

27-29 May 2022: FEAMC symposium: Challenges of
Competence and Compassion in Contemporary Medicine

Hepatology, Liver Transplantation, and Compassion

Helena Glasova, MD, PhD

Department of Clinical Pharmacology

Outpatient Clinic for Clinical Pharmacology and Hepatology

Slovak Medical University in Bratislava, Slovakia

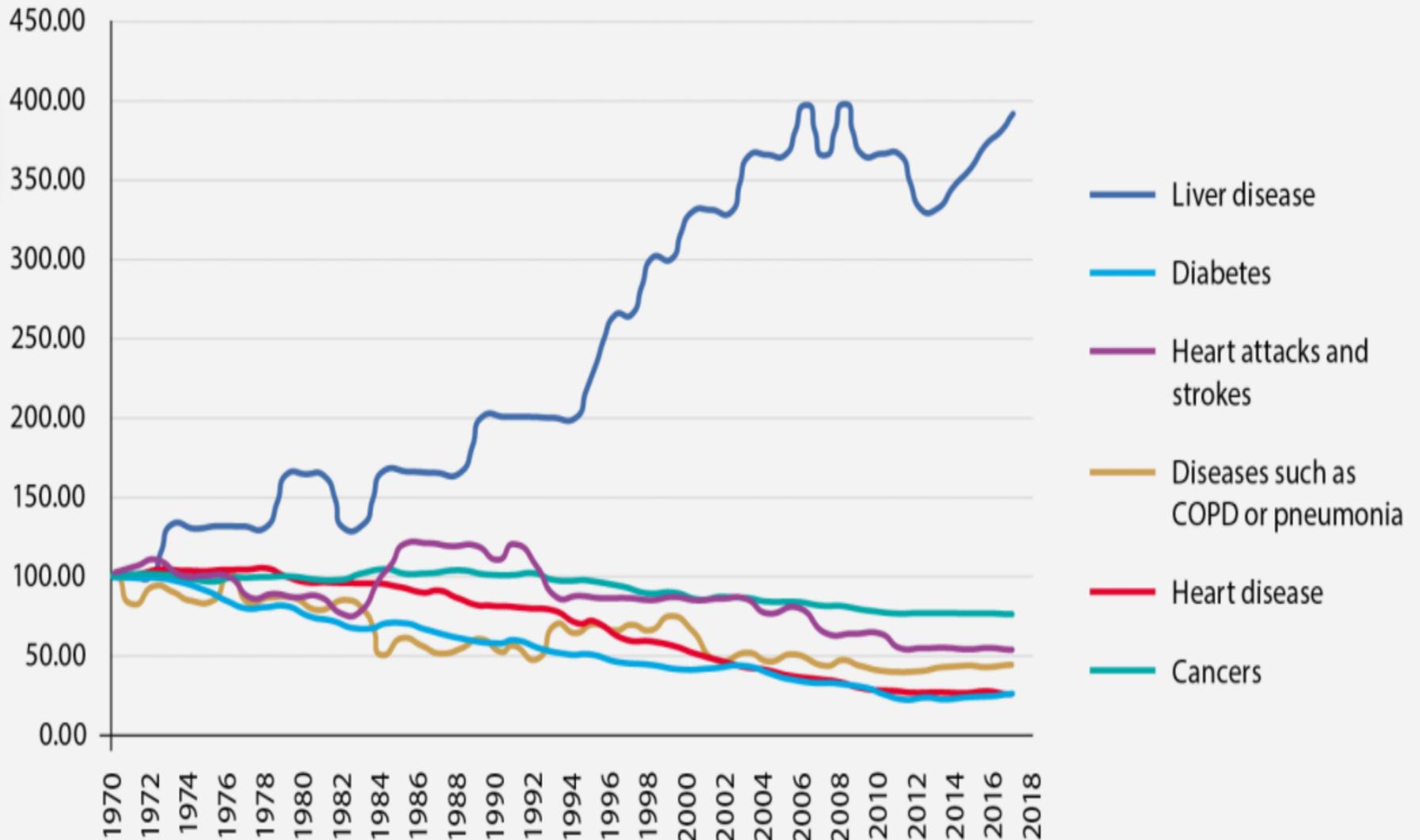
Numerous and Profound Challenges, Disputes, and Shifts in Hepatology

- amazing progress in the discipline over the past few decades
- major paradigm shifts transforming hepatology -- from the cellular to the societal levels
- genomic and epigenomic discoveries
 - can classify diseases in new ways that will enable treatments to be increasingly customized
 - clarify how the environment, the microbiome, social interactions, and even parental behaviours influence gene expression in development, health, and disease
 - personalize medicine by identifying genetic risks, which may lead to a more effective liver diseases prevention
 - concept of “precision medicine”
- application of big data AND artificial intelligence solutions to prevent, diagnose, and treat liver diseases

