, AO, MP, PG, AAz, FA, FC, CS, IF, MJD, MQ, RSP, RSS, AAs, DB, SJ, ABG, DG, HJ, DH, PS, SG, AS, MS, TSS, HR, IE, MN, LT, PG, RS, ALC, GO, RB, FC, MRM, RLP: Data collection, critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Imported Malaria in Portugal: A Retrospective Analysis from a Tertiary Public Hospital

Malária Importada em Portugal: Uma Análise Retrospetiva de um Hospital Público Terciário

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ABSTRACT

Imported malaria remains a clinical and public health challenge in non-endemic countries. This retrospective study analyzed all adult malaria cases diagnosed at Hospitais da Universidade de Coimbra between 2020 and 2024, and the aim was to characterize the epidemiological profile, assess the impact of previous malaria history, and identify biomarkers associated with disease severity. A total of 88 patients were included, mostly male expatriates, with exposure primarily in Angola. Previous malaria history was reported in 52.3% of cases. Severe malaria was diagnosed in 25.0% of patients, being significantly more frequent among those without a prior history of the disease ($p = 0.027$). These patients had significantly higher creatinine ($p = 0.009$) and lactate dehydrogenase ($p = 0.038$) levels, suggesting an increased risk of complications. Urea and parasitemia were independently associated with longer hospital stay ($p < 0.001$ and $p = 0.016$, respectively), used here as a proxy for severity. These findings support the hypothesis of semi-immunity in previously exposed individuals and highlight the potential of laboratory biomarkers for clinical risk stratification. Continuous surveillance and targeted prevention strategies for non-immune and semi-immune travelers remain essential, especially in countries like Portugal, where malaria reintroduction can be a real concern.
Keywords: Communicable Diseases, Imported/epidemiology; Emigrants and Immigrants; Immunity; Malaria/epidemiology; Portugal

RESUMO

A malária importada continua a representar um desafio clínico e de saúde pública em países não endémicos. Este estudo retrospetivo analisou todos os casos de malária diagnosticados em adultos nos Hospitais da Universidade de Coimbra, entre 2020 e 2024, com o objetivo de caracterizar o perfil epidemiológico, avaliar o impacto da história prévia de malária e identificar biomarcadores associados à severidade da doença. Foram incluídos 88 doentes, maioritariamente homens expatriados, expostos sobretudo em Angola, dos quais 52,3% apresentava história prévia de malária. Classificaram-se 25.0% dos casos como malária severa, sendo esta mais frequente nos doentes sem história prévia ($p = 0,027$). Nestes, os níveis de creatinina ($p = 0,009$) e desidrogenase lática ($p = 0,038$) foram significativamente mais elevados, sugerindo maior risco de complicações. Ureia e parasitémia mostraram associação independente com a duração do internamento ($p < 0,001$ e $p = 0,016$, respetivamente), utilizadas como marcadores indiretos de gravidade. Estes dados apoiam a hipótese de semi-imunidade em doentes previamente expostos e realçam o potencial de marcadores laboratoriais na estratificação do risco clínico. A vigilância contínua e estratégias de prevenção dirigidas a viajantes não imunes e semi-imunes permanecem essenciais, especialmente em países como Portugal, onde a reintrodução da malária pode ser uma preocupação real.
Palavras-chave: Doenças Transmissíveis Importadas/epidemiologia; Emigrantes e Imigrantes; Imunidade; Malária/epidemiologia; Portugal

Malaria, caused by *Plasmodium* spp. and transmitted by *Anopheles* mosquitoes, is endemic to tropical regions, but globalization and climate change have increased the risk of reintroduction in malaria-free areas, including Europe.[1,2]

In Portugal, endemic malaria transmission ceased in 1959.[2] In recent decades, international travel to tropical destinations and migratory flows between Portugal and malaria-endemic regions, particularly from lusophone African countries, have contributed to the occurrence of imported malaria.[3] Among migrants and expatriates who spend extended periods in endemic areas, repeated exposure to the parasite can occur. Such cumulative exposure may lead to partial immunity (semi-immunity), reducing disease severity, while differences in immunity can affect presentation, treatment, and prognosis.[4]

Across Portugal, competent *Anopheles* vectors coexist with imported malaria cases. Clusters combining high vector density and imported infections have been documented in Condeixa-a-Nova (Coimbra) and other regions of the country. Given that Condeixa-a-Nova falls within our hospital's catchment area, this case underscores the local relevance of investigating imported malaria.[2,5]

The aim of this study was to characterize imported malaria cases diagnosed at Hospitais da Universidade de Coimbra (HUC) between 2020 and 2024. We focused on geographic origin, prior malaria history, as well as disease severity. In addition, we explored the association between laboratory markers and hospitalization outcomes, under the hypothesis that specific biomarkers may reflect severity and predict length of stay. These insights may ultimately support better clinical practice in a setting with a considerable burden of imported malaria, where reintroduction remains a concern.[5]

This retrospective cohort study included every adult (≥ 18 years) patient with laboratory-confirmed malaria diagnosed at HUC, Portugal, between 2020 and 2024. Data was

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extracted from the hospital electronic records.

The diagnosis of malaria was made by microscopic examination of thick/thin blood smears, with parasitemia as percentage of infected red blood cells. The diagnosis of severe *Plasmodium falciparum* malaria was defined according to current World Health Organization (WHO) criteria.[6]

Descriptive statistics were used to summarize demographic, clinical, and laboratory data. Comparisons used chi-square/Fisher's for categorical and t-test/Mann-Whitney for continuous variables. Variables associated with hospitalization length in univariate analysis were entered into linear regression; due to multicollinearity, blood creatinine and lactate dehydrogenase (LDH) were excluded. The model included urea, bilirubin, platelets, age, and parasitemia. Linear regression assumptions were verified.

Analyses were two-tailed, with $p < 0.05$ considered significant, and performed in SPSS v29.

A total of 88 malaria cases were recorded between 2020 and 2024. Fig. 1 shows the annual trend in total and severe malaria cases and Table 1 details the demographic, biological, and clinical characteristics of the study population according to previous malaria history. The cohort (mean age 47.4 years) was mostly male (86.4%), Portuguese (75.0%), with exposure mainly in Sub-Saharan Africa (97.7%). Angola accounted for 59 cases (67.1%), followed by Mozambique (6; 6.8%) and the Ivory Coast (3; 3.4%). Uganda, Central African Republic, Mali, Equatorial Guinea, Gabon, and Ghana each contributed two cases (2.3%), while single cases were imported from Tanzania, Democratic Republic of Congo, Sierra Leone, Guinea-Bissau, Nigeria, São Tomé and Príncipe and India. A previous history of malaria was reported in 46 (52.3%) patients; among expatriates, 58.3% had previous episodes of malaria.

Lower blood LDH ($p = 0.038$) and creatinine ($p = 0.009$) levels were significantly associated with previous malaria episodes. Severe malaria was diagnosed in 25.0% of patients, most commonly due to jaundice and hyperparasitemia (50.0% and 41.0% of severe cases, respectively), as defined by WHO criteria; and was significantly more frequent in those without a prior history of malaria ($p = 0.027$). All severe malaria cases were due to *P. falciparum*.

Hospitalization length was positively associated with urea, LDH, creatinine, bilirubin, parasitemia and age, and negatively with platelet count in univariate analysis (all $p < 0.05$). In the multivariate model, urea ($p < 0.001$) and parasitemia ($p = 0.016$) remained independently associated with longer stays.

Between 2020 and 2024, we observed a rising number of imported malaria cases at our hospital, with a marked increase post-COVID-19. This trend reflects Portuguese and European data, where malaria resurged after travel restrictions eased.[7]

Prior malaria exposure influenced disease presentation. In our expatriate group, 58.3% had a history of malaria, in line with findings from another Portuguese study.[3] Consistent with the semi-immunity hypothesis, our data indicate that patients with a prior history of malaria were more likely to present with milder disease, aligning with previous reports.[4,8,9]

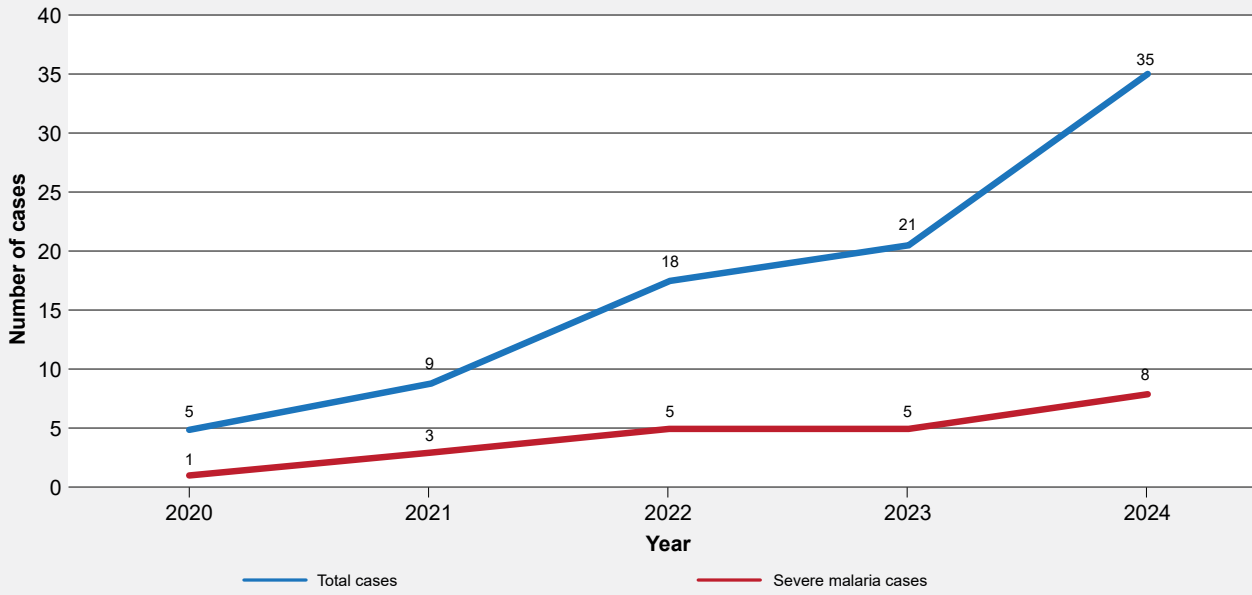

Figure 1 – Trends in total and severe malaria cases, by year, at Unidade Local de Saúde Coimbra (2020 - 2024)

Table 1 – Demographic, biological characteristics and outcomes of malaria cases diagnosed at HUC, all and according to history of malaria (section 1 of 2).

Analytical markers, treatment and outcomes	All	Previous malaria	No previous malaria	*p*-value
Number of cases, n (%)	88	46 (52.27)	42 (47.73)	
Age in years, Mean (SD)	47.44 (14.29)	49.17 (13.29)	45.55 (15.24)	0.237
Age group, n (%)				
18 - 24	6 (6.82)	2 (4.35)	4 (9.52)	0.419
25 - 34	14 (15.91)	5 (10.87)	9 (21.43)	0.245
35 - 44	17 (19.32)	11 (23.91)	6 (14.29)	0.253
45 - 54	21 (23.86)	10 (21.74)	11 (26.19)	0.625
55 - 64	21 (23.86)	13 (28.26)	8 (19.05)	0.311
> 64	9 (10.23)	5 (10.87)	4 (9.52)	1
Male, n (%)	76 (86.36)	41 (89.13)	35 (83.33)	0.429
Country of exposure, n (%)				
Angola	59 (67.05)	31 (67.39)	28 (66.67)	0.942
Others	28 (31.82)	14 (30.43)	14 (33.33)	0.771
Unknown	1 (1.14)	1 (2.17)	0 (0.00)	1
Nationality, n (%)				
Portuguese	66 (75.00)	34 (73.91)	32 (76.19)	0.805
Angolan	15 (17.00)	9 (19.57)	6 (14.29)	0.511
Other	6 (6.82)	3 (6.52)	3 (7.14)	1
Unknown	1 (1.14)	0 (0.00)	1 (2.38)	0.477
Type of traveler, n (%)				
Expatriates	48 (54.55)	28 (60.87)	20 (47.62)	0.284
Short trip	22 (25.00)	8 (17.39)	14 (33.33)	0.093
Mission	4 (4.55)	2 (4.35)	2 (4.76)	1
Recent immigrant	10 (11.36)	6 (13.04)	4 (9.52)	0.603
Unknown	4 (4.55)	2 (4.35)	2 (4.76)	1
Species, n (%)				
P. falciparum	73 (82.95)	35 (76.09)	38 (90.48)	0.073
P. ovale	6 (6.82)	4 (8.70)	2 (4.76)	0.678
P. vivax	3 (3.41)	2 (4.35)	1 (2.38)	1
P. malariae	2 (2.27)	2 (4.35)	0 (0)	0.495
P. falciparum + P. ovale	2 (2.27)	2 (4.35)	0 (0)	0.495
Unknown	2 (2.27)	1 (2.17)	1 (2.38)	1
Symptoms evolution, days **Median** (IQR)	4.00 (2.00 - 4.00)	4.00 (2.25 - 5.00)	4.00 (2.00 - 6.75)	0.521
Parasitemia, % **Median** (IQR)	1.50 (0.30 - 5.00)	1.50 (0.25 - 3.95)	1.00 (0.48 - 5.50)	0.809
Platelet count, 10^3/(µL) **Median** (IQR)	56.00 (35.00 - 100.00)	64.70 (38.75 - 101.75)	48.00 (26.00 - 96.00)	0.073
Hemoglobin, g/dL **Mean** (SD)	13.46 (2.20)	13.18 (2.00)	13.77 (2.40)	0.216
Creatinine, mg/dL **Median** (IQR)	0.94 (0.83 - 1.13)	0.90 (0.83 - 0.99)	1.05 (0.85 - 1.79)	**0.009***
Urea, mmol/L **Median** (IQR)	2.80 (2.13 - 3.88)	2.75 (2.08 - 3.60)	2.85 (2.15 - 4.25)	0.561
Bilirubin, mg/dL **Median** (IQR)	1.60 (1.10 - 2.69)	1.55 (1.10 - 2.78)	1.70 (1.00 - 2.66)	0.808
Creatine kinase, U/L **Median** (IQR)	72.00 (41.00 - 113.00)	55.00 (40.00 - 99.00)	73.00 (46.00 - 128.50)	0.192
LDH, U/L **Median** (IQR)	355.00 (270.00 - 519.00)	326.00 (252.00 - 458.00)	400.50 (293.00 - 551.25)	**0.038***

A/L: artemeter-lumefrantine; ICU: intensive care unit; IMCU: intermediate care unit; IQR: interquartile range; P.: *Plasmodium*; SD: standard deviation

*: *p*-value < 0.05 and therefore statistically significant. The tests performed are the Student's *t*-test or the non-parametric Wilcoxon-Mann-Whitney test, Pearson's chi-squared test or Fisher's exact test depending on the type of variables.

Table 1 – Demographic, biological characteristics and outcomes of malaria cases diagnosed at HUC, all and according to history of malaria (section 2 of 2).

Analytical markers, treatment and outcomes	All	Previous malaria	No previous malaria	*p*-value
Cases with severe malaria at admission, n (%)	22 (25.00)	7 (15.22)	15 (35.71)	**0.027***
Outcome, n (%)				
Outpatient	15 (17.05)	10 (21.74)	5 (11.90)	0.220
Ward	52 (59.09)	28 (60.87)	24 (57.14)	0.722
IMCU	15 (17.05)	5 (10.87)	10 (23.81)	0.107
ICU	6 (6.82)	3 (6.52)	3 (7.14)	1
Length of hospitalization, days **Median** (IQR)	4.00 (3.00 - 7.00)	4.00 (3.00 - 6.00)	5.00 (3.00 - 7.50)	0.308
Antimalarial treatment, n (%)				
Artesunate, then A/L	42 (47.73)	17 (36.96)	25 (59.52)	**0.034***
A/L alone	39 (44.32)	26 (56.52)	13 (30.95)	**0.016***
Other combinations	5 (5.68)	2 (4.35)	3 (7.14)	0.666
Unknown	2 (2.27)	1 (2.17)	1 (2.38)	1

A/L: artemeter-lumefrantine; ICU: intensive care unit; IMCU: intermediate care unit; IQR: interquartile range; P.: *Plasmodium*; SD: standard deviation
*: *p*-value < 0.05 and therefore statistically significant. The tests performed are the Student's *t*-test or the non-parametric Wilcoxon-Mann-Whitney test, Pearson's chi-squared test or Fisher's exact test depending on the type of variables.

Our results indicated that patients without prior *Plasmodium* spp. exposure showed a higher risk of organ complications, such as acute kidney injury (AKI), with elevated creatinine levels. This aligns with reports showing that non-immune patients are more prone to AKI.[10] Similarly, patients without prior malaria had higher LDH levels.

We also evaluated whether admission laboratory values could predict outcomes, using length of hospital stay as a surrogate for severity. Urea and parasitemia emerged as independent predictors in multivariate analysis. Elevated urea and hyperparasitemia are recognized by the WHO as severity markers for malaria.[6] Our findings align with these definitions, as both biomarkers were independently associated with longer hospital stays.

Beyond individual clinical management, these findings have broader implications. The predominance of expatriates and exposure mainly in Angola highlight the need for targeted preventive strategies for high-risk groups. Strengthening awareness among healthcare providers and travelers could contribute to earlier diagnosis and improved outcomes. At the public health level, continuous surveillance is essential to promptly detect imported cases and mitigate the risk of local reintroduction.

