

# Ethical Decisions in Transplantation

*P.-A. Clavien*

Department of Surgery  
University Hospital Zurich

- **Determination of death**
- **Allocation of organs**
- **Living donation**
- **Selection of patients for transplantation**
- **Drug abuse / compliance**
- **Retransplantation**



# Determination of brain death

## Ethic of donors

- Cerebral and brain stem functions must be absent
- The cause of the lack of brain functioning must be determined to be **irreversible**
- The absence of all brain function must have **persisted** during a period of observation

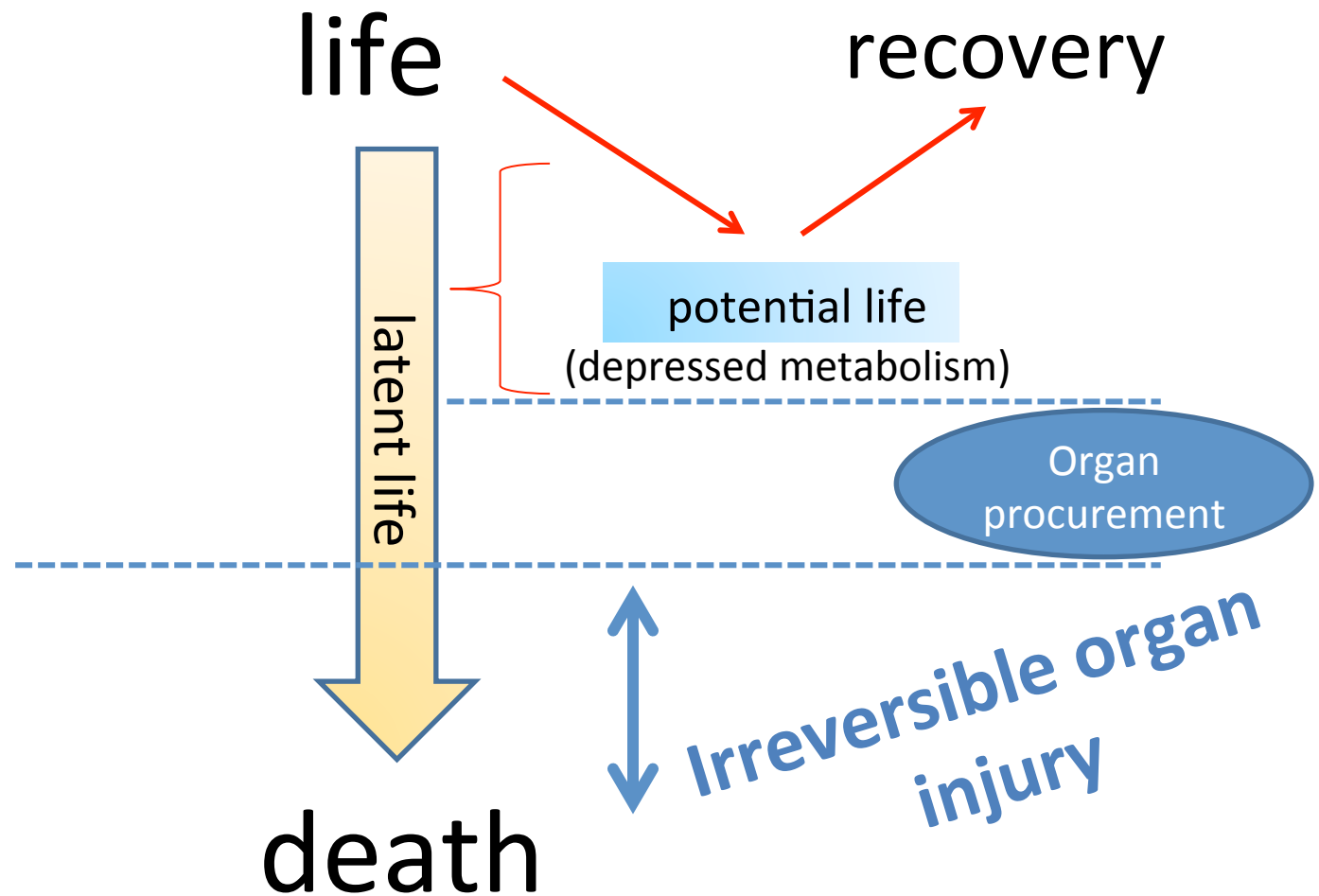
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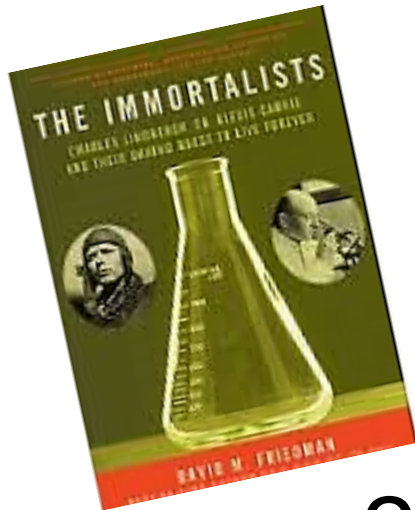
# Definition of biological life

Alexis Carrel „the secret of life 1912“



# The secret of life, A. Carrel

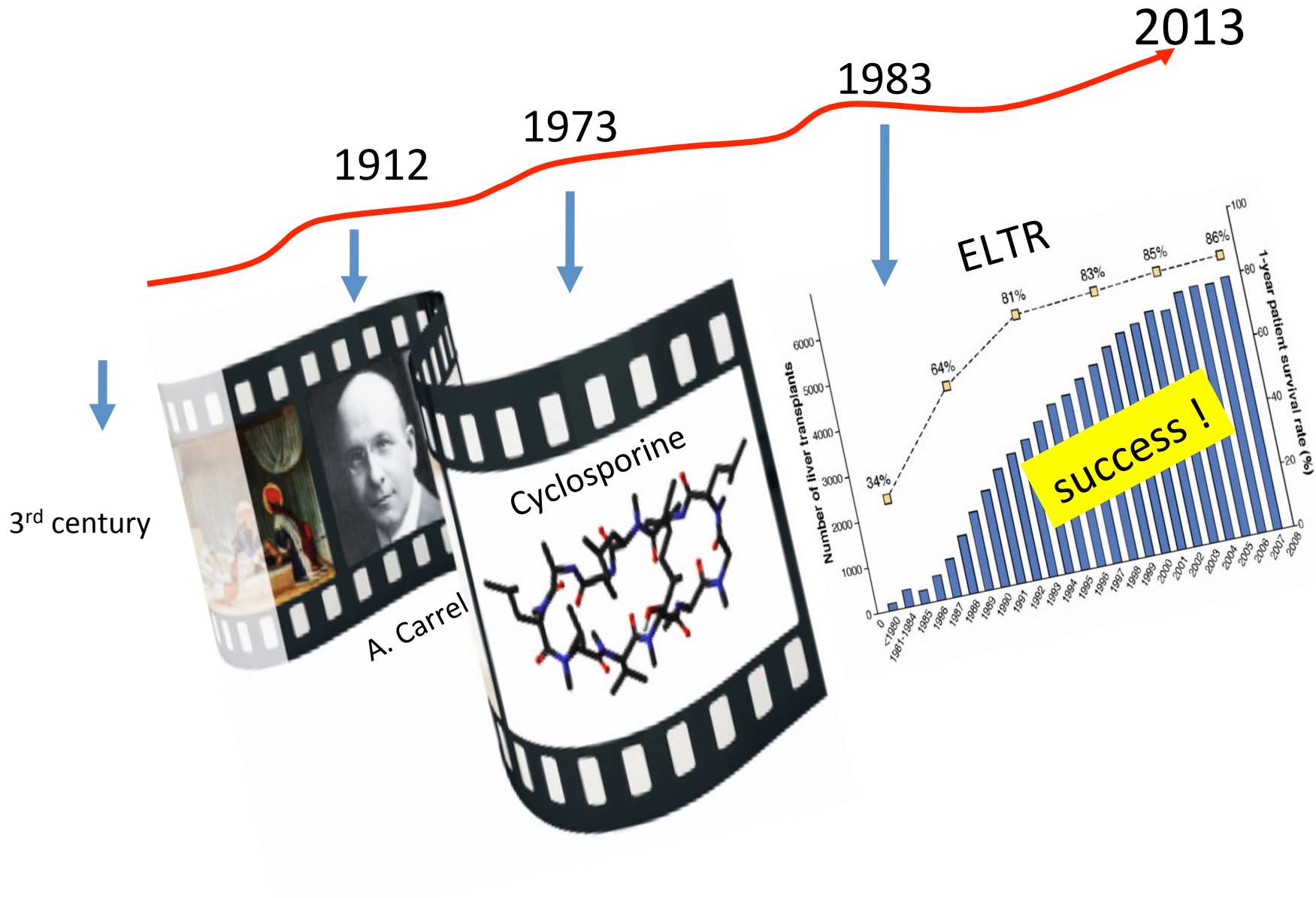
'If it were possible immediately after death to transplant the tissues and organs. . . into other organisms of identical character, no elemental (meaning no irreversible) death would occur, and all the constituent part of the body would continue to live'



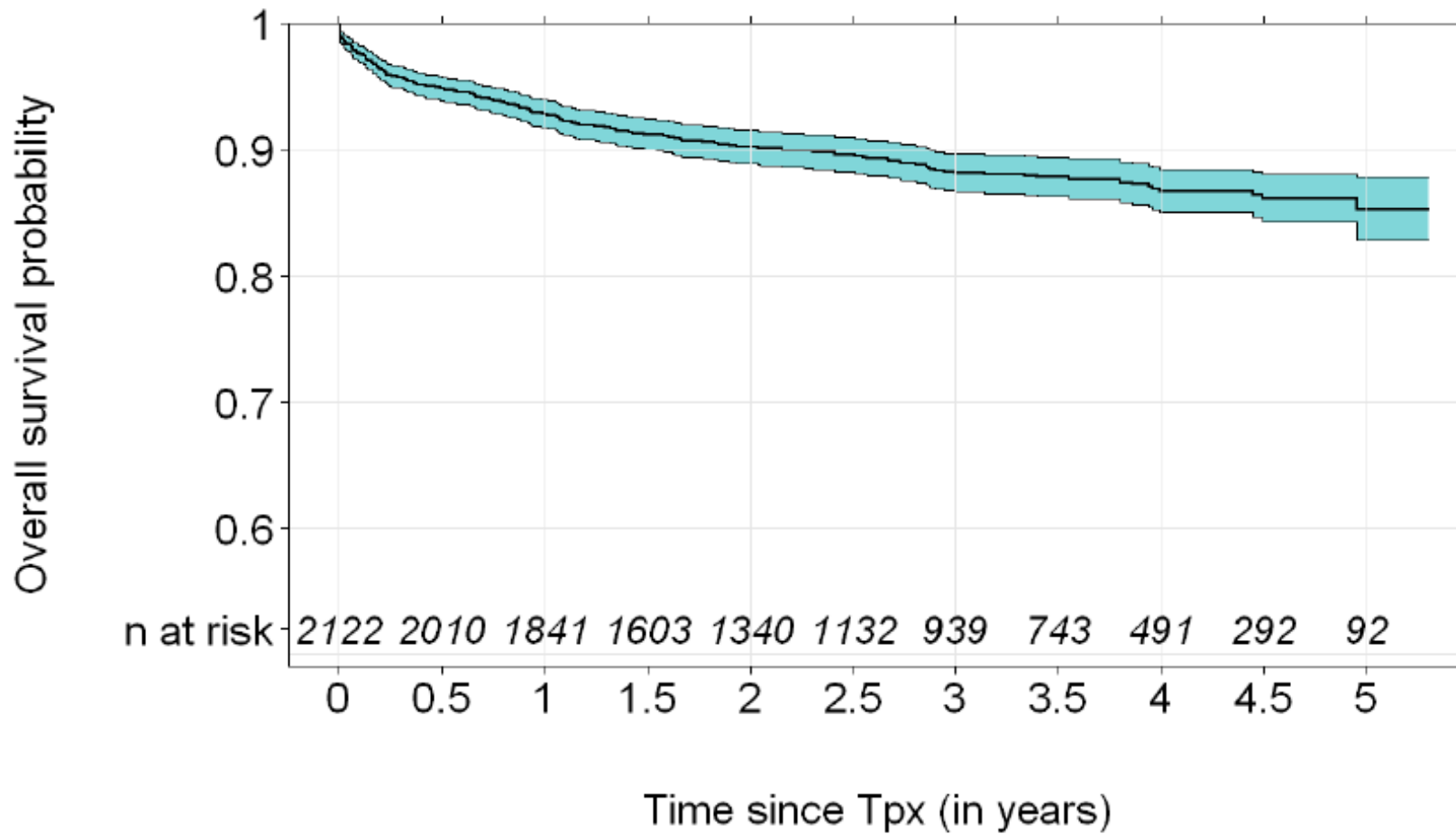
Ethic of recipients?

organ transplantation after cardiac death (DCD)