Numerous and Profound Challenges, Disputes, and Shifts in Hepatology

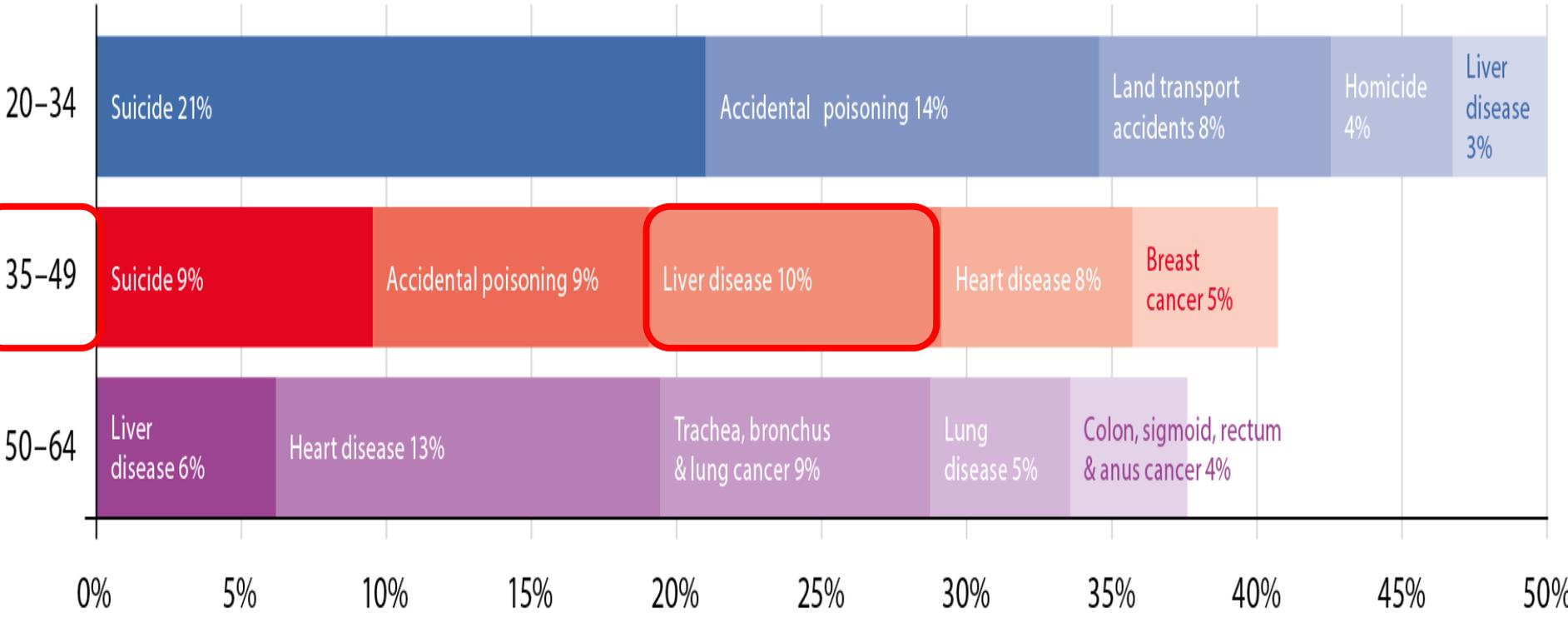
- highly effective oral therapies to cure **hepatitis C** and suppress **hepatitis B** with future prospect of curative HBV therapies
- other diseases become more prominent - among these are both alcoholic and nonalcoholic liver diseases
- **alcoholic liver disease (ALD)** remains a terribly neglected public health threat, as reflected in inability to either curtail high-risk drinking or to prevent severe liver injury in those who drink to excess, with no imminent prospects for improvement
- **nonalcoholic steatohepatitis (NASH)** is likely to eclipse all other liver diseases in the near future, owing to the astonishing rise in obesity, which now affects more individuals worldwide than malnutrition
- **NASH** is a particular threat among South and East Asians, and in Hispanics, where the genetic risk of disease appears to be greater and occurs at lower body mass indexes than in individuals of European descent

The rise in deaths from liver disease compared with other major diseases



Standardised UK Mortality Rate Data - All Ages

Liver disease is now the biggest cause of death in those aged between 35-49 years old



Source: Health Foundation analysis using ONS. Deaths registered in England and Wales, 2017

Top five causes of death by age, England and Wales 2017 – proportion of deaths in age group

<https://britishlivertrust.org.uk/wp-content/uploads/The-alarming-impact-of-liver-disease-FINAL-June-2019.pdf>



Deaths from liver cancer have tripled in past 20 years in England

- **Among men**, there were 2.73 cases of HCC diagnosed and 1.93 deaths per 100,000 of the population in 1997, but by 2016 this had increased to 8.82 and 5.97 respectively, per 100,000.
- **Among women**, there were 0.82 cases diagnosed and 0.51 deaths per 100,000 of the population in 1997; this increased to 2.2 and 1.4 respectively in 2016, per 100,000.
- Overall, **25% of HCC cases were from the most deprived fifth of the population; of these at least 58% of cases had cirrhosis and, of these, 42% had decompensated cirrhosis, the most severe form when the liver has developed so much scarring that complications set in.**

