nationwide survey

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# Abstract

**Background:** Hemoglobinopathies, such as sickle cell disease and thalassemia, are genetic disorders that affect hemoglobin structure or production, leading to various health complications, including an increased risk of infections. Vaccinations play a crucial role in managing these conditions by providing essential protection against preventable diseases. Ensuring timely and appropriate immunizations is vital for reducing infection-related morbidity and improving the overall health and quality of life for affected individuals. **Objectives:** Our objective was to assess vaccination coverage, as well as knowledge, attitudes, and practices toward vaccination in Greek patients with hemoglobinopathies.

**Design and methods:** A nationwide survey of hemoglobinopathy patients in Greece using a 37item questionnaire was conducted anonymously via Google Forms. It covered demographics, previous vaccinations, vaccine-preventable infections, beliefs about vaccines, and antibiotic prophylaxis post-splenectomy. The survey was distributed through Thalassemia and Sickle Cell Units and organizations.

**Results:** Participants were predominantly university-educated married women aged 30– 50 years with transfusion-depended thalassemia (n = 149, 60.5%) or sickle cell anemia (n = 52, 21.1%). Reported childhood vaccination rates aligned with Greece's national immunization program. However, adult coverage was suboptimal across all age groups for measles (10%), varicella (27%), zoster (2% for over 50 years old individuals), hepatitis A (13.9% of those with chronic liver disease) and hepatitis B (41%), pneumococcal (81.3%), meningococcal (37%), tetanus (20.3%), and influenza (67.1%) vaccines compared to guidelines. Participants relied predominantly on healthcare providers for vaccine information but perceived limited engagement. Those over age 50 demonstrated lower adult vaccination rates and higher misconceptions compared to younger cohorts.

**Conclusion:** Addressing educational and access gaps could help protect this vulnerable population. Our findings highlight the need for coordinated efforts to optimize adult immunization for those with hemoglobinopathies.

# Plain language summary

### Vaccination Habits of Greek Adults with Hemoglobin Disorders

We surveyed 246 adults in Greece with hemoglobin disorders like thalassemia and sickle cell anemia. Most were educated women aged 30–50. When it came to childhood vaccinations, they followed Greece's guidelines. But as adults, they weren't getting vaccinated enough. For instance, only a small percentage got vaccines for measles,

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Original Research

varicella, hepatitis A and B, among others. They mostly relied on doctors for vaccine info but felt they weren't getting enough guidance. Older adults were less likely to get vaccinated and had more misconceptions. To help, we need better education and easier access to vaccines.

Keywords: sickle cell disease, vaccineshemoglobinopathies, thalassemia

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# Introduction

Hemoglobinopathies, a group of genetic disorders in which there is abnormal production or structure of the hemoglobin molecule, including thalassemia and sickle cell disease (SCD), are among the most prevalent inherited disorders worldwide.<sup>1</sup> Recent surveys suggest that between 300,000 and 400,000 babies are born with a serious hemoglobin disorder each year and these conditions affect an estimated 7% of the population worldwide.<sup>2</sup> For Europe, the annual incidence of symptomatic individuals is estimated at between 1 in 10,000 for  $\beta$ -thalassemia and 1 to 5 in 10,000 for SCD.<sup>3</sup> Greece has a high burden, with carrier rates up to 12% in some regions and the total number of patients surviving today is estimated to be around 4000, most of them suffering from thalassemia.4

These diseases cause chronic hemolytic anemia and end-organ damage from hemolysis or recurrent sickling.<sup>5,6</sup> Both thalassemia and SCD also increase infection susceptibility. Splenic dysfunction and inflammatory changes lead to immune deficits.7-9 Vaccination represents a vital preventive strategy.<sup>8,9</sup> Hepatitis B virus (HBV) and hepatitis C virus (HCV) were of major concern in the previous decades, resulting from blood transfusion therapy and leading to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Infections with encapsulated bacteria, such as pneumococcus and meningococcus, have devastating effects on patients who have surgical or functional asplenia. In addition, viral infections of the young age may present with serious and permanent complications in adults with hemoglobinopathies.<sup>10</sup> In Greece, vaccination strategies for these patients follow those of the National Healthcare Vaccination program for adults at increased risk for serious infections and include measles-mumps-rubella

