Recommendations for

Quality Assessment of Surgical Interventions

Pierre-Alain Clavien

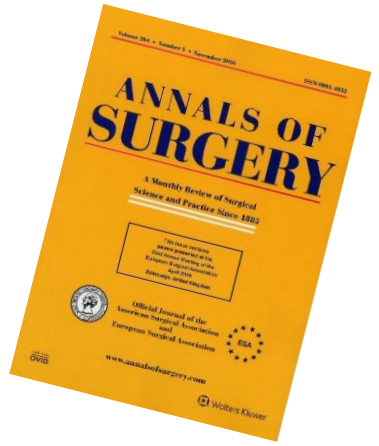
MD, PhD, FACS (Hon), ASA (Hon), FRCS (Engl), FRCS (Ed)

Professor of Surgery and Transplantation
Member of the National Academy of Medicine (USA)

ORIGINAL ARTICLE

Distinguishing Clinical From Statistical Significances in Contemporary Comparative Effectiveness Research

Ajami Gikandi, BA, Julie Hallet, MD, MSc,† Bas Groot Koerkamp, MD,‡ Clancy J. Clark, MD,§ Keith D. Lillemoe, MD,‖ Raja R. Narayan, MD, MPH,¶ Harvey J. Mamon, MD, PhD,# Marco A. Zenati, MD, MSc,** Nabil Wasif, MD,†† Dana Gelb Safran, ScD,‡‡ Marc G. Besselink, MD, PhD, MSc,§§ David C. Chang, PhD, MPH, MBA,‖ Lara N. Traeger, PhD,‖‖ Joel S. Weissman, PhD,¶¶ and Zhi Ven Fong, MD, MPH, PhD††✉*



Ann Surg 2024; 279: 913-914

EDITORIAL Ann Surg 2024; 279: 913-914

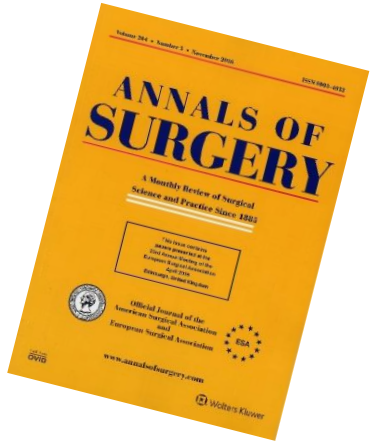
Is Statistical Significance Alone Obsolete?

Let's Turn to Meaningful Interpretation of Scientific and Real-world Evidence on Surgical Care

Milo A. Puhan, MD, PhD ✉ and*
Pierre-Alain Clavien, MD, PhD† ✉

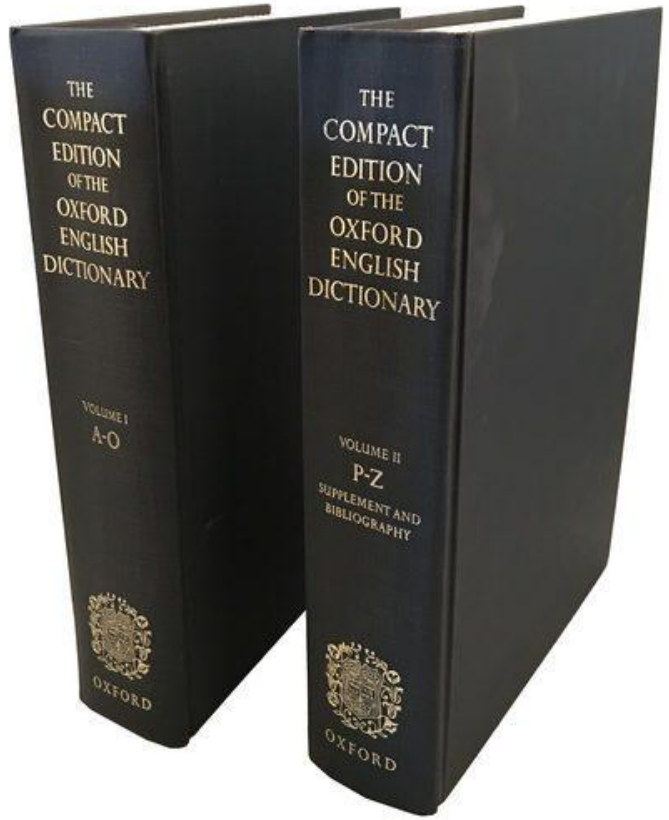
The Concept

minimal important difference (MID)