<https://abstracts.ncri.org.uk/abstract/the-landscape-of-hepatocellular-carcinoma-in-the-uk-in-the-past-20-years-the-hccuk-ncras-partnership/>



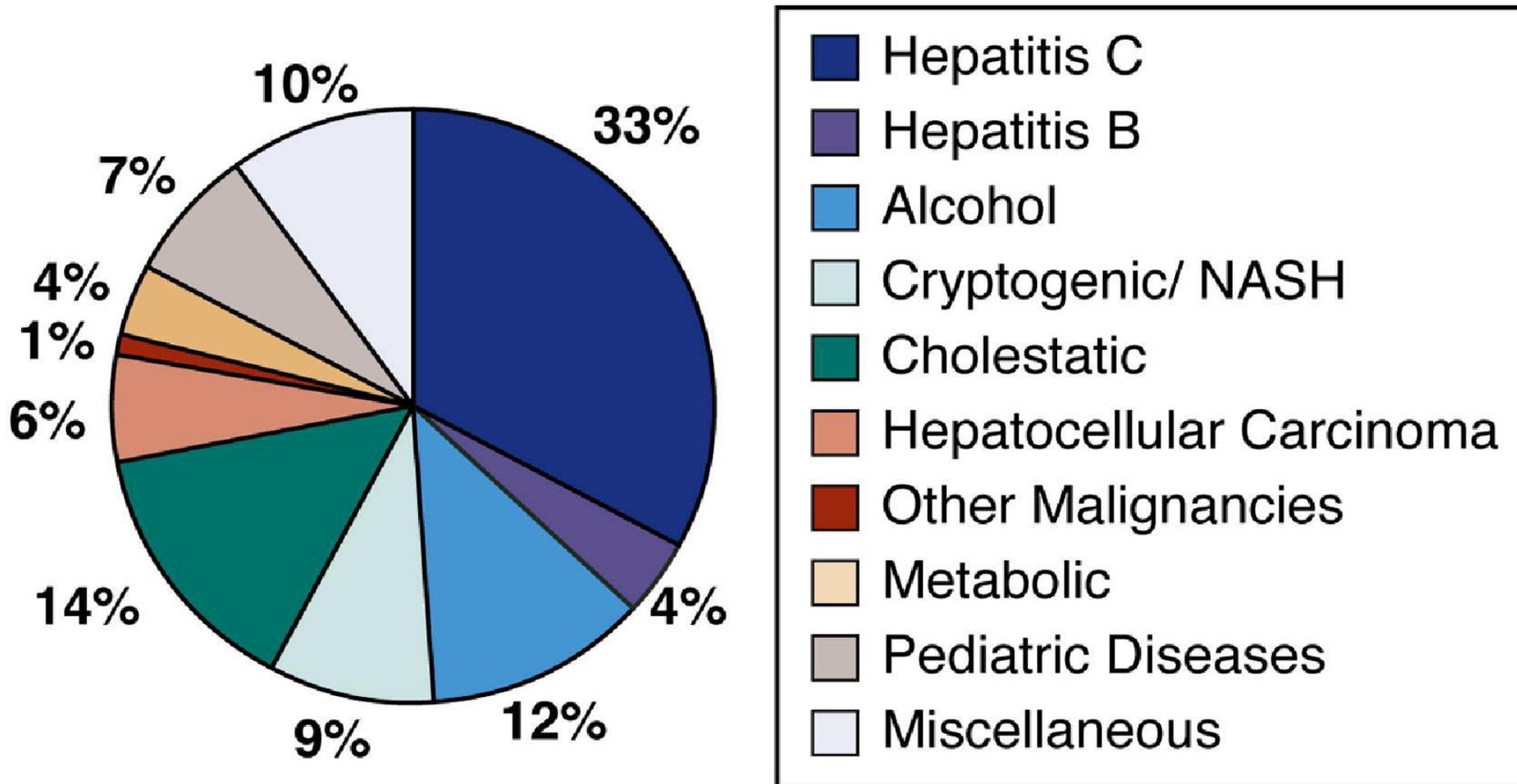
Review

Genetic predisposition similarities between NASH and ASH: Identification of new therapeutic targets

Cristiana Bianco ¹, Elia Casirati ², Francesco Malvestiti ², Luca Valenti ^{1, 2}  

- NASH can be triggered by a combination of excess alcohol, dysmetabolism, and other environmental cues, which can lead to steatohepatitis and can evolve to acute/chronic liver failure and hepatocellular carcinoma, especially in the **presence of shared inherited determinants**
- **PNPLA3 I148M risk variant**
- identification of the genetic causes of steatohepatitis → more effective risk stratification
- discovery of the mechanisms underpinning the detrimental effect of causal mutations led to some breakthroughs in the comprehension of the pathophysiology of steatohepatitis: hepatocellular fat accumulation, altered lipid droplet remodelling and lipotoxicity have now taken centre stage, and the role of adiposity and gut-liver axis alterations have been independently validated
- this could ignite a virtuous research - starting from human genomics, through omics approaches, molecular genetics and disease models - may lead to the development of new therapeutics targeted to patients at higher risk
- although this precision medicine drug discovery pipeline is mainly being applied to NASH, there is hope that successful products could be repurposed to treat also ALD

