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Does Peptide Receptor Radionuclide Therapy treatment extend the life expectancy in patients with Neuroendocrine Tumors?

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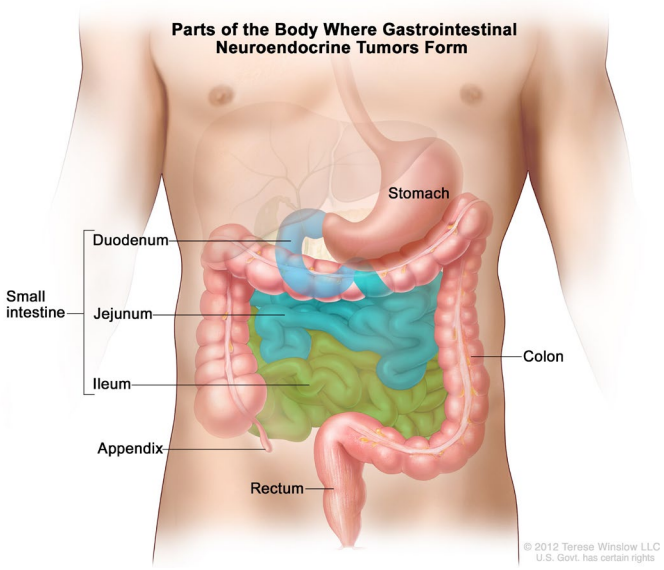
Background

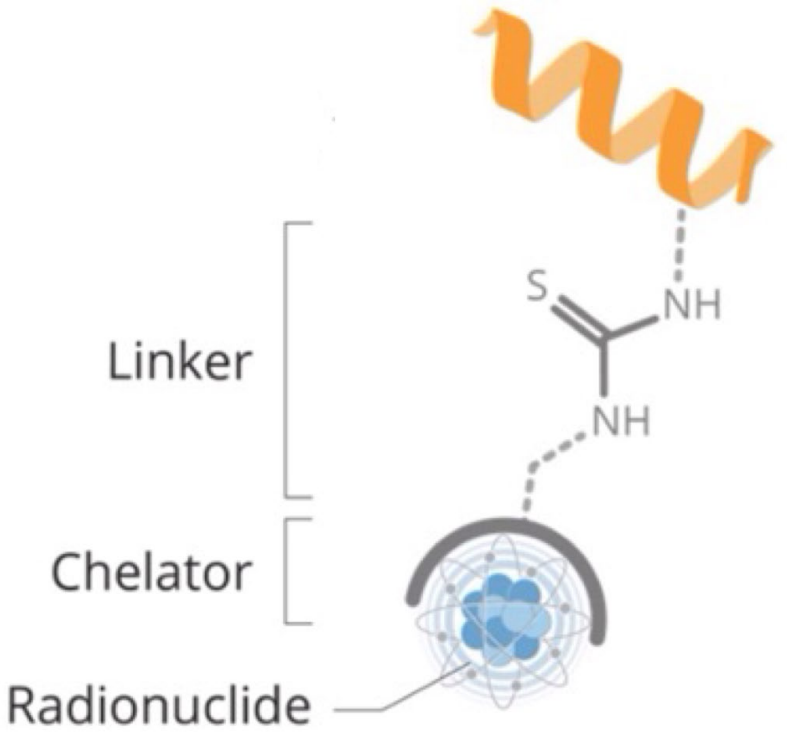
What are NENs?

- Neuroendocrine neoplasms(NENs) are a group of cancer tumors which originate from organs that produce and secrete hormones
- About 2% of all metastasized cancers each year are NENs with a prevalence of <200,000 in the US



What is PRRT?

- Peptide Receptor Radionuclide Therapy (PRRT) is a treatment used to treat specific cancers (such as NENS)
- FDA approved in 2018
- Used in Europe and Australia for around a decade



Survival Analysis

Research Question:

Does PRRT treatment extend the life expectancy in patients with NENs?

