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Care standards for non-alcoholic fatty liver disease in the United Kingdom 2016: a cross-sectional survey.

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Keywords: non-alcoholic fatty liver disease (NAFLD); non-alcoholic steato-hepatitis (NASH); liver biopsy; guidelines; transient elastography, staging

Abstract:

Objective: Guidelines for assessment of non-alcoholic fatty liver disease (NAFLD) have been published in 2016 by NICE and EASL-EASD-EASO. Prior to publication of these guidelines we performed a cross-sectional survey of Gastroenterologists and Hepatologists regarding NAFLD diagnosis and management.

Design: An on-line survey was circulated to members of BASL and BSG between February-May 2016.

Results: 175 Gastroenterologists / Hepatologists responded, 116 completing the survey, representing 84 UK centres. 22% had local NAFLD guidelines. 45% received >300 referrals per-year from primary care for investigation of abnormal liver function tests (LFTs).
Clinical assessment tended to be performed in secondary rather than primary care including BMI (82% vs 26%) and non-invasive liver screen (86% vs 32%) and ultrasound (81% vs 37%).
Widely used tools for non-invasive fibrosis risk-stratification were AST/ALT ratio (53%), Fibroscan® (50%), and NAFLD-Fibrosis score (41%). 78% considered liver biopsy in selected cases.
50% recommended 10% weight-loss target as first-line treatment. Delivery of lifestyle interventions was mostly handed back to primary care (56%). A minority have direct access to community weight-management services (22%).
Follow-up was favoured by F3/4 fibrosis (72.9%), and high-risk non-invasive fibrosis tests (51%). Discharge was favoured by simple steatosis at biopsy (30%), and low-risk non-invasive scores (25%).

Conclusions: The survey highlights areas for improvement of service provision for NAFLD assessment including improved recognition of NASH in people with type-2 diabetes, streamlining abnormal LFTs referral pathways, defining non-invasive liver fibrosis assessment tools, use of liver biopsy, managing metabolic syndrome features, and improved access to lifestyle interventions.

Summary 'box'

What is already known about this subject?	New clinical guidelines for NAFLD assessment, diagnosis and treatment were published in 2016 from NICE and EASL
What are the new findings?	This national cross sectional survey captured opinion on the state of NAFLD assessment in the UK, before guideline publication
How might it impact on clinical practice in the foreseeable future?	The survey has identified priority areas for service improvement and implementation of recent guidelines

INTRODUCTION

NAFLD is highly prevalent, affecting ~25% of the population and is likely to increase further due to the obesity epidemic [1]. NAFLD occurs due to accumulation of liver fat (steatosis) in the context of obesity and insulin resistance leading to generation of lipotoxic intermediates, and a cycle of liver cell stress, inflammation and fibrosis. This can progress ultimately to decompensated cirrhosis and/or hepatocellular carcinoma (HCC) [2]. NAFLD is typically asymptomatic and therefore the majority of patients remain undiagnosed. However, other associated features of metabolic syndrome including obesity, insulin resistance, type 2 diabetes, hyperlipidaemia and hypertension may frequently come to medical attention, and also affect prognosis, increasing risk of cardiovascular mortality in this group of patients [3]. Thus the typical patient with NAFLD crosses many of the boundaries between primary and secondary care and between traditional clinical specialities.

The first line intervention to treat NAFLD is lifestyle changes to lose weight, although many patients with NAFLD find support for lifestyle interventions difficult to access or achieve [4].

Although there are currently no licensed drug therapies to treat NASH, several agents are in phase 2 and 3 clinical trials. Therefore, the major priorities of healthcare providers at present are to identify those at risk of NAFLD, establish a definite diagnosis, initiate lifestyle interventions, identify those with advanced disease for HCC surveillance, and identify those with earlier fibrosis but potentially progressive NASH who may benefit from new treatments in the future.

In 2016 two clinical guidelines for the assessment and treatment of non-alcoholic fatty liver disease (NAFLD) have been published; NICE clinical guideline 49 [5] and the joint European Associations for the study of the Liver (EASL), European Association for the study of Diabetes (EASD) and the European Association for the study of Obesity (EASO) [6]. The publication of both these guidelines represents an important landmark in NAFLD clinical practice and research. It also highlights the many challenges and uncertainties in the existing evidence base posed by this important clinical problem.

The aim of the present survey was to understand the degree to which practice varies across the UK in identifying patients with NAFLD, diagnosis, risk stratification and treatment. Additionally, this data provides a context for the subsequent recommendations of NICE and EASL-EASD-EASO guidelines for assessment and treatment of NAFLD. We have utilised the survey findings to recommend an ‘action plan’ to improve NAFLD management.

METHOD

Survey questions were agreed by the UK-NAFLD group. A 10 question on-line survey was circulated to members of the British Association for the Study of the Liver (BASL) (859 members) and British Society of Gastroenterology

(BSG) Liver Section (561 members) between February 2016 and May 2016. This was prior to the publication of NICE guideline 49 and contemporary to the EASL-EASD-EASO guideline release. The full list of questions included in the survey is provided online supplemental appendix.

Results:

Respondents Sample of opinion. 175 gastroenterologist / hepatologists responded to the survey. 116 respondents provided complete responses, and there were 59 incomplete questionnaires. 84 separate NHS organisations across England, Scotland, Wales and Northern Ireland responded (Appendix). 30 (17%) considered themselves district general hospital (DGH) Gastroenterologists, 50 (29%) were DGH Gastroenterologists with a hepatology interest, 67 (38%) were Hepatologists in a specialist liver unit, and 28 (16%) in a liver transplant centre. There was no significant variance in completion rates by type of centre (table 1).

38/175 respondents (22%) stated that their centre had local guidelines for NAFLD management. All the respondents that stated they had local NAFLD guidelines completed the survey. More respondents from specialist hepatology units (34%) and liver transplant centres (35%) stated they had local NAFLD guidelines than those in DGH gastroenterology (3%) or DGH with hepatology interest (8%) (table 1).

NAFLD Assessment.
The majority of new diagnoses of NAFLD are made following investigation of abnormal liver function tests (LFTs), that have typically been performed in primary care for some indication other than suspected NAFLD [7]. The UK NAFLD survey data indicates a high demand for secondary care services to investigate abnormal LFTs with 49/110 (45%) of respondents reporting >300 referrals per year from primary care for investigation of abnormal LFTs.

Referrals from diabetes / metabolic services for investigation of abnormal LFTs are fewer than from primary care, with 63/99 (64%) of respondents reporting <50 referrals per year from these services. This supports the perception that NAFLD is under recognised in this high-risk population with type-2 diabetes (figure 1).

