

How to Define Success of a Liver Transplant

Carl L Berg, MD

Medical Director of Abdominal Transplantation
Duke University Health System



CUTTING EDGE OF TRANSPLANTATION

TRANSPLANT SUMMIT 2020
BALANCING EQUITY AND UTILITY IN THE FACE OF AN ORGAN SHORTAGE

How to Define Success for a Liver Transplant Candidate



CUTTING EDGE OF TRANSPLANTATION

TRANSPLANT SUMMIT 2020

BALANCING EQUITY AND UTILITY IN THE FACE OF AN ORGAN SHORTAGE

How to Define Success for a Patient with ESLD



CUTTING EDGE OF TRANSPLANTATION

TRANSPLANT SUMMIT 2020
BALANCING EQUITY AND UTILITY IN THE FACE OF AN ORGAN SHORTAGE

Disclosure

Nothing to disclose.

Learning Objectives

1. Review commonly utilized measures of liver transplant success
2. Review longer term outcomes of liver transplantation
 - a. Graft or patient survival
 - b. Health care related quality of life
3. Recognize deficiencies in patient centered contributions to defining success of liver transplantation

Do we really have any consensus
regarding the definition of transplant
success?

Definitions of success

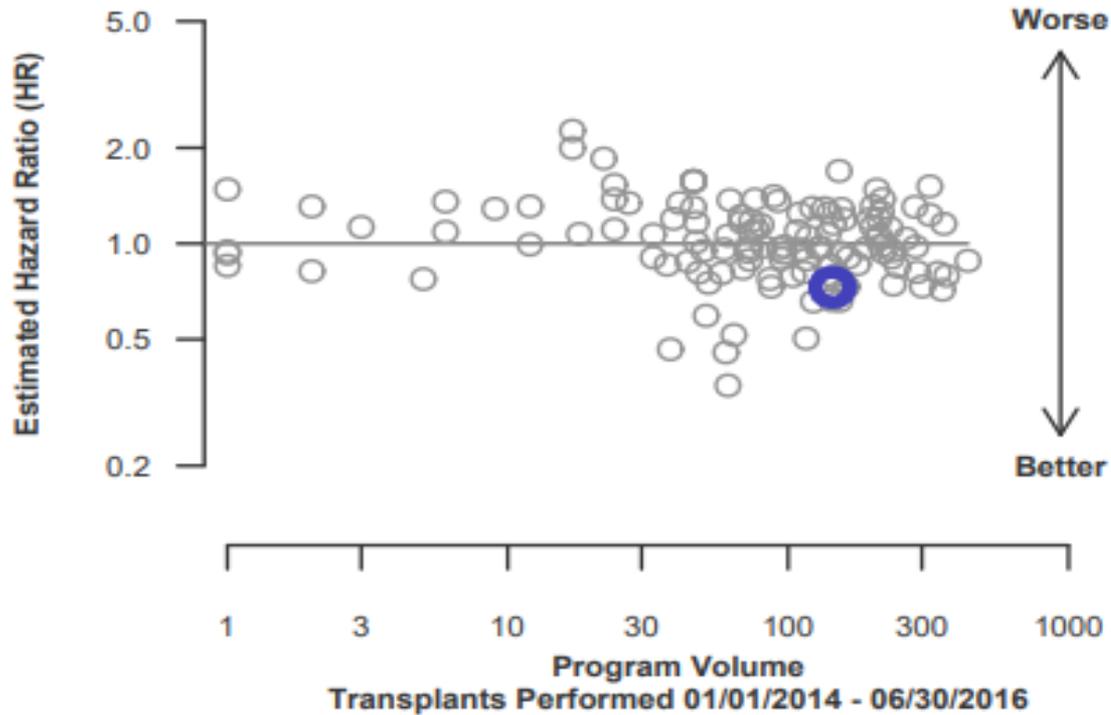
- From a systematic/regulatory perspective
- Patient perspective
 - Quality of life
 - Employment
 - Physical functioning
- Cost/benefit analysis-value based thinking

