Emerging Trend in Epidemiology of NAFLD and Long- term Outcome

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Introduction

- Nonalcoholic fatty liver disease(NAFLD) has emerged as the most prevalent liver disease worldwide, mainly because of the massive parallel global increase in obesity

- Extensive public-health and political efforts will be needed in the near future to counteract this disturbing development

- Traditionally, obesity and its related diseases have been considered a problem in Western countries

- In the past two decades, urbanisation in many Asian countries has led to a sedentary lifestyle and overnutrition, setting the stage for the epidemic of obesity

- The term NASH was coined in 1989

- After another decade, it was recognized that NASH is a part of the clinicopathologic spectrum of NAFLD

Definition

- Accumulation of fat within the liver (hepatic steatosis) with no other known cause of hepatic fat accumulation

- No evidence of excessive alcohol use

  Men: 3 drinks / day Women: 2 drinks / day

- Presence of fat defined by imaging or biopsy of liver

- NAFLD can be found in non-obese individuals

- **lack of secondary causes** of hepatic fat accumulation such as significant alcohol consumption, longterm use of a steatogenic medication, or monogenic hereditary disorders

- commonly associated with metabolic comorbidities such as obesity, diabetes mellitus, and dyslipidemia

- **NAFLD** ---histologically into nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis

- **NAFL** ---the presence of 5% HS **without** evidence of hepatocellular injury in the form of hepatocyte ballooning

- **NASH** --- presence of 5% HS and inflammation **with** hepatocyte injury (e.g., ballooning),with or without any fibrosis
- For defining “advanced” fibrosis--referring specifically to stages 3 or 4, that is, bridging fibrosis or cirrhosis.

NAFLD in the West and Asia

	Western countries	Asian countries
Prevalence of NAFLD	25%	25%
Proportion of NAFLD patients with NASH	20–30%	10–20%
Proportion of NAFLD patients with F3-4 fibrosis	10%	3–5%
Prevalence of NAFLD in subjects with BMI<25	10%	7–19%

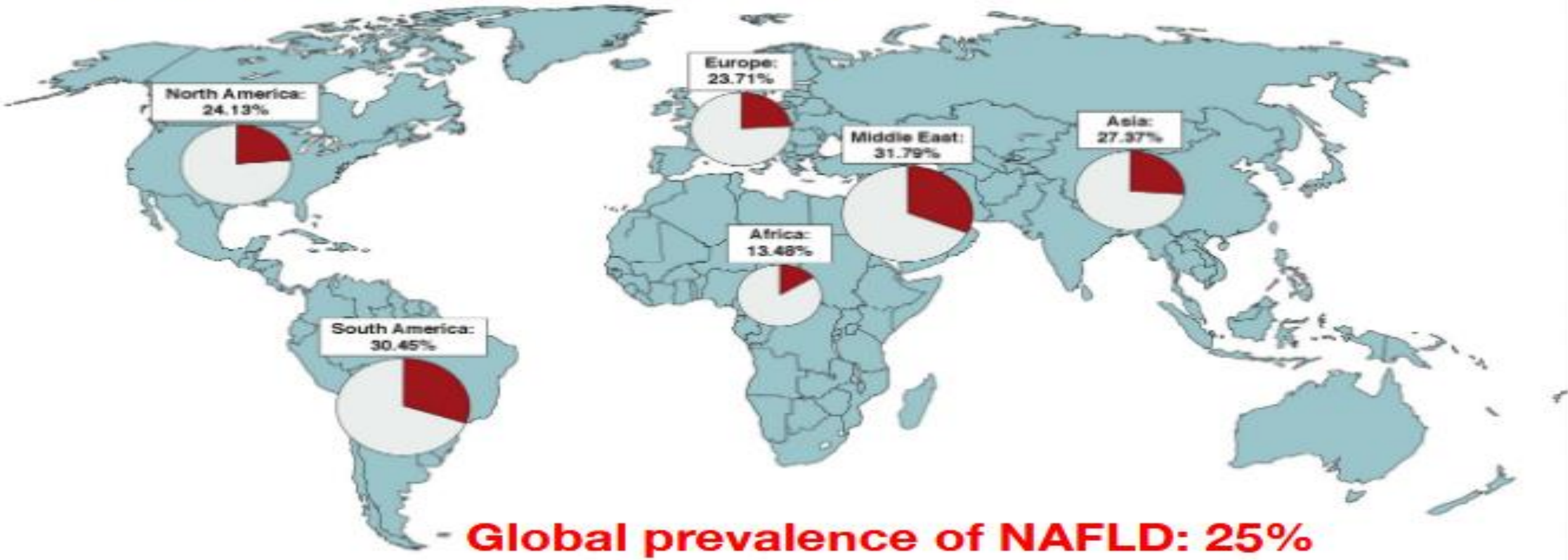
- Currently, the population prevalence of NAFLD in Asia is around 25%, like many Western countries. While hepatocellular carcinoma and end-stage liver disease secondary to NAFLD remain uncommon, a rising trend has emerged

