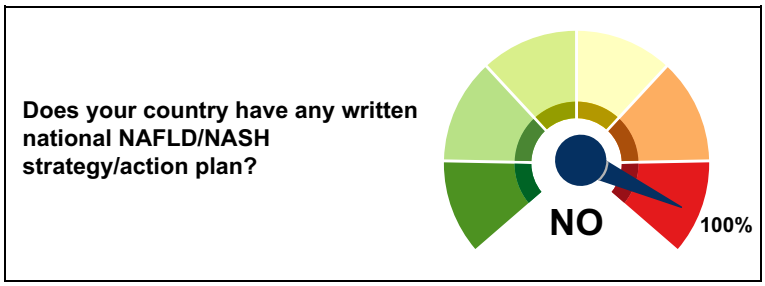
Research Article
NAFLD and Alcohol-Related Liver Diseases

JOURNAL OF HEPATOLOGY

A cross-sectional study of the public health response to non-alcoholic fatty liver disease in Europe

Graphical abstract



Highlights

- A comprehensive public health response to NAFLD is lacking in the 29 countries.
- Major gaps include strategies, clinical guidelines, awareness and education.
- Only 7 countries reported structured lifestyle programmes aimed at NAFLD.
- Four countries reported active collaboration with civil society groups on NAFLD issues.

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Lay summary

We conducted a survey on non-alcoholic fatty liver disease with experts in European countries, coupled with data extracted from official documents on policies, clinical guidelines, awareness, and monitoring. We found a general lack of national policies, awareness campaigns and civil society involvement, and few epidemiological registries.

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NAFLD and Alcohol-Related Liver Diseases

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A cross-sectional study of the public health response to non-alcoholic fatty liver disease in Europe

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Background & Aims: Non-alcoholic fatty liver disease (NAFLD) is a growing public health problem worldwide and has become an important field of biomedical inquiry. We aimed to determine whether European countries have mounted an adequate public health response to NAFLD and non-alcoholic steatohepatitis (NASH).

Methods: In 2018 and 2019, NAFLD experts in 29 European countries completed an English-language survey on policies, guidelines, awareness, monitoring, diagnosis and clinical assessment in their country. The data were compiled, quality checked against existing official documents and reported descriptively.

Results: None of the 29 participating countries had written strategies or action plans for NAFLD. Two countries (7%) had mentions of NAFLD or NASH in related existing strategies (obesity and alcohol). Ten (34%) reported having national clinical guidelines specifically addressing NAFLD and, upon diagnosis, all included recommendations for the assessment of diabetes and liver cirrhosis. Eleven countries (38%) recommended screening for NAFLD in all patients with either diabetes, obesity and/or metabolic syndrome. Five countries (17%) had referral algorithms for follow-up and specialist referral in primary care, and 7 (24%) reported structured lifestyle programmes aimed at NAFLD. Seven (24%) had funded awareness campaigns that specifically included prevention of liver disease. Four countries (14%) reported having civil society groups which address NAFLD and 3 countries (10%) had national registries that include NAFLD.

Conclusions: We found that a comprehensive public health response to NAFLD is lacking in the surveyed European countries. This includes policy in the form of a strategy, clinical guidelines, awareness campaigns, civil society involvement, and health systems organisation, including registries.

Lay summary: We conducted a survey on non-alcoholic fatty liver disease with experts in European countries, coupled with data extracted from official documents on policies, clinical guidelines, awareness, and monitoring. We found a general lack of national policies, awareness campaigns and civil society involvement, and few epidemiological registries.

Keywords: Non-alcoholic fatty liver disease (NAFLD); Non-alcoholic steatohepatitis (NASH); Guidelines as topic; Health Policy; Review; Europe.
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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a growing challenge to global public health. It is defined as the increased accumulation of hepatic triglyceride (>5%) in the absence of excessive alcohol consumption or other causes of liver disease. The NAFLD spectrum encompasses steatosis (non-alcoholic fatty liver, NAFL) and non-alcoholic steatohepatitis (NASH), an inflammatory form of the condition marked by the presence of hepatocyte damage and progressive fibrosis that may lead to cirrhosis.[1,2] Although NAFLD may occur in patients with normal weight, it is closely associated with the presence of the metabolic syndrome, and therefore with obesity, type 2 diabetes

mellitus, hypertension and dyslipidaemia.[3] The prevalence estimates of NAFLD vary widely according to the modality used to detect NAFLD and the geographical area.[3,4] Most of the larger studies on NAFLD prevalence are based on ultrasonography,[5] which is insensitive to modest increases in hepatic lipid accumulation at levels <30%, and do not employ diagnostic tools recommended by current guidance (*e.g.* transient elastography, NAFLD fibrosis score, magnetic resonance imaging, or the gold standard, liver biopsy).[1] Nevertheless, a recent meta-analysis estimated the global prevalence of NAFLD to be 25%, with the highest estimates in the Middle East and South America (32% and 31%, respectively) and the lowest estimates in the African continent (14%); the estimates for Asia, the USA, and Europe were 27%, 24% and 23%, respectively.[4]

