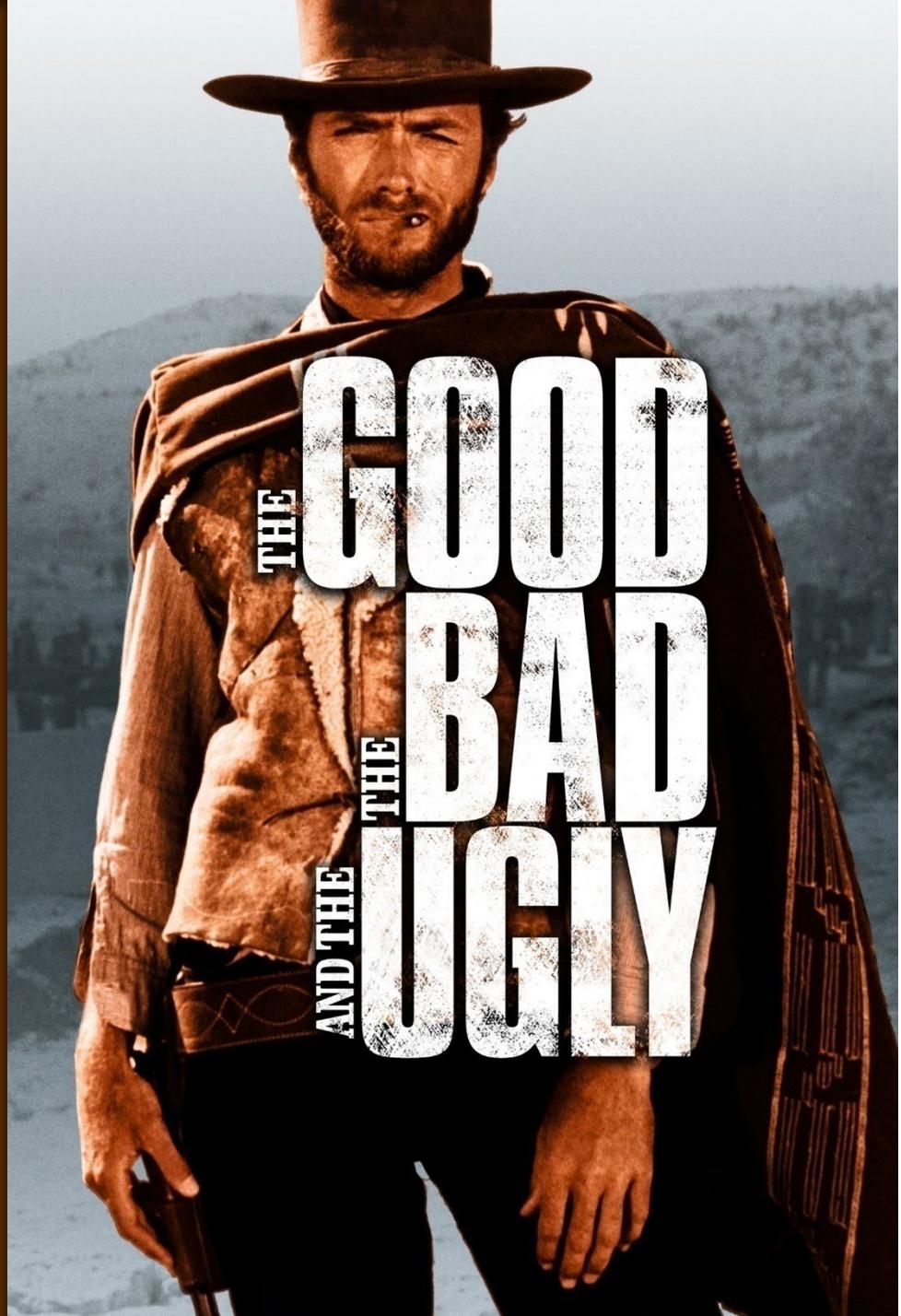


NAFLD
versus
MAFLD



S P SINGH

Chairman, NAFLD Research Centre

KALINGA GASTROENTEROLOGY FOUNDATION

Cuttack, INDIA.



My Disclosures

- Committed to Evidence based Science
- Aversion to Eminence based Whataboutery.
- Chairman, INASL Taskforce on NAFLD [Not MAFLD].
- Chairman, Indian Consortium on NAFLD (ICON-D); [Not MAFLD].
- Authored Multiple NAFLD versus MAFLD rants!

**The
GOOD**

The Good

- There has been a huge spurt in activity in NAFLD related publications.
- Increase in NAFLD related CMEs/Symposia /Educational Programs including Webinars.
- Increase in awareness about NAFLD as an entity.
- Increased awareness and understanding of the pathogenesis of NAFLD.

MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease



Mohammed Eslam¹



Arun J. Sanyal²



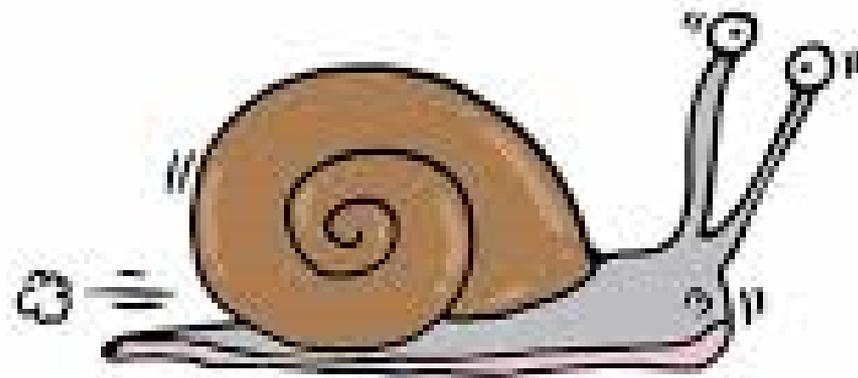
Jacob George¹, on behalf of the International Consensus Panel

Metabolic Associated!



Foot fault Sir!



