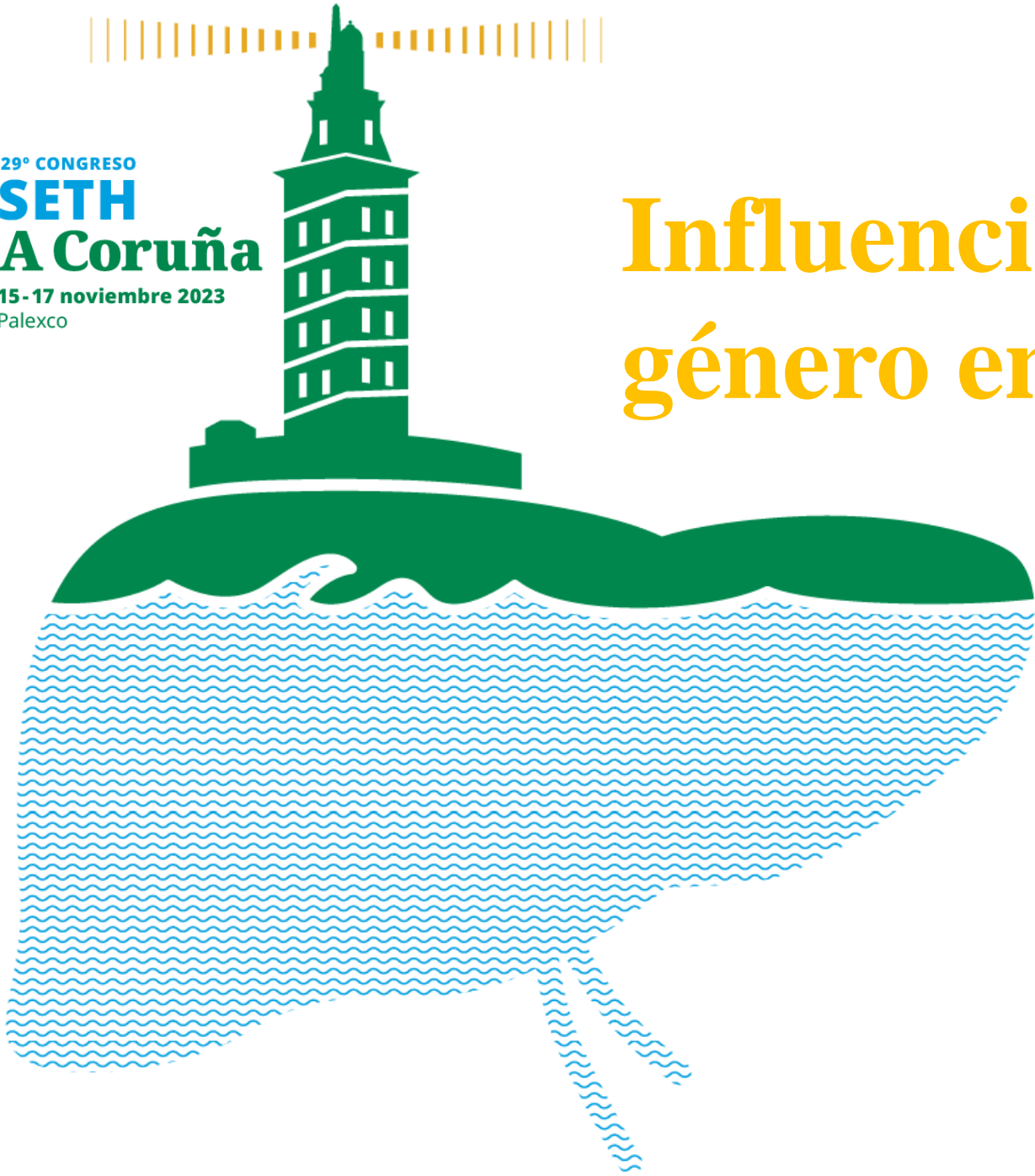


29º CONGRESO
SETH
A Coruña
15-17 noviembre 2023
Palexco



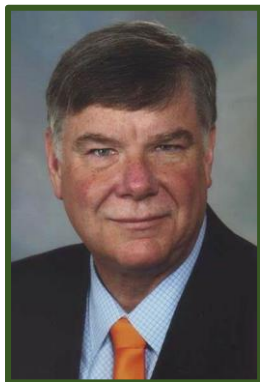
Influencia de la disparidad de género en el trasplante hepático

Manuel L. Rodríguez Perálvarez
Hospital Reina Sofía y Universidad de Córdoba





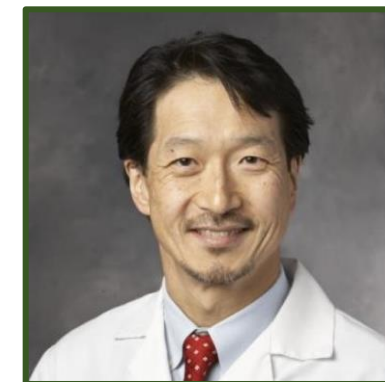
Historia del MELD



MELD and PELD: Application of Survival Models to Liver Allocation

REVIEW ARTICLE

Russell H. Wiesner, Sue V. McDiarmid, Patrick S. Kamath, Eric B. Edwards, Michael Malinchoc, Walter K. Kremers, Ruud A.F. Krom, and W. Ray Kim



- **Previo a 1998:** Priorización según tiempo en lista de espera (“first come, first served”)
- **1998-2002:** Child-Pugh define 3 categorías.
- **2000:** El tiempo en lista de espera no se relaciona con la mortalidad.
- **2000:** “The severity index should be based on a few, readily available objective variables to determine the risk of dying”
- **2000:** Se publica el modelo MELD (TIPS)
- **2001:** Se valida MELD en trasplante hepático
- **2002:** Se adopta MELD para priorizar lista de espera en EEUU





El problema se da a conocer en 2008



Disparities in Liver Transplantation Before and After Introduction of the MELD Score

Cynthia A. Moylan, MD, Carla W. Brady, MD, MHS, Jeffrey L. Johnson, MS, Alastair D. Smith, MB, ChB, Janet E. Tuttle-Newhall, MD, and Andrew J. Muir, MD, MHS
Division of Gastroenterology (Drs Moylan, Brady, Smith, and Muir), Comprehensive Cancer Center (Mr Johnson), and Division of General Surgery and Critical Care (Dr Tuttle-Newhall), Duke University Medical Center, Durham, North Carolina

JAMA. 2008 November 26; 300(20): 2371–2378.

**PRE-MELD
1996-2000**

VS

**POST-MELD
2002-2006**

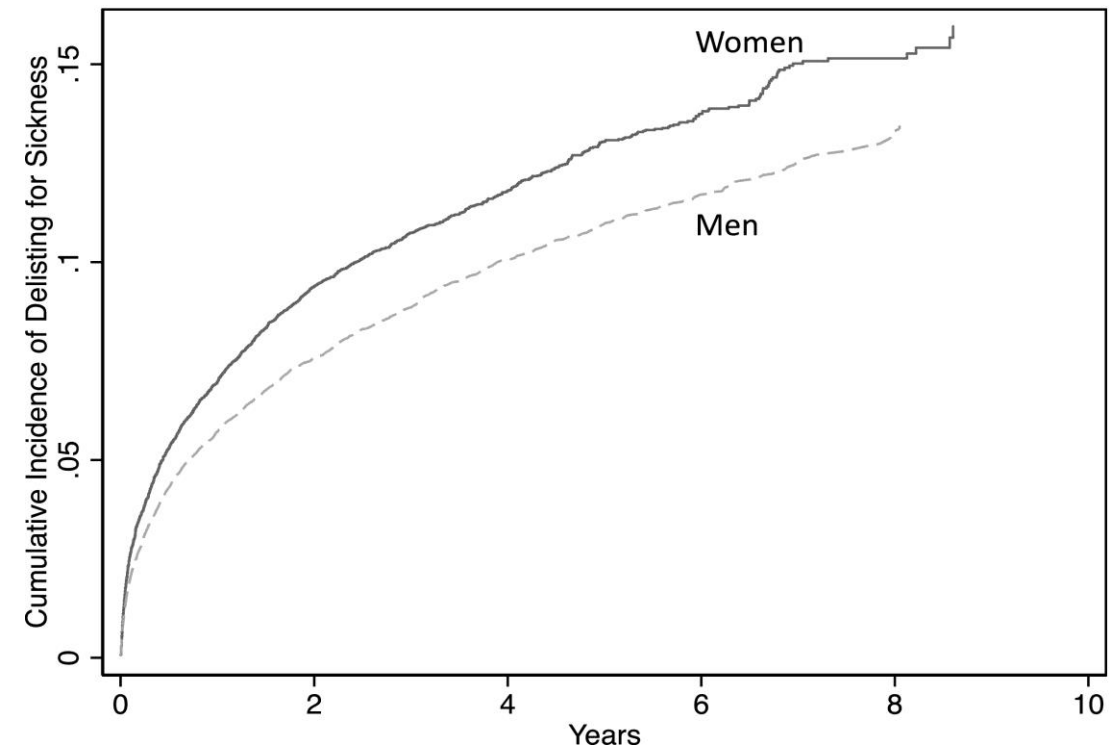
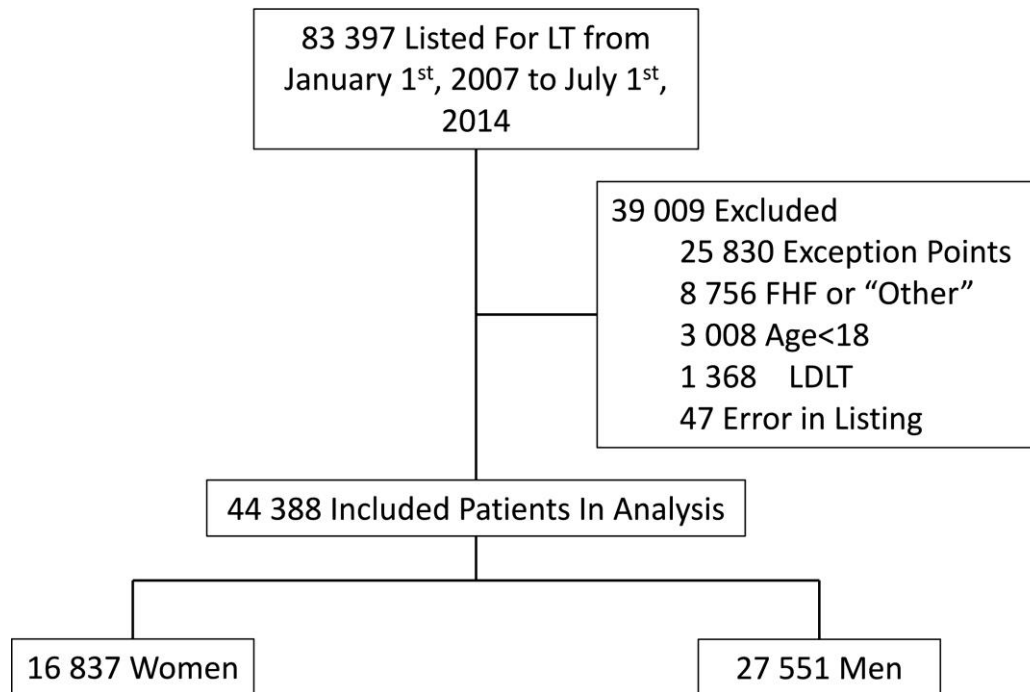
	Frequency (%)		Adjusted OR (95% CI) ^a	P Value
	Women	Men		
Death or becoming too sick for liver transplantation				
Without hepatocellular carcinoma ^b				
Pre-MELD cohort (n = 4066)	353 (22.4)	548 (21.9)	1.08 (0.91–1.26)	.37
Post-MELD cohort (n = 5163)	437 (23.7)	739 (21.4)	1.30 (1.08–1.47)	.003
With hepatocellular carcinoma				
Pre-MELD cohort (n = 91)	4 (14.8)	23 (35.9)	0.28 (0.07–0.99)	.05
Post-MELD cohort (n = 387)	9 (10.0)	41 (13.8)	NA	
Liver transplantation				
Without hepatocellular carcinoma				
Pre-MELD cohort (n = 4067)	1109 (64.8)	1686 (67.6)	0.80 (0.70–0.92)	.002
Post-MELD cohort (n = 5289)	736 (39.9)	1679 (48.7)	0.70 (0.62–0.79)	<.001
With hepatocellular carcinoma				
Pre-MELD cohort (n = 91)	19 (70.4)	31 (48.4)	2.48 (0.91–7.30)	.08
Post-MELD cohort (n = 387)	67 (74.4)	233 (78.4)	0.72 (0.41–1.31)	.27