NAFLD is a cause of significant morbidity and mortality, although it is not widely appreciated as being a major health threat. NAFLD-related cirrhosis can result in end-stage liver disease and hepatocellular carcinoma (HCC).[6,7] Recently, NAFLD became one of the main causes of liver transplantation in the United States.[2,8,9] While this is not yet the case in Europe, NAFLD is an increasingly common underlying cause of end-stage liver disease, which contributes substantially to hospital admissions.[6,10] This difference in prevalence may, at least in part, be due to an epidemiological lag in obesity rates in Europe coupled with the potential lack of recognition of the disease in European disease-coding data.[11]

Modelling studies predict a steady increase in the incidence of NAFLD at the global level, accompanied by a proportionally larger increase in NASH cases, liver transplantation, HCC and mortality from liver and non-liver causes.[4,12,13] This, combined with the advent of highly efficacious antiviral agents against hepatitis C, has contributed to the trend towards NAFLD becoming the leading cause of liver transplantation in the near future.[14] The economic burden associated with the NAFLD epidemic is enormous and will continue to increase as societies become progressively affected by this global public health problem.[15–17]

To assess this growing public health threat, we aimed to determine the existence of policy documents either specifically focused on NAFLD/NASH or encompassing them in related disease/condition policies. We also aimed to explore NAFLD awareness, and capture details of clinical guidelines for prevention, monitoring, testing, diagnosis and treatment in European countries.

Patients and methods

Survey instrument

To design the survey instrument, the European Association for the Study of the Liver (EASL) International Liver Foundation (EILF) convened a study group of NAFLD experts at the first EASL NAFLD Summit in November 2017. The survey instrument was then revised through multiple rounds of feedback from the study group over a 3-month period. The English-language 24-item survey questionnaire had a mix of multiple choice and open-ended questions and was grouped into 6 categories: (i) policies/guidelines; (ii) continuing medical education and awareness; (iii) monitoring and data; (iv) prevention, testing and diagnosis; (v) clinical assessment; and (vi) treatment. This questionnaire was piloted in 2018 with 8 countries (France, Germany, Italy, Portugal, Slovenia, Spain, Sweden and the United Kingdom) and subsequently simplified into a 17-item questionnaire for the second phase of the study and employed with all 29 participating countries.

Data collection and analysis

Data were collected from 29 countries: Norway, Switzerland and all European Union countries expect for Malta. Data were collected during late 2018 (pilot) and early 2019 (all countries).

Survey participants were recruited through a purposive sampling process. A NAFLD expert was selected from each study country. Each survey lead was tasked with completing a single survey for their country. They received written guidance recommending that they create an informal country-specific team of up to 6 members (*e.g.* clinicians, government representatives, and patient society representatives) to assist them in completing the survey and, to the extent possible, drawing responses from existing documentation.

After the surveys were completed, 2 of the authors performed a quality check. Participants were then e-mailed to seek clarification for inconsistent/unclear responses and to provide documentation to support answers when possible. Data collection for all countries closed on June 2019.

The data were compiled and descriptively analysed using Microsoft Excel. The results are presented in 6 sections: national or regional strategies on NAFLD and other conditions; national clinical guidelines for NAFLD and assessment of other conditions; national clinical guidelines for conditions other than NAFLD; NAFLD management; NAFLD awareness; monitoring and data.

Results

National or regional strategies on NAFLD and other conditions

None of the 29 participating countries had official national strategies for NAFLD. Thirteen countries (45%) had written national or regional strategies for obesity; 10 (34%) for alcohol; 12 (42%) for cardiovascular disease; 4 (14%) for liver disease; 15 (48%) for diabetes; and 14 (48%) for healthy habits/nutrition. However, NAFLD was specified in only 2 obesity strategies and in 1 alcohol strategy (Table 1).