Indications for Liver Transplantation - *PAST*

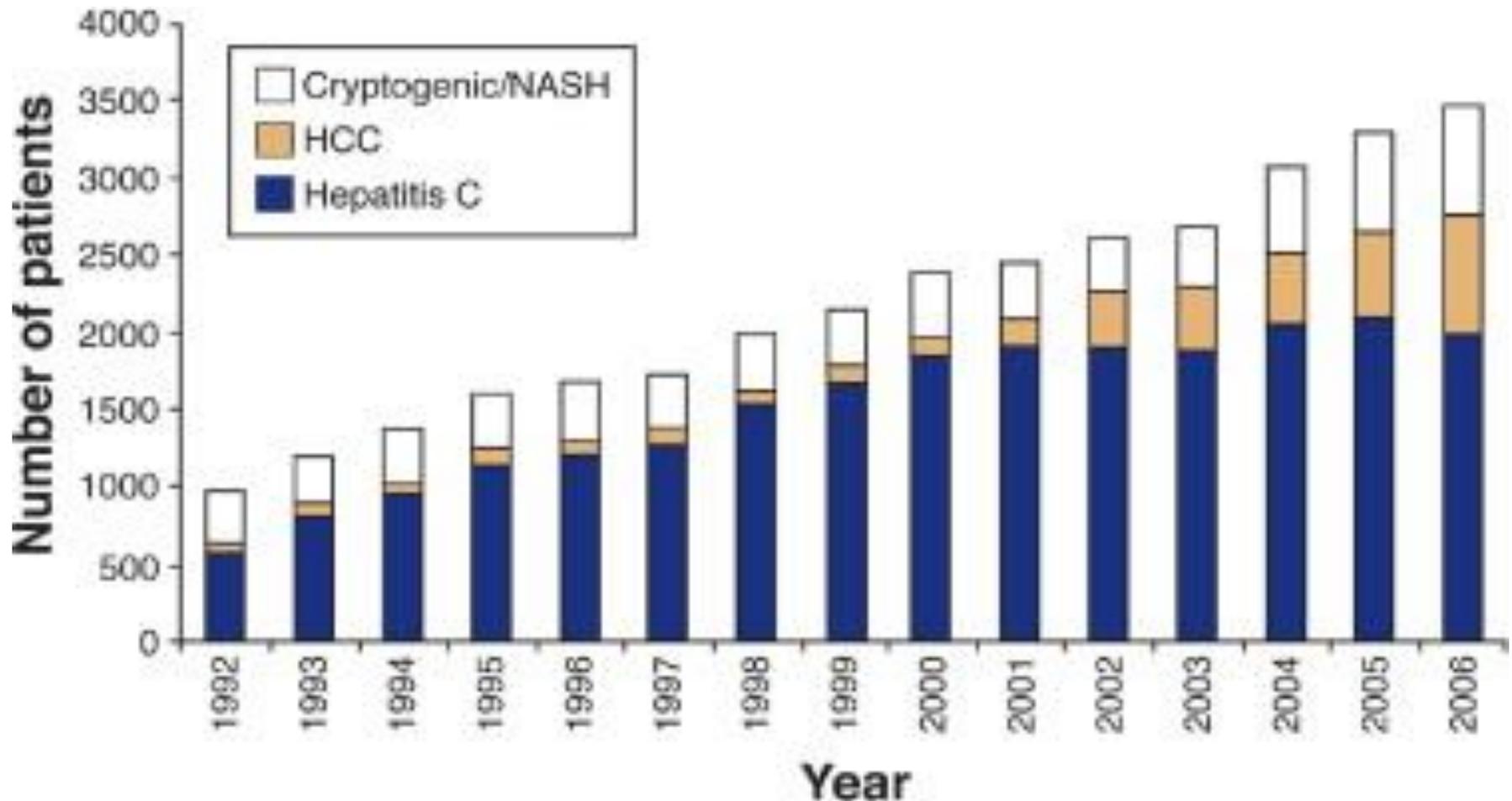


Jacqueline G. O'Leary, Rita Lepe, Gary L. Davis

Gastroenterology, Volume 134 Issue 6 Pages 1764-1776 (May 2008)

DOI: 10.1053/j.gastro.2008.02.028

Number of transplants for cryptogenic cirrhosis, HCC, and chronic hepatitis C by year - *PAST*



Jacqueline G. O'Leary, Rita Lepe, Gary L. Davis

Gastroenterology, Volume 134 Issue 6 Pages 1764-1776 (May 2008)

DOI: 10.1053/j.gastro.2008.02.028

Causes of liver disease and HCC among adult liver transplant recipients in the U.S. from 2010 to 2019 by frequency and percentage