MELD y disparidades de género

La probabilidad de mortalidad o exclusión de lista de espera por agravamiento es un 30% superior en mujeres





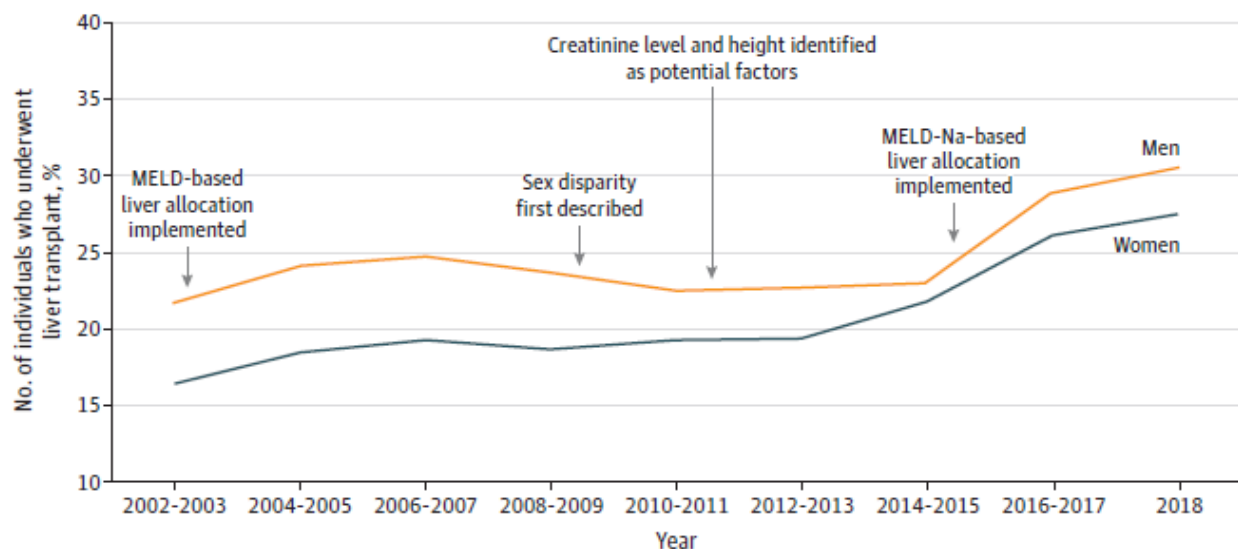
Evolución de las disparidades

VIEWPOINT

Time for Action to Address the Persistent Sex-Based Disparity in Liver Transplant Access

JAMA Surgery Published online May 20, 2020

Figure. Proportion of Women and Men Who Underwent Deceased Donor Liver Transplant and Timeline of Important Events in Liver Transplant



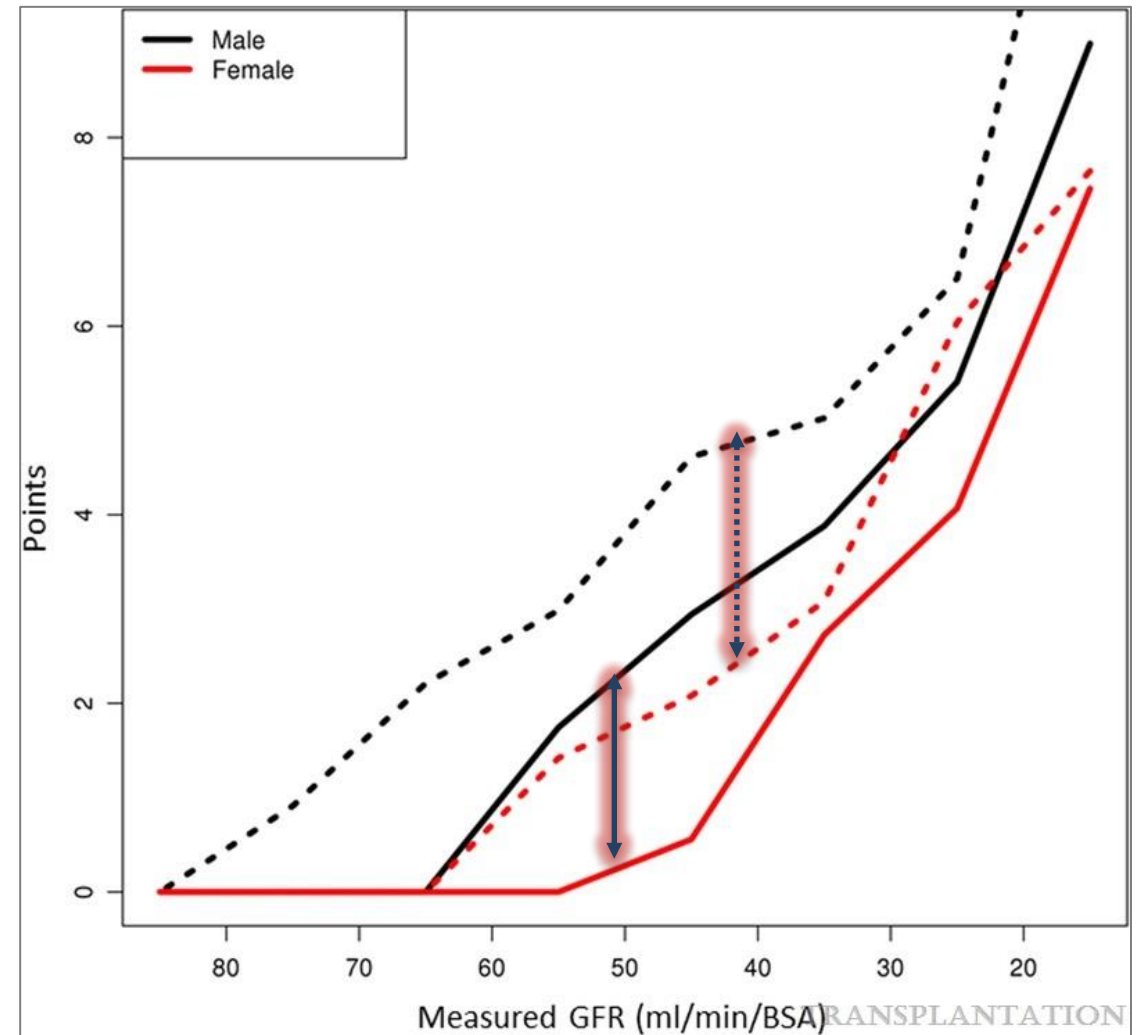
Si existiese un acceso paritario al trasplante, podría haberse evitado el fallecimiento de 800 mujeres en EEUU en la última década





