21S104 Health-care burden of NAFLD in UK hospital-based outpatient hepatology clinics:

Real-world prospective data from the CONSTANS study

Marie Boyle [1] Vlad Ratziu [2], Quentin Anstee [1]. Members of EPoS consortium

[1] Institute of Cellular Medicine, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom.
[2] Institute of Cardiometabolism and Nutrition, Pitié-Salpêtrière Hospital, Paris, France

INTRODUCTION & AIMS

NAFLD has an estimated global prevalence of 25%. In Europe, real-time data on the economic burden of NAFLD is lacking. Care provision for patients with NAFLD patients is largely conducted in an ambulatory setting.

- The study will characterize a typical OPD encounter. This will involve summarizing patient profiles, categories of new patient referrals and clinical investigations ordered. Patients with both 'known' and 'suspected' NAFLD will be identified. These cohorts will be followed over the subsequent 11 months and a bottom-up micro-costing study conducted, with a set of ALD patients acting as a comparator group.
- The sample of patients recorded will involve patients along the full spectrum of NAFLD related liver disease and thus will be representative of clinical care in Europe.

METHODS

Study Cohort: A prospective observational study of patients attending the outpatient hepatology clinic over a consecutive 4-week period at the Freeman hospital, Newcastle was conducted. Suspected NAFLD was defined as referrals for steatosis, increased LFTs, hyperferritinemia or cryptogenic cirrhosis. Suspected or already confirmed NAFLD patients were included in a 12 months follow-up study which recorded the final diagnosis, severity of the disease, diagnostic/monitoring work-up with an ALD cohort as a comparator group.

Cost of illness study: The method selected was the "bottom-up approach" where the estimation of costs involved quantification of health inputs and subsequent derivation of unit costs. The model used a "prevalence based" approach, estimating the financial burden over 1 year and was conducted from the 'Health care system' perspective concerned only with the medical costs of NAFLD.

Statistical Analysis: To investigate associations between patient characteristics at the index appointment and the total number of hepatology clinic appointments, a Poisson regression model was used. To determine the main cost drivers in NAFLD patient care, a multivariable regression model was generated to establish the variables contributing to direct costs.

RESULTS

Summary of Patients presenting to Hepatology Outpatients

664 patients attended general hepatology outpatient appointments in the Freeman Hospital. A detailed breakdown of the spectrum of liver disease referrals is shown in **table 1.** 145 patients were eligible for follow up from the known (n=97) and suspect (n=62) NAFLD patient cohorts. The investigations requested at the initial consultation are summarized in **table 2.**

Table 1: Reason for Consultation (n=664)

Mean age	58 +/- 15.6 years		
Alcoholic Liver Disease	91	14%	
Chronic Viral Hepatitis	63	9%	
Suspected NAFLD	62	9%	
Altered Liver Function Tests	28	4%	
Cryptogenic Cirrhosis	9	1%	Combined NAFLD 24%
Hyperferritinaemia	5	1%	
Steatosis on Imaging	20	3%	
Known NAFLD	97	15%	
Suspected Malignancy	23	3%	
Other	328	49%	
Autoimmune Hepatitis	61	9%	
Haemachromatosis	32	5%	
Liver Transplant follow-up	81	12%	
Primary Biliary Cirrhosis	73	11%	
Miscellaneous Hepatic Pathologies	81	12%	

Table 1: Liver Disease Referrals

Table 2: Services

Total cohort (n=159)	Known NAFLD (n=97)	Suspected NAFLD (n=62)
Mean age	62.8+/-11.9 years	58.5 +/- 17.6 years
Blood tests	91 (93.8%)	54 (87.1%)
Imaging	45 (46.4%)	17 (27.4%)
Ultrasound	39 (87%)	16 (94%)
CT Scan	5 (11%)	
MRI Scan	1 (2%)	1 (6%)
Fibroscan	12 (12.4%)	23 (37.1%)
Liver Biopsy	4 (4.1%)	1 (1.6%)
New Patient	15 (15.5%)	38 (61.3%)
Review Patient	82 (84.5%)	24 (38.7%)
Eligible for follow-up	89 (92%)	49 (79%)
Time to first OPD follow-up	215 +/- 103 days	204 +/- 115 days
Number of OPD follow-ups	2.3	2.4

Table 2: Investigations Requested

Patient Profiles; Suspect and Known NAFLD Cohort

Diagnosis and Stage of Liver Disease

Suspect NAFLD Cohort (n=49)	
Confirmed NAFLD	40 (82%)
NASH Cirrhosis	6 (12.2%)
NAFLD	22 (44.9%)
NAFLD and Alcohol	12 (24.5%)
Other	9 (12%)
De novo Liver Biopsy	6 (12.2%)
Diagnosis (n=6)	
NASH Cirrhosis	1 (17%)
NAFLD	3 (50%)
NAFLD and Alcohol	1 (17%)
Other (Autoimmune Hepatitis)	1 (17%)
Liver Disease Stage	
F0	3 (6.1%)
F1	0
F2	1 (2%)
F3	3 (6.1%)
F4	11 (22.4%)
Undetermined	31 (63.4%)
Undetermined Category	
Fibroscan	17 (55%)
Mean reading	7.46KPa +/- 4.0