# Organ transplantation

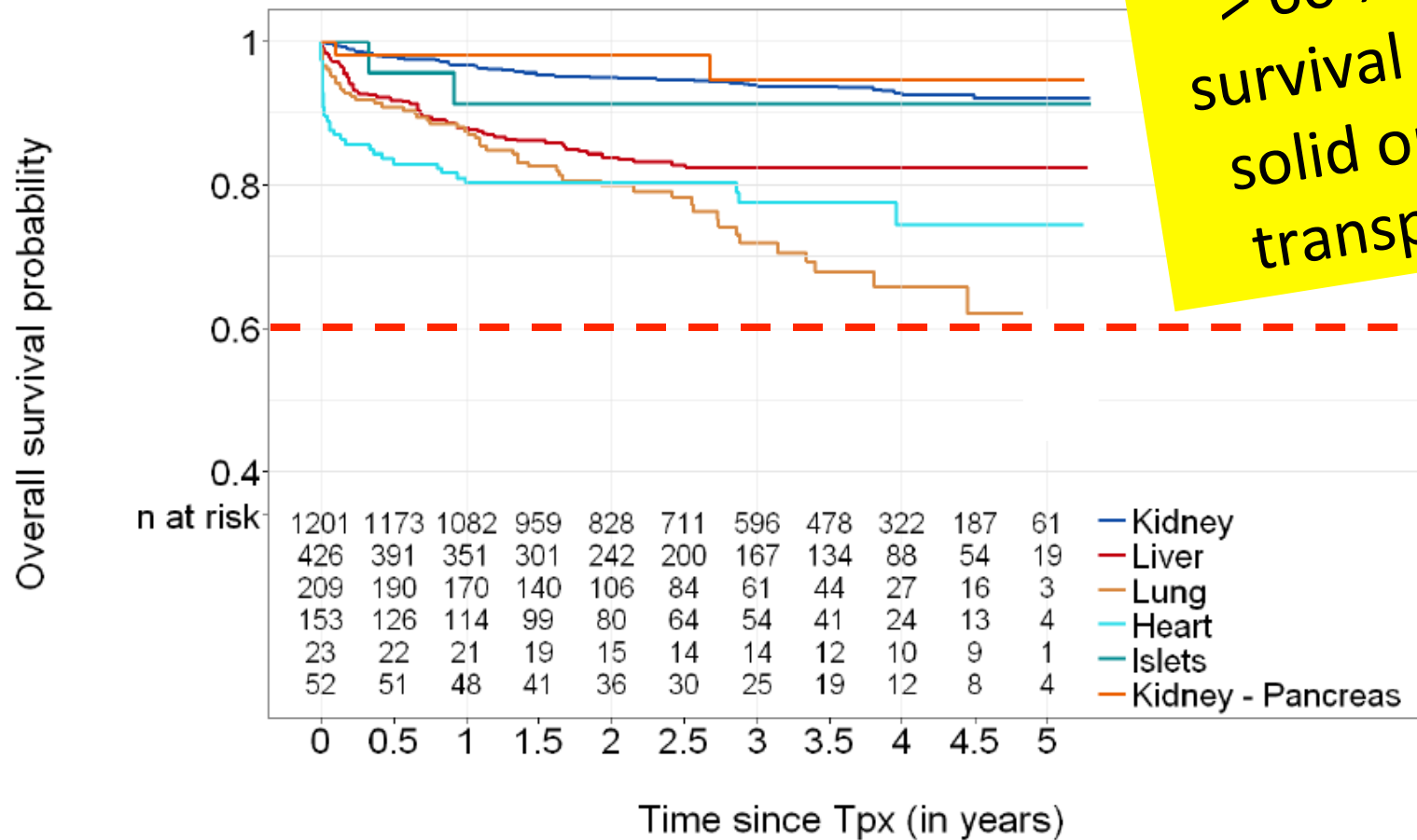


# Outcome after Transplantation



*Swiss Cohort study*

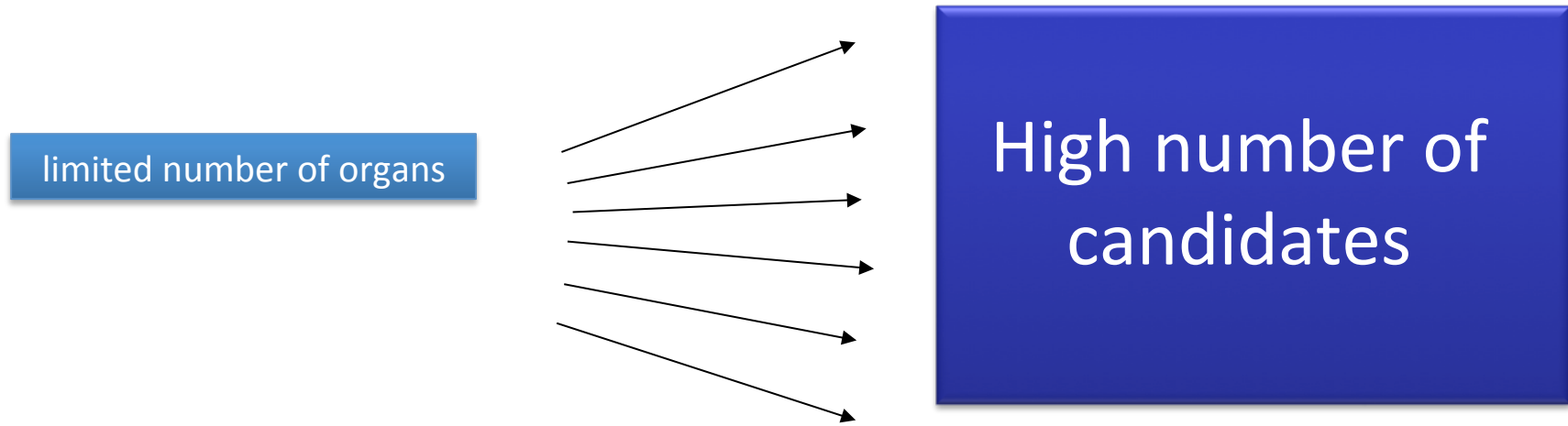
# Survival after Transplantation



> 60 % 5 y survival in all solid organ transplant



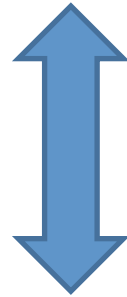
# Problem



Living donation

Split liver

Selection of donors?

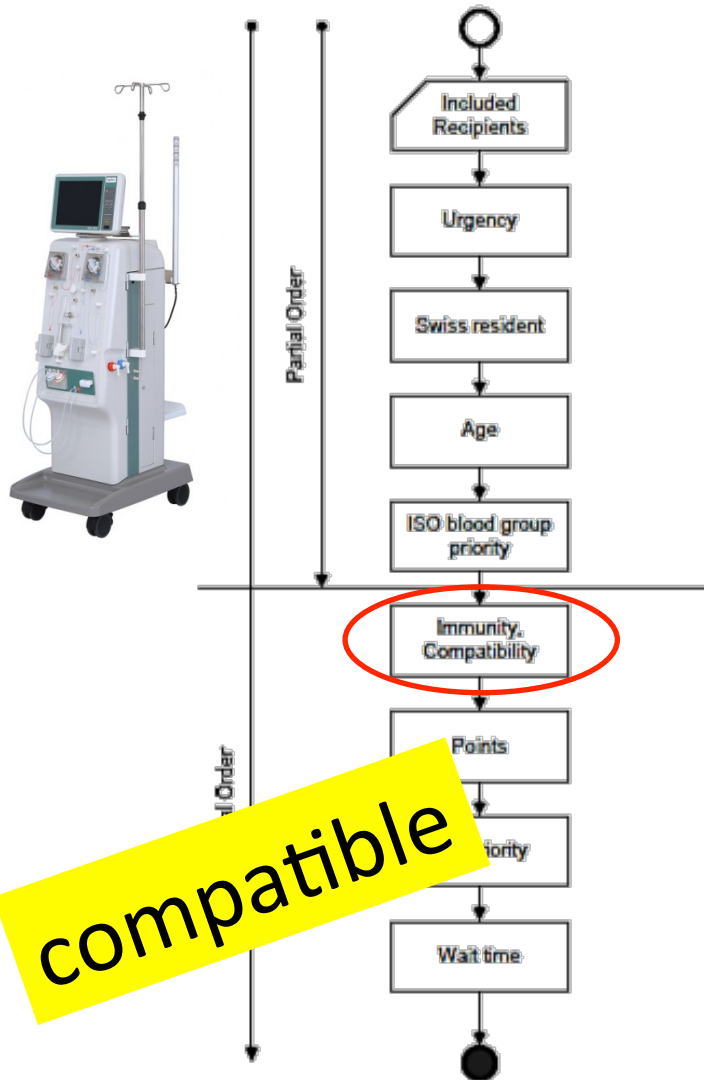


Selection of recipients?

Marginal Organs  
Cardiac death (DCD)  
organs

Indication?

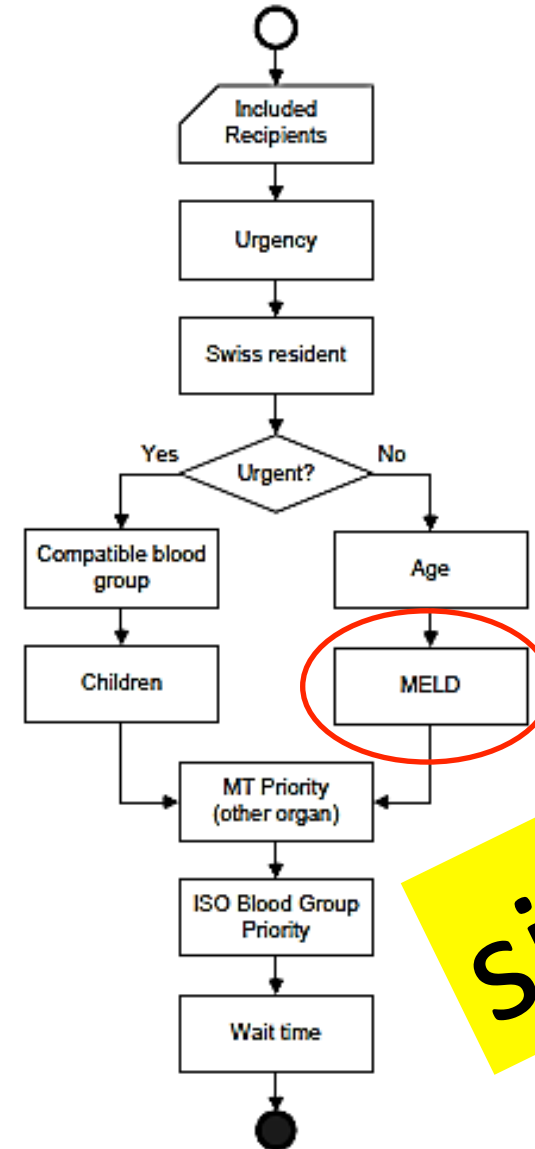
# Kidney allocation



compatible



# Liver allocation



sick



*Tim Pruitt, Waiting for liver transplantation. The Titanic effect. Liver Transplantation 2005*

# Organ transplantation



## Criteria for donation

- No transmission of tumor or untreatable infection
- Estimated sufficient post transplant organ function

Donor risk index  
Graft appearance

Prediction of graft function?

## Criteria for transplant candidates

- Compliance
- Residence in Switzerland

**Post transplant survival after liver transplantation  
more than 50 % after 5 year (BAG)**

Prediction of recipient outcome?

# Current challenge

## Donor

- High donor age
- Race
- Extended cold ischemia
- Warm ischemia
- Graft steatosis
- Infectious disease
- Cause of death



## Recipient

- End stage liver disease
- Hepatitis C
- Liver Cancer
- High recipient age
- Obesity
- Previous transplant
- Portal vein thrombosis

## Marginal graft



?