Causa principal: Creatinina sérica

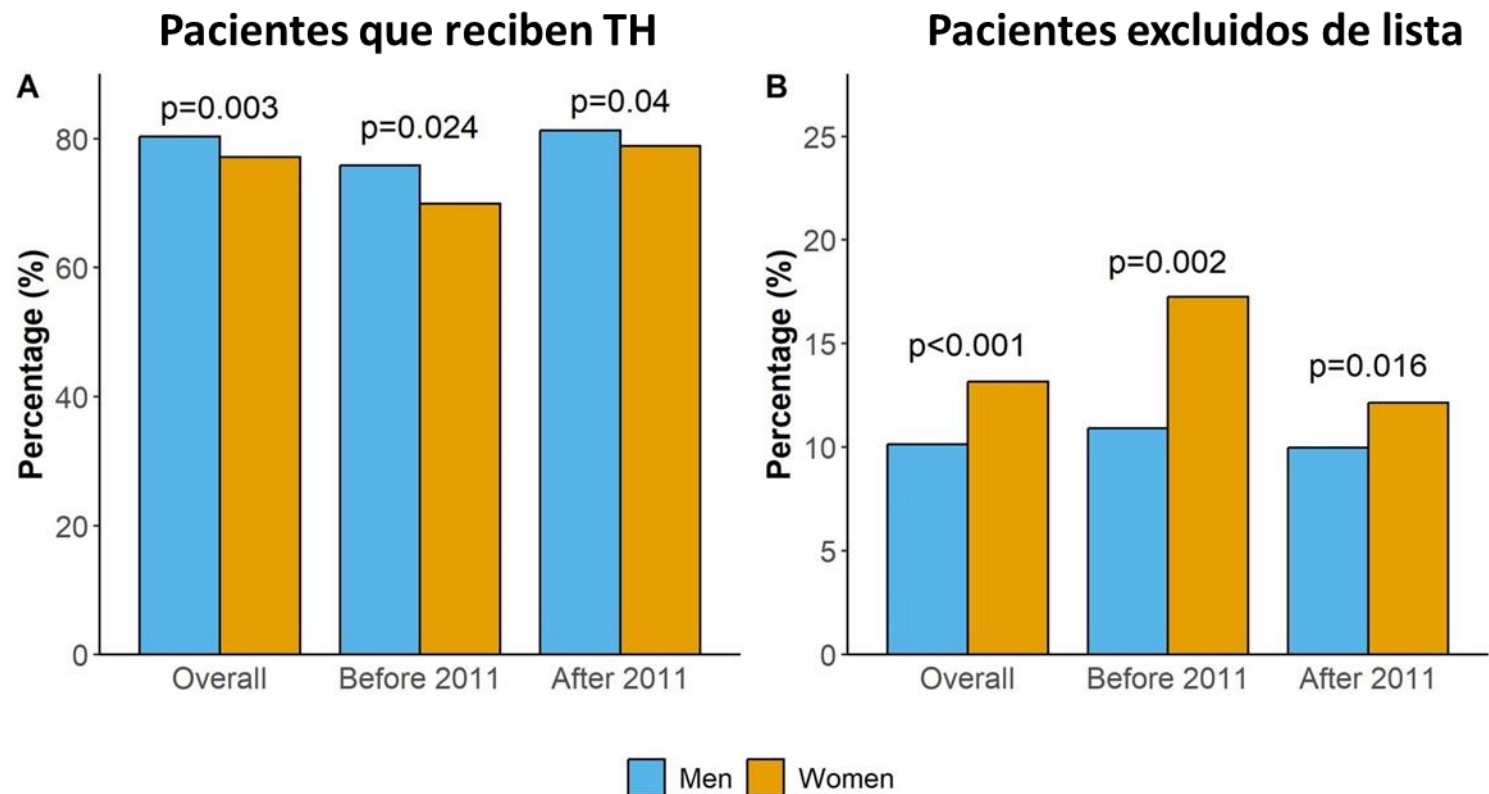
A idéntica función renal, las mujeres reciben menos puntuación MELD





¿Y en nuestro medio?

Registro Español de Trasplante Hepático 2000-2017: **9427** pacientes



	Antes de 2011	Después de 2011
Probabilidad de TH siendo hombre	OR 1.5 (p=0.018)	OR 1.1 (NS)
Probabilidad de exclusión de lista siendo mujer	HR 1.5 (p=0.043)	HR 1.2 (NS)



Otros factores: sarcopenia

Gastroenterology 2019;156:1675-1682

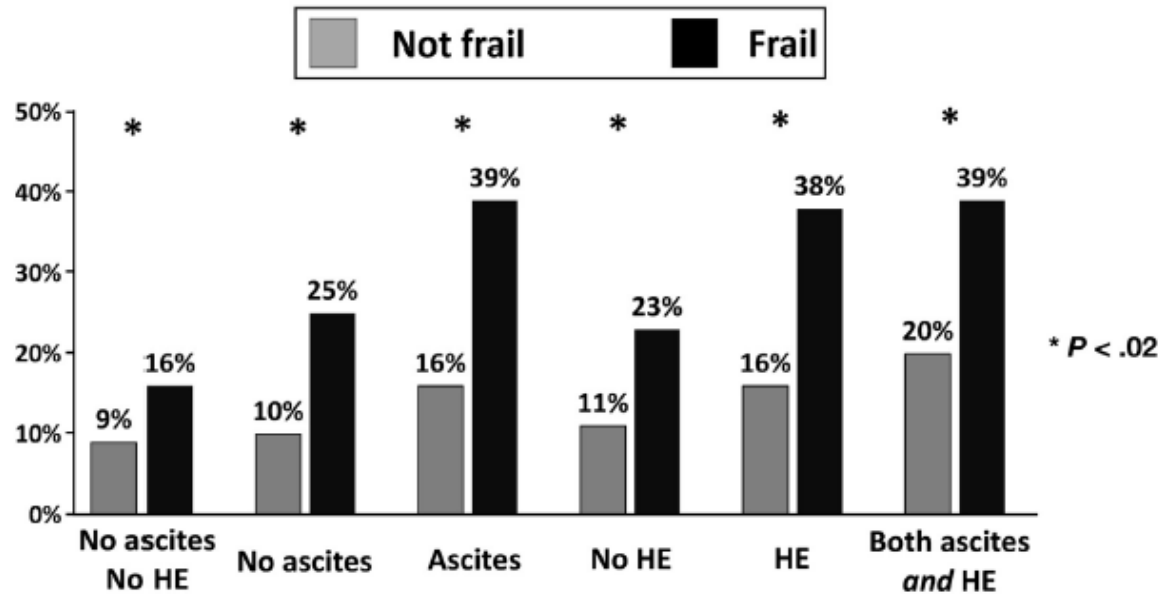
CLINICAL—LIVER

Frailty Associated With Waitlist Mortality Independent of Ascites and Hepatic Encephalopathy in a Multicenter Study

Jennifer C. Lai,¹ Robert S. Rahimi,² Elizabeth C. Verna,³ Matthew R. Kappus,⁴ Michael A. Dunn,⁵ Mara McAdams-DeMarco,^{6,7} Christine E. Haugen,⁷ Michael L. Volk,⁸ Andres Duarte-Rojo,⁹ Daniel R. Ganger,¹⁰ Jacqueline G. O'Leary,¹¹ Jennifer L. Dodge,¹² Daniela Ladner,¹³ and Dorry L. Segev⁷



The Liver Frailty Index
liverfrailtyindex.ucsf.edu



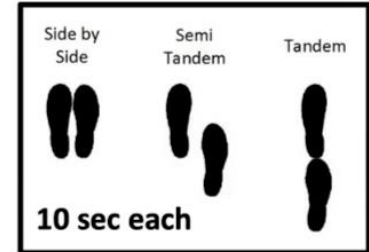
Nutrition

+



Muscle strength

+



Neuromotor coordination





MELD-GRAIL

Sustitución de creatinina por GRAIL
(creatinina, BUN, edad, género, raza y albúmina)



N=17.095
(2014-2015)



Elimina la creatinina del modelo
Demuestra calibración

HEPATOLOGY

HEPATOLOGY, VOL. 71, NO. 5, 2020



LIVER FAILURE/CIRRHOSIS/PORTAL HYPERTENSION

**MELD-GRAIL-Na: Glomerular
Filtration Rate and Mortality on
Liver-Transplant Waiting List**



No validación externa
La raza entra en el modelo
¿Periodo influenciado por antivirales?
Solo mejora a MELD-Na en score >25





MELD 3.0

Adición de género y albúmina
(mantiene la creatinina en el modelo)

CLINICAL—LIVER

MELD 3.0: The Model for End-Stage Liver Disease Updated for the Modern Era



N=29.410
(2016-2018)

OPTN

ORGAN PROCUREMENT AND
TRANSPLANTATION NETWORK



Datos más recientes
Elevado tamaño muestral
Aceptado para implantar en EEUU

No validación externa
No demuestra calibración
Priorización excesiva de mujeres





El modelo GEMA

Development and validation of the Gender-Equity Model for Liver Allocation (GEMA) to prioritise candidates for liver transplantation: a cohort study



Manuel Luis Rodríguez-Perálvarez*, Antonio Manuel Gómez-Orellana*, Avik Majumdar, Michael Bailey, Geoffrey W McCaughan, Paul Gow, Marta Guerrero, Rhiannon Taylor, David Guijo-Rubio, César Hervás-Martínez, Emmanuel A Tsochatzis



NHS

Blood and Transplant

N=7,682

(2010-2020)

Training and internal
validation (3:1)



Austin
HEALTH



Royal Prince
Alfred Hospital

N=1,638

(1998-2020)