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Total # of liver transplants (%) | 5731 | 5806 | 5731 | 5921 | 6200 | 6547 | 7268 | 7483 | 7687 | 8345 |
| BMI ≥30 at listing for LT | 2120 (37.0%) | 2130 (36.7%) | 2189 (38.2%) | 2181 (36.8%) | 2374 (38.3%) | 2425 (37.0%) | 2838 (39.1%)† | 3056 (40.8%)† | 3038 (39.5%)† | 3406 (40.8%)† |
| BMI ≥35 at listing for LT | 792 (13.8%) | 819 (14.1%) | 814 (14.2%) | 860 (14.5%) | 893 (14.4%) | 972 (14.9%) | 1165 (16.0%)† | 1276 (17.1%)† | 1257 (16.4%)† | 1391 (16.7%)† |
| Causes of liver disease | | | | | | | | | | |
| HCV** | 2548 (44.5%) | 2518 (43.4%) | 2613 (45.6%) | 2528 (42.7%) | 2623 (42.3%)† | 2468 (37.7%)† | 2247 (30.9%)† | 2124 (28.4%)† | 1857 (24.2%)† | 1563 (18.7%)† |
| ALD* | 727 (12.7%) | 764 (13.2%) | 754 (13.2%) | 811 (13.7%) | 917 (14.8%)† | 1158 (17.7%)† | 1496 (20.6%)† | 1694 (22.6%)† | 1920 (24.5%)† | 2399 (28.8%)† |
| NAFLD* | 519 (9.1%) | 534 (9.2%) | 595 (10.4%)† | 698 (11.8%)† | 792 (12.8%)† | 912 (13.9%)† | 1264 (17.4%)† | 1370 (18.3%)† | 1544 (20.1%)† | 1795 (21.5%)† |
| Cholestatic* | 481 (8.4%) | 544 (9.4%) | 464 (8.1%) | 492 (8.3%) | 480 (7.7%) | 551 (8.4%) | 641 (8.8%) | 651 (8.7%) | 591 (7.7%) | 641 (7.7%) |
| HBV*** | 325 (5.7%) | 354 (6.1%) | 296 (5.2%) | 323 (5.5%) | 324 (5.2%) | 298 (4.6%)† | 315 (4.3%)† | 327 (4.4%)† | 346 (4.5%)† | 355 (4.3%)† |
| Cryptogenic* | 270 (4.7%) | 270 (4.7%) | 208 (3.6%)† | 208 (3.5%)† | 180 (2.9%)† | 210 (3.2%)† | 264 (3.6%)† | 245 (3.3%)† | 270 (3.5%)† | 259 (3.1%)† |
| Autoimmune* | 148 (2.6%) | 155 (2.7%) | 171 (3.0%) | 167 (2.8%) | 147 (2.4%) | 177 (2.7%) | 212 (2.9%) | 203 (2.7%) | 215 (2.8%) | 234 (2.8%) |
| Metabolic* | 148 (2.6%) | 170 (2.9%) | 167 (2.9%) | 164 (2.8%) | 181 (2.9%) | 171 (2.6%) | 218 (3.0%) | 224 (3.0%) | 200 (2.6%) | 243 (2.9%) |
| Acute hepatic necrosis (non-HBV/HCV) | 180 (3.1%) | 149 (2.6%) | 137 (2.4%)† | 146 (2.5%)† | 155 (2.5%)† | 143 (2.2%)† | 153 (2.1%)† | 150 (2.0%)† | 165 (2.2%)† | 179 (2.1%)† |
| Unspecified causes of HCC | 77 (1.3%) | 62 (1.1%) | 68 (1.2%) | 91 (1.5%) | 100 (1.6%) | 80 (1.2%) | 63 (0.9%)† | 99 (1.3%) | 108 (1.4%) | 132 (1.6%) |

The (il)legal (?)/criminal (?) use of organs from executed prisoners

• China

- „officially“ outlawed in 2015
- very likely still occurs ...
- *International Coalition to End Transplant Abuse in China (ETAC)*
- *Independent Tribunal into Forced Organ Harvesting from Prisoners of Conscience in China*
https://chinatribunal.com/Tribunal_JUDGMENT_1stMarch_2020.pdf

• USA

- illegal, still debated
- prisoners on the death row to be accepted as organ donors (?)

• Globally

- still many countries, where organs are “trafficked”
- reality of the “transplant tourism”

BMJ Open Compliance with ethical standards in the reporting of donor sources and ethics review in peer-reviewed publications involving organ transplantation in China: a scoping review

[1]

Wendy Rogers,^{1,2} Matthew P Robertson,³ Angela Ballantyne,⁴ Brette Blakely,⁵ Ruby Catsanos,⁶ Robyn Clay-Williams,⁷ Maria Fiatarone Singh⁸

- 445 included studies reported on outcomes of 85,477 transplants
- 412 (92.5%) failed to report whether or not organs were sourced from executed prisoners
- 439 (99%) failed to report that organ sources gave consent for transplantation
- *324 (73%) reported approval from an IRB (= Ethics Committee)
- *Roche Pharmaceuticals* – 2010 “Shaming Award”
- “Of the papers claiming that no prisoners’ organs were involved in the transplants, 19 of them involved 2688 transplants that took place prior to 2010, when there was no volunteer donor program in China.”

