

Development of an open-access web platform to visualise IMPROVEMENT study results and provide a calculator for outcomes based on individual patient data.

*Elisa Schirra¹, *Alfonso W. Avolio^{1,2}, Marco Maria Pascale¹, Quirino Lai³, Patrizia Burra⁴, Umberto Cillo⁵, Martin De Santibanes⁶, Mikel M. Gastaca⁷, Zhiyong Guo⁸, Hiroto Egawa⁹, Paulo N. Martins¹⁰, Gabriel Oniscu¹¹, Wojtek Polak¹², Mohamed Rela¹³, Cristiano Quintini¹⁴, Gonzalo Sapisochin^{15,16}, Julio Wiederkehr^{17, 18}, Umberto Baccarani¹⁹, Deniz Balci²⁰, Louise Barbier²¹, Ilka de Fatima Santana Ferreira Boin²², Felix Braun²³, Lucio Caccamo²⁴, Amedeo Carraro²⁵, Matteo Cescon²⁶, Zhishui Chen²⁷, Olga Ciccarelli²⁸, Luciano De Carlis²⁹, Fabrizio Di Benedetto³⁰, Burcin Ekser³¹, Giuseppe Maria Ettorre³², Deng Feiwen³³, Davide Ghinolfi³⁴, Salvatore Gruttadauria³⁵, John Hammond³⁶, Michal Grat³⁷, Zemin Hu³⁸, Sunhawit Junrungsee³⁹, Nguyen Quang Nghia⁴⁰, Xiaoshun He⁸, Takashi Ito⁴¹, Mickael Lesurtel⁴², Laura Llado⁴³, Bunthoon Noonthasoot⁴⁴, Jean Yves Mabrut⁴⁵, Daniel Maluf⁴⁶, Vincenzo Mazzaferro⁴⁷, Gilberto Mejia⁴⁸, Artem Monakhov⁴⁹, Silvio Nadalin⁵⁰, Brian M Nguyen⁵¹, Thamara Perera⁵², Domenico Pinelli⁵³, Marcos Vinicius Perini⁵⁴, Carlo Pulitano⁵⁵, Renato Romagnoli⁵⁶, Massimo Rossi⁵⁷, Ephrem Salame⁵⁷, Gupta Subhash⁵⁸, Surendran Sudhindran⁵⁹, Francesco Tandoi⁶⁰, Timucin Taner⁶¹, Giuliano Testa⁶², Giovanni Vennarecci⁶³, Marco Vivarelli⁶⁴, Roberta Angelico⁶⁵, Massimo Arcerito⁶⁶, Giammauro Berardi³², Mikhail Boldyrev⁴⁹, Yang Bo²⁷, Eliano Bonaccorsi-Riani²⁸, Marco