Familial Hypercholesterolemia

Country Mapping Survey

Preliminary Analysis of Submitted Data

7 April 2022

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DISCLAIMER

The present paper is not an official document of the World Heart Federation or FH Europe. The report serves as a preliminary analysis of the data collected through the WHF / FH Europe Country Mapping Survey 2020.

The paper presents the data, as reported by the survey respondents. Therefore, the World Heart Federation and FH Europe are not responsible and accountable for the data.

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BACKGROUND

In 1998, the World Health Organization (WHO) officially recognized familial hypercholesterolemia (FH) as a global public health issue and published a set of recommendations to address its burden (1). In the past two decades, tremendous scientific progress has been achieved in the fields of genetics, lipidology, cardiology, and drug development. In spite of these breakthroughs, implementation of the WHO recommendations has been largely insufficient in many countries and regions.

Familial hypercholesterolemia affects approximately 34 million individuals worldwide (2). Nevertheless, low levels of awareness and education among both the general public and the medical community have resulted in only 10% of people living with FH being diagnosed and treated (2). Early diagnosis and treatment of the condition are of paramount importance, as untreated patients are at severe risk of developing premature cardiovascular disease (3).

In recent years, many countries have developed and implemented a number of successful FH initiatives and programmes, including universal children screening programmes, cascade screening programmes, patient-centred care, and evidence-based guidelines. Moreover, programmes benefiting from governmental support and funding were generally more successful (2).

In January 2020, representatives from the global FH community published a Global Call to Action and highlighted a set of recommendations, in 9 areas of priority, to reduce the clinical and public health burden of familial hypercholesterolemia (2).

1. **Awareness**
2. **Advocacy**
3. **Screening, Testing, and Diagnosis**
4. **Treatment**
5. **Severe and Homozygous FH**
6. **Family-Based Care**
7. **Registries**
8. **Research**
9. **Value and Cost**

In light of the continued need to raise awareness of FH and disseminate information on progress made, the World Heart Federation (WHF), in partnership with FH Europe, the European FH Patient Network (FHE), conducted an international survey to map the state of FH advocacy around the world. The survey was completed by representatives of FH advocacy organizations, patients, healthcare professionals, nurses, caregivers, and researchers.

OBJECTIVES

The country mapping survey aims to provide data on the burden of FH to a wide range of stakeholders. The present report summarizes the results of the survey, focusing on 7 out of the 9 areas of priority identified in the Global Call to Action. The main objectives of the country mapping analysis are to:

- Map the state of FH advocacy across the globe
- Identify trends and opportunities
- Identify gaps and challenges
- Recommend areas of priority for investments

METHODS

Survey Design

A total of 31 questions were included in the survey. Most questions were multiple choice or close-ended questions. For some questions, respondents had the possibility of adding comments, if necessary. The survey questions can be consulted in Appendix 1. The questionnaire was divided into 6 sections, each dedicated to a specific area of interest.

- Section 1: Information on the respondents and their organizations was collected.
- Section 2: Information on the prevalence, underdiagnosis, and undertreatment of FH was collected.
- Section 3: Information on screening strategies and methods of diagnosis was collected.
- Section 4: Information on referral pathways, treatments, insurances, and reimbursement schemes was collected.
- Section 5: Information on national FH registries was collected.
- Section 6: Information on national advocacy efforts and support for FH was collected.

To ensure the validity of the responses, all participants were invited to contact a representative from FHE in case of uncertainty or confusion. In addition, the responses were further reviewed with the survey participants via email, after submission.

Participants

The survey was sent out to collaborators from 102 countries. Selected individuals represented a range of stakeholders, including patients, advocates, physicians, nurses, and researchers among others. Selected individuals were also requested to forward the survey to other suitable national experts, as appropriate. In turn, some country data were provided by more than one participant.

Some of the authors of the Global Call to Action and leaders of the FH Europe's Network organisations were invited to participate. Other contacts were supplemented from the European Atherosclerosis Society (EAS) Familial Hypercholesterolemia Studies Collaboration (FHSC) National Lead Investigators list. Lastly, contacts from the Global Survey on Cholesterol Testing Infrastructure for Identifying Familial Hypercholesterolemia were added.

Respondents were invited to participate in the survey in late September 2020. A second wave of invitations was sent out in late October 2020. Reminders were also sent out on a regular basis. Over time, further respondents were identified and contacted in order to increase the geographical coverage and diversity. Individual follow-ups and data verification were conducted until June 2021. In November 2021, survey participants were re-contacted by the World Heart Federation in order to re-confirm the validity of the information on their respective countries.

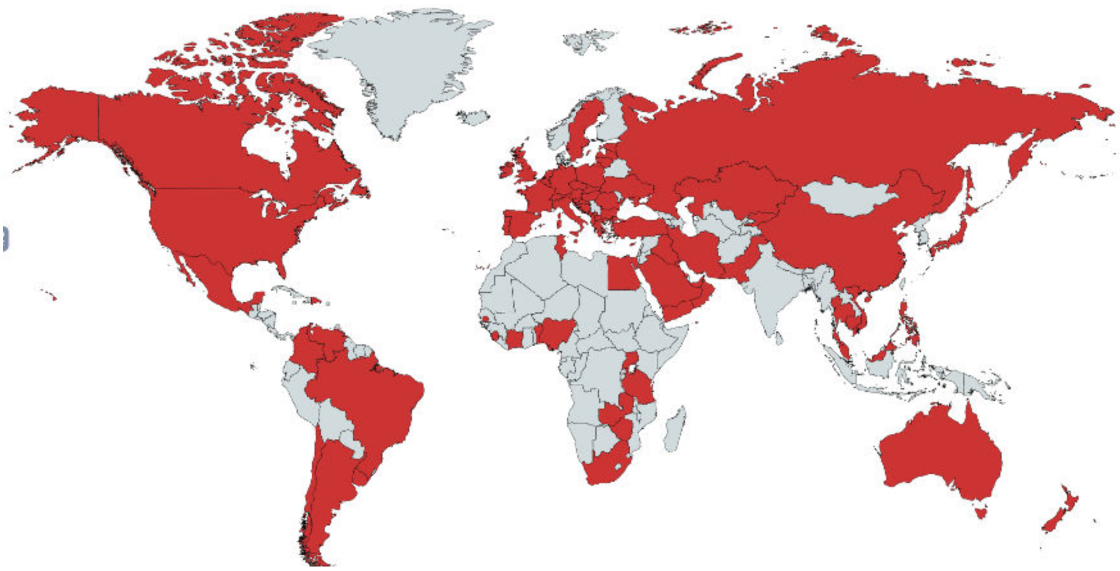

Figure 1: Mapping of survey respondents

Tools

WHF and FH Europe used SurveyMonkey® to build and disseminate the country mapping survey. Maps featured in the report were generated with MapChart.

Analysis

To structure and facilitate the analysis of the data, countries were grouped into 5 regions (similar to the WHO regions). Data on the following countries and regions were collected:

African Region – Benin, Ivory Coast, Nigeria, Rwanda, Sierra Leone, South Africa, Tanzania, The Gambia, Uganda, Zambia, and Zimbabwe.

Americas Region – Argentina, Brazil, Canada, Chile, Colombia, Dominican Republic, Mexico, United States, Uruguay, and Venezuela.

Eastern Mediterranean Region – Bahrain, Egypt, Iran, Iraq, Kuwait, Oman, Pakistan, Saudi Arabia, Tunisia, United Arab Emirates, and Yemen.

European Region – Albania, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, North Macedonia, Poland, Portugal, Romania, Russia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine, and the United Kingdom.

Asia-Pacific Region – Australia, Cambodia, China, Japan, Malaysia, New Zealand, Philippines, Thailand, and Vietnam.

RESULTS

The country mapping survey was completed by 95 respondents, representing 78 countries, between 21 September 2020 and 9 December 2020. The data was subsequently exported into a Microsoft Excel spreadsheet and **partially** cleaned prior to analysis. In total, 5 sets of responses were considered non-valid and removed from the analysis:

- 3 sets of duplicates
- 1 set of incomplete data
- 1 set of data from a test-run

As a result, the survey involved 90 true respondents from 78 countries.

In terms of distribution, data were collected from low-, middle-, and high-income countries. However, most of the data were provided by countries in the European region:

- The 12 respondents from the African region represented a total of 11 countries
- The 15 respondents from the Americas region represented a total of 10 countries
- The 12 respondents from the Eastern Mediterranean region represented a total of 11 countries
- The 42 respondents from the European region represented a total of 37 countries
- The 9 respondents from the Asia-Pacific region represented a total of 9 countries

Responses were immediately reviewed with survey respondents via email until June 2021. In November 2021, survey participants were re-contacted by the World Heart Federation to re-confirm the validity of the data.

1. Awareness

FH has been recognized as a global public health issue. Unfortunately, the condition remains severely underdiagnosed and undertreated. As such, the Global Call to Action recommends raising awareness of both forms of familial hypercholesterolemia among the general population and healthcare professionals (2). Awareness about the importance of early diagnosis and treatment of FH is needed in order to prevent FH-related premature cardiovascular events and reduce the burden of FH worldwide. FH Awareness Day was established on 24 September.