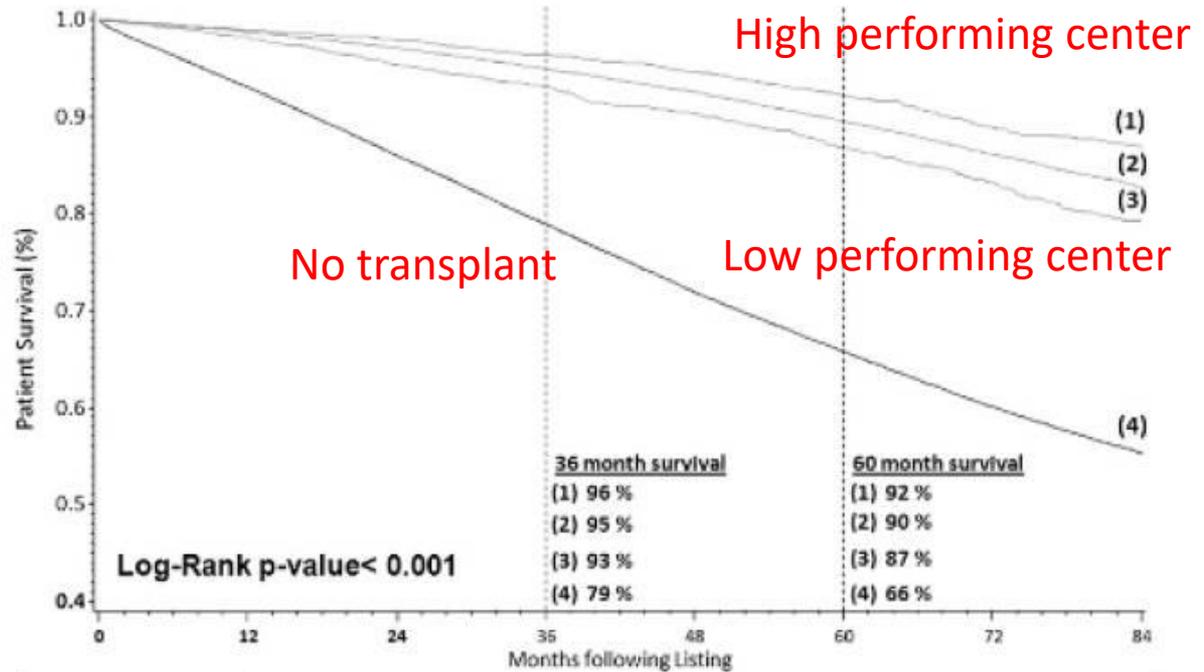
Simplest binary definition



- Are we alive or dead?

Figure C6. Adult (18+) 3-year graft failure HR program comparison





Schold JD, et al.,
Clin J Am Soc Nephrol.
 2014;9(10):1773-80.

January 2020 Liver SRTR report

| | DISTANCE | DECEASED DONOR TRANSPLANTS IN A YEAR | LIVING DONOR TRANSPLANTS IN A YEAR | SURVIVAL ON THE WAITLIST | GETTING A DECEASED DONOR TRANSPLANT FASTER | 1-YEAR LIVER SURVIVAL |
|---|----------|--|--|-----------------------------|--|--------------------------|
| View Summary Data View Complete Report (PDF) | N/A | 128 ADULTS | 1 ADULTS | | | |
| View Summary Data View Complete Report (PDF) | N/A | 100 ADULTS | 0 ADULTS | | | |
| View Summary Data View Complete Report (PDF) | N/A | 22 ADULTS | 0 ADULTS | | | |
| View Summary Data View Complete Report (PDF) | N/A | 138 ADULTS | 0 ADULTS | | | |

i For liver transplant candidates, this measure has the **largest impact on survival after listing** among these three measures. 1 year liver survival includes only candidates who received a transplant.

Regulatory oversight and definition of success

- CMS Conditions of Participation
- UNOS MPSC oversight
- SRTR Public reporting
- Focus has been on 1 year survival

What about longer term survival/success?