This study has limitations. Its retrospective, single-center design may limit generalizability. Prior malaria history was self-reported and not verified serologically.

This short article updates the profile of imported malaria in Portugal, showing that patients without prior malaria episodes had more severe disease and worse biomarker profiles, suggesting partial protection from semi-immunity. Urea and parasitemia were independently associated with the outcome and may serve as useful markers for clinical risk stratification. Pre-travel counselling should be strengthened not only for tourists and business travelers, but also for expatriates and immigrants returning to endemic regions, as they remain at risk and may contribute to the reintroduction of malaria in Portugal.

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The authors have declared that no AI tools were used during the preparation of this work.

AUTHOR CONTRIBUTIONS

TVF: Data collection, analysis and interpretation, drafting of the manuscript.

GAS: Data analysis and interpretation, critical review of the manuscript.

VD: Data analysis, critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

ETHICS

The study was approved by the Ethics Committee of the ULS Coimbra (170/25 CE).

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Managing Data in Screening Programs: Challenges and Solutions

Gerir Dados em Programas de Rastreio: Desafios e Soluções

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ABSTRACT

Population-based screening programs are vital public health initiatives that enable the early detection of diseases, significantly reducing both morbidity and healthcare costs. As these programs expand, the management of the extensive data they generate becomes increasingly complex, highlighting the need for structured digital solutions. This narrative review article presents a pragmatic framework aimed at clarifying big data analytics tailored to the needs and practices of healthcare professionals and administrators, focusing on effective integration into routine screening workflows. To achieve effective data utilization, the process begins with systematic archiving, which involves cloud-based storage solutions capable of securely maintaining various data formats in compliance with regulatory standards, thus ensuring long-term accessibility and continuity. Subsequent real-time processing of screening data facilitates rapid decision-making and patient management by providing immediate validation and analysis, essential for maintaining the responsiveness of screening services. Transformation processes play a critical role in converting diverse data inputs into standardized, consistent formats, enabling seamless communication and exchange among multiple healthcare systems. Integration further builds upon this standardization, merging data from different healthcare providers and diagnostic centers into centralized analytical platforms. This unified approach enables comprehensive patient monitoring and supports predictive modeling for early identification of at-risk individuals. Advanced analytics, particularly process mining and predictive techniques, reveal inefficiencies within screening workflows, highlighting areas needing improvement. These methods help healthcare managers to streamline operations, optimize resources, and enhance overall program performance. Real-time visualization tools provide administrators with continuous, practical insights into operational dynamics, despite existing challenges related to data governance and system interoperability. This article illustrates these concepts through concrete examples from the colorectal cancer screening program in Northern Portugal and the response to the COVID-19 pandemic. The colorectal cancer screening scenario demonstrates how structured data management significantly boosts operational efficiency and healthcare accessibility. Meanwhile, the COVID-19 experience highlights the importance of having flexible digital infrastructures capable of quickly adapting to unexpected crises. Finally, ongoing investments in digital infrastructure, professional training, and comprehensive data governance are crucial for sustaining these improvements. This review provides clear, actionable knowledge to support healthcare professionals in adopting big data analytics effectively within preventive healthcare programs.

Keywords: Big Data; Data Management; Diagnostic Screening Programs; Public Health

RESUMO

Os programas de rastreio populacional permitem a deteção precoce de doenças, contribuindo para a redução da morbilidade e custos. Contudo, à medida que ganham escala, o enorme volume e heterogeneidade dos dados exigem soluções digitais robustas. Este artigo de revisão narrativa oferece um enquadramento pragmático para a aplicação de *big data* em rastreios, adaptado às práticas clínicas e de gestão com foco na integração eficaz nos fluxos de trabalho. A utilização eficaz dos dados inicia-se com o seu arquivo sistemático em plataformas de armazenamento na nuvem, seguras e em conformidade com as normas regulamentares, capazes de preservar múltiplos formatos de informação e garantir a acessibilidade a longo prazo. O processamento em tempo real possibilita decisões céleres sobre convocatórias, confirmação de diagnósticos e triagem subsequente, mantendo a capacidade de resposta dos serviços. Os processos de extração-transformação-carregamento normalizam dados provenientes de sistemas heterogéneos, assegurando consistência semântica e interoperabilidade. Esta normalização suporta a integração de registos clínicos, laboratoriais e administrativos em repositórios analíticos digitais que se encontram centralizados, permitindo uma visão longitudinal do percurso do utente. Com esta infraestrutura, é possível agilizar técnicas de mineração de dados e de modelação preditiva que ajudam a identificar indivíduos de maior risco, antecipar picos de afluência e identificar barreiras operacionais. Estes dados apoiam a alocação de recursos e o redesenho de processos, contribuindo para ganhos de eficiência e equidade. O recurso a ferramentas de visualização interativas traduz informação complexa em relatórios dinâmicos intuitivos, facilitando a monitorização contínua de indicadores e a tomada de decisões baseadas na evidência. Persistem desafios de governação de dados, financiamento e capacitação, exigindo políticas claras, formação contínua e mecanismos de auditoria regular a estes sistemas digitais. Este artigo ilustra estes conceitos através de exemplos concretos do programa de rastreio do cancro colorretal na região Norte de Portugal. Os investimentos sustentados em infraestrutura digital, formação profissional e governação de dados são essenciais para assegurar a sustentabilidade e o impacto operacional destes programas. Esta revisão oferece orientações práticas para apoiar profissionais de saúde na adoção eficaz de análises de *big data* em iniciativas de prevenção.

Palavras-chave: Big Data; Gestão de Dados; Programas de Rastreio; Saúde Pública

INTRODUCTION

Framing the problem

Population-based screening programs are essential public health initiatives aimed at early disease detection, particularly in asymptomatic populations. By enabling timely interventions, they significantly enhance health outcomes, reduce morbidity, and decrease long-term healthcare costs. Diseases such as cancer, diabetes, and cardiovascular conditions benefit greatly from structured screening

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efforts, as early detection and interventions are associated with reduced mortality and a lower burden on healthcare services.[1,2] However, as programs expand, they generate massive and diverse datasets that are increasingly difficult to manage using traditional systems. Without scalable digital infrastructures, the success of screening efforts risks becoming a logistical burden, delaying interventions, and straining public health services.

Effective health programs are guided by rigorous frameworks, which uphold evidence-based and regularly updated protocols that reflect the advances in research. In cancer screening, for instance, the application of new detection technologies such as genomics and liquid biopsies has improved awareness and accessibility to screening options. However, these do not come without challenges, such as managing the risks of overdiagnosis and false positives. Balancing the benefits against potential harms requires a nuanced approach, guided by robust data systems and transparent methodologies.[3-5] Adhering to guidelines and aligning with population health goals ensures maximum benefit with minimal harm.[6]

Integrated data infrastructure enhances program effectiveness by tracking participation, compliance, and outcomes, while also addressing disparities driven by socioeconomic and demographic barriers. However, achieving a high level of integration demands sophisticated tools capable of handling the multifaceted challenges of what is often referred to as 'big data'.[7,8]

Big data in healthcare

As screening programs expand, the resulting data increases not only in volume but also in complexity, posing significant challenges for storage, integration, and analysis.[3,9] These datasets, sourced from various clinical, administrative, and diagnostic systems, present challenges rooted in the core characteristics of big data, that healthcare professionals must increasingly navigate as part of routine practice. Integrating big data techniques into screening programs enhances their efficiency and scalability, but only if such techniques are well understood and embedded into everyday workflows.[10,11] Digital platforms facilitate data collection, integration, and processing, enabling real-time analytics that drive proactive decision-making (Fig. 1). This capacity transforms data from a passive record into an active tool for clinical and managerial insight, guiding early interventions and optimizing resource use. One way to approach this is by viewing data flows as a continuous pipeline, from capture to insight. In this model, each phase, from data generation to final analysis, must be intentionally designed to avoid fragmentation and delays that could compromise patient care. The challenges can be analyzed through the five key characteristics of big data: volume, velocity, variety, veracity, and value. Each of these traits presents specific requirements for healthcare systems.

- A high **volume** of data is generated while harnessing big data in healthcare, which entails leveraging diverse datasets, including electronic health records (EHRs), imaging, and laboratory results.
- **Velocity** in data processing is essential for real-time decision-making and timely follow-up with patients.
- Data **variety** requires interoperable systems to integrate the diversity of data sources, from electronic health records to mobile health devices.
- Ensuring data **veracity** is critical, as inaccuracies and inconsistencies can lead to erroneous decisions and adverse patient outcomes.
- All the while, extracting **valuable** insights – which are important to provide meaningful perceptions that support preventive healthcare, refine screening strategies, and guide policy decisions - requires advanced analytics.

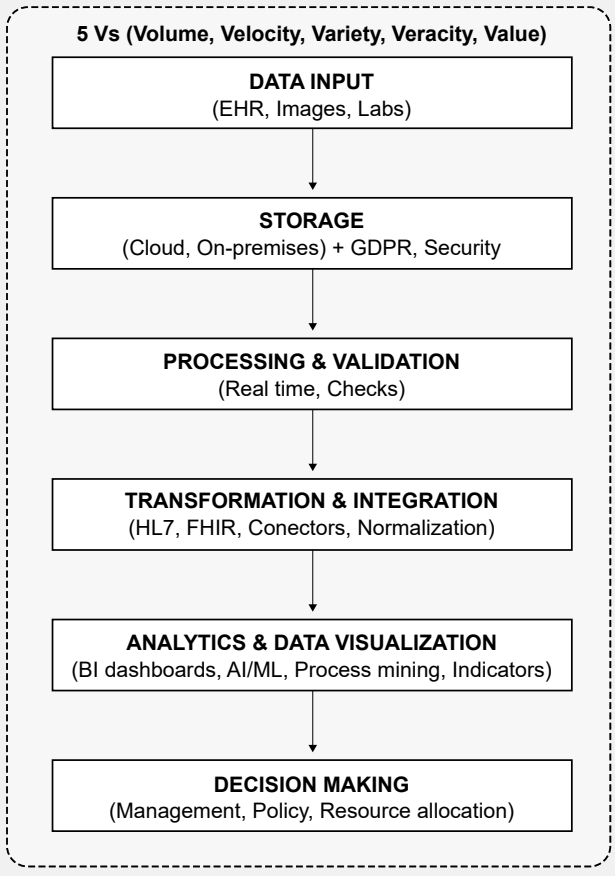

Figure 1 – The 'data pipeline'
EHR: electronic health record; GDPR: general data protection regulation; HL7: health level seven (a set of international standards for the exchange, integration, sharing, and retrieval of electronic health information); FHIR: fast healthcare interoperability resources (a standard describing data formats and elements for exchanging electronic health records); BI: business intelligence; AI/ML: artificial intelligence/machine learning

For healthcare professionals, understanding these concepts is no longer optional. They underpin the technologies that now influence everything from triage to follow-up scheduling. Tools like predictive analytics can flag patients at higher risk and prompt timely actions. Meanwhile, process mining techniques optimize workflow efficiency, reduce delays in patient follow-ups and resource allocations.[12] Advanced computational statistical models, including machine learning (ML) and artificial intelligence (AI), further enhance the capacity to uncover actionable patterns, refine protocols and improve program outcomes.[13,14]

However, the transition to big data-driven infrastructure does not come without challenges and requires more than access to software. It requires an alignment between data systems and clinical practice, ensuring that tools support – not replace – professional judgement. Therefore, integrating diverse data sources requires adherence to standardized data models.[15] Privacy regulations such as the General Data Protection Regulation (GDPR) introduce stringent requirements to safeguard sensitive health information. Furthermore, while advanced analytic methods hold promises, they must also address potential biases and maintain transparency to ensure patient trust and equity in healthcare delivery.[16]

To address these challenges, screening programs must implement structured, data-driven strategies that prioritize security, interoperability, and analytical rigor. Digital platforms play a key role in supporting the various needs of screening programs, including:

- Clinical needs: Facilitating patient care through EHRs and decision support systems.[17]
- Administrative needs: Optimizing scheduling, resource allocation, and reporting.[18]
- Process monitoring needs: Tracking workflow efficiency and program performance.[19]
- Data management: Ensuring data quality, security, and compliance with regulatory standards.[20]
- Financial oversight: Managing costs, billing, and financial analytics.[21]

By leveraging these principles in everyday operational realities, screening programs can improve operational efficiency, enhance equity in healthcare access, and maximize the impact of preventive interventions.[14] Drawing on lessons from Portugal's colorectal cancer screening program, this narrative review aimed to synthesize recent evidence and practice-based insights into a five-phase data management framework that can strengthen preventive medicine services. Colorectal cancer remains one of the leading causes of cancer death in Europe, presenting the need for robust screening strategies supported by effective digital systems. We present a practical overview of big data integration in real-world screening programs, highlighting both the persistent barriers and the solutions that have contributed to sustainable, outcome-oriented models.[22]

Handling data

To overcome the data management challenges of modern screening programs, we propose a structured, five-phase framework (archiving, processing, transformation, integration, analytics – Fig. 2) capable of addressing the unique challenges posed by the nature of this data.[3] In the following sections, we detail how each phase contributes to building resilient, interoperable, and insight-driven screening programs – drawing from real-world implementations in Northern Portugal.

Archiving: ensuring data longevity and compliance

Effective long-term data storage is critical for screening programs, as data must be retained for patient follow-ups, epidemiological studies, and quality control processes. Given the scale of these programs, traditional storage methods are insufficient, requiring cloud-based solutions that provide scalability, redundancy, and compliance with data protection regulations such as GDPR. Screening data often spans a wide range of formats, including structured EHRs, unstructured imaging files, and laboratory tests, all of which require tailored storage solutions. Modern storage solutions, such as cloud-based infrastructures, can enhance data accessibility and scalability. These systems should incorporate role-based access permissions and embedded security protocols to ensure compliance with confidentiality standards and data protection regulations.[23]

One of the persistent challenges in data archiving is managing legacy systems. Older databases were often designed without significant future expansions in mind, leading to difficulties when integrating with modern digital platforms. Additionally, storage costs increase over time, especially as screening programs expand their reach and generate more data, including high-resolution medical imaging.[24] Screening data in our experience grew from just a few megabytes per month to over dozens of GB within five years – making cloud scalability a non-negotiable requirement.

Addressing these challenges requires initiative-taking budget planning for storage infrastructure, periodic system upgrades, and interoperability frameworks that allow seamless data retrieval from both old and new systems.

Real-time processing: unlocking insights and enhancing efficiency

Timely data processing is a critical requirement in screening workflows, where delays in analyzing test results can impact early intervention efforts. Screening data flows continuously, from appointments to test results, which requires immediate validation and feedback loops.[25]

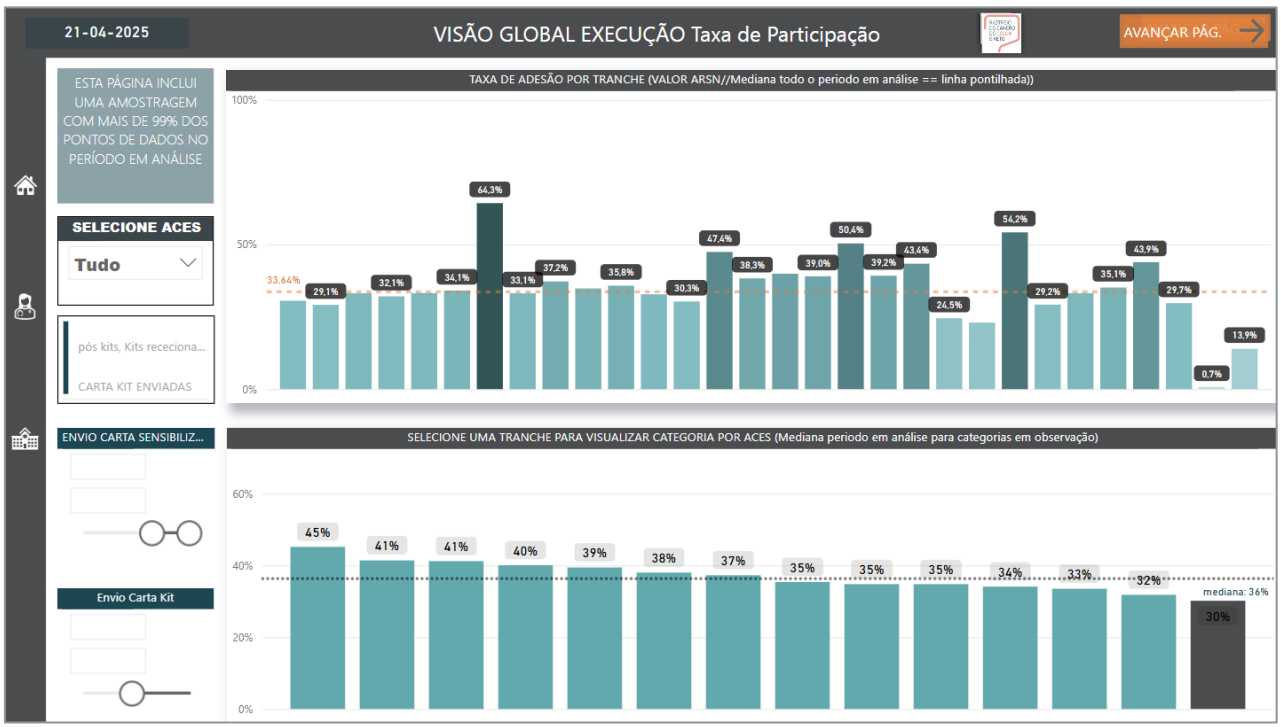

Figure 2 – Dynamic business intelligence "BI" report with multiple calculated metrics with different management perspectives to visualize patient enrollment in the screening program. Other pages of the report can provide more granular data or wider analytical perspectives. (hidden variables due to data sensitivity issues)

The complexity of screening workflows means that multiple healthcare professionals interact with patient data daily, requiring constant access to updated information. For example, radiologists reviewing mammograms, lab technicians processing blood tests, and administrative teams managing patient scheduling all rely on rapid and error-free data flow. To support this, automated data validation mechanisms should be implemented to ensure that input from various sources is accurate and actionable, reducing the risk of administrative errors and clinical misinterpretations. For example, real-time lab results are obtained by connecting lab machines to the same digital platform for screening management, errors in analysis are automatically provided to human technical experts and reviewed. System monitoring is critical to identify process bottlenecks and enable timely corrective action.