African Region

Data on the prevalence of familial hypercholesterolemia were only available for 2 out of 11 countries. South Africa reported the existence of founder effects in some subpopulations.

Table 1: FH prevalence in the African region

	Number of countries	Percentage
1 in 500 people	1/11	9.1%
1 in 250 people	1/11	9.1%
Data availability	2/11	18.2%

International guidelines for the management of dyslipidaemia were followed in 10 out of 11 countries, with 6 countries using the ESC/EAS guidelines and 2 others using the AHA/ACC guidelines. South Africa followed both national and international guidelines. Unfortunately, one country did not follow any guidelines.

Table 2: Adopted guidelines for the management of dyslipidaemia in the African region

	Number of countries	Percentage
No guidelines	1/11	9.1%
National guidelines	1/11	9.1%
International guidelines	10/11	90.9%

FH Awareness Day on 24 September was not officially recognized in any of the countries in the African region.

Table 3: Recognition of FH Awareness Day in the African region

	Number of countries	Percentage
Not recognized	10/11	90.9%
Partially recognized	0/11	0.0%
Fully recognized	0/11	0.0%

Americas Region

Data on the prevalence of FH in the Americas region were available in 9 out of 10 countries. Most countries reported a prevalence of 1 in 250 to 300 people. Brazil and Colombia reported a prevalence of 1 in 263 people and 1 in 160 people, respectively (4).

Table 4: FH prevalence in the Americas region

	Number of countries	Percentage
1 in 250 to 300 people	5/10	50.0%
1 in 250 people	2/10	20.0%
Other	2/10	20.0%
Data availability	9/10	90.0%

Every country followed either a national or an international guideline for the management of dyslipidaemia. Argentina, Mexico, the United States, and Uruguay followed both national and international guidelines (e.g., ACC/AHA, ESC/EAS, or the Spanish guidelines). Brazil indicated that its national guidelines were in line with other international guidelines.

Table 5: Adopted guidelines for the management of dyslipidaemia in the Americas region

	Number of countries	Percentage
No guidelines	0/10	0.0%
National guidelines	8/10	80.0%
International guidelines	6/10	60.0%

FH Awareness Day was partially or formally recognized in most countries.

Table 6: Recognition of FH Awareness Day in the Americas region

	Number of countries	Percentage
Not recognized	1/10	10.0%
Partially recognized	4/10	40.0%
Fully recognized	5/10	50.0%

Eastern Mediterranean Region

Data on the prevalence of FH were available in 10 out of 11 countries. Saudi Arabia reported a prevalence of 1 in 112 people, the highest in the region. Iraq indicated that experts were still evaluating the prevalence of FH.

Table 7: FH prevalence in the Eastern Mediterranean region

	Number of countries	Percentage
1 in 500 people	1/11	9.1%
1 in 250 to 300 people	4/11	36.4%
1 in 250 people	1/11	9.1%
1 in less than 250 people	3/11	27.3%
Other	1/11	9.1%
Data availability	10/11	90.1%

Every country followed an international guideline for the management of dyslipidaemia. Oman used the *Middle-East and North African Regional Recommendations for the Management of Lipid Disorders and FH*. Egypt followed both national and international guidelines.

Table 8: Adopted guidelines for the management of dyslipidaemia in the Eastern Mediterranean region

	Number of countries	Percentage
No guidelines	0/11	0.0%
National guidelines	1/11	9.1%
International guidelines	11/11	100.0%

FH Awareness Day was partially or fully recognized in most countries. Oman reported that its National Society for Lipid and Atherosclerosis managed various aspects related to awareness raising and advocacy for FH.

Table 9: Recognition of FH Awareness Day in the Eastern Mediterranean region

	Number of countries	Percentage
Not recognized	3/11	27.3%
Partially recognized	4/11	36.4%
Fully recognized	3/11	27.3%

European Region

Data on the prevalence of FH were available for 34 out of 37 countries. Most countries reported a prevalence of 1 in 250 to 300 people. Nonetheless, 11 countries notified a prevalence of 1 in less than 250 people. In addition, Portugal and Switzerland reported a prevalence of 1 in 250 to 500 people and 1 in 125 to 135 people, respectively.

Table 10: FH prevalence in the European region

	Number of countries	Percentage
1 in 500 people	1/37	2.7%
1 in 250 to 300 people	9/37	24.3%
1 in 250 people	11/37	29.7%
1 in less than 250 people	11/37	29.7%
Other	2/37	5.4%
Data availability	34/37	91.9%

Guidelines for the management of dyslipidaemia were followed in 35 out of 37 countries. International guidelines were followed by most countries, sometimes concurrently with national guidelines. The respondents from Bulgaria and Ireland did not provide any responses regarding the guidelines.

Table 11: Adopted guidelines for the management of dyslipidaemia in the European region

	Number of countries	Percentage
No guidelines	0/37	0.0%
National guidelines	12/37	32.4%
International guidelines	33/37	89.2%

A number of countries formally recognized FH Awareness Day. In Cyprus, activities are organized by the National Society of Atherosclerosis. In Hungary, activities are organized on World Heart Day. In Latvia, activities are organized by the national FH patient organization.

Table 12: Recognition of FH Awareness Day in the European region

	Number of countries	Percentage
Not recognized	5/37	13.5%
Partially recognized	7/37	18.9%
Fully recognized	25/37	67.6%

Asia-Pacific Region

Data on the prevalence of FH was available in 8 out of 9 countries. Malaysia reported a prevalence of 1 in 244 to 250 people. The Philippines indicated that the estimated prevalence of 1 in 500 people was probably an underestimation.

Table 13: FH prevalence in the Asia-Pacific region

	Number of countries	Percentage
1 in 500 people	1/9	11.1%
1 in 250 to 300 people	2/9	22.2%
1 in 250 people	2/9	22.2%
1 in less than 250 people	1/9	11.1%
Other	1/9	11.1%
Data availability	8/9	88.9%

Every country followed either a national or an international guideline for the management of dyslipidaemia. Malaysia, the Philippines, Thailand, and Vietnam used both national and international guidelines.

Table 14: Adopted guidelines for the management of dyslipidaemia in the Asia-Pacific region

	Number of countries	Percentage
No guidelines	0/9	0.0%
National guidelines	7/9	77.8%
International guidelines	6/9	66.7%

FH Awareness Day was partially or officially recognized in most countries.

Table 15: Recognition of FH Awareness Day in the European region

	Number of countries	Percentage
Not recognized	2/9	22.2%
Partially recognized	1/9	11.1%
Fully recognized	6/9	66.7%

2. Advocacy

In 2020, the global FH community called for the establishment of additional advocacy organizations across the world (2). Advocacy organizations have an essential role to play in awareness raising, education, fundraising, government lobbying, etc. (2).

African Region

All the respondents were physicians. Two of them were researchers and one represented an international non-governmental organization.

Table 16: Affiliations of survey respondents in the African region

	Number of respondents	Percentage
Patients	0/12	0.0%
Patient organization	0/12	0.0%
Physician	12/12	100.0%
Other	3/12	25.0%

Sources of funding for advocacy were relatively diverse. The organization located in Zimbabwe received funding from the government.

Table 17: Sources of funding for advocacy in the African region

	Number of organizations	Percentage
Organizational membership	3/12	25.0%
Individual donations	5/12	41.7%
Public fundraising	2/12	16.7%
Industry sponsorship / grants	3/12	25.0%
Scientific society funding	1/12	8.3%
Government funding	1/12	8.3%
Research programme	2/12	16.7%

Patient advocate or FH ambassador programmes were not established in any of the countries. However, the respondent from Sierra Leone was interested in developing such a programme.

Table 18: Established patient advocate or FH ambassador programmes in the African region

	Number of countries	Percentage
Not implemented	10/11	90.9%
Partially implemented	0/11	0.0%
Fully implemented	0/11	0.0%

Americas Region

Respondents were principally physicians and researchers. Some participants were involved in national FH registries or programmes. In addition, one respondent was a patient affiliated with a patient organization.

Table 19: Affiliations of survey respondents in the Americas region

	Number of respondents	Percentage
Patients	1/15	6.7%
Patient organization	3/15	20.0%
Physician	9/15	60.0%
Other	6/15	40.0%

Advocacy efforts were mostly funded by industry sponsorships and research programmes. Some activities in Colombia were funded by a Foundation. The respondents from Uruguay received support and funding from the government. Unfortunately, the respondent from Chile did not receive any funding for advocacy activities in 2020.

Table 20: Sources of funding for advocacy in the Americas region

	Number of organizations	Percentage
Organizational membership	2/15	13.3%
Individual donations	5/15	33.3%
Public fundraising	2/15	13.3%
Industry sponsorship / grants	8/15	53.3%
Scientific society funding	1/15	6.7%
Government funding	2/15	13.3%
Research programme	8/15	53.3%

Patient advocate or FH ambassador programmes were partially or fully established in 7 out of 10 countries.