Quality of Health Care

Quality



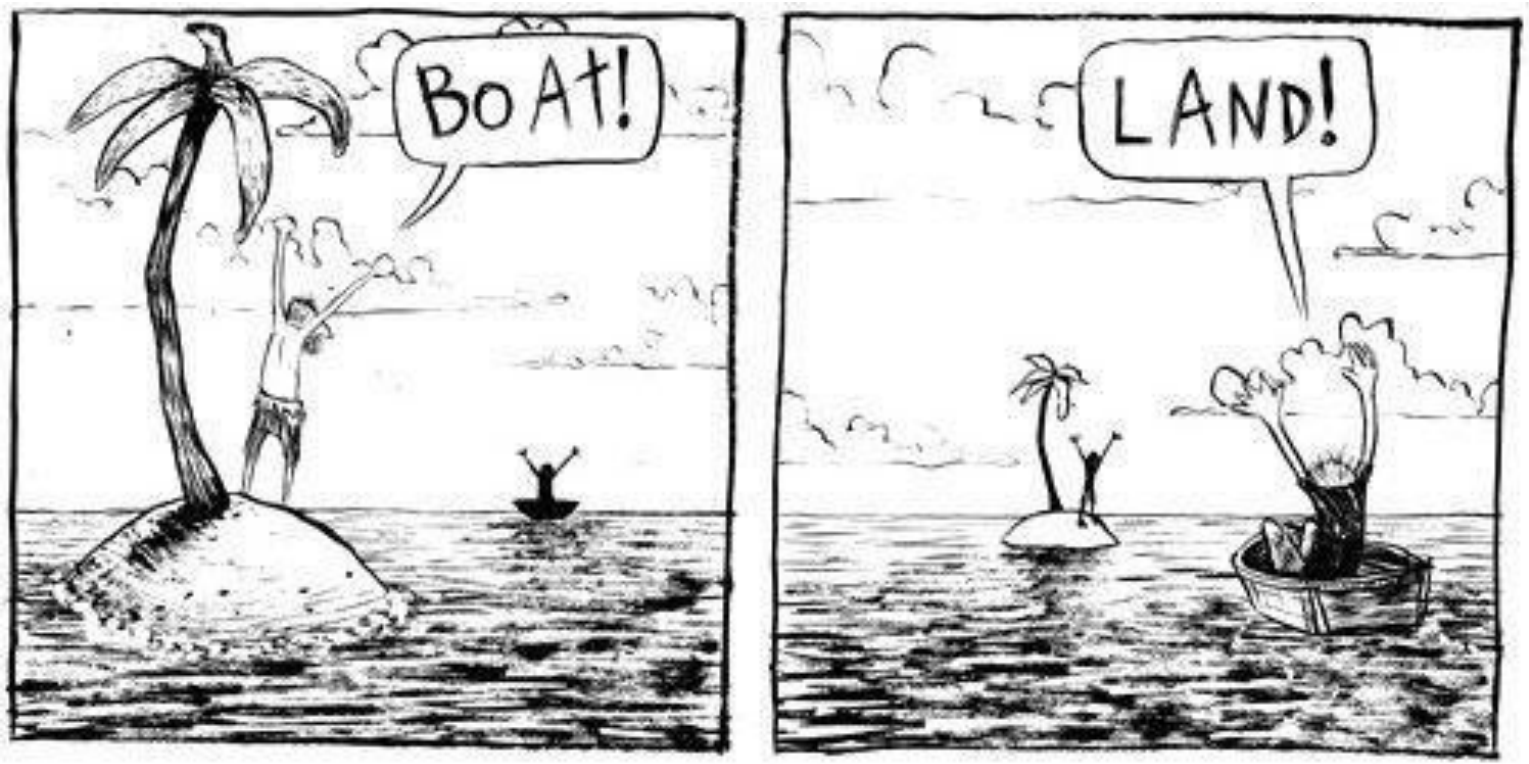
The standard of **SOMETHING**

when it is compared to other things like it.

….. ***how good or bad something is***.

https://www.oxfordlearnersdictionaries.com/

What means Quality?



https://writingpanther.wordpress.com/2017/03/09/article-5-angle-of-vision/

What means Quality - **for Society & Economy**?

BMJ Publishing group Ltd, 2016.
http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf

What means Quality - **for Doctors**?

Complication = any deviation from the normal postoperative course

What means Quality - **for the Patient**?

Johann Wolfgang von Goethe

No two people see the world exactly alike. Even one and the same person won’t always maintain the same views and judgments

What is Quality? for the PATIENT

Effect of Orthotopic Liver Transplantation on Employment and Health Status

Christine M. Hunt, Julie S. Tart,† Elaine Dowdy,‡ Barbara Philips Bute,* Diane M. Williams,* and Pierre-Alain Clavien†*

Liver Transplantation and Surgery, Vol 2, No 2 (March), 1996: pp 148-153

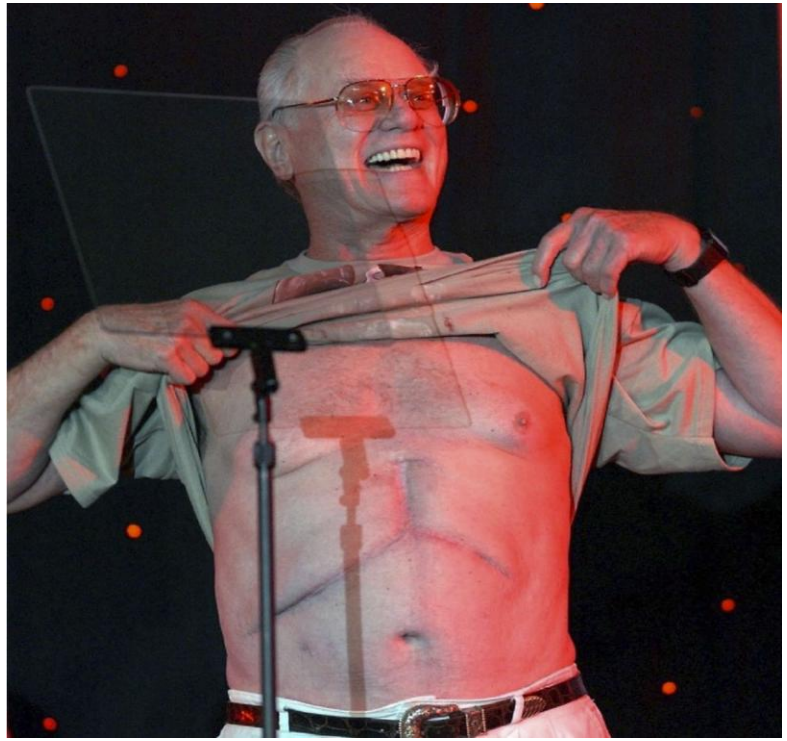
What means Quality - **for the patient**?