- Around 8–19% of Asians with body mass indexes less than 25 kg/m2 are also found to have NAFLD, a condition often described as ‘‘lean’’ or ‘‘non-obese’’ NAFLD

- Although this condition is generally less severe than that in more obese patients, steatohepatitis and fibrotic disease are well recognized

Global prevalence of NAFLD

Global prevalence of overweight and obesity: 39%



- **Global prevalence of NAFLD: 25%**

Younossi et al., Hepatology 2016

- **Central adiposity, insulin resistance and weight gain** are major risk factors, and

  genetic predisposition, such as the PNPLA3 polymorphism appears to be more important in the development of NAFLD in the non-obese population

- Lifestyle modification remains the cornerstone of management for obesity and NAFLD, but few patients can achieve adequate weight reduction and even fewer can maintain the weight in the long run

- Recent advances in chronic hepatitis B and C therapies, combined with increasing prevalence of the obesity epidemic and of other metabolic disorders, such as type 2 diabetes mellitus (T2DM) and hyperlipidemia, have led to → dramatic rise in NAFLD

- Today, NAFLD is a major global health problem and has emerged as the 2nd most common indication for liver transplantation (LT) in the USA, and is projected to become number 1 soon

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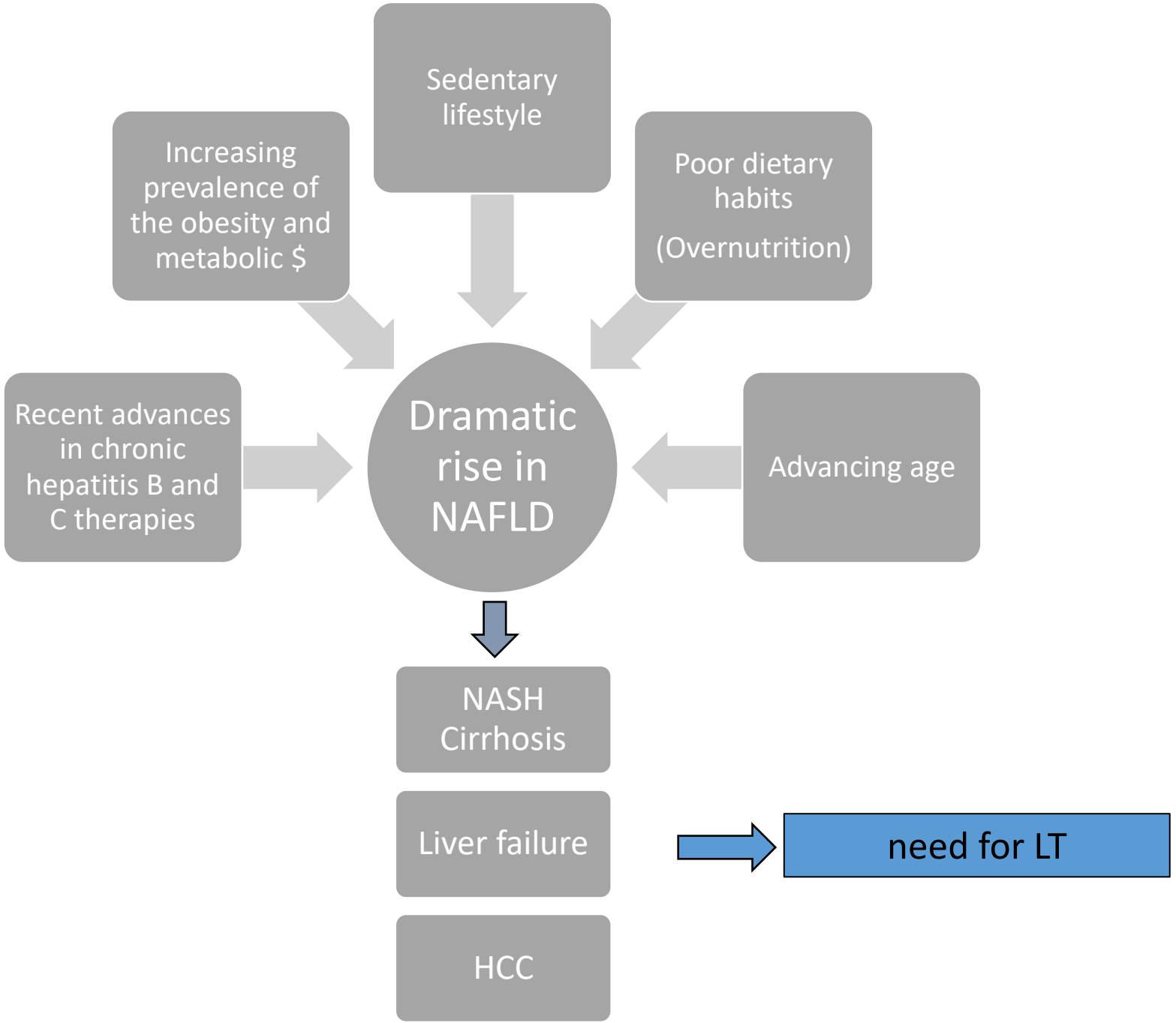