Bongini⁴⁷, Jessica Bronzoni³⁴, Petru Bucur⁵⁷, Stefania Camagni⁵³, Francesca Caputo²⁶, Daniela Caracciolo³⁰, Davide Chiappori³², Lorenzo Cocchi⁴², Joris Couillero⁴⁵, Christopher S. Chandler⁶⁶, Michael Crawford⁵⁵, Giulia Cirillo⁵, Kristopher P Croome⁶⁷, Femke De Goeij¹², Jeroen de Jonge¹², Andrea Della Penna⁵⁰, Elaine Cristina De Ataide²², Riccardo De Carlis²⁹, Nicola De Stefano⁵⁶, Stefano Di Sandro³⁰, Rajesh Dey⁵⁸, Daniele Dondossola²⁴, Emanuele Felli⁵⁷, Daniele Ferraro⁶³, Michael Fink⁵⁴, Michele Finotti⁶², Marta Garcia-Guix⁴⁹, Vasanthakumar Gunasekaran¹³, Do Hai Dang⁴⁰, Jan Paul Gundlach²³, Amanda Habermann¹¹, Noah Kelleher¹⁰, Elvan Onur Kirimker⁶⁸, Jagadeesh Krishnamurthy⁵⁸, Emilia Kruk³⁷, Shekhar A. Kubal³¹, Robert Jones⁵⁴, Jacopo Lanari⁵, Andrea Lauterio²⁹, Ian Leipnitz²¹, Songming Li⁸, Andrew Massutti¹⁸, Fabio Melandro³⁴, Luca Miele⁶⁹, Isabel Miglior³⁶, Stephanie Nguyen⁵¹, Duilio Pagano³⁵, Tommaso Partipilo¹, Madhukar Patel⁷⁰, Arkaitz Perfecto Valero⁷, Damiano Patrono⁵⁶, Niv Pencovici⁶¹, Jai Prasad¹⁹, Riccardo Pravisani¹⁹, Ashwin Rammohan¹³, Maria E. Ramos⁴⁸, Matteo Ravaioli²⁶, Maria Rendina⁶⁰, Roberta Rossi⁶⁴, Rebeca Sanabramateos⁵², Nair Saraswathy⁵⁹, Patrizia Silvestri¹, Qiang Sun³⁸, Li-Ying Sun⁷¹, Asara Thepbunchonchai³⁹, Luca Toti⁶⁵, Mathias Vidgren¹¹, Paola Violi²⁵, Claire West⁵⁵, Yoichiro Uchida⁴¹, Athaya Vorasitha⁴⁴, Jimmy Walker Uno⁶, Liu Ying³³, Gloria Zaffaroni⁵³, Zhi-Jun Zhu⁷¹, Zieniewicz Krzysztof⁶⁷, Daniela Markovic⁶⁶, Diana Giannarelli⁷², Tina Pasciuto^{73, 74}, Vatche G. Agopian⁶⁶