External validation

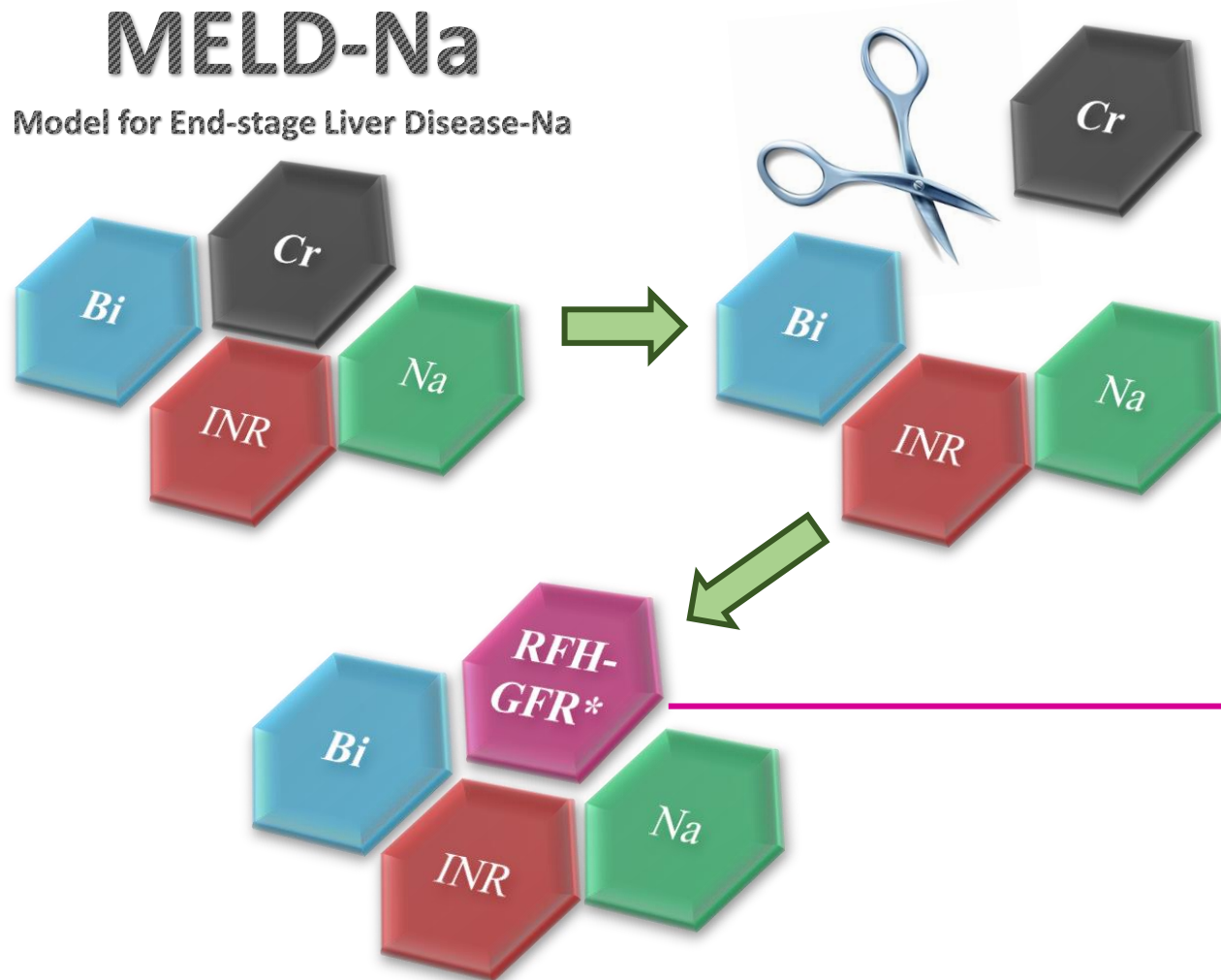




El modelo GEMA

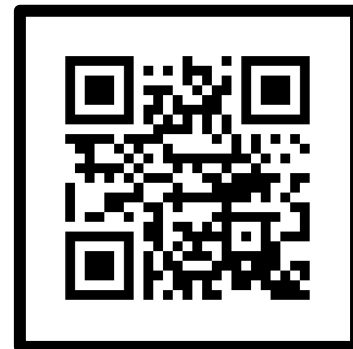
MELD-Na

Model for End-stage Liver Disease-Na



GEMA-Na
Gender-Equity Model for Liver Allocation-Na

GEMA (gema-transplant.com)



Calc: Gender-Equity model for Liver Allocation

Creatinine* 1.6 mg/dl
 Bilirubin* 7.8 mg/dl
 INR* 1.4
 Sodium* 137 mmol/L
 Urea 24 mg/dl
 Gender Female Male
 Age* 55 Years
 Ascites No Moderate or Severe Yes

RESULTS

RFH-GFR: **33.55**

GEMA: **24** GEMA-Na: **25**

MELD: **22** MELD-Na: **23**

Calculate Restart

Royal Free London
NHS Foundation Trust

<http://rfh-cirrhosis-gfr.ucl.ac.uk/>

Creatinine	Age
Urea	Sodium
INR	Sex
Ascites (mod-severe)	

HEPATOLOGY
HEPATOLOGY, VOL. 45, NO. 2, 2017

Development and Validation of a Mathematical Equation to Estimate Glomerular Filtration Rate in Cirrhosis: The Royal Free Hospital Cirrhosis Glomerular Filtration Rate





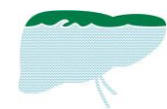
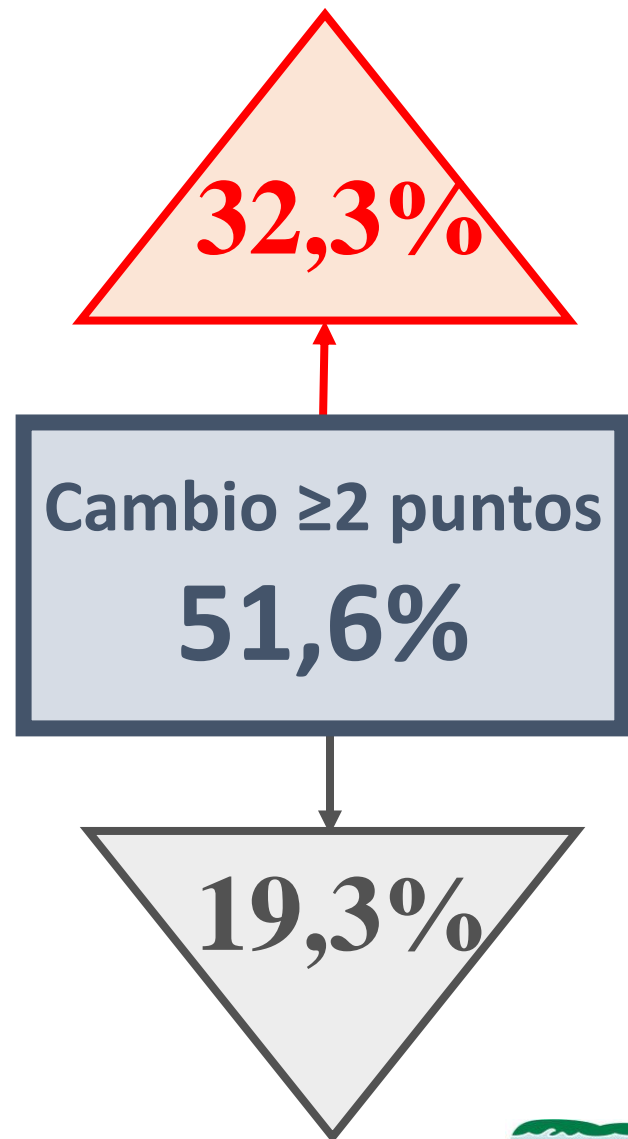
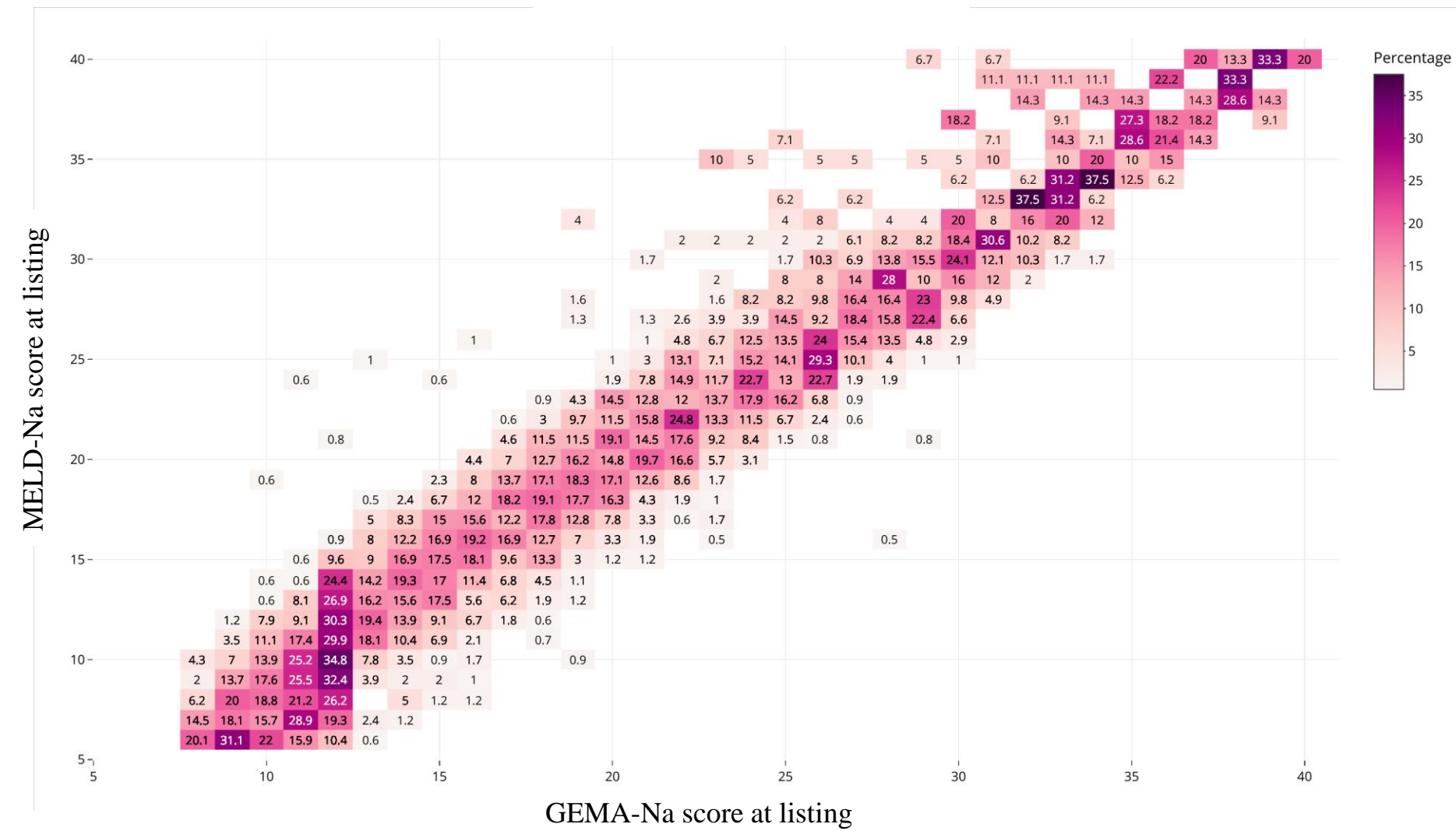
GEMA: discriminación