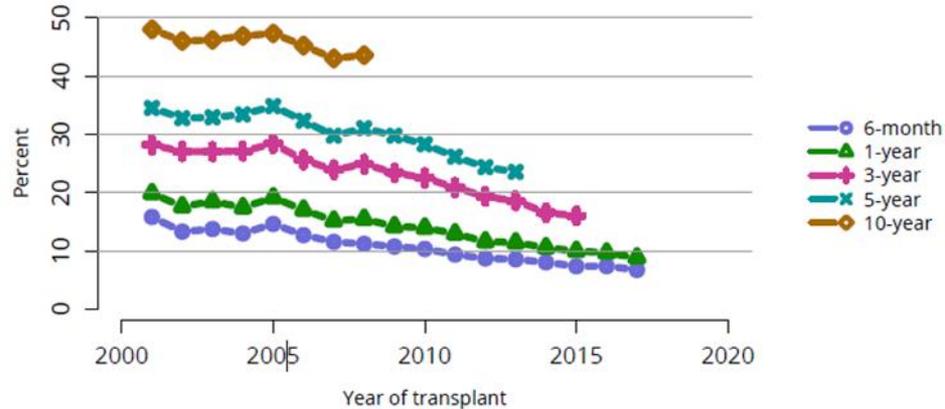


Figure LI 67. Graft failure among adult deceased donor liver transplant recipients. All adult recipients of deceased donor livers, including multi-organ transplants. Patients are followed until the earliest of retransplant, death, or December 31, 2018.

2018 SRTR
Annual report

How good is good enough?

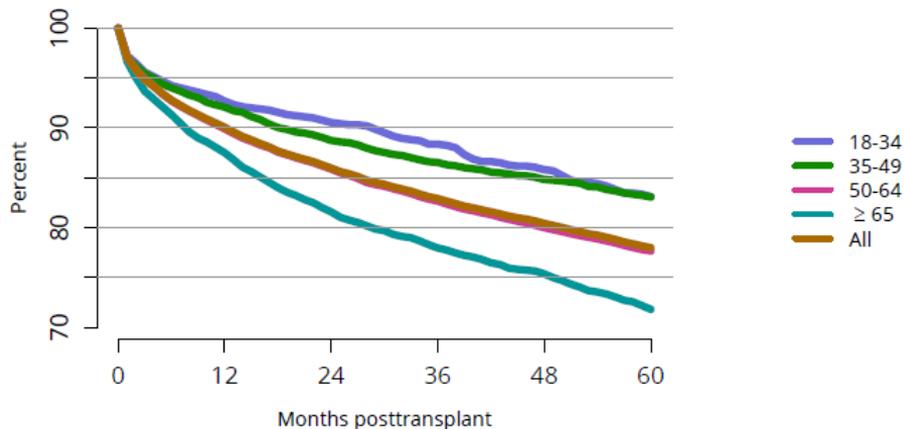


Figure LI 86. Patient survival among adult deceased donor liver transplant recipients, 2011-2013, by age. Patient survival estimated using unadjusted Kaplan-Meier methods. For recipients of more than one transplant during the period, only the first is considered.