Transformation: standardizing data for consistency and usability

One of the most significant obstacles in screening data management is the variety of data formats and sources. Each screening modality – whether mammography, colonoscopy, or diabetic retinopathy detection – generates data in different structures, requiring transformation processes that standardize information for further analysis. Without transformation, screening data remains fragmented – hindering cross-institutional insights and automated reporting.

To facilitate this, standardized health data exchange frameworks such as HL7[26] and FHIR[27] must be employed, allowing seamless communication between different healthcare information systems.[28,29] Additionally, data preprocessing techniques should be used to clean, normalize, and structure raw data, ensuring that irrelevant or erroneous information is filtered out before integration. A key part of this process is ensuring semantic consistency, meaning that medical terminologies and classifications remain uniform across different systems. The alternative is to extract and manipulate data later, decreasing efficiency and increasing errors.

A major challenge in transformation is the presence of inconsistencies in primary data input formats, such as variations in date formats or different character sets in administrative records. Delays often stem from the lack of uniform transformation rules, especially when merging legacy data with evolving standards.

Integration and connectors: unifying data sources for holistic insights

After transformation, integration brings together data from diverse systems into a unified analytical environment,

enabling patient monitoring, performance evaluation, and predictive insights. Population-wide programs rely on integration to combine data from hospitals, labs, registries, and administrative platforms. Integration efforts ensure that screening data is not siloed and simply stored but rather accessible for holistic patient monitoring, predictive modeling, and program evaluation. Data from more than 30 institutions was consolidated and connected daily, changing reporting lags from weeks to minutes, making it possible to monitor thousands of different processes close to real time.

To achieve this, data lakes and relational databases should be used to store and unify data, allowing healthcare providers to retrieve both individual patient records and aggregated population-level insights. Additionally, data connectors are deployed to enable automated merging of screening data across multiple platforms, minimizing the need for manual reconciliation. These connectors facilitate cross-institutional interoperability.

However, integration presents challenges, particularly when connecting digital systems that rely on different technical standards. Numerous systems, including database management systems (DBMS), use proprietary protocols and data structures, thus making data exchange intricate and time-consuming. For example, differences between structured databases (such as those using SQL) and more common file formats like spreadsheets often require additional steps to align and prepare the data. Technical mismatches caused delays, errors, and duplications, slowing down analytics pipelines.

Analytics: unlocking actionable insights

The goal of screening data management is to extract valuable insights that improve program efficiency and patient outcomes. Process mining techniques are particularly useful in screening programs, as they allow managers to identify inefficiencies in operational workflows, such as delays in test processing, scheduling gaps, or bottlenecks in follow-up procedures.[30] Tools like Power BI,[31] MicroStrategy,[32] and R[33]/Python[34]-based dashboards enable healthcare administrators to monitor screening program performance dynamically.

Several challenges persist despite these advancements. The absence of clear application programming interface (API) integrations, standardized data governance policies, and well-defined analytical workflows often delay the implementation of advanced solutions. Additionally, the risk of biases in machine learning models must be carefully managed to prevent disparities in screening access and outcomes. Lastly, the effectiveness of data-driven insights is dependent on high-quality, clean, and well-structured datasets, which remain a significant challenge in real-world healthcare environments.

By following the principles described above, we will provide evidence of the experience of the implementation of such techniques in screening programs and solutions found in alignment with best practices.[35]

Lessons learned: data-driven health interventions

In the northern region of Portugal, screening programs were implemented using the discussed methods. These programs covered most of the eligible population over more than ten years and included both oncological and non-oncological areas.

Data archiving and storage challenges

Archiving has played a critical role since the inception and evaluation of screening programs. However, legacy systems have struggled to scale effectively, leading to bottlenecks as screening volumes increased. Initially, available server storage seemed sufficient. However, as the screening program expanded, growing storage needs and renewed processing demands underscored the need for strategic planning in acquiring more robust digital systems.

However, legacy databases posed difficulties in retrieval and integration due to outdated formats and limited compatibility with modern digital platforms. Solutions included targeted infrastructure upgrades and interoperability frameworks to bridge gaps with legacy databases.

Data integration and standardization

Digital platforms have facilitated the expansion of local implementations to broader populations by standardizing data processes and enhancing transparency. Real-time dashboards provide regional health program managers with immediate insights into underperforming areas, allowing targeted interventions to boost screening uptake.

A major challenge (Table 1) in data integration stemmed from disparate DBMS, inconsistent protocols, and variations in language formats and file structures. Lack of clear connectors to data forced manual data reviews, slowing issue detection and requiring high technical expertise. Overcoming these obstacles required continuous standardization efforts and signaled the need to accelerate the adoption of interoperability frameworks such as HL7 and FHIR.

Nevertheless, these platforms also supported the automation of routine processes, freeing up resources for strategic tasks and enabling faster deployment of updated workflows, providing more time to audit processes, replying to queries from local program coordinators or other healthcare professionals and even providing the opportunity to innovate. To provide a concrete figure, automating data collection of eligible patients can represent a task taking weeks to less than a few hours or even minutes. This enabled more accurate cost analysis and adjustments, ensuring

Table 1 – Summary of key challenges encountered in big data management for screening programs and the solutions implemented to address them

Concepts	Challenges in big data management	Experience
Archiving	Considering the volume of patients by the millions per year, multiple data sources are stored across servers in a widely distributed area.	It is required to define the format of data being stored; the size of the files (image files to be attached to reports can be sized by Gb or Tb); and additional budgeting might be required as technology improves not only in terms of the size of the software programs but also record size.
Processing	Servers dedicated to various aspects of data processing, as well as for image rendering, may be necessary.	If thousands of healthcare professionals work in multiple places and see patients every day, or if tests are performed daily, queries to the database to check administrative identification or validate past values are a constant.
Transformation	Primary data might be stored in wide table formats, or secondary data be the result of table merging during processing - to match records with new test results.	This requires a middle layer of specific processing to guarantee that data quality is assessed and that data values comply to regulatory standards. Indicators are also processed in this stage, where granular data is aggregated and computed to simplify signals or provide visual alerts.
Integration (connectors)	To view data from its multiple sources, where data is stored, and to transform data and provide the possibility of analyzing it, data must be integrated into a middle layer dedicated to the creation of semantic models.	Connectors from different DBMS are not mapped or established in protocols, this means that certain loaded files show differences in language formatting or type (e.g., .xls *versus* .xlsx) which delays the data handling process.
Analytics	Data Science is an end and a window to all the processes related to data. The abstraction of data into understandable concepts produces information and knowledge	Due to the lack of clear API and User profiles, mapped entities, or standard data protocols to ensure quality, analytics is a “delayed” product. Where it is easier to provide descriptive analysis, and more advanced methods lack timely usefulness.

resource allocation closely matched demand, thereby avoiding overspending or underspending. These operational improvements, combined with standardized data pipelines, automation of routine processes, and structured training for key users improve capacity in scaling the framework across diverse institutional settings.

Advanced analytics and data utilization

Advanced analytics enabled descriptive, comparative, and scenario-based analysis, helping transform raw data into strategic decisions. Tools like Power BI allowed managers to explore large datasets and deliver tailored insights (example of dynamic dashboards presented in Fig. 2). For instance, visualizations of patient journeys helped identify drop-outs in screening adherence, allowing targeted outreach to improve follow-up rates.

Furthermore, process mining techniques revealed workflow bottlenecks and reduced operational delays through timely alerts and resource reallocation. This capacity to identify bottlenecks helped reduce the number of operational delays by facilitating timely adjustments in response to workflow dynamics. For example, whenever unexpected disruptions to services were detected, different resources responsible for ‘upstream’ or ‘downstream’ activities could be warned of the delays and adjust accordingly.

The robust data ecosystem also enabled more equitable access to healthcare services. Vulnerable populations, previously underrepresented, were provided free-of-cost screening tests, diagnostics, and treatment plans through the National Health System, supplemented by private care procurement agreements. By leveraging these tools and strategies, program managers ensured that the entire eligible population was included within a span of less than three years for each screening program. This comprehensive inclusion significantly enhanced the accessibility and impact of screening services, particularly in underserved regions.

Response capacity during COVID-19 and inclusive program maintenance

The adaptability of digital platforms proved essential in maintaining screening continuity during the COVID-19 pandemic. The ability to rapidly analyze large datasets and modify workflows ensured service resilience. The crisis exposed gaps in integration and coordination, reinforcing the need for interoperable, crisis-resilient systems. At the onset of the pandemic, disruptions to routine appointments and diagnostic follow-ups threatened to stall screening activities. Yet, digital infrastructure – equipped with centralized

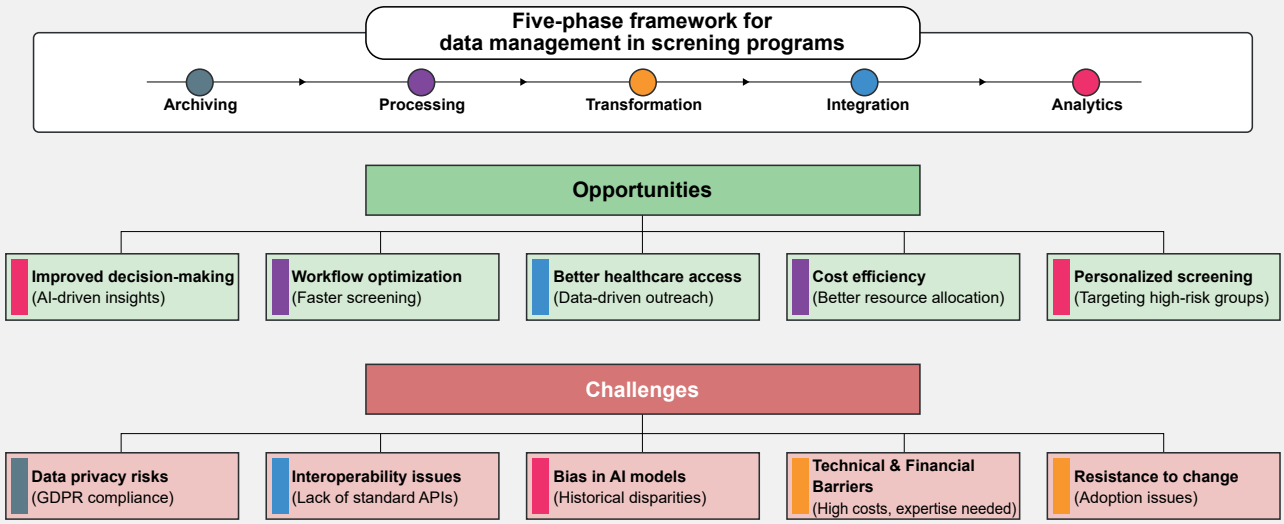

Figure 3 – Five-phase data-management framework (Archiving → Processing → Transformation → Integration → Analytics) and its relationship to the main opportunities and challenges of big data in screening programmes.
Each side colour bar reflects the data-management phase most closely associated with the corresponding opportunity or challenge. This mapping illustrates how each phase contributes to specific programme benefits, while simultaneously shaping the nature of the challenges encountered.

dashboards and automated data connectors – helped reschedule and reorganize screening appointments with minimal delays. Real-time dashboards helped coordinators detect service gaps and adjust schedules, avoiding prolonged care delays.

The pandemic experience reinforced that flexible data architectures, continuous workflow auditing, and stakeholder collaboration are key components in sustaining screening effectiveness under extreme circumstances. Going forward, building crisis-resilient infrastructure and workflows, with these tools and application of the concepts presented in this paper, will be instrumental for protecting public health and minimizing disruptions to essential services, even beyond COVID-19.

Training and capacity building for digital platforms

Even with strong digital platforms, success hinged on training healthcare professionals to use them effectively. Training programs were developed to enhance user proficiency in handling screening management tools and business intelligence (BI) dashboards.[36] Business intelligence tools had to be adapted to different user needs, from clinical staff to regional managers. Providing structured training sessions helped bridge digital skill gaps, ensuring seamless adoption and use of these technologies. Structured training, aligned to user roles, helped balance depth with practicality. Based on user profile and providing key users with the capacity to train others was essential to scale up faster digital platform usage.

Data driven screening programs

Big data strategies significantly improved efficiency, responsiveness, and equity in screening programs. However, the transition from traditional data handling to advanced digital ecosystems is not without challenges (Fig. 2), particularly in the context of critical healthcare scenarios where rapid adaptability is essential. Often, barriers such as limited funding and digital skills, not the technology itself, hinder implementation. This highlights the need for targeted investments in capacity-building and digital literacy.[37]

By integrating real-time dashboards, program managers could identify underperforming areas and bottlenecks, implementing targeted interventions with minimal delay. For instance, during periods of increased demand, such as flu seasons or post-pandemic recovery, quick access to updated data prevented the system from becoming overwhelmed, allowing for adequate distribution of resources. However, reliance on digital tools introduces vulnerabilities, including potential system downtimes, data input errors, and risks related to data integrity. Implementing strong data governance frameworks and redundancy measures is critical to mitigating these risks. Furthermore, privacy concerns and compliance with regulations like GDPR add layers of complexity, particularly in the context of cross-platform data sharing. Balancing transparency with data security remains a delicate and ongoing challenge.

Another key area of discussion is equitable access. Results show that big data tools enabled significant improvements in reaching underserved populations. This raises the

question of how such systems can maintain inclusivity as they scale up further. Critical situations, such as natural disasters or sudden economic downturns, could exacerbate existing disparities. Proactive measures, such as incorporating geographic information systems to identify and address spatial inequities, could further strengthen the inclusiveness of these programs.[38]

Predictive analytics and process mining have greatly optimized screening workflows, but biases inherent to historical data can inadvertently perpetuate healthcare disparities.[39] Transparency in algorithm development and continuous model auditing are necessary to maintain fairness in care delivery. Additionally, maintaining historical data consistency is important, as structural changes in data catalogs over time can introduce analytical gaps, affecting long-term decision-making. Similarly, while process mining has proven effective in identifying inefficiencies, its reliance on comprehensive and accurate workflow data means that gaps in data coverage can lead to incomplete or misleading insights. Considering the time that these programs have been present, changes in the data catalogue or table structure might have introduced historical gaps in knowledge.

The COVID-19 pandemic highlighted both the strengths and weaknesses of digital screening infrastructures. While rapid adaptation and workflow flexibility ensured continuity, the crisis underscored the need for enhanced intersectoral collaboration, interoperability, and contingency planning to ensure seamless service delivery during future disruptions. Further underscoring the significance and potential for broader application, these results have been previously presented at European Public Health congress.[40]

Further research is needed to validate this framework in different national and regional contexts, particularly regarding its operational impact and scalability. Exploring how it performs across varied digital infrastructures and screening program designs will help determine its broader applicability. In parallel, assessing the role of advanced analytics and real-time monitoring in improving clinical outcomes remains a critical area for continued investigation.

CONCLUSION

Successful screening programs depend on integrating digital infrastructure with skilled professionals, ensuring that technology enhances – rather than replaces – clinical decision-making. Ongoing investment in training and capacity-building will ensure that expertise keeps pace with technological advancements.

Leveraging big data management techniques can further enhance program effectiveness. Patient engagement improves service quality and fosters trust, while quick, valuable insights and their integration into the decision-making process enable targeted interventions, ensuring equitable access and efficient resource allocation.

The discussion published here demonstrates the amount of investment required, not only in technological tools but also in highly skilled professionals. There is a further need to research how to innovate while compelling workers to keep up with innovative technology (like new generative AI tools), as well as how to procure technologies that are as future-proof as possible, so that there is significant value for money in a relevant period.

Finally, integrating process mining techniques into digital platforms supports continuous monitoring and optimization of workflows.[40] This initiative-taking approach enhances responsiveness and sets the stage for AI-driven automation, enhancing scalability, equity, efficiency, and impact of screening programs in tackling public health challenges. Health authorities should prioritize structured data management as a strategic pillar in scaling equitable and resilient screening services.

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The authors declare that AI-assisted technologies were used solely to generate code for workflow figures; no AI tools were used in writing, editing, or reviewing the manuscript.

AUTHOR CONTRIBUTIONS

HM: Data interpretation, writing and critical review of the manuscript.

MO, RM, CM: Writing and critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

ETHICS

The study was conducted in accordance with relevant ethical guidelines. No direct patient involvement occurred, and all data used were anonymized and obtained from

authorized institutional datasets. All procedures complied with legal regulations and were approved by the Health Ethics Committee of the Regional Health Administration of Northern Portugal (CE/2023/96).