A positive diagnosis of NAFLD is made on the basis of imaging evidence of hepatic steatosis, and exclusion of other causes of liver disease including alcohol related liver disease, viral hepatitis, autoimmune liver disease and haemochromatosis. NAFLD diagnosis therefore requires an initial clinical assessment for features of the metabolic syndrome, an alcohol history and a negative 'non-invasive liver screen' and abdominal ultrasound scan [8]. The UK NAFLD survey questions sought to understand where in the diagnostic pathway an assessment for BMI, alcohol consumption and waist circumference are being made. BMI (82.6%) and alcohol history (79.1%) are usually performed in secondary care rather than in primary care, but waist circumference is not routinely performed in most units (56.5%) (Supplemental figure 1A). For diagnosis of NAFLD, the Fatty Liver Index (FLI) score, (an

algorithm based on BMI, waist circumference, GGT and fasting Triglycerides) is not routinely performed in 89.3% of respondents, although had been suggested by NICE as useful for NAFLD diagnosis.

The survey data indicates that the non-invasive liver screen including ferritin (87.7%), hepatitis B and C serology (86%), liver auto-antibodies (91.2%), immunoglobulins (91.2%) and liver ultrasound (80.9%) are performed in the majority of cases by secondary rather than primary care (Supplemental figure 1B).

Assessment of Liver Fibrosis

Various scoring systems/tools are available for the non-invasive assessment of liver fibrosis. Many require measurement of the AST, whereas others include transient elastography (fibroscan®) and serum fibrosis tests including serum Enhanced Liver Fibrosis (ELF) test. NICE recommends offering testing for advanced liver fibrosis to people with NAFLD using the ELF test[5].
The UK NAFLD survey attempted to capture data on which tools are currently most widely used for non-invasive fibrosis assessment (figure 2). The survey found that the AST is routinely performed by the hospital team in 71.4% of cases, and in 33.9% of primary care cases. The survey indicates that primary care do not routinely perform any assessment of liver fibrosis, with only 7.9% routinely performing AST/ALT ratio in primary care. The tools most commonly used routinely in secondary care are: AST/ALT ratio (53%), Transient Elastography (Fibroscan®) (50%), NAFLD Fibrosis score (41%), FIB-4 score (16%), APRI score (6%) and ELF test or other serum fibrosis markers (5%). There was variation in modalities used for liver fibrosis assessment according to type of centre, notably Fibroscan more likely to be performed in Specialist hepatology centres (71%) and transplant units (67%), than DGH gastroenterology (16%) or DGH hepatology interest (32%) centres (table 1).

Liver Biopsy.

Liver biopsy is an important tool for NAFLD assessment to establish a diagnosis of NASH by histological features of steatosis, hepatocyte ballooning and inflammation, and to stage degree of liver fibrosis. Neither the NICE nor EASL-EASD-EASO guidelines make specific recommendations regarding when to use liver biopsy in NAFLD assessment, although the EASL-EASD-EASO guidance advocates the approach of applying non-invasive methods first, to avoid biopsy in low risk cases [6]. In the UK NAFLD survey, 78% of respondents said they would consider liver biopsy in selected cases. The strength of agreement with a series of statements regarding use of liver biopsy in NAFLD was asked to attempt to understand the boundaries and indications for liver biopsy. The hierarchy of factors for which respondents agreed or strongly agreed with is shown in figure 3. There was general agreement that liver biopsy is indicated when an alternative diagnosis is in the differential, and/or where there are high non-invasive scores of fibrosis. There was also general disagreement that liver biopsy is poorly tolerated by patients. There does not appear to be a consensus of views regarding the utility of liver biopsy in those with escalating features of the metabolic syndrome and in those with intermediate non-invasive risk scores.

Extrahepatic conditions
Extraheptic conditions are relevant to holistic care in NAFLD patients. NICE guidance highlights awareness that NAFLD is a risk factor for type 2 diabetes, hypertension and chronic kidney disease. Furthermore, there should be awareness that in people with Type 2 diabetes, NAFLD is a risk factor for atrial fibrillation, myocardial infarction, ischaemic stroke and death from cardiovascular causes [5]. The survey sought to understand who manages features of the metabolic syndrome in patients with NAFLD. The survey data indicate that only in a minority does secondary care take ownership of these extra-hepatic conditions, the majority either providing advice to GP, or leaving extrahepatic conditions entirely for the GP to manage (Supplmental figure 2).

Alcohol
NICE guidelines state that people with NAFLD should stay within the national recommended limits for alcohol consumption. Most respondents of the survey are providing advice consistent with this, advising on both <14 units per week in those without advanced fibrosis (70.6%) and the calorific nature of alcohol (63%) should be moderated to help lose weight.

Lifestyle modification
Currently, lifestyle intervention to lose weight by diet and exercise is the first line treatment for NAFLD [9]. The survey sought to identify whether services can provide access to effective lifestyle interventions. The majority of respondents relied on referral by GP to community weight management services (56.3%) to facilitate delivery of lifestyle interventions. A minority of respondents in secondary care had direct access to either a multidisciplinary clinic with dieticians and physiotherapists (20.9%) input, or tier 2 (26%), tier 3 (23%) and / or tier 4 (26%) community weight management services. The survey indicates that most respondents give general advice on diet (93%) and exercise (94%), but fewer set specific weight loss targets of >5% or >10% (Supplemental figure 3).

Pharmacotherapy
In the absence of any licensed drugs for NASH, most respondents never prescribe any specific pharmaco-interventions including vitamin E, insulin sensitizers, omega 3 supplements or probiotics. 55% occasionally give advice on specific lipid lowering therapy (Supplemental figure 4).

Follow up decision making.
The survey sought to capture data of factors that influence decisions in secondary care to follow up a case of NAFLD, or discharge back to primary care. Those factors most strongly favouring secondary care follow-up were: NASH with F3/ F4 fibrosis, high risk non-invasive fibrosis test scores, NASH with F2 fibrosis, and a child or young person with evidence of NAFLD (figure 4A). Factors favouring discharge included simple bland steatosis at liver biopsy, low risk non-invasive fibrosis tests, current pressures on clinic capacity and individual unlikely or unable to lose weight (figure 4B).

DISCUSSION.

The publication of clinical practice guidelines for assessment and treatment of NAFLD from NICE and EASL- EASD-EASO provides an impetus to improve care and service provision for patients with NAFLD. Prior to publication of these guidelines, the responses indicate that only a minority of centres had local recommendations for NAFLD assessment, particularly district general hospitals (3-8%), although only 34% of respondents from specialist liver units and 35% from liver transplant centres had local NAFLD guidelines.
This is the first national cross-sectional survey which attempted to provide some context for implementation of the recent NICE guidelines. In light of the survey findings we have summarised recommendations to implement changes in practice locally that will help move from the position described by this survey to improved services for patients with NAFLD (table 2).

The major demand to assess probable NAFLD in secondary care is coming from primary care referral to investigate abnormal LFTs. The evidence from this survey suggests a likely under recognition of NAFLD in high risk individuals, such as those attending diabetes clinics. A significant proportion of asymptomatic patients attending type 2 diabetes clinics have undiagnosed NAFLD and advanced liver fibrosis [10] and therefore diabetic clinics may be an appropriate setting for case-finding.