(MMR), varicella, zoster, hepatitis A and B, pneumococcal, meningococcal, tetanus–diphtheria– pertussis (Tdap), influenza, and haemophilus influenza type b.<sup>11</sup> However, studies show vaccination knowledge and coverage gaps worldwide, despite recommendations.<sup>12–16</sup> A small audit from England reported that only 2.5% of the adult population with SCD had a complete up-to-date vaccination profile, with lower rates of vaccination concerning meningococcal and HepB vaccines.<sup>16</sup> Reported barriers include safety concerns, logistical obstacles, costs, and insufficient patient and provider awareness.<sup>18–20</sup>

The literature review revealed a shortage of data concerning vaccination coverage and practices among adults affected by hemoglobinopathies. Individuals with hemoglobinopathies do not precisely match the criteria defining immunocompromised patients, leading to overlooked vaccination practices by both patients themselves and healthcare professionals. Despite a substantial body of literature addressing immunocompromised patients, there is a notable absence of equivalent attention for individuals with hemoglobinopathies, despite the high prevalence of these conditions, particularly in the Mediterranean region. We conducted this nationwide survey in Greece during 2018-2019 to assess adult vaccination practices, knowledge, and attitudes among patients with hemoglobinopathies, shortly before the COVID-19 pandemic. Our goal was to identify deficiencies to guide public health efforts toward better protecting this vulnerable group.

# Methods

A nationwide sample of patients with hemoglobinopathies was surveyed using a 37-item questionnaire designed to assess their knowledge, attitudes, and practices related to vaccination. In Greece, mandatory immunization shots are completely paid for by health insurance, are prescribed by private general practitioners, and are administered in clinics or pharmacies. The documentation of vaccines is stored inside the patient's medical record. The questions included demographic characteristics (age, sex, marital status, educational level, type of hemoglobinopathy), previous vaccinations [measles-mumps-rubella (MMR), varicella, zoster, hepatitis A and B, pneumococcal, meningococcal, tetanus-diphtheria-pertussis (Tdap), influenza and haemophilus influenza type b], previous infections with vaccine-preventable diseases, beliefs concerning benefits and vaccination side effects and antibiotic prophylaxis after splenectomy. The survey was conducted anonymously to ensure participant confidentiality. In March 2018, the questionnaire was uploaded onto the Google Forms platform and distributed to patients associated with Thalassemia and Sickle Cell Units around Greece. Only one completion of the questionnaire was permitted per patient. Invitation for participation has been prolonged for the second semester of 2019. Study inclusion criteria were all patients with hemoglobinopathies previously diagnosed by hemoglobin electrophoresis or genetic testing, and who were given the link to the questionnaires. Exclusion criteria were late completion of the questionnaire beyond the specified date, as well as patients being followed in Thalassemia and Sickle Cell Units without a documented diagnosis. The statistical analysis of the results was done with the program IBM SPSS Statistics Standard Grandpack version 28 for Windows, using descriptive analysis and a chi-square test for comparison between groups. Findings were reported as statistically significant at p < 0.05.

# Results

# Participant characteristics

We enrolled 246 participants aged 18–71 years across Greece, predominantly women (n=170, 69%). Most of the patients were aged 30–50 years (n=182, 73.9%), married (n=132, 53.6%), and university graduates (n=156, 63.4%). Diagnoses included transfusion-depended thalassemia (n=149, 60.5%), thalassemia intermedia (n=34, 13.8%), sickle cell anemia (n=52, 21.1%), and other hemoglobinopathies (n=11, 4.5%) (Table 1).

 Table 1. Sociodemographic characteristics of the participants.

Characteristics	n (%)
Age range (years)	18–71
Age distribution	
18-29 years	15 (6.1)
30–50 years	182 (73.9)
51-71 years	49 (19.9)
Gender	
Male	76 (31)
Female	170 (69)
Marital status	
Married	132 (53.6)
Unmarried	114 (46.4)
Educational level	
University Graduates	156 (63.4)
Non-university graduates	90 (36.6)
Diagnosis	
Transfusion-dependent thalassemia	149 (60.5)
Non-transfusion dependent thalassemia	34 (13.8)
Sickle cell disease	52 (21.1)
Other hemoglobinopathies	11 (4.5)

#### Childhood vaccinations

Overall, 84% (n=207) provided childhood vaccine history, with most born 1970–1990 likely vaccinated per Greece's 1997 schedule. This introduced hepatitis B, haemophilus influenza type b, acellular pertussis, mumps, and hepatitis A vaccines. However, varicella, meningococcal, second MMR doses, and HPV vaccination came later. Table 2 presents the breakdowns in relation to childhood vaccination.