## MELD > 35



# Example tumor size

25 y, suspected 12 x 6 cm  
diffuse HCC, Hep B, Child A



Liver transplant 2011 (donor age 88 y)

**Histology post transplant: 4 cm HCC**

2014: tumor free, back to full work

# Example tumor size

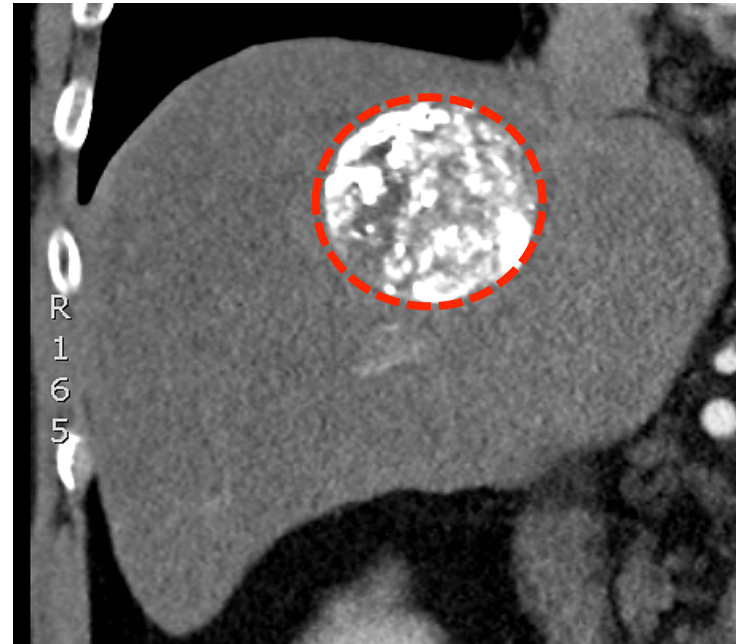
**25 y**, suspected 12 x 6 cm  
diffuse HCC, Hep B, Child A



Liver transplant 2011 (**donor age 88 y**)  
**Histology post transplant: 4 cm HCC**

2014: tumor free, full work

**43 y**, 7 x 6 cm central HCC,  
Hep C, Liver cirrhosis Child B



Liver transplant 2005,  
**Histology post transplant: 4 cm HCC**

2014 : tumor free, Hep c free, full work



# Liver Cancer

Criteria	Features	5-year Survival
<b>Milan<sup>68</sup></b>	Single tumor $\leq 5\text{cm}$ Up to 3 tumors each $\leq 3\text{cm}$	>80%
<b>UCSF<sup>73</sup></b>	Single tumor $\leq 6.5\text{cm}$ , or Two tumors $\leq 4.5\text{cm}$ or Total diameter $\leq 8\text{cm}$	75%
<b>Hangzhou<sup>80</sup></b>	Tumor $< 8\text{cm}$ in total or Tumor $\geq 8$ and AFP $\leq 400\text{ng/ml}$ and well differentiated	72%
<b>Toronto<sup>71</sup></b>	Any tumor size or number and No macrovascular invasion and No extra-hepatic disease and Well or moderate differentiated (when beyond Milan)	70%
<b>Up to Seven<sup>69,78</sup></b>	Largest tumor size $\leq 7\text{cm}$ or Tumor number $\leq 7$	71%
<b>Asan Medical Center<sup>82</sup></b>	Largest tumor size $\leq 5\text{cm}$ or Tumor number $\leq 6\text{cm}$ with macrovascular invasion	82%
<b>Kyoto<sup>81</sup></b>	Largest tumor diameter $\leq 5\text{cm}$ Tumor number $\leq 10\text{cm}$	87%
<b>Tokyo University<sup>79</sup></b>	Largest tumor size $< 5\text{cm}$ Tumor number $\leq 5\text{cm}$	75%

Milan as benchmark ?

# Ethical dilemma

wasteful transplantation?

25 Jahre Swisstransplant

WEITER

UND INSTITUTIONEN

Dringlichkeit vs. N  
von Organen

er Allokation

gesetz und den darin festgelegten Zuteilungskriterien  
konsequenzen. Dass medizinisch dringliche Patienten bei  
organen prioritär behandelt werden, birgt auch Probleme. Es gibt  
schkeiten zur Allokation der spärlich vorhandenen Spenderorgane.

# Introduction of „MELD“ Policy

„sickest first“



US  
2/2002

North Italian  
Transplant  
3/2006

Euro  
Transplant  
12/2006

Etablissement  
français des Greffes  
3/2007

Swiss  
Transplant  
7/2007

# Example too sick?

63 J, BMI 17.9,  
MELD 32,  
hemofilter, ICU

Liver transplant  
2008



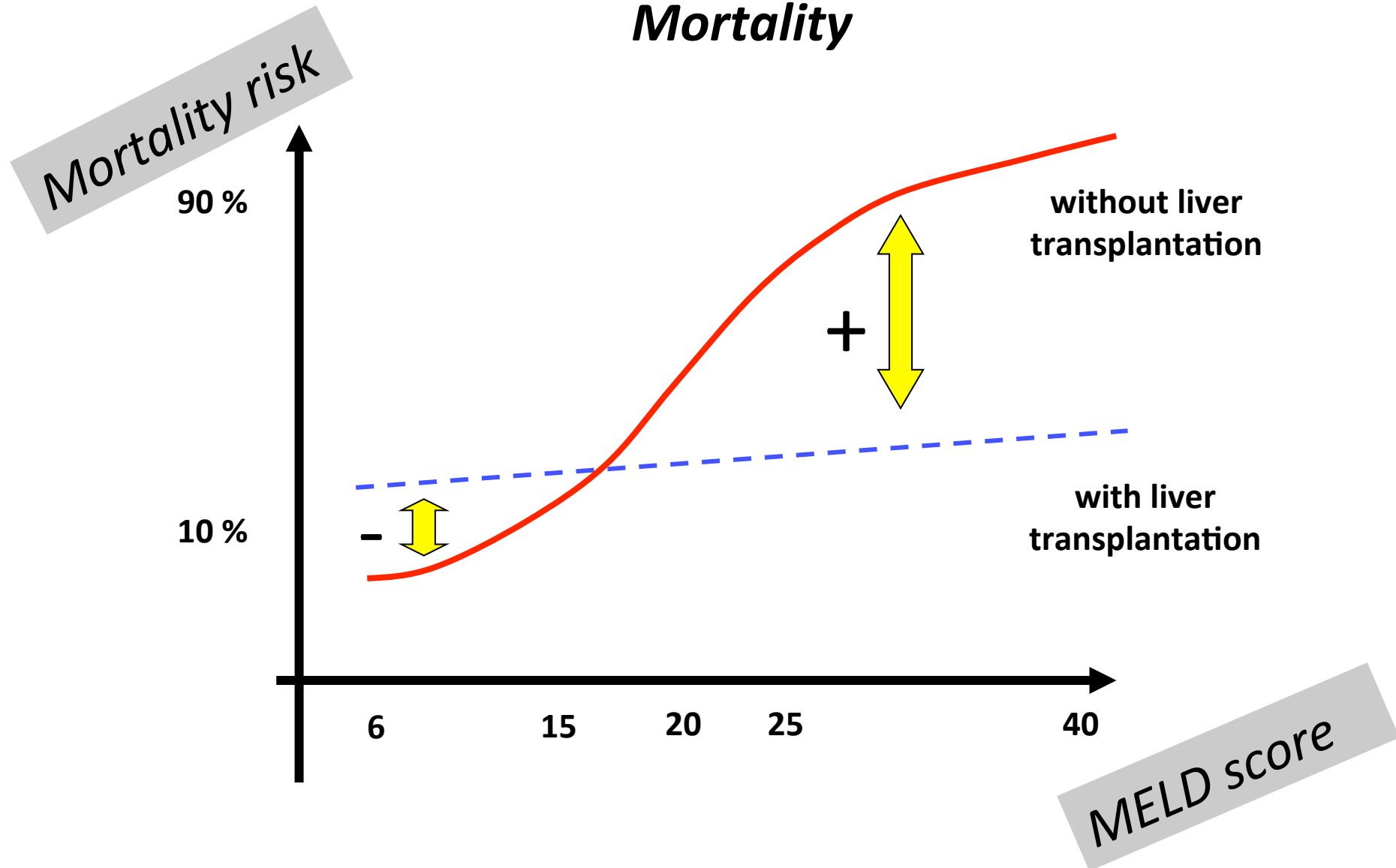
1 year after  
Transplantation



6 years after  
Transplantation

# Survival benefit ?

*Mortality*

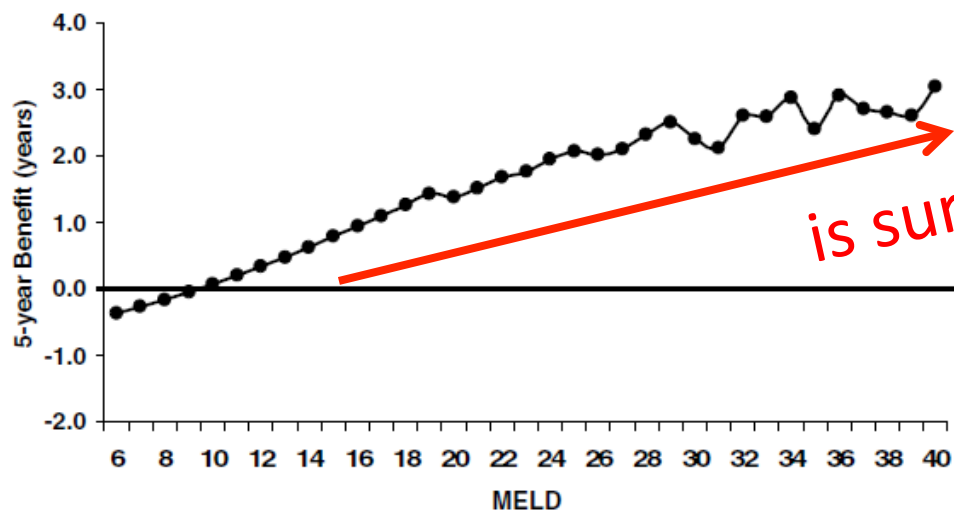


# Survival Benefit-Based Deceased-Donor Liver Allocation

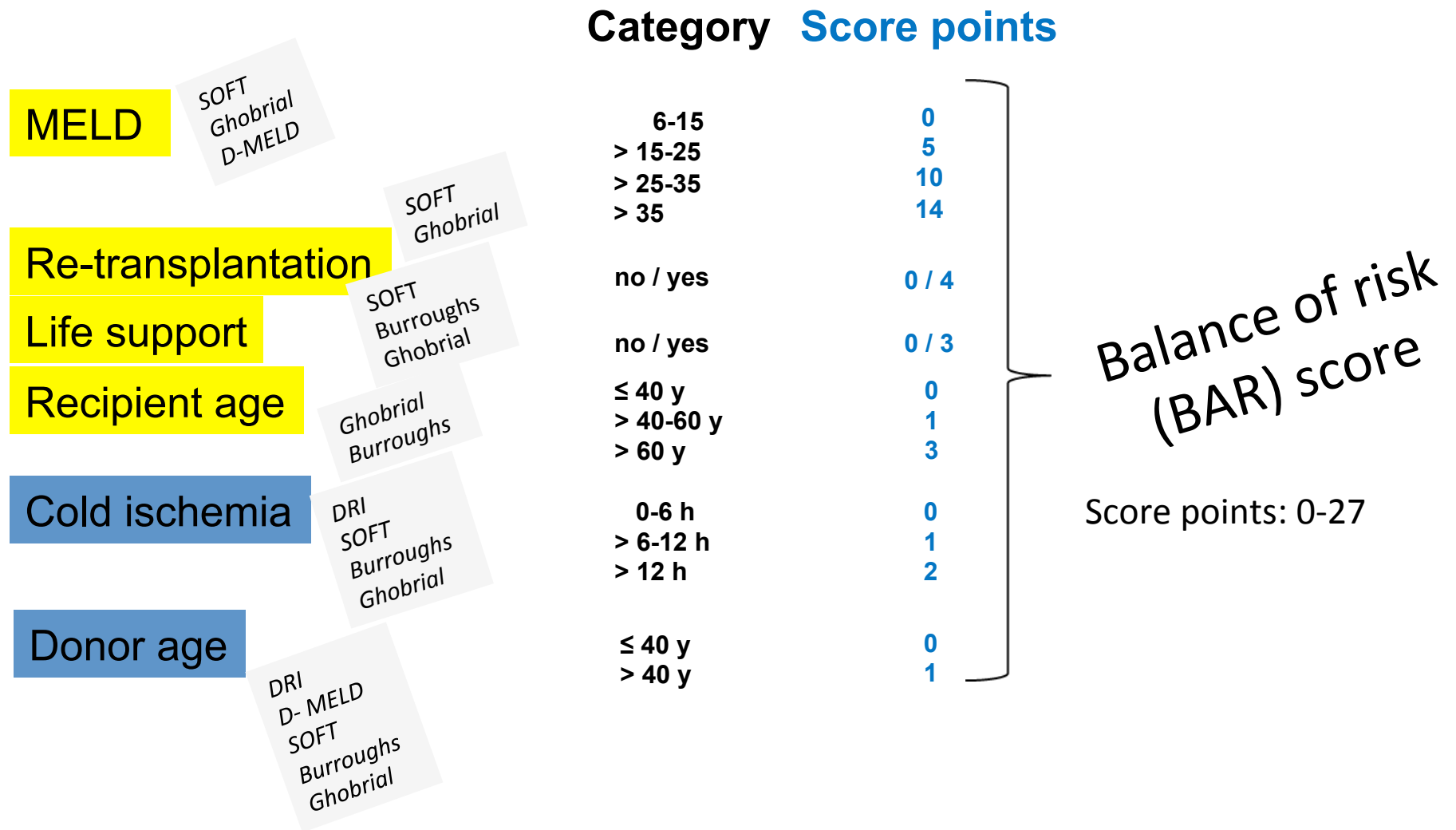
D. E. Schaubel<sup>a,b,\*</sup>, M. K. Guidinger<sup>b,c</sup>,  
S. W. Biggins<sup>d</sup>, J. D. Kalbfleisch<sup>a,b</sup>,  
E. A. Pomfret<sup>e</sup>, P. Sharma<sup>f</sup> and R. M. Merion<sup>b,g</sup>

Organ Procurement and Transplantation Network  
(OPTN), Scientific Registry of Transplant Recipients  
(SRTR), waiting list