BMJ Open Compliance with ethical standards in the reporting of donor sources and ethics review in peer-reviewed publications involving organ transplantation in China: a scoping review

[2]

Wendy Rogers,^{1,2} Matthew P Robertson,³ Angela Ballantyne,⁴ Brette Blakely,⁵ Ruby Catsanos,⁶ Robyn Clay-Williams,⁷ Maria Fiatarone Singh⁸

- transplant research community has failed to implement ethical standards banning publication of research using material from executed prisoners
- as a result, a large body of unethical research now exists, raising issues of complicity and moral hazard to the extent that the transplant community uses and benefits from the results of this research
- call for retraction of this literature pending investigation of individual papers

EXECUTION BY ORGAN PROCUREMENT

BREACHING THE DEAD DONOR RULE IN CHINA

Matthew P. Robertson, Research Fellow in China Studies,
Victims of Communism Memorial Foundation

Jacob Lavee, Ph.D., Director, Heart Transplantation Unit,
Sheba Medical Center

Published in the American Journal of Transplantation

April 4, 2022

ORIGINAL ARTICLE

Execution by organ procurement: Breaching the dead donor rule in China

Matthew P. Robertson¹  | Jacob Lavee² 

- The dead donor rule is fundamental to transplant ethics. The rule states that organ procurement must not commence until the donor is both dead and formally pronounced so, and by the same token, that procurement of organs must not *cause* the death of the donor.
- In a separate area of medical practice, there has been intense controversy around the participation of physicians in the execution of capital prisoners.
- These two apparently disparate topics converge in a unique case: **the intimate involvement of transplant surgeons in China in the execution of prisoners via the procurement of organs. We use computational text analysis to conduct a forensic review of 2838 papers drawn from a dataset of 124 770 Chinese-language transplant publications.**
- Our algorithm searched for **evidence of problematic declarations of brain death** during organ procurement. We find **evidence in 71 of these reports, spread nationwide, that brain death could not have properly been declared.** In these cases, the removal of the heart during organ procurement must have been the proximate cause of the donor's death. Because these organ donors could only have been prisoners, findings strongly suggest that physicians in the People's Republic of China have participated in executions by organ removal.

„ There Was a Wedding in Cana ... “ John 2:1–11



... on importance of a good wine...

The Marriage Feast at Cana
Bartolomé Esteban Murillo (1617–1682)
The Barber Institute of Fine Arts
Artuk.org

(Luke 7:34)

The Son of man has come eating and drinking, and you say, Behold, a gluttonous wine-drinking man, a friend of publicans and sinners.

... on our Lord **Jesus** being **unfairly judged** by the Scribes and Pharisees... **because** (also) of His humane-divine **compassion** ...

Stigma of a Liver Disease

- liver diseases are considered to be stigmatizing
- well-documented problem in certain liver pathologies
- associated with alcoholism and drug abuse
- patients affected by hepatitis C and B are often stigmatized regardless of the way of acquiring the virus
- patients with liver cirrhosis are stigmatized regardless of the etiology of the original liver disease

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

[1]

Stigmatization is common in patients with non-alcoholic fatty liver disease and correlates with quality of life

Marta Carol, Martina Pérez-Guasch, Elsa Solà, Marta Cervera, Sara Martínez, Adrià Juanola, Ann T. Ma, Emma Avitabile, Laura Napoleone, Elisa Pose, Isabel Graupera, Maria Honrubia, Marko Korenjak, [...],