#### Adult vaccinations

Concerning measles-mumps-rubella vaccination, while 74.9% (n=155) reported childhood MMR vaccination, only 10% (n=25) had adult **Table 2.** Patients' vaccination coverage duringchildhood.

Vaccination	n (%)
MMR	155 (74.9)
Varicella	76 (37.1)
Zoster	7 (3.3)
Hepatitis A	86 (41.5)
Hepatitis B	111 (53.6)
Pneumococcal	115 (55.6)
Meningococcal	84 (40.6)
Tetanus-diphtheria-pertussis	113 (54.6)
Influenza	97 (46.9)
H. influenza b	32 (15.5)

 Table 3. Patients' vaccination coverage in adulthood.

Vaccination	n (%)	
MMR	25 (10)	
Varicella	66 (27)	
Zoster vaccine awareness	212 (86)	
Hepatitis A	6 (13.9)ª	
Hepatitis B	101 (41)	
Pneumococcal	200 (81.3)	
Meningococcal	91 (37) <sup>ь</sup>	
Tetanus-diphtheria-pertussis	50 (20.3)	
Influenza	165 (67.1)	
H. influenza b	75 (30.5)	
°4 out of 28 patients with liver disease, 2 out of 15 patients		

with cirrhosis or portal thrombosis. <sup>b</sup>18 out of 86 (20.9%) patients with prior splenectomy.

doses. Instead, 90% (n=221) were unvaccinated as adults, despite recommendations for those born after 1970 without immunity. Adult varicella coverage was low, with 73% (n=180) unvaccinated. Adults over 50 years old lacked childhood vaccination, and only 20% of those aged 20–50 years (n=49) had a childhood infection. Among those eligible, only 15.4% aged 30–50 years (n=28) received the recommended doses (Table 3, Figure 1).

Zoster vaccine awareness was very low, with 86% (n=212) seemingly unaware of it. Only 13% (n=32) had been recommended the vaccine, which is advised for all adults over 60 years. Coverage was very low among over 50-year-olds (2%) (Table 3 and Figure 1).

Most participants were unvaccinated for hepatitis A as adults, including only 13.9% of those with liver disease and any stage of cirrhosis or portal thrombosis (n=4/28 and n=2/15, respectively).The majority of participants aged 50 and above indicated a history of hepatitis B infection (45%) or a record of vaccination (22.4%). Nevertheless, the vaccination coverage was found to be insufficient in the under-20 age group, with 12 out of 20 individuals (60%) remaining unvaccinated. Similarly, among individuals aged 18-30, the vaccination coverage was also inadequate, with 80% remaining unvaccinated. Overall, 41% (n=101/246) were vaccinated against hepatitis B. The majority of vaccinated individuals underwent regular antibody testing on an annual basis (Table 3 and Figure 1).

Reported pneumococcal vaccine coverage appeared reasonably high (60%–90%) across all age groups. However, most were uncertain about which specific vaccines they had received, confusing appropriate use.

Meningococcal vaccination was low, with 60%– 80% unvaccinated across age groups. Only 20.9% of those with prior splenectomy (n=18/86) had received the vaccine, which is advised for functional or anatomic asplenia.

Alarmingly, few participants reported adult tetanus vaccinations. Most under 60 years were unvaccinated (21.4%, 33.3%, and 12.2% vaccination coverage for age groups 30–50, 18–30, and over 50 years, respectively). Most incorrectly indicated receiving tetanus immunoglobulin over the vaccine (Table 3, Figure 1).

A total of 165 individuals, accounting for 67.1% of the sample population, have received the annual influenza vaccine and 32 (15.5%, the vaccine for haemophilus influenza type b (Table 3, Figure 1).



Figure 1. Adult vaccination coverage by age group.



Figure 2. Patients' beliefs toward vaccination.