National clinical guidelines for NAFLD and assessment of other conditions

Ten countries (35%) had national clinical guidelines for NAFLD (Table 2). Upon NAFLD diagnosis, all 10 included specific recommendations for the assessment of diabetes and liver cirrhosis. Almost all also included specific recommendations for the assessment of hypertension, dyslipidaemia, levels of alcohol use, cardiovascular disease and HCC (Table 3).

National clinical guidelines for conditions other than NAFLD

Almost all countries (n = 25, 86%) had national guidelines for diabetes. The most common existing clinical guidelines were for dyslipidaemia (n = 19, 65%), hypertension (n = 19, 65%) and obesity (n = 18, 62%). There were guidelines for alcohol in 14 countries (48%), ischaemic heart disease in 13 (45%), liver transplant in 11 (38%) and end-stage liver disease/cirrhosis in 7 (24%). NAFLD/NASH was specifically mentioned in approximately half of the existing guidelines for end-stage liver disease/cirrhosis and liver transplant, whereas for the other conditions NAFLD/NASH was mentioned in a much smaller number of existing guidelines (Table 2). Eleven countries (38%) recommended screening for NAFLD in all patients with either diabetes, obesity and/or metabolic syndrome (Not shown in tables).

Table 1. National or regional strategies for NAFLD/NASH, key diseases or conditions related to NAFLD/NASH and their inclusion of NAFLD/NASH.

	NAFLD/ NASH	Obesity		Alcohol		Cardiovascular disease		Liver disease		Diabetes		Healthy habits/ nutrition	
	Strategy	Strategy	NAFLD/ NASH*	Strategy	NAFLD/ NASH*	Strategy	NAFLD/ NASH*	Strategy	NAFLD/ NASH*	Strategy	NAFLD/ NASH*	Strategy	NAFLD/ NASH*
Austria	–	m	m	m	m	m	m	–	n.a.	m	m	m	m
Belgium	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Bulgaria	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Croatia	–	–	n.a.	–	n.a.	X	–	–	n.a.	X	–	–	n.a.
Czech Republic	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Denmark	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	X	–	X	–
Estonia	–	X**	–	X**	–	X	–	X**	–	X**	–	X**	–
Finland	–	m	m	m	m	m	m	m	m	m	m	m	m
France	–	X	–	X	–	–	n.a.	–	n.a.	m	m	m	m
Germany	–	X	–	X	–	–	n.a.	–	n.a.	–	n.a.	X	–
Greece	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Hungary	–	DK	n.a.	–	n.a.	DK	n.a.	–	n.a.	DK	n.a.	DK	n.a.
Ireland	–	X	–	DK	n.a.	DK	n.a.	–	n.a.	X	–	X	–
Italy	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	X	–	X	–
Latvia	–	–	n.a.	DK	n.a.	DK	n.a.	X	–	–	n.a.	X	–
Lithuania	–	X	–	X	–	X	–	–	n.a.	X	–	–	n.a.
Luxembourg	–	X	–	–	n.a.	X	–	–	n.a.	X	–	–	n.a.
Netherlands	–	X	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Norway	–	X	–	X	–	X	–	–	n.a.	X	–	X	–
Poland	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Portugal	–	X	X	X	X	X	–	–	n.a.	X	–	X	–
Republic of Cyprus	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Romania	–	DK	n.a.	–	n.a.	X	–	X	–	DK	n.a.	DK	n.a.
Slovakia	–	X	–	X	–	X	–	–	n.a.	X	–	X	–
Slovenia	–	X	–	–	n.a.	X	–	–	n.a.	X	–	X	–
Spain	–	X	–	X	–	X	–	–	n.a.	X	m	X	–
Sweden	–	–	n.a.	X	–	X	–	–	n.a.	X	–	X	–
Switzerland	–	–	n.a.	–	n.a.	–	n.a.	X	–	–	n.a.	X	–
United Kingdom	–	X	X	X^	–	X	–	–	n.a.	X	–	X	–
Total of affirmative answers (%)	**0/0 (0%)**	**13/29 (43%)**	**2/13 (15%)**	**10/29 (34%)**	**1/10 (10%)**	**12/29 (42%)**	**0/12 (0%)**	**4/29 (14%)**	**0/4 (0%)**	**14/29 (48%)**	**0/14 (0%)**	**14/29 (48%)**	**0/14 (48%)**

Notes: Possible answers include yes (X), no (–), do not know (DK) and missing value (m). n.a., not applicable; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.
*Denotes specific inclusion of information or mention of NAFLD/NASH in the strategy.
**Denotes that the disease or condition does not have a specific strategy although it is covered in another wider strategy.
^Previously an alcohol strategy in place up to 2012 but now only a "Youth Alcohol Strategy" and some inclusion in crime strategy.