Key Concepts

- Time to event data
- Censoring
  - Event of interest not observed for all individuals
  - When patient doesn't experience death by end of study

Main Goal of Survival Analysis

- Estimate the probability of not experiencing an event of interest over a given period of time

The Data

Site: Where the tumors originated in the body

Met: The spread of cancer cells from the place of origin

tOS: Time of overall survival measured in years when a patient entered the study

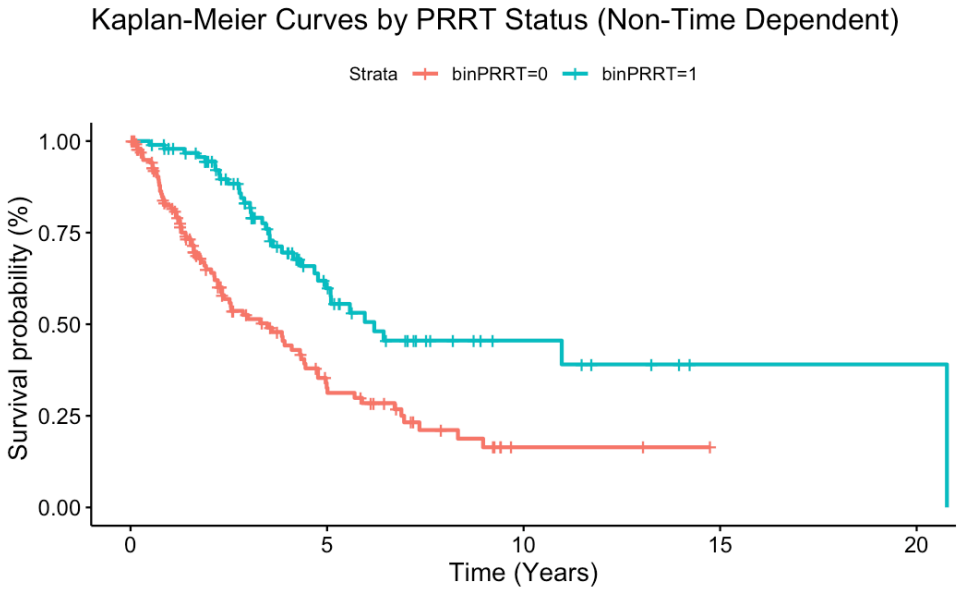
dOS: If the patient has experienced death

tPRRT: Time when the patient received treatment within the study in years

	Age	Site	Met	tOS	dOS	tPRRT
1	58.4	Pancreas	FALSE	14.23	FALSE	0.71
2	73.5	Pancreas	FALSE	6.96	TRUE	*NA*
3	84.6	Pancreas	FALSE	4.97	TRUE	*NA*
4	60.9	Stomach	TRUE	3.92	TRUE	*NA*
5	57.6	Pancreas	FALSE	7.14	FALSE	*NA*
6	62.0	Pancreas	TRUE	1.68	TRUE	*NA*
7	54.9	Pancreas	TRUE	5.10	TRUE	0.44
8	61.0	Pancreas	TRUE	4.45	TRUE	*NA*
9	52.9	Pancreas	TRUE	0.50	TRUE	*NA*
10	89.4	Pancreas	FALSE	1.92	FALSE	*NA*

