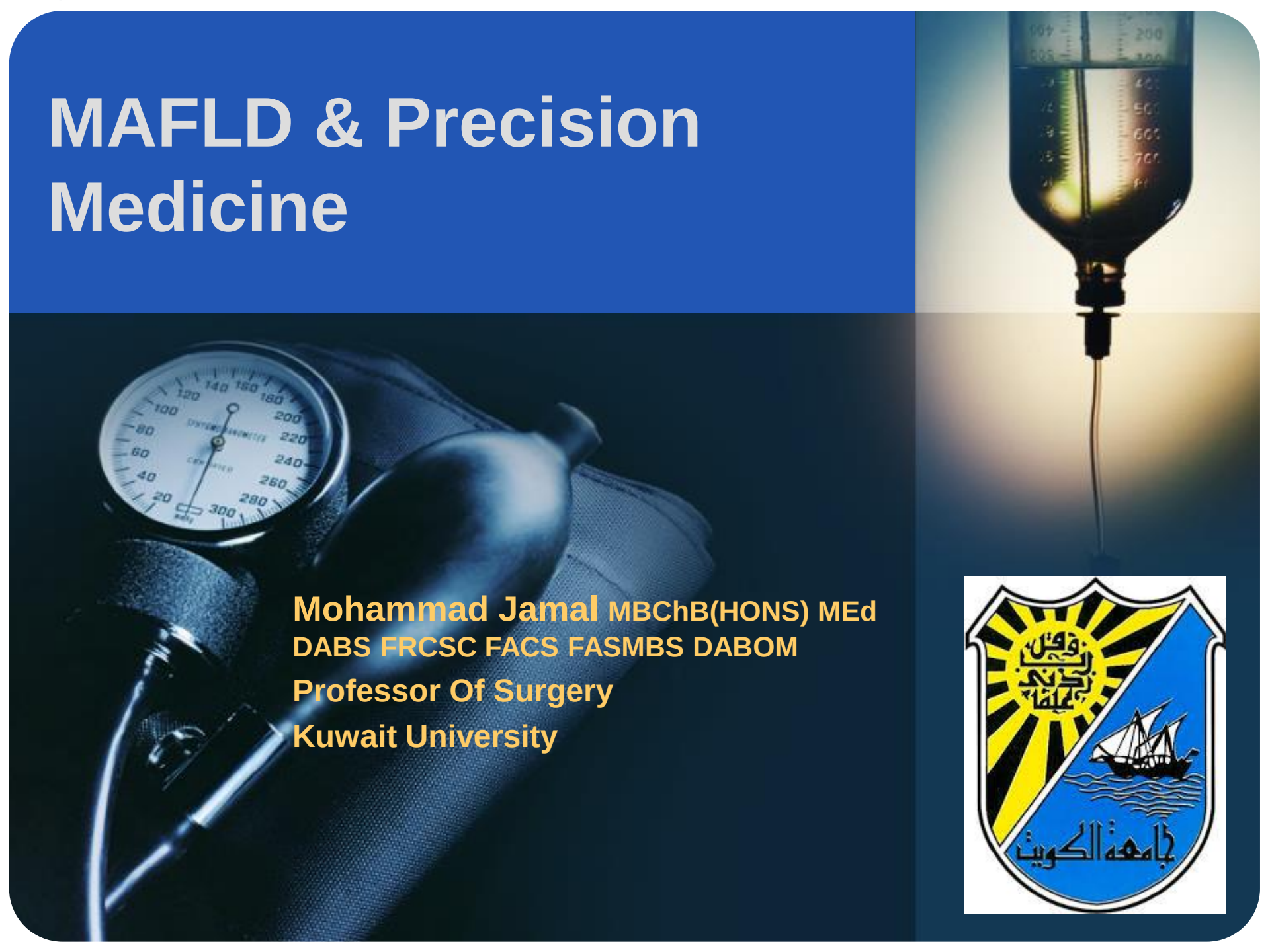
# MAFLD & Precision Medicine