Simple steps can be implemented into most local referral guidelines and pathways to improve standards. These include improved simple clinical assessment including alcohol history, measurement of BMI and waist circumference in all cases.
Abnormal LFTs pathways can be streamlined, recognising that NAFLD is the most common reason for referral from primary care for investigation of abnormal LFTs[7]. NAFLD diagnosis can be made in primary care, by exclusion of other causes of liver disease. Thus an alcohol history, non-invasive liver screen and ultrasound scan to exclude biliary pathology and confirm hepatic steatosis are mandatory. Streamlined abnormal LFTs referral pathways between primary and secondary care should be developed in all localities to prevent unnecessary follow-up appointments. The focus of secondary care assessment of NAFLD should be on staging, managing the metabolic syndrome and delivering lifestyle interventions.

Following NAFLD diagnosis, non-invasive assessment of liver fibrosis is required. NICE advocate the use of ELF testing which could be performed exclusively in primary care. However, the survey indicates that only 5% of respondents were routinely using ELF. The assessment of fibrosis is generally perceived as an added value exercise of a secondary care referral and the most widely used tools identified from the survey were transient elastography (Fibroscan®), AST / ALT ratio, NFS and Fib-4 scores. All of these modalities have an evidence base for having good (>90%) negative predictive values to 'rule-out' advanced fibrosis in those with low scores, but poor positive predictive values to 'rule-in' NASH with fibrosis in those with higher scores in secondary care cohorts [11].

Current NICE and EASL-EASD-EASO guidelines do not specify when liver biopsy should be undertaken, but histology is required to diagnose NASH with

fibrosis. Most survey respondents indicated that there is a role for liver biopsy, which was most strongly favoured when an alternative diagnosis was being considered, and in those with high risk non-invasive scores. Liver biopsy has an important role in defining eligibility to clinical trials and should be reported according to an agreed framework [12 13].

The survey indicates variation in delivery of lifestyle intervention and specific management of features of the metabolic syndrome. In many instances respondents indicated that secondary care gastroenterologists and hepatologists consider this the responsibility for primary care to deliver. We advocate that secondary care gastroenterologists and hepatologists assessing patients with NAFLD should prescribe a target of 10% weight loss over 12 weeks by diet and exercise as first line treatment for NAFLD, and re-assess response. This can be facilitated in most districts by closer working and referral pathways to tier 2 and 3 community weight management services, in line with the NICE obesity guidance[14]. Furthermore, the survey highlights variation in ownership of management of features of the metabolic syndrome. We advocate a more holistic approach to managing the metabolic syndrome by all physicians assessing patients with NAFLD.

The strengths of this survey are that it is representative of opinion of membership of BSG and BASL gastroenterologists and hepatologists in secondary care. The study is limited by not including representation from primary care, and the data remains qualitative and subjective. It is the intention of the UK NAFLD group to repeat the survey, a year after publication of NICE guidelines to determine if management of NAFLD patients is improving.

In conclusion, the survey has highlighted priorities for service development to adopt recent guidance for NAFLD management, including improved recognition of NAFLD in type 2 diabetes, streamlining abnormal LFTs referral pathways, defining non-invasive fibrosis assessment, when to perform liver biopsy, increasing ownership of managing metabolic syndrome and improving access and delivery of lifestyle interventions.

Table 1: Responses by centre type for NAFLD guidelines and Liver Fibrosis assessment modalities. # Missing responses in completed questionnaires counted as 'not routine'.

		All centres	DGH Gastro	DGH Hepatology Interest	Specialist Hepatology	Liver Transplant Units
Response	Completed	116 (66%)	19 (63%)	34 (68%)	48 (72%)	15 (54%)
	Incomplete	59 (34%)	11 (37%)	16 (32%)	19 (28%)	13 (46%)
Local NAFLD guidelines	Yes	38 (22%)	1 (3%)	4 (8%)	23 (34%)	10 (35%)
	No#	137 (78%)	29 (97%)	46 (92%)	44 (66%)	18 (65%)
NAFLD Fibrosis Score	Performed in all	48 (41%)	4 (21%)	14 (41%)	22 (46%)	8 (53%)
	Selected cases	29 (25%)	4 (21%)	12 (35%)	10(21%)	3 (20%)
	Not routine#	39 (34%)	11 (58%)	8 (24%)	16 (33%)	4 (27%)
APRI score	Performed in all	8 (6%)	0 (0%)	3 (9%)	2 (4%)	3 (20%)
	Selected cases	18 (16%)	1 (5%)	6 (18%)	10 (21%)	1 (7%)
	Not routine#	90 (78%)	18 (95%)	25 (73%)	36 (75%)	11 (73%)
FIB-4	Performed in all	19 (16%)	1 (5%)	3 (9%)	9 (19%)	6 (40%)
	Selected cases	15 (13%)	1 (5%)	2 (6%)	10 (21%)	2 (13%)
	Not routine#	82 (71%)	17 (90%)	29 (85%)	29 (60%)	7 (47%)
Fibroscan	Performed in all	58 (50%)	3 (16%)	11 (32%)	34 (71%)	10 (67%)
	Selected cases	46 (40%)	12 (63%)	17 (50%)	12 (25%)	5 (33%)
	Not routine#	12 (10%)	4 (21%)	6 (18%)	2 (4%)	0 (0%)
AST / ALT ratio	Performed in all	62 (53%)	9 (47%)	16 (47%)	28 (58%)	9 (60%)
	Selected cases	24 (21%)	4 (21%)	8 (24%)	10 (21%)	2 (13%)
	Not routine#	30 (26%)	6 (32%)	10 (29%)	10 (21%)	4 (27%)
Liver Biopsy	Performed in all	7 (6%)	3 (16%)	0 (0%)	2 (4%)	2 (13%)
	Selected cases	90 (78%)	12 (63%)	22 (65%)	43 (90%)	13 (87%)
	Not routine#	19 (16%)	4 (21%)	12 (35%)	3 (6%)	0 (0%)
ELF test	Performed in all	6 (5%)	0 (0%)	1 (3%)	0 (0%)	5 (33%)
	Selected cases	10 (9%)	2 (11%)	1 (3%)	4 (8%)	3 (20%)
	Not routine#	100 (86%)	17 (89%)	32 (94%)	44 (92%)	7 (47%)