Table 21: Established patient advocate or FH ambassador programmes in the Americas region

	Number of countries	Percentage
Not implemented	3/10	30.0%
Partially implemented	5/10	50.0%
Fully implemented	2/10	20.0%

Eastern Mediterranean Region

Most of the participants were physicians and represented a range of organizations, including a patient organization in one instance. The respondent from Pakistan represented the EAS FH Studies Collaboration (FHSC) and a patient organization.

Table 22: Affiliations of survey respondents in the Eastern Mediterranean region

	Number of respondents	Percentage
Patients	0/12	0.0%

Patient organization	2/12	8.3%
Physician	9/12	75.0%
Other	2/12	16.7%

Advocacy activities were funded by different sources. The respondent from Kuwait received some funding from the government.

Table 23: Sources of funding for advocacy in the Eastern Mediterranean region

	Number of organizations	**Percentage**
Organizational membership	0/12	0.0%
Individual donations	3/12	25.0%
Public fundraising	0/12	0.0%
Industry sponsorship / grants	3/12	25.0%
Scientific society funding	2/12	16.7%
Government funding	1/12	8.3%
Research programme	3/12	25.0%

Patient advocate or FH ambassador programmes were not implemented in most countries. The respondents from Saudi Arabia and the United Arab Emirates indicated that patient advocacy organizations did not exist in their countries. Participants from Iraq and Saudi Arabia explained that the absence of funding and the presence of stigma were major barriers to the implementation of such programmes. In Oman, various advocacy and educational activities are managed by the National Society for Lipid and Atherosclerosis.

Table 24: Established patient advocate or FH ambassador programmes in the Eastern Mediterranean region

	Number of countries	**Percentage**
Not implemented	6/11	54.5%
Partially implemented	3/11	27.3%
Fully implemented	1/11	9.1%

European Region

Most respondents were physicians and/or representatives of patient organizations. Austria, Bulgaria, France, Germany, the Russian Federation, and Sweden were represented by FH patients. The respondent from Switzerland represented both a research institute and a patient organization.

Table 25: Affiliations of survey respondents in the European region

	Number of respondents	**Percentage**
Patients	6/42	14.3%
Patient organization	20/42	47.6%

Physician	23/42	54.8%
Caregiver	1/42	2.4%
Other	3/42	7.1%

Advocacy efforts were principally funded by industry sponsorships and grants. The respondents from Austria, Kosovo, Lithuania, the Netherlands, Slovenia, and Sweden received support and funding from their respective governments. The participants from Bosnia and Herzegovina, Kazakhstan, Kyrgyzstan, Latvia, Luxembourg, and Turkey did not receive any funding for their advocacy activities.

Table 26: Sources of funding for advocacy in the European region

	Number of organizations	Percentage
Organizational membership	14/42	33.3%
Individual donations	15/42	35.7%
Public fundraising	6/42	14.3%
Industry sponsorship / grants	31/42	73.8%
Scientific society funding	7/42	16.7%
Government funding	7/42	16.7%
Research programme	7/42	16.7%

Patient advocate or FH ambassador programmes were partially or fully implemented in most countries. Unfortunately, patient organizations did not exist in Malta and Luxemburg. The development of patient advocate or FH ambassador programmes is a priority in Hungary.

Table 27: Established patient advocate or FH ambassador programmes in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	9/37	27.0%
Partially implemented	14/37	37.8%
Fully implemented	13/37	35.1%

Asia-Pacific Region

The majority of the respondents were physicians. One of the physicians also represented a patient organization. The respondent from Australia was a researcher who represented a patient organization. The participant from New Zealand was a clinical nurse specialist employed in a lipid disorder service.

Table 28: Affiliations of survey respondents in the Asia-Pacific region

	Number of respondents	Percentage

Patients	0/9	0.0%
Patient organization	2/9	22.2%
Physician	7/9	77.8%
Nurse	1/9	11.1%
Other	1/9	11.1%

Advocacy activities were mainly funded by organizational memberships, individual donations, and industry sponsorships and grants. The participant from Malaysia received government funding for health screening programmes.

Table 29: Sources of funding for advocacy in the Asia-Pacific region

	Number of organizations	Percentage
Organizational membership	4/9	44.4%
Individual donations	4/9	44.4%
Public fundraising	1/9	11.1%
Industry sponsorship / grants	5/9	55.6%
Scientific society funding	3/9	33.3%
Government funding	1/9	11.1%
Research programme	3/9	33.3%

Patient advocate or FH ambassador programmes were partially or fully implemented in most countries. Patient advocacy groups did not exist in New Zealand.

Table 30: Established patient advocate or FH ambassador programmes in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	2/9	22.2%
Partially implemented	4/9	44.4%
Fully implemented	2/9	22.2%

3. Screening, Testing, and Diagnosis

Early diagnosis and treatment of familial hypercholesterolemia can prevent the development of FH-related premature cardiovascular events. Evidence suggests that universal screening of children and cascade screening of first- and second-degree relatives are cost-effective approaches (2). Screening strategies should be adapted to each country (e.g., depending on the setting, guidelines, available resources, etc.). Insofar as possible, results from metabolic tests should be confirmed by a genetic test.

African Region

The estimated diagnosis rates were below 5% in 5 countries, with 2 countries reporting a 0% rate. South Africa, Nigeria, Uganda, and Zimbabwe reported a diagnosis rate of 5%. Zambia notified that approximately 30% of individuals with FH were detected nationally. The Gambia indicated that the national diagnosis rate was unknown.

Table 31: Estimated FH diagnosis rate in the African region

	Number of countries	Percentage
<5%	5/11	45.5%
5-10%	4/11	36.4%
>10%	1/11	9.1%

There were no national efforts to screen for FH in most countries. National efforts were partially implemented in Nigeria.

Table 32: National FH screening efforts in the African region

	Number of countries	Percentage
Not implemented	10/11	90.9%
Partially implemented	1/11	9.1%
Fully implemented	0/11	0.0%

Cascade screening programmes were not implemented in 10 out of 11 countries. Cascade screening was fully implemented in Nigeria.

Table 33: Cascade screening programmes in the African region

	Number of countries	Percentage
Not implemented	10/11	90.9%
Partially implemented	0/11	0.0%
Fully implemented	1/11	9.1%

Universal screening for children was not implemented in any of the countries.

Table 34: Universal children screening programmes in the African region

	Number of countries	Percentage
Not implemented	11/11	100.0%
Partially implemented	0/11	0.0%
Fully implemented	0/11	0.0%

Individuals with FH were principally diagnosed at the specialist level. South Africa reported that FH patients were often detected through opportunistic screening. The respondent from The Gambia indicated that the probability of being diagnosed depended on various factors.

Table 35: Levels at which FH individuals are diagnosed in the African region

	Number of countries	Percentage
Screening programme	2/11	18.2%
Paediatric	1/11	9.1%
General Practitioner	2/11	18.2%
Specialist	8/11	72.7%

Metabolic tests were used to confirm the diagnosis of FH in every country. However, the tests were only reimbursed in South Africa and Zimbabwe. Genetic tests were not used to confirm FH in any of the countries. South Africa indicated that genetic testing was performed in some research programmes between 1986 and 2005.

Table 36: Testing for FH in the African region

	Number of countries	Percentage
Blood testing	11/11	100.0%
Reimbursed blood testing	2/11	18.2%
Genetic testing	0/11	0.0%
Reimbursed genetic testing	0/11	0.0%

Americas Region

The diagnosis rate of FH varied substantially from one country to another. Respondents from Mexico reported a rate between 1% and 5%. Respondents from Uruguay reported a rate between 2% and 10%. The United States reported that approximately 15% of individuals with FH were detected nationally.

Table 37: Estimated FH diagnosis rate in the Americas region

	Number of countries	Percentage
<5%	3/10	30.0%
5-10%	6/10	60.0%
>10%	1/10	40.0%

National efforts to screen for FH were inexistent in 8 out of 10 countries. National efforts were partially implemented in Argentina and fully implemented in Uruguay.

Table 38: National FH screening efforts in the Americas region

	Number of countries	Percentage
Not implemented	8/10	80.0%
Partially implemented	1/10	10.0%
Fully implemented	1/10	10.0%

Cascade screening programmes were partially implemented in Mexico and fully implemented in Brazil and Uruguay. Chile reported that cascade screening was available locally in Concepcı́on and Santiago.

Table 39: Cascade screening programmes in the Americas region

	Number of countries	Percentage
Not implemented	7/10	70.0%
Partially implemented	1/10	10.0%
Fully implemented	2/10	20.0%

Universal screening for children was not implemented in any of the countries.

Table 40: Universal children screening programmes in the Americas region

	Number of countries	Percentage
Not implemented	10/10	100.0%
Partially implemented	0/10	0.0%
Fully implemented	0/10	0.0%

Individuals with FH were mainly detected at the specialist level in all countries. However, patients were also diagnosed in screening programmes, or at the paediatric and GP levels in some countries.

Table 41: Levels at which FH individuals are diagnosed in the Americas region

	Number of countries	Percentage
Screening programme	4/10	40.0%
Paediatric	4/10	40.0%
General Practitioner	4/10	40.0%
Specialist	10/10	40.0%

Metabolic tests were used to confirm FH in all countries and were reimbursed in 9 out of 10 countries. Genetic tests were performed in 7 countries and reimbursed in 5 countries. In Chile, genetic tests were only conducted in universities for research purposes.