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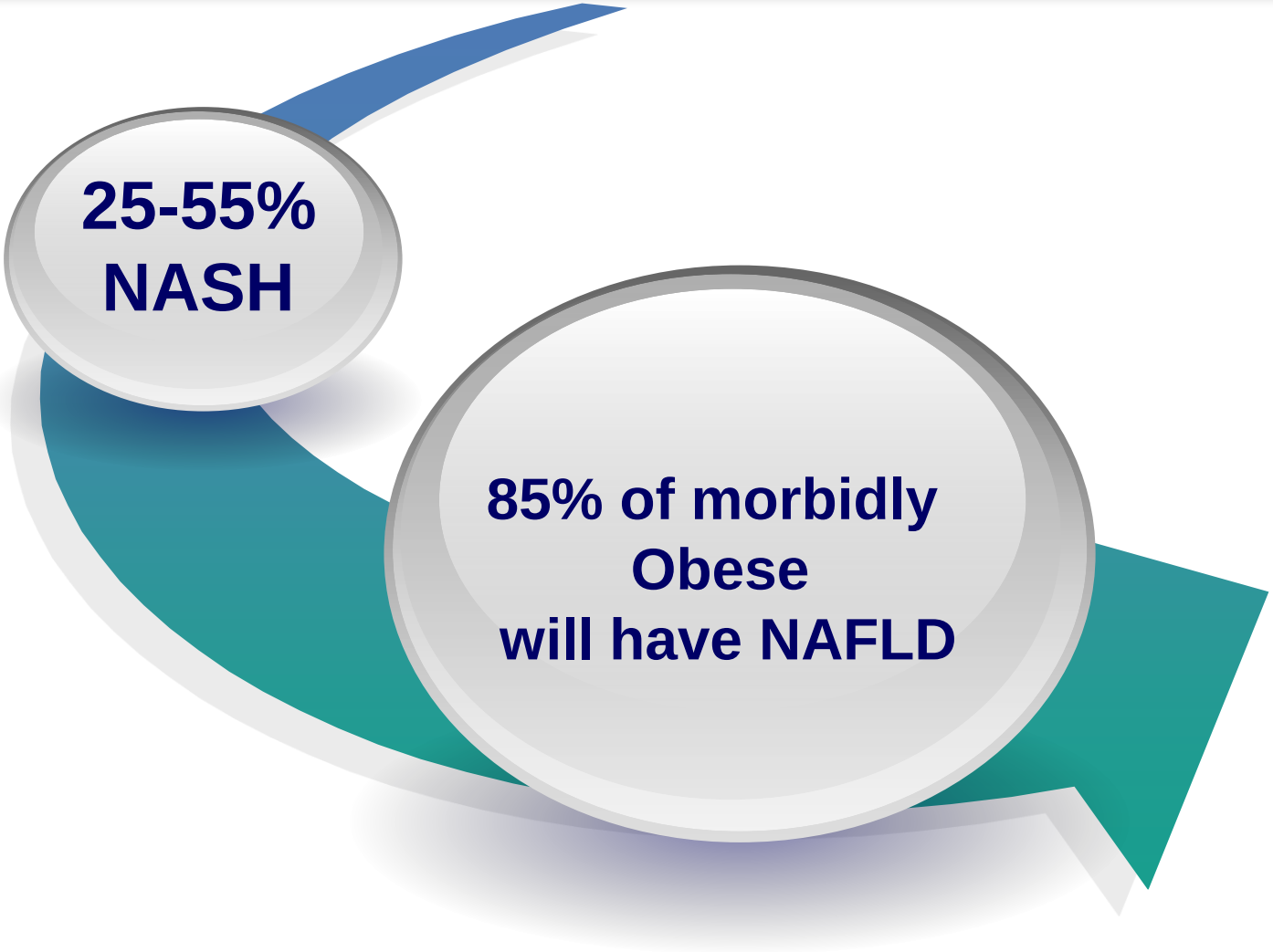