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Disentangling a Functional Speech Disorder in the Context of another Neurological Disease: A Case Report

Perturbação Funcional da Fala no Contexto de outra Doença Neurológica: Caso Clínico

Beatriz STEIN [1,2], Filipa SOTERO [1,2], José FONSECA [2]
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ABSTRACT

This clinical case describes the communication profile of a functional speech disorder. A 48-year-old woman was admitted to the emergency service due to sudden changes in speech, generalized dystonia and gait ataxia. Magnetic resonance imaging showed multiple supra and infratentorial inflammatory lesions involving the posterior occipito-temporal lobes bilaterally, frontal convexity bilaterally, insula and paramedian frontal cortex on the left, diencephalon, rhombencephalon. On the third day, a speech pathology evaluation was conducted, revealing inconsistencies in speech: repetitions of initial sounds, without characteristics of an acquired stutter, a clenched articulation, not justified by an orofacial motor disorder, an inconsistent pattern in voice and prosody. Three days later, another assessment was carried out, showing a significant improvement in speech intelligibility. There was a marked variability in speech features defects found over the days, as well as in their severity. These behaviors appear simultaneously with a speech pattern that is not justified by any of the neurological lesions found.
Keywords: Conversion Disorder; Psychophysiologic Disorders; Speech; Speech Disorders

RESUMO

Este caso descreve o perfil comunicativo de uma perturbação funcional da fala. Uma mulher de 48 anos foi admitida no serviço de urgência com alterações súbitas da fala, distonia generalizada e ataxia da marcha. A ressonância magnética mostrou múltiplas lesões supra e infratentoriais inflamatórias envolvendo lobos occipitotemporais bilateralmente, ínsula e córtex frontal paramediano esquerdos, diencéfalo e rombencéfalo. No terceiro dia, foi avaliada em Terapia da Fala, revelando inconsistências: repetições de sons iniciais, sem características de gaguez adquirida, articulação cerrada, sem defeitos de motricidade orofacial, flutuações na voz e prosódia. Passados três dias, foi efetuada nova avaliação, verificando-se uma melhoria significativa na inteligibilidade do discurso. Existe uma flutuação dos defeitos de fala encontrados ao longo dos dias, bem como da sua gravidade. Estes comportamentos surgem em simultâneo com um padrão de fala que não é justificado por nenhuma das lesões neurológicas.
Palavras-chave: Fala; Perturbação Conversiva; Perturbações da Fala; Perturbações Psicofisiológicas

INTRODUCTION

Functional speech disorders (FSD) are a subtype of functional neurological disorders. They can be characterized by speech manifestations that resemble those observed in other neurological disorders but cannot be fully explained by the underlying neurological or mental condition.[1] Some studies of FSDs suggested that the main manifestations include dysfluencies (pauses, hesitations and repetitions) articulatory errors, dysphonia (changes in vocal quality), and atypical prosody (changes in rhythm and melody).[2] The characteristics associated with motor speech disorders and FSD often overlap and can co-occur.[2,3] The literature regarding the identification and clinical evaluation of these disorders remains limited. Detailed case reporting is essential, as it provides valuable insights that enhance diagnostic accuracy and improve clinical decision-making.

CASE REPORT

A 48-year-old right-handed female patient, native European Portuguese speaker, with 12 years of formal education, was admitted to the emergency department. The patient was oriented, exhibiting an apparent stutter and marked changes in prosody. Moreover, she disclosed mild generalized dystonia as well as a postural and intentional tremor, a gait instability characterized by retropulsion (postural instability) and a widened base.

Brain magnetic resonance imaging (MRI) identified multiple supra- and infratentorial lesions in T2 FLAIR in cortico-pial topographies, predominantly in the posterior occipito-temporal lobes bilaterally and the frontal convexity bilaterally, insula and paramedian frontal cortex on the left, diencephalon, rhombencephalon, especially the thalamus, hippocampus, and internal capsule on the left (Fig. 1). A cerebrospinal fluid (CSF) analysis revealed 48 cel/mm^3 (< 5 cel/mm^3) with normal glucose and protein levels. Multiplex polymerase chain reaction (PCR) for infectious agents was negative. Serum serologies, as well as anti-MOG and anti-AQP4 antibodies, were also negative.

On the first day, a speech and language assessment was conducted, with an acquired neurogenic stuttering considered as being the most probable syndromic diagnosis. Various tasks were performed, including automatic speech, spontaneous and descriptive discourse, reading a text

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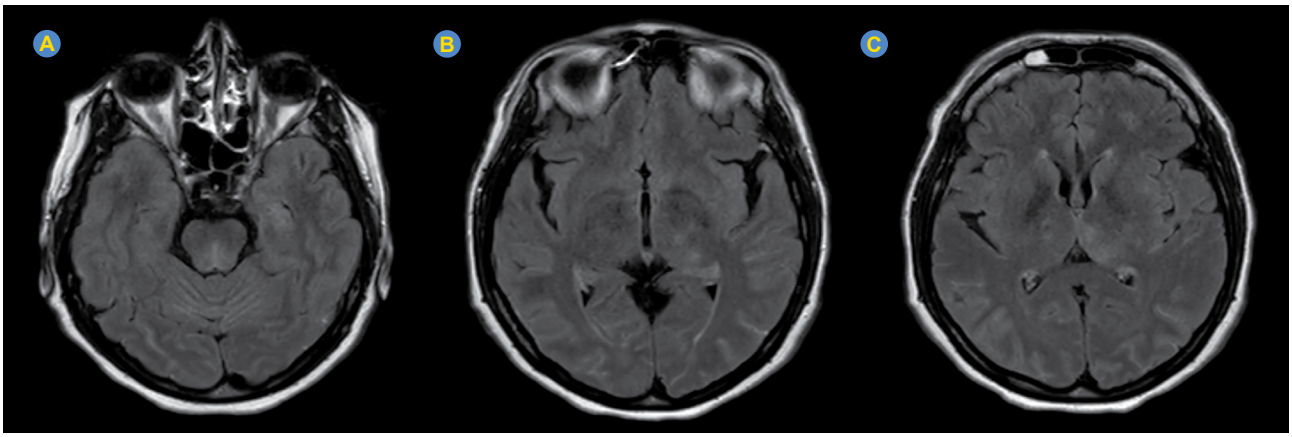

Figure 1 – Brain MRI (T2 FLAIR axial) showing multiple supra- and infratentorial lesions in posterior occipito-temporal lobes bilaterally and insula and paramedian frontal cortex on the left, along with hyperintensities on the left hippocampus and internal capsule. There are also hyperintensities in diencephalon and rhombencephalon, especially in the left thalamus.

aloud, singing, naming, auditory comprehension, word and phrase repetition.

In this first observation, the patient presented with disfluency (repetitions of syllables and initial sounds) in spontaneous speech, but not in narrative speech. Also, when asked to repeat words and phrases or even sing, the patient showed no dysfluency, a pattern that is not consistent with what is typically found in acquired stuttering.

Her speech was initially characterized by atypical features in articulation, phonation and prosody. Specifically, a clenched articulation in speech production was evident, marked by a low range of movement, a loss of articulatory precision and hypernasality, but again with an inconsistent behavioral pattern throughout the tasks. Phonation was characterized by fluctuations in pitch and intensity during a prolonged vowel production and prosody assessment revealed significant impairments: a monotonous speech and an inability to replicate various speech patterns or intonations.

The first language assessment revealed no difficulties in discourse, word finding, repetition, auditory comprehension, reading comprehension or writing abilities. All communicative behaviors were inconsistent, varying across tasks.

Given the clinical picture, the hypothesis of a FSD was considered by the multidisciplinary team (speech therapists, neurologists and psychiatrists). No correlations were found between the speech alterations and the neurological or imaging abnormalities. In addition, despite the higher prevalence of psychiatric comorbidities among patients with functional neurological disorders, no psychopathological findings were identified.

On the sixth day, the patient underwent a formal evaluation of language, speech and fluency, with an overall improvement in the clinical presentation. Regarding fluency, the disfluencies initially observed were no longer present upon reassessment. In terms of language, the patient produced grammatical errors, such as omission of constituents of the sentence, and also demonstrated difficulty identifying prosodic features and melodic contours associated with various phrases in a subtest of the Montreal Assessment Battery. Speech exhibited minimal impairments, such as fluctuations in articulatory performance, hypernasality, and prosody. As observed previously, there was no impairment in orofacial motor skills that could justify the noted defects. The patient used, predominantly, a low-intensity voice, but was able to increase loudness when asked. Occasionally, abrupt and exaggerated movements were observed during the assessment in performing rapid and alternating oral motor movement sequences.

Between the initial and second assessments, no treatment that could impact the clinical picture was administered. Although, given the possibility of inflammatory lesions on MRI and the presence of coordination and gait impairments, the patient was administered methylprednisolone 1 g IV for five days, resulting in a complete clinical, CSF and imaging resolution.

DISCUSSION

The patient exhibited a complete resolution of the initial dysfluencies and an improvement in speech intelligibility without any medical treatment. This included the complete resolution of the initial dysfluencies and an improvement in speech intelligibility. Although this might be considered a case of spontaneous recovery, the observed characteristics cannot be explained solely by a speech-related condition, as there were inconsistent error patterns, including disfluencies that improved with melody or repetition, features that are not characteristic of acquired stuttering. Additionally, there was an absence of orofacial abnormalities that would explain the observed speech motor features, along

with variable articulatory precision throughout tasks. These findings are not consistent with a typical motor speech disorder. Furthermore, the patient displayed specific language difficulties in identifying prosodic traits, in the absence of other linguistic impairments. This isolated language impairment is difficult to classify under any type of language or speech disorder.

The findings suggest the presence of a FSD, which is characterized by: a speech pattern that does not correspond to any type of known motor speech disorder and cannot be explained by a neurological lesion; a discrepancy between the orofacial motor assessment and the speech patterns; a variable speech rhythm; a reversible speech pattern within a brief time frame; presence of isolated grammatical errors without other linguistic impairments; an inconsistent hypernasality and a variation in prosody and/or phonation.[3] The clinical findings presented in this case are in line with the existing case descriptions in the literature, emphasizing an inconsistent speech pattern that is not attributable to any other impairment. The differences in the pattern features and severity of impairments are context-dependent, demonstrating variability across assessments.

The diagnosis of a FSD can be challenging, particularly when other neurological symptoms and structural brain lesions are present. Therefore, this case highlights the importance of multidisciplinary evaluations to establish an accurate diagnosis, as this may influence subsequent therapeutic decisions. This case contributes to the literature with information on the identification and assessment of FSDs.

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All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

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Conjunctival Extranodal Marginal Zone Lymphoma Presenting as Entropion

Linfoma de Zona Marginal Extranodal da Conjuntiva Mascarado de Entrópion

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Keywords: Conjunctival Neoplasms; Entropion; Lymphoma, B-Cell, Marginal Zone
Palavras-chave: Entrópion; Linfoma de Zona Marginal Tipo Células B; Neoplasias da Conjuntiva

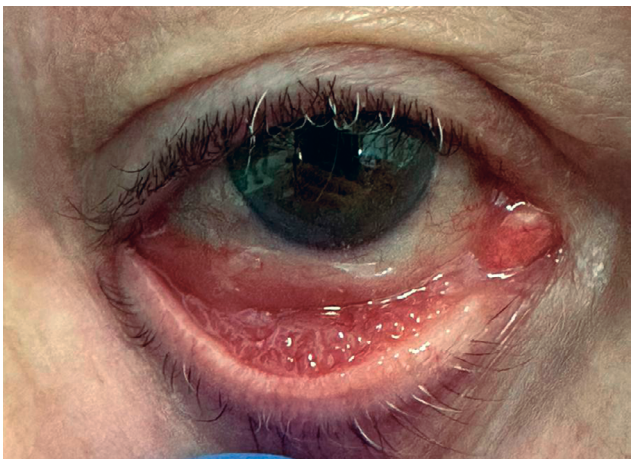

Figure 1 – Upon lid eversion, a multinodular, salmon-pink mass is observed extending along the entire length of the right conjunctival fornix

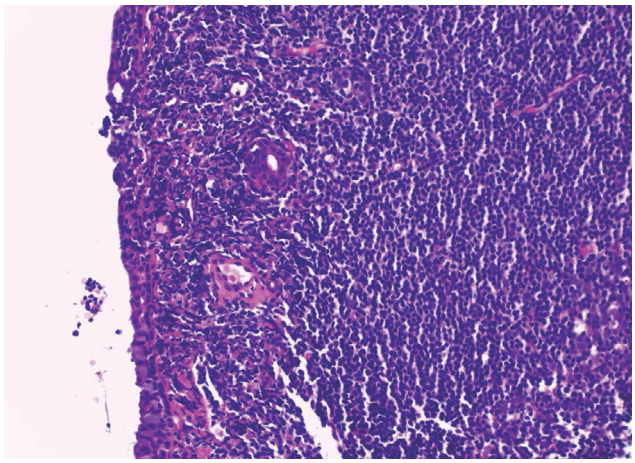

Figure 2 – Histopathology (H&E 200x) showing small- to medium-sized lymphocytes in the *substantia propria*, in a towel disposition, occasionally forming germinal centers. Immunohistochemistry was diffusely positive for CD20, BCL2 and CD43; and negative for CD3, CD5, CD10, CD23, BCL6, cyclin D1 and SOX-11. The Ki-67 proliferation index was 10%. The lining epithelium had focal lymphoid infiltration, without atypia.

A 78-year-old woman presented with a one-year history of painless, progressively enlarging entropion (a condition where an eyelid, most often the lower one, turns inwards) in the right eye. Her medical history was unremarkable.

Previous records of the patient, carried out in another health facility, included histology showing follicles and a computed tomography reporting thickening soft tissue. No immunohistochemistry test had been done. She had been treated with topical corticosteroids without improvement.

Examination revealed a multinodular, salmon-pink mass causing mechanical entropion across the right fornix (Fig. 1), with a smaller, similar lesion in the left eye.

Bilateral conjunctival biopsies revealed lymphoid infiltration of the *substantia propria* (the connective tissue layer beneath the conjunctival epithelium), with positive CD20, BCL2 and CD43 on immunohistochemistry (Fig. 2). Extranodal marginal zone B-lymphoma of the conjunctive was diagnosed. Since oncohematology staging was negative, rituximab treatment was initiated.

Ocular adnexal lymphomas represent 2% of non-Hodgkin lymphomas, with conjunctival involvement in 25%.[1] These lesions often mimic benign, inflammatory conditions. Ophthalmologists should include lymphoma in the differential diagnosis for cases of chronic conjunctivitis or atypical entropion, especially in older patients. Early biopsy is essential, as prognosis is favorable, with high recurrence-free survival.[2]

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ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Vacinação de Adultos Mais Velhos em Portugal: Recomendações do Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna

Vaccination of Older Adults in Portugal: Recommendations from the Geriatrics Study Group of the Portuguese Society of Internal Medicine

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RESUMO

As pessoas mais velhas são mais suscetíveis a infeções e apresentam maior risco de complicações graves, com pior prognóstico funcional e vital. A vacinação é uma estratégia eficaz e com perfil de segurança favorável na prevenção de infeções, contribuindo para um envelhecimento saudável. Considerando a evidência clínica e as vacinas disponíveis em Portugal no primeiro semestre de 2025, o Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna apresenta uma proposta de vacinação nos adultos com idade igual ou superior a 65 anos e alerta para a necessidade de criar um programa nacional de vacinação ao longo da vida que inclua as pessoas mais velhas, para aumentar a cobertura vacinal e diminuir o impacto das infeções nesta população. Embora o documento foque as pessoas com idade igual ou superior a 65 anos, a vacinação contra algumas doenças deve começar mais cedo. Este artigo elabora cinco recomendações principais: 1) Vacinação anual contra a gripe e a COVID-19 em todos os adultos com idade igual ou superior a 50 anos, devendo aqueles com idade igual ou superior a 65 anos receber a vacina trivalente de dose elevada contra a gripe; 2) Vacinação contra o vírus sincicial respiratório em todos os adultos com idade igual ou superior a 60 anos e adultos com 18 - 59 anos com fatores de risco, priorizando pessoas com idade igual ou superior a 75 anos e aqueles com idade igual ou superior a 50 anos com fatores de risco; 3) Vacinação com a vacina pneumocócica conjugada 20-valente ou 21-valente em todos os adultos com idade igual ou superior a 50 anos e adultos com 18 - 49 anos com fatores de risco; 4) Vacinação com a vacina recombinante contra o herpes zoster em todos os adultos com idade igual ou superior a 50 anos e adultos com 18 - 49 anos com risco elevado de herpes zoster; 5) A partir dos 65 anos, vacinação de reforço contra o tétano, difteria e tosse convulsa de 10 em 10 anos.
Palavras-chave: Idoso; Imunossenescência; Meia-Idade; Portugal; Vacinação; Vacinas

ABSTRACT

Older persons are more susceptible to infections and have a higher risk of serious complications, with a worse functional and vital prognosis. Vaccination is an effective strategy with a favorable safety profile for preventing infections and promoting healthy aging. In view of the clinical evidence and the vaccines available in Portugal in the first half of 2025, the Geriatrics Study Group of the Portuguese Society of Internal Medicine presents a proposal for vaccination of adults aged 65 years or older. The experts also point out the need to create a national lifelong vaccination program that includes older people to increase vaccination coverage and reduce the impact of infections in this population. Although the document focuses on people aged 65 years or older, vaccination against some diseases should start earlier. This article outlines five main recommendations: 1) Annual influenza and COVID-19 vaccination for all adults aged 50 years or older, with those aged 65 years or older receiving the high-dose trivalent influenza vaccine; 2) Respiratory syncytial virus vaccination for all adults aged 60 years or older and adults aged 18 - 59 years with risk factors, prioritizing people aged 75 years or older and those aged 50 years or older with risk factors; 3) Pneumococcal vaccination with the 20-valent or 21-valent pneumococcal conjugate vaccine for all adults aged 50 years or older and adults aged 18 - 49 years with risk factors; 4) Herpes zoster vaccination with the recombinant vaccine for all adults aged 50 years or older and adults aged 18 - 49 years at high risk of herpes zoster; 5) From the age of 65 years, booster vaccination against tetanus, diphtheria and pertussis every 10 years.
Keywords: Aged; Immunosenescence; Middle Aged; Portugal; Vaccination; Vaccines