# Vaccine attitudes

The majority of participants (ranging from 87% to 99%, with a sample size ranging from 214 to 243) denied the erroneous beliefs that vaccines are unnecessary, cause cancer, or that alternative medicine can serve as an alternative to them. However, 6% (n=15) still believed hemoglobinopathies were a vaccine contraindication. Nearly all (97%, n=239) agreed that vaccines benefit those with blood disorders (Figure 2). Patients

had a significantly higher level of trust in their doctor (87.5%) for both receiving information about vaccines and getting vaccinated, compared to their trust in nurses (5%) or pharmacists (7.5%); Figure 3).

Individuals aged 50 and above exhibited a higher propensity for harboring misconceptions regarding vaccines compared to younger age groups (17% vs 2%, p < 0.05). Furthermore, this older



**Figure 3.** The trust of patients in relation to information and the implementation of vaccinations.

cohort demonstrated insufficient coverage of adult vaccinations, ranging from 0% to 22% to 10% to 42% across different vaccines (p < 0.05).

Finally, a notable prejudice against vaccines was evident among individuals without a university education in the patient group, as 15 out of 90 (16.7%) were against vaccination compared to 10 out of 156 (6.4%) from those with a university education (p < 0.05).

### Antibiotic prophylaxis

Within the cohort of individuals who had previously undergone splenectomy, only 42% (n=36/86) were administered antibiotic prophylaxis. However, most people would take antibiotics for fever as suggested by their doctors after a splenectomy. Only a small proportion of individuals, specifically 3% (n=2), would choose not to seek medical evaluation for fever.

### Discussion

Our findings reveal significant adult vaccination coverage and knowledge gaps among patients with hemoglobinopathies in Greece compared to guidelines,<sup>21–35</sup> likely elevating infection risks. Deficiencies spanned all vaccines but were most pronounced for varicella, zoster, meningococcal,

tetanus, and influenza.<sup>21</sup> Participants over age 50 showed heightened susceptibility, with lower adult vaccination rates (0%-22% vs 10%-42% for those under 50 years old) and higher misconception rates compared to younger groups. In addition, 17% of over-50s harbored vaccine misconceptions, markedly higher than the 2% among vounger participants (p < 0.05). Older patients were raised under earlier childhood immunization schedules with fewer contemporary vaccine options.<sup>26</sup> They have also historically faced more vaccine hesitancy and access limitations.27-29 Targeted educational and catch-up vaccination initiatives focused on older adults with hemoglobinopathies could help address these pronounced deficiencies. Reported childhood vaccinations aligned with Greece's evolving national immunization schedule.<sup>23-25</sup> New vaccine introductions over recent decades have gradually expanded recommendations. However, limitations contributed to the adult deficiencies observed. Many participants completed childhood immunizations before the second MMR, varicella, and adolescent booster doses were introduced.20 Most adults also received childhood vaccines prior to universal varicella and zoster vaccination in Greece.33 Furthermore, combination vaccines were unavailable until recently. Thus, many participants likely entered adulthood under-immunized, requiring catch-up adult vaccines that were suboptimally delivered.<sup>30</sup> Even for widely available vaccines like influenza, tetanus, and hepatitis B with longstanding guidelines, most eligible adults remained unvaccinated.33-35

Comparing vaccination rates within the Greek population, two significant studies conducted in 2020 and 2023 focused on elderly and high-risk groups. The findings revealed variations in coverage across different vaccines. Influenza vaccination rates ranged from 56% to 83%, indicating a relatively high level of uptake. Pneumococcal vaccination, on the other hand, showed a wider range of coverage, from 36% to 73%, suggesting variability in accessibility or awareness. Zoster vaccine coverage remained notably low, ranging from 12% to 20%, indicating potential areas for improvement in immunization outreach or education. Tetanus vaccination rates were also relatively low, ranging from 7% to 21%, suggesting a need for increased emphasis on adult immunization programs. Measles coverage hovered around 33%, indicating room for improvement in achieving

herd immunity against this highly contagious disease. Hepatitis B vaccination coverage was notably low, ranging from 3% to 11%, highlighting the importance of targeted efforts to increase awareness and access to this crucial vaccine. These findings underscore the importance of ongoing public health efforts to enhance vaccination coverage and protect vulnerable populations from preventable diseases.<sup>36,37</sup> Our findings align with those mentioned above regarding the Greek population's susceptibility to serious infections. In our research, we observed elevated rates of pneumococcal and HepB vaccination coverage, alongside notably reduced coverage for measles vaccination.