COHORT	N*	MELD-Na	MELD-3.0	GEMA-Na	<i>p</i> (vs -Na) <i>p</i> (vs 3.0)
Training (overall)	5,762	0.783 (0.755-0.810)	0.770 (0.740-0.780)	0.796 (0.769-0.823)	<i>p</i> =0.022 <i>p</i> <0.001
Training (women)	1,955	0.784 (0.739-0.829)	0.766 (0.718-0.815)	0.821 (0.781-0.860)	<i>p</i> <0.001 <i>p</i> <0.001
Internal validation (overall)	1,920	0.742 (0.686-0.797)	0.720 (0.657-0.784)	0.766 (0.715-0.818)	<i>p</i> =0.006 <i>p</i> =0.001
Internal validation (women)	623	0.779 (0.688-0.871)	0.763 (0.660-0.867)	0.802 (0.716-0.888)	<i>p</i> =0.087 <i>p</i> =0.164
External validation (overall)	1,638	0.745 (0.690-0.800)	0.749 (0.696-0.802)	0.774 (0.720-0.827)	<i>p</i> =0.014 <i>p</i> =0.008
External validation (women)	432	0.714 (0.592-0.835)	0.732 (0.625-0.839)	0.796 (0.698-0.895)	<i>p</i> =0.009 <i>p</i> =0.007



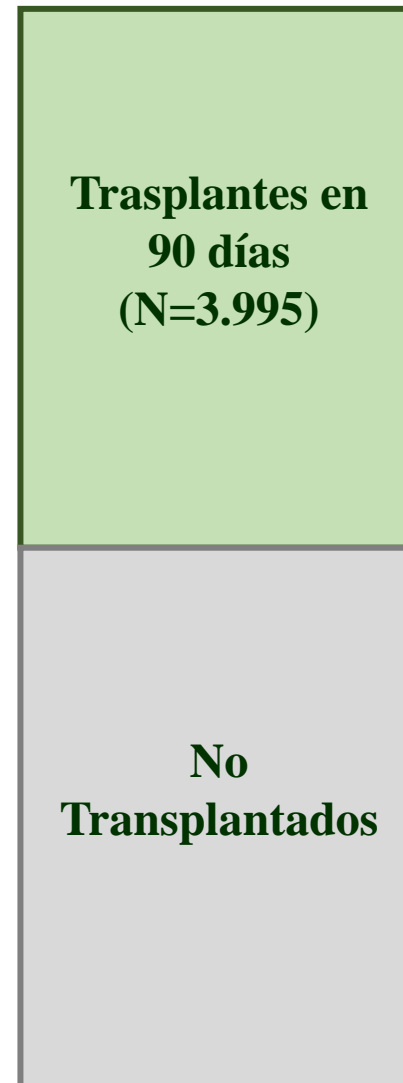


GEMA: Reclasificación

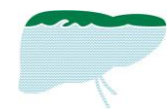
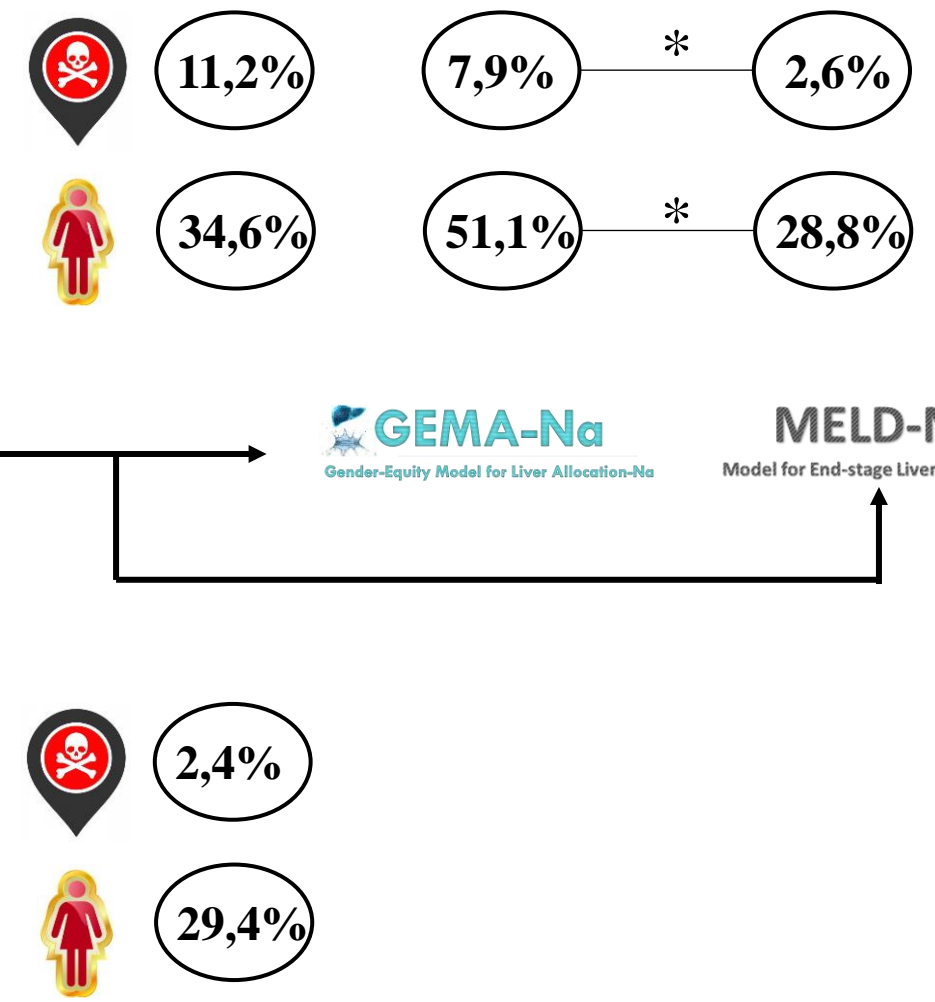
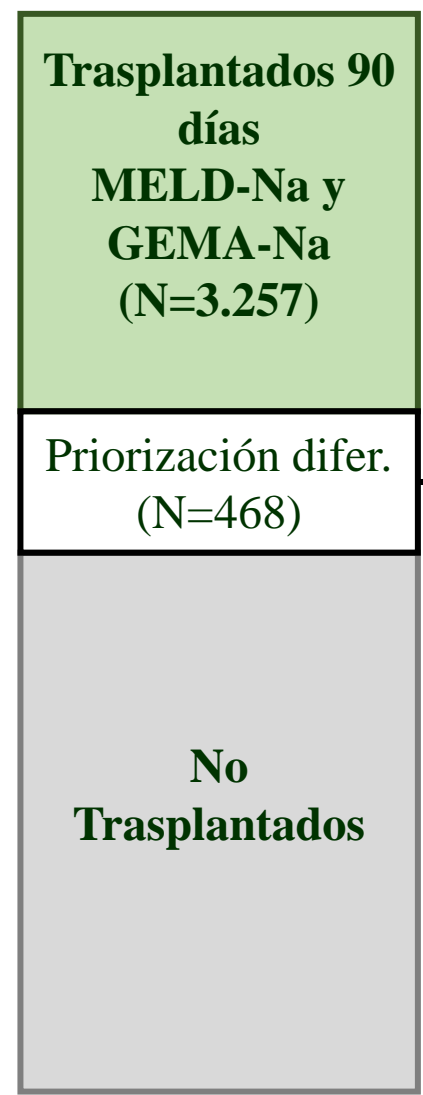
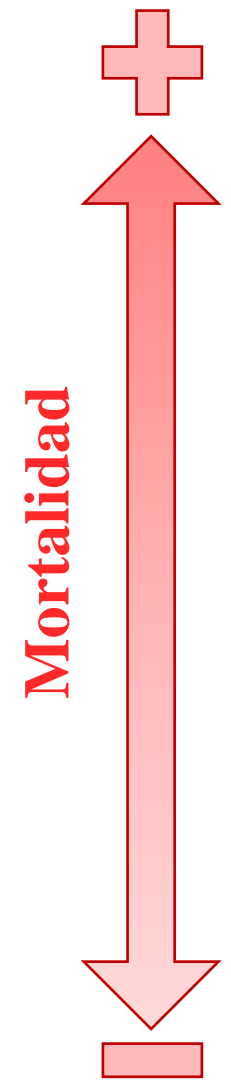
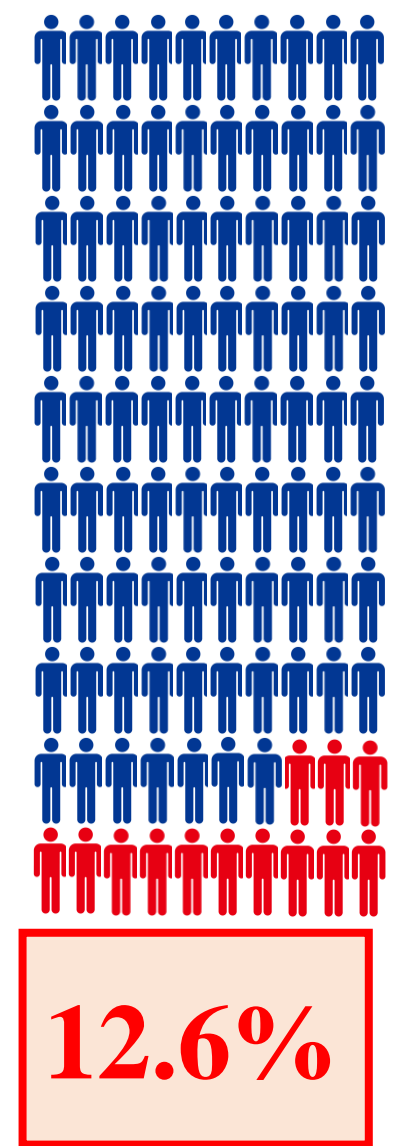