INTRODUÇÃO

Portugal é o segundo país europeu com maior rácio de pessoas com idade igual ou superior a 65 anos, estando entre os países com menos anos de vida saudável.[1,2] Sendo as doenças infeciosas uma causa significativa de morbilidade e mortalidade nos adultos mais velhos, é fundamental abordar a vacinação nesta população.[3] Trata-se de um grupo etário com maior risco de infeção, devido a alterações anatomofisiológicas do envelhecimento (como a imunossenescência), comorbilidades, síndromes geriátricas (destacando-se a polimedicação e a fragilidade) e exposição aumentada a agentes infeciosos em serviços de saúde, rede nacional de cuidados continuados integrados (RNCCI) e estabelecimentos residenciais para pessoas idosas (ERPI).[4,5] Por outro lado, a apresentação

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caracteristicamente atípica da doença nos mais velhos pode levar ao subdiagnóstico.[6]

A maior vulnerabilidade da população geriátrica traduz-se em maior gravidade da infeção, frequentemente implicando hospitalização.[4] Verifica-se também um risco elevado de descompensação de doenças crónicas devido à diminuição da reserva fisiológica, complicações, nomeadamente cardiovasculares, e síndromes geriátricas agravadas ou *de novo* (ex., *delirium*, imobilidade, malnutrição, sarcopenia), potenciando a deterioração funcional e o risco de institucionalização.[6,7] Assim, as infeções apresentam pior prognóstico funcional e vital nos adultos mais velhos, sendo considerável o seu impacto nos serviços de saúde e económico.[3,6]

As vacinas são uma estratégia eficaz, custo-efetiva e com bom perfil de segurança na prevenção de infeções, contribuindo para um envelhecimento saudável.[3,8] O retorno económico da vacinação é evidente, com programas de imunização de adultos a renderem até 19 vezes o seu investimento inicial, promovendo a sustentabilidade.[9] A prevenção de doenças infeciosas, especialmente das formas graves, é particularmente relevante quando não existe tratamento dirigido ou a eficácia do tratamento é limitada. A nível populacional, a prevenção de doenças transmissíveis beneficia ainda os contactos da pessoa vacinada, particularmente em contexto de ERPI e serviços de saúde.

O programa nacional de vacinação (PNV) em vigor foca predominantemente a infância, sendo a vacina contra o tétano e difteria a única a integrar o esquema geral recomendado na população geriátrica.[10] Complementarmente, a Direção-Geral da Saúde (DGS) tem emitido normas de orientação clínica relativas à vacinação contra a gripe, COVID-19 e *Streptococcus pneumoniae*, incluindo as pessoas mais velhas.[11-13]

Com o objetivo de aumentar a cobertura vacinal neste escalão etário, o Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna (NEGERMI) elaborou o presente documento, propondo um plano de vacinação para pessoas com idade igual ou superior a 65 anos. Estas recomendações referem-se às doenças preveníveis por vacinação com impacto global na população mais velha, de acordo com a evidência disponível, e incluem apenas vacinas disponíveis em Portugal no primeiro semestre de 2025. Os autores decidiram referir as vacinas através do nome comercial para facilitar a operacionalização destas recomendações na prática clínica. Embora os adultos com idade igual ou superior a 65 anos sejam o foco do artigo, para algumas doenças, a imunização deve começar mais precocemente, com vista à promoção do envelhecimento saudável, preservação da reserva fisiológica e prevenção de doenças agudas e crónicas. A vacinação de profissionais de saúde, cuidadores, familiares e conviventes é também fundamental para proteger os mais velhos.

MÉTODOS

Um painel composto por cinco especialistas em Medicina Interna com competência em Geriatria pela Ordem dos Médicos analisou a evidência relativa ao impacto das doenças preveníveis por vacinação e à eficácia e segurança das vacinas em adultos mais velhos. A evidência recolhida incluiu metanálises, ensaios clínicos, estudos observacionais, orientações nacionais e internacionais e a experiência clínica dos peritos. Após discussão, os autores, em nome do NEGERMI, elaboraram as recomendações propostas neste documento.

VACINAÇÃO DE ADULTOS MAIS VELHOS

Vacinação contra a gripe

Em Portugal, entre 2008/2009 e 2017/2018, 46,2% dos internamentos por gripe foram de adultos com idade igual ou superior a 65 anos.[14] Nesta faixa etária, a duração média do internamento foi de 12,0 dias, a taxa de mortalidade hospitalar de 9,5% e o custo médio do internamento de €3327 por doente.[14] Nos mais velhos, a gripe pode levar à exacerbação de doenças crónicas e síndromes geriátricas e à deterioração física, cognitiva e funcional, impactando a qualidade de vida e a autonomia.[15]

Na época 2024/2025, a DGS recomendou a vacinação sazonal contra a gripe em pessoas com idade igual ou superior a 60 anos, com posterior alargamento àquelas entre os 50 e os 59 anos.[12] A vacina de dose elevada (Efluelda Tetra®[16]) gratuita esteve reservada a pessoas com idade igual ou superior a 85 anos e a residentes em ERPI, instituições similares e RNCCI; os restantes adultos deveriam ser vacinados com uma vacina de dose padrão (Fluarix Tetra®[17], Influvac Tetra®[18] ou Vaxigrip Tetra®[19]).[12]

As recomendações portuguesas elaboradas por seis sociedades científicas, incluindo a Sociedade Portuguesa de Medicina Interna (SPMI), propõem que a vacina de dose elevada seja priorizada em todos os adultos com idade igual ou superior a 65 anos, pois a imunossenescência aumenta a suscetibilidade à gripe e reduz a eficácia das vacinas, sendo a vacina de dose elevada mais imunogénica em pessoas mais velhas comparativamente com as vacinas de dose padrão.[15] No estudo DANFLU-1, em indivíduos entre os 65 e os 79 anos, as taxas de hospitalização por gripe ou pneumonia e a mortalidade foram menores no grupo que recebeu a vacina de dose elevada *versus* grupo que recebeu a vacina de dose padrão, demonstrando a eficácia clínica superior da vacina de dose elevada nos mais velhos.[20]

Devido à elevada variabilidade genética do vírus da gripe e variação dos vírus em circulação, a Organização Mundial de Saúde (OMS) atualiza periodicamente as estirpes de vírus que devem constar da vacina contra a gripe

para garantir a sua eficácia. Em 2024, a OMS recomendou que a linhagem B/Yamagata fosse excluída das vacinas por não se encontrar em circulação desde 2020.[21] Consequentemente, a OMS recomenda a transição das vacinas quadrivalentes para trivalentes no hemisfério norte (contendo antigénios do vírus influenza A subtipo H1N1, A subtipo H3N2 e B/Victoria).[21]

Atualmente, estão autorizadas em Portugal quatro tipos de vacinas inativadas trivalentes contra a gripe: de dose padrão (Fluarix®[22], Influvac®[23], Vaxigrip®[24]); de dose elevada (Efluelda®[25]); adjuvada (Fluad®[26]); e preparada em culturas celulares (Flucelvax®[27]).

Na última atualização, o Centers for Disease Control and Prevention (CDC) recomenda a vacinação contra a gripe dos indivíduos com idade igual ou superior a 65 anos preferencialmente com uma vacina trivalente de dose elevada, adjuvada ou recombinante, existindo mais evidência científica da dose elevada.[28,29] Em Portugal, apenas está disponível a vacina trivalente de dose elevada [Efluelda®[25] – Apêndice 1, Tabela 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)].

Recomendações

- Recomenda-se a vacinação anual contra a gripe em todos os adultos com idade igual ou superior a 50 anos, preferencialmente entre outubro e novembro.[30]
- Nos adultos com idade igual ou superior a 65 anos, recomenda-se a vacina trivalente de dose elevada. Quando esta não é gratuita, se houver incapacidade para a adquirir, recomenda-se a vacina de dose padrão, habitualmente gratuita.
- A vacinação após doença deve ocorrer assim que possível, considerando as contraindicações referidas no resumo das características do medicamento.[25]
- Tendo em vista a proteção das pessoas mais velhas, recomenda-se a vacinação de todos os profissionais de saúde e outros prestadores de cuidados que lidam com adultos mais velhos, bem como de todos os conviventes.

Vacinação contra a COVID-19

A idade é o maior fator de risco para COVID-19 grave: o risco de morte por COVID-19 é 60 vezes superior nos adultos entre os 65 e os 74 anos, e 140 vezes superior naqueles com 75 - 84 anos, comparativamente com indivíduos na faixa etária dos 18 aos 29 anos.[31]

Em Portugal, atualmente, a primovacinação contra a COVID-19 dos adultos elegíveis decorre durante todo o ano, com uma dose única da vacina de RNA mensageiro (mRNA) adaptada à época (Comirnaty®[32]).[13]

Na época 2024/2025, a DGS recomendou a vacinação sazonal contra a COVID-19 para pessoas com idade igual ou superior a 60 anos (com posterior alargamento àquelas entre os 50 e os 59 anos) e esquema vacinal primário completo com a única vacina disponível à data, que era de mRNA adaptada à época (Comirnaty®[32]), independentemente do número de reforços anteriores e de história prévia de COVID-19.[13]

Atualmente, estão aprovadas pela Agência Europeia de Medicamentos (EMA) e autorizadas em Portugal cinco vacinas contra a COVID-19: duas de mRNA (Comirnaty®[32] e Spikevax®[33]), uma de mRNA autoamplificante (Kostaive®[34]) e duas proteicas recombinantes adjuvadas [Bimervax®[35] (apenas para reforço) e Nuvaxovid®[36]]. Em Portugal, só está disponível a Comirnaty®[32] [Tabela 1 do Apêndice 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)].

Na última atualização, o CDC recomenda a primovacinação contra a COVID-19 dos indivíduos com idade igual ou superior a 65 anos com uma dose de vacina de mRNA 2024/2025 (Comirnaty®[32] ou Spikevax®[33]) ou duas doses de vacina recombinante adjuvada 2024/2025 (Nuvaxovid®[36]), seguida de uma dose de reforço com qualquer uma das vacinas contra a COVID-19 2024/2025 seis meses depois (mínimo dois meses).[29] Nesta faixa etária, a vacinação sazonal consiste em duas doses de uma das vacinas contra a COVID-19 2024/2025, com intervalo de seis meses (mínimo dois meses).[29]

Recomendações

- Recomenda-se a vacinação sazonal anual contra a COVID-19 em todos os adultos com idade igual ou superior a 50 anos, pessoas com patologias de risco ou condições de imunossupressão grave e moderada, profissionais dos serviços de saúde e utentes/residentes em ERPI e instituições similares.[13] Nas pessoas com idade igual ou superior a 65 anos, deverá equacionar-se a vacinação de seis em seis meses.
- Os esquemas de vacinação deverão ser adaptados às vacinas disponíveis em Portugal na época sazonal, considerando a autonomia de prescrição do médico e o perfil de eficácia e segurança das vacinas.
- A vacinação após doença está indicada e deverá acontecer quatro a seis meses depois.[13]
- Em situações clínicas específicas (ex., antes do início de terapêuticas imunossupressoras), o reforço vacinal pode ser encurtado para três meses após a última dose de vacina ou quatro semanas após a última infeção por SARS-CoV-2.[13]

Vacinação contra o vírus sincicial respiratório

A relevância do vírus sincicial respiratório (VSR) nas pessoas mais velhas é cada vez mais reconhecida, existindo evidência crescente do seu impacto em termos de infeção das vias respiratórias inferiores, internamento e mortalidade.[37-41] Um estudo realizado na Unidade Local de Saúde de Matosinhos, entre 2018 e 2024, revelou que 91,4% dos internamentos associados ao VSR em adultos ocorreram em pessoas com idade igual ou superior a 60 anos.[42] Nesta faixa etária, a duração mediana do internamento foi de nove dias, com um custo de €4768 por doente; a taxa de mortalidade hospitalar foi de 20,6%.[42] A nível nacional, estimam-se 3095 internamentos associados ao VSR, por ano, em pessoas com 65 anos ou mais.[43]

Por outro lado, uma metanálise de 16 estudos observacionais em indivíduos com 60 anos ou mais demonstrou taxas de hospitalização e mortalidade semelhantes para o VSR e para o vírus da gripe.[40] A idade igual ou superior a 75 anos associou-se a maior risco de hospitalização, maior duração do internamento e maior mortalidade devido a infeção pelo VSR.[37,38,41] Os adultos com determinadas comorbilidades também apresentam maior risco de infeção grave.[37,38,41]

Atualmente, estão aprovadas pela EMA três vacinas contra o VSR: uma de mRNA com nucleósido modificado (mRESVIA®[44]) e duas recombinantes [uma adjuvada (Arexvy®[45]) e outra bivalente (Abrysvo®[46])], não existindo estudos comparativos diretos entre as mesmas. Apenas as vacinas recombinantes estão disponíveis em Portugal [Apêndice 1, Tabela 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)].[45,46] Em adultos com idade igual ou superior a 60 anos, a eficácia da vacina adjuvada foi mantida durante três épocas[47]; a vacina bivalente foi eficaz durante duas épocas.[48] Vários estudos comprovam a efetividade de ambas as vacinas em pessoas mais velhas, em termos de prevenção de hospitalizações, episódios de urgência e doença crítica.[49-51]

A SPMI, conjuntamente com outras cinco sociedades científicas portuguesas, recomendou recentemente a vacinação contra o VSR em todas as pessoas com idade igual ou superior a 60 anos e pessoas com idade igual ou superior a 50 anos com fatores de risco, priorizando aquelas com idade igual ou superior a 75 anos ou com idade igual ou superior a 50 anos com fatores de risco.[52] Estas recomendações basearam-se no elevado impacto do vírus nestas populações e no perfil de eficácia e segurança das vacinas contra o VSR.[52]

A necessidade de revacinação contra o VSR ainda não está estabelecida.[45,46] É expectável que a revacinação venha a ser recomendada e que o intervalo entre doses varie consoante a vacina administrada.[53]

Recomendações

- Recomenda-se a vacinação contra o VSR em todos os adultos com idade igual ou superior a 60 anos e naqueles entre os 18 e os 59 anos com fatores de risco (doença pulmonar obstrutiva crónica, asma, insuficiência cardíaca, doença arterial coronária, diabetes, doença renal crónica, doença hepática crónica, imunossupressão, fragilidade, demência, residência em ERPI/RNCCI).
- Adultos com idade igual ou superior a 60 anos e adultos entre os 50 e os 59 anos com fatores de risco podem receber qualquer uma das vacinas recombinantes; adultos entre os 18 e os 49 anos com fatores de risco só podem receber a vacina recombinante bivalente.[45,46]
- A vacinação deverá ser priorizada em adultos com idade igual ou superior a 75 anos e adultos com idade igual ou superior a 50 anos com fatores de risco.
- A vacina pode ser administrada em qualquer altura do ano; caso seja necessário articulá-la com outras vacinas, poderá considerar-se o final do verão/início do outono como o período de maior benefício.[54]
- A necessidade de reforço é provável, mas o intervalo de administração ainda não está definido.[45,46]
- A vacinação após doença está indicada, pois a imunidade adquirida após infeção não é substancial,[39] mas desconhece-se o momento ideal de vacinação.

Vacinação contra *Streptococcus pneumoniae*

A infeção por *Streptococcus pneumoniae* (pneumococo) é uma importante causa de morbilidade e mortalidade mundial, com peso considerável nas pessoas mais velhas.[55] A doença pneumocócica varia desde formas não invasivas (pneumonia, otite média, sinusite) a doença invasiva pneumocócica (DIP), definida pelo isolamento da bactéria num local do organismo habitualmente estéril.[55,56] Em Portugal, mais de metade dos isolados de *S. pneumoniae* responsáveis por DIP na população adulta entre 2009 e 2011 ocorreu em indivíduos com idade igual ou superior a 65 anos.[57]

Embora a DIP constitua a forma mais grave de infeção por *S. pneumoniae*, a pneumonia é a apresentação mais comum de doença pneumocócica.[56] Dados nacionais revelaram que, em 2015, na população adulta, a mediana de idade dos doentes admitidos por pneumonia foi de 80 anos e a mortalidade hospitalar por pneumonia foi superior em indivíduos com mais de 75 anos; o pneumococo foi o isolado bacteriano mais frequente (41,2%).[58] Também as comorbilidades, imunodeficiência e determinados comportamentos estão associados a maior risco de doença pneumocócica.[56]

Em Portugal, existem cinco vacinas pneumocócicas comercializadas para prevenção da doença pneumocócica

em adultos: quatro conjugadas – 13-valente (Pn13; Prevenar 13®[59]), 15-valente (Pn15; Vaxneuvance®[60]), 20-valente (Pn20; Prevenar 20®[61]) e 21-valente (Pn21; Capvaxive®[62]) – e uma polissacárida 23-valente (Pn23; Pneumovax 23®[63]).