Patient 1

1 year after Liver Transplantation

Severe disatisfaction

Patient 2



1 year after Liver Transplantation

Very happy

What means Quality?

→ Assessment goes beyond Mortality

- Complications
- Quality of life
- Patient satisfaction
- Costs
- …

Domenghino et al. Nature Medicine 2023

THE LANCET

Volume 347, 984–985; 1996

Horton, R.

Surgical research or comic opera:

Many questions, but few answers.

Outcome reporting in 2002

119 articles reporting outcomes in 22,530 patients after pancreatectomy, esophagectomy & hepatectomy

Follow-up information	**60%**
Procedure specific complications	**57%**
Definitions of complications	**34%**
Severity of complication	**20%**
Patient reported outcomes	**NA**

Martin RC et al. Ann Surg 2002

Outcome reporting TODAY

627 articles repo[illegible]rgical proced[illegible]

ORIGINAL ARTICLE

Surgical Outcome Reporting. Moving From a Comic to a Tragic Opera?

Fariba Abbassi, MD,*† Matthias Pfister, MD,* Anja Domenghino, MD, PhD,*†
Milo A. Puhan, MD, PhD,† and Pierre-Alain Clavien, MD, PhD‡✉

[illegible]		55%
[illegible]	20%	61%
[illegible] reported outcomes	NA	17%

Abbassi F, Clavien PA, Ann Surg 2024

EDITORIALS

Surgical outcome assessment — the need for better and standardized approaches?

Henrik Kehlet, MD, PhD · Pierre-A. Clavien, MD, PhD

Kehlet H, Clavien PA, Can J Anesth 2021

nature medicine

Consensus Statement

https://doi.org/10.1038/s41591-023-02237-3

Consensus recommendations on how to assess the quality of surgical interventions

Received: 24 October 2022

Accepted: 26 January 2023

Published online: 17 April 2023

Anja Domenghino[1,2], Carmen Walbert[3], Dominique Lisa Birrer[1], Milo A. Puhan[2] ✉, Pierre-Alain Clavien[1] ✉ & The Outcome4Medicine consensus group*

how should **outcomes** be **measured, interpreted, and communicated** to improve **patient care** worldwide

ETH zürich

University of Zurich[UZH]

SAMW ASSM
Schweizerische Akademie der Medizinischen Wissenschaften

LGID Foundation
Liver and Gastrointestinal Disease Foundation

SWISS MEDICAL NETWORK

nature medicine

Jury recommendations: the seven final statements

(1) Record outcome parameters at standardized time points.
(2) Routinely use PROMS and PREMS in clinical care.
(3) Record individual and global morbidity according to the Clavien–Dindo classification and by using the CCI.
(4) Define benchmark values and compare results.
(5) Conduct routine interdisciplinary mortality and morbidity conferences.
(6) Appoint a 'data quality guarantor' at every institution.
(7) Follow the TRACK principle in case of unwarranted outcomes: Transparency, Respect, Accountability, Continuity and Kindness must be applied.

ETH zürich

University of Zurich[UZH]

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SWISS MEDICAL NETWORK

Domenghino A et al. Nat Med 2023

Clinical perspective

How to assess?

→ Assessment tools must be

- Precise
- Reproducible
- Intuitive
- Quantitative
- …

Clavien-Dindo Classification

Grade	Description
1	No need for pharmacological treatment or inter
2	Pharmacological treatment
3	Surgical, endoscopic or radiological intervention
3a	*Regional or local anesthesia*
3b	*General anesthesia*
4	Life-threatening complication requiring ICU management
4a	*Single-organ dysfunction*
4b	*Multi-organ dysfunction*
5	Patient demise

Invasiveness of the therapy

Cited: > 40,000 x

Dindo D, Clavien PA. Ann Surg 2004

Clavien-Dindo Classification

Drawback: What about multiple complications?

Which patient had the "worse" postoperative course?