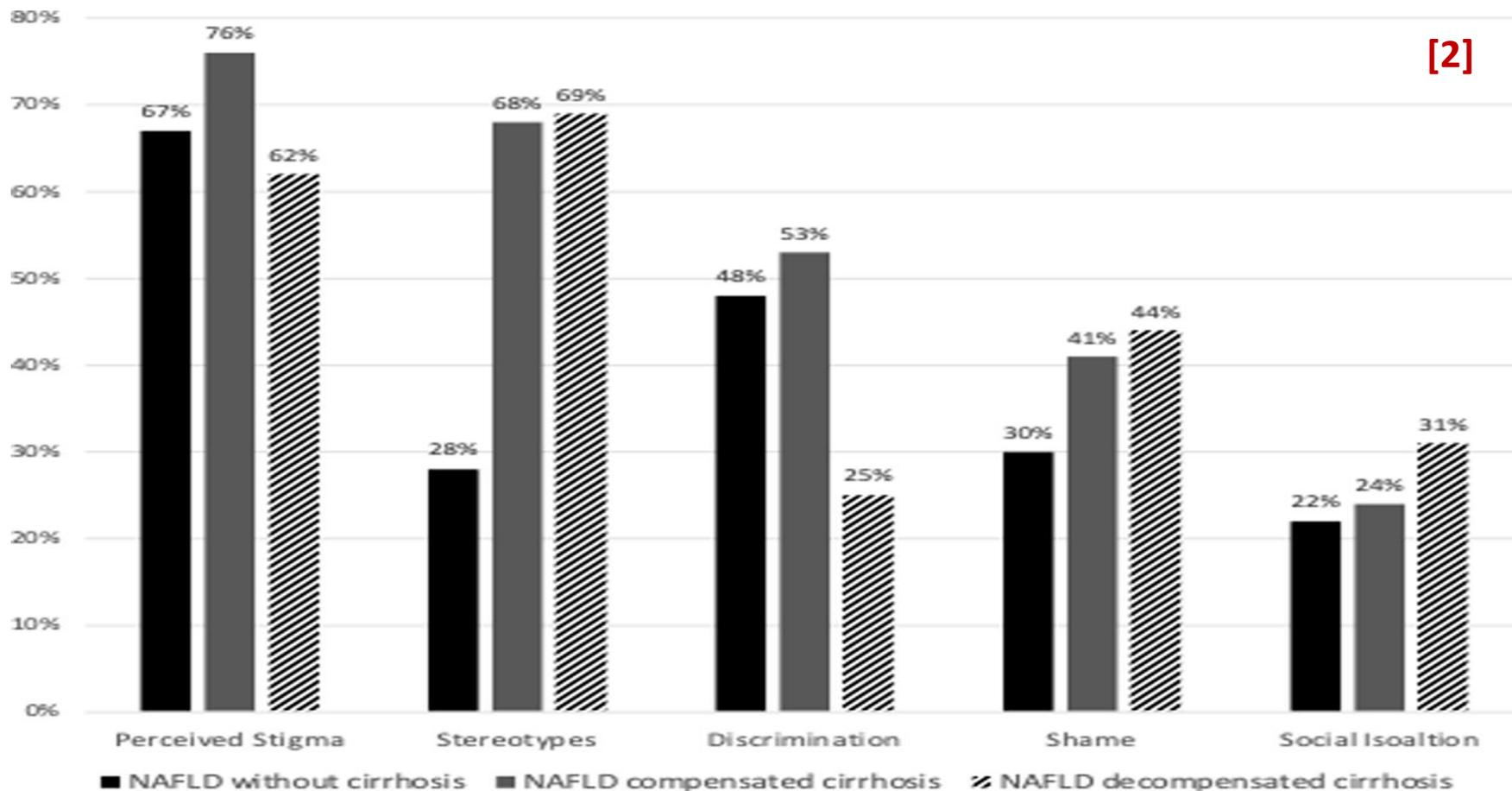
for the LiverHope Consortium Investigators 

[view all]

Published: April 6, 2022 • <https://doi.org/10.1371/journal.pone.0265153>

- the study aimed to finding the frequency and features of the perceived stigma among patients with **NAFLD** (non-alcoholic fatty liver disease)
- collected data from 197 patients from the Hepatology Department of Hospital Clínic de Barcelona, 114 of them affected by non-alcoholic fatty liver disease (**NAFLD**) and 53 with alcohol-related cirrhosis (**ALD**)
- Since **NAFLD** is usually associated with an impaired quality of life, a potential relationship between the perceived stigma and the quality of life of these patients was also explored
- the perceived stigma was evaluated through a specific questionnaire listed in four domains: stereotypes, discrimination, shame, and social isolation
- **7** out of **10** patients with NAFLD felt stigmatized

Frequency of perceived stigma in patients with NAFLD - overall and in 4 different domains, without cirrhosis, NAFLD with compensated cirrhosis and NAFLD with decompensated cirrhosis



Carol M, Pérez-Guasch M, Solà E, Cervera M, Martínez S, Juanola A, et al. (2022) Stigmatization is common in patients with non-alcoholic fatty liver disease and correlates with quality of life. PLoS ONE 17(4): e0265153. <https://doi.org/10.1371/journal.pone.0265153>

Stigma-related questions that were answered affirmatively by more than 20% of patients with NAFLD without cirrhosis (panel A), compensated cirrhosis (panel B) and decompensated cirrhosis (panel C), classified according to the different domains **[3]**

| QUESTIONS | |
|--|----------|
| A | |
| STEREOTYPES | |
| Other people think I am partially to blame for my liver disease. | 23 (25%) |
| DISCRIMINATION | |
| People with liver disease are looked down upon by society | 43 (47%) |
| SHAME | |
| I feel like I am partially to blame for my liver disease | 20 (22%) |
| B | |
| STEREOTYPES | |
| Some people assume that because I have liver disease, I must have been a drinker | 9 (26%) |
| DISCRIMINATION | |
| People with liver disease are looked down upon by society | 16 (47%) |
| SHAME | |
| I feel like I am partially to blame for my liver disease | 9 (26%) |
| I feel less competent that I did before I was diagnosed with liver disease | 7 (21%) |
| C | |
| STEREOTYPES | |
| Other people think I am partially to blame for my liver disease. | 5 (33%) |
| DISCRIMINATION | |
| People with liver disease are looked down upon by society | 4 (27%) |
| SHAME | |
| I feel like I am partially to blame for my liver disease | 3 (20%) |
| I feel less competent that I did before I was diagnosed with liver disease | 7 (47%) |
| SOCIAL ISOLATION | |
| I avoid telling other people about my liver disease | 4 (27%) |