Table 42: Testing for FH in the Americas region

	Number of countries	Percentage
Blood testing	10/10	100.0%

Reimbursed blood testing	9/10	90.0%
Genetic testing	7/10	70.0%
Reimbursed genetic testing	5/7	71.4%

Eastern Mediterranean Region

Bahrain, Iraq, Tunisia, the United Arab Emirates, and Yemen reported a diagnosis rate of 31-45%, 30%, 50%, 40%, and 11%, respectively. The respondent from Pakistan indicated that the percentage of people diagnosed with FH was unknown.

Table 43: Estimated FH diagnosis rate in the Eastern Mediterranean region

	Number of countries	Percentage
<5%	2/11	18.2%
5-10%	3/11	27.3%
>10%	5/11	45.5%

National efforts to screen for FH were reported in 2 countries. In addition, national efforts were partially implemented in 4 other countries.

Table 44: National FH screening efforts in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	5/11	45.5%
Partially implemented	4/11	36.4%
Fully implemented	2/11	18.2%

Cascade screening was partially implemented in 3 out of 11 countries. Cascade screening strategies were fully implemented in Saudi Arabia and Tunisia.

Table 45: Cascade screening programmes in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	6/11	54.5%
Partially implemented	3/11	27.3%
Fully implemented	2/11	18.2%

Universal screening for children was not implemented in 10 out of 11 countries. Iraq reported that nonmandatory universal children screening was available for children aged 2.

Table 46: Universal children screening programmes in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	10/11	90.9%

Partially implemented	1/11	9.1%
Fully implemented	0/11	0.0%

FH patients were mostly identified at the specialist level. Oman indicated that some individuals were detected in lipid clinics and/or research programmes. Pakistan reported that some patients were also diagnosed through opportunistic screening.

Table 47: Levels at which FH individuals are diagnosed in the Eastern Mediterranean region

	Number of countries	Percentage
Screening programme	0/11	0.0%
Paediatric	3/11	27.3%
General Practitioner	1/11	9.1%
Specialist	10/11	90.9%

Metabolic tests were used to confirm FH in all of the countries. Nonetheless, the tests were only reimbursed in 6 out of 11 countries. Genetic testing was available in Oman and Saudi Arabia. The reimbursement status of the test, outside of research programmes, is unknown.

Table 48: Testing for FH in the Eastern Mediterranean region

	Number of countries	Percentage
Blood testing	11/11	100.0%
Reimbursed blood testing	6/11	54.5%
Genetic testing	2/11	18.2%
Reimbursed genetic testing	N/A	N/A

European Region

The estimated diagnosis rate varied across the European region. A total of 15 countries reported a diagnosis rate above 10%. In addition, Belgium, Bulgaria, Greece, Ireland, Montenegro, the Netherlands, Slovenia, Spain, and Sweden reported a diagnosis rate above 20%. The Netherlands led the efforts with a rate of 55%. France, Germany, and Latvia had multiple respondents and reported a rate of 10-12%, 5-10%, and 4.0-5.5%, respectively.

Table 49: Estimated FH diagnosis rate in the European region

	Number of countries	Percentage
<5%	11/37	29.7%
5-10%	11/37	29.7%
>10%	15/37	40.5%

National efforts to screen for FH were partially implemented in 10 out of 37 countries and fully implemented in 13 others.

Table 50: National FH screening efforts in the European region

	Number of countries	Percentage
Not implemented	14/37	37.8%
Partially implemented	10/37	27.0%
Fully implemented	13/37	35.1%

Cascade screening was partially or fully implemented in most countries. Only 7 out of 37 countries did not implement cascade screening strategies.

Table 51: Cascade screening programmes in the European region

	Number of countries	Percentage
Not implemented	7/37	18.9%
Partially implemented	13/37	35.1%
Fully implemented	17/37	45.9%

Universal screening for children was not implemented in most countries. The strategy was only fully implemented in the Czech Republic, Portugal, Slovenia, and Slovakia. Germany reported the existence of regional non-systematic screening programmes for children.

Table 52: Universal children screening programmes in the European region

	Number of countries	Percentage
Not implemented	26/37	70.3%
Partially implemented	7/37	18.9%
Fully implemented	4/37	10.8%

Individuals with FH were diagnosed at the specialist level in almost every country. However, many countries indicated that patients were also identified through screening programmes or at the paediatric and GP levels. In Latvia, adults were generally diagnosed by cardiologists, while children were identified by paediatric endocrinologists.

Table 53: Levels at which FH individuals are diagnosed in the European region

	Number of countries	Percentage
Screening programme	12/37	32.4%
Paediatric	19/37	51.4%
General Practitioner	17/37	45.9%
Specialist	36/37	97.3%

Metabolic tests were used to confirm FH in 31 out of 37 countries and were reimbursed in 29 countries. Genetic tests were used in 24 out of 37 countries and were reimbursed in 20 countries. Hungary reported that its national budget for FH genetic tests was extremely limited and covered approximately 50 tests every year. Latvia reported that genetic tests were only conducted for patients with suspected homozygous familial hypercholesterolemia and/or paediatric patients with suspected FH, as part of a national rare disease programme.

Table 54: Testing for FH in the European region

	Number of countries	Percentage
Blood testing	31/37	83.8%
Reimbursed blood testing	29/31	93.5%
Genetic testing	24/37	64.9%
Reimbursed genetic testing	20/24	83.3%

Asia-Pacific Region

The estimated percentage of diagnosed individuals were below 5% in most of the countries. Cambodia and Japan reported a diagnosis rate of 25% and 42%, respectively. The diagnosis rate for the Philippines was unknown.

Table 55: Estimated FH diagnosis rate in the Asia-Pacific region

	Number of countries	Percentage
<5%	5/9	55.6%
5-10%	1/9	11.1%
>10%	2/9	22.2%

National efforts were partially implemented in 2 out of 9 countries and fully implemented in 2 others. The Philippines reported that FH had been officially integrated into its National Clinical Practice Guidelines for the Management of Dyslipidaemia in 2020.

Table 56: National FH screening efforts in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	5/9	55.6%
Partially implemented	2/9	22.2%
Fully implemented	2/9	22.2%

Cascade screening strategies were partially or fully implemented in most countries. The Philippines indicated that cascade screening had been introduced in its National Clinical Practice Guidelines for the Management of Dyslipidaemia in 2020.

Table 57: Cascade screening programmes in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	1/9	11.1%
Partially implemented	5/9	55.6%
Fully implemented	3/9	33.3%

Universal screening for children was partially implemented in Japan and fully implemented in the Philippines. The respondent from the Philippines indicated that universal screening was implemented in collaboration with the National Paediatric Society.

Table 58: Universal children screening programmes in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	6/9	66.7%
Partially implemented	1/9	11.1%
Fully implemented	1/9	11.1%

Individuals with FH were detected at different levels of care across the region. Nevertheless, every country reported the diagnosis of patients at the specialist level. New Zealand reported that screening programmes were only conducted in Canterbury.

Table 59: Levels at which FH individuals are diagnosed in the Asia-Pacific region

	Number of countries	Percentage
Screening programme	6/9	66.7%
Paediatric	4/9	44.4%
General Practitioner	5/9	55.6%
Specialist	9/9	100.0%

Metabolic tests were performed in 7 out of 9 countries and were reimbursed in 5 countries. Genetic tests were used in 7 out of 9 countries and were reimbursed in 4 countries. New Zealand reported that patients needed to meet a set of criteria to be eligible for genetic testing.

Table 60: Testing for FH in the Asia-Pacific region

	Number of countries	Percentage
Blood testing	7/9	77.8%
Reimbursed blood testing	5/7	71.4%
Genetic testing	7/9	77.8%
Reimbursed genetic testing	4/9	57.1%

4. Treatment

Treatment and management of familial hypercholesterolemia are cost-effective and lifelong interventions that aim to avert the development of premature cardiovascular disease (2). In order to ensure high coverage, medications and care must be available, accessible, affordable, patient-centred, and of high quality. Treatments for FH should be initiated as early as possible.

African Region

National or regional referral pathways only existed in 3 countries. South Africa reported that referrals within the state system were only possible in Cape Town and Johannesburg. FH patients were typically referred to a specialist in 5 countries. The respondent from The Gambia indicated that there were no FH specialists in the country.

Table 61: National or regional referral pathway in the African region

	Number of countries	Percentage
Not implemented	7/11	63.6%
Partially implemented	1/11	9.1%
Fully implemented	3/11	27.3%
Referral to a specialist	5/11	45.5%

Statins were available in 10 out of 11 countries and reimbursed in 6 countries. Statins were fully reimbursed in Ivory Coast and Tanzania.

Table 62: Availability and affordability of statins in the African region

	Number of countries	Percentage
Available	10/11	90.9%
Not reimbursed	4/10	40.0%
Partially reimbursed	4/10	40.0%
Fully reimbursed	2/10	20.0%

Ezetimibe was available in 7 out of 11 countries and reimbursed in 2 countries. Ezetimibe was fully reimbursed in Ivory Coast.