Table 2 UK NAFLD Group Recommendations for implementation

Guideline Domain	Proposed Actions for implementation	Impact	Research priorities
Identification of NAFLD in high risk groups	Screening Primary care populations with known type 2 diabetes for significant NAFLD with liver fibrosis as part of the existing diabetes QOF.	Increased NAFLD diagnosis in high risk patients with type 2 diabetes	Does earlier diagnosis of NASH with liver fibrosis alter outcomes in patients with T2DM?
Diagnosis	Review and streamline referral pathways for assessment of abnormal LFTs. Perform routine diagnostic investigations to establish NALFD diagnosis, including abdominal ultrasound and non-invasive liver screen blood tests (hepatitis B & C serology), ALT, AST, ferritin, auto-antibody profile and immunoglobulins) in primary care.	Streamline referral pathways to decrease number of hospital outpatient appointments.	Evaluation of community based programmes for NAFLD diagnosis and risk stratification
Staging for advanced disease	Perform a non-invasive test with high negative predictive value to exclude advanced liver fibrosis in primary care, or at point of referral for assessment to secondary care. Fib 4, NFS, ELF, and Transient Elastography all suitable depending upon local availability.	Facilitates discharge of low risk cases, and decision to biopsy and follow up intermediate and high risk cases.	Evaluate the diagnostic performance and cost effectiveness of non-invasive fibrosis risk scores vs ELF vs transient elastography
Liver biopsy	Offer liver biopsy to those with intermediate and high risk scores to diagnose NASH with Fibrosis, or re-classify as low risk, and reporting using standardised criteria.	Definitive NASH diagnosis, access to clinical trials and those that may benefit for future licensed therapies.	Evaluation of biomarkers and imaging as an alternative to biopsy for NASH diagnosis and staging
Extra-hepatic conditions	Pro-active management of features of the metabolic syndrome by both primary and secondary care.	Improved cardiovascular risk reduction	Specific evidence base on which insulin sensitizers, lipid lowering therapies and anti-hypertensive are best in NAFLD cases.
Lifestyle intervention	Set target of 10% weight loss by diet and exercise as first line treatment for all cases of NAFLD Increase access to tier 2 and 3 weight management services to deliver weight loss as first line NAFLD treatment	Improved efficacy of lifestyle intervention to treat NASH. Define lifestyle non-responders who may benefit from trials and future therapies	What factors influence response /non-response to lifestyle intervention?
Trials	Individuals with NASH and ≥F2 fibrosis should be offered access to clinical trials, and long term follow up in secondary care to assess fibrosis progression	Evidence base for NASH specific therapies	Which interventions are most efficacious, in which populations? Factors that determine response and non-response?

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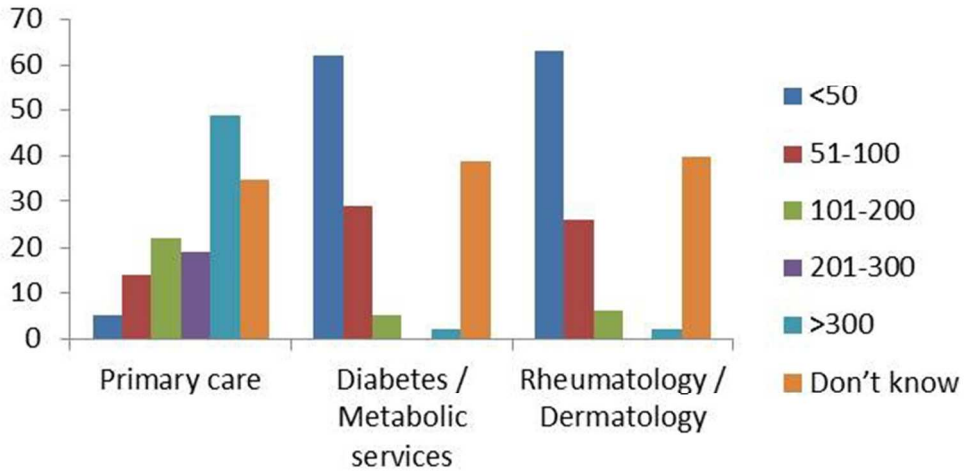
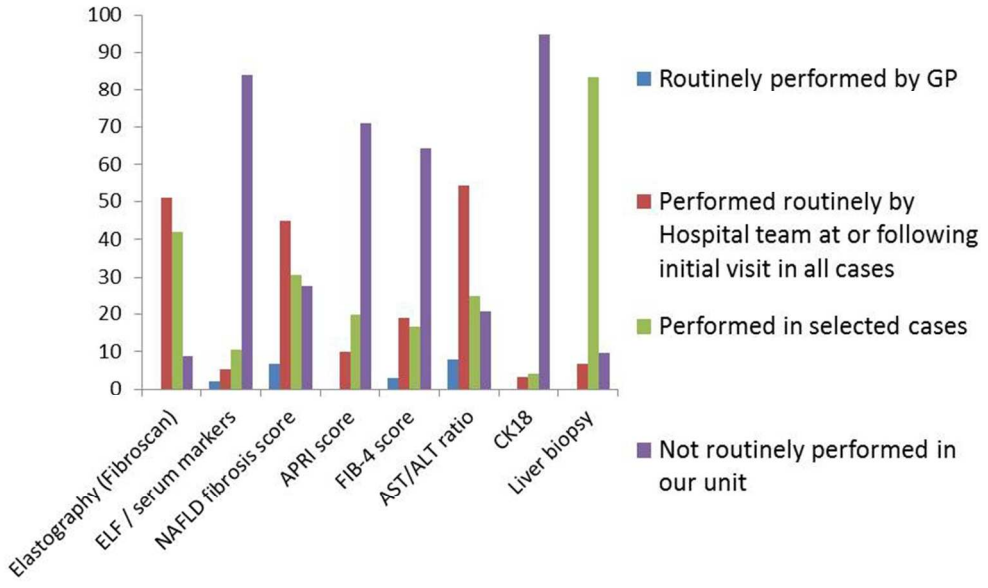
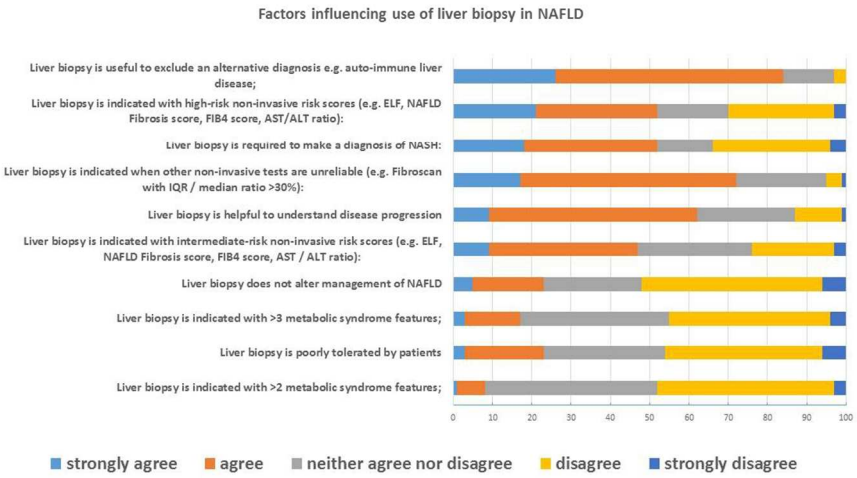