Patient A		Patient B	
Wound infect	1	Urinary infect	2
Abscess	3a	Severe pain	2
Gastric ulcer	3a	Bleeding	3b

Comprehensive Complication Index (CCI®)

A Novel Continuous Scale to Measure Surgical Morbidity

Ksenija Slankamenac, MD, Rolf Graf, PhD,* Jeffrey Barkun, MD,† Milo A. Puhan, MD, PhD,‡ and Pierre-Alain Clavien, MD, PhD**

Ann Surg 2013

Summarizes **all complications** and their **relative severity** in **one single number**

CCI®:

0
no complication

100
death

Postoperative Complications

Clavien-Dindo classification vs. CCI®

Pancreas surgery

Patient A		Patient B	
Wound infect	1	Urinary infect	2
Abscess	3a	Severe pain	2
Gastric ulcer	3a	Bleeding	3b

Postoperative Complications

Clavien-Dindo classification vs. CCI®

Pancreas surgery

	Patient A	Patient B
CCI®	38	45

Postoperative Complications

Longitudinal follow-up with CCI®

Pancreas surgery

Discharge	***3 months***	***6 months***	***1 year***
38.1	***43.4***	***55***	***55.7***
Clavien-Dindo compl.	***(+ 2)***	***(+ 3b)***	***(+1)***

Slankamenac K et al. Ann Surg 2013

Most sensitive endpoints in RCTs

PAPER OF THE 21ST ANNUAL ESA MEETING

The Comprehensive Complication Index

A Novel and More Sensitive Endpoint for Assessing Outcome and Reducing Sample Size in Randomized Controlled Trials

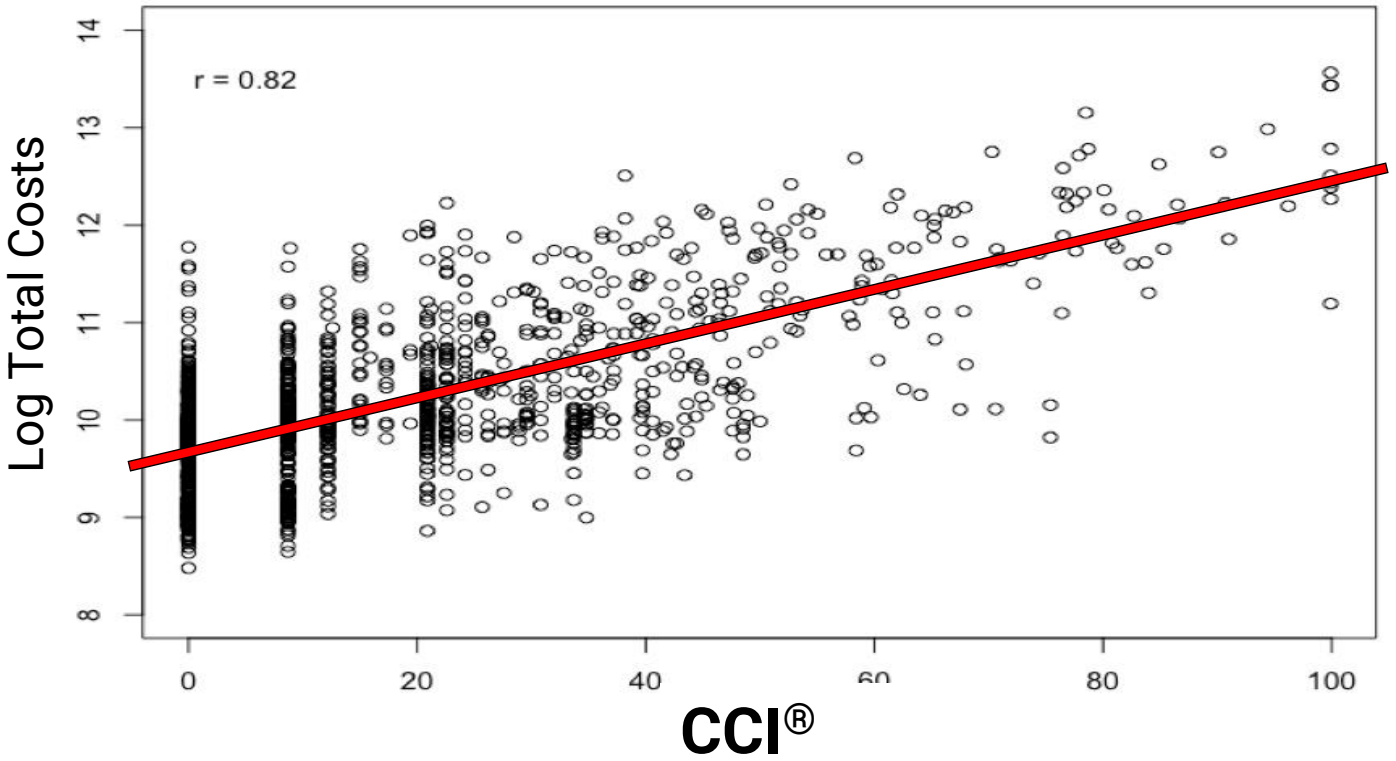
Ksenija Slankamenac, MD, PhD, Nina Nederlof, MD,† Patrick Pessaux, MD,‡ Jeroen de Jonge, MD, PhD,† Bas P. L. Wijnhoven, MD, PhD,† Stefan Breitenstein, MD,* Christian E. Oberkofler, MD,* Rolf Graf, PhD,* Milo A. Puhan, MD, PhD,§ and Pierre-Alain Clavien, MD, PhD*¶*