Table 63: Availability and affordability of Ezetimibe in the African region

	Number of countries	Percentage
Available	7/11	63.6%
Not reimbursed	5/7	72.4%
Partially reimbursed	1/7	14.3%

Fully reimbursed	1/7	14.3%

PCSK9 inhibitors were available in 4 countries and reimbursed in none.

Table 64: Availability and affordability of PCSK9 inhibitors in the African region

	Number of countries	Percentage
Available	4/11	36.4%
Not reimbursed	4/4	100.0%
Partially reimbursed	0/4	0.0%
Fully reimbursed	0/4	0.0%

Bempedoic acid was available in 4 countries and reimbursed in none.

Table 65: Availability and affordability of bempedoic acid in the African region

	Number of countries	Percentage
Available	4/11	36.4%
Not reimbursed	4/4	100.0%
Partially reimbursed	0/4	0.0%
Fully reimbursed	0/4	0.0%

Americas Region

National or regional referral pathways were fully established in 3 countries and partially implemented in Colombia and Mexico. GPs and paediatricians typically referred FH patients to a specialist in 9 out of 10 countries. Brazil reported that some areas in the country were limited to the GP level. Chile indicated that patients were usually referred to an endocrinologist, a paediatrician, or a lipidologist. The respondent from the United States reported that referrals to specialists varied widely between health systems and individual clinicians.

Table 66: National or regional referral pathway in the Americas region

	Number of countries	Percentage
Not implemented	5/10	50.0%
Partially implemented	2/10	20.0%
Fully implemented	3/10	30.0%
Referral to a specialist	9/10	90.0%

Statins were available in every country. Statins were partially reimbursed in 2 out of 10 countries and fully reimbursed in 7 others.

Table 67: Availability and affordability of statins in the Americas region

	Number of countries	Percentage
Available	10/10	100.0%
Not reimbursed	1/10	10.0%
Partially reimbursed	2/10	20.0%
Fully reimbursed	7/10	70.0%

Ezetimibe was available in every country and reimbursed in 9 out of 10 countries. Chile reported that ezetimibe was usually reimbursed by private insurances.

Table 68: Availability and affordability of Ezetimibe in the Americas region

	Number of countries	Percentage
Available	10/10	100.0%
Not reimbursed	1/10	40.0%
Partially reimbursed	5/10	50.0%
Fully reimbursed	4/10	10.0%

PCSK9 inhibitors were available in 8 out of 10 countries and reimbursed in 4 countries. Respondents from Colombia indicated that some PCSK9 inhibitors will be reimbursed in the future.

Table 69: Availability and affordability of PCSK9 inhibitors in the Americas region

	Number of countries	Percentage
Available	8/10	80.0%
Not reimbursed	4/8	50.0%
Partially reimbursed	4/8	50.0%
Fully reimbursed	0/8	0.0%

Bempedoic acid was only available in 2 countries. The medication was not reimbursed in Brazil and partially reimbursed in the United States.

Table 70: Availability and affordability of bempedoic acid in the Americas region

	Number of countries	Percentage
Available	2/10	20.0%
Not reimbursed	1/2	50.0%
Partially reimbursed	1/2	50.0%
Fully reimbursed	0/2	0.0%

Eastern Mediterranean Region

National or regional referral pathways were partially implemented in 5 out of 11 countries and fully implemented in Egypt and Oman. GPs and paediatricians referred FH patients to a specialist in 10 out of 11 countries. The respondent from Iraq indicated that the Iraqi Network of Lipid Clinics organized various social media activities in order to promote visits to lipid clinics. Oman indicated that the lipid clinic at the Sultan Qaboos University was the National Referral Centre for all suspected FH cases.

Table 71: National or regional referral pathway in the Eastern Mediterranean region

	Number of countries	**Percentage**
Not implemented	3/11	27.3%
Partially implemented	5/11	45.5%
Fully implemented	2/11	18.2%
Referral to a specialist	10/11	90.9%

Statins were available in all of the countries. The drugs were partially reimbursed in 2 countries and fully reimbursed in 6 others.

Table 72: Availability and affordability of statins in the Eastern Mediterranean region

	Number of countries	**Percentage**
Available	11/11	100.0%
Not reimbursed	3/11	27.3%
Partially reimbursed	2/11	18.2%
Fully reimbursed	6/11	54.5%

Ezetimibe was available in 10 out of 11 countries and reimbursed in 7 countries.

Table 73: Availability and affordability of Ezetimibe in the Eastern Mediterranean region

	Number of countries	**Percentage**
Available	10/11	90.9%
Not reimbursed	3/10	30.0%
Partially reimbursed	3/10	30.0%
Fully reimbursed	4/10	40.0%

PCSK9 inhibitors were available in 8 out of 11 countries and reimbursed in 4 countries.

Table 74: Availability and affordability of PCSK9 inhibitors in the Eastern Mediterranean region

	Number of countries	**Percentage**
Available	8/11	72.7%
Not reimbursed	4/8	50.0%
Partially reimbursed	1/8	12.5%
Fully reimbursed	3/8	37.5%

Bempedoic acid was available in 3 countries and reimbursed in none.

Table 75: Availability and affordability of bempedoic acid in the Eastern Mediterranean region

	Number of countries	Percentage
Available	3/11	27.3%
Not reimbursed	3/3	100.0%
Partially reimbursed	0/3	0.0%
Fully reimbursed	0/3	0.0%

European Region

National and regional referral pathways were partially or fully implemented in most countries. One respondent from Latvia indicated that, even though no official pathways existed, most physicians were aware that suspected FH cases could be referred to lipid clinics. Patients in Latvia could also be referred to a Rare Disease Centre for genetic testing if homozygous FH was suspected. The respondent from Switzerland indicated that the Swiss Society for Familial Forms of Hypercholesterolemia delivered a screening programme called SAPPHIRE at the national FH centre. Portugal reported the existence of several National Centres for Referral.

Most GPs and paediatricians referred FH patients to a specialist. Luxemburg reported that paediatric patients were typically referred to a paediatric endocrinologist. A number of countries indicated that referrals were not systematic and heavily depended on the referrers.

Table 76: National or regional referral pathway in the European region

	Number of countries	Percentage
Not implemented	11/37	29.7%
Partially implemented	10/37	27.0%
Fully implemented	14/37	37.8%
Referral to a specialist	31/37	83.8%

Statins were available and reimbursed in every country. The drugs were partially reimbursed in 12 countries and fully reimbursed in 25 others.

Table 77: Availability and affordability of statins in the European region

	Number of countries	Percentage
Available	37/37	100.0%
Not reimbursed	0/37	0.0%
Partially reimbursed	12/37	32.4%
Fully reimbursed	25/37	67.6%

Ezetimibe was available in 36 out of 37 countries and reimbursed in 28 countries. The respondent from Bulgaria was not certain about the reimbursement status of ezetimibe.

Table 78: Availability and affordability of Ezetimibe in the European region

	Number of countries	Percentage
Available	36/37	97.3%
Not reimbursed	7/36	19.4%
Partially reimbursed	8/36	22.2%
Fully reimbursed	20/36	55.6%

PCSK9 inhibitors were available in 34 out of 37 countries and reimbursed in 25 countries. Albania and Ireland reported that PCSK9 inhibitors will be reimbursed in the near future. Malta indicated that the drugs could be reimbursed in some exceptional cases.

Table 79: Availability and affordability of PCSK9 inhibitors in the European region

	Number of countries	Percentage
Available	34/37	91.9%
Not reimbursed	9/34	26.5%
Partially reimbursed	6/34	17.6%
Fully reimbursed	19/34	55.9%

Bempedoic acid was available in 24 out of 37 countries and reimbursed in 5 countries. Albania, Italy, Luxemburg, the Netherlands, and the United Kingdom reported that the medication will be reimbursed in the near future. Many respondents were not certain about the reimbursement status of the drug in their countries.

Table 80: Availability and affordability of bempedoic acid in the European region

	Number of countries	Percentage
Available	24/37	64.9%
Not reimbursed	14/24	58.3%
Partially reimbursed	2/24	8.3%
Fully reimbursed	3/24	12.5%

Asia-Pacific Region

National or regional referral pathways were partially or fully implemented in most countries. New Zealand indicated that the pathways could vary depending on the cities or regions.

GPs and paediatricians typically referred patients to a specialist in 7 out of 9 countries. New Zealand reported that referrals were minimal in some regions due to the limited amount of specialist services.

Table 81: National or regional referral pathway in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	1/9	11.1%
Partially implemented	4/9	44.4%
Fully implemented	4/9	44.4%
Referral to a specialist	7/9	77.8%

Statins were available in every country and reimbursed in 8 out of 9 countries. The Philippines indicated that the reimbursement of statins depended on the health insurance. Cambodia reported that statins were in the process of becoming reimbursed.

Table 82: Availability and affordability of statins in the Asia-Pacific region

	Number of countries	Percentage
Available	9/9	100.0%
Not reimbursed	1/9	11.1%
Partially reimbursed	3/9	33.3%
Fully reimbursed	5/9	55.6%

Ezetimibe was available in all of the countries and reimbursed in 8 out of 9 countries. Cambodia reported that ezetimibe was also in the process of becoming reimbursed.