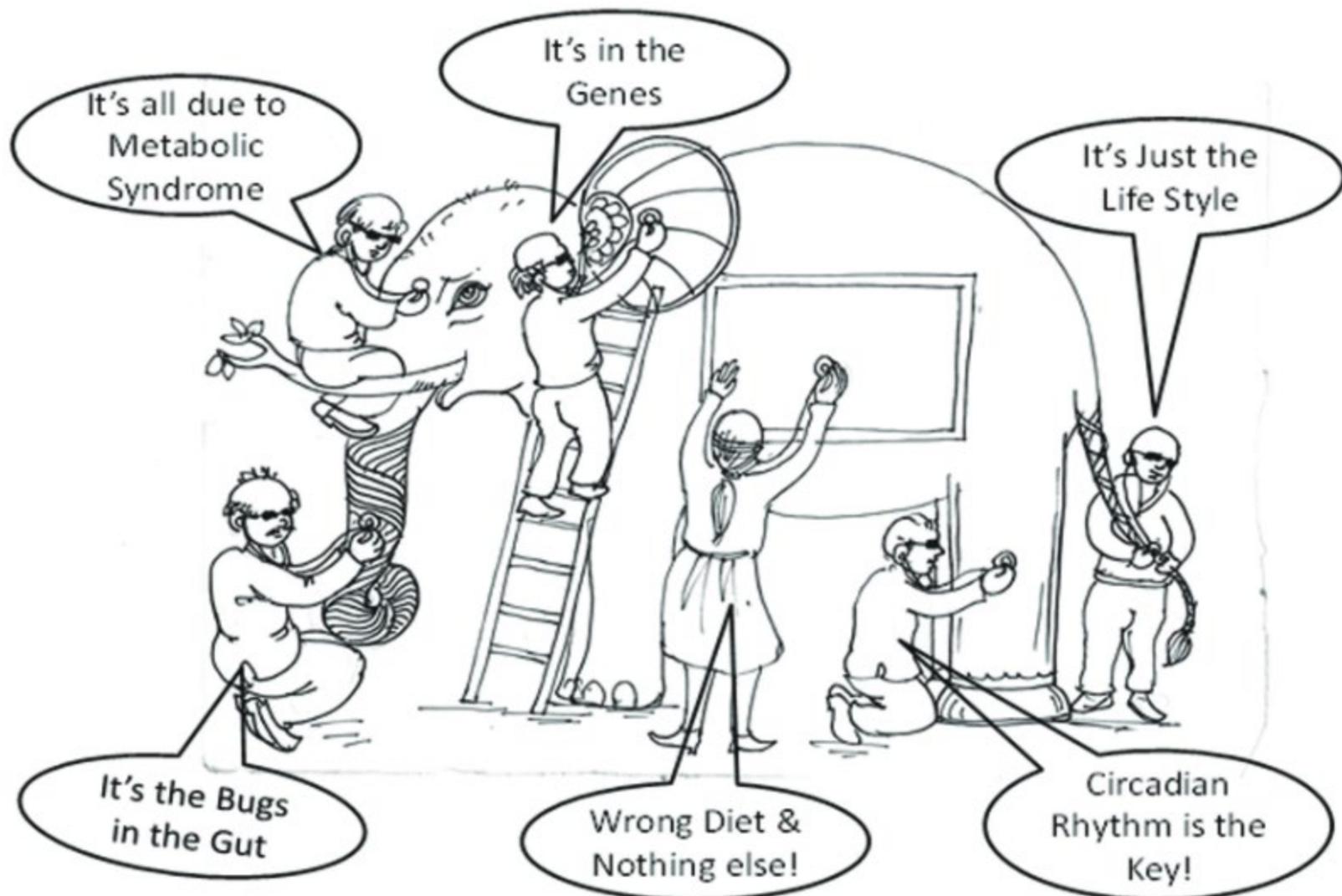


BETTER LATE THAN NEVER

SPECIAL ARTICLE | HEPATOLOGY, VOL. 0, NO. 0, 2021

From NAFLD to MAFLD: Implications of a **Premature Change** in Terminology

Zobair M. Younossi ^{1,2}, Mary E. Rinella ³, Arun J. Sanyal,⁴ Stephen A. Harrison,⁵ Elizabeth M. Brunt,⁶ Zachary Goodman,^{1,2}
David E. Cohen,⁷ and Rohit Loomba⁸