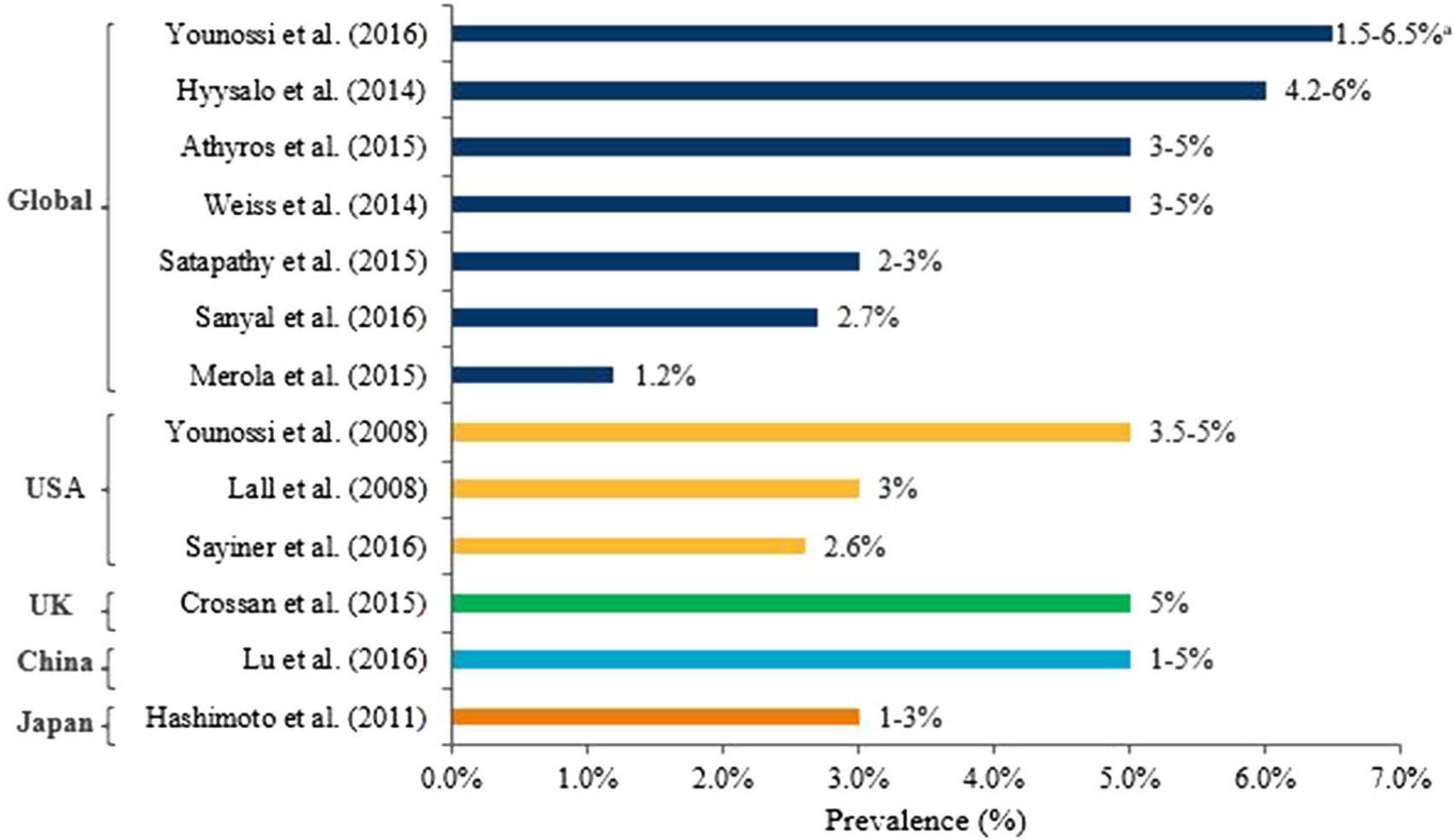
Kuwait University