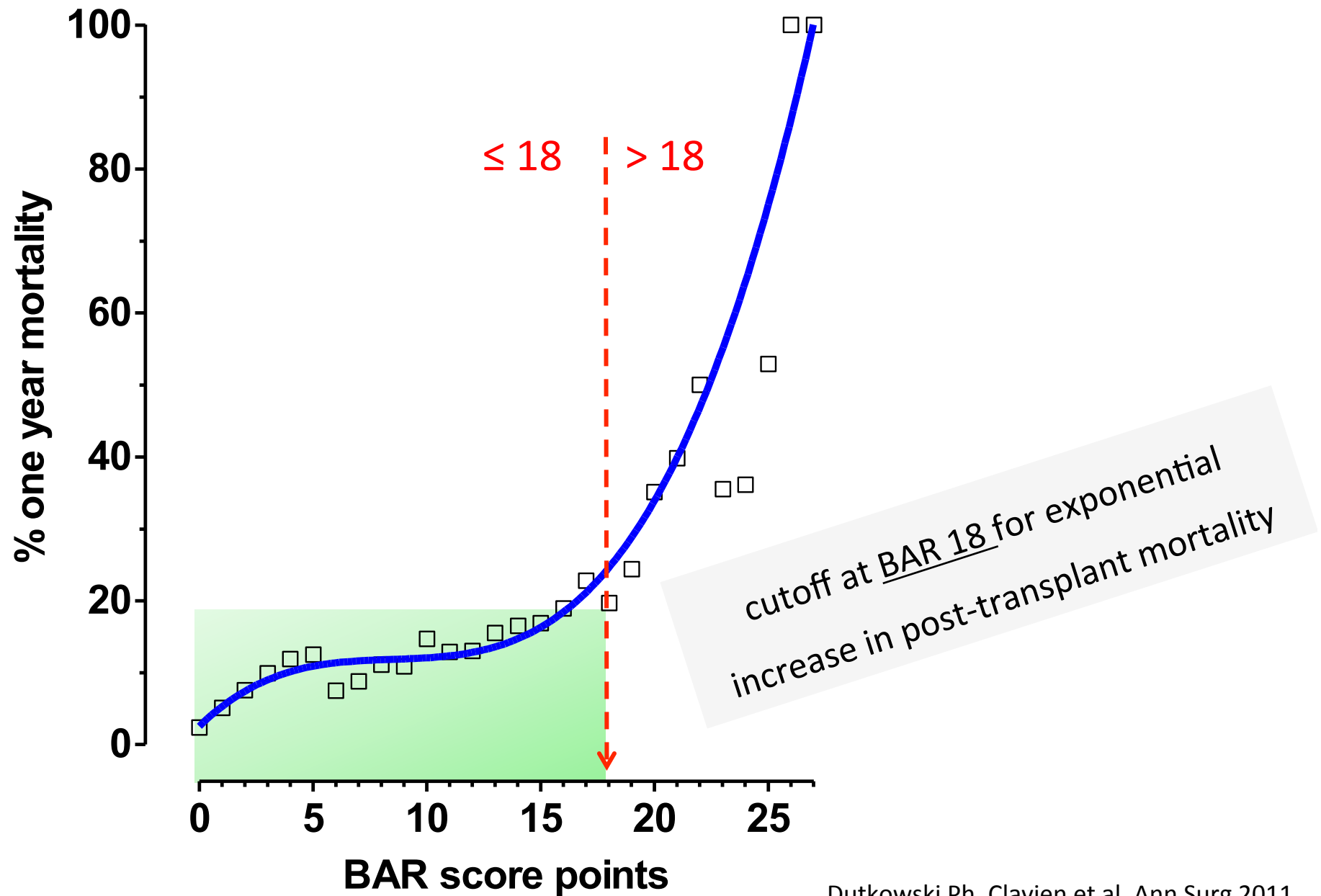
Schaubel et al.



# New calculation of categorized key risk factors Adult UNOS population, n= 37255

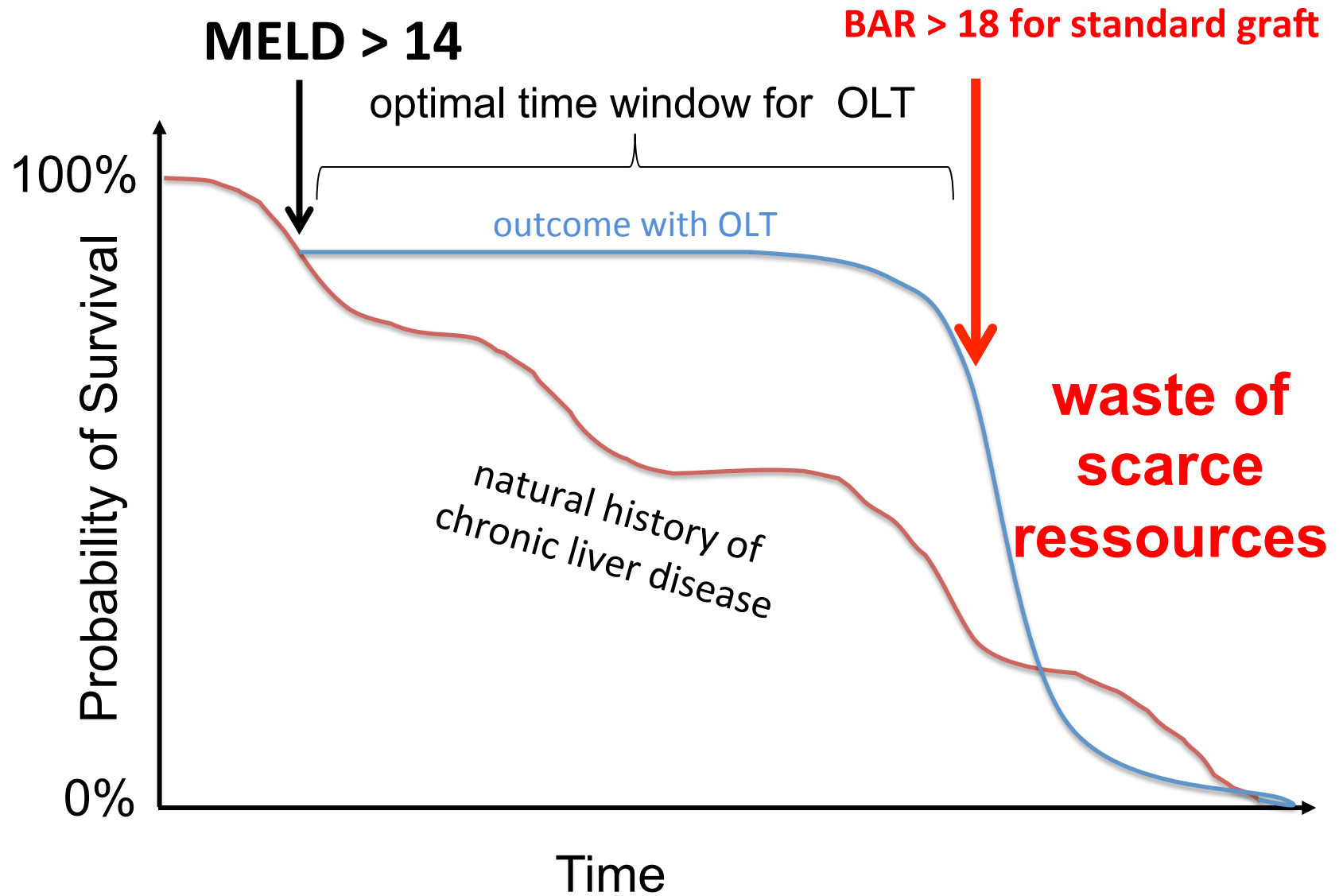


# Threshold of increasing mortality after OLT





# Current policy



# Individual vs collective benefit

The goal of liver transplantation is to maximize the benefits that can be provided to patients through the most judicious and fair use of the limited supply of donor organs. In practice, the problem of the donor organ shortage influences the indications for liver transplantation. In this context, it is necessary to make choices that favor collective benefits rather than individual benefits for patients while we attempt to

# Triage ?

Startseite

**TagesAnzeiger**

WISSEN

Aboservice · Marktplatz

ZÜRICH BÖRSE SCHWEIZ AUSLAND WIRTSCHAFT SPORT KULTUR PANORAMA LEBEN AUTO

Medizin & Psychologie Natur Technik Geschichte Bildstreifen Weiterbildungs-Spezial

## Erst die junge Mutter, dann der Senior

Von Daniel Friedli, Bern. Aktualisiert am 25.09.2010 65 Kommentare

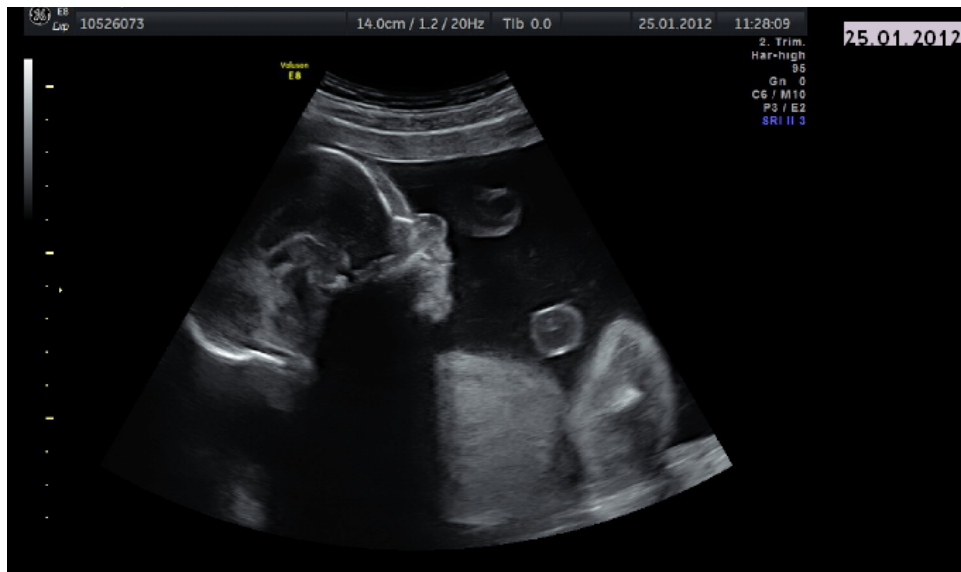
Bislang stehen auf der Warteliste für Spender-Organen jene zuoberst, die am schwersten krank sind. Die Stiftung Swisstransplant will das ändern. Sie wirft eine heikle Frage auf: Sind alle Leben gleich viel wert?



# Example acute liver failure during pregnancy

Acute Hepatitis B

21 weeks of pregnancy, MELD 30

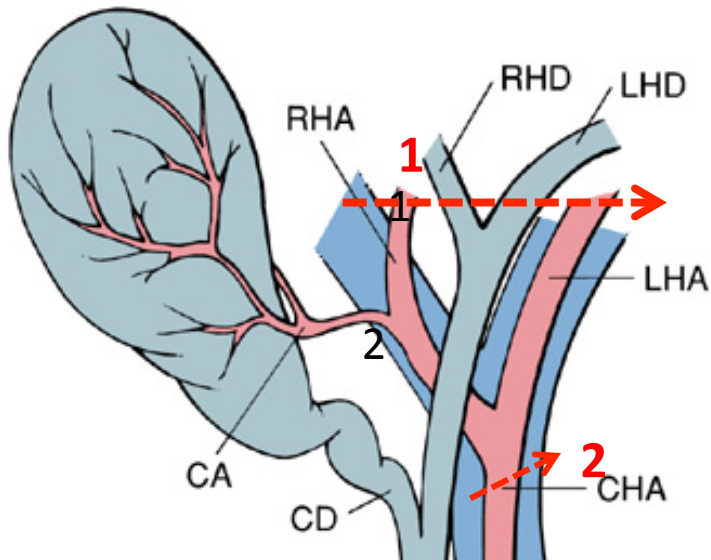


14 cases world wide,  
most with fatal outcome  
for the fetus



- Liver transplant 2012 with super urgent listing (graft offer from France)
- Sectio 3 months later with healthy child