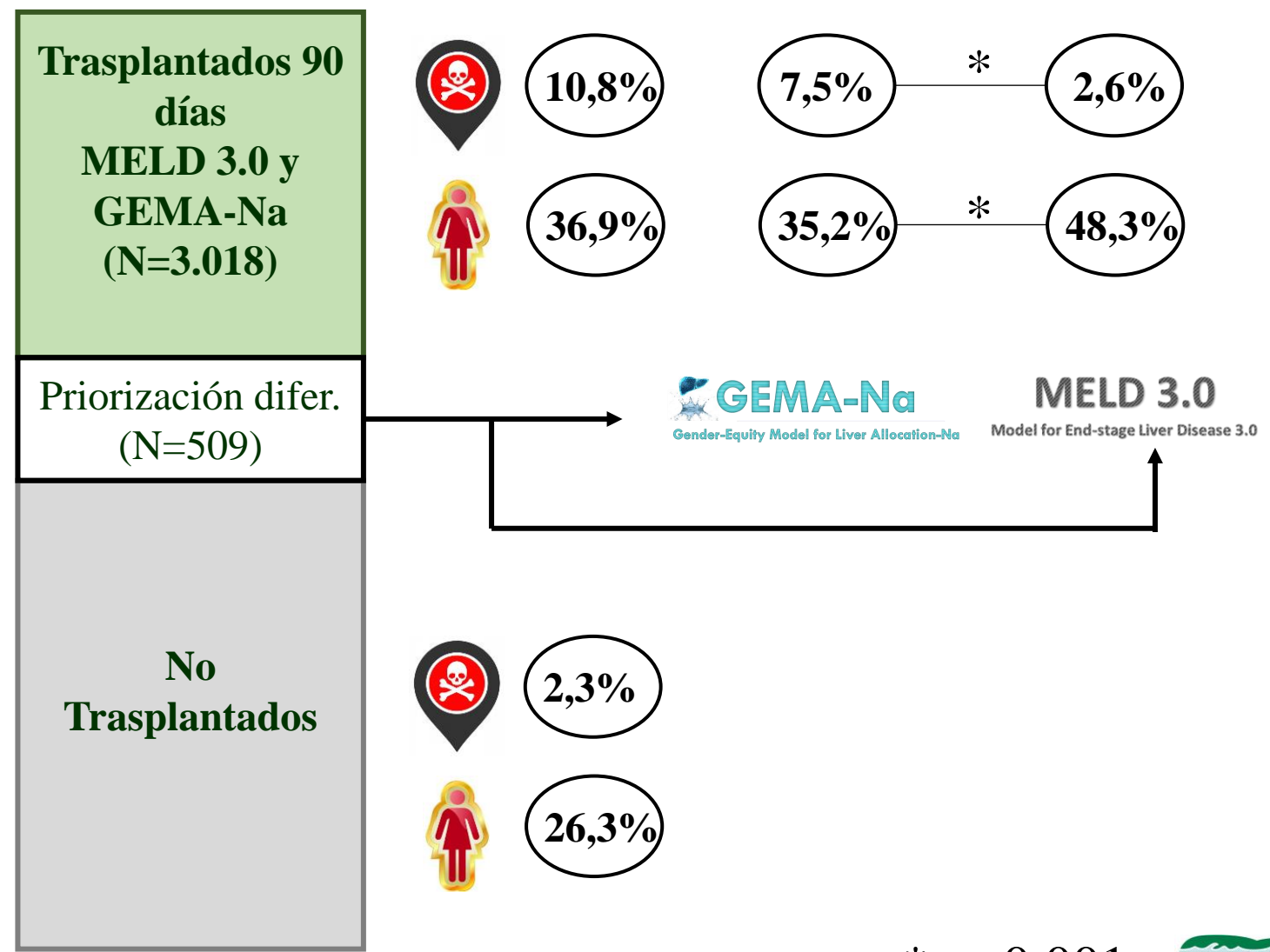
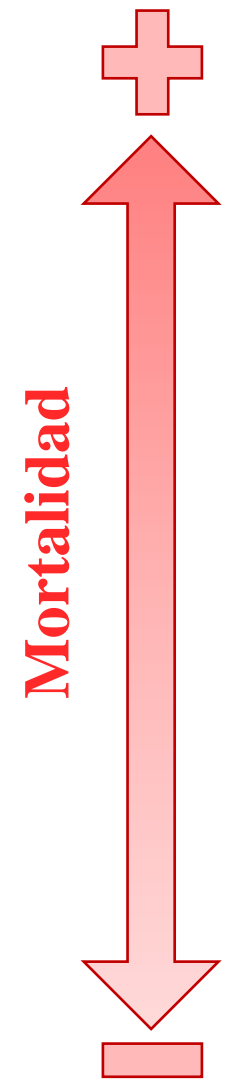
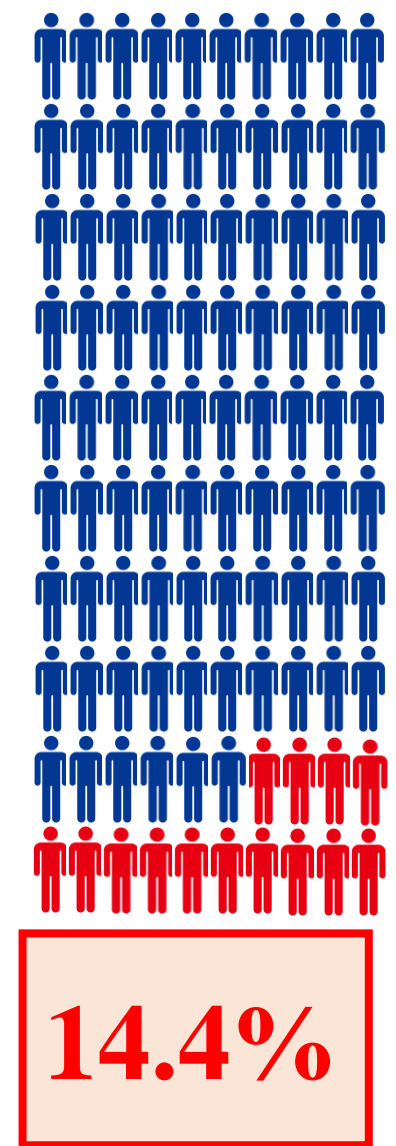
Priorización diferencial



Priorización diferencial (vs. MELD-Na)



Priorización diferencial (vs. MELD-3.0)