# MAFLD and MASH In Obesity

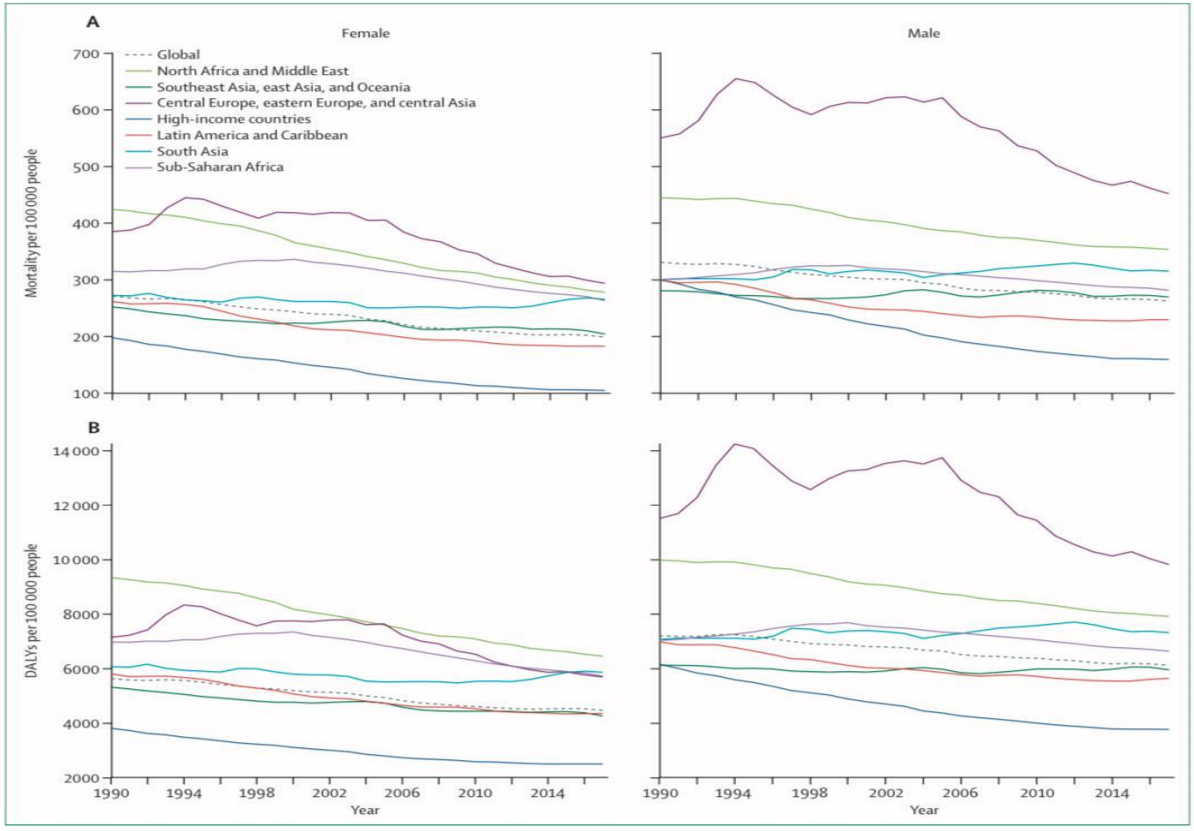



Clark JM. The epidemiology of nonalcoholic fatty liver disease in adults. *J Clin Gastroenterol*. 2006;40 Suppl 1:S5–10.

# Mash In General Population



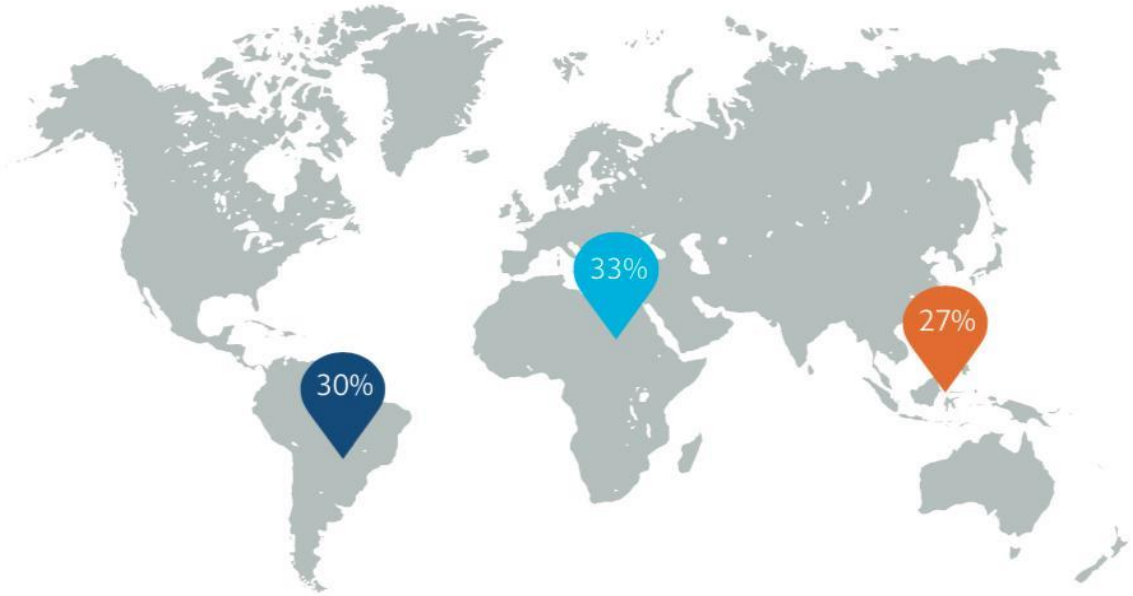
# Metabolic Risk Factors in The ME




Azizi F, Hadaegh F, Hosseinpanah F, et al. Metabolic health in the Middle East and north Africa. Lancet Diabetes Endocrinol 2019; 7: 866–79

# MAFLD Prevalence

**Figure 2: NAFLD prevalence in Asia-Pacific, Latin America and the Middle East (2019)**




Source: Younossi Z, Tacke F, Arrese M, et al. Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Hepatology. 2019;69(6):2672-82.

**The Economist Intellegence Unit Report, NAFLD:Sounding the alarm on a global public health challenge**

# Fatty Liver IN Kuwait

- According to the Global Burden of Disease Study, mortality related to chronic liver disease ranked 11th in all-cause DALYs, resulting in 524 years of life lost per 100000 population.

- Men in Kuwait and Qatar had the highest prevalence of cirrhosis, more than twice the global estimates.