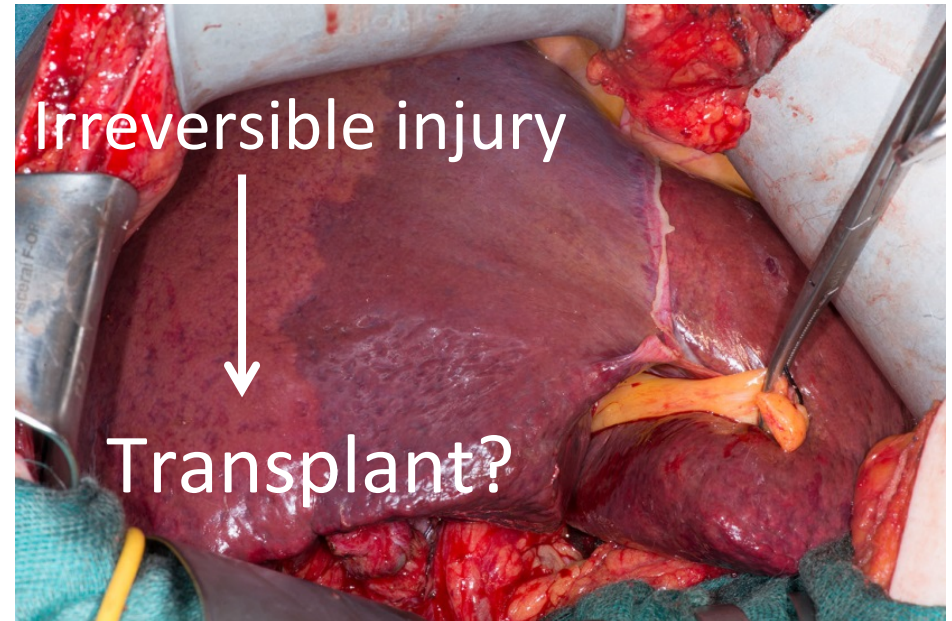
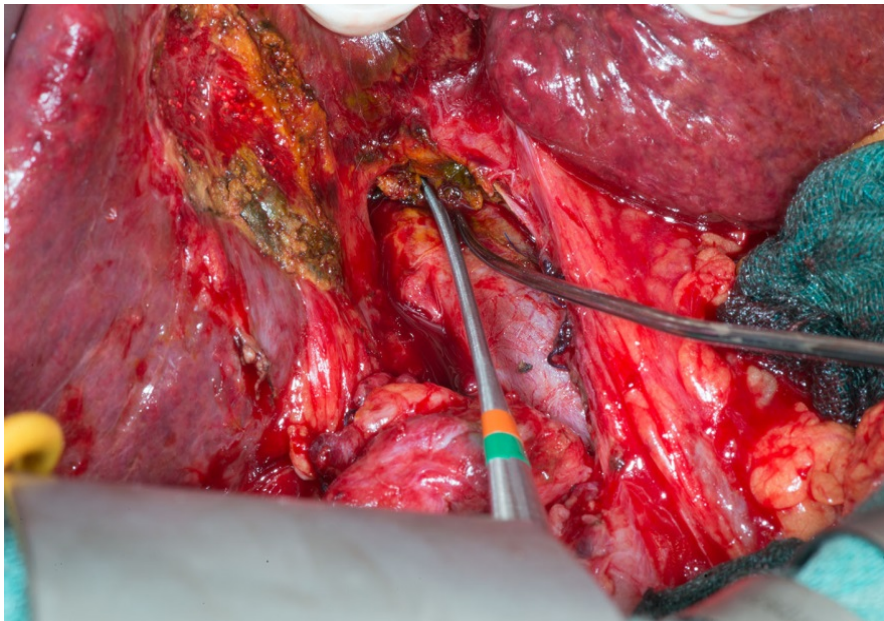
# Example iatrogenic injury after lap. cholecystectomy



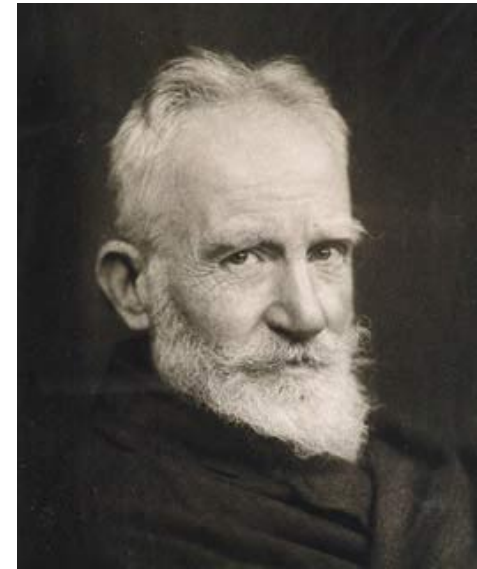
**80 y**, benign disease

Send from another hospital after iatrogenic injury

**Complete transection of the biliary bifurcation  
& the common hepatic artery**



*G. B. Shaw 1906*  
*The Doctor's dilemma*



«I have had to consider not only whether the man could be saved but whether he was worth saving.

There were fifty cases to choose from and forty had to be condemned to death»

# Steve Jobs Liver Transplant—Is That Ethical?

posted by hfields



UPDATE: Interesting NY Times article asking some of the same questions as my original post about Steve Jobs' liver transplant. [Check the NY Times piece out!](#) Because of this article, and because of the many comments I received on my own, I'm putting up an updated version of my prior post today (below), but with some changes to reflect better information. Unfortunately, by putting up this new version, the old one was deleted, so some of the comments on it may no longer apply. Anyhow, enough disclaimers!

# Example chronic drug abuse & tumor

- **45 y**, Hep C
- Chronic drug abuse from 1998 -2000, currently Methadon program
- Suspicion on hilar cholangiocarcinoma (bile duct cancer)
- No disease outside the liver

Radio-Chemotherapy after staging (Mayo protocol)

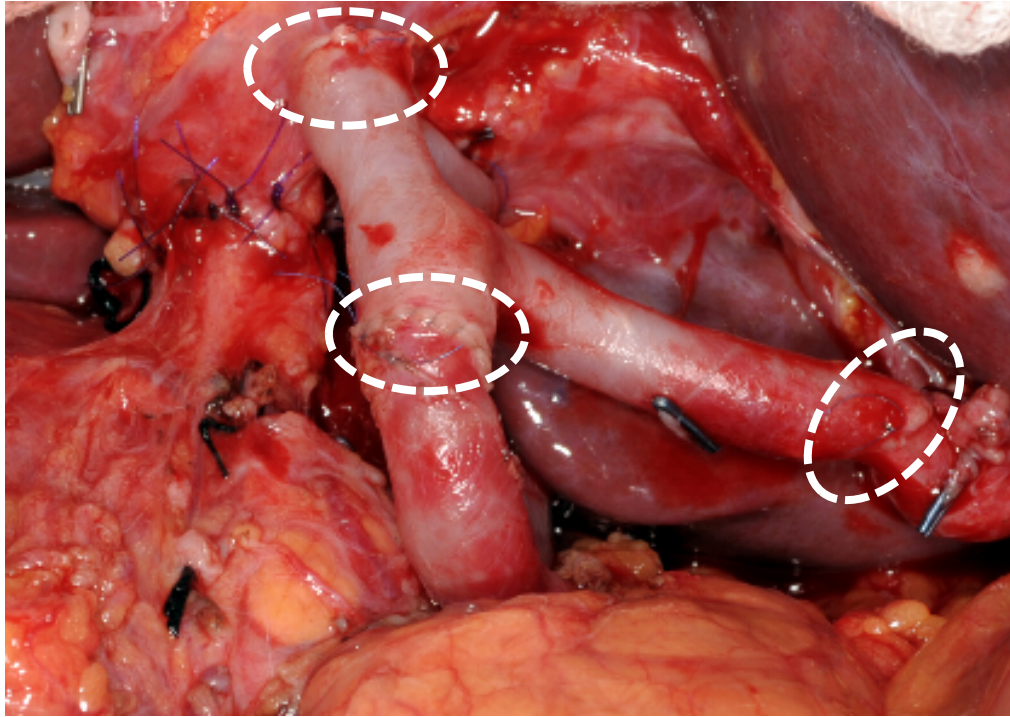


## Recht auf Rettung

Von Mario Stäubli. Aktualisiert am 05.03.2012 14 Kommentare

Menga V. war drogensüchtig, leidet an Depressionen und hat zwei Suizidversuche hinter sich. Nun die Diagnose: Krebs. Sie braucht eine neue Leber, aber Spenderorgane sind knapp. Soll sie eine erhalten?





Liver transplant 2011 with poor artery requiring complex reconstruction (**liver graft rejected by all other centers**)

# Example sick & drug abuse

- 34 y, acute alcoholic steatohepatitis, lab MELD 38  
Intubated, on hemofilter, 20 y Noradrenalin
- On list 09/2013 after **repeated discussions with parents, psychologists, hepatologists, Anaesthesists, Ethicists**
- Liver transplant 10/2013,  
**Donor age 70 y + graft fibrosis**

2014 : full recovery, back to work

ORIGINAL ARTICLE

## Early Liver Transplantation for Severe Alcoholic Hepatitis

Philippe Mathurin, M.D., Ph.D., Christophe Moreno, M.D., Ph.D.,  
Didier Samuel, M.D., Ph.D., Jérôme Dumortier, M.D., Ph.D., Julia Salleron, M.S.,  
François Durand, M.D., Ph.D., Hélène Castel, M.D., Alain Duhamel, M.D., Ph.D.,  
Georges-Philippe Pageaux, M.D., Ph.D., Vincent Leroy, M.D., Ph.D.,  
Sébastien Dharancy, M.D., Ph.D., Alexandre Louvet, M.D., Ph.D.,  
Emmanuel Boleslawski, M.D., Ph.D., Valerio Lucidi, M.D., Thierry Gustot, M.D., Ph.D.,  
Claire Francoz, M.D., Christian Letoublon, M.D., Denis Castaing, M.D.,  
Jacques Belghiti, M.D., Vincent Donckier, M.D., Ph.D.,  
François-René Pruvot, M.D., and Jean-Charles Duclos-Vallée, M.D., Ph.D.

**6 month abstinence pretransplant?**



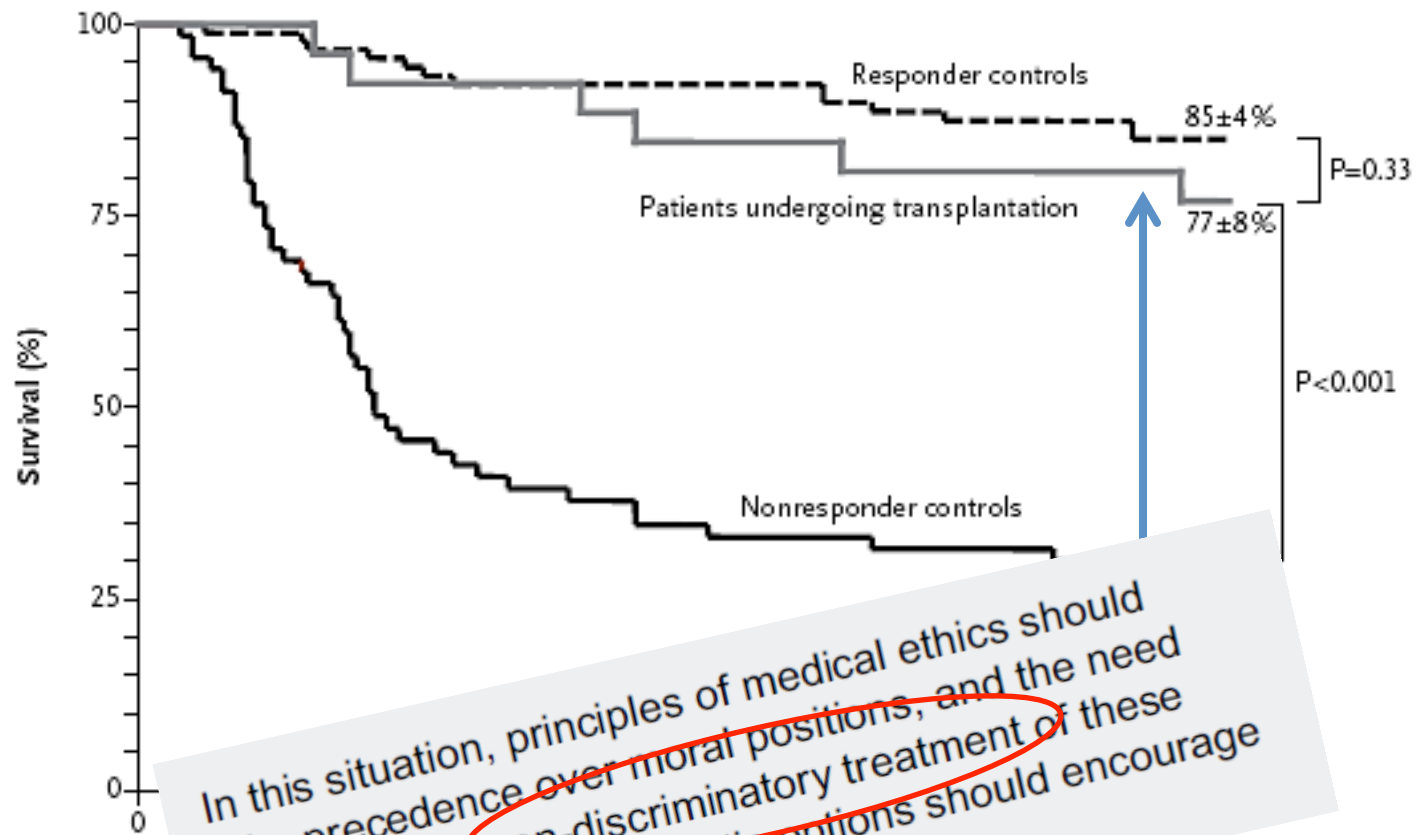
## **Ethical considerations regarding early liver transplantation in patients with severe alcoholic hepatitis not responding to medical therapy**