Table 2. National clinical guidelines for NAFLD/NASH and related key diseases or conditions and their inclusion of NAFLD/NASH.

	NAFLD/ NASH	Dyslipidaemia		Obesity		Diabetes		Alcohol		Hypertension		Ischaemic heart disease		End-stage liver disease/cirrhosis		Liver transplant	
	Guideline	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*	Guideline	NAFLD/ NASH*
Austria	– ***	m	m	m	m	m	m	m	m	m	m	m	m	m	m	m	m
Belgium	X	X	–	–	n.a.	X	–	X	–	X	–	–	n.a.	–	n.a.	–	n.a.
Bulgaria	– ***	– ***	n.a.	X	–	X	–	X	X	– ***	n.a.	– ***	n.a.	X	X	X	X
Croatia	–	–	n.a.	–	n.a.	X	–	–	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.
Czech Republic	X	X	–	X	X	X	–	X	–	X	–	X	–	–	n.a.	X	X
Denmark	X	X	–	X	X	X	–	X	–	X	–	X	–	X	–	DK	n.a.
Estonia	– ***	X	–	X	–	X	–	X	–	X	–	X	–	– ***	n.a.	X	X
Finland	– ^	m	m	m	m	m	m	m	m	m	m	m	m	m	m	m	m
France	–	X	–	X	–	X	–	X	–	X	–	X	–	X	–	X	–
Germany	X	X	–	X	X	X	–	X	–	X	–	X	–	X	–	– ^	n.a.
Greece	– ^	X	–	–	n.a.	X	–	–	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.
Hungary	–	X	DK	DK	n.a.	X	DK	–	n.a.	X	DK	DK	n.a.	–	n.a.	– ***	n.a.
Ireland	–	–	n.a.	X	–	X	–	X	–	X	–	X	–	–	n.a.	–	n.a.
Italy	X	–	n.a.	X**	X	X	X	X	–	–	n.a.	X	–	X	X	X	X
Latvia	–	– ***	n.a.	m	m	m	m	m	m	m	m	– ***	n.a.	– ***	n.a.	– ^	n.a.
Lithuania	–	X	–	X	–	X	–	–	n.a.	X	–	X	–	–	n.a.	X	–
Luxembourg	–	X	–	X	–	X	–	–	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.
Netherlands	–	X	–	X	–	X	–	X	–	X	–	X	–	–	n.a.	–	n.a.
Norway	–	–	n.a.	X	X	X	X	X	–	X	–	X	–	–	n.a.	X	–
Poland	X	X	–	X	–	DK	n.a.	–	n.a.	DK	n.a.	–	n.a.	–	n.a.	–	n.a.
Portugal	–	X	–	X	–	X	–	X	–	X	–	X	–	–	n.a.	X	–
Republic of Cyprus	–	–	n.a.	–	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	–	n.a.
Romania	X	X	X	DK	n.a.	X	–	DK	n.a.	X	–	DK	n.a.	X	X	–	n.a.
Slovakia	X	X	–	– ***	n.a.	X	–	DK	n.a.	– ***	n.a.	– ***	n.a.	– ***	n.a.	– ***	n.a.
Slovenia	–	X	–	–	n.a.	X	–	–	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.
Spain	X	–	n.a.	X	–	X	–	–	n.a.	–	n.a.	–	n.a.	–	n.a.	X	X
Sweden	–	X**	–	X**	–	X	–	X	–	–	n.a.	X	–	–	n.a.	X	–
Switzerland	–	X	–	X	–	X	–	DK	n.a.	X	–	–	n.a.	–	n.a.	–	n.a.
United Kingdom	X	X	X	X	X	X	–	X	–	X	–	X	X	X	X	X	X
Total of affirmative answers (%)	**10/29 (35%)**	**19/29 (66%)**	**2/19 (11%)**	**18/29 (62%)**	**6/18 (33%)**	**25/29 (86%)**	**2/25 (8%)**	**14/29 (48%)**	**1/14 (7%)**	**19/29 (66%)**	**0/19 (0%)**	**13/29 (45%)**	**1/13 (8%)**	**7/29 (24%)**	**4/7 (57%)**	**11/29 (38%)**	**6/11 (55%)**

Notes: Possible answers include yes (X), no (–), do not know (DK) and missing value (m). n.a., not applicable; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.
*Denotes specific inclusion of information or mention of NAFLD/NASH in the strategy.
**Denotes that the disease or condition does not have a specific national guideline although it is covered in another clinical guideline.
***Denotes the use of international clinical guidelines instead of national ones.
^Denotes a clinical guideline being in development.