Institute for Health Metrics and Evaluation. Compare GBD. 2015. http://vizhub.healthdata.org/gbd-compare

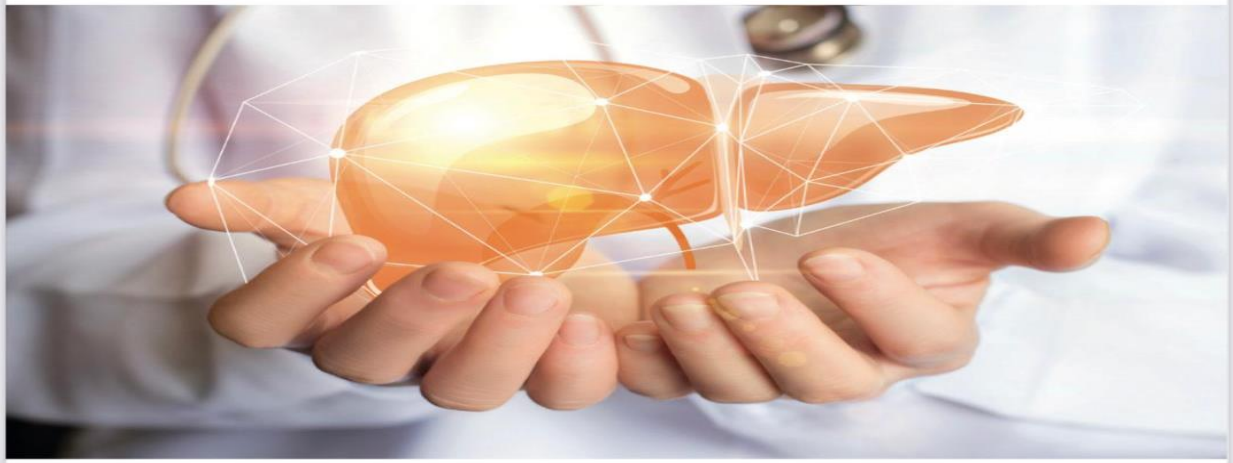
# January 17th 2018

**Characteristics of transplanted patients (n=11)**
*MELD-Na: Model of End Stage Liver Disease-Sodium

| | |
|---|---|
| Sex | Male- 7<br>Female- 4 |
| Age | Youngest- 33years<br>Oldest- 70 years<br>Median- 56 years |
| Blood group | Type 0- 6<br>Type A- 3<br>Type B- 2 |
| Diagnosis | NASH- 9 (82%)<br>Alcohol- 1 (9%)<br>Hepatitis C- 1 (9%) |
| MELD-Na | Lowest- 16<br>Highest- 31<br>Median- 21 |
| Donor age | Youngest- 24 years<br>Oldest- 54 years<br>Median- 47 years |

The Economist INTELLIGENCE UNIT

# NAFLD: Sounding the alarm on a global public health challenge



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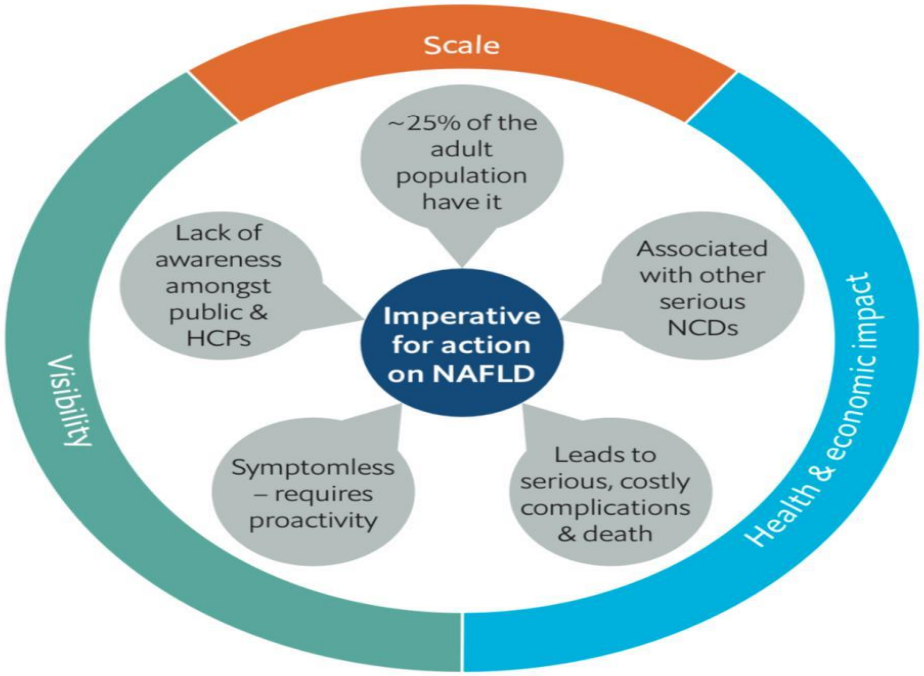
**The Economist Intellegence Unit Report, NAFLD:Sounding the alarm on a global public health challenge**