Vincent Donckier<sup>1,\*</sup>, Valerio Lucidi<sup>1</sup>, Thierry Gustot<sup>2</sup>, Christophe Moreno<sup>2</sup>

<sup>1</sup>Department of Abdominal Surgery, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium; <sup>2</sup>Department of Gastroenterology, Liver Transplant Unit, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium

- Severe alcoholic hepatitis refers to a life-threatening syndrome of liver failure and systemic inflammation arising in persons who have been consuming excess amounts of alcohol. In this condition, the absence of response to medical therapy is associated with extremely high early mortality

# Estimates of Survival among 26 study patients and randomly selected matched controls



No. at Risk	
Responder controls	92
Patients undergoing transplantation	26
Nonresponder controls	69

**Interdisciplinary & ethical decision**

# Example retransplant

- 51 y, Hep C
- First liver transplant 2004
- Recurrent Hep C cirrhosis, second liver transplant 2009

Chronic rejection and severe graft injury, persisting Hep C

**Third liver transplant 2011**

*Justified?*

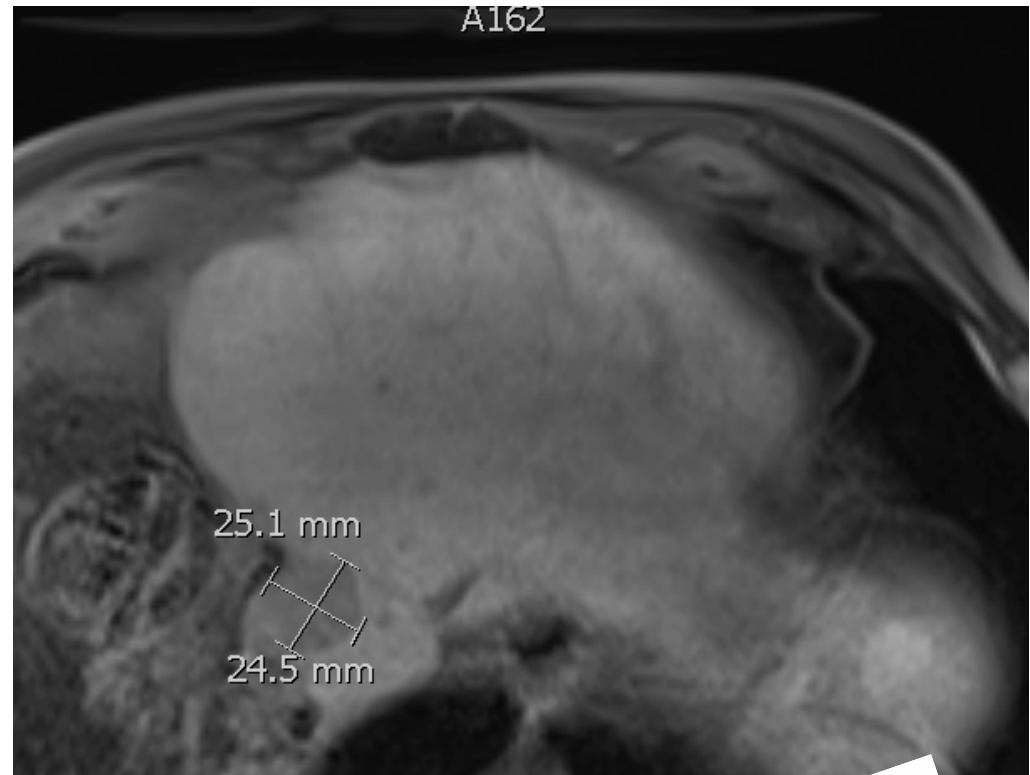
Normal graft function, Hep C treatment with new nucleotide polymerase inhibitor sofosbuvir

# Example ECD/DCD organ, rejected by others

71 y, Liver fibrosis,  
HCC wedge resection 2008  
Recurrent HCC, 6 x TACE  
Right Hepatectomy 2010

Recurrent HCC near the v. cava

Liver transplant 2013



**Donor offer rejected by all other centers:**

**Suizid, ALT 1016 U/l, Quick 32**

Machine  
liver  
perfusion  
for 3h

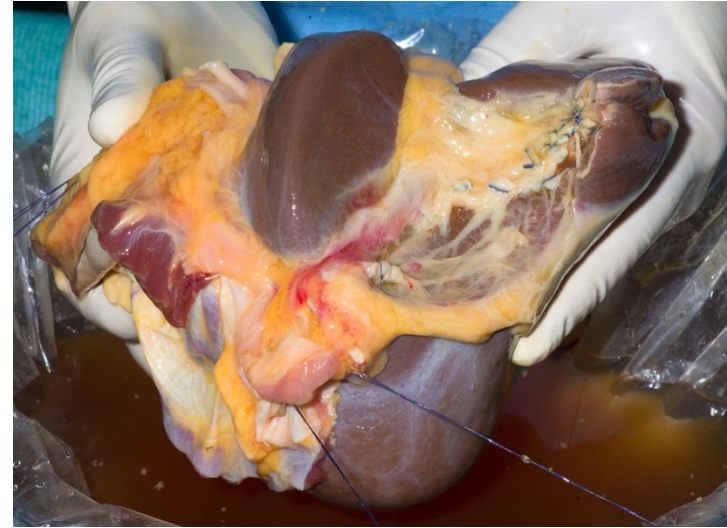
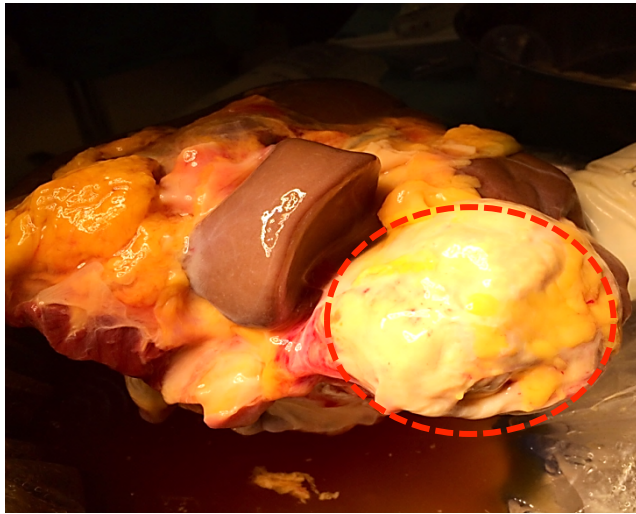




# Example ECD/DCD organ, rejected by others

Ultrasound  
report donor:

Regelrechte Darstellung der Leber ohne Nachweis fokaler Läsionen.



- **8 cm cystic lesion in left lobe**
- Resection on backtable

Recipient with HCC, expected waiting time > 1 y

**final histology: benign cyst**

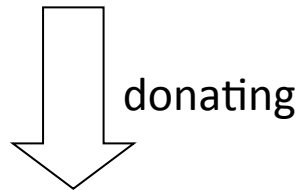


# Ethics in **Living** donor transplant

Ethical acceptable

Ethical unacceptable

Adult



Pediatric recipient

Cancer outside the liver

Expected donor mortality risk > 0.5 %

# Double equipoise



R: 75yr man,  
Liver cancer *above Milan*

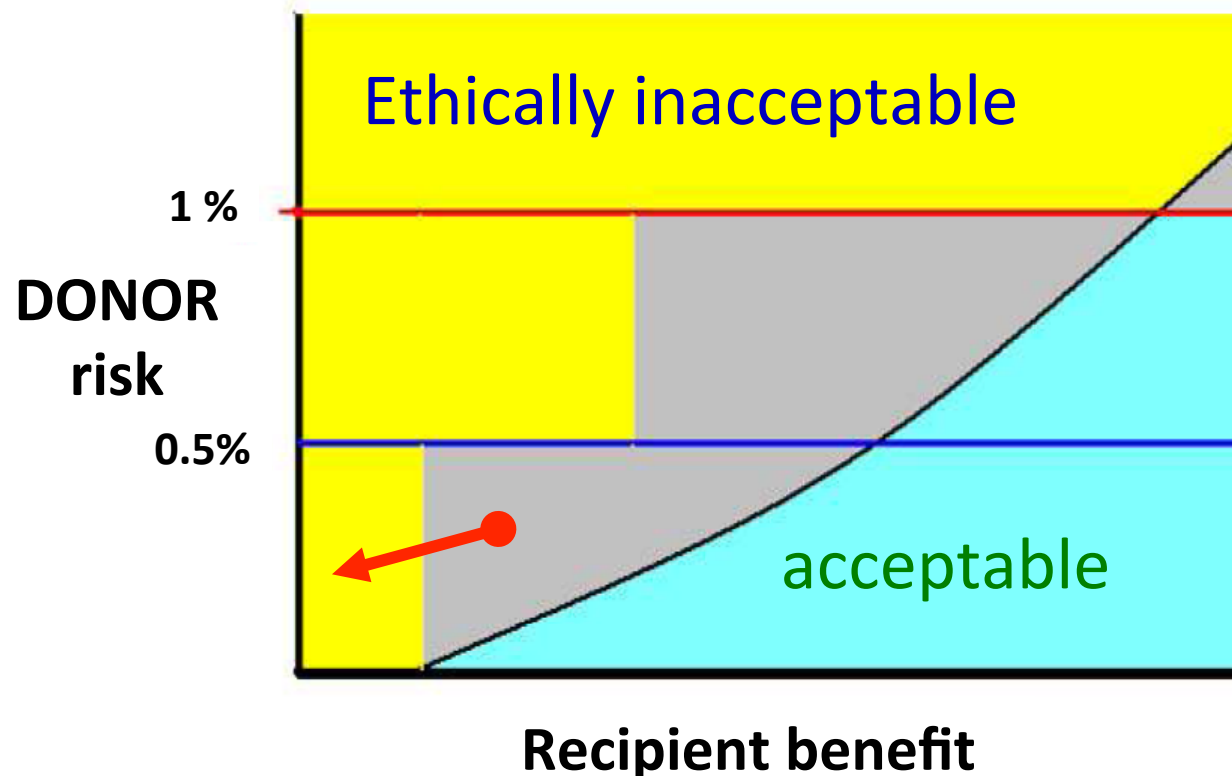
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D: 20 yr loving grand child

## Should We Use Living Donor Grafts for Patients With Hepatocellular Carcinoma? Ethical Considerations

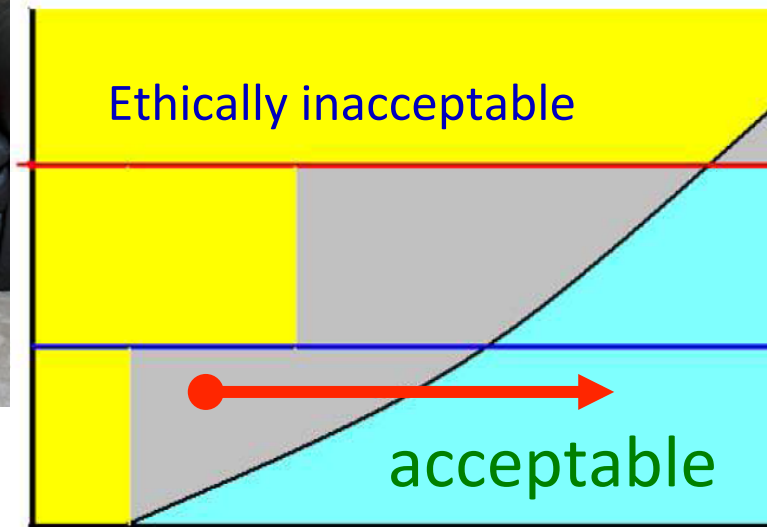
Elizabeth A. Pomfret,<sup>1</sup> J. Peter A. Lodge,<sup>2</sup> Federico G. Villamil,<sup>3</sup> and Mark Siegler<sup>4</sup>



# Double equipoise



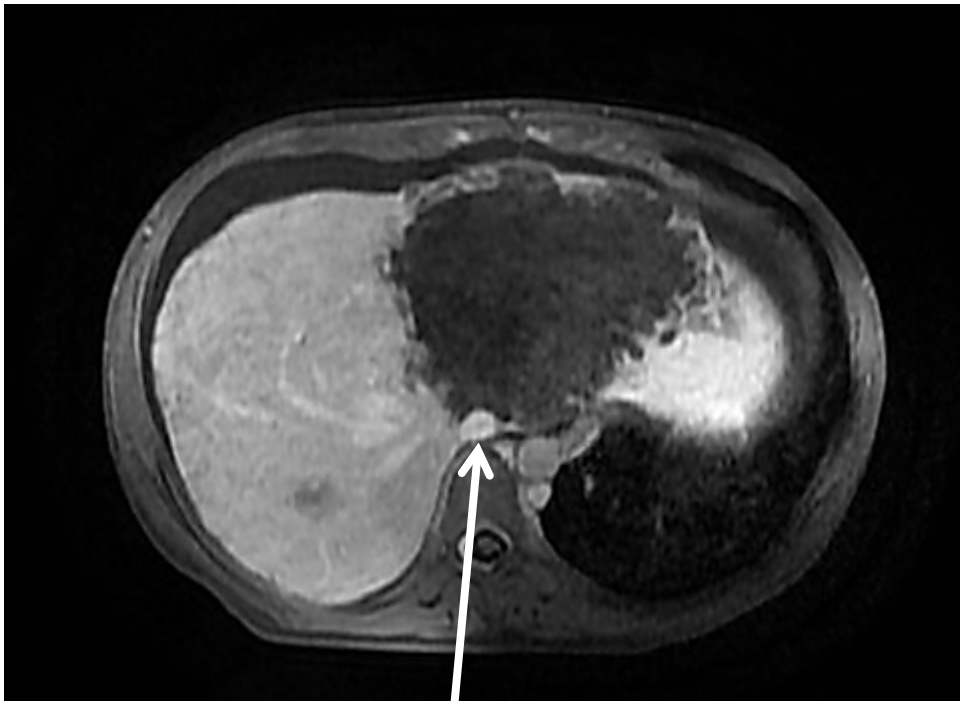
R: mother of 3 children  
**Liver cancer above UCSF**  
D: father