2018 SRTR
Annual report

Long term “success”: ELTR

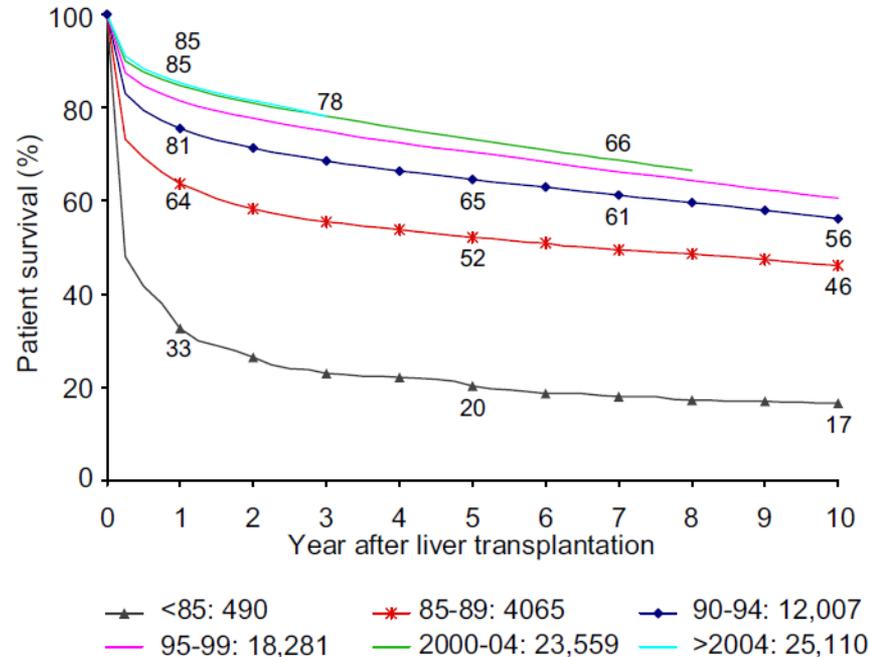
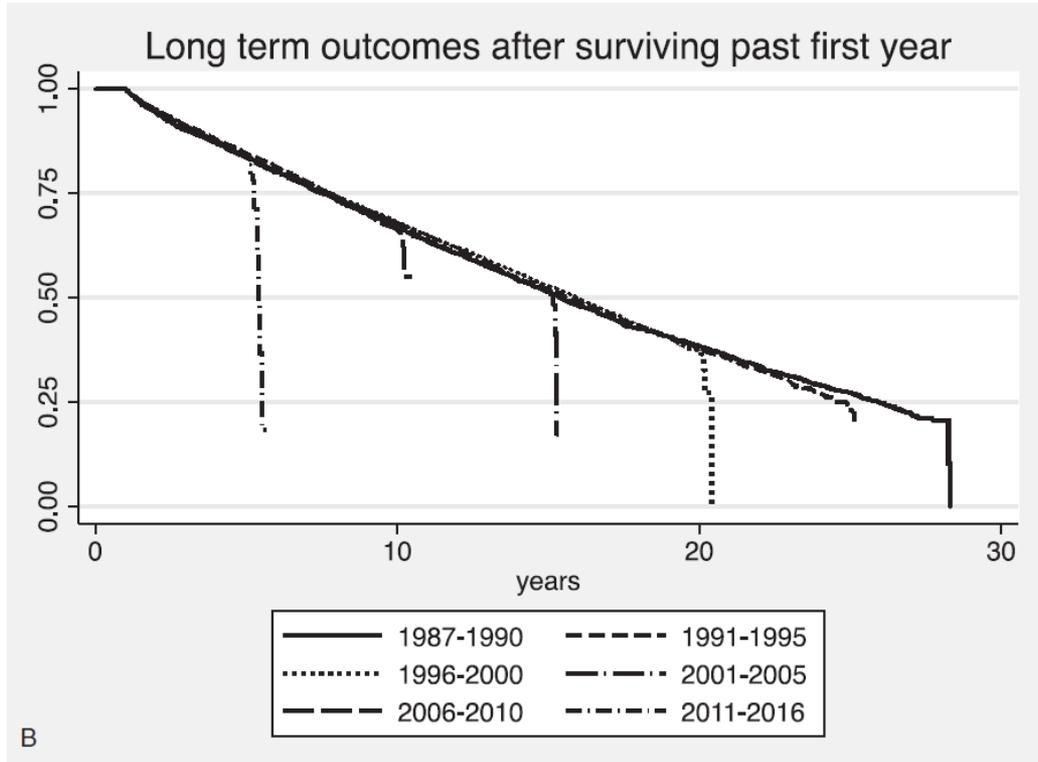


Fig. 7. Patient survival according to year of LT.