Ann Surg 2014

Correlation to costs

Cost Assessment Tool

The Comprehensive Complication Index (CCI®) is a Novel Cost Assessment Tool for Surgical Procedures



Staiger R et al. Ann Surg 2018

ESA PAPER

Milestones in Surgical Complication Reporting. Clavien-Dindo Classification 20 Years & Comprehensive Complication Index (CCI®) 10 Years

Abbassi, Fariba MD[*,†]; Pfister, Matthias MD[*,‡]; Lucas, Katharina L MD[§]; Domenghino, Anja MD, PhD[‖]; Puhan, Milo A MD, PhD[†]; Clavien, Pierre-Alain MD, PhD[*,‡]; the Outcome Reporting Group

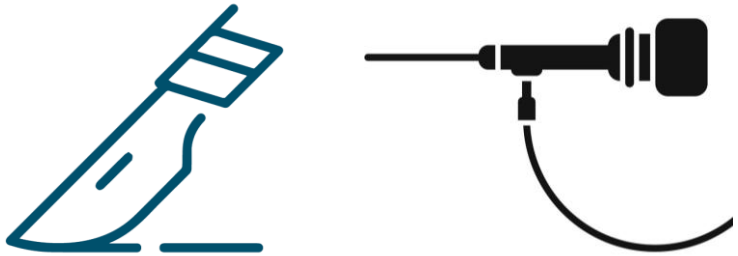
→ Guidance on how to count and rate complications

Abbassi F et al. Ann Surg 2024

Recommendation 1

→ Negative invasive diagnostics

Diagnostics



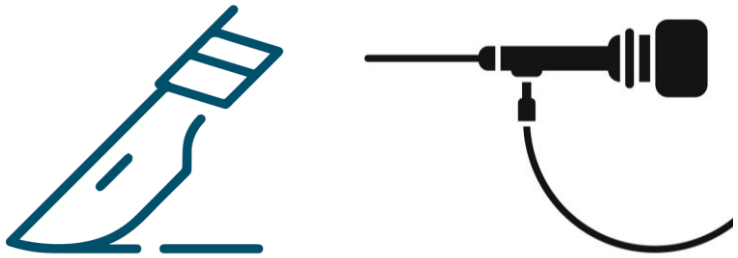
No Complication

Abbassi F et al. Ann Surg 2024

Recommendation 1

→ Negative invasive diagnostics

Diagnostics



No Complication

Diagnostics
+ Treatment

Complication

Abbassi F et al. Ann Surg 2024

Recommendation 2

→ Complications requiring multiple interventions

Complication vs. **number of therapeutic interventions** needed

→ Risk to underestimate the cumulative morbidity

each individual intervention should be included in the CCI®

Abbassi F et al. Ann Surg 2024

Recommendation 2

→ Complications requiring multiple interventions

- Necrotizing pancreatitis after right sided hemicolectomy

  → 3 re-looks

3 x CD grade 3b

- Anastomotic leak after esophagectomy

  → 4 sponge placements

4 x CD grade 3a

Abbassi F et al. Ann Surg 2024

AssessSurgery
Design by Gottfried Honegger

Home | CCI® Calculator | About the CCI® | The Clavien-Dindo Classification | About us | Contact | Buy Premium | Login

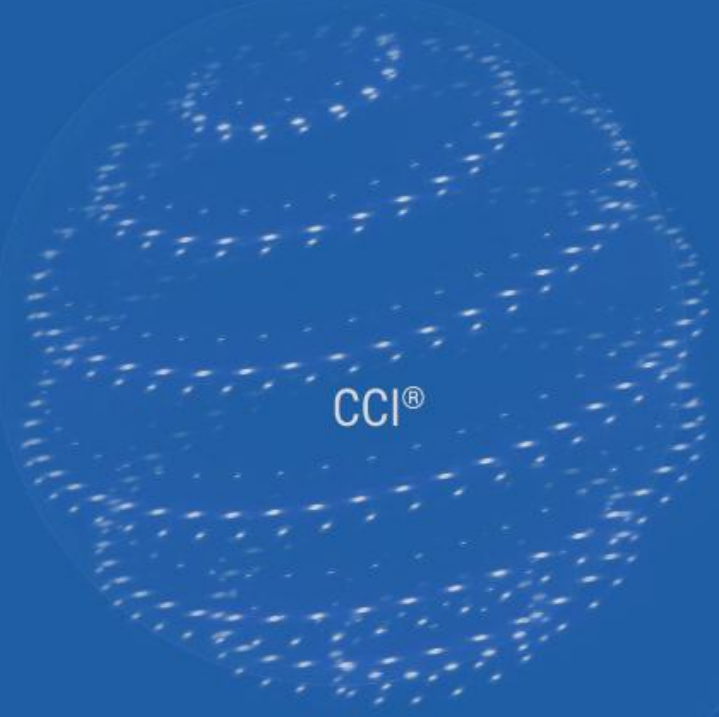
Free available

The only validated measure to assess patient's overall morbidity

- Sensitive endpoint for RCTs
- Reduced sample size requirements
- Selected as a yardstick in jury-based consensus recommendations on how to assess the quality of surgical interventions (Domenghino et al., Nature Medicine, 2023 , doi: 10.1038/s41591-023-02237-3)