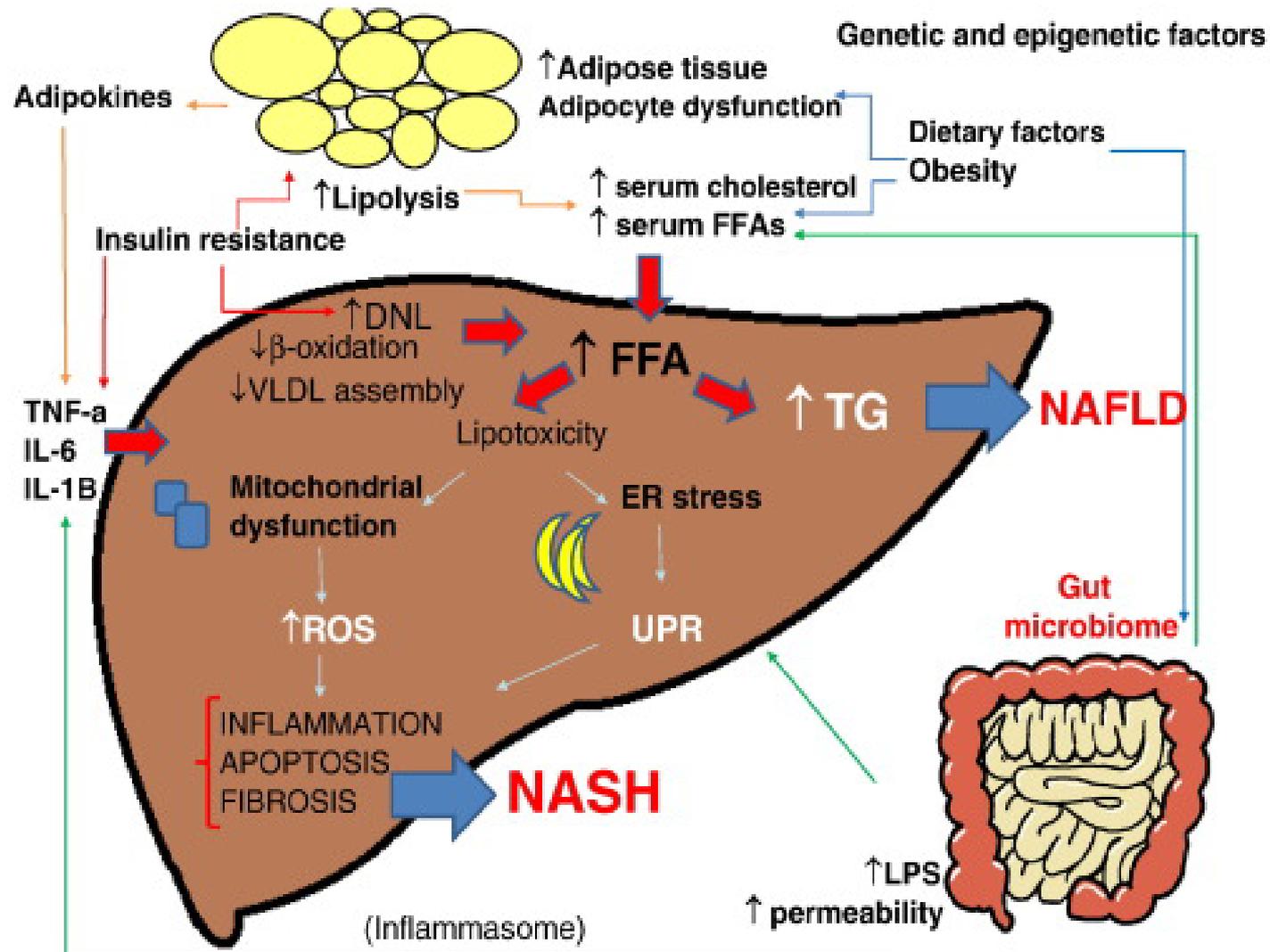


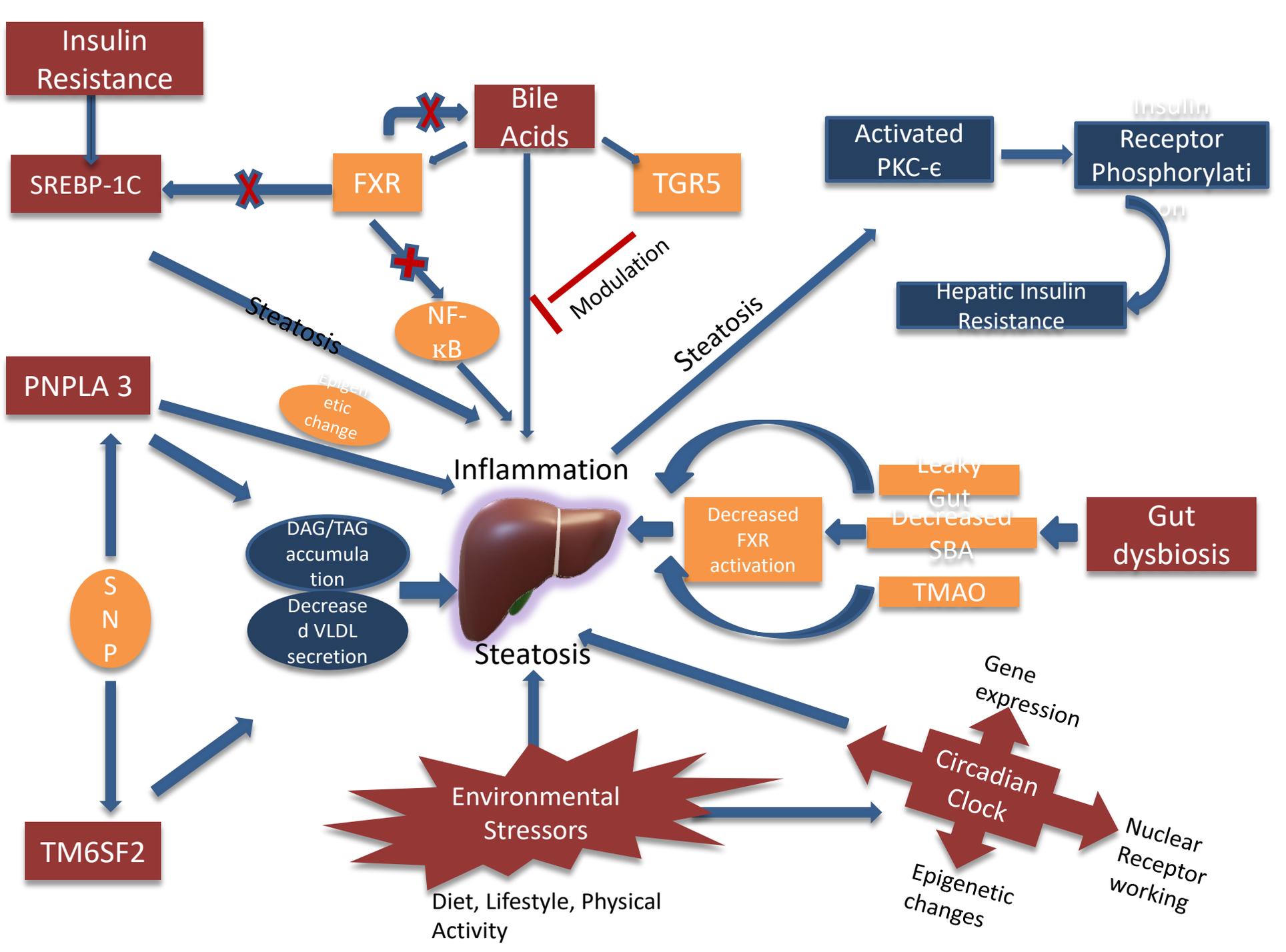
NAFLD: Pathogenesis

*And so these men of Indostan
Disputed loud and long,
Each in his own opinion
Exceeding stiff and strong,
Though each was partly in the right,
And all were in the wrong!*



Multi-hit hypothesis





East versus West

MAFLD is a Western Concept



NAFLD: Not merely the hepatic manifestation of Metabolic Syndrome

Comparative Study > Clin Res Hepatol Gastroenterol. 2015 Sep;39(4):482-8.

doi: 10.1016/j.clinre.2014.08.014. Epub 2014 Dec 17.

Nonalcoholic fatty liver disease (NAFLD) without insulin resistance: Is it different?

Shivaram Prasad Singh ¹, Bijay Misra ², Sanjib Kumar Kar ², Manas Kumar Panigrahi ²,
Debasis Misra ², Pallavi Bhuyan ³, Kaumudee Pattnaik ³, Chudamani Meher ⁴,
Omprakash Agrawal ⁴, Niranjan Rout ⁵, Manorama Swain ⁶

Conclusion: Nearly half of our NAFLD population was without IR; one third of them had significant fibrosis. NAFLD is probably a heterogeneous disease and IR is not the sole factor responsible for NAFLD; further studies are needed to find out other possible etiological factors.

Original Article

Insulin Resistance in Nonalcoholic Fatty Liver Disease: Experience from Bangladesh

Golam Azam¹, Shahinul Alam², SKM Nazmul Hasan³, Sheikh Mohammad Noor-E-Alam⁴, Jahangir Kabir⁵, AKM Khorshed Alam⁶

- **Insulin Resistance [IR] was normal in 132 (60.3 %) and was raised in 87 (39.7%).**
- **Liver biopsy was performed in 110 cases with elevated ALT; of these biopsied NAFLD patients, IR was normal in 63 (57.3%) and was raised in 47 (42.7%).**

NAFLD: Genetics

- In subjects with PNPLA3 polymorphism, steatosis occurs independent of IR and serum lipid concentration.
- SNP (rs738409) in PNPLA3 was only moderately associated with elevated serum liver enzymes and did not correlate with serum lipids.
- The SNP was not associated with insulin resistance.

Kantartzis et al. Diabetes. 2009

NAFLD: Environmental stressors

- **Soft drink** consumption and smoking have also been associated with development of fatty liver independent of obesity, diabetes and hyperlipidemia.
- **Soft drink** consumption is a strong predictor of fatty liver (odds ratio: 2.0; $p < 0.04$) independent of metabolic syndrome.
- **Smoking** pack-years associated with increased risk for NAFLD plus intermediate or high fibrosis score.

NAFLD: Bile acids

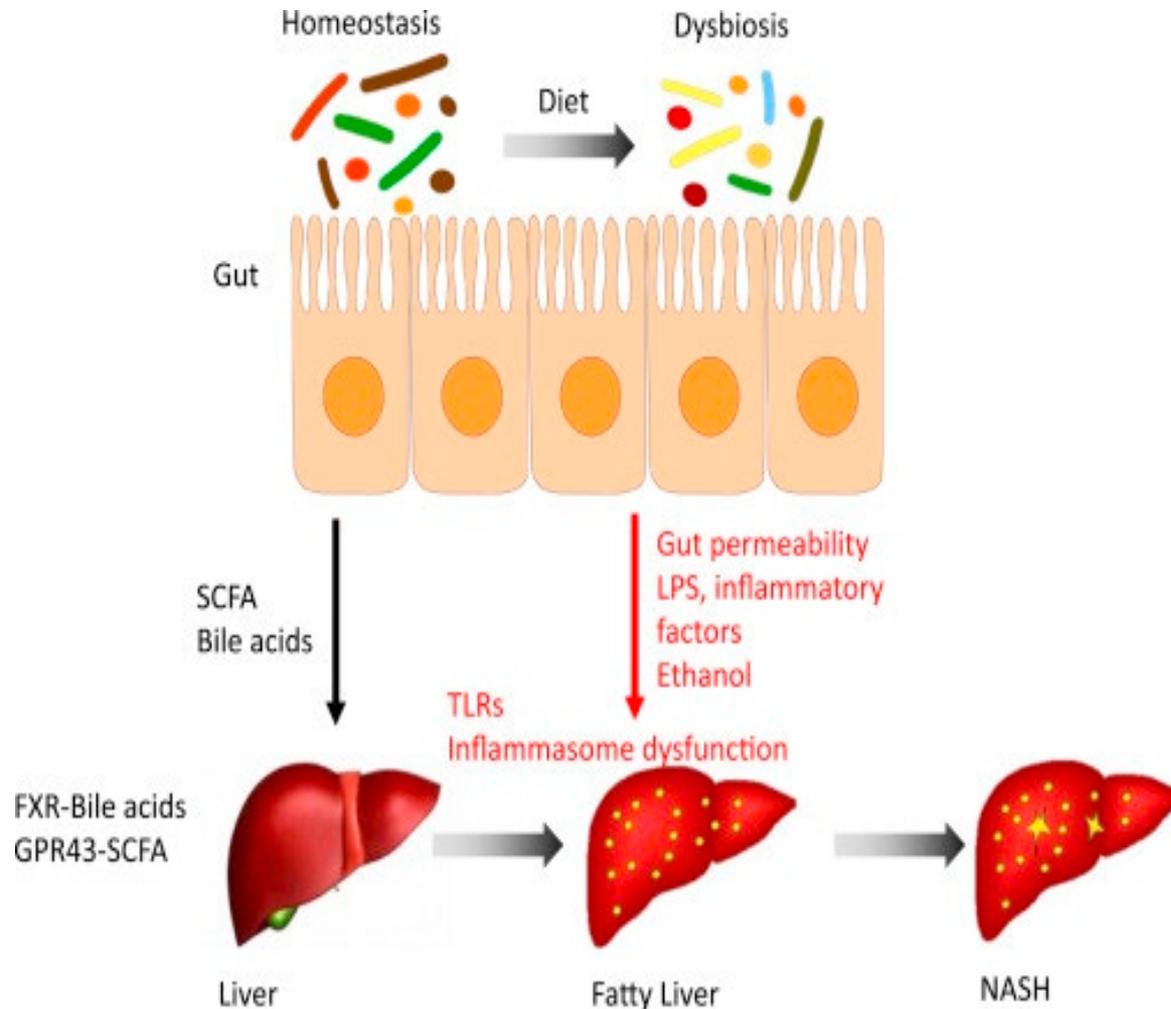
- Increased serum bile acid levels too seem to be independently associated with NASH in non-diabetics.
- NASH patients exhibited higher serum TBA level compared to NAFL patients.
- Serum TBA has been seen to be independently associated with NASH in only non-diabetes patients - not in diabetes patients.

Li et al 2020.