As vacinas pneumocócicas conjugadas apresentam bom perfil de segurança e tolerabilidade e conferem imunogenicidade mais robusta e duradoura, pois induzem uma resposta imunitária T-dependente.[55,56,64-66] Esta característica é especialmente relevante nas pessoas mais velhas, devido à imunossenescência. Contrariamente à Pn23, as vacinas conjugadas diminuem ainda a taxa de colonização orofaríngea, protegendo indiretamente os não vacinados.[55,56]

A Pn20 [Tabela 1 do Apêndice 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)] contempla os principais serotipos causadores de DIP na população portuguesa com idade igual ou superior a 65 anos (3, 8, 22F, 14, 19A).[61,67] Esta vacina engloba ainda cinco dos serotipos mais comuns causadores de pneumonia pneumocócica não invasiva na referida população (3, 11A, 19F, 22F, 10A).[61,68] Por sua vez, a Pn23 inclui o serotipo 9N, responsável por 4,1% dos casos de DIP e 5,5% dos casos de pneumonia não invasiva em pessoas com idade igual ou superior a 65 anos, em Portugal.[63,67,68] A Pn21 [Tabela 1 do Apêndice 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)], além dos serotipos 3, 8, 22F, 19A, 9N, 11A e 10A, anteriormente referidos, inclui ainda os serotipos 23B, 23A, 15A e 35B, responsáveis por 4,0% - 7,1% dos casos de pneumonia não invasiva nesta população.[62,68]

Em 2024, a DGS atualizou a norma da vacinação pneumocócica, que inclui apenas a Pn20 e a Pn23.[11] Para pessoas com idade igual ou superior a 65 anos saudáveis é apenas recomendada a Pn23.[11] A vacinação sequencial com Pn20 e Pn23 (intervalo de seis a 12 meses, mínimo oito semanas) é recomendada para doentes com comorbilidades, nomeadamente, doença cardíaca crónica, doença hepática crónica, diabetes, doença respiratória crónica e doentes imunodeprimidos ou com risco acrescido de meningite bacteriana.[11]

Considerando o cenário epidemiológico nacional e o custo-efetividade das vacinas, o Grupo de Doenças Respiratórias da Associação Portuguesa de Medicina Geral e Familiar (GRESP) propõe uma estratégia de vacinação universal com Pn20 para todos os adultos com idade igual ou superior a 65 anos e adultos com 18 anos ou mais que apresentem fatores de risco.[56] Em alternativa, o GRESP considera o esquema sequencial com Pn15 seguida de Pn23, passado pelo menos 12 meses.[56]

O CDC preconiza a vacinação pneumocócica única com Pn20 ou Pn21, ou, em alternativa, a vacinação sequencial com Pn15 seguida de Pn23, em todos os adultos com idade igual ou superior a 50 anos e igual ou superior a 19 anos com fatores de risco, sem vacinação pneumocócica prévia.[69]

Recomendações

- Recomenda-se a vacinação pneumocócica com a vacina Pn20 ou Pn21 em todos os adultos com idade igual ou superior a 50 anos (Tabela 1) e adultos entre os 18 e os 49 anos com fatores de risco.
- Tendo em conta a Norma n.º 13/2024 de 19/12/2024 da DGS,[11] o painel considera a possibilidade de, em adultos vacinados com Pn20, continuar o esquema de vacinação com Pn23, com intervalo entre vacinas de seis a 12 meses (mínimo oito semanas), se tal não atrasar a vacinação contra outras doenças.
- Em alternativa, a vacinação poderá ser efetuada com Pn15 seguida de Pn23, com intervalo igual ou superior a 12 meses entre vacinas (Tabela 1). Em imunocomprometidos, este intervalo poderá ser encurtado para um mínimo de oito semanas.
- Após utilização de qualquer um destes esquemas (Pn20, Pn21 ou Pn15+Pn23), a revacinação não é necessária.
- Em indivíduos previamente vacinados com Pn13 e/ou Pn23, o esquema de vacinação deverá ser completado com Pn20 ou Pn21, num período igual ou superior a 12 meses após a última vacinação

Tabela 1 – Recomendações do Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna para a vacinação pneumocócica em pessoas com idade ≥ 65 anos em Portugal, considerando as vacinas disponíveis no primeiro semestre de 2025

Vacinação pneumocócica prévia	Esquema preferencial[a]	Esquema alternativo[a]
Naïve	Pn20[b] ou Pn21	Pn15 + Pn23 (intervalo ≥ 12 meses[c])
Pn13	Pn20[b] ou Pn21 (intervalo ≥ 12 meses)	-
Pn23	Pn20 ou Pn21 (intervalo ≥ 12 meses)	-
Pn13 + Pn23	Pn20 ou Pn21 (intervalo ≥ 12 meses)	-

Pn13: vacina pneumocócica conjugada 13-valente; Pn15: vacina pneumocócica conjugada 15-valente; Pn20: vacina pneumocócica conjugada 20-valente; Pn21: vacina pneumocócica conjugada 21-valente; Pn23: vacina pneumocócica polissacárida 23-valente.
a: Após utilização de qualquer um destes esquemas, a revacinação não é necessária.
b: Tendo em conta a Norma n.º 13/2024 de 19/12/2024 da Direção-Geral da Saúde,[11] o painel considera a possibilidade de continuar o esquema de vacinação com a Pn23, com um intervalo entre vacinas de 6 - 12 meses (mínimo de oito semanas), desde que tal não atrase a vacinação contra outras doenças.
c: Em indivíduos imunocomprometidos, o intervalo entre vacinas poderá ser encurtado para um mínimo de oito semanas.

pneumocócica (Tabela 1).[70]

- Excecionalmente, a vacinação isolada com Pn23 poderá ser equacionada se houver incapacidade de aquisição das vacinas conjugadas.
- A vacinação após doença está indicada.[11] Recomenda-se que seja realizada no momento da alta hospitalar do internamento por doença pneumocócica, como medida de adesão à vacinação.[71]

Vacinação contra o herpes zoster

O herpes zoster (HZ), ou zona, resulta da reativação do vírus varicela zoster (VVZ) latente e pode originar complicações crónicas potencialmente incapacitantes, sendo a nevralgia pós-herpética (NPH) a principal.[72] A idade é um dos maiores fatores de risco de HZ e suas complicações, devido ao declínio da imunidade celular específica para o VVZ.[73] Em indivíduos com HZ entre os 50 e os 59 anos, o risco de desenvolver NPH é de 4% - 15%, aumentando para 7% - 26% na faixa etária entre os 60 e os 69 anos e para 14% - 34% em pessoas com idade igual ou superior a 70 anos.[72]

Em Portugal, 99,3% das pessoas com idade igual ou superior a 65 anos apresentam evidência serológica de infeção pelo VVZ.[74] Entre julho de 2023 e junho de 2024, 62 985 adultos receberam tratamento para o HZ, dos quais 67% tinham idade igual ou superior a 50 anos e 50% igual ou superior a 60 anos.[75] Em 2017, registaram-se 191 internamentos com diagnóstico primário de HZ, 69% dos quais em pessoas com 50 anos ou mais.[76] Nesta faixa etária, a duração média do internamento foi de 14,8 dias, com um custo médio de €3422 por doente.[76]

Atendendo à elevada carga da doença, a SPMI e a Associação Portuguesa de Medicina Geral e Familiar recomendaram, em 2023, a vacina recombinante contra o HZ [Shingrix®[77]; Tabela 1 do Apêndice 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)] em todos os adultos com idade igual ou superior a 50 anos e adultos entre os 18 e os 49 anos com risco elevado de HZ.[78] A vacina viva atenuada contra o HZ foi descontinuada em Portugal em 2024.[79]

Recomendações

- Recomenda-se a vacina recombinante contra o HZ em todos os adultos com idade igual ou superior a 50 anos e em adultos entre os 18 e os 49 anos com risco elevado de HZ, nomeadamente, doentes com comorbilidades médicas ou imunossupressão.
- Indivíduos com antecedentes de HZ devem ser vacinados contra a doença, com intervalo igual ou superior a 12 meses desde a resolução dos sintomas.[78] Em indivíduos com HZ recorrente ou imunocomprometidos, deve ponderar-se encurtar este intervalo para um mínimo de oito semanas.[78] No caso de HZ oftálmico, recomenda-se avaliação por Oftalmologia antes e após vacinação contra o HZ, devendo a vacinação ser protelada até a doença ocular estar bem controlada.[80]
- Indivíduos previamente imunizados com a vacina viva atenuada devem ser imunizados com a vacina recombinante, devido à sua eficácia elevada e persistente.[77] O intervalo entre vacinas deverá ser igual ou superior a 12 meses.[78]

Vacinação contra o tétano, difteria e tosse convulsa

O tétano, a difteria e a tosse convulsa são infeções potencialmente fatais, mas preveníveis através da vacinação. A proteção conferida pela vacinação não é vitalícia, sendo necessário reforçá-la ao longo da vida.[8,81,82] Na idade adulta, segundo o PNV, a vacina contra o tétano, difteria e tosse convulsa acelular com conteúdo reduzido de antigénios [Tdpa; Boostrix®[83] ou Triaxis®[84]; Tabela 1 do Apêndice 1 (Apêndice 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/23786/15853)] está reservada a grávidas.[10] Após primovacinação, o PNV preconiza que os restantes adultos recebam a vacina contra o tétano e difteria com conteúdo reduzido de antigénios [Td; D.T. Vax Adulto®[85] ou diTeBooster®[86] (não comercializada em Portugal)] aos 25, 45 e 65 anos e, posteriormente, a cada 10 anos.[10] A vacinação contra a tosse convulsa não contempla, assim, faixas etárias mais elevadas.[10]

Contudo, dados do Centro Europeu de Prevenção e Controlo das Doenças (ECDC) revelam um aumento do número de casos de tosse convulsa, causada por *Bordetella pertussis*, em vários países da UE/EEE, nos últimos anos.[87] Segundo o ECDC, os adultos mais velhos enfrentam risco acrescido de doença grave e hospitalização.[87]

Vários estudos documentam taxas de hospitalização de 11% - 14% em adultos com idade igual ou superior a 75 anos com tosse convulsa.[88] Em Portugal, um estudo de vigilância conduzido entre 2000 e 2015 reportou uma mortalidade de 17,4% em adultos com idade igual ou superior a 65 anos internados com tosse convulsa.[89] Um estudo retrospetivo em Inglaterra revelou ainda um aumento significativo da utilização de recursos de cuidados de saúde em indivíduos com 50 ou mais anos de idade, diagnosticados com tosse convulsa.[90]

Enquanto a seroproteção contra o tétano e a difteria se mantém elevada durante pelo menos 10 anos, os níveis de anticorpos contra a tosse convulsa diminuem mais rapidamente, sendo esta redução mais acentuada com a idade.[81,82] Dez anos após a dose de reforço com Tdpa, a taxa de seropositividade para o toxoide da tosse convulsa foi de 48,3% em adultos.[82]

Perante estes dados, vários países europeus, como

Áustria, Bélgica, Chéquia, Itália, Luxemburgo, Noruega e Polónia, preconizam o reforço da vacinação contra a tosse convulsa a cada cinco a 10 anos na idade adulta.[91]

Recomendações

- Recomenda-se a vacina Tdpa em todos os adultos com idade igual ou superior a 65 anos, com reforço de 10 em 10 anos.
- Se houver incapacidade de adquirir a Tdpa, recomenda-se a vacina Td incluída no PNV.

Estratégias para promover a vacinação

No sentido de promover a adesão à vacinação nas pessoas mais velhas, é fundamental privilegiar a comunicação médico-doente, incentivando a literacia em saúde e permitindo o esclarecimento de mitos sobre vacinação, tais como: que as reações adversas às vacinas são piores nos mais velhos ou que as vacinas causam doença. Importa também realçar que as reações adversas às vacinas são maioritariamente ligeiras e que as contraindicações são raras.[10] Neste contexto, a monitorização de possíveis efeitos adversos da vacinação é essencial.

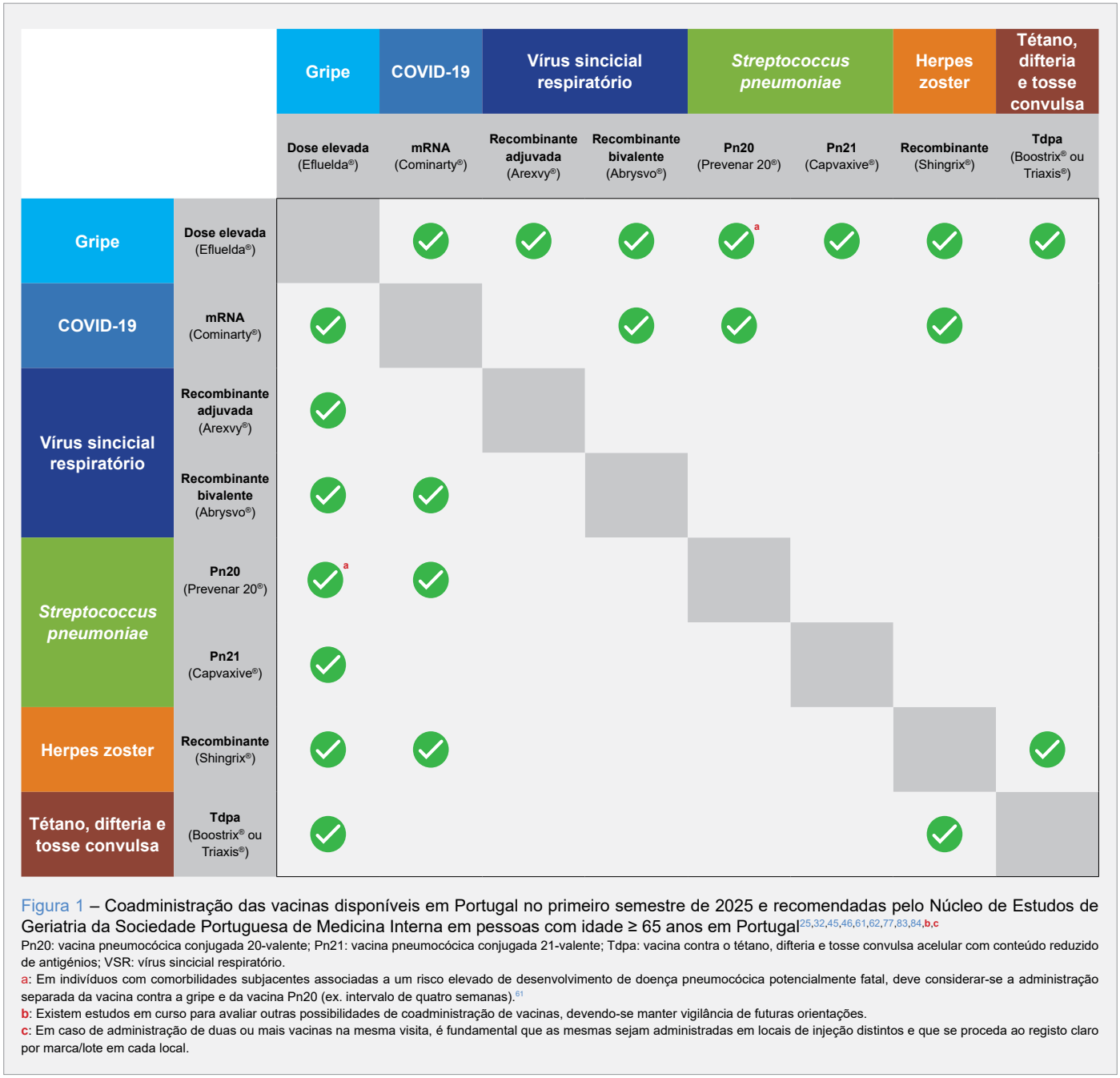

Figura 1 – Coadministração das vacinas disponíveis em Portugal no primeiro semestre de 2025 e recomendadas pelo Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna em pessoas com idade ≥ 65 anos em Portugal[25,32,45,46,61,62,77,83,84,b,c]

Pn20: vacina pneumocócica conjugada 20-valente; Pn21: vacina pneumocócica conjugada 21-valente; Tdpa: vacina contra o tétano, difteria e tosse convulsa acelular com conteúdo reduzido de antigénios; VSR: vírus sincicial respiratório.

a: Em indivíduos com comorbilidades subjacentes associadas a um risco elevado de desenvolvimento de doença pneumocócica potencialmente fatal, deve considerar-se a administração separada da vacina contra a gripe e da vacina Pn20 (ex. intervalo de quatro semanas).[61]

b: Existem estudos em curso para avaliar outras possibilidades de coadministração de vacinas, devendo-se manter vigilância de futuras orientações.

c: Em caso de administração de duas ou mais vacinas na mesma visita, é fundamental que as mesmas sejam administradas em locais de injeção distintos e que se proceda ao registo claro por marca/lote em cada local.

Dever-se-á aproveitar qualquer oportunidade de contacto para informar, propor e prescrever a vacinação, considerando que esse poderá ser o último contacto antes de uma infeção. Destacam-se situações de particular alteração imunitária (como doenças oncológicas ou autoimunes) em que a vacinação assume especial importância para impedir complicações e permitir a continuidade e sucesso dos tratamentos.[8,10]

Por outro lado, é crucial planear uma estratégia personalizada de hierarquização de vacinas, baseada tanto nas comorbilidades pré-existentes e epidemiologia, sazonalidade e gravidade das doenças preveníveis, como na disponibilidade, possibilidade de coadministração (Fig. 1) e custo das vacinas. O registo vacinal deverá ser efetuado no boletim individual do registo de saúde eletrónico.

Finalmente, a vacinação dos profissionais de saúde, familiares, cuidadores e conviventes é fundamental para proteger a população geriátrica, sendo necessário apostar na sensibilização destes intervenientes.