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Table 3. National clinical guidelines recommending assessment of the following diseases and conditions in patients with NAFLD upon diagnosis.

	Diabetes	Hypertension	Dyslipidaemia	Cardiovascular disease	Liver cirrhosis	Hepatocellular carcinoma	Levels of alcohol use
Belgium	X	X	X	X	X	X	X
Czech Republic	X	X	X	X	X	–	X
Denmark	X	X	X	–	X	X	X
Germany	X	X	X	X	X	X	X
Italy	X	X	X	X	X	X	X
Poland	X	–	–	–	X	X	–
Romania	X	X	X	X	X	X	X
Slovakia	X	X	X	X	X	X	X
Spain	X	X	X	X	X	X	X
United Kingdom	X	X	X	X	X	–	X
Total of affirmative answers (%)	**10/10 (100%)**	**9/10 (90%)**	**9/10 (90%)**	**8/10 (80%)**	**10/10 (100%)**	**8/10 (80%)**	**9/10 (90%)**

Notes: Possible answers include yes (X), no (–), do not know (DK) and missing value (m). n.a., not applicable; NAFLD, non-alcoholic fatty liver disease.

NAFLD management

The healthcare providers specifically managing NAFLD included hepatologists (86% of the countries) and gastroenterologists (83%); less frequently, primary care physicians (48%), internal medicine physicians (45%) and multi-disciplinary teams (24%) (Table 4). Primary healthcare providers were typically responsible for the care of obesity (76%), diabetes (72%), metabolic syndrome (72%) and harmful alcohol use (62%) (Not shown in tables). Five countries (17%) had algorithms for NAFLD management in primary care centres. Regarding treatment, 7 countries (24%) had structured lifestyle programmes for patients with NAFLD (Table 5).

NAFLD awareness

Seven countries (24%) had funded public health awareness campaigns specifically including preventive aspects of liver disease. Only France, the Netherlands, Portugal and Switzerland reported having any in-country civil society group focused on NAFLD (Table 5).

Monitoring and data

Three countries (10%) reported national disease registries that include NAFLD. Although only 8 countries (28%) had national or regional NAFLD cohorts, some reported having local cohorts in university hospitals. Eight countries (28%) had conducted population-based epidemiological studies on NAFLD in the past 5 years and 2 (7%) have ongoing nationwide epidemiological studies to assess NAFLD prevalence (Table 5).

Discussion

Our study is the first to comprehensively review national policies and guidelines on NAFLD. Despite the high burden of NAFLD, earlier studies have primarily focused on clinical aspects, laboratory findings and molecular pathways leading to liver fibrosis. Our results demonstrate that while clinical guidelines are available and epidemiological studies have been conducted in some European countries, policies and the involvement of civil society, as well as nationwide campaigns are limited or non-existent in most countries. This is of particular concern in light of the estimated prevalence of NAFLD in Europe of 23.7%.[3]

The absence of national or regional strategies addressing NAFLD is probably the most worrying finding. This reflects either a lack of appreciation of the high prevalence and potential health economic impact of this condition or a lack of prioritisation of this growing public health problem by international and national institutions, or both. There is also a dearth of high-quality epidemiological and health economic data to support decision-makers. For example, estimates of NAFLD were not provided by the Global Burden of Disease studies until its 2017 causes of death study, and no disability-adjusted life years (DALYs) were calculated for it.[18]

Despite the strong relationship between NAFLD and obesity, diabetes and cardiovascular risk, and the existence of well-established strategies addressing the latter in most countries, there is a paucity of strategies or guidelines on NAFLD. This is probably because its potential for severity and progression has been recognised only recently.

In spite of the absence of national and regional government strategies, EASL[2] and countries such as Germany,[19] Italy,[20] Spain[21] and the UK[22] do have clinical guidelines addressing NAFLD. However, the majority of these guidelines, either specific for NAFLD or for other conditions closely linked to NAFLD, do not universally recommend key measures such as systematic screening for NAFLD in patients with metabolic risk factors like type 2 diabetes and obesity. Nor do they recognise metabolic syndrome associated liver disease, *i.e.* NAFLD, as a potential contributory factor for liver damage in harmful alcohol use.[7] Importantly, they also do not call for assessment of the presence of other metabolic conditions after a diagnosis of NAFLD.