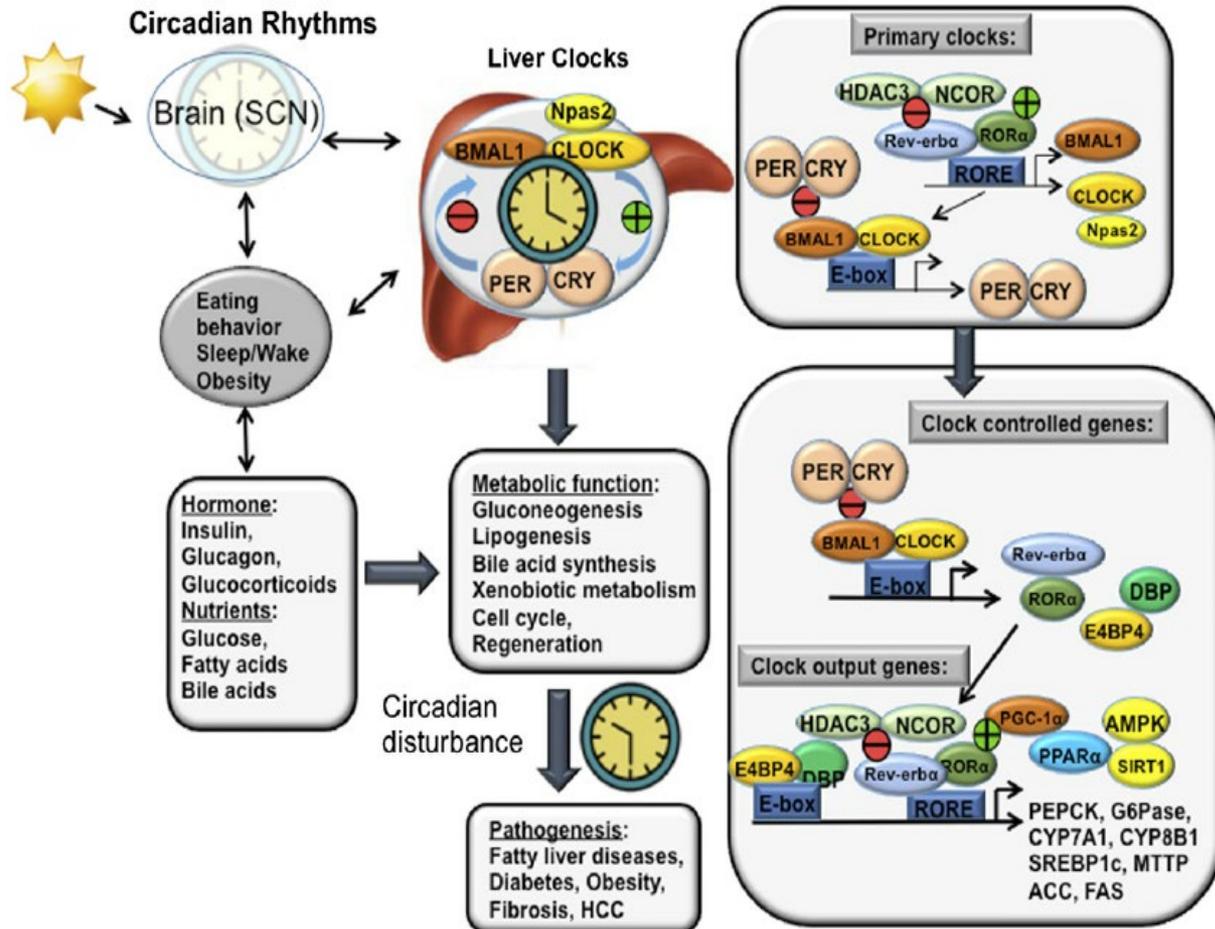
NAFLD: Gut microbiota

- NAFLD is associated with gut dysbiosis.
- NAFLD has been found to be associated with reduced abundance of several bacterial taxa (*Ruminococcus*, *Coprococcus* and *F. prausnitzii*) **independent of BMI & insulin resistance.**
- NAFLD patients have higher concentrations of select fecal and serum metabolites, indicating a specific intestinal microbiome community.

Intestinal Dysbiosis and NAFLD



Circadian Rhythm In NAFLD!



NAFLD: The story of six blind men



Patients' Perspective

- European Liver Patients Association (ELPA) “expressed displeasure” with the term NAFLD to the European Commission in 2018.
- Repeated queries to ELPA as regards how this was decided, the % of patients who felt uncomfortable with such terminology and whether the diverse pathogenesis of NAFLD - especially in non-Caucasians - was considered.
- **No response from ELPA.**

What do our* patients feel about it?

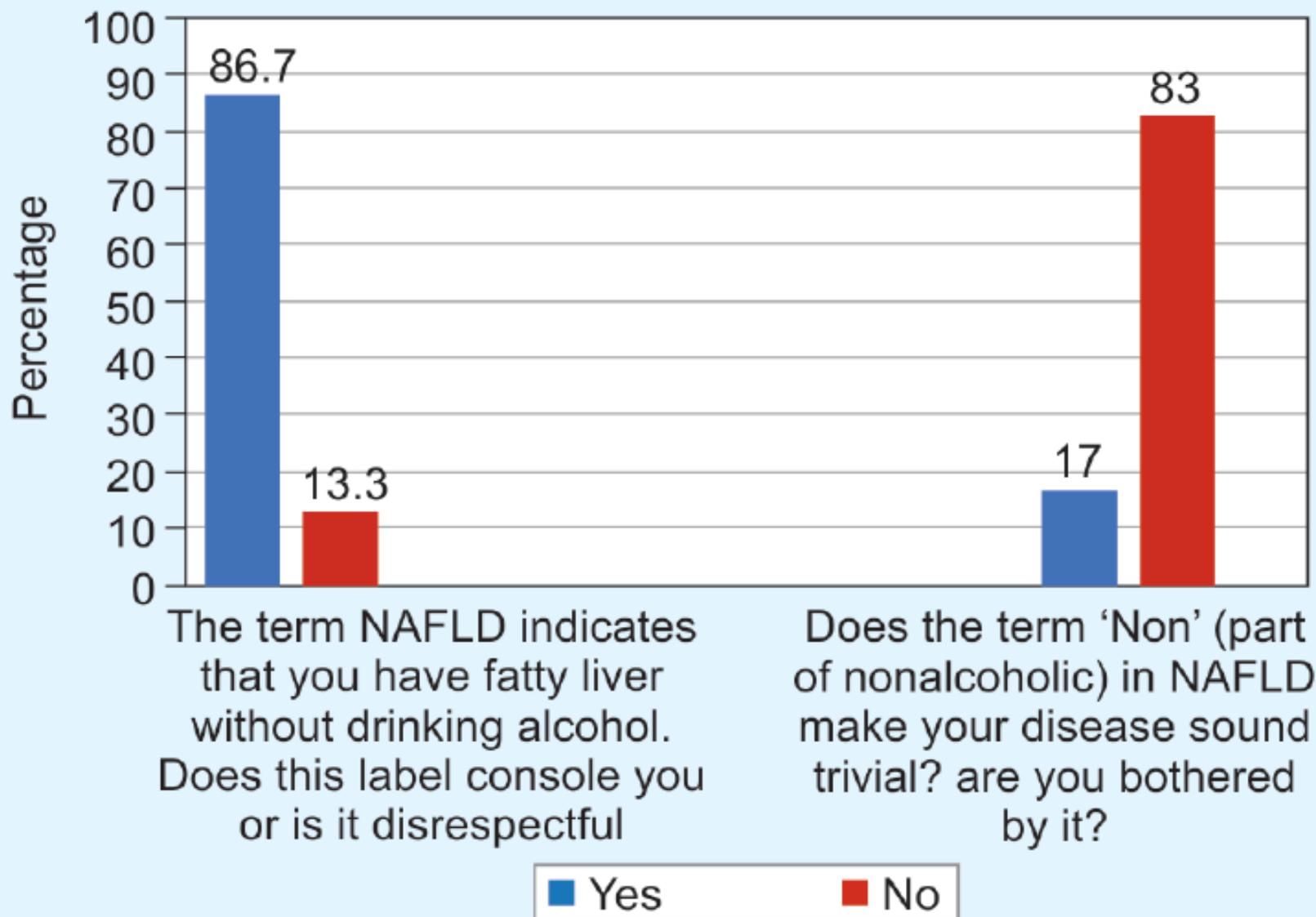
***South Asian**

NAFLD vs MAFLD: South Asian NAFLD Patients don't Favor Name Change

Shivaram P Singh¹, Prajna Anirvan², Amna S Butt³^{ORCID}, Ananta Shrestha⁴^{ORCID}, Anuradha S Dassanayake⁵^{ORCID}, Bashir A Shaikh⁶, Mamun A Mahtab⁷^{ORCID}

Corresponding Author: Shivaram P Singh, Department of Gastroenterology, SCB Medical College and Hospital, Cuttack, Odisha, India, Phone: +91 6712505466, e-mail: spsingh.cuttack@gmail.com

Singh SP, Anirvan P, Butt AS, et al. NAFLD vs MAFLD: South Asian NAFLD Patients don't Favor Name Change. *Euroasian J Hepato-Gastroenterol* 2022;12(Suppl 1):S15–S18.