Sedentary lifestyle
Increasing prevalence of the obesity and metabolic $
Poor dietary habits
(Overnutrition)
Recent advances in chronic hepatitis B and C therapies
Dramatic rise in NAFLD
Advancing age
NASH Cirrhosis
Liver failure
HCC
need for LT

- As noted previously, due to the growing obesity epidemic now affecting more than 1.9 billion adults globally

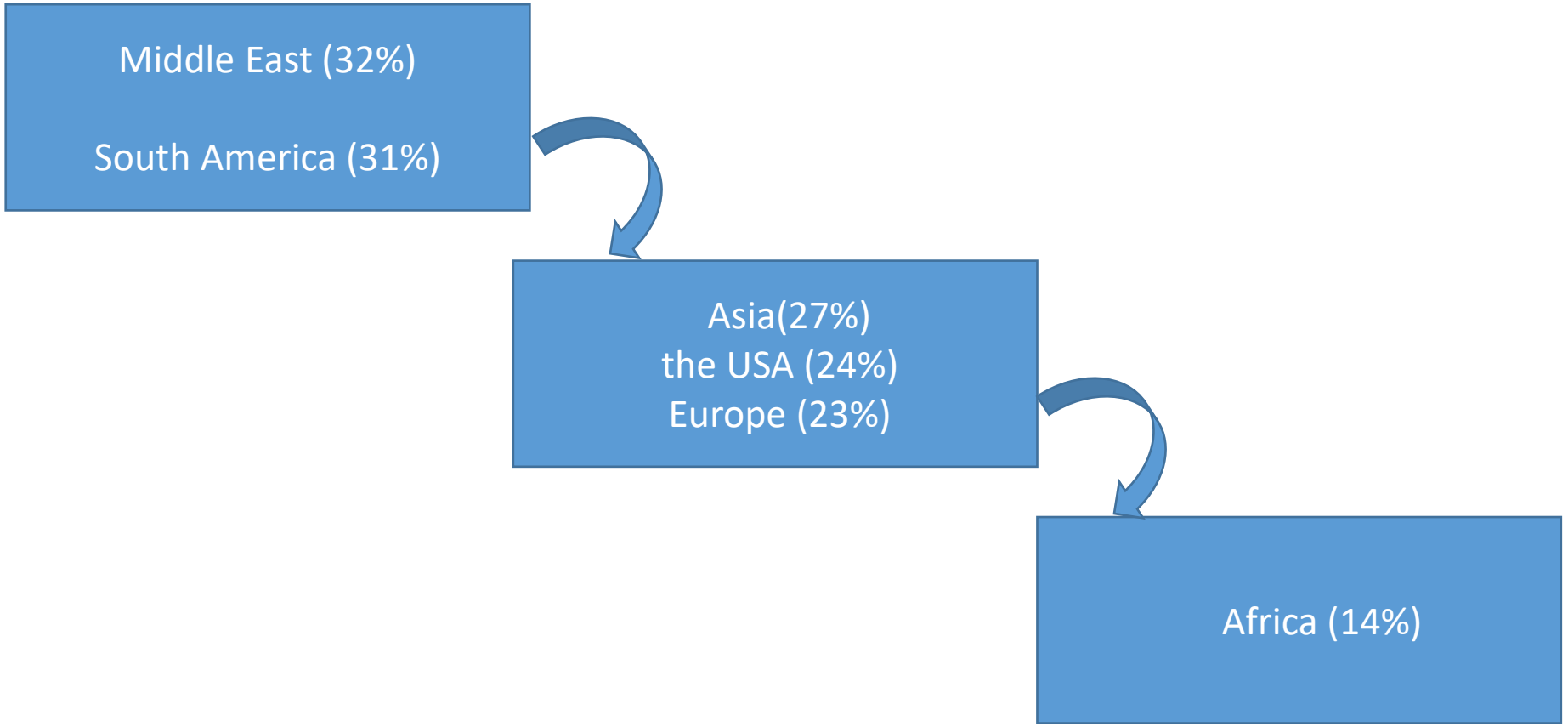
- According to recent estimates, NAFLD affects as many as one billion individuals throughout the world

