Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

Restricted Mean Survival Time in Practice: An Easy-to-Understand Approach

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Dana-Farber Cancer Institute

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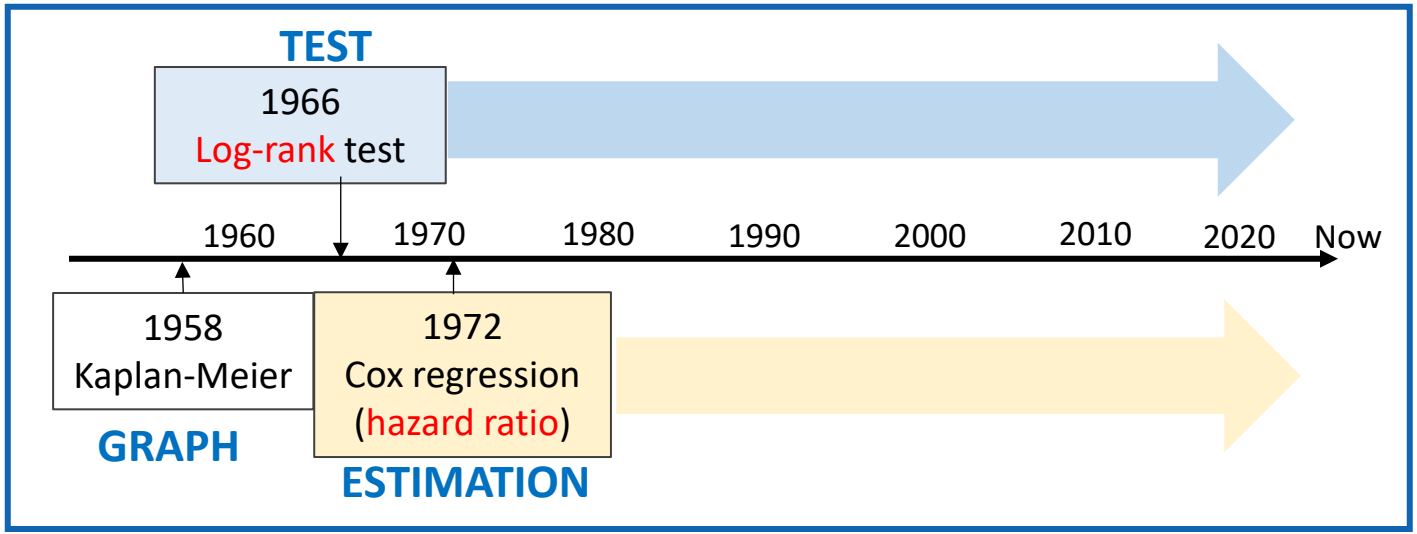
Data Science Training 2025

Welcome!