**Recipient benefit**

# Example Living donor liver transplantation + heart resection

- 22 year old, female patient, unresectable echinococcus alveolaris in the liver
- Incidence of echinococcus in Switzerland: 10-20 cases/y, 90 % mortality (untreated)



Infiltration of suprahepatic vena cava  
and right atrium

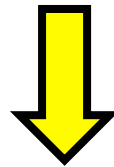


# Regular treatment options?

**None**

Liver transplantation with resection of right atrium and vena cava

But.....no perspective for an organ offer



Evaluation: Living donor liver transplantation

**Never done before, mortality ?**

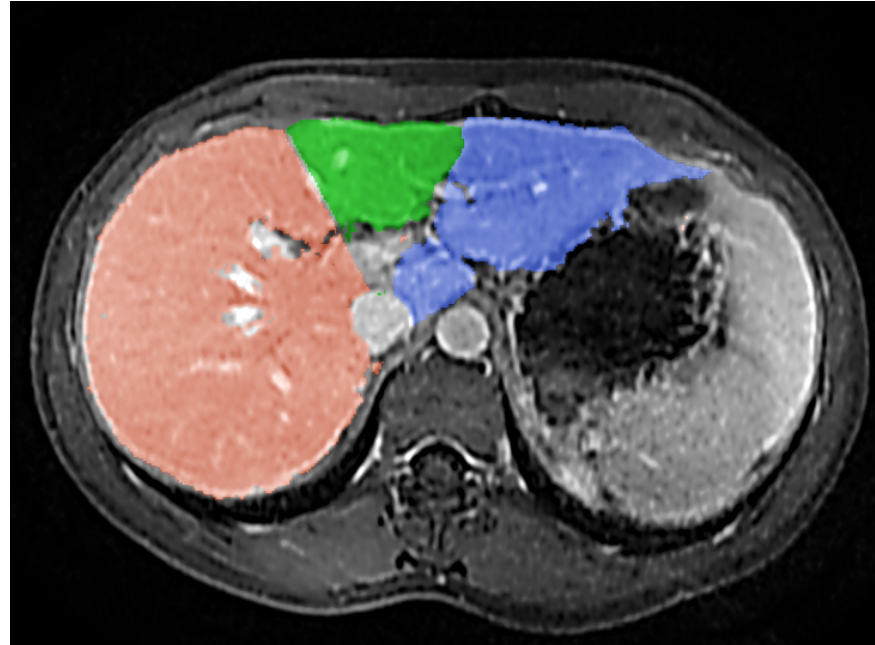
# Donor Evaluation

- Sister, 26 years

**1: Segment (V, VI, VII, VIII): 624 cm<sup>3</sup>**

**2: Segment IV: 101cm<sup>3</sup>**

**3: Segment I, II, III: 223 cm<sup>3</sup>**



- Operation in parallel:

**Team 1:** Donor operation (resection of right hemiliver)

**Team 2:** Recipient operation (resection liver including right atrium, cava vein and implantation of right hemiliver from donor)