A Success Story: Primary Biliary Cholangitis (PBC) ~~Primary Biliary Cirrhosis (PBC)~~

Position Paper



 EASL | JOURNAL OF HEPATOLOGY

Changing nomenclature for PBC: From 'cirrhosis' to 'cholangitis'☆☆

Ulrich Beuers^{1,*}, M. Eric Gershwin², Robert G. Gish³, Pietro Invernizzi⁴, David E.J. Jones⁵,
Keith Lindor⁶, Xiong Ma⁷, Ian R. Mackay⁸, Albert Parés⁹, Atsushi Tanaka¹⁰,
John M. Vierling¹¹, Raoul Poupon¹²

¹Department of Gastroenterology & Hepatology and Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; ²Division of Rheumatology, Allergy and Clinical Immunology, The University of California School of Medicine, Davis, CA, USA ³Department of Medicine, Division of Gastroenterology & Hepatology, Stanford University, Stanford, CA, USA ⁴Center for Autoimmune Liver Diseases, Humanitas Clinical and Research Center, Rozzano (Milan), Italy; ⁵Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; ⁶College of Health Solutions, Arizona State University, Phoenix, AZ, USA; ⁷Division of Gastroenterology & Hepatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai Institute of Digestive Disease, Shanghai, China; ⁸Department of Biochemistry & Molecular Biology, Monash University, Clayton, Vic 3800, Australia; ⁹Liver Unit, Hospital Clinic, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain; ¹⁰Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan; ¹¹Departments of Medicine and Surgery, Baylor College of Medicine, Houston, TX, USA; ¹²Reference Center for Inflammatory Biliary Diseases, Service d'Hépatologie, Saint-Antoine Hospital, Paris, France

See Editorial, pages 1066–1067

Change From 'Cirrhosis' to 'Cholangitis'

→ de-stigmatization of PBC

- the change has critical implications for patients
- removes the stigmata of cirrhosis and its implications of alcohol abuse
- removes the stigmata of a poor prognosis
- reminds patients that they are living with this liver syndrome, not necessarily dying of it
- improves patient's opportunities in the workplace and in their everyday social lives
- *“Thus, we sincerely call on all medical professionals and all patients and their families and friends worldwide to use from this moment on the name “primary biliary cholangitis” for the disease known by its abbreviation PBC! We owe this to our patients and to further our role as caring physicians.”*

St. Paul's Call to Compassion

Be kind and compassionate to one another, forgiving each other, just as in Christ God forgave you.

(Ephesians 4:32)

Pope Francis attends funeral of his personal doctor **Fabrizio Soccorsi** who died of Covid-related causes on 9 January 2021. The funeral Mass was celebrated by Vatican Secretary of State, Cardinal Pietro Parolin.



NEWSFEED

Pope Francis Picks Liver Disease Specialist as His Private Doctor

August 14, 2015

[News](#) [Resources](#) [Columns](#) [Podcasts](#) [Video](#) [CNA Newsletter](#)

Soccorsi, 73, is the Emeritus Chief of Hepatology at the San Camillo Hospital in Rome and is an adviser of Health and Hygiene for the Governorate of Vatican City. He is also an expert on the Medical Committee for the Congregation of the Causes of Saints.

Since St. John Paul II's pontificate, it has been customary that the position as director of the Vatican City State's healthcare facilities was tied to the post of the Pope's personal doctor. However, Francis has branched out from the tradition by selecting a new doctor who is not in charge of the Vatican healthcare system.

Born Feb. 2, 1942 in Rome, Soccorsi graduated from Rome's La Sapienza University in 1968 with a degree in Medicine and Surgery, and received his license to practice the following year.

Thank you for your attention!

One more advice of St. Paul

(1 Timothy 5:23)

Stop drinking only water and use a little wine because of your stomach and your frequent illnesses.

ON COMPASSION

James V. Schall, S.J. (1928–2019)

TUESDAY, FEBRUARY 17, 2015



JAMES V. SCHALL, S.J. (1928–2019)

James V. Schall, S.J., who served as a professor at Georgetown University for thirty-five years, was one of the most prolific Catholic writers in America. Among his many books are *The Mind That Is Catholic*, *The Modern Age*, *Political Philosophy and Revelation: A Catholic Reading*, *Reasonable Pleasures*, *Docilitas: On Teaching and Being Taught*, *Catholicism and*

Intelligence, and, most recently, *On Islam: A Chronological Record, 2002–2018*.

<https://www.thecatholicthing.org/2015/02/17/compassion/>