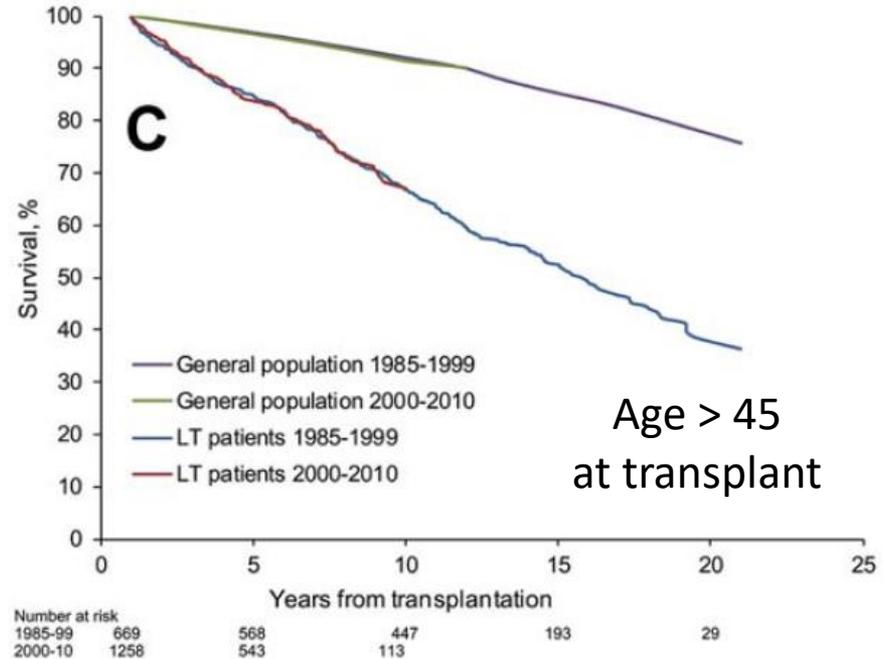
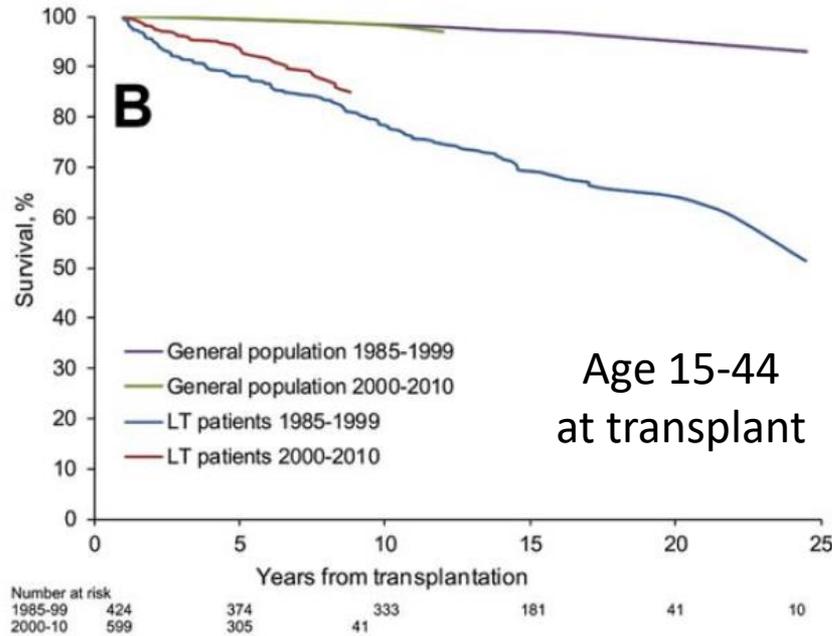
Adam R, et al.,
J Hepatol 2012;
57:675-688

Long term “success”: US

Ranas A, et al.,
Ann Surg 2019;
269:20-17



Success compared to what?



Aberg F, et al., Hepatology 2015;61:668-677

If we have survived, what is the expected QOL that defines success?



Changing definitions of successful outcomes in pediatric liver transplantation

Nanda Kerkar^{a,b} and Tanaz Danialifar^b

The focus of success after transplantation is moving toward achieving 'normality' posttransplant.

