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Evaluating a clinical care pathway for the screening, diagnosis and treatment of fatty liver disease among primary care patients

Submission date 11/05/2020	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 27/05/2020	**Overall study status** Completed	
Last Edited 22/02/2023	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NAFLD) are important clinical issues that have not received prompt attention from GPs. Although GPs are central to the identification and management of NAFLD, they seldom address the risk of advanced fibrosis in patients with frequent NAFLD comorbid conditions, including obesity, type 2 diabetes mellitus and dyslipidemia. European clinical practice guidelines suggest the use of non-invasive tests to improve the early detection of advanced fibrosis and reduce unnecessary referrals. While strong collaboration between primary and speciality care is necessary for the effective diagnosis and management of NASH, respective pathways are currently limited. There is, as such, a need to establish and evaluate easily implementable, multidisciplinary, patient-centered models to enhance primary care screening and linkage to specialty care for high-risk NAFLD/NASH patients, to inform policies and drive decisions. Such models need to be evidence-informed and theory-driven, incorporating concepts of 'risk perception' and 'health literacy', which can affect health behavior and information communication. The aim of this study is to evaluate the impact of an evidence-informed and locally adapted NASH Model of Care implemented by trained healthcare providers in increasing the numbers of patients screened for and diagnosed with NAFLD/NASH in primary care and linkage to specialty care compared to usual care.

Who can participate?
Adults who have at least one of the following conditions, including metabolic dysfunction, liver dysfunction, NAFLD or cardiovascular disease.

What does the study involve?
A total of 12 primary care practices, four from each country (Greece, Spain), are randomly assigned (like the toss of a coin) to either the NAFLD/NASH Model of Care group or the control group. All GPs in the NASH Model of Care group will receive the NAFLD/NASH training intervention and be supported in implementing it. The NAFLD/NASH Model of Care includes

criteria for screening, diagnosis and referral of patients using a calculator. In the control group, GPs will follow their usual care procedures, tools and tests. In both groups outcomes will be assessed at baseline and at 12 weeks.

What are the possible benefits and risks of participating?
The study cannot promise any benefits to participants but the information from this study will help improve the treatment of people with NAFLD/NASH.

Where is the study run from?
University of Crete (Greece)

When is the study starting and how long is it expected to run for?
May 2020 to March 2023

Who is funding the study?
Gilead Sciences (USA)

Who is the main contact?
Prof. Christos Lionis
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
EU-989-5753

Study information

Scientific Title
Evaluating a clinical care pathway for NASH/NAFLD primary care patients: a multi-centre randomized controlled trial

Study objectives
It is hypothesized that the proposed evidence-informed and locally adapted NASH Model of Care implemented by trained health care providers will increase the numbers of patients screened for and diagnosed with NASH in primary care (PC) and linked to specialty care compared to usual care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/06/2020, Research Ethics Committee University of Crete (Research Ethics Board, University of Crete, University Campus Voutes, 70013, Heraklion, Crete, Greece; +30 (0)2810 545206 (ext. 5206); ehde@uoc.gr), ref: 48/05.03.2020, 144/23.06.2020

Study design
Multi-centre parallel-group randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH)

Interventions
Current interventions as of 15/02/2023:
Twelve PC practices (four practices per country) will participate in the model evaluation. Practices will be randomized to intervention and control groups in a 1:1 ratio.

From all intervention and control practices, the researchers will recruit a representative sample of patients at high risk for NFLD/NASH (obesity, type 2 diabetes or metabolic syndrome, cardiovascular disease, liver dysfunction).

Intervention group: Primary care providers will be asked to implement the NAFLD/NASH model of care which includes a standardized care pathway which involves a protocol defining different HP tasks for the screening, diagnosis, referral and management of patients at high risk for NAFLD/NASH.

All GPs in practices randomized to the intervention group will be exposed to NAFLD/NASH training intervention and supported by implementing the Model of Care.

The NAFLD/NASH Model of Care includes screening algorithms which assess serum biomarkers and calculation of FIB-4 score (next-to-patient). Patient auto-calculation will be promoted. Patients with FIB-4 < 1.30 will be considered as having no sufficient evidence of liver fibrosis, thus not requiring referral to specialists. However, they will be advised to modify their diet and lifestyle and repeat FIB-4 every 2 years. For indeterminate FIB-4 values, patients will be referred to hospital care for transient elastography. Hospital specialists will interpret elastography results jointly with serum markers.

Control group: In the control group, GPs will follow their usual care procedures, tools and tests.

Previous interventions:
Twelve PC practices (four practices per country) will participate in the model evaluation.

Practices will be randomized to intervention and control groups in a 1:1 ratio. The randomization is computer generated by a faculty not involved in the study.

From all intervention and control practices, the researchers will recruit a representative sample of patients at high risk for NASH (age >50 years, obesity, type 2 diabetes or metabolic syndrome).