**Figure 1: Imperative for action on NAFLD**

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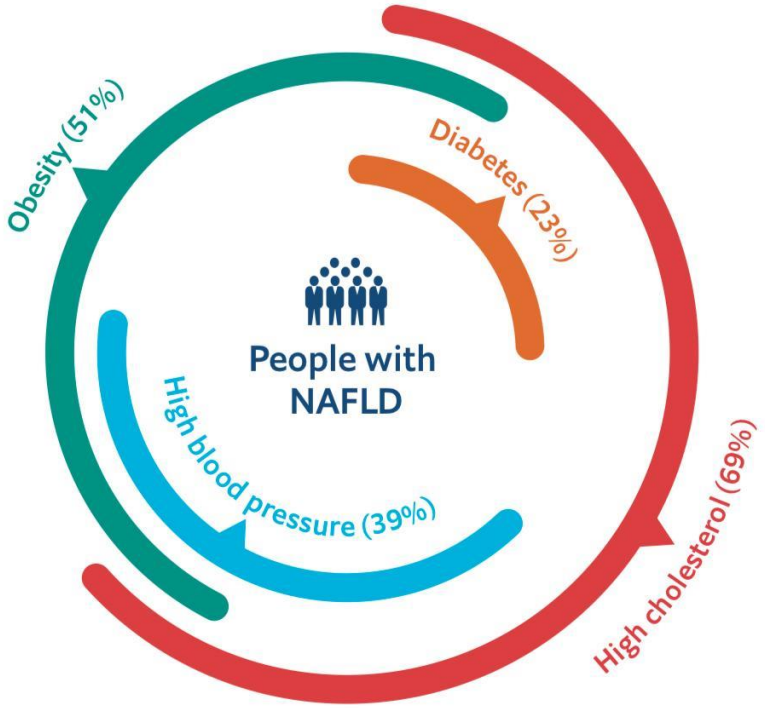
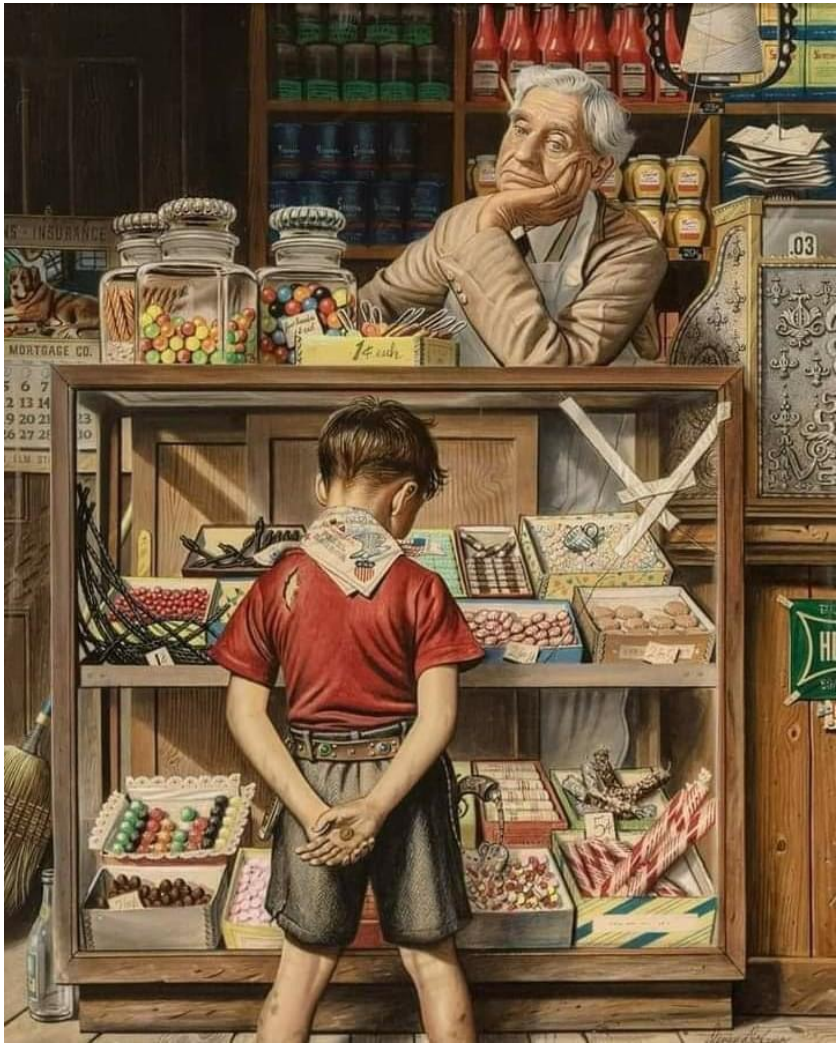
# MAFLD Comorbidities