*Equally contributed.

[§] Members of the International Steering Committee.

1. General Surgery and Transplantation Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS; Rome, Italy
2. Università Cattolica del Sacro Cuore; Roma, Italy
3. Hepato-biliary-pancreatic and Liver Transplant Unit, Department of Surgery, Sapienza University; Roma, Italy
4. Multivisceral Transplant Unit, Azienda Ospedaliera Universitaria; Padua, Italy
5. General Surgery 2 Hepatobiliopancreatic Surgery and Liver Transplant Unit, Azienda Ospedaliera Universitaria; Padua, Italy
6. Cirugía Hepato-Bilio-Pancreática, Trasplante Hepático, Hospital Italiano de Buenos Aires; Buenos Aires, Argentina
7. Unidad de Cirugía Hepatobiliar y Trasplante Hepático, Hospital Universitario Cruces-Bilbao; Bilbao, Spain
8. Organ Transplant Center, The First Affiliated Hospital of Sun Yat-sen University; Guangzhou, China
9. Hamamatsu Rosai Hospital, Shogen-cho, Chuoku, Hamamatsu; Shizuoka, Japan
10. Transplant Division, Dept of Surgery, University of Massachusetts; Worcester, MA, USA
11. Transplant Division, Department of Clinical Science, Intervention and Technology, Karolinska Institutet; Stockholm, Sweden
12. Department of Surgery, Division of HPB and Transplant Surgery, Erasmus MC Transplant Institute, University MC Rotterdam; Rotterdam, the Netherlands
13. Dr. Rela Institute & Medical Centre; Chennai, India
14. Department of Liver Transplantation, Cleveland Clinic; Cleveland, OH, USA
15. Multiorgan Transplantation, Toronto General Hospital; Toronto, Canada
16. Cirugía General y del Aparato Digestivo, Trasplante Hepático, Hospital Universitario Vall d'Hebron; Barcelona, Spain
17. Federal University of Paraná; Blumenau, Brazil
18. Liver Transplant Division, Hospital Santa Isabel; Blumenau, Brazil
19. Liver-Kidney Transplant Unit, Università di Udine – ASUFC; Udine, Italy
20. Department of Surgery and Transplantation, Bahcesehir University School of Medicine, Medical Park Goztepe Hospital; Istanbul, Turkey
21. NZ Liver Transplant Unit - Te Toka Tumai, Auckland City Hospital; Auckland, New Zealand
22. Liver Transplantation Unit, University of Campinas-UNICAMP, San Paolo, Brazil
23. Sektion Klinische Transplantationsmedizin, Klinik für Allgemeine, Viszeral, Thorax, Transplantations und Kinderchirurgie, Universitätsklinikum Schleswig-Holstein, Campus Kiel
24. General and Liver Transplant Surgery, Fondazione IRCCS Cà Grande Ospedale Maggiore Policlinico Milano; Milan, Italy
25. Liver Transplant Unit, University Hospital Trust of Verona; Verona, Italy
26. General Surgery and Transplant Unit, Azienda Ospedaliero-Universitaria di Bologna, Policlinico di Sant'Orsola; Bologna, Italy
27. Laboratory of Organ Transplantation, Institute of Organ Transplantation, Tongji Hospital; Wuhan, China
28. Service de Chirurgie et Transplantation Abdominale, Cliniques Universitaires Saint-Luc, Louvain, Belgium
29. General Surgery and Abdominal Transplantation Unit, University of Milano-Bicocca and Niguarda-CàGranda Hospital; Milan, Italy