Currently, risk factors that indicate a need to screen for NAFLD remain poorly defined and recommendations are inconsistent. The current EASL/European Association for the Study of Diabetes (EASD)/European Association for the Study of Obesity (EASO) guidelines recommend screening in high-risk groups where metabolic risk factors are present.[2] The German[19] and UK[22] guidelines, developed as a joint effort between different specialists, do incorporate clear algorithms for NAFLD screening in high-risk populations (*e.g.* those with type 2 diabetes and obesity). In contrast, societies such as the American Association for the Study of Liver Diseases (AASLD) do not recommend routine screening in high-risk groups from primary care (typically understood as general practitioners [GPs]), diabetes or obesity clinics, although they acknowledge that there should be a high suspicion of NAFLD and NASH in patients with type 2 diabetes. This lack of consensus regarding the efficacy and/or cost-effectiveness of systematic NAFLD screening among patients with metabolic syndrome conditions, *e.g.* obesity[23] and diabetes,[24] reduces the likelihood of recommendations being uni-

Table 4. Most common healthcare providers typically responsible for the care of NAFLD.

	Gastroenterology	Internal Medicine	Hepatology	Primary care	Multi-disciplinary team	Diabetologist	Nutritionist	Endocrinologist	Cardiologist	Department of infectious diseases
Austria	–	X	X	X	–	–	–	–	–	–
Belgium	X	–	X	–	–	–	–	–	–	–
Bulgaria	X	X	X	X	X	–	–	–	–	–
Croatia	X	–	X	–	–	–	–	–	–	–
Czech Republic	X	X	X	–	–	–	–	–	–	–
Denmark	X	–	X	X	–	–	–	–	–	–
Estonia	X	X	–	X	–	–	–	–	–	–
Finland	X	–	–	X	–	–	–	–	–	–
France	X	–	X	–	–	–	–	–	–	–
Germany	X	X	X	X	–	X	X	–	–	–
Greece	X	X	X	–	X	–	–	–	–	–
Hungary	X	X	X	X	–	–	–	–	–	–
Ireland	X	–	X	–	–	–	–	–	–	–
Italy	X	X	X	–	X	–	–	–	–	–
Latvia	–	–	X	–	–	–	–	–	–	–
Lithuania	X	–	X	–	–	–	–	X	X	–
Luxembourg	X	X	X	–	–	–	–	–	–	–
Netherlands	X	X	X	–	X	–	–	–	–	–
Norway	X	–	–	X	–	–	–	–	–	–
Poland	–	–	X	–	–	–	–	–	–	X
Portugal	X	X	X	X	X	–	–	–	–	–
Republic of Cyprus	X	X	X	X	–	–	–	–	–	–
Romania	X	–	X	–	–	–	–	–	–	–
Slovakia	X	–	X	–	–	–	–	–	–	–
Slovenia	–	–	X	–	–	–	–	–	–	–
Spain	X	–	X	X	–	–	–	–	–	–
Sweden	X	–	–	X	X	–	–	–	–	–
Switzerland	–	X	X	X	–	X	–	–	–	–
United Kingdom	X	–	X	X	X	–	–	–	–	–
Total of affirmative answers (%)	**24/29 (83%)**	**13/29 (45%)**	**25/29 (86%)**	**14/29 (48%)**	**7/29 (24%)**	**2/29 (7%)**	**1/29 (3%)**	**1/29 (3%)**	**1/29 (3%)**	**1/29 (3%)**

Notes: Possible answers include yes (X), no (–), do not know (DK) and missing value (m). n.a., not applicable; NAFLD, non-alcoholic fatty liver disease.

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Table 5. NAFLD management; awareness; and monitoring and data.