- Similarly, in the USA, NAFLD affects nearly 80-100 million individuals, making it the number 1 etiology of CLD

- Nearly 25% of patients with NAFL progress to NASH; however, the true prevalence of biopsy-proven NASH is difficult to determine, as the majority of NAFL patients do not undergo biopsy

- Although the prevalence of NAFLD is increasing throughout the world, there appears to be a significant geographical variation

- The global prevalence of NAFLD is currently estimated to be 25%



Younossi et al; Hepatology 2016

- Due to the increased prevalence of NAFL, the prevalence of NASH is expected to increase as well

- the proportion of NAFL cases that progress to NASH will increase from **20% to 27% by 2030**

- Similarly, incident of decompensated cirrhosis is predicted to increase by **168%**,from **39,230 cases annually in 2015 to 105,430 cases in 2030**

Estes et al; Hepatology 2018;67:123–133. doi: 10.1002/hep.29466.

- The prevalence of NAFLD continues to increase, and it is expected that NASH-related end-stage liver disease (ESLD) will become the leading indication for LT over the next several decades

- The corresponding burden of NASH cirrhosis on liver transplantation (LT) is expected to increase by **59%**

- Numerous recent studies have reported that NASH-related cirrhosis is the most rapidly growing indication for LT in the USA

Estes et al; Hepatology 2018;67:123–133. doi: 10.1002/hep.29466.

- In 2017, Cholankeril et al., using data from the United Network for Organ Sharing and Organ Procurement and Transplantation Network (commonly known as UNOS/OPTN) database, reported a **162%** increase in **LT secondary to NASH** from **2003 to 2014**

- while LT due to alcoholic liver disease (**ALD**) and hepatitis C virus **(HCV**) only increased by **54%** and **33%** respectively

- As the burden of NASH-related ESLD on the wait-list continues to rapidly grow, the risk of wait-list removal secondary to death or progression of comorbidities increases

Cholankeril G et al. Liver transplantation for nonalcoholic steatohepatitis in the US:
Patel YA, Berg CL, Moylan CA. Nonalcoholic fatty liver disease:2017

Long term outcome of NAFLD

Good outcome

- NASH resolution can be achieved by targeted weight loss
  - Diet
  - Physical exercise
  - Pharmacological treatment
  - Surgical intervention

- NAFLD without significant fibrosis can regress completely

Long term outcome of NAFLD

Bad outcome

- Liver related
  - NASH is the risk of
    - liver failure
    - liver fibrosis/cirrhosis
    - HCC
      - Advanced fibrosis
      - Higher age
      - Family history of HCC
      - Lower serum Albumin
      - Higher GGT
      - Insulin treatment for DM
      - Chronic viral hepatitis infection

Long term outcome of NAFLD

Bad outcome

- Non-liver related
    - CVD risks and complications (Cardiovascular diseases like MI, stroke) influenced by both nature (genetics) and nurture (environment and diet)
    - Obesity related complication like Obstructive sleep apnoea syndrome
    - Increased risk of developing DM and closely related to degree of glucose intolerance
    - Hyperuricaemia, gout, chronic kidney disease, gallstone disease
    - Poly cystic ovarian $
    - Colorectal adenomatous polyp and colorectal cancer

Hepatology international 7(1), 65-71,2013


THANK YOU