Learn more about the CCI® →

Explore Premium →



Comprehensive
Complication Index

50.6

Grade I	1
Grade II	0
Grade IIIa	1
Grade IIIb	0
Grade IVa	1
Grade IVb	0
Grade V	0

Comprehensive
Complication Index

0

Grade I	0
Grade II	0
Grade IIIa	0
Grade IIIb	0
Grade IVa	0
Grade IVb	0
Grade V	0

Comprehensive
Complication Index

0

Grade I	0
Grade II	0
Grade IIIa	0
Grade IIIb	0
Grade IVa	0
Grade IVb	0
Grade V	0

CCI® Calculator

Premium

NEW: Premium Versions

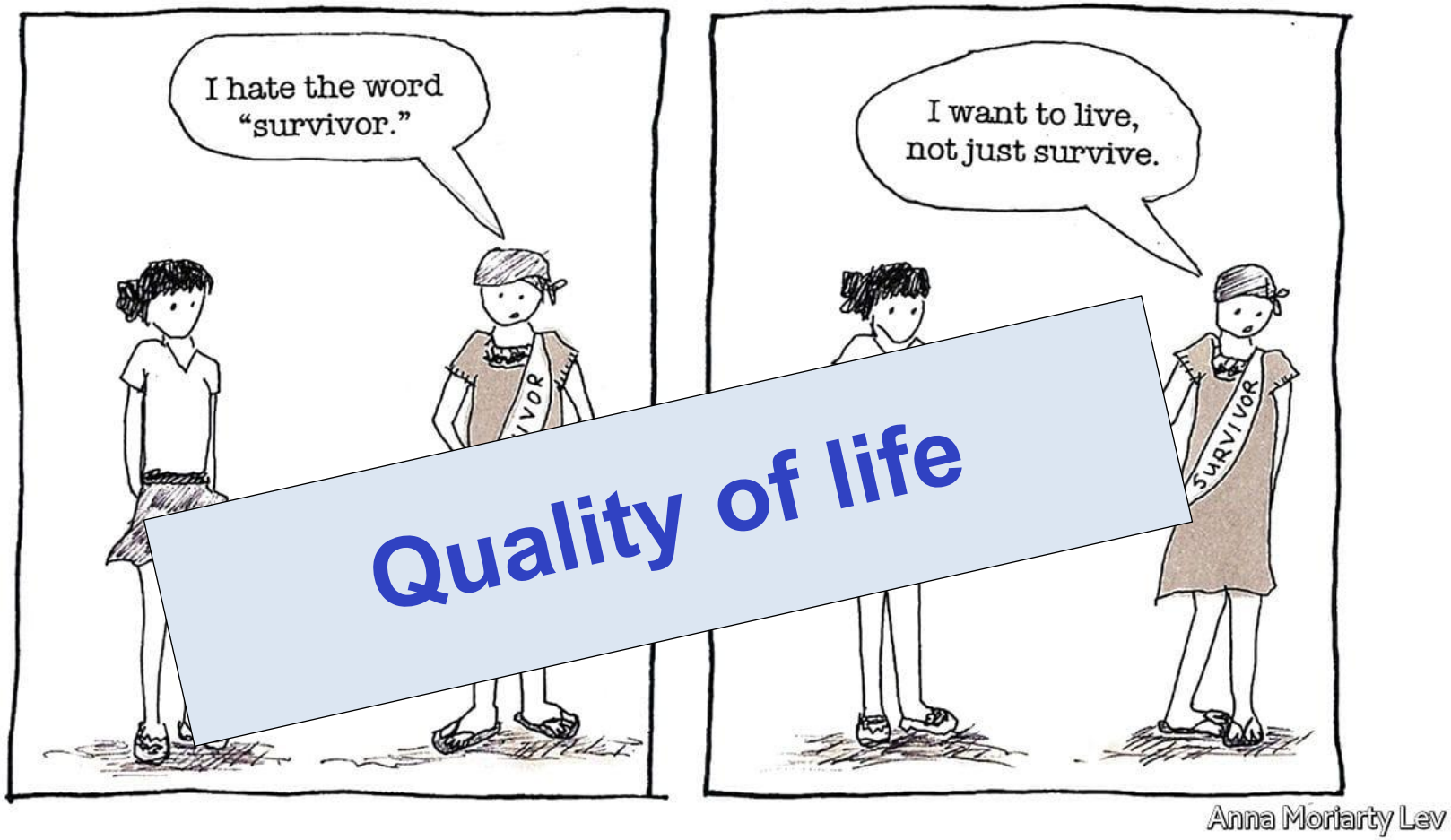
- For individuals or groups available
- Create your own databases
- Do longitudinal follow-ups for patients
- Export your data as Excel file
- Share your data with other users for multicenter studies

CCI® Calculator

Coming soon

- Integration of the CCI® **into hospital information system**
- Integration of the CCI® **into the REDCap**

Patient's Perspective



https://www.economist.com/culture/2022/05/18/doctors-and-therapists-are-turning-to-comic-books

Patients’ perspective

- Focus on **quality of life**
- More **home care**
- **Activities**
- **Comparative measures**

Patients' perspective

How to assess?