30. Hepato-Pancreato-Biliary Surgery and Liver Transplantation Unit, University of Modena and Reggio Emilia; Modena, Italy
31. Division of Transplant Surgery, Department of Surgery, Stritch School of Medicine, Loyola University Chicago; Chicago, IL, USA
32. Department of General Surgery and Transplantation Unit, Azienda Ospedaliera San Camillo Forlanini; Roma, Italy
33. Department of Hepatopancreatic Surgery, First People's Hospital of Foshan; Foshan, China
34. Division of Hepatic Surgery and Liver Transplantation, University of Pisa Hospital; Pisa, Italy
35. Abdominal Transplantation, IRCCS ISMETT - UPMC; Palermo, Italy
36. HPB and Transplant Surgery, Newcastle Hospital NHS Foundation Trust; Newcastle, UK
37. Department of General, Transplant and Liver Surgery, Medical University of Warsaw, Poland
38. General Surgery 1, Zhongshan People's Hospital; Zhongshan, China
39. Division of Hepato-Biliary-Pancreas Surgery, Chiang Mai University; Chiang Mai, Thailand
40. Organ Transplantation center, Viet Duc University Hospital; Hanoi, Vietnam
41. Dept of Surgery, Graduate School of Medicine, Kyoto University; Kyoto, Japan
42. Department of HPB Surgery & Liver Transplantation, Hôpital Beaujon, Université Paris Cité, Paris, France
43. Unitat d'Hepatologia, Hospital Universitari de Bellvitge, Barcelona, Spain
44. Department of Surgery, Faculty of Medicine, Chulalongkorn University; Bangkok, Thailand
45. Department of General Surgery and Liver Transplantation, Hôpital de la Croix-Rousse, Hospices Civils de Lyon, Lyon, France
46. Department of Surgery, University of Maryland; Baltimore, MD, USA
47. General Surgery and Liver Transplantation Unit, University of Milan and National Cancer Institute, IRCCS; Milan, Italy
48. Transplant Surgery, Fundacion CardioInfantil; Bogotá, Colombia
49. Surgical Department #2 (Liver Transplantation), National Medical Research Center of Transplantation and Artificial Organs named after V.I. Shumakov; Moscow, Russia
50. Transplantationscentrums und HB-Chirurgie, Universitätsklinik für Allgemein-, Viszeral- und Transplantationschirurgie Universitätsklinikum Tübingen, Germany
51. MedStar Georgetown Transplant Institute, MedStar Georgetown University Hospital; Georgetown, Washington DC, USA
52. Transplant Surgery, Queen Elizabeth Hospital; Birmingham, UK
53. Dept of Organ Failure and Transplantation, ASST Papa Giovanni XXIII; Bergamo, Italy
54. Department of Surgery, Austin Health - Medicine Dentistry and Health Sciences, The University of Melbourne; Melbourne, Australia
55. Transplantation and HPB Surgery, University of Sydney, Royal Prince Alfred Hospital; Sydney, Australia
56. General Surgery 2U, Liver Transplantation Center, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino; Torino, Italy
57. Pôle Pathologies Digestives et Endocriniennes, Service de Chirurgie Digestive, Oncologique et Endocrinienne, Transplantation Hépatique, CHU Tours; Tours, France
58. Department of Liver Transplant and HPB Surgeries, Max Super Speciality Hospital; Saket, New Delhi, India
59. Dept of GI Surgery, Amrita Institute of Medical Sciences (Amrita Hospital); Kochi, India
60. Hepatobiliary Surgery and Liver Transplantation, AOU Policlinico Consorziale di Bari; Bari, Italy
61. Center for Transplantation and Clinical Regeneration, Mayo Clinic; Rochester, MN, USA
62. Abdominal Transplant, Baylor Scott & White, All Saints Medical Center & Baylor University Medical Center, Ft. Worth & Dallas, TX, USA
63. Dept. Hepato-Biliary Surgery and Liver Transplant center, A.O.R.N.A. Cardarelli; Napoli, Italy
64. Hepatobiliary and Abdominal Transplantation Surgery, Ancona Hospital, Italy
65. HPB and Transplant Unit, Department of Surgical Sciences, University of Rome Tor Vergata; Rome, Italy
66. Division of Liver and Pancreas Transplantation, Department of Surgery, David Geffen School of Medicine at UCLA; Los Angeles, USA
67. Division of Transplant Surgery, Department of Transplant, Mayo Clinic; Jacksonville, FL, USA
68. Liver Transplantation Unit, Department of General Surgery, Faculty of Medicine, Ankara University; Ankara, Turkey
69. Department of Medicine, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS; Rome, Italy
70. Liver Transplantation Unit, UT Southwestern Medical Center; Dallas, TX, USA
71. Liver Transplantation Center, National Clinical Research Center for Digestive Diseases, Beijing Friendship Hospital, Capital Medical University, Beijing, China
72. Department of Epidemiology and Biostatistics, Fondazione Policlinico Universitario Agostino Gemelli, IRCCS, Rome, Italy
73. Hygiene Unit, University Department of Life Sciences and Public Health, Università Cattolica Del Sacro Cuore, Rome, Italy
74. Research Core Facility Data Collection G-STeP, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background