UK NAFLD survey data - estimated number of referrals to gastroenterology and hepatology with abnormal liver function tests.(Number of respondents)
Figure 1
111x57mm (150 x 150 DPI)



Modalities performed to assess for liver fibrosis (% of respondents)
Figure 2
155x94mm (150 x 150 DPI)



Factors influencing use of liver biopsy in NAFLD assessment.
Figure 3
270x152mm (120 x 120 DPI)

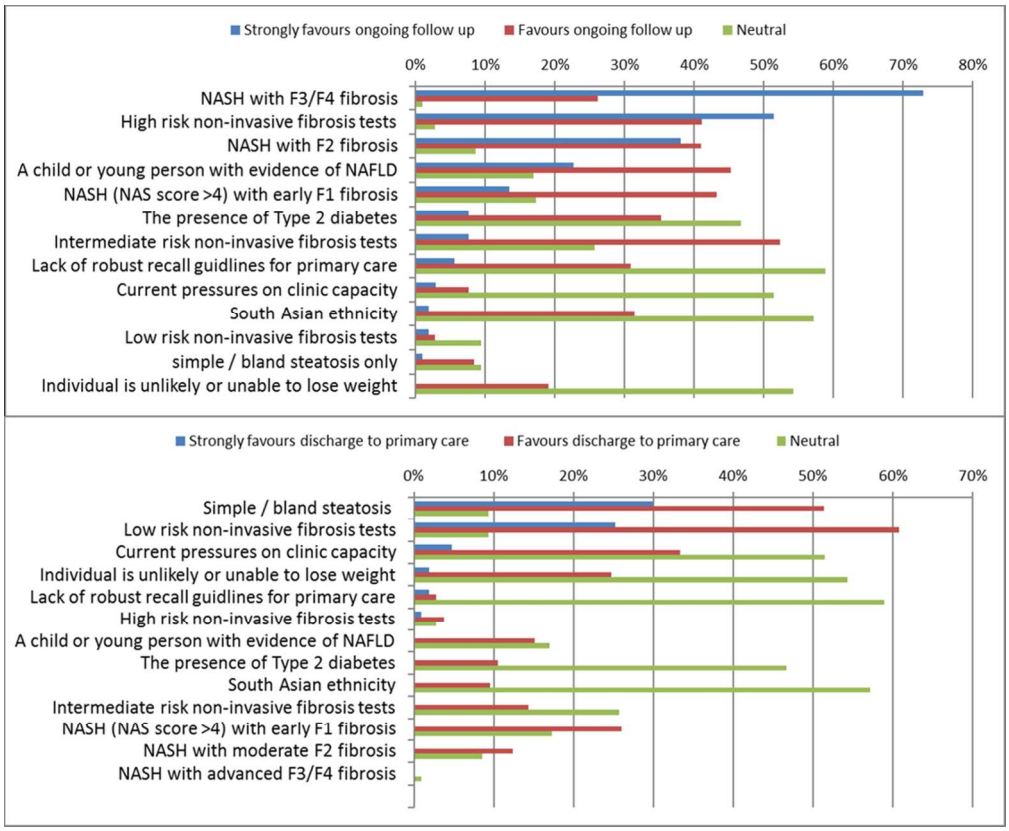
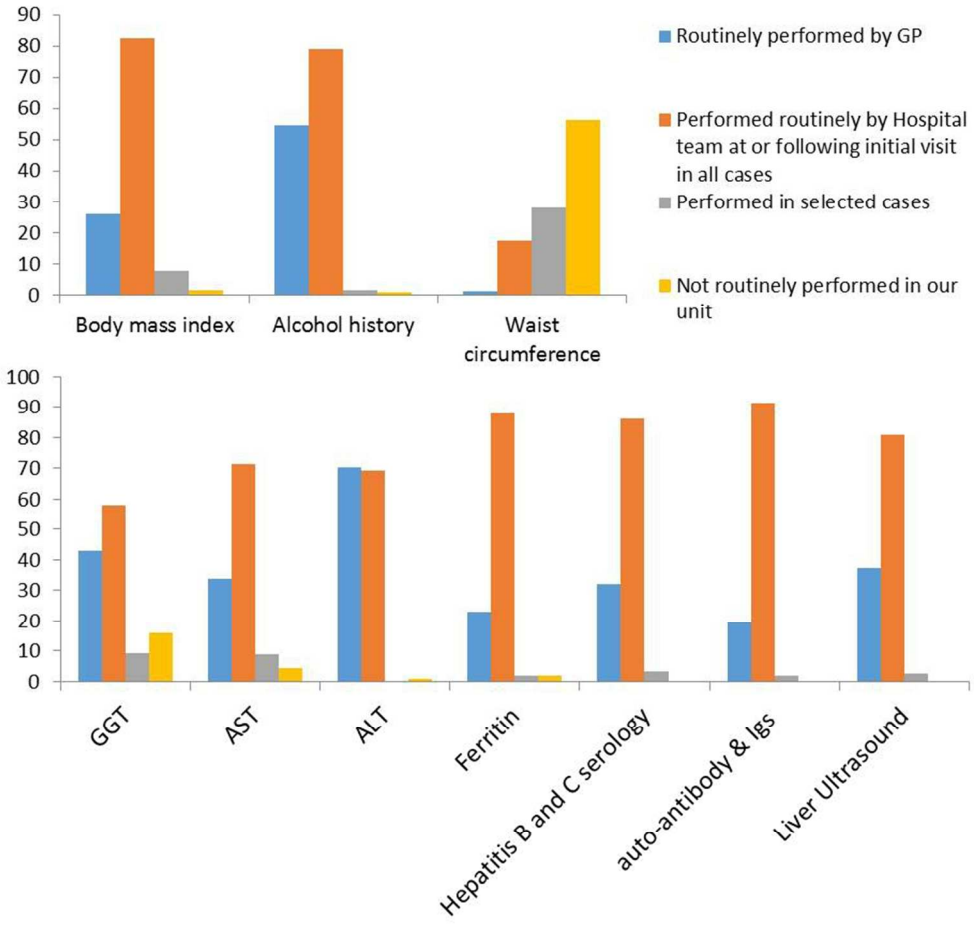


Figure 4A (top panel) factors favouring follow-up in secondary care. 4B (bottom panel) factors favouring discharge from secondary care.
Figure 4
196x161mm (150 x 150 DPI)