Patients' sentiments concerning NAFLD

The BAD

The Bad

- Brand NAFLD setback.
- Stigmatization of patients in South Asia.
- Journals full of unscientific reviews and ill informed advocacies.
- Confusion among other stakeholders.
- Setback to Research for Pharmacotherapy.
- Setback to Research for Biomarker.
- Increase permissiveness to alcohol.

What are the demerits of name change to MAFLD?

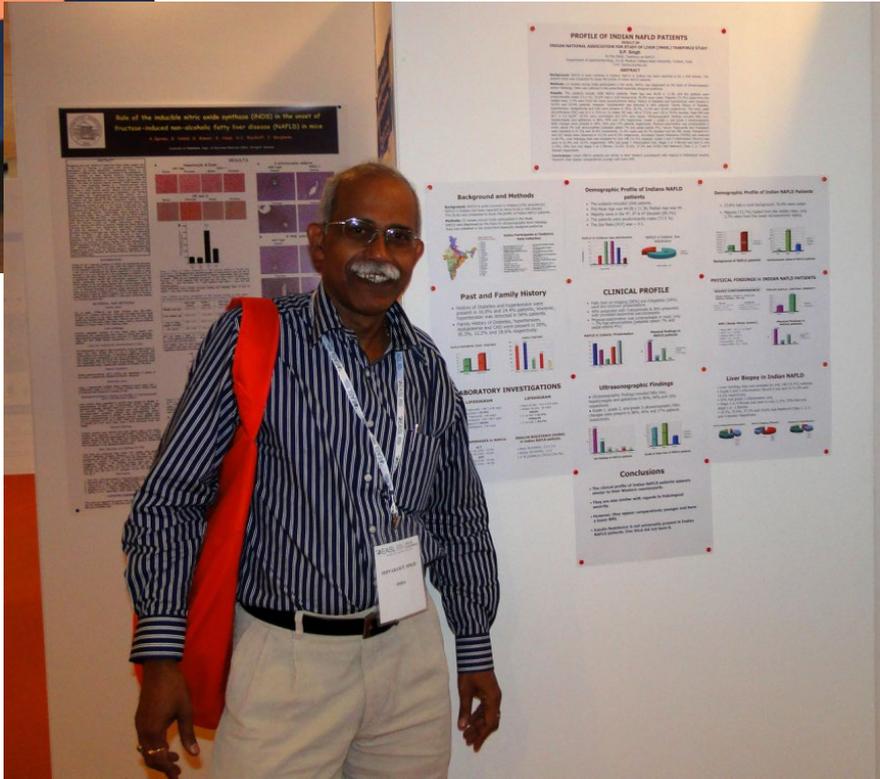
“A name change from NAFLD to MAFLD is replete with demerits”

**1st INASL NAFLD
Taskforce Meeting
at Chennai: 2007**

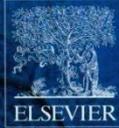




**2nd INASL NAFLD
Taskforce Meeting at
Bhubaneswar: 2007**

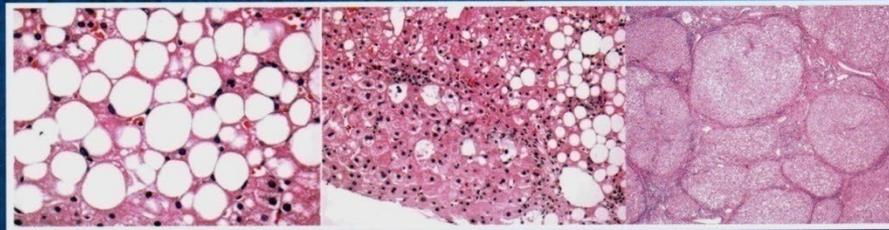


**EASL NAFLD/NASH
Special Conference at
Bologna: 2009**



Non-alcoholic Fatty Liver Disease and Metabolic Syndrome

Position Paper



Endorsed by





Release of INASL Position Paper during the NAFLD SIG Meeting today morning.

Non-alcoholic Fatty Liver Disease and Metabolic Syndrome – Position Paper of the Indian National Association for the Study of the Liver, Endocrine Society of India, Indian College of Cardiology and Indian Society of Gastroenterology



Ajay Duseja^{*}, Shivaram P. Singh[†], Vivek A. Saraswat[‡], Subrat K. Acharya[§], Yogesh K. Chawla^{*}, Subhankar Chowdhury^{||}, Radha K. Dhiman^{*}, Rohinivilasam V. Jayakumar[¶], Kaushal Madan[#], Sri P. Misra^{**}, Hrudananda Mishra^{††}, Sunil K. Modi^{‡‡}, Arumugam Muruganathan^{§§}, Banshi Saboo^{|||}, Rakesh Sahay^{¶¶}, Rajesh Upadhyay^{##}

^{}Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, [†]Department of Gastroenterology, SCB Medical College, Cuttack, Odisha, [‡]Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, [§]Department of Gastroenterology, All India Institute of Medical Sciences, New Delhi, ^{||}Department of Endocrinology, Institute of Postgraduate Medical Education & Research and SSKM Hospital, Kolkata, West Bengal, [¶]Department of Endocrinology, Amrita Institute of Medical Sciences, Kochi, Kerala, [#]Medanta Institute of Digestive and Hepatobiliary Sciences, Medanta—The Medicity, Gurgaon, Haryana, ^{**}Department of Gastroenterology, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, ^{††}Department of Cardiology, S.C.B. Medical College, Cuttack, Odisha, ^{‡‡}Department of Cardiology, Indraprastha Apollo Hospital, New Delhi, ^{§§}The Tamil Nadu Dr. M.G.R. Medical University & AG Hospital, Tirupur, Tamil Nadu, ^{|||}Department of Endocrinology, Diabetes Care & Hormone Clinic, Ahmedabad, Gujarat, ^{¶¶}Osmania Medical College & Osmania General Hospital, Hyderabad, Andhra Pradesh & MediCiti Hospital, Hyderabad, Andhra Pradesh and ^{##}Department of Gastroenterology, Max Super Speciality Hospital, Shalimar Bagh, New Delhi, India*

ICON-D

[Indian Consortium on NAFLD]



22 FEB 2021

“India has become the first country in the world to identify the need for action for NAFLD”



Dr. Harsh Vardhan Union Minister of Health & Family Welfare launches Operational Guidelines for integration of Non-Alcoholic Fatty Liver Disease (NAFLD) with NPCDCS (National Programme for Prevention & Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke).

Demerits of Name Change

- MAFLD Term is Suboptimal, leaving a great deal of ambiguity.
- It can have a Negative Impact on the field [Advocacy/Prevention/Research].
- It will create unnecessary Confusion.
- It will lose its destigmatizing effect [Majority of South Asian NAFLD patients prefer NAFLD].

“Re-Branding”

- A prominent demerit is the possibility of the ‘re-branding’ going wrong.
- The use of term ‘brand’ may seem inappropriate in the setting of medical academia!
- But we need to understand that changes in medical terminology is not all about academics.
- It has taken almost half a century of persistent advocacy efforts that non-hepatologists are beginning to recognize the importance of “NAFLD”.
- Changing name to another in absence of robust evidence either pathogenetic or perceptive can have serious deleterious effects akin to the re-branding exercises which went wrong!