Table 3: Suspect NAFLD Cohort

Known NAFLD Cohort (n=89)	
Confirmed NAFLD	89 (100%)
NASH Cirrhosis	44 (49%)
NAFLD	37 (42%)
NAFLD and Alcohol	8 (9%)
De novo Liver Biopsy	3 (3.4%)
Liver Disease Stage	
F0	1(1.1%)
F1	1(1.1%)
F2	5 (6%)
F3	6 (7%)
F4	44 (49.4%)
Undetermined	32 (36%)
Undetermined Category (n=32) Fibroscan	15 (47%)
Mean reading	8.05KPa +/- 4.6

Table 4: Known NAFLD Cohort

Trends observed in OPD appointments

Advanced disease was associated with a greater number of clinic appointments. The Poisson regression (IRR 0.617, p=0.019) indicated having a liver biopsy was predictive of a lesser number of appointments over a 12 month period.

Alcoholic liver disease - comparison cohort

Table 5	NAFLD (n=138)	ALD Cohort (n=79)	P value
Ultrasound	68 (49.3%)	62 (78.5%)	<0.0001
CT scan	14 (10.1%)	21 (26.6%)	<0.0001
MRI	10 (7.2%)	11 (13.9%)	0.054
Liver Function tests	136 (98.6%)	79 (100%)	0.283
Liver Screen	38 (27.5%)	10 (12.7%)	<0.0001
Lipids	98 (71%)	5 (6.3%)	<0.0001
Glucose	71 (51.4%)	5 (6.3%)	<0.0001
Fibroscan	50 (36.2%)	14 (17.7%)	0.005
Liver Biopsy	9 (6.5%)	0	0.030
Hospitalisation	33 (23.9%)	23 (29%)	0.418

Table 5 Service Utilization NAFLD versus ALD Cohort

Table 6	ALD (n=79)	NAFLD (n=138)	P-Values
Confirmed	79 (100%)	129 (93%)	
Cirrhosis	68 (86%)	55 (42%)	<0.0001
ALD/NAFLD	11 (14%)	54 (42%)	<0.0001
ALD + NAFLD		20 (16%)	
De novo Liver Biopsy	0	9	0.003
Liver Disease Stage			<0.0001
F0	0	4 (3%)	
F1	0	1 (1%)	
F2	1 (1%)	6 (4%)	
F3	2 (3%)	9(7%)	
F4	68 (86%)	55 (40%)	
Undetermined	8 (10%)	63 (46%)	

Table 6 Disease Stage NAFLD versus ALD Cohort

Micro-costing Study

Projected costs are summarised in **table 7.**

Table 7	NAFLD	ALD
Total Annual cost	£935,993	£1,309,214
Annual cost per patient	£565	£1,381
	NAFLD Cirrhotic	ALD Cirrhotic
Total Annual cost	£612,409	£1,261,084
Annual cost per patient	£927	£1,592
	Suspect NAFLD	Known NAFLD
Total Annual cost	£691084	£244908
Annual Cost per Patient	£364	£200.69

Table 7: Projected Costs

The direct medical costs associated with both NAFLD and ALD are substantial and increase exponentially with the presence of advanced disease. Higher costs in the ALD groups are likely due to the presence of a larger number of patients with cirrhosis (86% versus 42%).

Multivariate regression model to establish variables contributing to costs

Table 8	Direct costs		
Explanatory variable	Co-efficient	Z	p-value
Age	0.083	0.920	0.359
BMI	0.046	0.534	0.594
Suspected NAFLD	-0.167	-1.827	0.070
Time to first OPD	-0.137	-1.616	0.109
Number of OPD	0.177	2.053	0.042
Patient metabolic profile			
Type II Diabetes	0.107	1.091	0.278
Hypertension	0.032	0.307	0.759
Dyslipidaemia	-0.248	-2.262	0.026
Histological Stage			
Fibrosis Stage	0.322	3.569	0.001

Table 8: Multivariate Regression Model

From the regression model ***(Table 8)*** a statistically significant increase in the mean total direct costs in patients was observed in patients with each unit change in fibrosis (0.322, p=0.001).

A similar trend is observed with the number of OPD appointments (p=0.042).

CONCLUSIONS

In a large, prospective real-life study of tertiary care outpatient hepatology clinics, 25% of patients are currently referred for known or suspected NAFLD which is confirmed in 82% of cases after multiple diagnostic procedures. 28% have advanced fibrosis and 22% cirrhosis. Both NAFLD and ALD have a high prevalence at referral. The direct medical costs associated with both NAFLD and ALD are substantial and increase exponentially with the presence of advanced disease. This study, with a detailed description of health service utilisation provides cost estimate data which will be potentially useful to clinicians and policy makers. The study is conducted in a manner to provide a framework for cost of illness (COI) studies in different health care systems and constitutes the UK arm of the pan-European CONSTANS study.