Low vaccination rates among individuals with hemoglobinopathies in Greece have significant implications for both public health and the affected population. Low vaccination rates leave individuals with hemoglobinopathies more vulnerable to vaccine-preventable diseases such as influenza, meningococcal disease, varicella, and tetanus. These individuals often have compromised immune systems, making them more susceptible to severe complications from these infections.10 Furthermore, with low vaccination rates, there is a higher likelihood of outbreaks of vaccine-preventable diseases within this population. This not only poses a direct risk to the health and well-being of affected individuals but also increases the burden on healthcare systems. Unvaccinated individuals serve as potential reservoirs for vaccine-preventable diseases, increasing the risk of transmission to others in the community, including those who may be unable to receive vaccinations due to medical reasons or age. Moreover, individuals with hemoglobinopathies are at increased risk of experiencing severe complications or even mortality if they contract vaccine-preventable diseases. Complications can include pneumonia, encephalitis, sepsis, and other serious conditions, which can be particularly dangerous for those with underlying health conditions. In addition, outbreaks of vaccine-preventable diseases can impose significant economic costs on both individuals and healthcare systems. This includes expenses related to medical treatment, hospitalization, lost productivity, and public health interventions to control the spread of disease. Low vaccination rates among individuals with hemoglobinopathies can strain healthcare resources, leading to increased demand

for medical services, hospital admissions, and intensive care management during disease outbreaks. This can potentially overwhelm healthcare facilities, especially during peak flu seasons or outbreaks of other infectious diseases.<sup>38</sup> Finally, communities with low vaccination rates may face stigmatization or discrimination from others who perceive them as a higher risk for spreading infectious diseases. This can lead to social isolation and further barriers to accessing healthcare services and support.

Addressing low vaccination rates among individuals with hemoglobinopathies requires a multifaceted approach, including targeted education and outreach efforts, improved access to vaccines and healthcare services, addressing vaccine hesitancy and misinformation, and strengthening healthcare infrastructure to support vaccination initiatives. Participants valued provider vaccine counseling but perceived limited engagement, potentially hindering adult coverage. Optimizing provider recommendation practices through reminders, audits, and incentives could strengthen guideline adherence. Standardizing documentation via registries could empower patients to initiate vaccine discussions. Financial obstacles may also factor in, given adult vaccine cost-sharing in Greece. Ensuring health insurance coverage could increase protection for this vulnerable group. Finally, educational initiatives targeting misconceptions are needed, especially among older patients. A coordinated national effort is essential to address these gaps through improved awareness, access, and adherence to optimize adult vaccination and prevent infections in those with hemoglobinopathies. Our findings highlight vaccination as an unmet need requiring prioritization among this high-risk population.

The study's constraints stem from its retrospective nature, relying on patient-completed questionnaires, potentially impacting the reliability of vaccination data. In addition, as the questionnaires were anonymous, people without hemoglobinopathies may have completed them, although this possibility is not considered very likely, as the link was shared by the Thalassemia and Sickle Cell Units. Furthermore, vaccination records, particularly among elderly participants, may have been inadequately maintained or updated.

### Declarations

## Ethics approval and consent to participate

All participants consented to participate in the study by answering the corresponding question at the beginning of the questionnaire. Ethics committee approval was not deemed necessary, as the questionnaire was anonymous and the study did not involve any therapeutic intervention for the patients.

#### Consent for publication

All participants completed the questionnaires voluntarily and anonymously, knowing in advance that the data would be used for the writing of this document.

## Author contributions

**Sophia Delicou:** Conceptualization; Formal analysis; Methodology; Supervision; Visualization; Writing – review & editing.

**Konstantinos Manganas:** Data curation; Investigation; Software; Writing – original draft.

**Aikaterini Xydaki:** Data curation; Formal analysis; Methodology; Resources; Validation; Writing – original draft.

**Loukia Evliati:** Data curation; Investigation; Methodology; Software.

**Ioanna Myrilla:** Data curation; Investigation; Methodology; Resources; Software; Writing – original draft.

**Leonidas Rubatis:** Data curation; Formal analysis; Investigation; Methodology.

**Stavroula Kostaridou:** Conceptualization; Project administration; Supervision; Visualization; Writing – review & editing.

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#### Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials All data are available upon request.

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