Curr Opin Organ Transplant 2014;19:480-485

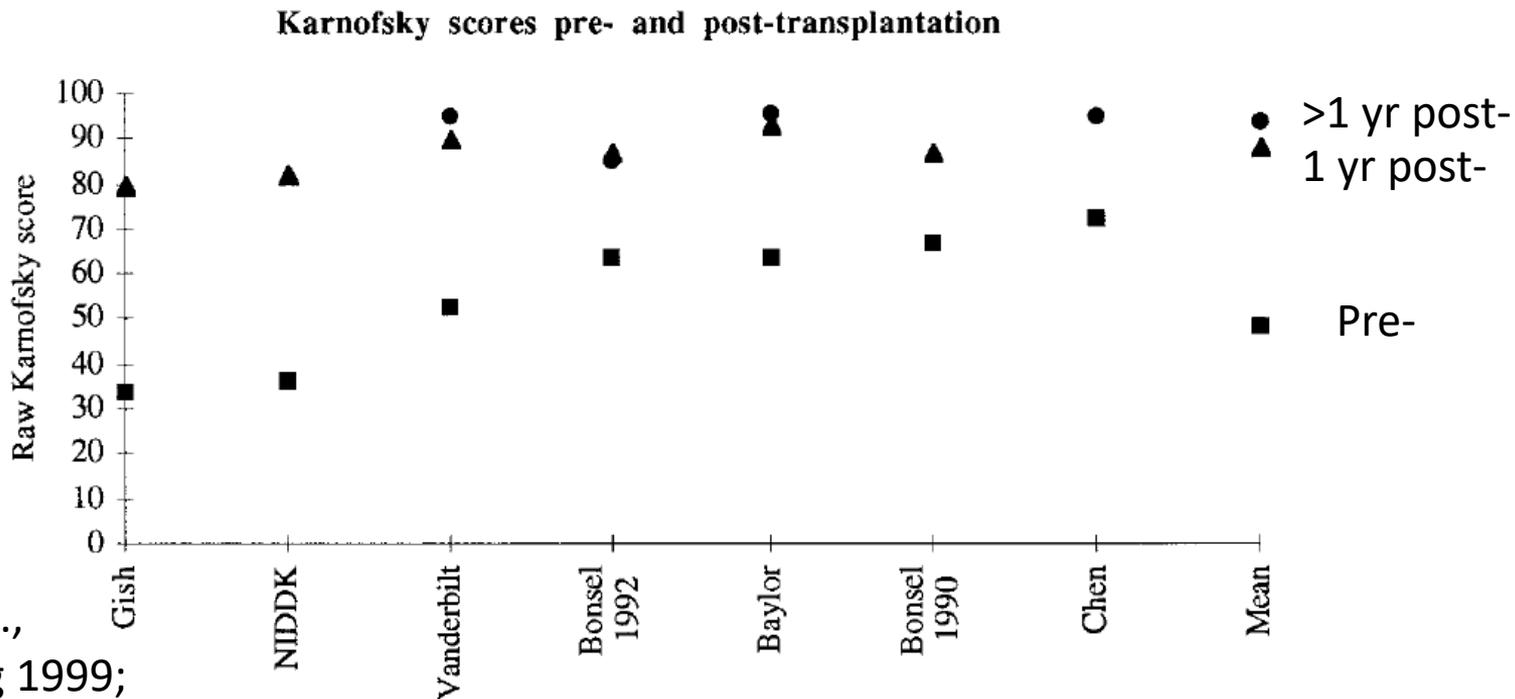
“Successful” outcome:

In the Eye of the Beholder

- Majority of cancer patients more concerned about QOL than longevity
- More than 50% of patients consider a severe stroke worse than death
- Physician perception of QOL often at odds with patient perception