Methods for time-to-event data

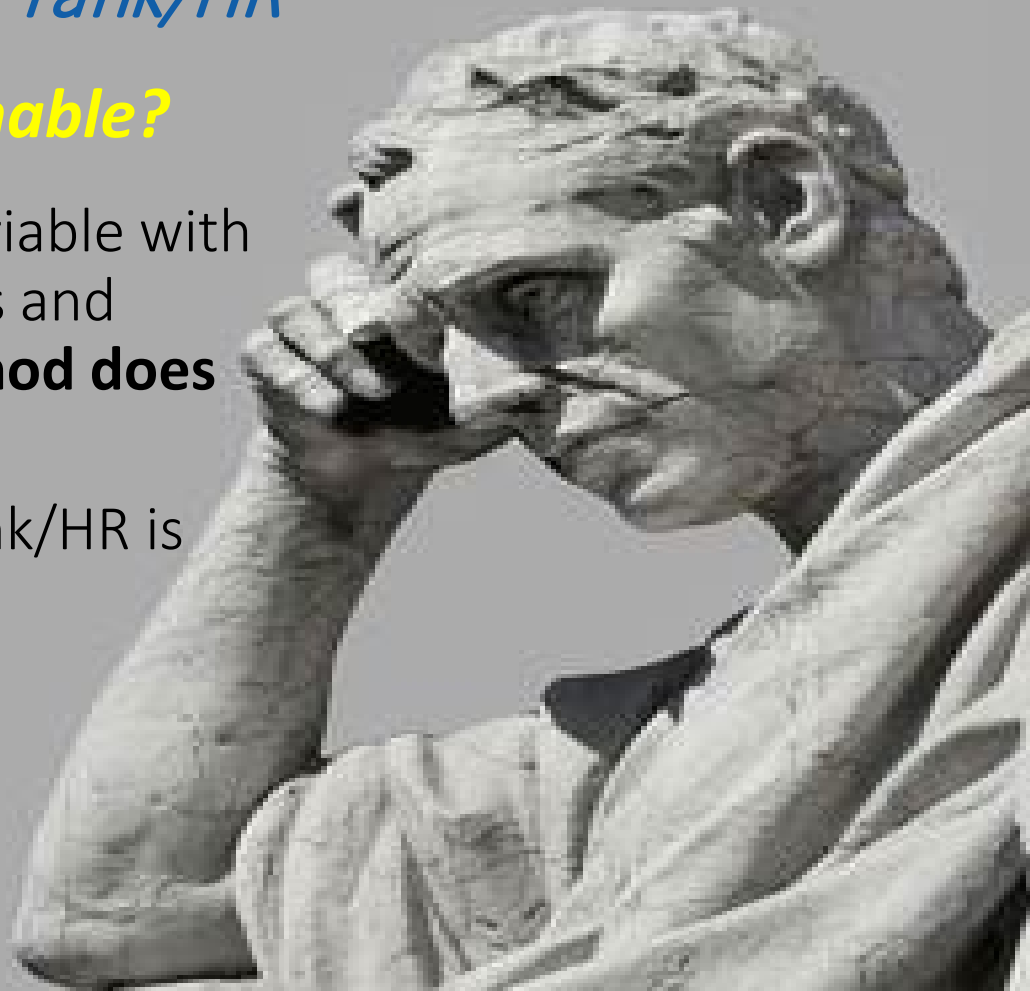


>95% of cancer RCTs (ph3) were using this Test/Estimation method (Uno et al. 2020, Oncologist)

Near universal use of log-rank/HR

Is this tradition reasonable?

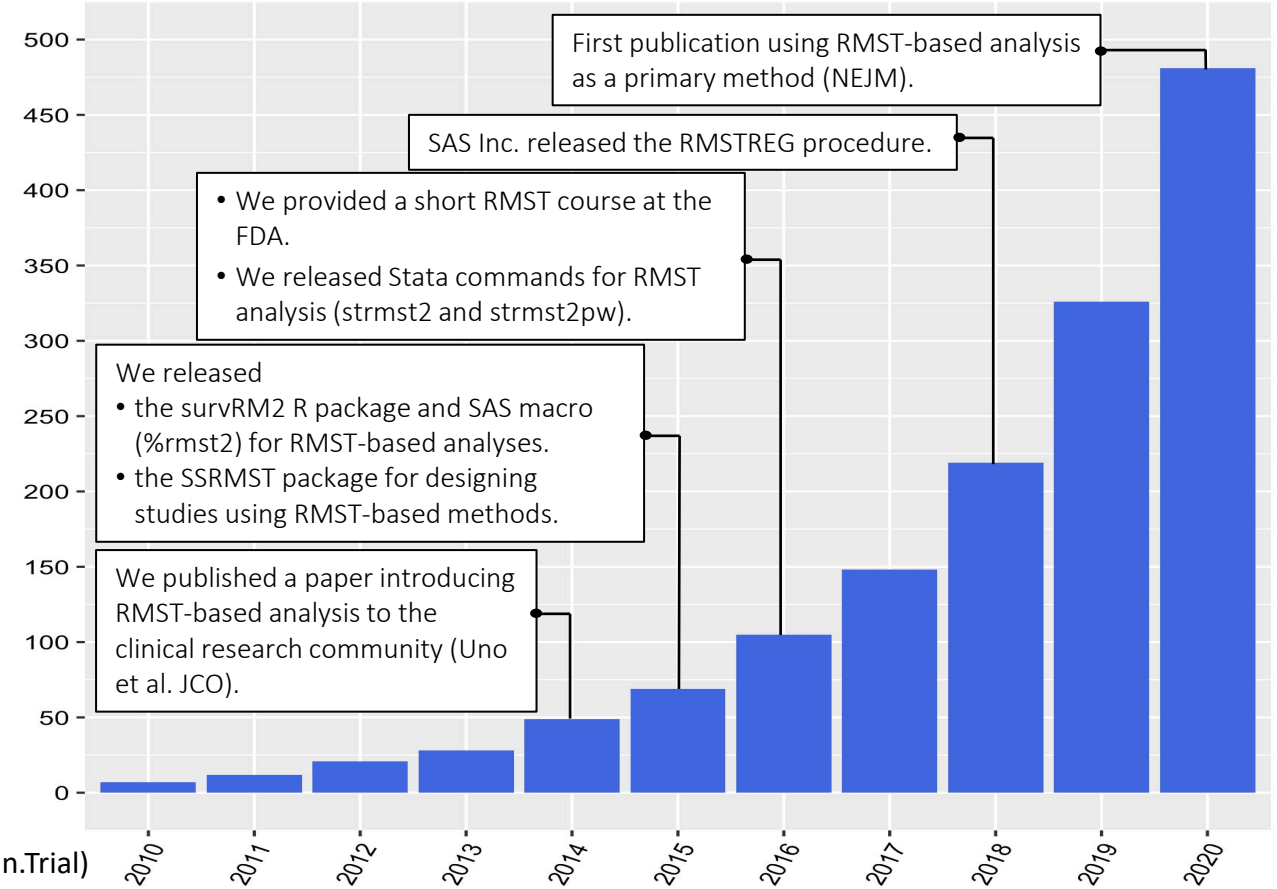
- Clinical research are highly variable with respect to their characteristics and research questions. **One method does not fit all.**
- ***No method is perfect.*** Log-rank/HR is not an exception.