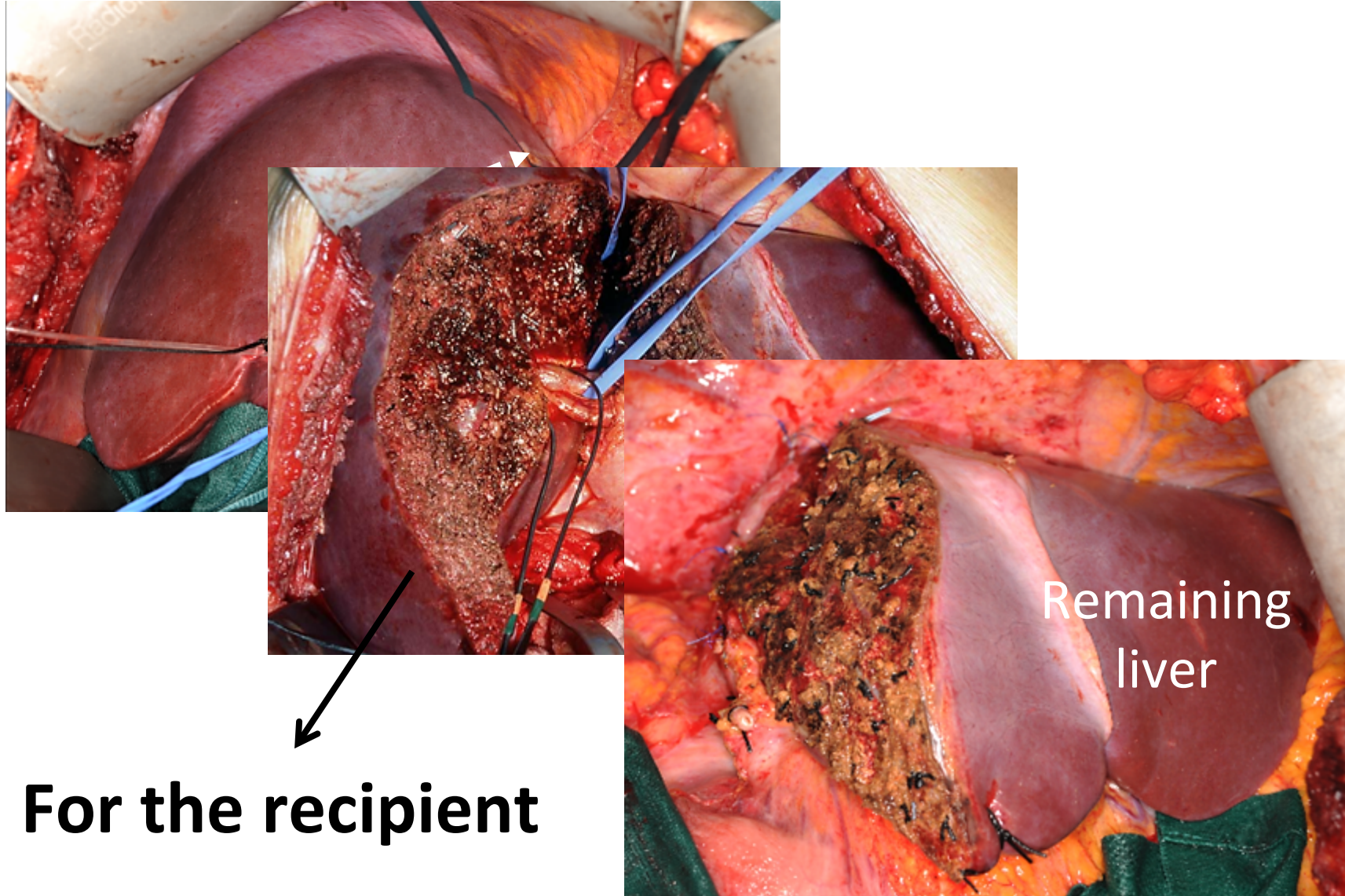
+

**Team 3:** In cooperation with Heart/Vascular Surgeon (Prof. Lachat)



# Living Donor Liver transplantation

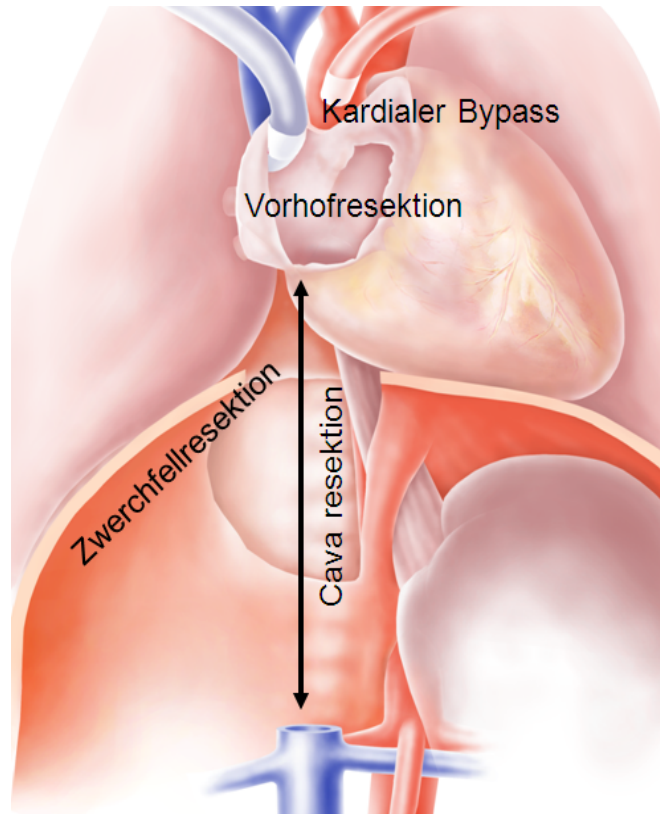
Donor operation



# Operation

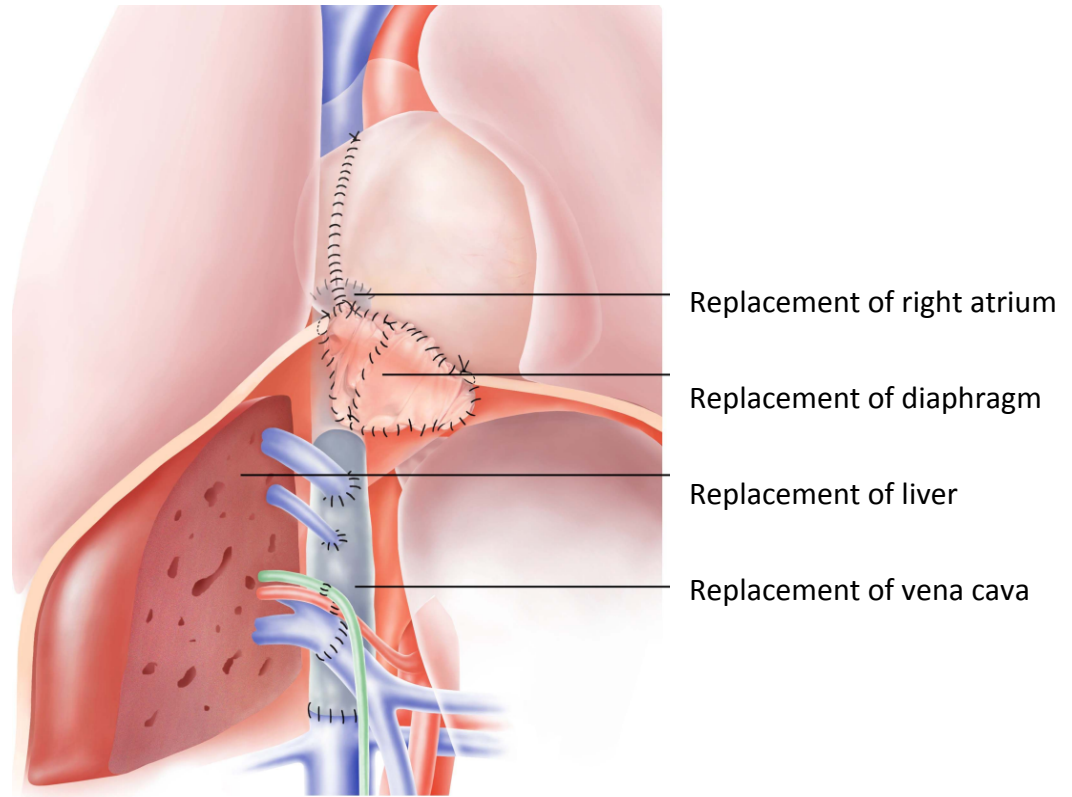
**Team 1: Donor operation**

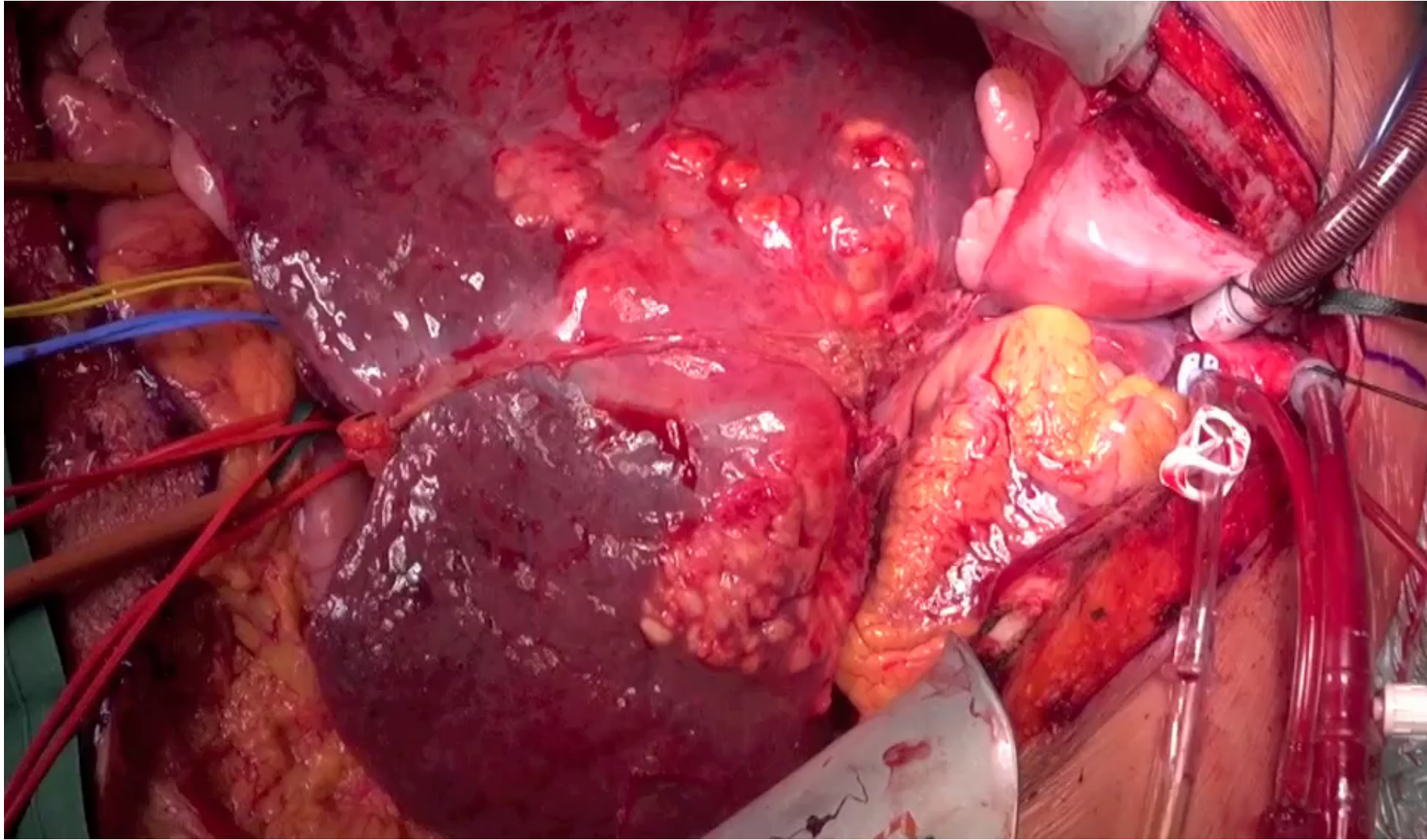
**Resection**



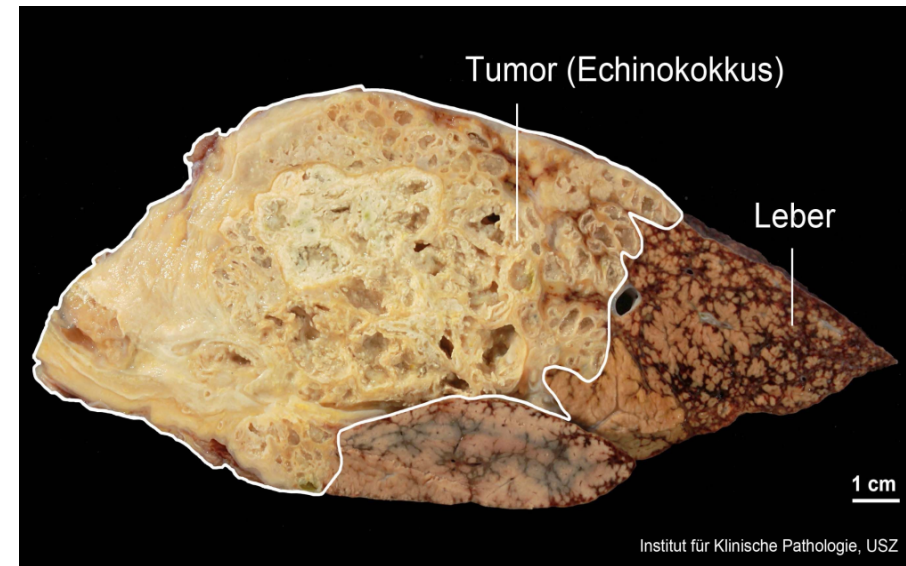
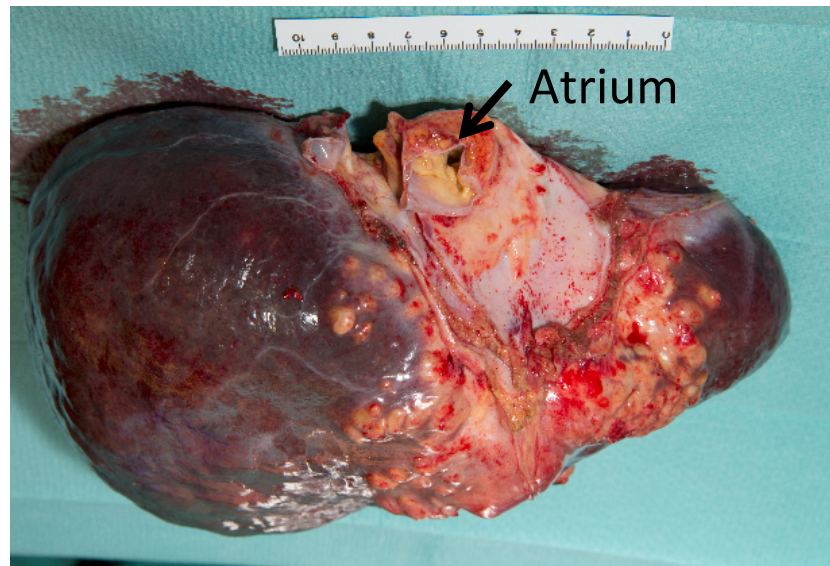
**Team 2: Recipient operation**

**Reconstruction**





# Diseased liver of recipient with echinococcus



- Complete recovery of the patient (1.5 year follow-up)
- No immunosuppression
- HLA-Identity of donor and recipient



Nina Germann (links) spendete Kinza Sigrist einen Teil ihrer Leber und rettete damit das Leben ihrer Schwester. (Foto: Hans Guterstorfer)

Montag, 30. Dezember 2013

Eine **Leberspende** bewahrte

**Blick** 5

**Kinza Sigrist (25)** aus Bürglen TG vor dem Tod

«Meine Schwester  
schenkte mir ein  
zweites Leben»



Nina Germann (L.)  
spendete ihrer  
Schwester Kinza  
Sigrist einen  
Teil ihrer Leber.



# How to define thresholds? How to move forward?

- Immune response
- New technology
- Artificial organs
- Donor / recipient risk
- Infection
- Quality of life

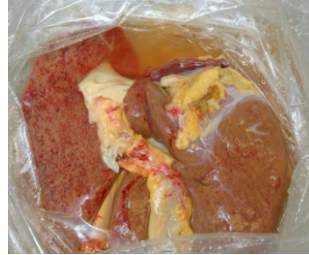


# Marginal Organs

cold Ischemia ↑



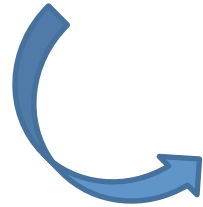
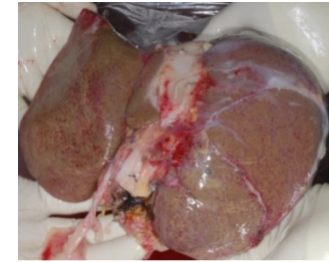
warm Ischemia ↑



steatosis ↑



age ↑



## Optimization ?

**Machine liver perfusion**



Dutkowi, Clavien, et al. Gastroenerology 2014

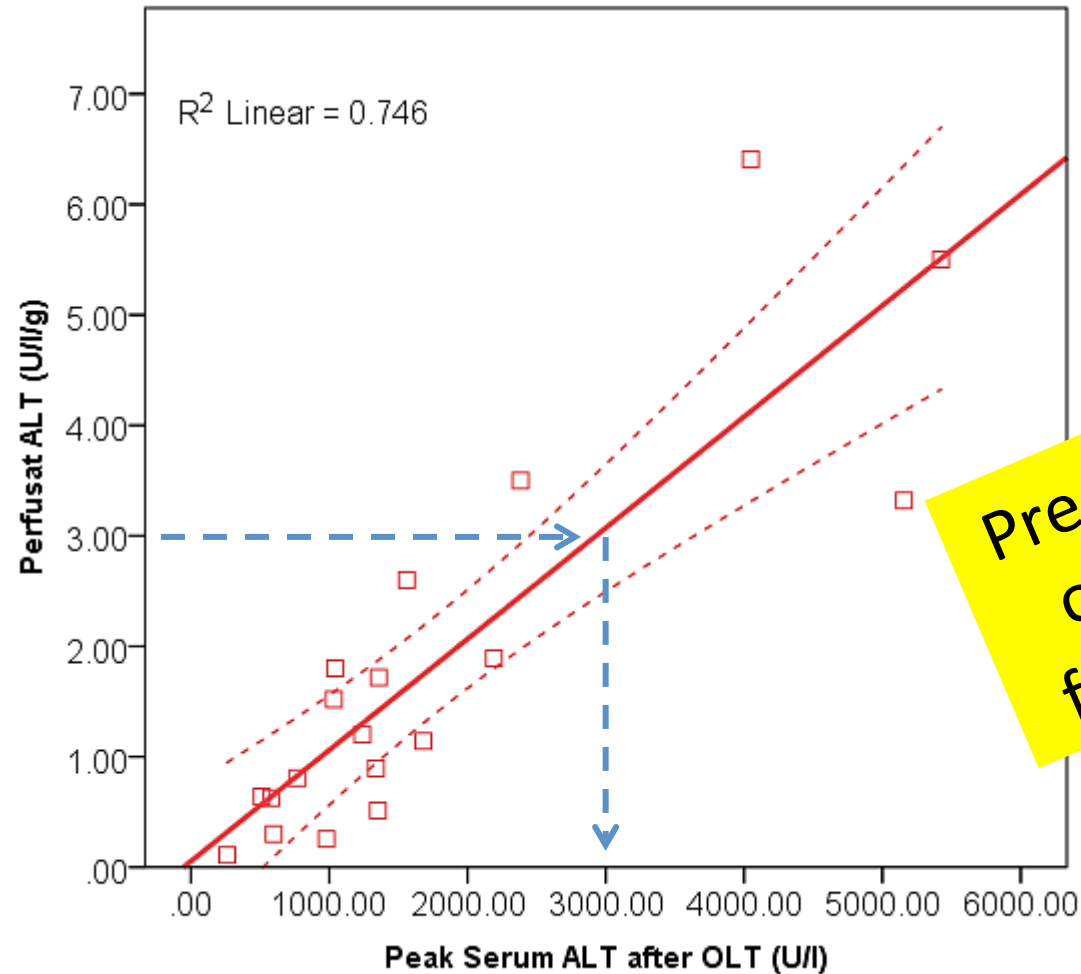


Hypothermic oxygenated machine perfusion, Case 1-20:



# Assessment of injury **before** implantation?

AST/ALT release during machine liver perfusion



Prediction  
of graft  
function?

# Ethical decisions in transplantation

Future interdisciplinary research needed ...

- Indications for transplant
- Allocation principles
- Retransplantation for early graft failure
- Donation after cardiac death
- Living donor transplantation
- Acute liver failure after suicide/drug abuse

tumor limits?  
recurrent chronic drug abuse?

...to the sickest recipient?

second chance?

donor treatment?  
graft injury limits?

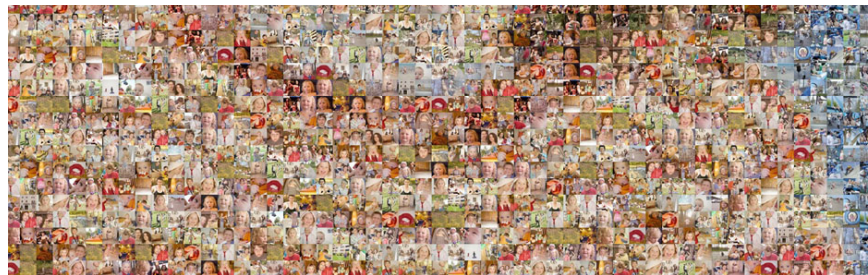
donor risk?  
recipient benefit?

justified?

# big picture



**HSM including  
Transplantation should be  
permitted only in centers  
performing credible  
research**





Thank you