Owens DK. Hepatology 1998;27:292-293

Mean Karnofsky scores following LT



Bravata DM, et al.,
Liver Transpl Surg 1999;
5:318-331

QOL after liver transplant

Bravata DM, et al.,
Liver Transpl Surg 1999;
5:318-331

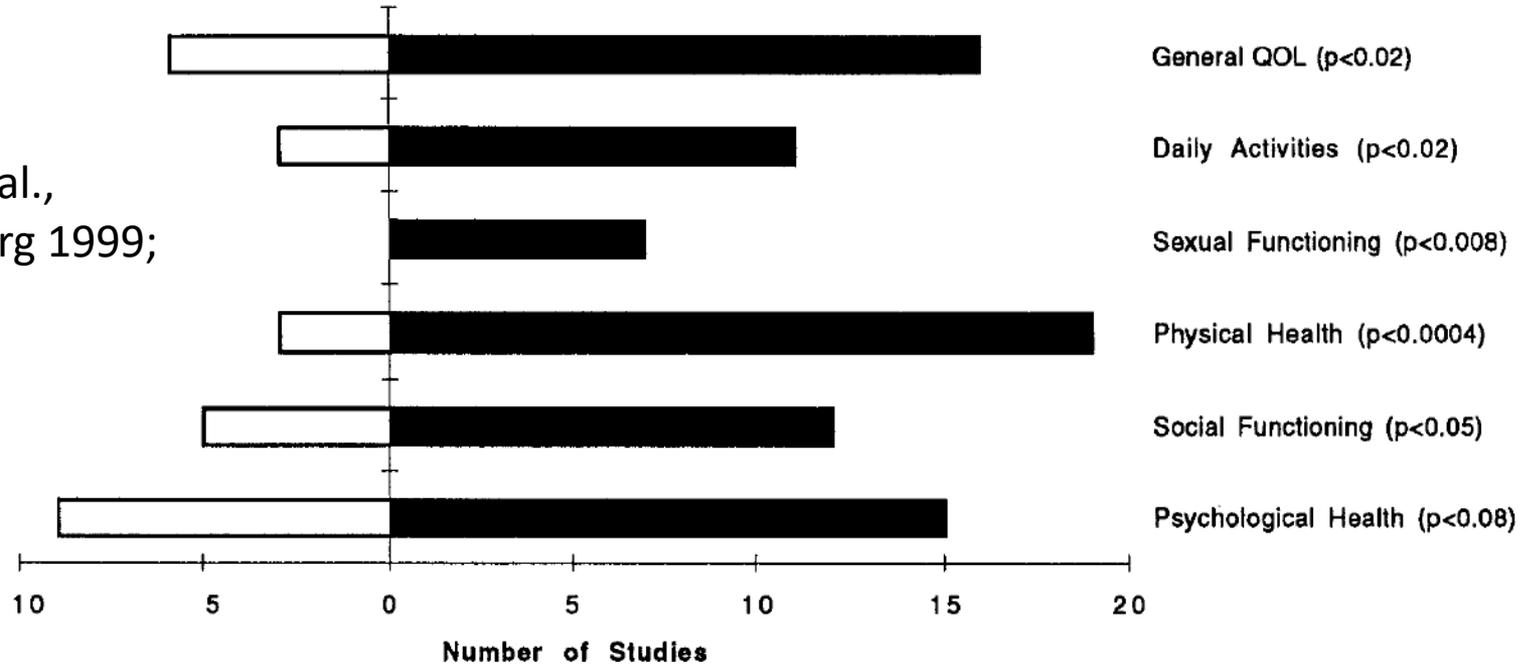
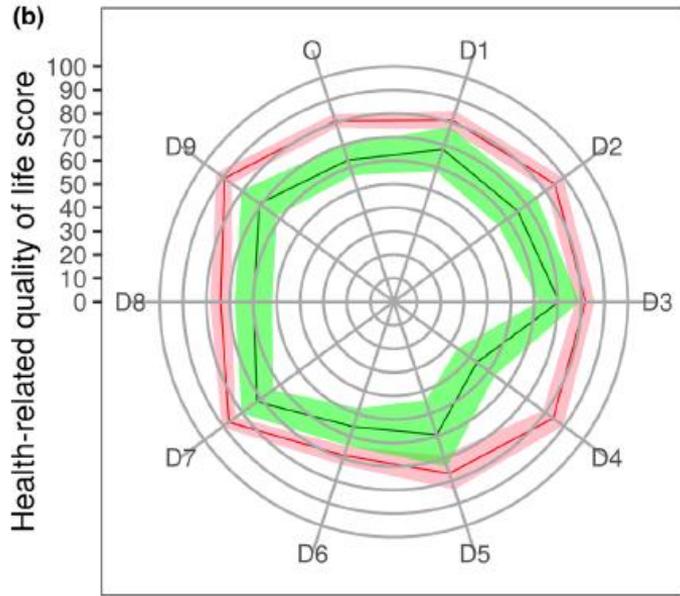
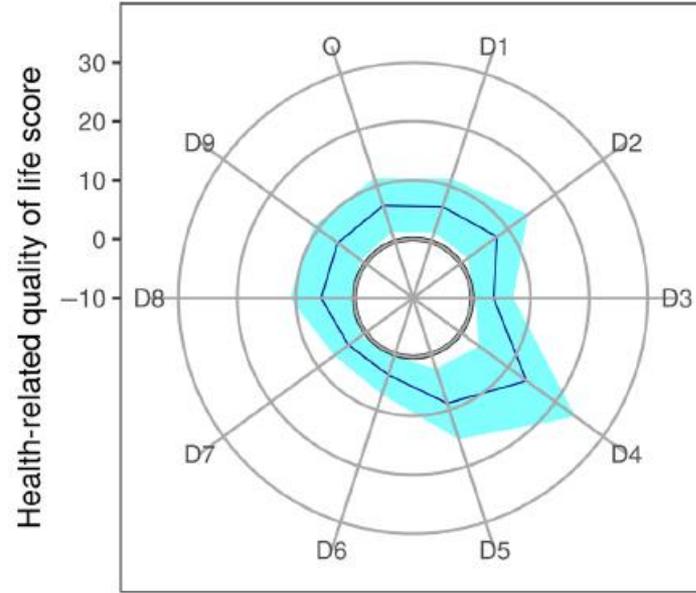