The IMPROVEMENT study is a global project aimed at providing a snapshot of liver transplant (LT) risk factors and predicting outcomes using multivariable algorithms. A manuscript with the study results has been submitted to a journal for peer review and publication. To date, nor a web platform to describe the propensity to the risk and the implementation of mitigation strategies in LT patients nor a global algorithm with prognostic factors predictive of outcome have been developed.

Methods

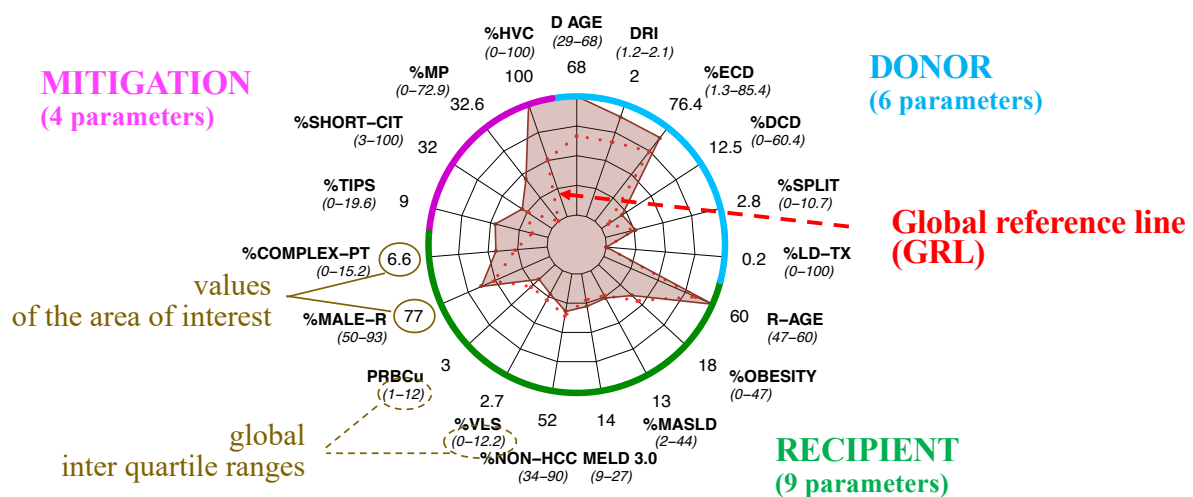
The IMPROVEMENT study enrolled 5218 patients from Europe, Asia, Oceania, North America, and South America. Patients were recruited in a retrospective cohort for LTs performed from 2017–2019 and in a

prospective cohort for those performed from July 2022 to December 2023. The median follow-up was 56 months (IQR 37-72).

The study focused on donor and recipient risk factors identified according to the literature (visualised with the radar graphs) and includes four prognostic algorithms developed according to stepwise logistic regression analysis: 1. mortality at 90-day, 2. mortality at 365-day, mortality at 730-day and 4. high complication rate according to Comprehensive Complication Index ≥ 72 .

A web-based platform, available also on smartphones, has been developed to divulge the results of the study, to allow easy comparison of donor-recipient profiles among macroregions, countries, and individual centres and to allow individual predictions according to the prognostic algorithms. The website is available online as a work-in-progress at *improvementstudy.pages.dev*.

Figure 1 illustrates a radar graph example, while Figure 2 illustrates the website's content.



The parameters are grouped into three blocks (donor factors, light blue; recipient factors, green; mitigation strategies, pink). The values of the area of interest are shown on the outer arc. For each parameter, the global inter quartile range is reported in brackets. Values are compared with the values shown in red on the dotted line that constitute the global reference values.

The global reference line (GRL, red-dotted line) summarises the weighted medians. The GRL are 55 for Donor-AGE (D-AGE), 1.8 for Donor Risk Index (DRI), 64% for Extended Criteria Donors (ECD), 4% for Donors from Circulatory Death (DCD), 2.7% for SPLIT, 0.1% for Living Donor Liver Transplant (LD-LT), 58 for Recipient-AGE (R-AGE), 21% for OBESITY, 12% for Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD), 13 for Model for End-stage Liver Disease score (MELD 3.0), 54% for % non-hepatocellular carcinoma (NON-HCC), 3.4% for Ventilatory Life-Support (VLS), 4 for PRBCu, 72% for MALE-Recipient (MALE-R), 4.1% for complex portal vein thrombosis (COMPLEX-PT), 2.7% for Transjugular Intrahepatic Portal Shunt (TIPS), 27% for short-Cold Ischemia Time (SHORT-CIT), 0% for machine perfusion (MP), 51% for High Volume Centre (HVC, ≥ 65 cases per year). The illustrative radar refers to the Italian prospective data collection (2022-2023).

Figure 1 – Radar graph example (Italy, prospective data collection) illustrating the different components and variable definitions.