Some of The Worst Corporate Rebrands Ever



OLD



NEW



OLD



NEW



NETFLIX

OLD

Qwikster
a Netflix company

NEW

Most customers struggled to understand the move & described the decision as confusing and pointless. Luckily, it only lasted a few months as the CEO soon decided to abandon the plan and leave things as they were.



Re-BRANDING!



1991

Leningrad changes its name back to St Petersburg

Name Change

- Name change of an important disease cannot be decided like a 100 m Sprint or a raucous boxing bout.
- Name change requires Quiet systematic brainstorming without any Conflict of Interest.
- It should be inclusive: the process should honestly involve all stake holders.
- No Role of “Prejudging”

The UGLY

The Ugly

- The NAFLD MAFLD debate has degenerated into a no holds barred scuffle.
- The opponents have dug in into irretrievable unrelenting positions [bunkers].
- Recourse to unacceptable.



MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease



*Mohammed Eslam*¹



*Arun J. Sanyal*²



*Jacob George*¹, on behalf of the International Consensus Panel

The NAFLD-MAFLD Wars

Time to Take The Bull By The Horns

**TAKE THE
BULL BY
THE
HORNS**





Time to Take The Bull By The Horns

Letter to the Editor

JOURNAL
OF HEPATOLOGY

Non-alcoholic fatty liver disease: Not time for an obituary just yet!

Shivaram Prasad Singh^{1,*}
Prajna Anirvan¹
K. Rajender Reddy²
Hari S. Conjeevaram³
Giulio Marchesini⁴
Mary E. Rinella⁵
Kaushal Madan⁶
Maria Letizia Petroni⁴
Mamun Al-Mahtab⁷
Stephen H. Caldwell⁸
Guruprasad P. Aithal⁹
Saeed S. Hamid¹⁰
Geoffrey C. Farrell¹¹
Sanjaya K. Satapathy¹²
Ajay Duseja¹³
Subrat Kumar Acharya¹⁴
Anuradha Supun Dassanayake¹⁵
Khean-Lee Goh¹⁶

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Published: 2022.08.15

Editorial: The Metabolic (Dysfunction) Associated Fatty Liver Disease (MAFLD)-Non- Alcoholic Fatty Liver Disease (NAFLD) Debate: A Forced Consensus and The Risk of a World Divide

CDEF 1 Nahum Méndez-Sánchez

CDF 2 Ming-Hua Zheng

CDF 3 Takumi Kawaguchi

CF 4 Shiv K. Sarin

- 1 Liver Research Unit, Medica Sur Clinic & Foundation and Faculty of Medicine, National Autonomous University of Mexico, Mexico City, Mexico
- 2 MAFLD Research Center, Department of Hepatology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, PR China
- 3 Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Fukuoka, Japan
- 4 Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Corresponding Authors: Nahum Méndez-Sánchez, e-mail: nmendez@medicasur.org, mx/nah@unam.mx, Ming-Hua Zheng, e-mail: zhengmh@wmu.edu.cn, Takumi Kawaguchi, e-mail: takumi@med.kurume-u.ac.jp, Shiv K Sarin, e-mail: shivsarin@gmail.com

Conflict of interest: None declared

Editorial: The Metabolic (Dysfunction) Associated Fatty Liver Disease (MAFLD)-Non- Alcoholic Fatty Liver Disease (NAFLD) Debate: A Forced Consensus and The Risk of a World Divide

Abstract

During the past two years, the redefinition of non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) have been endorsed by international societies of hepatology, patient advocacy associations, and stakeholders. More recently, the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) have attempted to achieve a consensus. Three main fundamental issues raise concerns regarding the validity of the current consensus process. First, the development of the process and the selection of experts in the consensus panels remain unclear. Second, there is a concern regarding the quantity and quality of the evidence considered by the consensus panels. Third, there has been a lack of input to the consensus panel decisions from the academic and clinical community. This Editorial aims to raise an urgent note of caution regarding the consensus process used by the AASLD and EASL regarding fatty liver disease, to prevent world divide and different global definitions and guidelines from being adopted.

Keywords: **Guidelines • Consensus • Metabolic Dysfunction-Associated Fatty Liver Disease • Non-Alcoholic Fatty Liver Disease • Editorial**

What Conceit!

- We acknowledge our comments are iconoclastic but we believe them sensible.
- We conclude with a quote from the Harvard economist, **John Galbraith**:
- “One of my greatest pleasures in my writing has come from the thought that perhaps my work might annoy someone of comfortably **pretentious** position. Then comes the realization that such people rarely read”.

What does Pretentious mean?

Someone trying to appear better or more important than is really the case: a pretentious snob

What was the method followed? For Selection of Participants ? For Reaching of Consensus ?? Who was representing South Asia???

Gastroenterology 2020;158:1999–2014

MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease



Mohammed Eslam¹



Arun J. Sanyal²



Jacob George¹, on behalf of the International Consensus Panel

**Why (all) the hurry?
Preemptive strike!**

Hepatology International (2020) 14:889–919
<https://doi.org/10.1007/s12072-020-10094-4>

GUIDELINES



The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease

Mohammed Eslam¹ · Shiv K. Sarin² · Vincent Wai-Sun Wong³ · Jian-Gao Fan⁴ · Takumi Kawaguchi⁵ · Sang Hoon Ahn⁶ · Ming-Hua Zheng^{7,8} · Gamal Shiha^{9,10} · Yusuf Yilmaz^{11,12} · Rino Gani¹³ · Shahinul Alam¹⁴ · Yock Young Dan¹⁵ · Jia-Horng Kao^{16,17,18,19} · Saeed Hamid²⁰ · Ian Homer Cua²¹ · Wah-Kheong Chan²² · Diana Payawal²³ · Soek-Siam Tan²⁴ · Tawesak Tanwandee²⁵ · Leon A. Adams²⁶ · Manoj Kumar² · Masao Omata^{27,28} · Jacob George¹

Received: 8 July 2020 / Accepted: 6 September 2020 / Published online: 1 October 2020

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Jumping The GUN!



**Questions? Questions &
Questions?**



Questions?

- What methodology was used by this group to replace NAFLD with MAFLD?
- How was the selection of 23 experts who are shown as authors made?
- Why is there a preponderance of the Chinese among this group: 4 from China & 4 from Taiwan [over one third].
- Even countries like Phillipines /Malaysia /Turkey /Egypt had 2 representatives each.

Questions?

- Why was Indian Hepatology [India has a total population of 1,567,281,163,838 with NAFLD prevalence as high as 38.6%] literally kept out?
- Why were the Chairpersons & Convenors of the INASL Taskforce on NAFLD & ICON-D kept out?
- In the Learned Group of 23, there were only 2 Indians: The 'mover' and 'shaker' – a First author and his institutional subordinate.



The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease

Mohammed Eslam¹ · Shiv K. Sarin² · Vincent Wai Jun Wong³ · Jian-Gao Fan⁴ · Takumi Kawaguchi⁵ · Sang Hoon Ahn⁶ · Ming-Hua Zheng^{7,8} · Gamal El Hefny⁹ · Yusuf M. Mazza^{10,12} · Rino Gani¹³ · Shahinul Alam¹⁴ · Yock Young Dan¹⁵ · Jia-Horng Kao^{16,17,18,19} · Ezzat Hamid²⁰ · Han Hsin Hsu²¹ · Wah-Kheong Chan²² · Diana Payawal²³ · Soek-Siam Tan²⁴ · Taweeak Tanwanitakul²⁵ · John A. Adams²⁶ · Manoj Kumar² · Masao Omata^{27,28} · Jacob George¹

Received: 8 July 2020 / Accepted: 6 September 2020 / Published online: 1 October 2020
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Bangladesh has one of the highest rates of MAFLD in South Asia.