Table 83: Availability and affordability of Ezetimibe in the Asia-Pacific region

	Number of countries	Percentage
Available	9/9	100.0%
Not reimbursed	1/9	11.1%
Partially reimbursed	4/9	44.4%
Fully reimbursed	4/9	44.4%

PCSK9 inhibitors were available in 8 out of 9 countries. The drugs were partially reimbursed in 3 out of 8 countries.

Table 84: Availability and affordability of PCSK9 inhibitors in the Asia-Pacific region

	Number of countries	Percentage
Available	8/9	88.9%
Not reimbursed	5/8	62.5%
Partially reimbursed	3/8	37.5%
Fully reimbursed	0/8	0.0%

Bempedoic acid was available in Cambodia and New Zealand. The drug was not reimbursed in any of the countries.

Table 85: Availability and affordability of bempedoic acid in the Asia-Pacific region

	Number of countries	Percentage
Available	2/9	22.2%
Not reimbursed	2/2	100.0%
Partially reimbursed	0/2	0.0%
Fully reimbursed	0/2	0.0%

5. Severe and Homozygous FH

Severe and homozygous FH are rare and life-threatening forms of familial hypercholesterolemia. In particular, homozygous FH (HoFH) affects approximately 1 in 160 000 to 320 000 individuals (3). HoFH patients require unique care and resources, such as special guidelines, novel or unconventional drugs (e.g., lomitapide, etc.), and specialized interventions (e.g., LDL-apheresis, etc.) (2).

African Region

Separate guidelines for the management of severe and homozygous familial hypercholesterolemia did not exist in any of the countries.

Table 86: Guidelines for the management of severe and homozygous FH in the African region

	Number of countries	Percentage
Special guidelines	0/11	0.0%

Lipid or FH clinics were established in South Africa. South Africa also reported that FH clinics were poorly supported and affiliated with the national health system.

Table 87: Established specialized lipid and/or FH clinics in the African region

	Number of countries	Percentage
Specialized lipid or FH clinic	1/11	9.1%

Lomitapide was available in 5 out of 11 countries. The drug was not reimbursed in any of the countries. The respondent from Zimbabwe was not certain about its reimbursement status.

Table 88: Availability and affordability of lomitapide in the African region

	Number of countries	Percentage
Available	5/11	45.5%

Not reimbursed	4/5	80.0%
Partially reimbursed	0/5	0.0%
Fully reimbursed	0/5	0.0%

LDL-apheresis was available in 5 out of 11 countries. The procedure was not reimbursed in any of the countries. The respondent from Zimbabwe was not certain about its reimbursement status.

Table 89: Availability and affordability of LDL-apheresis in the African region

	Number of countries	**Percentage**
Available	5/11	45.5%
Not reimbursed	4/5	80.0%
Partially reimbursed	0/5	0.0%
Fully reimbursed	0/5	0.0%

Americas Region

Dedicated guidelines for severe and homozygous FH were available in 2 countries. In Brazil, HoFH guidelines were provided by the Brazilian Society of Cardiology. The United States reported the existence of multiple sets of guidelines for HoFH.

Table 90: Guidelines for the management of severe and homozygous FH in the Americas region

	Number of countries	**Percentage**
Special guidelines	2/10	20.0%

Specialized lipid and FH clinics were established in 8 out of 10 countries. Chile reported that such clinics were mostly located in private institutions and university hospitals. The Dominican Republic indicated that its first lipid clinic was recently launched and involved a group of specialists in metabolic diseases (i.e., cardiologists, lipidologists, geneticists, specialists in rare diseases, endocrinologists, nutritionists, and nephrologists).

Table 91: Established specialized lipid and/or FH clinics in the Americas region

	Number of countries	**Percentage**
Specialized lipid or FH clinic	8/10	80.0%

Lomitapide was available in 6 out of 10 countries and was partially or fully reimbursed in 3 countries. Lomitapide was fully reimbursed in Colombia.

Table 92: Availability and affordability of lomitapide in the Americas region

	Number of countries	**Percentage**

Available	6/10	60.0%
Not reimbursed	3/6	50.0%
Partially reimbursed	2/6	33.3%
Fully reimbursed	1/6	16.7%

LDL-apheresis was available in 6 out of 10 countries. The procedure was partially reimbursed in 3 countries and fully reimbursed in Colombia.

Table 93: Availability and affordability of LDL-apheresis in the Americas region

	Number of countries	Percentage
Available	6/10	60.0%
Not reimbursed	2/6	33.3%
Partially reimbursed	3/6	50.0%
Fully reimbursed	1/6	16.7%

Eastern Mediterranean Region

Special guidelines for the management of severe and homozygous FH only existed in Oman. The respondent from Oman also indicated that the guidelines needed to be updated.

Table 94: Guidelines for the management of severe and homozygous FH in the Eastern Mediterranean region

	Number of countries	Percentage
Special guidelines	1/11	9.1%

Specialized lipid and FH clinics were established in 6 out of 11 countries. The respondent from Iraq established a network of lipid clinics in 2017 through non-governmental efforts and support. Pakistan indicated that cardiology outpatient departments were considered as lipid clinics.

Table 95: Established specialized lipid and/or FH clinics in the Eastern Mediterranean region

	Number of countries	Percentage
Specialized lipid or FH clinic	6/11	54.5%

Lomitapide was available in 6 out of 11 countries. The medication was partially reimbursed in Saudi Arabia and fully reimbursed in the United Arab Emirates.

Table 96: Availability and affordability of lomitapide in the Eastern Mediterranean region

	Number of countries	Percentage
Available	6/11	54.5%
Not reimbursed	4/6	66.7%
Partially reimbursed	1/6	16.7%

Fully reimbursed	1/6	16.7%

LDL-apheresis was available in 7 out of 11 countries. The procedure was partially reimbursed in Egypt and fully reimbursed in Oman and Saudi Arabia.

Table 97: Availability and affordability of LDL-apheresis in the Eastern Mediterranean region

	Number of countries	Percentage
Available	7/11	63.6%
Not reimbursed	4/7	57.1%
Partially reimbursed	1/7	14.3%
Fully reimbursed	2/7	28.6%

European Region

Special guidelines were only available in 11 out of 37 countries. France and Portugal reported that separate guidelines on HoFH were being developed.

Table 98: Guidelines for the management of severe and homozygous FH in the European region

	Number of countries	Percentage
Special guidelines	11/37	29.7%

Specialized lipid and FH clinics were established in 26 out of 37 countries. Cyprus reported the establishment of combined diabetes and lipid clinics. Lithuania indicated that preventative cardiology subdivisions were considered as lipid clinics/units. Poland explained that regular check-ups were performed by GPs and cardiologists.

Table 99: Established specialized lipid and/or FH clinics in the European region

	Number of countries	Percentage
Specialized lipid or FH clinic	26/37	70.3%

Lomitapide was available in 27 out of 37 countries and reimbursed in 9 out of 27 countries. Respondents from Bulgaria, Cyprus, Hungary, Ireland, Luxemburg, the Netherlands, and Portugal were not certain about its reimbursement status. Lomitapide was in the process of becoming reimbursed in Albania and Spain.

Table 100: Availability and affordability of lomitapide in the European region

	Number of countries	Percentage
Available	27/37	72.9%
Not reimbursed	11/27	40.7%

Partially reimbursed	2/27	7.4%
Fully reimbursed	7/27	25.9%

LDL-apheresis was available in most countries. The procedure was also fully reimbursed in more than half of the countries. Albania indicated that the procedure will be reimbursed in the near future. Poland reported that LDL-apheresis were generally performed in cardiological clinics.

Table 101: Availability and affordability of LDL-apheresis in the European region

	Number of countries	**Percentage**
Available	32/37	86.5%
Not reimbursed	6/32	18.8%
Partially reimbursed	4/32	12.5%
Fully reimbursed	17/32	53.1%

Asia-Pacific Region

Separate guidelines for the management of severe and homozygous familial hypercholesterolemia existed in 2 out of 9 countries. Malaysia reported that HoFH guidelines were being developed. New Zealand indicated that the guidelines were not fully implemented due to limited resources.

Table 102: Guidelines for the management of severe and homozygous FH in the Asia-Pacific region

	Number of countries	**Percentage**
Special guidelines	2/9	22.2%

Specialized lipid and FH clinics were established in 7 out of 9 countries. New Zealand reported that some regions were not serviced due to limited resources.

Table 103: Established specialized lipid and/or FH clinics in the Asia-Pacific region

	Number of countries	**Percentage**
Specialized lipid or FH clinic	7/9	77.8%

Lomitapide was available in 4 out of 9 countries. The medication was partially reimbursed in Japan.

Table 104: Availability and affordability of lomitapide in the Asia-Pacific region

	Number of countries	**Percentage**
Available	4/9	44.4%
Not reimbursed	3/4	75.0%
Partially reimbursed	1/4	25.0%
Fully reimbursed	0/4	0.0%

LDL-apheresis was available in 7 out of 9 countries. The procedure was partially reimbursed in Japan and Thailand, as well as fully reimbursed in Australia and New Zealand.