→ PROMs and PREMs

- Questionnaires filled out by patients
- Standardized format
- Validation according to a rigorous methodology

Gerteis M et al. JHQ 1997
Mokkink LB et al. QoL Research 2010

ESA Session

EUROPEAN SURGICAL ASSOCIATION

Outcomes from Patient Perspective

Description: Which patient reported outcome should be used? Importance of PROMs and PREMs.

ESA Speaker: **Laurence Chiche, MD**
Institution: University Hospital of Bordeaux
City, Country: Pessac, France

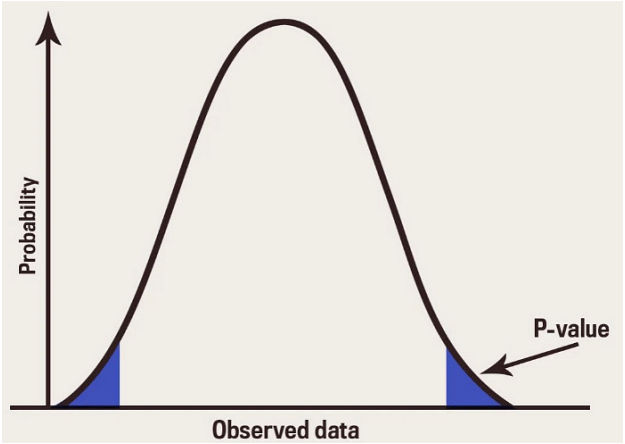
ASA Discussant: **Leigh A. Neumayer, MD, MS, MBA**
Institution: University of Florida Jacksonville
City, State: Jacksonville, FL

The Central Question

How should results be **interpreted**?

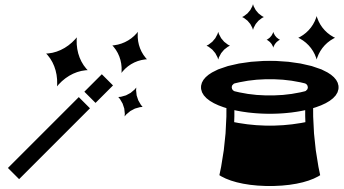
Data Interpretation

Statistical significance



P-Value <0.05

The magic number



The probability of **obtaining test results** at least as extreme as the observed difference **is <5%**, if the **null hypothesis is true**.

Does not reveal the magnitude of the effect size

Data Interpretation

Clinical significance

- **Smallest change** in outcome that is **meaningful to patients**
- Based on many outcome measures, e.g., PROMs

Distinguishing Clinical From Statistical Significances in Contemporary Comparative Effectiveness Research

Ajami Gikandi, BA, Julie Hallet, MD, MSc,† Bas Groot Koerkamp, MD,‡ Clancy J. Clark, MD,§ Keith D. Lillemoe, MD,‖ Raja R. Narayan, MD, MPH,¶ Harvey J. Mamon, MD, PhD,# Marco A. Zenati, MD, MSc,** Nabil Wasif, MD,†† Dana Gelb Safran, ScD,‡‡ Marc G. Besselink, MD, PhD, MSc,§§ David C. Chang, PhD, MPH, MBA,‖ Lara N. Traeger, PhD,‖‖ Joel S. Weissman, PhD,¶¶ and Zhi Ven Fong, MD, MPH, PhD††✉*

Ann Surg June 2024

- Analysis of 5 surgical and medical journals published in 2022
- 307 comparative effectiveness research studies

- **All** primary outcome = **statistical significance**
- **Only 2 with defined minimal clinical significance (MID)**

Statistical *vs.* clinical significance

Problematic

- P values only reveal whether [illegible] the
- [illegible] a

☛ could lead to flawed recommendations that increase health care costs, treatment toxicity, and surgical harm.

→ Statistically significance may or may not be clinically significant

Erlotinib Plus Gemcitabine Compared With Gemcitabine Alone in Patients With Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group

Malcolm J. Moore, Pawel Murawa, L... Theodora Voskogl... ...llinger, Heather J. Au, ...ing, Gary Clark,

JOURNAL OF CLINICAL ONCOLOGY

- 569 patients with advanced pancreatic cancer
- Randomization to **erlotinib plus gemcitabine or gemcitabine alone**

→ Statistically significant improvement in survival (**P=0.038**)

→ Clinical outcome: Survival **6.2** *vs.* **5.9 months**

Erlotinib Plus Gemcitabine Compared With Gemcitabine Alone in Patients With Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group

Malcolm J. Moore, Pawel Murawa, L… Theodora Voskogl… …llinger, Heather J. Au, …ing, Gary Clark,