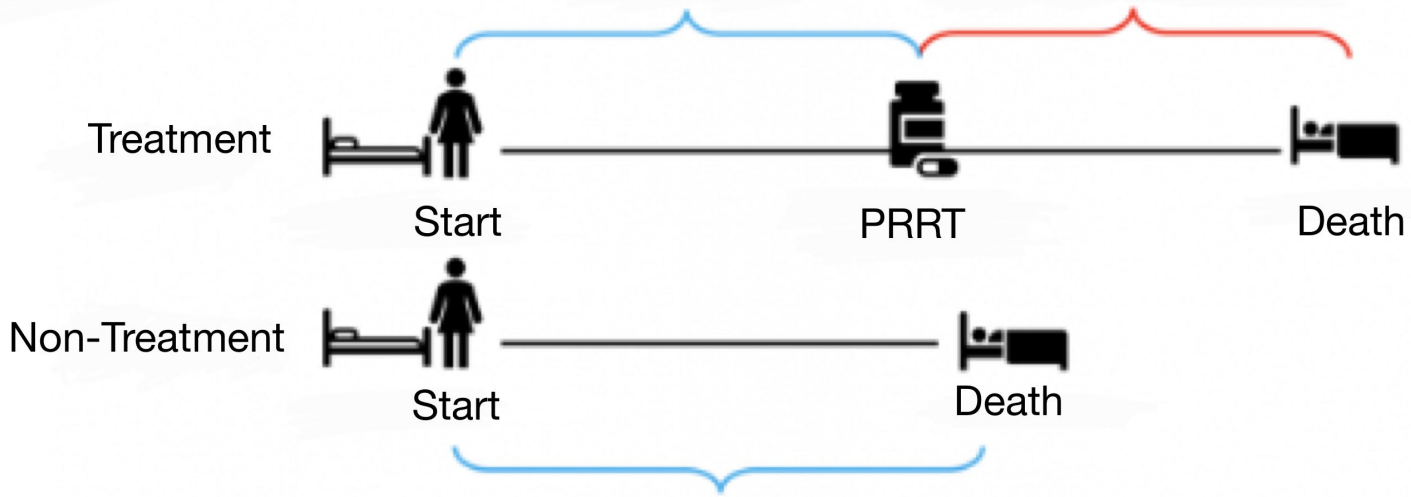
Kaplan-Meier Estimates/Curve

- Fundamental tool used to estimate survival probabilities
- Handles censoring by considering the number of individuals at risk over time then adjusting survival based on observed events
- Non-parametric method: Doesn't assume a specific distribution of survival times and can make survival probabilities estimations at given times



Immortal Time Bias

- “Immortal Time” is when patients in a study cannot experience the outcome during the follow-up time
- If immortal time is not properly accounted for it can lead to bias



Cox Proportional Hazard Model

Equation: $\lambda_i(t) = \lambda_o(t)e^{(xi\beta i)}$

- $\lambda_i(t)$ = hazard of an individual
- $\lambda_o(t)$ = base hazard
- **xi** = covariates
- β_i = coefficient

-an equation that gives you a value based on the different factors in your study

-λ_o does not need to be calculated to calculate the overall hazard of a person

Cox Proportional Hazard Model Cont.

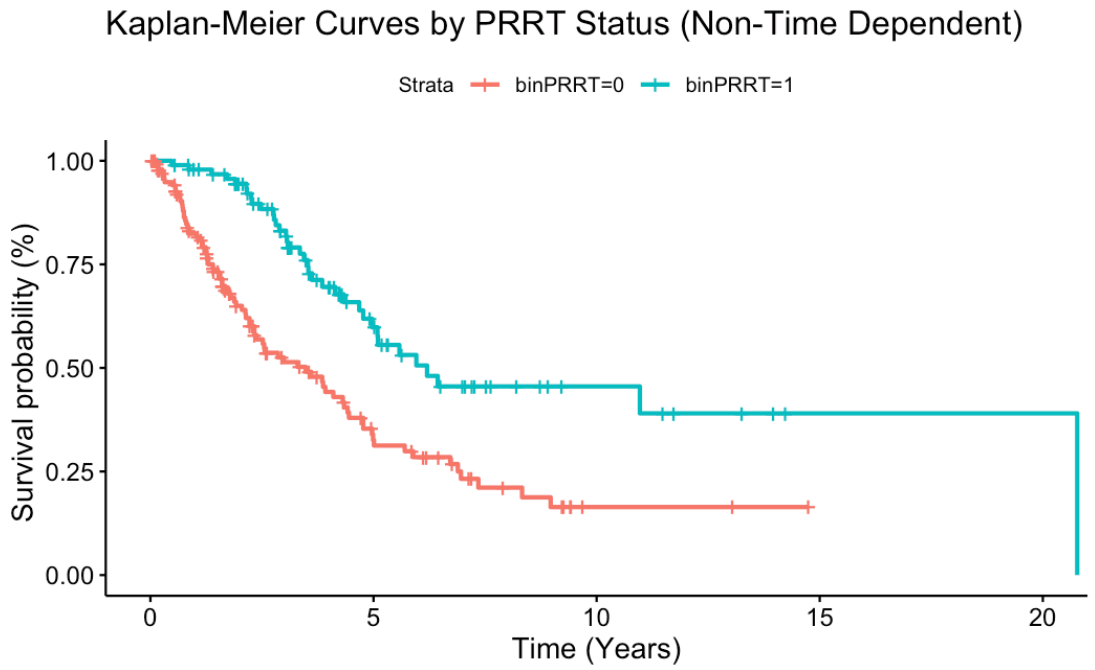
Equation: $\lambda_i(t) = \lambda_o(t)e^{(xi(t)\beta i)}$