Table 105: Availability and affordability of LDL-apheresis in the Asia-Pacific region

	Number of countries	Percentage
Available	7/9	77.8%
Not reimbursed	3/7	42.9%
Partially reimbursed	2/7	28.6%
Fully reimbursed	2/7	28.6%

6. Family-Based Care

FH is a lifelong condition and imposes various challenges at different stages in life. For instance, management of FH requires different interventions in childhood, pregnancy, adulthood, etc. Therefore, treatment and care should be patient- and family-centred (2).

African Region

FH patients were predominantly managed by cardiologists and endocrinologists in the African region.

Table 106: Management of FH in the African region

	Number of countries	Percentage
Cardiologists	7/11	63.6%
Endocrinologists	8/11	72.7%
Lipid specialists	1/11	9.1%
General Practitioner	7/11	63.6%
Gastroenterologists	1/11	9.1%
Paediatrician	5/11	45.5%
Other	0/11	0.0%

Americas Region

FH patients were principally managed by cardiologists and endocrinologists in the Americas region. Colombia reported that geneticists were also involved in the management of FH cases.

Table 107: Management of FH in the Americas region

	Number of countries	Percentage
Cardiologists	10/10	100.0%
Endocrinologists	9/10	90.0%

Lipid specialists	7/10	70.0%
General Practitioner	4/10	40.0%
Gastroenterologists	1/10	10.0%
Paediatrician	6/10	60.0%
Other	1/10	10.0%

Eastern Mediterranean Region

Individuals with FH were generally managed by cardiologists and endocrinologists in the Eastern Mediterranean region. Iraq reported that internists and members of the Iraqi lipid clinics network (i.e., multiple different specialties) were also trained to treat FH patients.

Table 108: Management of FH in the Eastern Mediterranean region

	Number of countries	Percentage
Cardiologists	9/11	81.8%
Endocrinologists	7/11	63.6%
Lipid specialists	5/11	45.5%
General Practitioner	3/11	27.3%
Gastroenterologists	0/11	0.0%
Paediatrician	5/11	45.5%
Other	1/11	9.1%

European Region

FH patients were mainly managed by cardiologists in the European region. However, endocrinologists, lipid specialists, general practitioners, and paediatricians were all regularly involved in the care of FH cases. In addition, Ireland reported that biochemists were also involved in the management of the disease. Latvia specified that adults were managed by cardiologists and children by paediatric endocrinologists. Luxemburg also indicated that paediatric endocrinologists were involved in the management of children living with FH. Portugal reported that medical geneticists, nephrologists, and vascular surgeons were also responsible for the care of FH patients. Lastly, internists were involved in the management of patients in Slovakia and Spain.

Table 109: Management of FH in the European region

	Number of countries	Percentage
Cardiologists	31/37	83.8%
Endocrinologists	15/37	40.5%
Lipid specialists	21/37	56.8%
General Practitioner	19/37	51.4%
Gastroenterologists	1/37	2.7%

Paediatrician	21/37	56.8%
Other	5/37	13.5%

Asia-Pacific Region

FH cases were principally managed by cardiologists, endocrinologists, and lipid specialists in the Asia-Pacific region. New Zealand reported that paediatric endocrinologists were also involved in the management of patients.

Table 110: Management of FH in the Asia-Pacific region

	Number of countries	Percentage
Cardiologists	9/9	100.0%
Endocrinologists	9/9	100.0%
Lipid specialists	8/9	88.9%
General Practitioner	5/9	55.6%
Gastroenterologists	0/9	0.0%
Paediatrician	5/9	55.6%
Other	1/9	11.1%

7. Registries

FH registries can be used to collect a range of valuable information on familial hypercholesterolemia. The establishment and adequate maintenance of registries are often correlated with improved practices and outcomes for patients (2). Data from registries are subjected to medical secrecy. As such, privacy and confidentiality must be ensured. Evidence suggests that governmental support and funding are essential to the sustainability of registries (2).

African Region

National FH registries for adult patients were not established in any of the countries. Nigeria and Tanzania reported that some efforts were underway.

Table 111: Established national registries for adult FH patients in the African region

	Number of countries	Percentage
Not implemented	9/11	81.8%
Several non-national registries	0/11	0.0%
Partially implemented	2/11	18.2%
Fully implemented	0/11	0.0%

National registries for children with FH were not established in any of the countries. Tanzania reported that some efforts were underway.

Table 112: Established national registries for paediatric FH patients in the African region

	Number of countries	Percentage
Not implemented	9/11	81.8%
Several non-national registries	0/11	0.0%
Partially implemented	1/11	9.1%
Fully implemented	0/11	0.0%

National registries for homozygous patients were not established in any of the countries. Nigeria indicated that some efforts were underway.

Table 113: Established national registries for homozygous FH patients in the African region

	Number of countries	Percentage
Not implemented	8/11	72.7%
Several non-national registries	0/11	0.0%
Partially implemented	1/11	9.1%
Fully implemented	0/11	0.0%

Americas Region

National registries for adults with FH were partially implemented in 2 out of 10 countries and fully implemented in 5 other countries. Brazil and Chile reported the existence of several regional and/or local registries.

Table 114: Established national registries for adult FH patients in the Americas region

	Number of countries	Percentage
Not implemented	1/10	10.0%
Several non-national registries	2/10	20.0%
Partially implemented	2/10	20.0%
Fully implemented	5/10	50.0%

National FH registries for paediatric patients were partially implemented in 2 countries and fully implemented in 4 others.

Table 115: Established national registries for paediatric FH patients in the Americas region

	Number of countries	Percentage
Not implemented	2/10	20.0%
Several non-national registries	1/10	10.0%
Partially implemented	2/10	20.0%

Fully implemented	4/10	40.0%

Registries of homozygous FH patients were established in 4 countries. Efforts to set up HoFH registries were underway in Argentina and Colombia. Brazil and Chile reported that several regional or local registries were established.

Table 116: Established national registries for homozygous FH patients in the Americas region

	Number of countries	Percentage
Not implemented	2/10	20.0%
Several non-national registries	2/10	20.0%
Partially implemented	2/10	20.0%
Fully implemented	4/10	40.0%

Eastern Mediterranean Region

National registries of adult patients were partially developed in 6 out of 11 countries and fully established in Iran and Saudi Arabia. Iraq reported the existence of several regional or local registries.

Table 117: Established national registries for adult FH patients in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	2/11	18.2%
Several non-national registries	1/11	9.1%
Partially implemented	6/11	54.5%
Fully implemented	2/11	18.2%

National registries for paediatric FH patients were available in Iran and Saudi Arabia. Nonetheless, 5 out of 11 countries reported that efforts were underway.

Table 118: Established national registries for paediatric FH patients in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	3/11	27.3%
Several non-national registries	1/11	9.1%
Partially implemented	5/11	45.5%
Fully implemented	2/11	18.2%

National registries of homozygous FH patients were partially established in 4 out of 11 countries. Saudi Arabia had already established a registry for HoFH patients.

Table 119: Established national registries for homozygous FH patients in the Eastern Mediterranean region

	Number of countries	Percentage
Not implemented	3/11	27.3%
Several non-national registries	1/11	9.1%
Partially implemented	4/11	36.4%
Fully implemented	1/11	9.1%

European Region

National registries for adults were partially established in 11 out of 37 countries and fully established in 16 others. Malta reported that a national FH registry was recently set up for a research study.

Table 120: Established national registries for adult FH patients in the European region

	Number of countries	Percentage
Not implemented	5/37	13.5%
Several non-national registries	4/37	10.8%
Partially implemented	11/37	29.7%
Fully implemented	16/37	43.2%

National registries for paediatric cases were available in 13 out of 37 countries. Efforts to set up a national registry for children were underway in Belgium, Greece, Lithuania, and the United Kingdom.

Table 121: Established national registries for paediatric FH patients in the European region

	Number of countries	Percentage
Not implemented	13/37	35.1%
Several non-national registries	1/37	2.7%
Partially implemented	4/37	10.8%
Fully implemented	13/37	35.1%

National FH registries for homozygous patients were available in 17 out of 37 countries. Belgium, Greece, Hungary, Kyrgyzstan, and Lithuania were in the process of setting up such registries.

Table 122: Established national registries for homozygous FH patients in the European region

	Number of countries	Percentage
Not implemented	9/37	24.3%
Several non-national registries	0/37	0.0%
Partially implemented	5/37	13.5%
Fully implemented	17/37	45.9%

Asia-Pacific Region

National FH registries for adults were available in 4 out of 9 countries. New Zealand reported that the country only had one local registry, in Canterbury. Efforts to set up a national registry were underway in Cambodia and the Philippines.

Table 123: Established national registries for adult FH patients in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	1/9	11.1%
Several non-national registries	2/9	22.2%
Partially implemented	2/9	22.2%
Fully implemented	4/9	44.4%

National registries for paediatric FH patients were available in 3 out of 9 countries. Malaysia reported that its national paediatric registry was only partially established.