	Follow-up and specialist referral algorithms in primary care	Structured lifestyles programmes	Government funded awareness campaigns that include any aspect of "liver health"	In-country civil society group focused on NAFLD	National disease registry that include NAFLD/ NASH	National or regional NAFLD/NASH cohort	Population-based epidemiological studies to assess NAFLD prevalence/ incidence in the last 5 years	Ongoing nationwide epidemiological studies assessing NAFLD prevalence
Austria	–	–	–	–	–	–	–	–
Belgium	X	X	–	–	–	–	–	–
Bulgaria	–	–	–	–	–	–	–	–
Croatia	–	X	X	–	–	X	X	–
Czech Republic	X	X	–	–	–	–	–	–
Denmark	X	–	–	–	–	–	–	–
Estonia	–	–	–	–	–	–	–	–
Finland	–	–	–	–	–	–	X	–
France	–	–	–	X	–	–	X	–
Germany	–	X	–	–	–	X	X*	X*
Greece	–	–	–	–	–	–	–	–
Hungary	DK	X	X	DK	–	DK	DK	DK
Ireland	–	–	–	–	–	–	–	–
Italy	–	–	–	–	–	–	–	–
Latvia	–	–	X	–	–	DK	–	–
Lithuania	–	–	–	–	X	–	–	–
Luxembourg	–	–	X	–	–	–	–	–
Netherlands	–	–	–	X	–	X	–	–
Norway	DK	–	–	–	–	–	–	–
Poland	–	–	–	–	–	–	–	–
Portugal	–	–	–	X	X	–	X	–
Republic of Cyprus	–	–	–	–	–	–	–	–
Romania	–	–	–	–	–	–	–	–
Slovakia	X	X	DK	–	–	X	–	–
Slovenia	–	–	X	–	–	–	–	DK
Spain	–	–	X	–	X	X	X	X
Sweden	–	–	–	–	–	X	X	–
Switzerland	m	DK	X	X	–	X	–	–
United Kingdom	X	X	–	–	–	X	X**	–
Total of affirmative answers (%)	5/29 (17%)	7/29 (24%)	7/29 (24%)	4/29 (14%)	3/29 (10%)	8/29 (28%)	8/29 (28%)	2/29 (7%)

Notes: Possible answers include yes (X), no (–), do not know (DK) and missing value (m). n.a., not applicable; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.
*Not national but deemed representative of the German population.
**UK Biobank: Not national but deemed representative of the UK.

formly included in clinical guidelines or consistently adopted into practice by GPs. There is indeed already emerging evidence that adherence to the guidelines in clinical practice is poor.[25] Research efforts that identify the pathophysiological links and epidemiological associations between NAFLD and other prevalent conditions such as type 2 diabetes, hypertension and dyslipidaemia in the European population may further elucidate risk factors and stratifiers to guide NAFLD screening.

One argument against screening for NAFLD or NASH is the lack of an effective pharmacological treatment specifically licensed for these conditions. However, dietary and lifestyle changes have a substantial impact on the natural course of the disease: weight reduction can lead to the regression of steatosis, steatohepatitis or even fibrosis.[26] Even without weight loss, healthier dietary habits, physical activity and avoiding a sedentary lifestyle have metabolic as well as hepatic benefits.[27] There are data supporting tailored selection of pharmaceutical agents for the treatment of associated metabolic conditions that may have additional liver-directed benefits, for example, the use of pioglitazone or liraglutide to treat type 2 diabetes may ameliorate coexistent NASH.[9] Therefore, not diagnosing NAFLD/NASH deprives patients of the opportunity to address their risk of progressive liver disease in the context of metabolic syndrome, of an opportunity to reinforce dietary and lifestyle changes, and, most importantly, of proper surveillance for liver-related complications in those that have disease that has progressed to undiagnosed cirrhosis.

Although the occurrence of HCC in non-cirrhotic NASH is well recognised, studies suggest that the individual risk of a patient with non-cirrhotic NAFLD developing HCC remains modest, irrespective of the presence of type 2 diabetes.[7,28] At present, there are no data to support a recommendation for routine HCC surveillance in the non-cirrhotic NAFLD population.[29,30] However, half of the participating countries did recommend an initial screen for HCC among patients when first diagnosed with NAFLD/NASH. Identifying effective diagnostic and prognostic biomarkers, such as markers for the risk of progression to HCC,[31] would help to underpin strategic plans to prevent and control NAFLD-related HCC.[7]

Our study found that hepatogastroenterologists were the main healthcare providers in charge of managing patients with NAFLD. However, the absence in most of the countries of algorithms for follow-up and specialist referral, as well as of structured lifestyle programmes, reflects important gaps in NAFLD management. Additionally, on average, awareness of NAFLD is poor among GPs, gastroenterologists and other clinicians.[32–34] This lack of awareness, in conjunction with the dearth of national strategies and guidelines, leads to the underdiagnosis of NAFLD.[35] Therefore, continuing education programmes and awareness campaigns are pivotal, as well as development and adaptation of clinical guidelines to protocols to identify patients who need specialist referral. Potential factors that need to be assessed in further studies are the role of non-liver specialists, including GPs, and the implementation of community-based initiatives and civil society involvement aimed at NAFLD education, prevention, detection and care (*e.g.* through community-based participatory research study designs).