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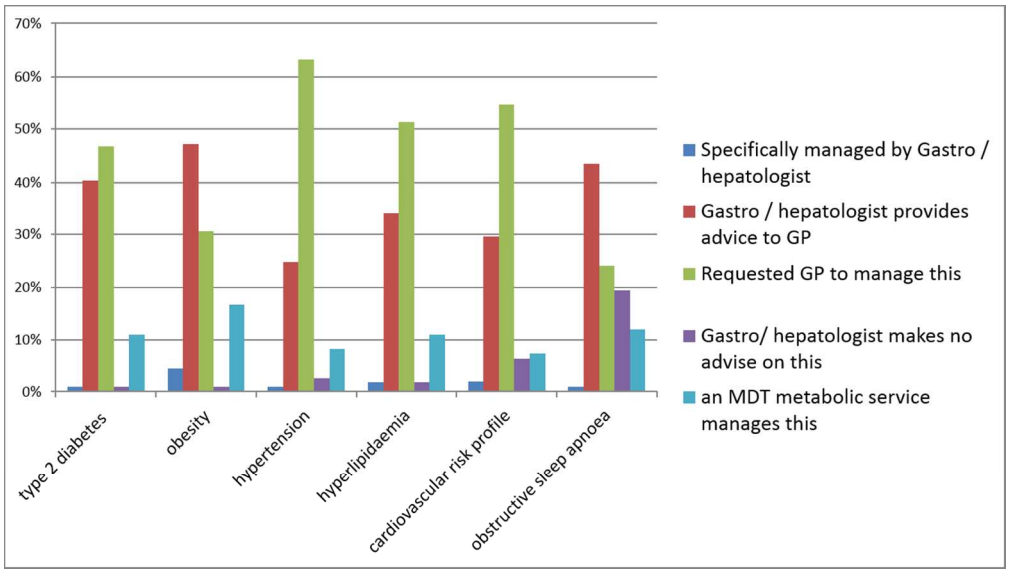

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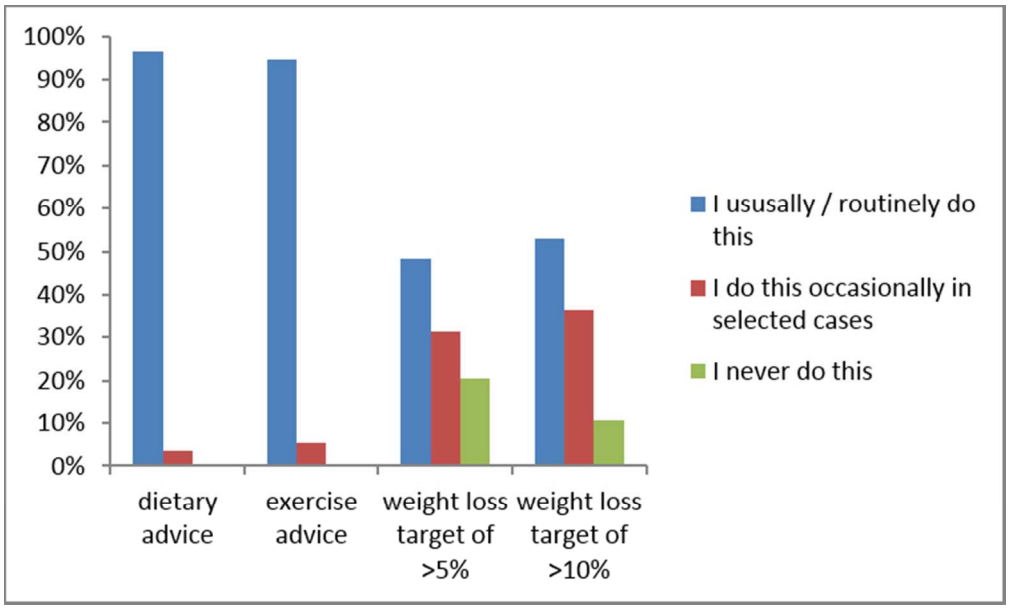
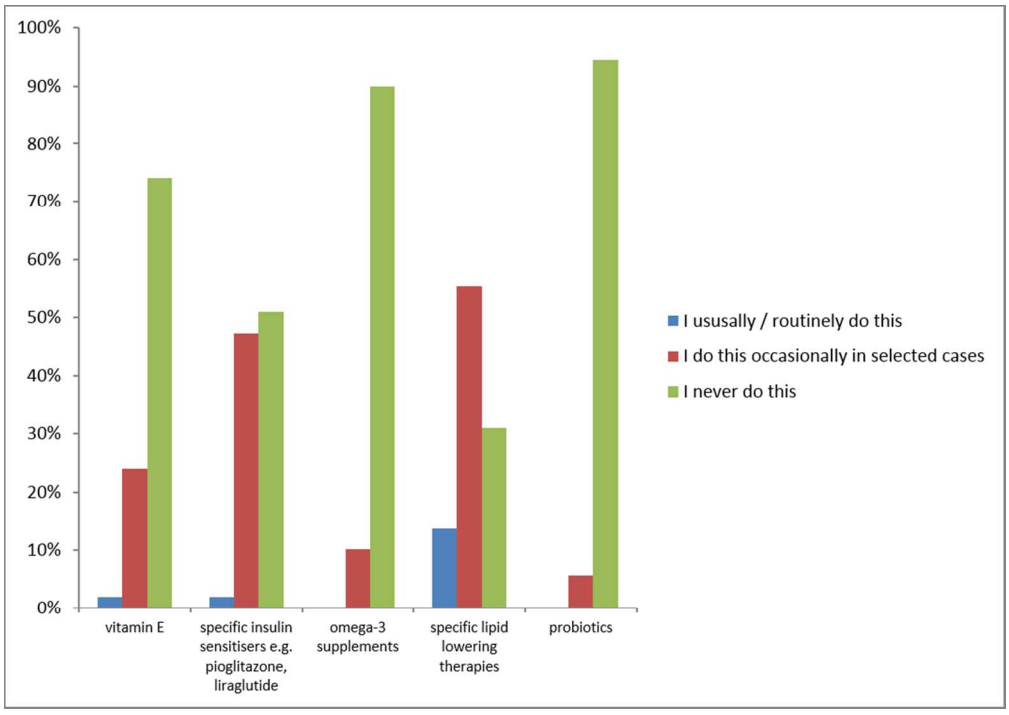


127x76mm (150 x 150 DPI)



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Appendix 1: Contributing centres:

We would like to thank respondents contributing to the survey from the following centres:

Aberdeen Royal Infirmary
Addenbrookes, Cambridge
Aintree University Hospital
Aneurin Bevan University Health Board
Arrowe Park Hospital
Ayreshire Hospital
Barnet Hospital
Barts Health NHS Trust
Birmingham Children's Hospital
Birmingham Heartlands Hospital
Borders General Hospital, Melrose
Brighton & Sussex University Hospitals
Broomfield Hospital, Mid Essex
Chesterfield Royal Hospital
Coventry Hospital
Ealing Hospital
East Kent Hospital
East Surrey Hospital
Fife NHS Trust
Gateshead NHS Foundation Trust
Glasgow Royal Infirmary
Gloucestershire Royal Hospital
Guys and St Thomas' Hospital
Hull and East Yorkshire NHS Trust
Kettering General Hospital
Kings College Hospital
Leeds
Lewisham & Greenwich NHS Trust
Lincoln County Hospital
Lister, Stevenage
London North West healthcare NHS Trust
Newcastle upon Tyne Hospitals NHS Foundation Trust
NHS Grampian
NHS Highland
NHS Lothian
NHS Tayside, Dundee
Norfolk & Norwich NHS Trust
North Bristol NHS Trust
North Cumbria University Hospitals
North Middlesex Hospital
North Tees & Hartlepool
Nottingham University Hospitals
Oxford, John Radcliffe