ORIGINAL ARTICLE

Prevalence and risk factors of non-alcoholic fatty liver disease in Bangladesh

Shahinul Alam,*  Shah Mohammad Fahim,[†] Muhammad Abdul Baker Chowdhury,[‡]  Md. Zakiul Hassan,[§] Golam Azam,[¶] Golam Mustafa,* Mainul Ahsan^{||} and Nooruddin Ahmad*

Departments of *Hepatology, ^{||}Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University, [†]Nutrition and Clinical Services Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), [‡]Programme for Emerging Infections, Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr, b), [¶]Department of Gastrointestinal Hepatobiliary and Pancreatic disorders (GHPD), BIRDEM, Dhaka, Bangladesh and [§]Department of Emergency Medicine, University of Florida College of Medicine, Gainesville, Florida, USA

- The overall prevalence of NAFLD was 33.86%. Females living in the rural areas and midlife adults (45–54 years) had the highest prevalence of NAFLD.
- Multivariable logistic regression model demonstrated that increasing age, diabetes, elevated body mass index, and married individuals are significantly associated with NAFLD.



Changing Nomenclature from Nonalcoholic Fatty Liver Disease to Metabolic Dysfunction-Associated Fatty Liver Disease – Not Only Premature But Also Confusing

Ajay Duseja, Sunil Taneja

Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

“Changing nomenclature from NAFLD to MAFLD thus may cause potential clouding of the diagnostics and drug development endeavours that will be left in the lurch with further delay in getting a pharmacological solution that we earnestly seek”

Need to Chart the road ahead



- Recognize the vast heterogeneity of NAFLD across populations and the presence of multiple pathophysiological pathways.
- Launch Collaborative efforts worldwide to better understand the different facets and nuances of this intricate entity.
- Bolster treatment arsenal - curb NAFLD pandemic.
- Intellectual exercise need of the hour - not semantic juggling!

ALICE IN WONDERLAND



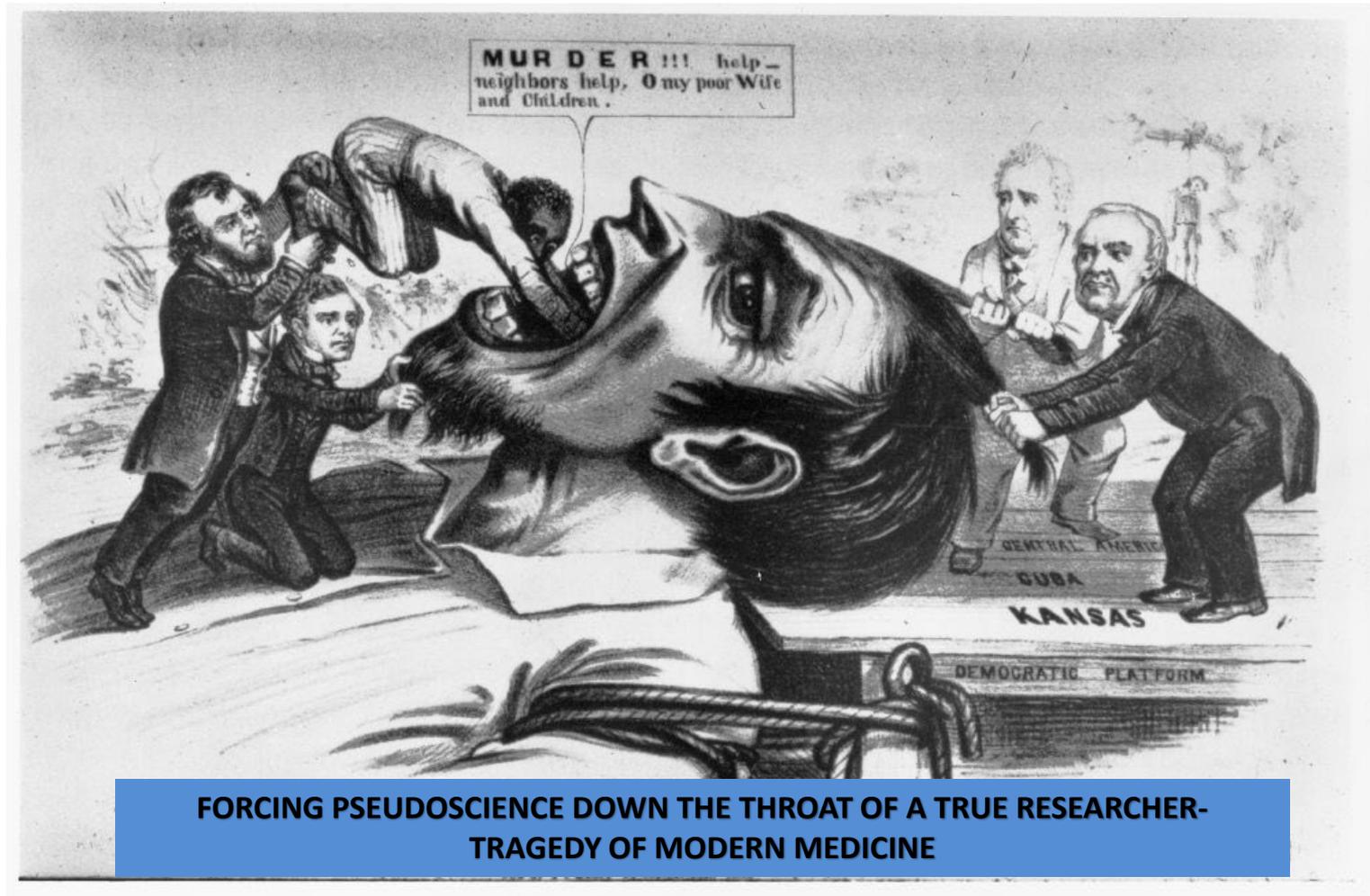
'Words mean what I want them to
mean!'



The Queen of
Hearts

**“Such an attitude
can have no place in
the world of
Medicine”**

NAFLD to MAFLD: Science or Scientific muscle flexing?



**FORCING PSEUDOSCIENCE DOWN THE THROAT OF A TRUE RESEARCHER-
TRAGEDY OF MODERN MEDICINE**

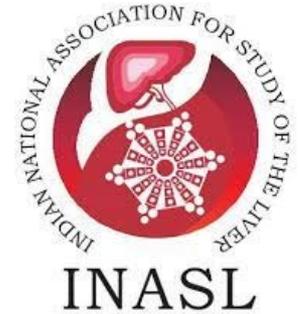


Thank You!

For all queries email to:
fattyliver@gmail.com

NAFLD vs MAFLD: South Asian NAFLD Patients don't Favor Name Change

- This study evaluated the perspectives of patients in South Asia.
- The response is a clear “No” to name change, reaffirming primacy of patients’ attitudes & beliefs before contemplating a change.
- Term “NAFLD” is comforting to patients, destigmatizes them & is acceptable to majority of South Asian patients.
- NAFLD would favour greater patients participation not only in NAFLD research but also in devising preventive strategies and programs.



NAFLD name change to MAFLD: SAASL – INASL Consensus

23 March 2022



Dr Manas Kumar Panigrahi



Shivaram Prasad Singh



Ananta Shrestha



Sanjaya Satapathy



Ajay Duseja



Dr Kaushal Madan



Mamun Al Mahtab



Guru P. Dhakal980156



Hasitha Wijewantha



Hasitha Wijewantha



amna subhan



amna subhan

Should NAFLD be changed to MAFLD?



The term NAFLD [Nonalcoholic Fatty Liver Disease] should not be changed to MAFLD

At a very personal level ...