CONCLUSÃO

Os adultos mais velhos são mais suscetíveis a infeções, devido às inúmeras particularidades clínicas, destacando-se a imunossenescência, e têm maior risco de complicações graves, que se associam a pior prognóstico funcional e vital, implicando menor qualidade de vida. As doenças infeciosas constituem, assim, uma causa significativa de morbilidade e mortalidade nesta faixa etária.

A vacinação é uma estratégia eficaz e segura, sendo fundamental na prevenção de infeções e promoção do envelhecimento saudável. Considerando a evidência clínica e as vacinas disponíveis em Portugal no primeiro semestre de 2025, o NEGERMI apresenta uma proposta de vacinação nas pessoas com idade igual ou superior a 65 anos (Fig. 2) e alerta para a necessidade de criar um PNV ao longo da vida, em Portugal, abrangendo os adultos mais velhos, para aumentar a cobertura vacinal e diminuir o impacto das doenças infeciosas nesta população. Esta proposta está alinhada com as recomendações da OMS, da Sociedade Europeia de Medicina Geriátrica e da Federação Internacional sobre o Envelhecimento.[92,93]

Estão em curso vários estudos para desenvolver novas vacinas, com diferentes combinações e tecnologias, especialmente dirigidas ao sistema imunitário dos utentes mais velhos, bem como novas vias de administração que potenciem a eficácia da vacinação nesta população.[3,94] Assim, é de esperar a revisão periódica deste documento, à luz de nova evidência científica sobre o impacto das doenças infeciosas em Portugal e sobre o desenvolvimento de novas vacinas. Numa sociedade cada vez mais envelhecida,

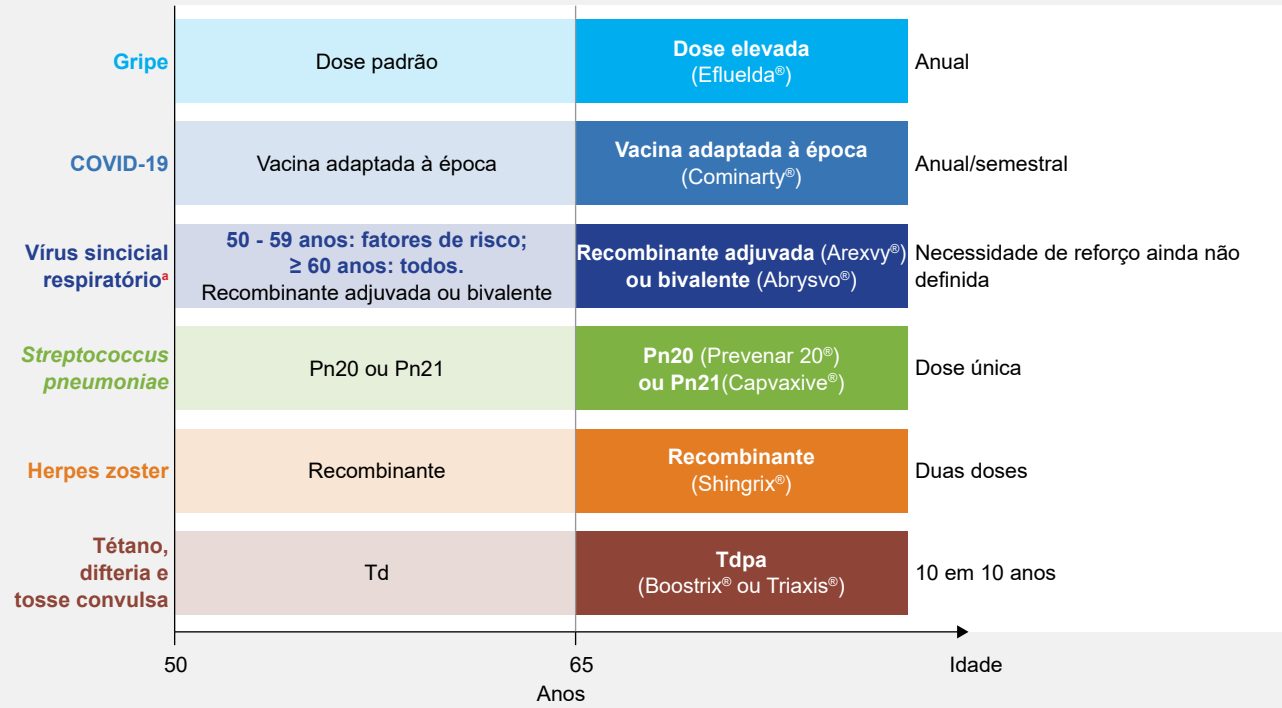

Figura 2 – Resumo das recomendações do Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna para a vacinação das pessoas com idade ≥ 65 anos em Portugal, considerando as vacinas disponíveis no primeiro semestre de 2025

Pn20: vacina pneumocócica conjugada 20-valente; Pn21: vacina pneumocócica conjugada 21-valente; Td: vacina contra o tétano e difteria com conteúdo reduzido de antigénios; Tdpa: vacina contra o tétano, difteria e tosse convulsa acelular com conteúdo reduzido de antigénios.

a: A vacinação contra o vírus sincicial respiratório deverá ser priorizada em adultos com idade ≥ 75 anos e adultos com idade ≥ 50 anos com fatores de risco.

todos os esforços são devidos para proteger esta população mais vulnerável, contribuindo para a sustentabilidade do sistema de saúde e social e para o envelhecimento bem-sucedido.

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CONFLITOS DE INTERESSE

PA recebeu pagamentos ou honorários de Pfizer, GSK e Sanofi para palestras, apresentações, escrita de manuscritos ou eventos educacionais; recebeu honorários de consultadoria de Pfizer, GSK e AstraZeneca.

GS recebeu pagamentos ou honorários de GSK, Sanofi, Pfizer, Zambon e Gilead para palestras, apresentações, escrita de manuscritos ou eventos educacionais; recebeu apoio de Sanofi e Medinfar para comparecer em reuniões/viagens.

HG recebeu pagamentos ou honorários de Pfizer para palestras; recebeu apoio de Novartis para comparecer em reuniões/viagens.

RV recebeu pagamentos ou honorários de Pfizer e GSK para palestras, apresentações, escrita de manuscritos ou eventos educacionais.

SD recebeu pagamentos ou honorários de GSK, Sanofi e Pfizer para palestras, apresentações, escrita de manuscritos ou eventos educacionais; recebeu honorários por integrar conselhos consultivos de Pfizer e HIPRA; recebeu apoio de GSK, Sanofi, Pfizer e HIPRA para comparecer em reuniões/viagens; é coordenadora do Núcleo de Estudos de Geriatria da Sociedade Portuguesa de Medicina Interna e *communication and website director* da European Geriatric Medicine Society.

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Neurocysticercosis Presenting with Seizures: Diagnostic Value of the Dot Sign in Non-Endemic Areas

Neurocisticercose e Crises Epiléticas: O Valor Diagnóstico do Dot Sign em Áreas Não Endémicas

Keywords: Neurocysticercosis/complications; Neurocysticercosis/diagnosis; Neurocysticercosis/diagnostic imaging; Seizures/etiology
Palavras-chave: Convulsões/etiologia; Neurocisticercose/complicações; Neurocisticercose/diagnóstico; Neurocisticercose/diagnóstico por imagem

A 26-year-old woman presented with new-onset tonic-clonic seizures and left-sided monoparesis. The patient was originally from Cape Verde and had been living in Portugal for six months, with access to drinking water and adequate hygiene conditions, no relevant past medical history, and no known similar cases among close contacts.

Brain computed tomography (CT) revealed a poorly defined right frontal cortico-subcortical cystic lesion measuring approximately 12 x 7 mm on the axial plane, with a millimetric central hyperdense focus and surrounding hypodensity.

Magnetic resonance imaging (MRI) (Fig. 1) revealed a solitary cystic lesion exhibiting a central 'dot sign' on T2 FLAIR, accompanied by peripheral enhancement and surrounding vasogenic edema – findings consistent with parenchymal neurocysticercosis (NCC) in the colloidal stage.[1]

Cerebrospinal fluid analysis showed mild pleocytosis with polymorphonuclear cell predominance; glucose and protein levels were normal. Microbiological tests and *Taenia solium* serology were negative. The MRI excluded intracranial extraparenchymal involvement, skeletal radiographs showed no evidence of muscular cysticercosis and cardiac involvement was excluded by cardiac MRI.

Combined albendazole-praziquantel therapy was initiated on admission and praziquantel was discontinued on day seven after exclusion of disseminated disease.[2] Dexamethasone and levetiracetam were also administered, with complete clinical stability and no seizure recurrence. Follow-up at three months demonstrated evolution to a calcified nodule, supporting the diagnosis.

Neurocysticercosis, caused by the larval stage of *Taenia solium*, is a leading cause of acquired epilepsy in endemic regions.[3] Most parenchymal cases are asymptomatic, with clinical manifestations largely determined by the stage of cyst evolution – vesicular, colloidal, granular nodular, or calcified.[4-7]

Among symptomatic patients, seizures are the most frequent presentation, occurring in 70% - 90% of cases.[8] The colloidal stage is especially symptomatic, as increased cyst-wall permeability elicits a strong inflammatory response, resulting in perilesional oedema, peak immune activation, and symptoms such as seizures and headache.[3-7]

Neuroimaging is central to diagnosis, with MRI optimal for detecting viable cysts and visualizing the scolex, which is the viable larval structure within the cyst and constitutes

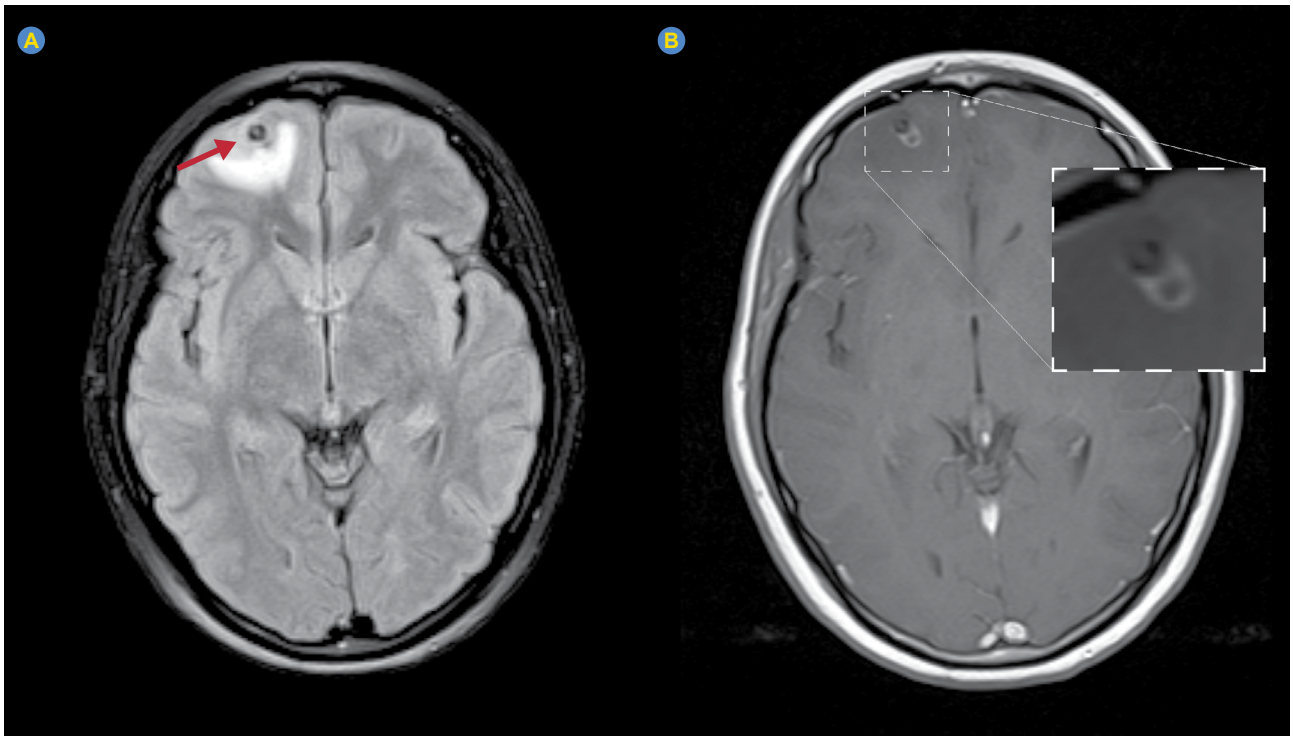

Figure 1 – (A) Cerebral MRI demonstrates a cystic lesion in the right frontal cortico-subcortical region, with a central 'dot sign' on T2-FLAIR (red arrow) representing the scolex and eliciting surrounding vasogenic oedema. No hemorrhage was evident on T1-weighted or T2* sequences (not shown). Post-contrast T1-weighted images (B) clearly depict peripheral wall enhancement of the cyst.
MRI: magnetic resonance imaging; FLAIR: fluid-attenuated inversion recovery

the hallmark imaging feature of neurocysticercosis. Its signal and density characteristics produce the classic 'hole-with-dot' appearance – best appreciated on MRI – widely regarded as pathognomonic of viable parenchymal cysticerci.[5,9]

On the other hand, CT is more sensitive for identifying calcifications, particularly in later disease stages.[5-8]

While NCC is endemic in low- and middle-income countries,[2] its prevalence is increasing in developed regions due to migration from endemic areas.[10] The unequivocal identification of the scolex on MRI enabled a confident diagnosis.

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Remembering PLEVA: An Old Disease in Need of Renewed Attention

Recordando a PLEVA: Uma Doença Antiga a Merecer Atenção Renovada

Keywords: Pityriasis Lichenoides/diagnosis
Palavras-chave: Pitiríase Liquenoide/diagnóstico

We present the case of a 9-year-old boy with a history of chickenpox two years prior who presented to the emergency department with a two-week history of a rapidly progressive papular eruption. The lesions were erythematous, scaly, and intensely pruritic, initially developing on the dorsum and subsequently spreading to the thorax and genital areas, while sparing the lower limbs, scalp, and face. The dermatosis was suggestive of pytiriasis lichenoides et varioliformis acuta (PLEVA). The mother declined skin biopsies, but laboratory workup including infectious serologies and TASO was performed, yielding normal results. The patient was treated with clarithromycin, with complete resolution of lesions within three weeks and no recurrence at two-month follow-up.

Pityriasis lichenoides is a rare self-limited autoinflammatory condition, with two main variants: pityriasis lichenoides chronica (PLC) and PLEVA. In rare cases, the disease progresses to febrile ulceronecrotic Mucha-Habermann disease (FUMHD), a severe variant, characterized by acute symptoms, rapidly necrotic lesions, and high mortality, requiring urgent systemic treatment.[1]

The exact cause of PLEVA is unknown, but it is thought to represent an inflammatory or lymphoproliferative process triggered by infections, immune dysregulation, medications or vaccines. Its lymphoproliferative nature is suggested by the presence of clonal T-cell populations in some lesions, histological similarities to cutaneous T-cell disorders, and rare cases that evolve into lymphoma.[2]

Pytiriasis lichenoides et varioliformis acuta presents as successive crops of small erythematous macules and papules, predominantly on the trunk and flexural areas, often at different stages of evolution – an important diagnostic clue. Lesions may develop fine scale or central puncta, or progress to vesiculopustules with hemorrhagic necrosis and crusting, usually healing without scarring, although varioliform scars may occur. Systemic symptoms are uncommon. Dermoscopy usually displays three concentric zones of central brownish cloud, an intermediate ring of white scale, and a peripheral vascular ring.[3]

It typically affects children, posing a significant diagnostic challenge due to its resemblance to more common conditions such as chickenpox, lymphomatoid papulosis, Gianotti-Crosti syndrome and arthropod bites.[4] The absence of pustules, sparing of face and scalp, and

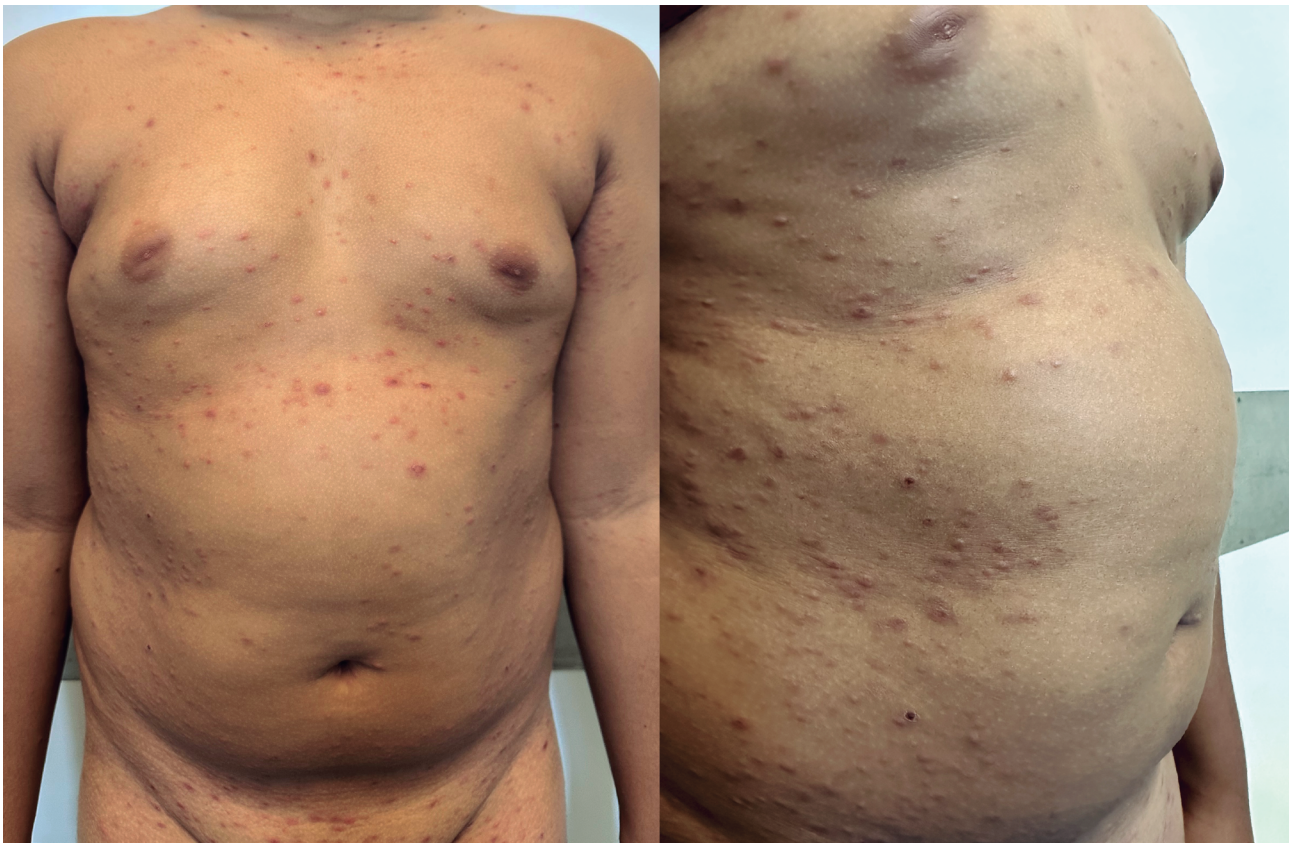

Figure 1 – Trunk showing discrete and confluent erythematous papules

characteristic necrotic papules favor PLEVA.