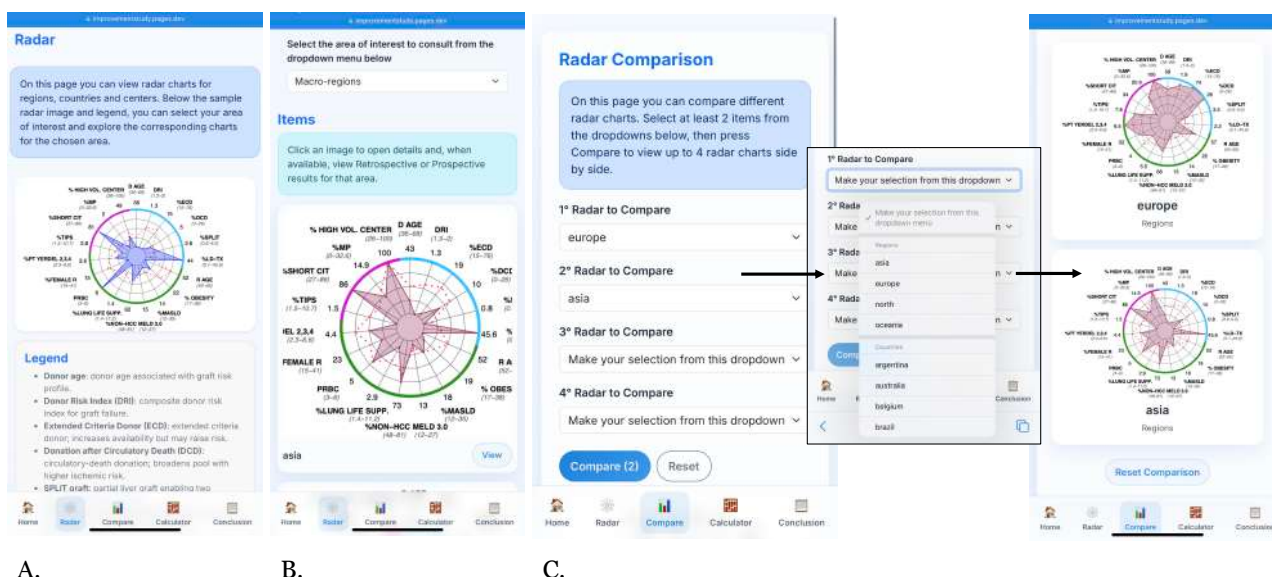


Figure 2 – Screenshots from the website. A. Example of a radar with the definition of each variable plotted. B. Selection example of a radar graph, selecting a macro-region or a country from the dropdown menu (e.g. Asia) C. Example of a comparison between two macro-regions via selection from the dropdown menu (e.g. Europe vs. Asia).

Expected results

After peer review and publication, the predictive algorithms will be available online and will allow risk estimation for the area of interest. Users will also be able to enter a few parameters for a single patient or for a group of patients (e.g., patients transplanted at a given center over x months), and the platform will instantly return their mortality and complication rates. The platform will allow comparison between the real case and cases registered on the IMPROVEMENT study in an area of interest. Finally, data concerning access to the website will provide information about the users' geographic location, to evaluate worldwide use.

Discussion

The platform currently illustrates part of the results of the IMPROVEMENT study and allows visualisation of patterns of the geographical area of interest. The user can visualize radar graphs illustrating the demographics of patients transplanted in a certain area. Each graph summarise 6 parameters related to the donor risk, 9 parameters related of the recipient risk and 4 parameters related to the mitigation strategies.

Data can be visualized according to three levels: (1) the geographic macroregion (Europe, Asia, Oceania, North America, and South America), (2) the country level (Italy, France, Spain, Germany, UK, Netherlands, Sweden, Belgium, Poland, Turkey, Russia, China, India, Vietnam, Thailand, Japan, Australia, New Zealand, USA, Brazil, Colombia, Argentina), and (3) the 82 patient series belonging to 61 centers.

Comparison among different geographical regions allows visualization of the different approaches to donor and recipient risk factors and mitigations strategies.

The prognosis calculator, once validated, will allow the risk-forecast of single patients and allow the visualisation of various scenarios according to donor-recipient match.