Pennine Acute Hospitals NHS Trust
Plymouth Hospitals NHS Trust
Poole Hospital
Portsmouth Hospital
Prince Charles Hospital, Cwm Taf, HB
Queen Elizabeth University Hospital, Glasgow
Queen Elizabeth Hospital Birmingham
Royal Alexandra Hospital, Paisley
Royal Berkshire Hospital
Royal Bolton Hospital
Royal Bournemouth Hospital
Royal Derby Hospital
Royal Devon & Exeter Hospital
Royal Free Hospital
Royal Infirmary of Edinburgh
Royal Liverpool Hospital
Royal London Hospital
Royal United Hospital, Bath
Royal Victoria Hospital, Belfast
Salisbury NHS Foundation Trust
Shaheed Ziaur Rahman Medical College Hospital
Sheffield
Solihull Hospital
South Tees NHS Foundation Trust
South Tyneside Hospital
St John's Hospital, Livingston
St Marys / Imperial Healthcare
Taunton Hospital
Torbay
Toronto General hospital
UHNM Royal Stoke Hospital
University Hospital Bristol
University Hospital of Wales
University Hospitals Leicester
Western Sussex Hospitals NHS Foundation Trust (Worthing & Chichester)
Wirral University Hospital
Wishaw General Hospital, Lanarkshire
Withybush Hospital, Hyel Dda HB
Worcester Hospital
Wrightinton, Wigan and Leigh NHS Foundation Trust
Wye Valley

Appendix 2: Full list of survey questions

Q1. Do you have local hospital guidelines for assessment of NAFLD?

Please describe your centre according to one of the following categories:

Answer Choices	Responses
District General Hospital, liver services provided by general gastroenterology	30
District General Hospital, liver services delivered by gastroenterologists with an interest in hepatology	50
A specialist centre providing designated hepatology services	67
A liver transplant unit	28
We have local NAFLD guidelines	38

Q2 How many referrals does your unit receive per year from for investigation of abnormal LFTs, from Primary Care; Diabetes / metabolic; Rheumatology / Dermatology?

	From Primary care–	From diabetes / metabolic medicine services–	From rheumatology / dermatology–
<50	5 (5%)	63(64%)	64 (65%)
51-100	14 (13%)	29 (29%)	26 (27%)
101-200	23 (21%)	5 (5%0	6 (6%)
201-300	19 (17%)	0	0
>300	49 (44%)	2 (2%)	2 (2%)
Total Responses	**110**	**99**	**98**
don't know	35	39	40

Q3 When triaging a referral with abnormal LFTs in your unit with suspected NAFLD, which of the following tests are performed routinely by the referring primary care team or receiving secondary care team?

	Routinely performed by GP before first hospital visit	Performed routinely by hospital team at or following initial visit in all patients	Performed in selected cases	Not routinely performed in our unit	Total Respondents	Missing / incomplete responses
Body Mass Index	25.86% 30	82.76% 96	7.76% 9	1.72% 2	116	0
Alcohol history	55.17% 64	79.31% 92	1.72% 2	0.86% 1	116	0
Waist circumference	1.16% 1	17.44% 15	29.07% 25	55.81% 48	86	30
GGT	42.59% 46	58.33% 63	9.26% 10	15.74% 17	108	8
AST	33.63% 38	71.68% 81	8.85% 10	4.42% 5	113	3
ALT	70.43% 81	69.57% 80	0.00% 0	0.87% 1	115	1
Ferritin	22.61% 26	87.83% 101	1.74% 2	1.74% 2	115	1
Hepatitis B and C serology	32.76% 38	86.21% 100	3.45% 4	0.00% 0	116	0
Liver auto-antibody screen and immunoglobulins	19.13% 22	91.30% 105	1.74% 2	0.00% 0	115	1
Liver and biliary tree ultrasound scan	37.07% 43	81.03% 94	2.59% 3	0.00% 0	116	0
Fibroscan	0.00% 0	50.88% 58	40.35% 46	8.77% 10	114	2
ELF test or other serum fibrosis marker	2.08% 2	6.25% 6	10.42% 10	83.33% 80	96	20
Fatty Liver Index (FLI) score	1.06% 1	5.32% 5	6.38% 6	89.36% 84	94	22
NAFLD Fibrosis score	6.60% 7	45.28% 48	27.36% 29	27.36% 29	106	10
APRI score	0.00% 0	8.79% 8	19.78% 18	71.43% 65	91	25
FIB-4 score	3.13% 3	19.79% 19	15.63% 15	63.54% 61	95	21
AST / ALT ratio	7.84% 8	57.94% 62	22.43% 24	19.63% 21	107	9
Cytokeratin 18	0.00% 0	3.16% 3	4.21% 4	94.74% 90	95	21

	Routinely performed by GP before first hospital visit–	Performed routinely by hospital team at or following initial visit in all patients–	Performed in selected cases–	Not routinely performed in our unit–	Total Respondents–	Missing / incomplete responses
(M30 and / or M65)						
Liver biopsy	0.00% 0	6.54% 7	84.11% 90	9.35% 10	107	9
random glucose	24.27% 25	67.96% 70	11.65% 12	7.77% 8	103	13
HbA1C	20.00% 21	60.95% 64	22.86% 24	6.67% 7	105	11
non-fasting lipid profile	17.35% 17	66.33% 65	11.22% 11	13.27% 13	98	18
fasting glucose	11.96% 11	28.26% 26	51.09% 47	14.13% 13	92	24
fasting lipid profile	15.15% 15	32.32% 32	48.48% 48	13.13% 13	99	17
fasting insulin	0.00% 0	2.17% 2	25.00% 23	73.91% 68	92	24

Q4 In respect to liver biopsy in cases of NAFLD

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
is indicated with intermediate-risk non-invasive risk scores (e.g. ELF, NAFLD Fibrosis score, FIB4 score, AST / ALT ratio)	8.93% 10	38.39% 43	28.57% 32	21.43% 24	2.68% 3
is indicated with high-risk non-invasive risk scores (e.g. ELF, NAFLD Fibrosis score, FIB4 score, AST/ALT ratio)	21.24% 24	31.86% 36	17.70% 20	26.55% 30	2.65% 3
is indicated when other non-invasive tests are unreliable (e.g. Fibroscan with IQR >30%)	16.96% 19	54.46% 61	23.21% 26	4.46% 5	0.89% 1
is indicated with >2 metabolic syndrome features	0.89% 1	7.14% 8	43.75% 49	45.54% 51	2.68% 3
is indicated with >3 metabolic syndrome features	2.70% 3	13.51% 15	37.84% 42	41.44% 46	4.50% 5
is useful to exclude an alternative diagnosis e.g auto-immune liver disease	25.66% 29	58.41% 66	12.39% 14	3.54% 4	0.00% 0
to required to make a diagnosis of NASH	18.02% 20	33.33% 37	13.51% 15	30.63% 34	4.50% 5
is poorly	3.57% 4	20.54% 23	30.36% 34	39.29% 44	6.25% 7