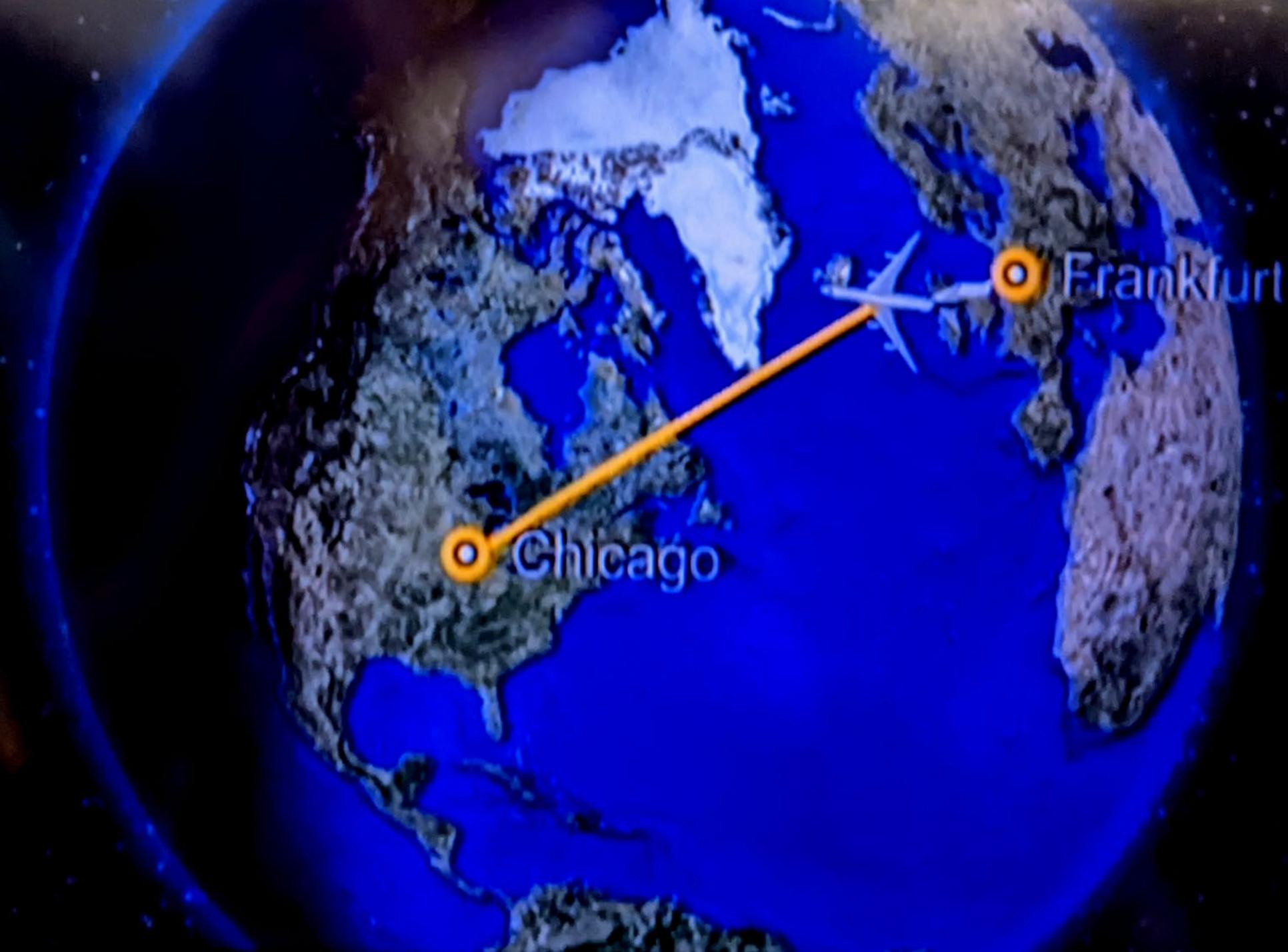


AASLD/EASL NAFLD NOMENCLATURE MEETING

8 & 9 JULY 2022



from CUTTACK to CHICAGO



Chicago

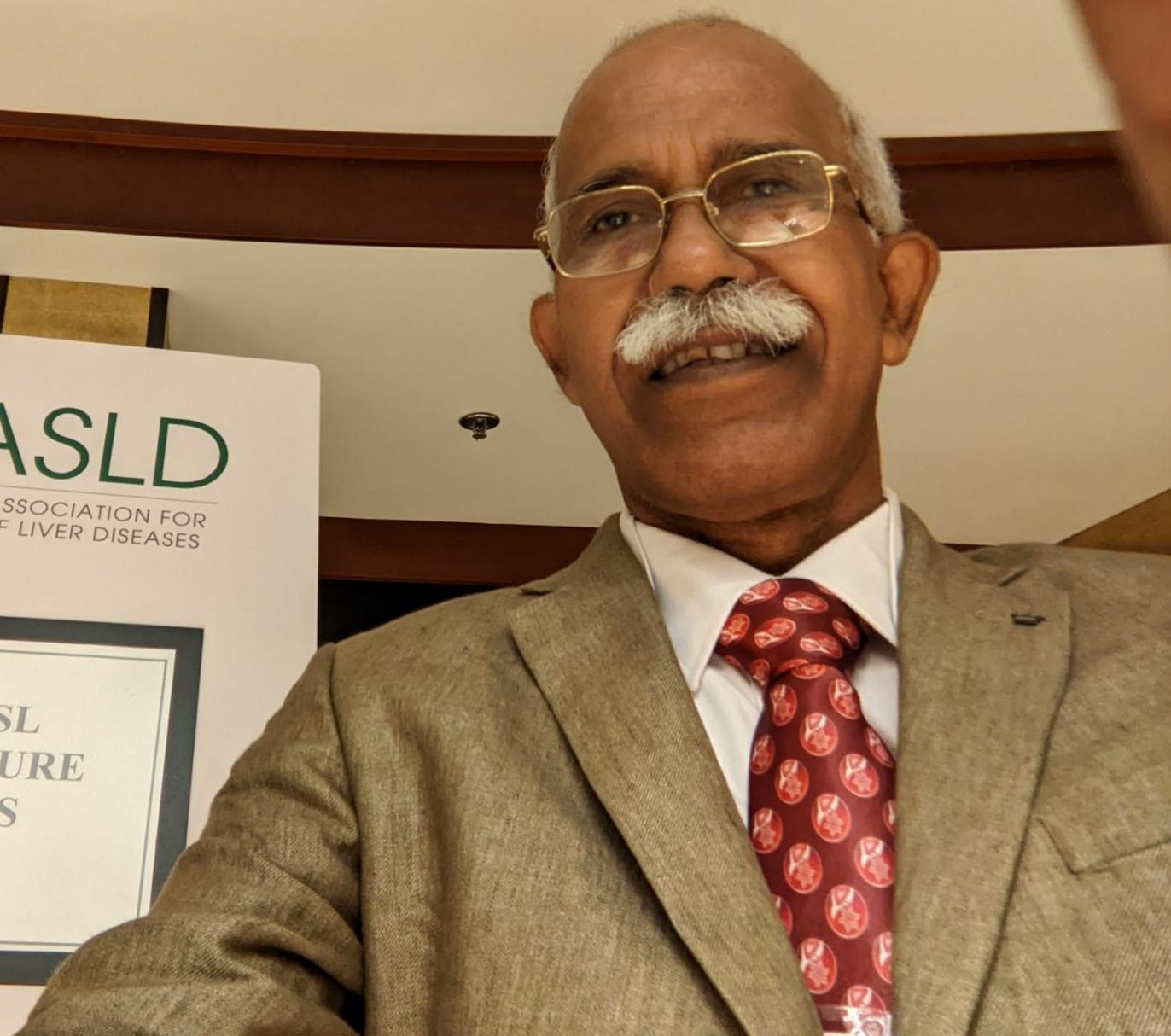
Frankfurt





AMERICAN ASSOCIATION FOR
THE STUDY OF LIVER DISEASES

**AASLD/EASL
NOMENCLATURE
CONSENSUS
MEETING**



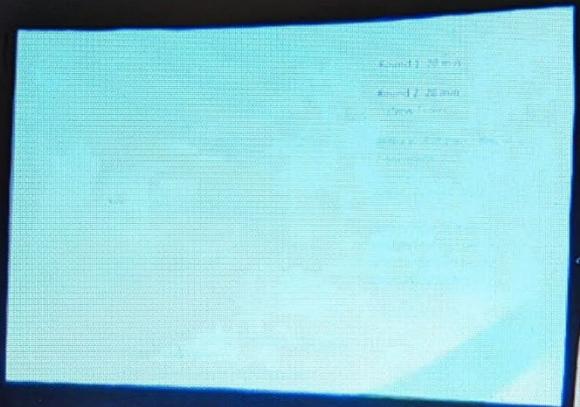
HOST

HOST

At the end of each round of discussion, we want to identify key takeaways or insights to share in all areas.

Capture each of these insights in a separate large sheet of paper. It's okay, and we want the full view.

Denis-Pagoda



Melissa Morrison



AASLD/EASL
NOMENCLATURE
CONSENSUS
MEETING

INASL Tie & Logo



Review Article

Nonalcoholic Fatty Liver Disease (NAFLD) Name Change: Requiem or Reveille?

Shivaram P. Singh^{1*}, Prajna Anirvan¹, Reshu Khandelwal¹ and Sanjaya K. Satapathy²