**Figure 3: NAFLD co-morbidities**

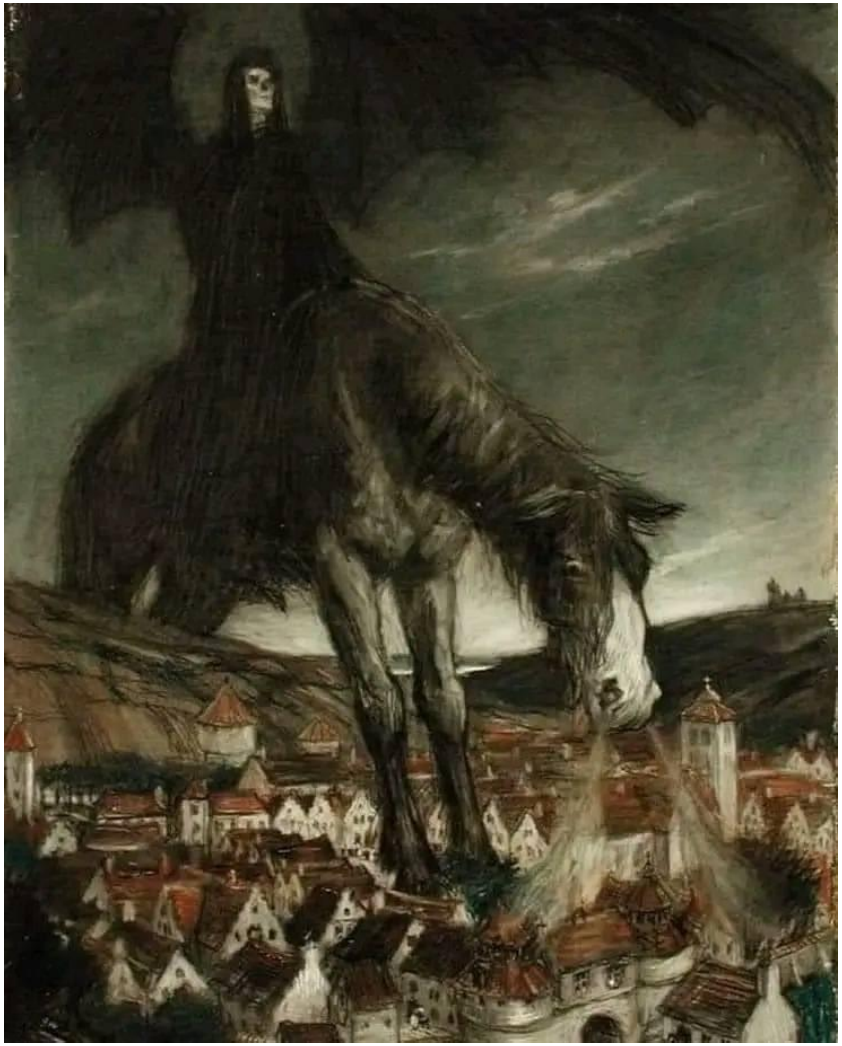



Source: Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84.

# Precision Medicine in MAFLD:Prevention



# Precision Medicine in MAFLD: The Environment



# Toxicant Associated Steatohepattis

- It occurs as a result of exposure to endocrine and metabolism disrupting chemicals (EDCs)

- One of the most recently discovered EDCs is Polychlorinated Biphenyls (PCBs)