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
tolerated by patients					
does not alter management of NAFLD	4.46% 5	17.86% 20	25.00% 28	45.54% 51	7.14% 8
is helpful to understand disease progression	8.93% 10	53.57% 60	25.00% 28	11.61% 13	0.89% 1

Q5. What lifestyle interventions and support do you regularly access for your patients with NAFLD? (tick all that apply)

Answer Choices	Responses
a multidisciplinary clinic with dieticans and physiotherapy	20.91% 23
direct access to tier 2 weight mamangement (BMI<35)	26.36% 29
direct access to tier 3 weight management services (BMI>35)	22.73% 25
direct access to tier 4 weight management services (BMI>40) including assessment for bariatric surgery	26.36% 29
access to weight management services by referral from GP	56.36% 62
no additional lifestyle intervention support available	

Q6. What advice do you give NAFLD patients about alcohol consumption?

Answer Choices	Responses
To always remain completely abstinent from alcohol	20.18% 22
To drink < 14 units per week in those without advanced fibrosis	70.64% 77
Explain that alcohol is calorific and should be moderated to help reduce weight	63.30% 69
There is insufficient evidence to make a recommendation	2.75% 3
I do not routinely advise on safe alcohol consumption	1.83% 2
Total Respondents: 109	

Q7. With respect to interventions in cases of NAFLD / NASH do you recommend and / or prescribe the following:

	I usually / routinely do this–	I do this occasionally in selected cases–	I never do this–
dietary advice	96.40% 107	3.60% 4	0.00% 0
exercise advice	94.59% 105	5.41% 6	0.00% 0
weight loss target of >5%	47.87% 45	30.85% 29	21.28% 20
weight loss target of >10%	53.40% 55	35.92% 37	10.68% 11
vitamin E	1.83% 2	23.85% 26	74.31% 81
specific insulin sensitisers e.g. pioglitazone, liraglutide	1.83% 2	46.79% 51	51.38% 56
omega-3 supplements	0.00% 0	10.00% 11	90.00% 99
specific lipid lowering therapies	13.51% 15	54.95% 61	31.53% 35
probiotics	0.00% 0	5.50% 6	94.50% 103

Q8. Who manages features of metabolic syndrome in the patients you see with NAFLD?

	Specifically managed by you	you provide advice to GP or other healthcare provider to manage this	you request GP to manage this	you don't advise on this	your centre has a multidisciplinary metabolic service to manage this
type 2 diabetes e.g. advice on specific treatments and glycaemic control e.g.HbA1c	0.91% 1	40.00% 44	47.27% 52	0.91% 1	10.91% 12
obesity	4.59% 5	46.79% 51	31.19% 34	0.92% 1	16.51% 18
hypertension	0.91% 1	24.55% 27	63.64% 70	2.73% 3	8.18% 9
hyperlipidaemia	1.82% 2	33.64% 37	51.82% 57	1.82% 2	10.91% 12
cardiovascular risk profile e.g. QRISK2 score & statin prescribing	1.83% 2	29.36% 32	54.13% 59	7.34% 8	7.34% 8
obstructive sleep apnoea	0.92% 1	43.12% 47	23.85% 26	20.18% 22	11.93% 13

Q9. Which of the following imaging modalities are available in your unit?

	Routinely available and used	Available, but used for selected cases only including research studies	Unavailable at our unit	Don't know
Transient Elastography (Fibroscan) M Probe	70.37% 76	6.48% 7	20.37% 22	2.78% 3
Transient Elastography (Fibroscan) XL Probe	63.89% 69	6.48% 7	24.07% 26	5.56% 6
Controlled attenuation parameter (CAP)	28.57% 30	4.76% 5	56.19% 59	10.48% 11
Acoustic radiation force impulse (ARFI)	5.61% 6	12.15% 13	71.03% 76	11.21% 12
MRI elastography	0.94% 1	15.09% 16	73.58% 78	10.38% 11
Magnetic Resonance Imaging estimated proton density fat fraction (MRI-PDFF)	0.93% 1	14.95% 16	68.22% 73	15.89% 17
Magnetic Resonance Spectroscopy – proton density fat fraction (MRS-PDFF)	0.93% 1	14.81% 16	68.52% 74	15.74% 17

Q10. Please describe to what extent the following factors influence your decision to follow up or discharge a patient with NAFLD from your clinic.

	Strongly favours ongoing follow up	Favours ongoing follow up	Neutral	Favours discharge to primary care	Strongly favours discharge to primary care
A child or young person with evidence of NAFLD	22.43% 24	45.79% 49	16.82% 18	14.95% 16	0.00% 0
The presence of Type 2 diabetes	7.55% 8	34.91% 37	47.17% 50	10.38% 11	0.00% 0
South Asian ethnicity	1.89% 2	31.13% 33	57.55% 61	9.43% 10	0.00% 0
Low risk non-invasive investigations for advanced fibrosis	1.85% 2	2.78% 3	9.26% 10	61.11% 66	25.00% 27
Intermediate risk non-invasive investigations for advanced fibrosis	7.55% 8	52.83% 56	25.47% 27	14.15% 15	0.00% 0
High risk non-invasive investigations for advanced fibrosis	51.85% 56	40.74% 44	2.78% 3	3.70% 4	0.93% 1
Current pressures on clinic capacity	2.83% 3	7.55% 8	51.89% 55	33.02% 35	4.72% 5
Individual is unlikely or unable to lose weight	0.00% 0	18.87% 20	54.72% 58	24.53% 26	1.89% 2
Liver biopsy showing simple / bland steatosis without inflammation, ballooning or fibrosis	0.93% 1	8.33% 9	9.26% 10	51.85% 56	29.63% 32
Liver biopsy showing NASH (NAS score >4) with early F1 fibrosis	13.33% 14	43.81% 46	17.14% 18	25.71% 27	0.00% 0
Liver biopsy showing NASH with moderate F2 fibrosis	38.68% 41	40.57% 43	8.49% 9	12.26% 13	0.00% 0
Liver biopsy showing NASH with advanced F3/F4 fibrosis	73.15% 79	25.93% 28	0.93% 1	0.00% 0	0.00% 0
Lack of robust recall guidelines for primary care	5.56% 6	31.48% 34	58.33% 63	2.78% 3	1.85% 2