Figure 3. Summary results of the sign test. The number of positive studies (■) and nonpositive studies (□) for each QOL domain are shown.

SF-LDQOL before/after LT



Health-related quality of life domains



Health-related quality of life domains

Avg
Treatment
effect

McLean KA, et al., Transplant International 2019;32:808-819

UCLA long-term “success”: QOL

TABLE 5. Short Form-36: Health-Related Quality of Life in 20-Year Liver Transplant Survivors Compared With US General Population and Patients With Chronic Liver Disease

| Category | 20-yr Survivors (n = 68) | US Population (n = 2474) | <i>P</i> | Chronic Liver Disease (n = 210) | <i>P</i> |
|----------------------------|-----------------------------|-----------------------------|----------|------------------------------------|----------|
| Physical functioning | 79 ± 26 | 84 ± 23 | 0.038 | 51 ± 29 | <0.001 |
| Role-physical | 67 ± 42 | 81 ± 34 | <0.001 | 38 ± 31 | <0.001 |
| Bodily pain | 72 ± 28 | 75 ± 24 | 0.315 | 50 ± 32 | <0.001 |
| General health | 62 ± 23 | 72 ± 20 | <0.001 | 54 ± 27 | 0.033 |
| Vitality | 63 ± 22 | 61 ± 21 | 0.329 | 52 ± 28 | 0.002 |
| Social functioning | 77 ± 26 | 83 ± 23 | 0.026 | 33 ± 21 | <0.001 |
| Role-emotional | 75 ± 39 | 81 ± 33 | 0.098 | 58 ± 20 | <0.001 |
| Mental health | 80 ± 20 | 74 ± 18 | 0.029 | 34 ± 22 | <0.001 |
| Physical component summary | 46 ± 12 | 50 ± 10 | <0.001 | — | — |
| Mental component summary | 52 ± 11 | 50 ± 10 | 0.124 | — | — |

Duffy JP, et al., Ann Surg 2010;252:652-661

UMinn long term “success”: QOL

20 year survivors

TABLE 3. HRQOL as Measured With the SF-12 Health Survey: PCS and MCS Scale Scores by Age Group

| | Adult Recipients (n = 12) | Pediatric Recipients (n = 24) | <i>P</i> Value |
|-----|---------------------------------|-------------------------------------|----------------|
| PCS | 39.3 ± 14.7 | 49.2 ± 12.0 | 0.04 |
| MCS | 54.6 ± 9.4 | 48.6 ± 11.0 | 0.12 |

NOTE: The values were standard-normalized to the US population with a mean of 50 and a standard deviation of 10. *P* values are based on the Mann-Whitney U test. Thirty-six of the 53 liver transplant recipients alive at the time of follow-up responded to an SF-12 Health Survey.

Sullivan KM, et al.
Liver Transplantation 2014;
20:649-654

“It would be ideal if a measure of HRQOL were included in transplant databases or clinical care. These data could be monitored over time and might enable therapeutic interventions or provide a better understanding of the challenges that remain for OLT”

Sullivan KM, et al. Liver Transplantation 2014;20:649-654

Summary

- Definition of success has largely been driven by regulatory bodies
- Success has been focused on short term end-point
- Success is more than being alive
- There is abundant opportunity to make liver transplantation more successful