- Separates base hazard from covariates
  - $\lambda_o(t)$ gets cancelled out
- Separation allows us to have a time-dependent covariates
  - We can graph $x_i(t)$, covariates over time and calculate individual hazard

Methods

Kaplan Meier Curve

- Non-Time Dependent p-value: 7*10^-6
- Time Dependent p-value: 0.114
- Not the final answer, PRRT mainly given to people with metastasis



Covariates

	HR	P
PRRT	0.6198	0.0239
Met	2.3896	0.0073
Sex	1.1893	0.3636
Age	1.6947	0.0762

Evaluating PRRT's Benefits

- From our data, we conclude that there is a decrease in death risk in regard to age, sex, and metastasis
- We used the cox proportional hazard model to present PRRT as a time-dependent variable
- PRRT reduced death risk by 38% p = 0.0239, compared to p = 7e-06, benefits are overblown

Shiny Model

https://ph-ivshiny.iowa.uiowa.edu/pbreheny/isib/

Citations

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NIH National Heart, Lung, and Blood Institute

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Questions?

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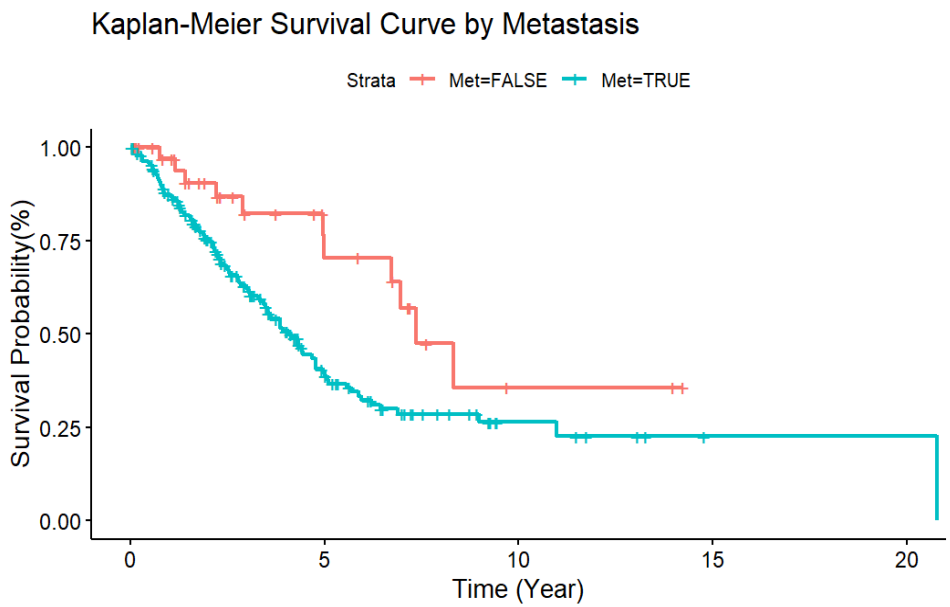
Cox Proportional Hazard Modeling

Kaplan-Meier Curve of Metastasis



Cox Proportional Hazard Model of Metastasis