Intervention group:
Primary care providers will be asked to implement the NASH model of care which includes a standardized care pathway which involves a protocol defining different HP tasks for the screening, diagnosis, referral and management of patients at high risk for NASH.

All GPs in practices randomized to the intervention group will be exposed to NASH training intervention and supported with implementing the Model of Care.

The NASH Model of Care includes Screening algorithms will include serum biomarkers and calculation of FIB-4 (next-to-patient). Patient auto-calculation will be promoted. Patients with FIB-4 < 1.30 will be considered as having no sufficient evidence of liver fibrosis, thus not requiring referral to specialists. However, they will be advised to modify their diet and lifestyle and repeat FIB-4 every 2 years. For indeterminate FIB-4 values, patients will be referred to hospital care for transient elastography. Hospital specialists will interpret elastography results jointly with serum markers.

Control group: In the control group, GPs will follow their usual care procedures, tools and tests.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 15/02/2023:
The following primary outcome measures will be assessed at 12 weeks:
1. Number of patients screened for NAFLD/NASH measured using prospective tracking of eligible patients
2. Number of patients diagnosed with advanced fibrosis measured using diagnostic criteria (case report form)
3. Number of patients referred to the specialist using GP report (case report form)

Previous primary outcome measure:
The following primary outcome measures will be assessed at 12 weeks:
1. Number of patients screened for NASH measured using prospective tracking of eligible

patients
2. Number of patients diagnosed with advanced fibrosis measured using diagnostic criteria (case report form)
3. Number of patients referred to the specialist using GP report (case report form)

Key secondary outcome(s))
Current secondary outcome measure as of 15/02/2023:
The following secondary outcome measures will be assessed:
1. Proportion of patients accepting assessment at PC, measured by GP report (case report form)
2. Proportion of patients accepting referral to specialists, measured by GP report (case report form)
3. Number of patients without advanced fibrosis (F1/F2) who did not need a referral to a specialist, measured using a GP report (case report form)
4. Number of patients with advanced fibrosis (F3/F4) receiving comprehensive care, measured using standardized criteria (case report form)
5. Number of high-risk patients screened for NAFLD/NASH allocated to PC, measured using GP report (case report form)

Previous secondary outcome measure:
The following secondary outcome measures will be assessed at 12 weeks:
1. Proportion of patients accepting assessment at PC, measured by GP report (case report form)
2. Proportion of patients accepting referral to specialists, measured by GP report (case report form)
3. Number of patients without advanced fibrosis (F1/F2) who did not need a referral to a specialist, measured using a GP report (case report form)
4. Number of patients with advanced fibrosis (F3/F4) receiving comprehensive care, measured using standardized criteria (case report form)
5. Number of high-risk patients screened for NASH allocated to PC, measured using GP report (case report form)
6. Direct/indirect costs of model implementation, measured by cost tracking of medical and non-medical expenses

Completion date
15/03/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/02/2023:
1. Metabolic dysfunction: overweight/obesity OR type 2 diabetes OR metabolic syndrome (MetS)
OR
2. Liver dysfunction: raised alanine aminotransferase (ALT) OR raised aspartate aminotransferase (AST)
OR
3. NAFLD: an ultrasonographic fatty liver indicator (US-FLI) >60 AND no other causes of liver disease AND no alcohol excess
OR
4. Cardiovascular disease (CVD): any diagnosis or medication for CVD

Previous inclusion criteria:
1. Registered as a patient in the practice of the participating GP

2. Age >=50 years
3. One or more of the following conditions:
3.1. Obesity (BMI>30)
3.2. Type 2 diabetes (T2DM)
3.3. Metabolic syndrome (MetS)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
220

Key exclusion criteria
1. Not registered in the selected GPs practice
2. Unwillingness or inability to provide signed informed consent and complete study procedures due to cognitive impairment, dementia and/or terminal illness

Date of first enrolment
21/11/2022

Date of final enrolment
22/12/2022

Locations

Countries of recruitment
Greece

Spain

Study participating centre
University of Crete
Clinic of Social and Family Medicine
Andrea Kalokerinou 13, Giofirakia
Heraklion
Greece
71500

Study participating centre
La Mina Primary Health Care Centre - IDIAP Jordi Gol
Gran Via Corts Catalanes
Barcelona
Spain
8708007

Sponsor information

Organisation
University of Crete

ROR
https://ror.org/00dr28g20

Funder(s)

Funder type
Industry

Funder Name
Gilead Sciences

Alternative Name(s)
Gilead, Gilead Sciences, Inc., Oligogen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the chief investigator Prof. Christos Lionis (Lionis@med.uoc.gr) on reasonable request. Data will be made available after the trial outcomes paper is published in a peer-reviewed journal; applicants must provide an as a minimum a publicly available pre-specified protocol describing the purpose,

methods and analysis of the secondary research; de-identified data will be available indefinitely; consent from participants for secondary use of data will be obtained; patient identifiable data will never be shared with third parties.

IPD sharing plan summary

Available on request