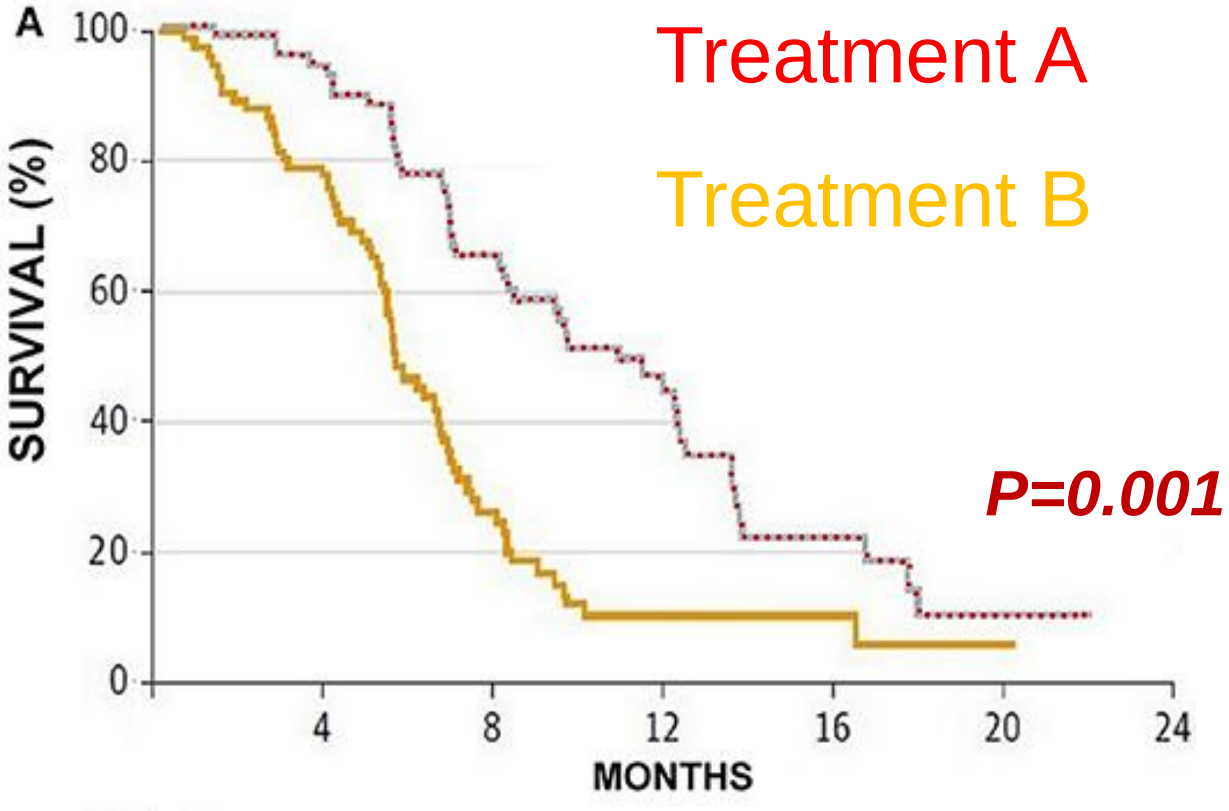
JOURNAL OF CLINICAL ONCOLOGY

- 569 patients with advanced pancreatic c…

…one

10-day difference in survival *vs.* toxicity and costs?

Benefit *vs.* Harm



CCI®

Treatment A: 20

Treatment B: 67

Is Statistical Significance Alone Obsolete?

Let's Turn to Meaningful Interpretation of Scientific and Real-world Evidence on Surgical Care

Milo A. Puhan, MD, PhD✉ and*
Pierre-Alain Clavien, MD, PhD†✉

Quality rather than Quantity

- Move away from single (benefit) outcome to ***benefit-harm analysis***

→ Next steps

Concerning Clinical Significance:

→ Defining Estimates of the MID for the CCI®

- RCTs with CCI® and PROMs as endpoint
- Anchor-based methods: MID of PROMs as anchor

***Submitted to ESA*: Major abdominal surgery: Submitted to ESA: MID = 12 CCI ®**

The credit goes to …..

Milo Puhan, MD, PhD

F. Abbassi

D. Dindo

K. Slankamenac

A.Domenghino

R. D. Staiger

D. Vetter

R. Vonlanthen

BJA
British Journal of Anaesthesia

Volume 131, Number 6, December 2023

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doi: 10.1016/j.bja.2023.09.014
Advance Access Publication Date: 23 October 2023

EDITORIALS

Perioperative outcome assessment from the perspectives of different stakeholders: need for reconsideration?

Fariba Abbassi[1,2], Carmen Walbert[3], Henrik Kehlet[4], Michael P. W. Grocott[5], Milo A. Puhan[2,†] and Pierre-Alain Clavien[6,*,†]

1ST WORLD CONSENSUS AND GUIDELINES MEETING ON PERIHILAR CHOLANGIOCARCINOMA

IMPROVING ONCOSURGICAL OUTCOMES THROUGH SCIENTIFIC EVIDENCE

MILAN
5 - 6 DECEMBER 2024

IGHETTI
AIN CLAVIEN

JURY-BASED ZURIC

Orga
Matt

Jury P sident:
Jordi Bruix (Spain)

Special lecture: Murray Brennan

How to interpret outcome in surgical oncology?

gnosis
egory Gores (USA)

Preoperative Planning and Surgical Resectability
Chair: Mickael Lesurtel (France)

Preoperative Optimization *(Including biliary groinage and hypertrophy techniques)*
Chair: Laurence Chiche (France)

Surgery *(Including minimally-invasive approach)*
Chair: Tomoki Ebata (Japan)

Morbidity / Mortality
Chair: Victoria Ardiles (Argentina)

Perioperative Oncological Treatments *(Including chemotherapy, radiotherapy and immunotherapy)*
Chair: Juan W. Valle (UK)

Transplantation
Chair: Julie K. Heimbach (USA)

Expected Outcomes
Chair: Chiara Braconi (UK)

Guidelines

WWW.CONSENSUS4PCCA.ORG

THANK YOU