**Table**. Demographic Characteristics by Liver Disease Status

| Characteristic | Liver Disease Status | | | p-value | Total (n ¼ 738) |
|---|---|---|---|---|---|
| | None (n ¼ 294) | TASH (n ¼ 359) | Other (n ¼ 85) | | |
| Age (years) | 54.1 ± 15.7 | 56.0 6 16.3a | 51.5 ± 15.1 | 0.04 | 54.7 15.9 |
| BMI (kg/m2) | 31.5 ± 7.8 | 30.9 6 7.7 | 32.1 ± 7.7 | 0.34 | 31.25± 7.7 |
| Gender | | | | 0.03 | |
| Male | 72 (24.5) | 123b (34.3) | 26 (30.6) | | 221 (30.0) |
| Female | 222 (75.5) | 236 (65.7) | 59 (69.4) | | 517 (70.1) |
| Race/ethnicity | | | | <.001 | |
| NonHispanic White | 117 (39.8) | 223b (62.1) | 53c (62.4) | | 393 (53.3) |
| African/American | 177 (60.2) | 136 (37.9) | 32 (37.7) | | 345(46.8) |
| **Age (years)** | | | | 0.13 | 63 (8.5) |
| <30 | 24 (8.2) | 31 (8.7) | 8 (9.4) | | 78 (10.6) |
| 30–40 | 41 (14.0) | 25 (7.0) | 12 (14.1) | | 132 (17.9) |
| 40–50 | 45 (15.3) | 69 (19.2) | 18 (21.2) | | 161 (21.8) |
| 50–60 | 66 (22.5) | 75 (20.9) | 20 (23.5) | | 153 (20.7) |
| 60–70 | 63 (21.4) | 75 (20.9) | 15 (17.7) | | 151 (20.5) |
| >70 | 55 (18.7) | 84 (23.4) | 12 (14.1) | | |
| **BMI (kg/m2)** | | | | 0.4 | |
| <18.5 | 3 (1.0) | 2 (0.6) | 0 (0.0) | | 5 (0.7) |
| 18.5–24.9 | 61 (20.8) | 67 (18.7) | 14 (16.5) | | 142 (19.3) |
| 25–29.9 | 62 (21.1) | 109 (30.4) | 20 (23.5) | | 191 (26.0) |
| 30–34.9 | 77 (26.2) | 90 (25.1) | 22 (25.9) | | 189 (25.7) |
| 35–39.9 | 48 (16.3) | 48 (13.4) | 15 (17.7) | | 111 (15.1) |
| >40 | 42 (14.3) | 42 (11.7) | 14 (16.5) | | 98 (13.3) |
| Missing | 1 (0.3) | 1 (0.3) | 0 (0.0) | | 2 (0.3) |
| **Number of drinks in last 30 days** | | | | 0.7 | |
| No drinks | 205 (69.7) | 254 (70.8) | 62 (72.9) | | 521 (70.6) |
| Within defined limitsd | 63 (21.4) | 73 (20.3) | 14 (16.5) | | 150 (20.3) |
| More than limit | 16 (5.4) | 23 (6.4) | 8 (9.4) | | 47 (6.4) |
| Missing | 10 (3.4) | 9 (2.5) | 1 (1.2) | | 20 (2.7) |
| **Current Smoker** | | | | 0.69 | |
| No | 208 (70.8) | 243 (67.7) | 58 (68.2) | | 509 (69.0) |
| Yes | 86 (29.3) | 116 (32.3) | 27 (31.8) | | 229 (31.0) |
| **West Anniston resident** | | | | **0.25** | |
| **No** | (14.6) 43 | (17.3) 62 | (14.1) 12 | | (15.9) 117 |
| **Yes** | (85.4) 251 | (82.7) 297 | (85.9) 73 | | (84.2) 621 |
| **CK18 M65 (U/l)** | 42.6 ± 233.6 | 430.6 ± 122.1a, b | 792.5 ± 584.9c | 001.> | 276.0 ± 393.8 |
| **CK18 M30 (U/l)** | 22.0± 97.9 | 124.0 ± 28.2a, b | 407.6 ± 324.6c | 001.> | 147.1 ± 146.3 |

Heather B. Clair, Christina M. Pinkston, Shesh N. Rai, Marian Pavuk, Nina D. Dutton, Guy N. Brock , Russell Russell A. Prough, Keith Cameron Falkner,kj,kk Craig J. McClain,§,kj,kk, and Matthew C. Cave. 2018. “Liver disease in a residential cohort with elevated polychlorinated biphenyl exposures”. TOXICOLOGICAL SCIENCES, 164(1), 2018, 39–49

# Precision Medicine in MAFLD: Diabetes Subtypes

- A study looking at comprehensive phenotyping of 1105 patients newly diagnosed with Type II DM

- Patients classified into 5 clusters:
  - Mild age related diabetes MARD 35%
  - Mild obesity related diabetes MOD 29%
  - Severe autoimmune diabetes SIRD 22%
  - Severe insulin deficient diabetes SIDD 3%
  - Severe insulin resistant diabetes SIRD 11%

Zaharia et al The Lancet Diabetes and endocrinology 2019

# Precision Medicine in MAFLD: Diabetes Subtypes

- These clusters use common variables such as autoimmunity, age at diagnosis, BMI, homeostasis model estimate of beta cell function (HOMA beta) and insulin resistance (HOMA IR)
- The clusters correlate better with diabetes complications than classic diabetes classification
- Intrahepatic fat content was more in the newly diagnosed SIRD and the 5 years followup showed more fibrosis in that group

# Diabetes subtypes in Qatar

- **More MOD in the QATARI cohort and at a younger age**

# Conclusions

- MAFLD is pandemic to the region
- Precision medicine questions can provide more reliable treatment answers


Thank You !