The dearth of algorithms for primary care referral is particularly concerning in view of the high prevalence of NAFLD in Europe. Primary care should play a key role in the management of NAFLD, not only because of its pivotal role in health promotion and community care but also because specialised liver care is not prepared to receive such a large number of patients. Simple and affordable algorithms to identify patients at high risk of complications could be implemented in primary care to determine patients needing specialised care.[36–38] This might contribute to managing the complexity of the spectrum of NAFLD-associated liver disease, including transplantation, within a health system that ensures early detection and excellent clinical management while maintaining economic sustainability and equity.

Lack of government-supported surveillance systems to detect and monitor NAFLD and its associated comorbidities in the countries surveyed is another example of how limited commitment of health authorities can influence the NAFLD response. This gap was partially addressed by the academically led international "European NAFLD Registry" that was established in 2010 with EASL and European Union funding to the *Fatty Liver: Inhibition of Progression* (FLIP), *Elucidating Pathways of Steatohepatitis* (EPoS) and *Liver Investigation: Testing Marker Utility in Steatohepatitis* (LITMUS) research consortia. This registry was recruiting in secondary/tertiary care environments in some countries. However, broadening the scope and geographical participation in this effort to collect data on NAFLD/NASH across the general European population would be beneficial. In the case of epidemiological knowledge, the most urgent issue, together with the necessity of implementing coordinated surveillance systems, is to complement the many studies providing highly valuable evidence on the clinical aspects of NAFLD with studies addressing the social, economic and cultural (including lifestyle) drivers of the epidemics. This might enable us to move from screening strategies based on high-risk clinical profiles to a combination of genetic, epidemiological and clinical profile approaches leading to value-based care of patients with NAFLD.[39]

From a public health perspective, arguably one of the most important aspects to focus on is modifying risk factors: to prevent and reduce obesity rates and to achieve better dietary habits.[11] In the participating countries, the prevalence of physical inactivity is estimated to be 25–45% and obesity 20–30%.[40] Childhood obesity is particularly worrying as NAFLD also affects young people,[41] with an estimated prevalence of 6–10%. As the EAT-Lancet Commission reported recently,[42] overweight and obesity rates are increasing globally, with 2.1 billion overweight or obese individuals currently. Estimates place unhealthy diets as the main contributor to the global burden of disease. Measures such as taxation, especially of sugar-sweetened beverages,[43] marketing regulation, improving nutritional labelling, reformulating food, conducting awareness campaigns as well as subsidies to increase consumption of healthier nourishment have been proven to be successful in improving healthy eating among the general population, including children.[32,44] Also, behavioural interventions that address both dietary habits and exercise at an individual level are likely to reduce obesity rates.[45] One study estimated that reducing the consumption of added sugars by 20% could prevent up to 770,000 DALYs due to its impact on NAFLD (considering NASH, HCC and cirrhosis), obesity, type 2 diabetes and coronary heart disease.[46] Further, structural changes in cities such as transportation policies may contribute to increased physical activity.[47]

This study has several limitations. Although data were provided by leading in-country experts in consultation with colleagues, they were not externally validated, and some findings may have been subject to interpretation, including when translating to English, or may have changed between data collection

and publication of the results. Nevertheless, as the overall study findings were similar in all countries, *i.e.* the limited attention to NAFLD in policies and practice, the data are consistent and plausible. Future studies should seek to address additional countries from around the world and also assess the economic burden and implications for health system organisation of the increasing prevalence of NAFLD in association with other conditions (*e.g.* obesity and diabetes).

In conclusion, our study analysing the policies, guidelines, health system organisation and epidemiological initiatives in place for NAFLD in 29 European countries found that an informed response was lacking. A comprehensive approach, including formulating policy, developing clinical practice guidelines and conducting research is needed to effectively tackle NAFLD in Europe. If the current growing prevalence of non-communicable diseases is any indication, health systems should turn their attention to NAFLD in order to raise awareness and promote healthy lifestyles.

Abbreviations

AASLD, American Association for the Study of Liver Diseases; DK, Do not know; EASD, European Association for the Study of Diabetes; EASL, European Association for the Study of the Liver; EASO, European Association for the Study of Obesity; EPoS, Elucidating Pathways of Steatohepatitis; HCC, hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

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Conflict of interest

The authors declare that they have no conflict of interest related to this manuscript. Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

JVL and JM designed the study and oversaw it. JVL, JM, JMP developed the questionnaire with input from all authors. JMP and JVL wrote the first draft with input from QMA and HCP. All authors contributed to the revision of the first draft and ER re-analysed the data and revised the tables with input from JVL. All authors reviewed and approved the final draft.

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Supplementary data

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