* $p < 0,001$



Muertes evitadas



GEMA-Na

Gender-Equity Model for Liver Allocation-Na

VS

MELD-Na

Model for End-stage Liver Disease-Na



1/21



1/8



GEMA-Na

Gender-Equity Model for Liver Allocation-Na

VS

MELD 3.0

Model for End-stage Liver Disease 3.0



1/19

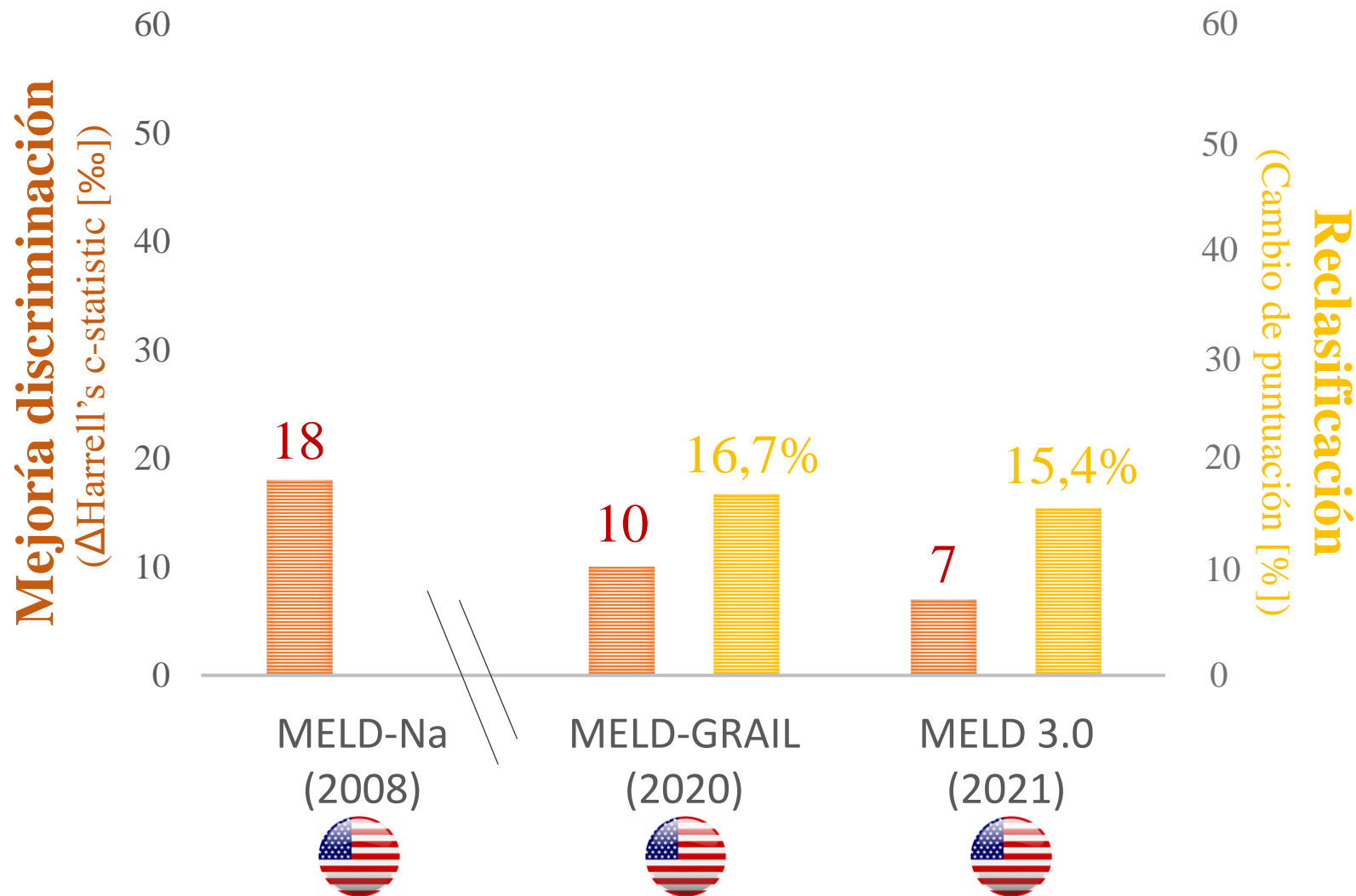


1/14



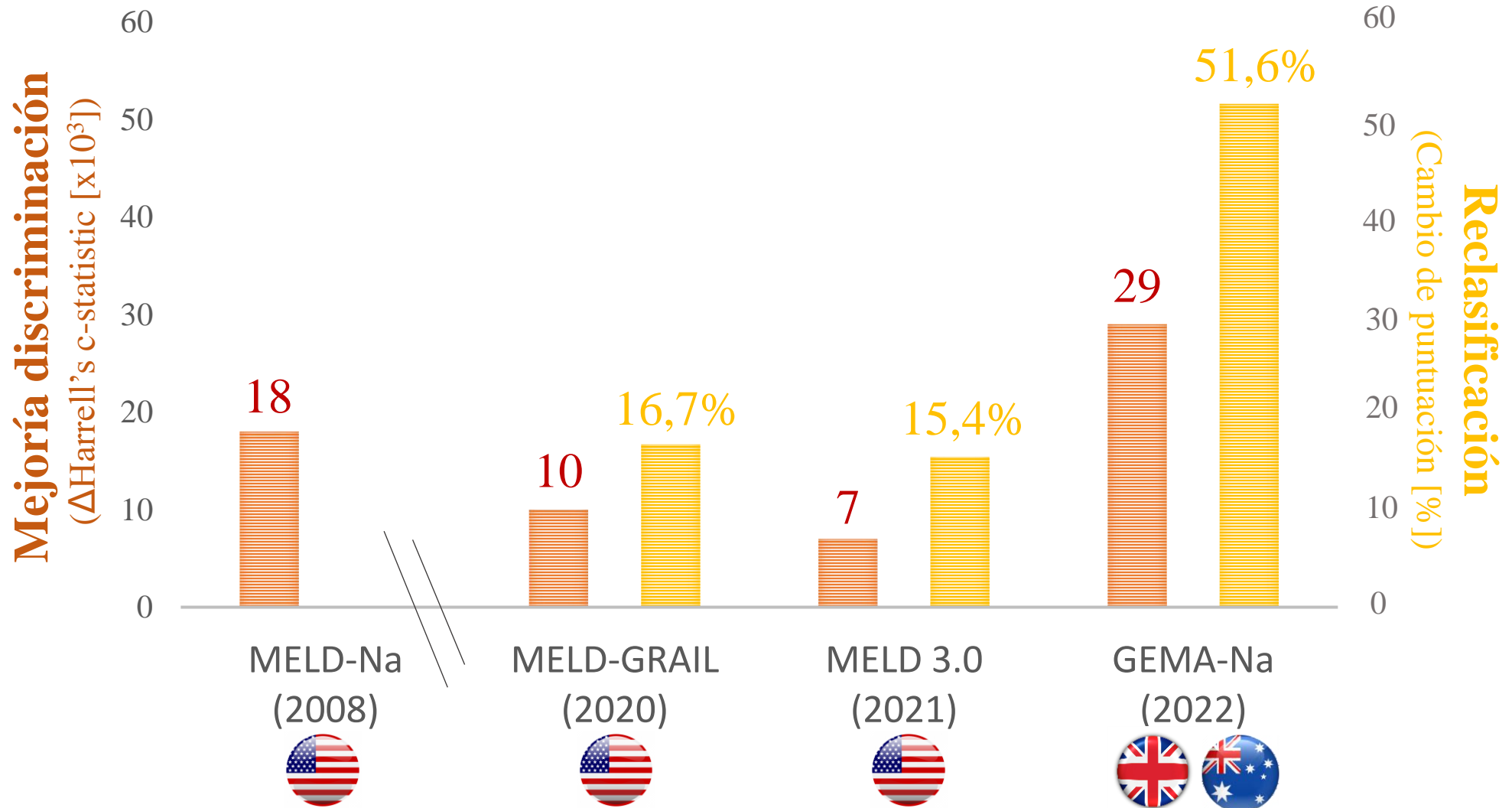


Comparación entre modelos





Comparación entre modelos

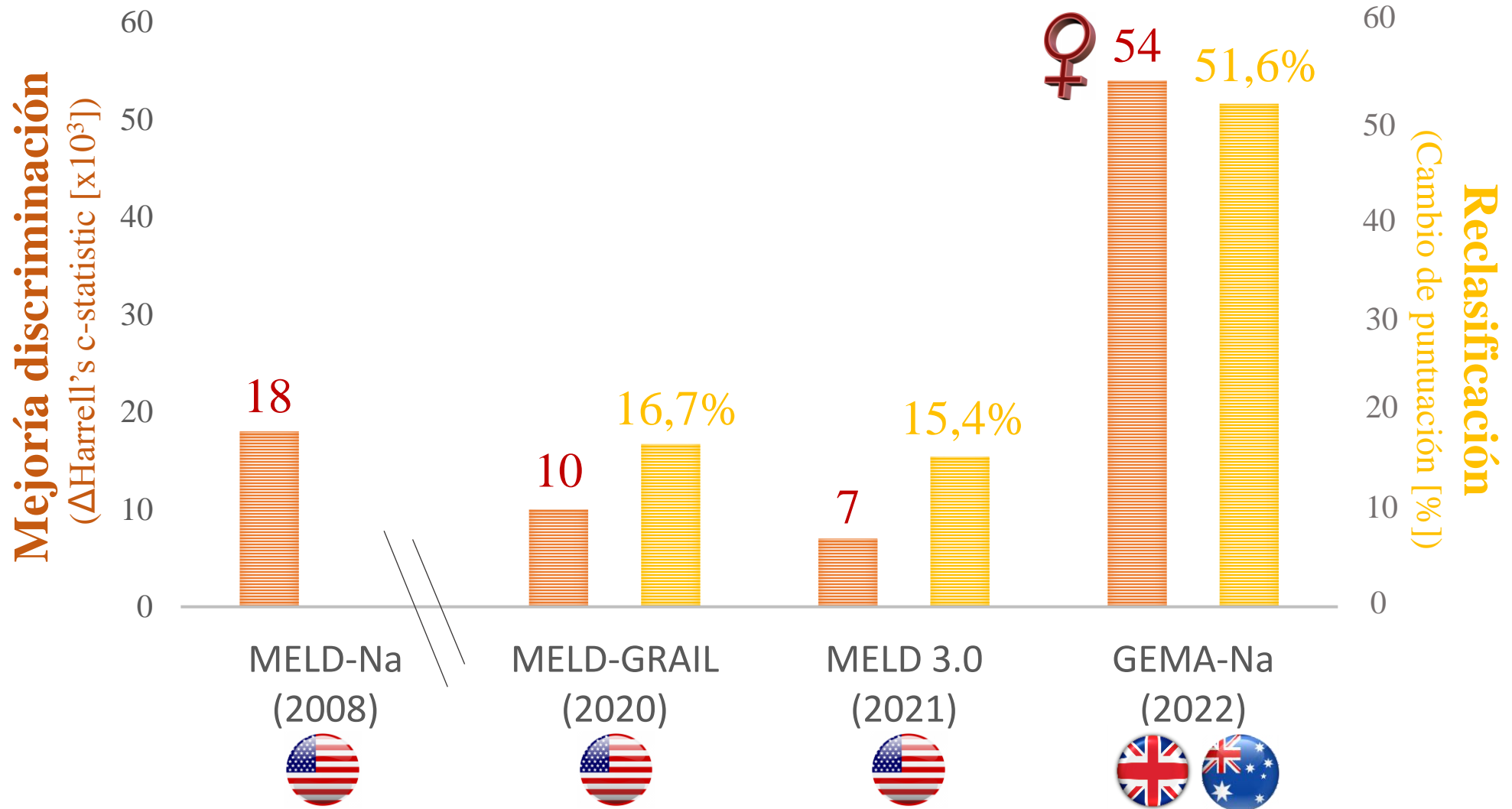


MELD-Na: Kim et al. *New Engl J Med* (2008); MELD-GRAIL: Asrani et al. *Hepatology* (2020); MELD 3.0: Kim et al. *Gastroenterology* (2021); GEMA: Rodríguez-Perálvarez et al. *The Lancet GH* (2023)