Signs of change

Google Scholar "restricted mean survival time"

RMST is getting popular…



Glasziou, Simes, Gelber (**1990**)
Partitioned survival curve
(Quality Adjusted Survival)

RMST was proposed by Irwin (**1947**)

Karrison (**1997**, Cont.Clin.Trial)

Guimarães et al. (November 14, 2020)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve

ABSTRACT

BACKGROUND

The effects of rivaroxaban in patients with atrial fibrillation and a bioprosthetic mitral valve remain uncertain.

METHODS

In this randomized trial, we compared rivaroxaban (20 mg once daily) with dose-adjusted warfarin (target international normalized ratio, 2.0 to 3.0) in patients with atrial fibrillation and a bioprosthetic mitral valve. The primary outcome was a composite of death, major cardiovascular events (stroke, transient ischemic attack, systemic embolism, valve thrombosis, or hospitalization for heart failure), or major bleeding at 12 months.

RESULTS

A total of 1005 patients were enrolled at 49 sites in Brazil. A primary-outcome event occurred at a mean of 347.5 days in the rivaroxaban group and 340.1 days in the warfarin group (difference calculated as restricted mean survival time, 7.4 days; 95% confidence interval [CI], –1.4 to 16.3; P<0.001 for noninferiority). Death from cardiovascular causes or thromboembolic events occurred in 17 patients (3.4%) in the rivaroxaban group and in 26 (5.1%) in the warfarin group (hazard ratio, 0.65; 95% CI, 0.35 to 1.20). The incidence of stroke was 0.6% in the rivaroxaban group and 2.4% in the warfarin group (hazard ratio, 0.25; 95% CI, 0.07 to 0.88). Major bleeding occurred in 7 patients (1.4%) in the rivaroxaban group and in 13 (2.6%) in the warfarin group (hazard ratio, 0.54; 95% CI, 0.21 to 1.35). The frequency of other serious adverse events was similar in the two groups.

CONCLUSIONS

In patients with atrial fibrillation and a bioprosthetic mitral valve, rivaroxaban was noninferior to warfarin with respect to the mean time until the primary outcome of death, major cardiovascular events, or major bleeding at 12 months. (Funded by PROADI-SUS and Bayer; RIVER ClinicalTrials.gov number, NCT02303795.)

RMST was used as the primary analysis

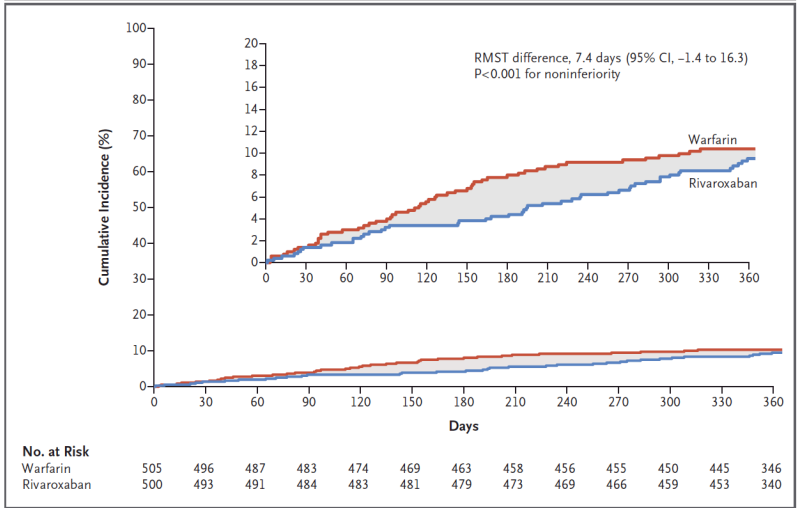


Figure 1. Kaplan–Meier Analysis of the Primary Outcome.