Table 124: Established national registries for paediatric FH patients in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	2/9	22.2%
Several non-national registries	2/9	22.2%
Partially implemented	1/9	11.1%
Fully implemented	3/9	33.3%

National registries of homozygous FH patients were available in Australia, Japan, Malaysia, and Thailand. China and Vietnam reported the existence of several regional or local registries for HoFH patients.

Table 125: Established national registries for homozygous FH patients in the Asia-Pacific region

	Number of countries	Percentage
Not implemented	2/9	22.2%
Several non-national registries	2/9	22.2%
Partially implemented	0/9	0.0%
Fully implemented	4/9	44.4%

DISCUSSION

Awareness

Data on the prevalence of familial hypercholesterolemia were available in most countries of the Americas, Eastern Mediterranean, European, and Asia-Pacific regions. Unfortunately, only 2 countries in the African region were able to provide such data. Overall, the reported figures were in line with the estimated prevalence of 1 in 200 to 250 people worldwide (2).

International guidelines were used in many countries and all regions. National guidelines were well-established in the Americas and Asia-Pacific regions. FH Awareness Day was well-recognized in most countries of the European and Asia-Pacific regions. The awareness day was modestly recognized in the Americas and Eastern Mediterranean regions. However, many countries in the Americas and Eastern Mediterranean regions have started to adopt 24 September.

Awareness raising activities and research on the prevalence of familial hypercholesterolemia are still sorely needed globally (especially in the African region).

Advocacy

In the absence of dedicated formal patient advocacy groups (PAG) and patient support organizations, most of the survey respondents were physicians. Unfortunately, patients and patient organizations were underrepresented in most regions. Patient advocate and FH ambassador programmes were scarce in all regions. Efforts to implement such programmes have been initiated in the Americas, European, Eastern Mediterranean, and Asia-Pacific regions. Unfortunately, responses related to organisational funding did not always specify whether the resources were allocated to advocacy activities for FH. However, considering the limited numbers of PAGs representatives in the survey, overall funding for advocacy and advocacy activities were probably insufficient.

Screening, testing, and diagnosis

Overall, the diagnosis rates of familial hypercholesterolemia were far too low, globally. Only a few countries in each region were able to achieve an over 10% diagnosis rate. In addition, most of the aforementioned countries were located in the European region. Unfortunately, efforts to screen for FH at the national level were absent in most regions. However, many countries in the European and Eastern Mediterranean regions have started to implement such programmes. Unfortunately, it was not possible to ascertain whether the aforementioned programmes were pilot, local, regional, or national programmes.

Although cost-effective, cascade screening programmes were only implemented in 25 out of 78 countries. Fortunately, efforts to implement cascade screening strategies were underway in most regions. Universal screening for children were only available in 5 out of 78 countries. Efforts to implement these programmes were underway in 9 other countries.

Metabolic tests were available in almost every country. In addition, the test was reimbursed in most countries of the Americas, European, and Asia-Pacific region. Genetic testing was mostly available and reimbursed in the Americas, European, and Asia-Pacific regions.

In conclusion, actions to improve the diagnosis rates of familial hypercholesterolemia are needed in every part of the globe.

Treatment

Statins were available in almost every country and were reimbursed in most countries and regions. Ezetimibe was available in most countries across all regions and was mainly reimbursed in the Americas, Eastern Mediterranean, European, and Asia-Pacific regions.

PCSK9 inhibitors were available in most countries of the Americas, Eastern Mediterranean, European, and Asia-Pacific regions. The drugs were only available in some countries of the African region. PCSK9 inhibitors were rarely reimbursed in the African, Americas, Eastern Mediterranean, and Asia-Pacific regions. Novel medicines, such as bempedoic acid, were only available in some countries globally and were rarely reimbursed.

The availability and affordability of cholesterol-lowering drugs remain insufficient and inadequate in most parts of the world. In particular, access to affordable novel and expensive medicines needs to be improved.

Severe and homozygous FH

Overall, most countries did not have separate guidelines for the management of severe and homozygous familial hypercholesterolemia. Lipid and FH clinics were rarely established in the African region. Specialized clinics were available in approximately half of the countries in the Eastern Mediterranean and European regions. Lipid and FH clinics were established in most countries of the Americas and Asia-Pacific regions.

Novel medicines for homozygous FH, such as lomitapide, were only available in some countries of the African, Americas, Eastern Mediterranean, and Asia-Pacific regions. In contrast, lomitapide was readily available in most countries of the European region. The drug was rarely reimbursed across all regions. LDL-apheresis was available in some countries of the African, Americas, and Eastern Mediterranean regions. The medical procedure was rarely reimbursed in the aforementioned regions. In contrast, LDL-apheresis was available in most countries of the European and Asia-Pacific regions. However, apheresis was only reimbursed in some of the countries.

Access to specialized centres for the management of severe and homozygous FH needs to be improved worldwide. In particular, access to affordable new medicines and other expensive medical procedures needs to be addressed.

Family-based care

FH patients were principally managed by cardiologists and endocrinologists across the world. Lipid specialists, general practitioners, and paediatricians were also regularly involved in the management of FH cases. The limited amount of involvement from general practitioners and paediatricians suggests that levels of awareness in some medical communities were still low. Diagnosis at the specialist level also implies that patients were detected late, often after experiencing a cardiovascular event. Gaps in prevention for FH-related cardiovascular disease and health promotion still need to be addressed.

Registries

National FH registries for adults, children, and homozygous patients were not established in most countries of the African region. Registries were fully implemented in approximately half of the countries in the Americas, European, and Asia-Pacific regions. National FH registries were partially implemented in many countries of the Eastern Mediterranean region.

Many countries have yet to establish reliable national FH registries for adults, children, and HoFH patients.

LIMITATIONS

The survey was essentially a self-reported questionnaire. As such, some responses may be subjected to recall bias. In addition, some questions may have been occasionally missed and/or incorrectly interpreted by participants. Questionnaires are generally inflexible by nature and opportunities to add comments were not always offered. Furthermore, the survey was only available in English and non-native speakers may have misunderstood or misinterpreted some questions.

In terms of statistical power, the survey was completed by 1 to 4 respondents for each country. Therefore, the answers will not necessarily reflect the opinions of every in-country expert due to the small sample size. This issue can be observed in the answers provided by two or more participants from the same country. Observer bias can also be observed as the best possible answer was systematically selected and reported when two or more respondents from the same country provided different responses.

Data on the prevalence of FH were not available for every country and some respondents reported an assumed figure. With regard to formal studies, the method of detection for familial hypercholesterolemia may also vary depending on population characteristics, awareness of FH, socio-cultural norms, diagnostic criteria, resources, etc. (5).

Many progresses and changes have occurred since the WHF / FH Europe country mapping survey was conducted. In fact, many newer treatments and therapies were still in development or in the process of being approved in 2020. In addition, data on the impact of COVID-19 on the FH community and/or FH advocacy were not collected. Furthermore, the survey did not cover aspects, such as advocacy barriers, available resources (i.e., funding, time, expertise, etc.), the genetic nature of the condition, stigma and discrimination, as well as public misconceptions. Furthermore, other critical areas, such as genetic counselling, health literacy, as well as wider advocacy and support were not covered. Lastly, further studies on patient behaviours, multidisciplinary collaborations, health literacy, engagement in guidelines development, and policy-making should be conducted.

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APPENDIX

Appendix 1: Survey Questions

Nr	Survey Questions
1	What area do you represent? I am…
2	What is the estimated population number in your country? E.g. 8.57 million
3	What is the estimated prevalence of FH in your country?
4	What percentage of estimated total of people with FH in your country are diagnosed?
5	What percentage of the diagnosed people receive treatment?
6	Are there national efforts, e.g., your government /ministry of health, to screen for FH in your country at the population level?
7	Is there cascade screening (FH screening of the family of a diagnosed FH patient) in place in your country?
8	Is there a universal child screening program for FH in your country?
9	If there is universal child screening program for FH - at what age is it?
10	At what level do patients get diagnosed with FH?
11	How do FH patients get typically diagnosed?
12	What type of testing is used in your country to confirm FH?
13	Is the testing reimbursed?
14	If yes, then how is it reimbursed?
15	How commonly is genetic testing used in your country?
16	Is there country-specific legislation related to access to the results of genetic testing?
17	Who has access to the patient's FH diagnosis results?
18	Is there a national / regional referral pathway?
19	If diagnosed at the GP/paediatrician level, are patients typically referred to a specialist?
20	Do specialized lipid clinics or FH clinics exist in your country?
21	What guidelines for dyslipidaemia management does your country follow?
22	Do the clinical guidelines your country follows on CVD management include FH as a risk factor?
23	Does your country have separate guidelines for severe and homozygous FH?
24	Are the following therapies generally available and reimbursed?
25	Who manages FH patients in your country?
26	Is there a National registry for FH?

27	**Do you collaborate with the Principal Investigators for any advocacy efforts?**
28	**Can your organization connect with the patients in the FH registry to promote your advocacy efforts?**
29	**Is FH Awareness Day, September 24th, recognized in your country?**
30	**Is there a dedicated Patient Advocate / Ambassador program for the FH community in your country?**
31	**How are your advocacy efforts funded?**