Comparación entre modelos

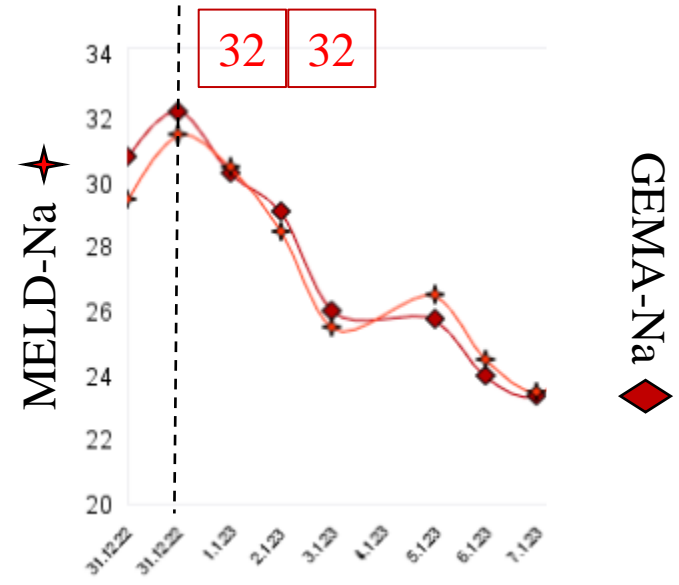




Caso clínico

Mujer de 61 años con sarcopenia y ascitis refractaria

Sepsis y
coagulopatía grave



TA 65/50
FC 119 lpm
Tª 37,8°C
FR 25 rpm
Encefalopatía grado II/IV



Noradrenalina
Ringer lactato
Piper/tazo
Parecentesis restrictiva



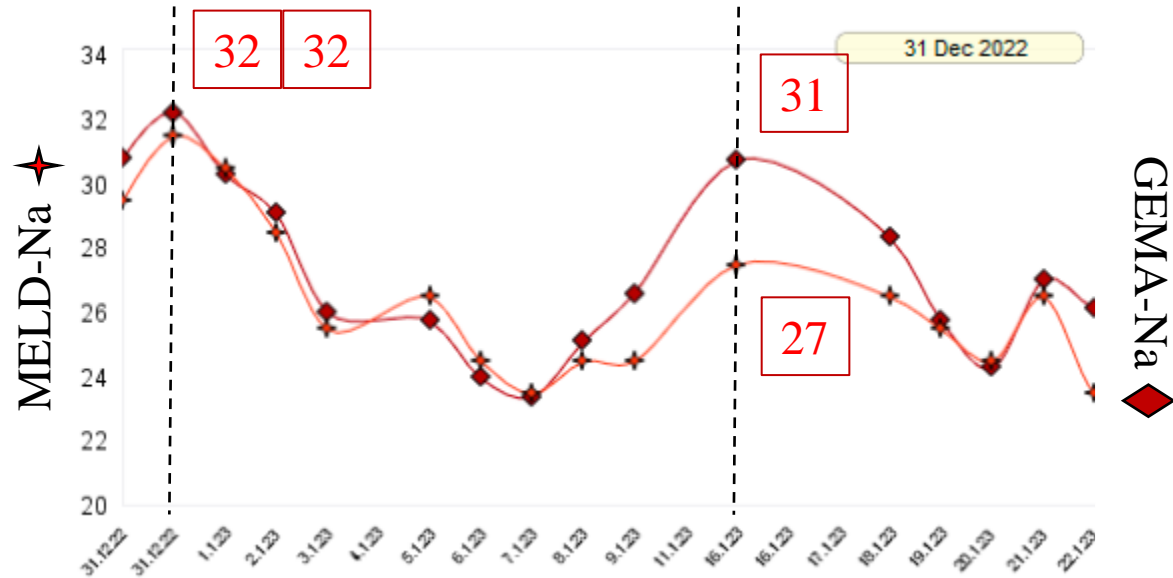


Caso clínico

Mujer de 61 años con sarcopenia y ascitis refractaria

Sepsis y
coagulopatía grave

Síndrome hepato-
renal



TA 95/60
 FC 87 lpm
 Tª 36,6°C
 FR 17 rpm
 Oligoanuria + emp. ascitis



Terlipresina (RCT)
 Albúmina
 Furosemida
 Nueva paracentesis 5L

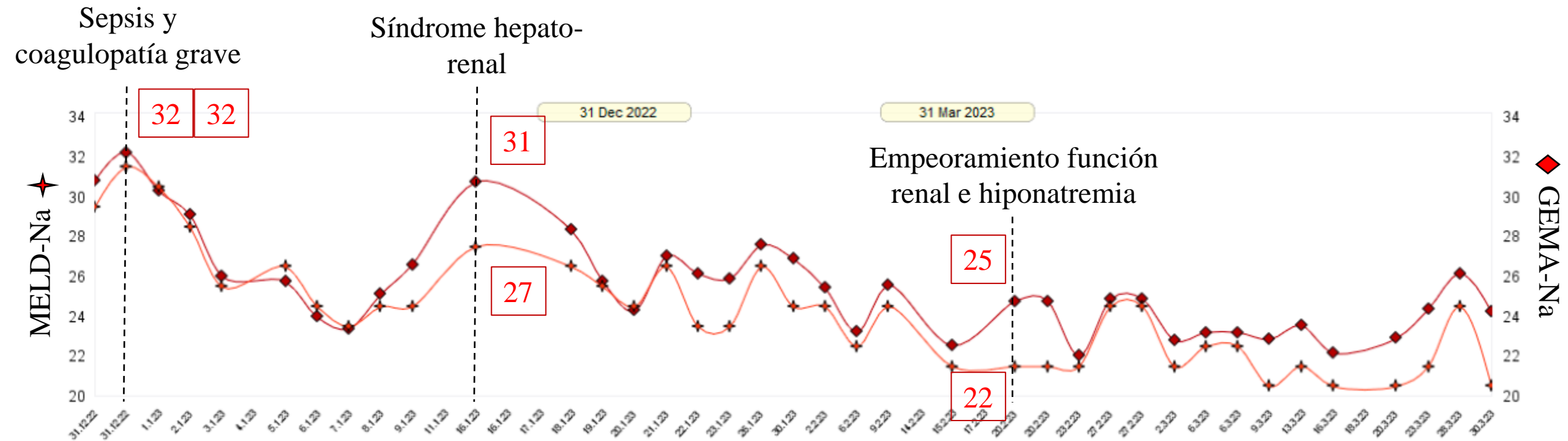


Cortesía del Dr. Avik Majumdar del Royal Prince Alfred Hospital, Sydney, Australia



Caso clínico

Mujer de 61 años con sarcopenia y ascitis refractaria





Received: 10 January 2023 | Revised: 10 August 2023 | Accepted: 2 September 2023

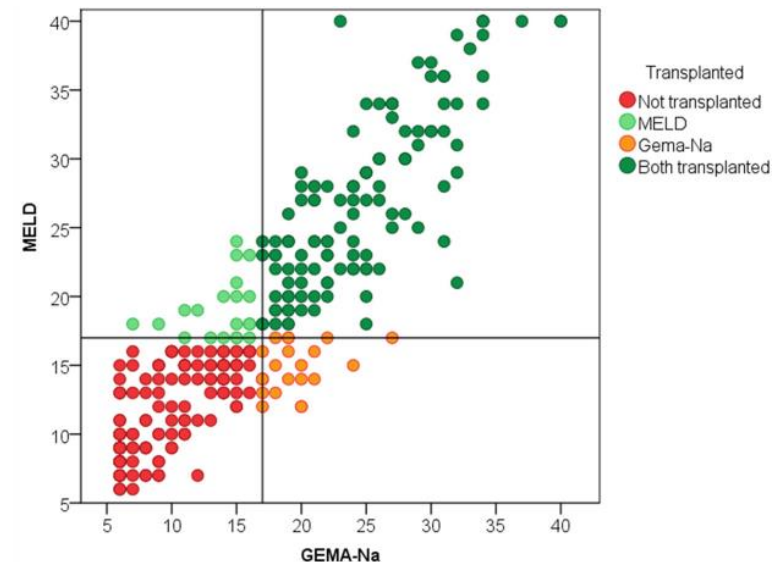
DOI: 10.1111/liv.15735

ORIGINAL ARTICLE



Superiority of the new sex-adjusted models to remove the female disadvantage restoring equity in liver transplant allocation

Giuseppe Marrone^{1,2} | Valerio Giannelli³ | Salvatore Agnes^{1,2} | Alfonso Wolfango Avolio^{1,2} | Leonardo Baiocchi⁴ | Giammauro Berardi³ | Giuseppe Maria Ettorre³ | Flaminia Ferri⁵ | Stefano Ginanni Corradini⁵ | Antonio Grieco^{1,2} | Nicola Guglielmo³ | Ilaria Lenci⁴ | Raffaella Lionetti⁶ | Gianluca Mennini⁵ | Martina Milana⁴ | Massimo Rossi⁵ | Gabriele Spoletini^{1,2} | Giuseppe Tisone⁴ | Tommaso Maria Manzia⁴ | Quirino Lai⁵



Scores	Brier skill score	Brier skill score (%)	Reclassification of transplanted cases, n (%)	Cases saved on the total number of dropouts
MELD	.333	Ref.	Ref.	Ref.
MELDNa	.280	+1.6	17/296 (5.7)	1 in 26
MELD 3.0 no albumin	.276	+1.7	17/296 (5.7)	1 in 26
Sex-adjusted MELDNa	.254	+2.4	19/296 (6.4)	1 in 13
MELD 3.0 albumin	.233	+3.0	13/296 (4.4)	1 in 13
GEMA-Na	.188	+4.4	36/296 (12.2)	1 in 9





Perspectivas futuras

Utilización del modelo GEMA basado en inteligencia artificial para corregir las disparidades de género en el acceso al trasplante hepático



FIS PI22/00312

HOSPITAL	IP
H. Virgen Rocío	Carmen Cepeda
H. Reina Sofía	M. Rodríguez
H. R. Málaga	Rocío González
H. Virgen Nieves	M. D. Espinosa
H. Lozano Blesa	Sara Lorente
H. Central Asturias	ML González D.
H. NS Candelaria	Elena Otón
H. M. Valdecilla	A. Cuadrado Lavín
H. Río Hortega	Carmen Alonso
H. Clinic	J. Colmenero
H. Bellvitge	Alba Cachero
H. Vall D'Hebrón	Itxarone Bilbao

HOSPITAL	IP
H. La Fe	Toya Aguilera
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H. A coruña	Francisco Suárez
H. Santiago	Santi Tomé
H 12 Octubre	Mónica Barreales
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H. Virgen Arrixaca	María L. Ortiz
CU Navarra	Amaya Redín
H. Cruces	Mikel Gastaca
ONT	Gloria De la Rosa






N=7.022
(2016-2021)
Validación GEMA y
modelos AI





Perspectivas futuras



MELD-3.0
OPTN | ORGAN PROCUREMENT AND
TRANSPLANTATION NETWORK 

GEMA-Na



MELD
MELD-Na



Consenso SETH 2024

Priorización en lista de espera de trasplante en España
26 de Abril de 2024... Os esperamos!!!



Manuel Rodríguez-Perálvarez

h02ropem@uco.es



@Rod_Peralvarez



[GEMA \(gema-transplant.com\)](http://gema-transplant.com)

Calc Gender-Equity model for Liver Allocation

Creatinine*	1.6	mg/dL
Bilirubin*	7.8	mg/dL
INR*	1.4	
Sodium*	137	mmol/L
Urea	24	mg/dL
Gender*	<input checked="" type="radio"/> Female <input type="radio"/> Male	
Age*	55	Years
Ascites	<input type="radio"/> No <input type="radio"/> Moderate or Severe <input checked="" type="radio"/> Yes	

Calculate Restart

RESULTS	
RFH-GFR	
33.55	
GEMA	GEMA-Na
24	25
MELD	MELD-Na
22	23