This condition may resolve spontaneously within weeks or months. Antibiotics like erythromycin or tetracycline are first-line options. Other options include topical steroids, phototherapy or systemic agents, used mainly for symptom control or refractory cases.[5]

The role of T-cell dyscrasia *versus* an inflammatory response to external antigens is still debated, with recent immunophenotyping studies showing a predominance of cytotoxic CD8+ T cells in PLEVA lesions, but without clear evidence of clonality. In the future, multiomics analysis will likely clarify the pathophysiology and etiology of this entity.[6]

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GAS: Study design, writing and critical review of the manuscript.

PF, JA: Critical review of the manuscript.

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Safety and Efficacy of Mepolizumab during Pregnancy and Postpartum

Segurança e Eficácia do Mepolizumab durante a Gravidez e Pós-Parto

Keywords: Anti-Asthmatic Agents/therapeutic use; Antibodies, Monoclonal, Humanized; Asthma/drug therapy; Postpartum Period/drug effects; Pregnancy
Palavras-chave: Anticorpos Monoclonais Humanizados; Asma/tratamento farmacológico; Antiasmáticos/tratamento farmacológico; Gravidez; Período Pós-Parto/efeitos dos fármacos

Asthma is the most common chronic respiratory disease complicating pregnancy, with symptoms worsening in approximately one third of women during early gestation. Poor asthma control increases adverse maternal and perinatal outcomes. Mepolizumab, an anti-interleukin-5 monoclonal antibody, is approved for the treatment of severe eosinophilic asthma. Despite established efficacy and safety in non-pregnant populations, limited pregnancy data have led to its precautionary avoidance.[1,2]

We describe a case in which mepolizumab was safely and effectively continued throughout pregnancy and the postpartum period in a patient with severe allergic eosinophilic asthma.

A 34-year-old non-smoking woman with childhood-onset allergic asthma and chronic rhinosinusitis without nasal polyps remained stable until adolescence, when respiratory symptoms worsened, with seven to eight annual exacerbations requiring oral corticosteroids (OCS). The assessment showed an allergic-eosinophilic phenotype with symptomatic sensitization to dog, cat and olive-tree pollen allergens, and irreversible bronchial obstruction. Omalizumab (300 mg/4w) was initiated; however, despite optimized therapy, she experienced worsening symptoms, recurrent exacerbations and OCS dependence. After five years, omalizumab was switched to mepolizumab (100 mg/4w), leading to improvement of exacerbations, pulmonary function, inflammatory biomarkers, and OCS withdrawal (Table 1).

After seven years of continuous mepolizumab therapy, the patient became pregnant. Following a multidisciplinary meeting at the Severe Asthma Unit, mepolizumab and budesonide/formoterol (400/12µg twice daily) were continued, with the hospital's Pharmacy and Therapeutics Committee approval and written informed consent. The pregnancy and delivery were uneventful. During the first and second trimesters, the patient reported intermittent dyspnea, wheeze and fatigue requiring short-acting bronchodilators, without exacerbations or OCS use. These symptoms were considered compatible with physiological changes of pregnancy, anxiety or transient disease variability. Fractional exhaled nitric oxide increased during the second trimester without clinical deterioration and oxygen saturation remained stable. A healthy infant was delivered vaginally at 39 weeks + three days (Apgar 9/10, weighting 3020 g). Asthma control remained excellent during seven months of postpartum follow-up. Breastfeeding was avoided due to uncertain risks, and the child developed normally.

To date, one case report supports the safety of mepolizumab during pregnancy and early lactation. Discontinuation before conception led to clinical decline; after

Table 1 – Pulmonary function tests and clinical parameters before, during and after pregnancy follow-up under mepolizumab treatment

	Pre-pregnancy		Pregnancy		Post-pregnancy		
	Pre-mepolizumab	Post-mepolizumab	1st trimester	2nd trimester	2 months	4 months	7 months
ACT	21/25	22/25	11/25	15/25	24/25	24/25	24/25
AQLQ	5.75/7	5.81/7	4.09/7		6.46/7	6.68/7	6.81/7
SNOT-22	20/110	22/110	17/110		10/110	19/110	7/110
VAS	25/100	20/100	40/100		30/100	25/100	20/100
TAI	45/50	46/50	50/50		45/50	44/50	47/50
Nijmegen questionnaire	11/64	9/64	11/64		9/64	4/64	2/64
AIRQ			5/10		0/10		0/10
FVC (L/%)	3.75/93	3.92/94			2.21/64	3.81/91	3.96/95
FEV1 (L/%)	2.01/53	2.35/68			1.78/52	2.21/64	2.52/73
FEV1/FVC (%)	53.0	60.1			57.6	58.0	76.0
FeNO (ppb)	232	114	116	146	122	99	123
Eosinophils (per mL)	640	60	50	80	120		
IgE (kU/L)	517	206					
ECP (µg/L)	134	55					
Prednisolone (mg/day)	10	0	0		0		
Exacerbations requiring OCS	7 - 8/year	0	0		0		

ACT: asthma control test; AQLQ: Asthma Quality of Life Questionnaire; SNOT-22: sinonasal outcome test; VAS: visual analogue scale for sino-nasal symptoms severity; TAI: test of adherence to inhalers; AIRQ: Asthma Impairment and Risk Questionnaire; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second; FeNO: fractional exhaled nitric oxide; ECP: eosinophilic cationic protein.

re-initiation, conception occurred four months later with two exacerbations, highlighting the risks of biologic interruption.[3] Pharmacovigilance data have yielded mixed pregnancy outcomes with asthma biologics. For mepolizumab, adverse outcomes were reported for 42% of cases (64/154; OR 0.23), with higher reporting of fetal death (OR 1.87) and spontaneous abortion (OR 2.75) but lower reporting of pregnancy and delivery complications (OR 0.17 and OR 0.21) compared to non-biologic asthma medications; however, spontaneous reporting limits causality assessment.[4] Ongoing prospective studies are expected to provide more definitive data.[5] Additionally, IgG monoclonal antibodies have limited first-trimester placental transfer and low breast milk concentration, with partial infant gastrointestinal degradation, supporting relative safety in pregnancy and lactation.[2,3,5]

Although limited to a single case, this report supports the potential safety and efficacy of continued mepolizumab therapy during pregnancy and postpartum, emphasizing the importance of multidisciplinary management. Further data is required to guide clinical decision-making in this population.

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JMS, DV: Literature review, writing of the manuscript.
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Clonally Related Chronic Myelomonocytic Leukemia and Erdheim-Chester Disease with *KRAS* Mutation: A Rare and Challenging Case

Leucemia Mielomonocítica Crónica e Doença de Erdheim-Chester com Mutação *KRAS*: Um Caso Raro e Desafiador

Keywords: Erdheim-Chester Disease; Leukemia, Myelomonocytic, Chronic; Mutation/genetics; Proto-Oncogene Proteins p21(ras)/genetics
Palavras-chave: Doença de Erdheim-Chester; Leucemia Mielomonocítica Crónica; Mutação/genética; Proteínas Proto-Oncogénicas p21(ras)/genética

Chronic myelomonocytic leukemia (CMML) is a myeloid neoplasm with features of both myelodysplastic and myeloproliferative syndromes, defined as persistent non-reactive peripheral blood monocytosis (≥ 500/μL and relative ≥ 10%), bone marrow (BM) dysplasia, in the absence of other myeloid neoplasms, with a risk of leukemic transformation. Recurrent mutations affect approximately 40 genes, most commonly *TET2, SRSF2, ASXL1*, and the *RAS* pathway.[1] Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis of adults, characterized by xanthelasma, bone pain, and multiorgan infiltration by foamy CD68+/CD1a- histiocytes, frequently carrying *BRAFV600E* or *RAS* pathway mutations.[2] Histiocytic neoplasms may coexist with hematological malignancies; up to 10% of adults with ECD have an associated myeloid neoplasm.[3]

A 59-year-old woman with periorbital and thoracic xanthelasmas (Fig. 1A) since age 25 was referred to the Hematology clinic for severe iron deficiency anemia. She presented mild pancytopenia with monocytosis (1350/μL, rising to 2040/μL).

Bone marrow examination showed hypercellularity with trilineage dysplasia, < 5% blasts, and a normal karyotype. No *BCR::ABL1, PDGFRA, PDGFRB, FGFR1, or PCM1::JAK2* rearrangements were detected, findings that did not meet criteria for other myeloid neoplasms and were consistent with low-risk CMML.

Due to painful subcutaneous nodules and recurrent cutaneous and mucosal infections, biopsies of skin and vulvar lesions were performed, showing foamy CD68+/CD1a-/S100- macrophages, consistent with cutaneous ECD (Fig. 1B). Fluorodeoxyglucose positron emission tomography (FDG-PET) revealed diffuse skeletal uptake and splenomegaly, without cardiac or central nervous system involvement.

Next-generation sequencing (Ion GeneStudio S5 Plus, Panel Oncomine Myeloid Research Assay) of vulvar tissue and peripheral blood identified the same *KRAS* p.Gly12Ala mutation (*VAF* 26% and 41%, respectively), supporting a shared clonal origin from a myeloid progenitor, as previously reported.[4,5] Given the stable course of CMML, PEG-interferon-α was initiated for ECD, resulting in initial clinical improvement. However, after six months, the patient experienced recurrence of cutaneous lesions. Since *KRAS* mutations activate the MAPK pathway, treatment was then switched to cobimetinib, a MEK inhibitor, with transient clinical and hematologic partial responses observed after eight months of therapy.

This case illustrates the coexistence of CMML and ECD sharing a single driver mutation, supporting a common myeloid progenitor origin. Papo *et al* reported myeloid neoplasms in 10% of adults with ECD,[3] and others described similar CMML-ECD associations involving *KRAS* mutations.[4] The biological link may reflect either transformation of a clonal CMML population into histiocytes or divergent differentiation from a mutant progenitor.[4,5]

Close clinical and hematologic monitoring remains crucial, as allogenic stem cell transplantation is the only curative approach for CMML. Despite reporting a single case with a short follow-up, we believe this case strengthens the evidence for a shared pathogenesis between myeloid neoplasms and histiocytic disorders.

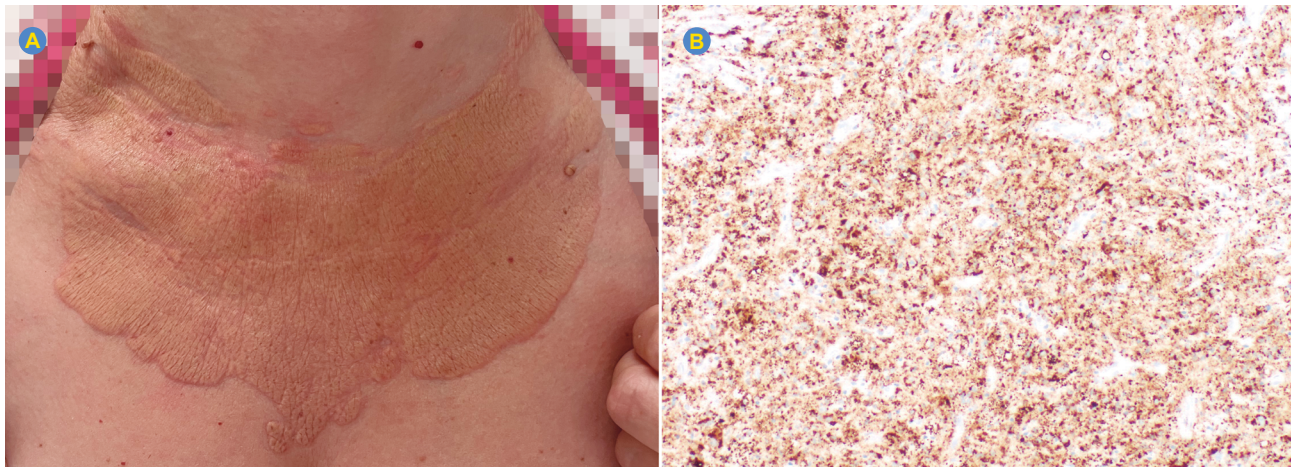

Figure 1 – Cutaneous and histopathological features of the thoracic lesion. Thoracic xanthelasma presenting as yellowish plaques on the upper chest (A). Skin biopsy of the thoracic lesion with hypercellular proliferation comprising CD68 positive foamy histiocytes (B).

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AUTHOR CONTRIBUTIONS

TMB: Data collection, writing of the manuscript.

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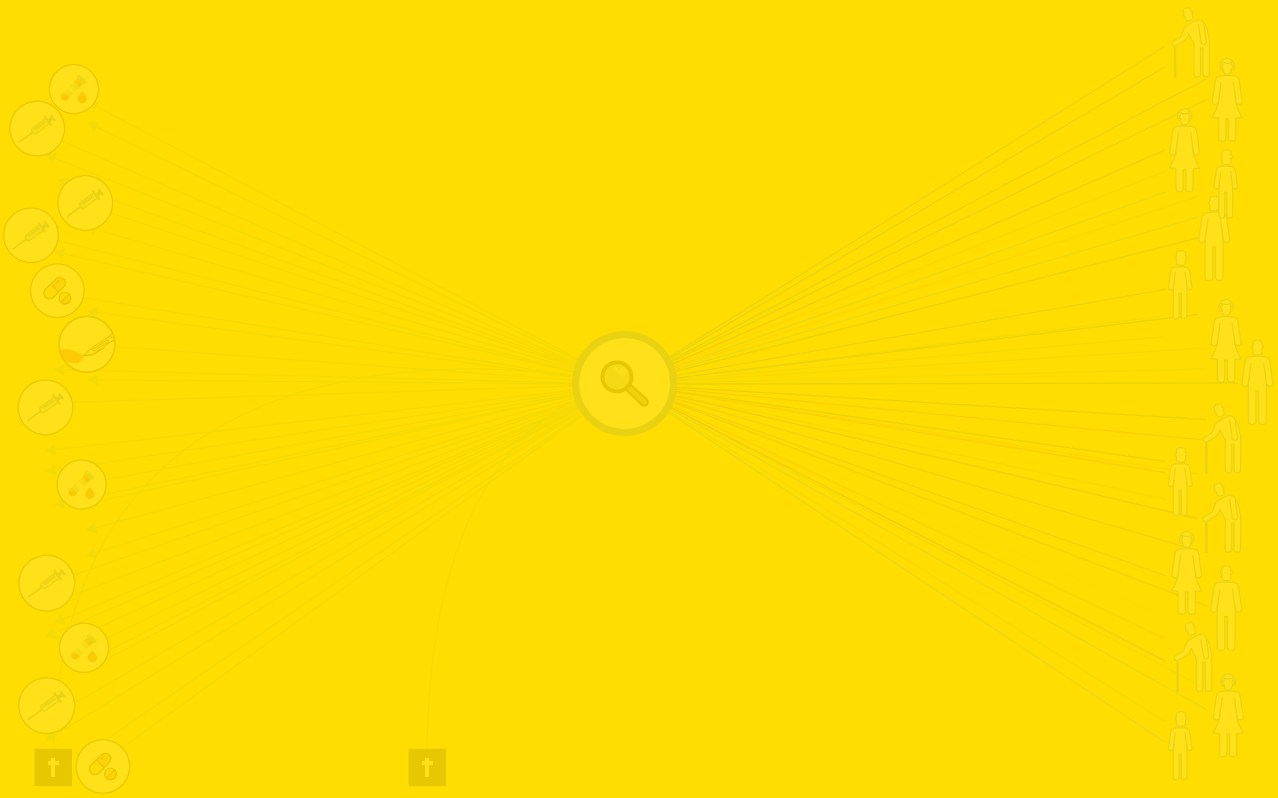

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