Shown is the primary outcome (death, major cardiovascular events, or major bleeding) in the rivaroxaban group and the warfarin group, as calculated according to the restricted mean survival time (RMST) method. The inset shows the same data on an expanded y axis.

Treatment-Free Survival: A Novel Outcome Measure of the Effects of Immune Checkpoint Inhibition—A Pooled Analysis of Patients With Advanced Melanoma

Regan et al. 2019 JCO

Meredith M. Regan, ScD[1,2]; Lillian Werner, MS[1]; Sumati Rao, PhD[3]; Komal Gupte-Singh, PhD[3]; F. Stephen Hodi, MD[1,2]; John M. Kirkwood, MD[4]; Harriet M. Kluger, MD[5]; James Larkin, PhD, FRCP[6]; Michael A. Postow, MD[7,8]; Corey Ritchings, PharmD[3]; Mario Sznol, MD[9]; Ahmad A. Tarhini, MD, PhD[10]; Jedd D. Wolchok, MD, PhD[7,8]; Michael B. Atkins, MD[11]; and David F. McDermott, MD[2,12]

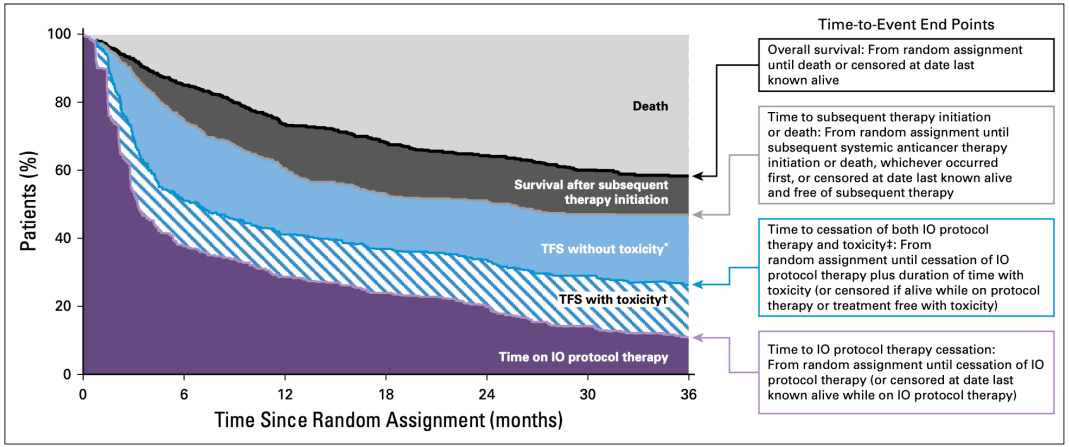


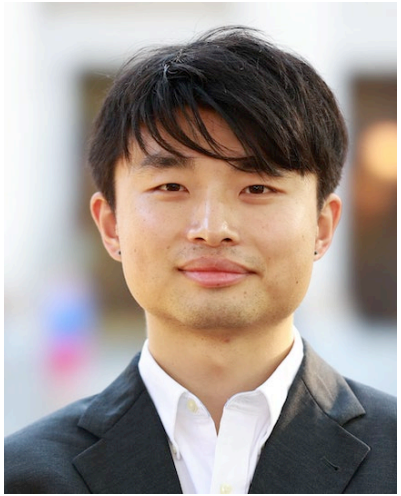
FIG 1. Illustration of the end points that partition the area under the overall survival curve into treatment-free survival (TFS) and other resulting health states. (*) Time after cessation of immuno-oncology (IO) protocol therapy without toxicity before initiation of subsequent systemic anticancer therapy or death. (†) Time after cessation of IO protocol therapy with toxicity while treatment free. (‡) Includes toxicity that persisted since protocol therapy and toxicity that newly presented after protocol therapy cessation.

Overview of the course

Goal: Participants can immediately apply the RMST methods in practice when appropriate.

Instructors:

Angel Cronin



Xiang Meng

Hajime Uno

Schedule

Date	Contents
2025-11-05 (120 min)	Part 1: Estimation of between-group difference - Limitation of Hazard Ratio - RSMT definition - Examples
2025-11-12 (120 min)	Part 2: More on RMST - Power considerations - Study design - Regression analysis - Stratified analysis - Other applications of RMST

SCAN ME

Each includes

- 10 min break
- Demo and exercise using R (all materials are on the DS Training webpage)
- Feedback and Q&A