

# Evaluating and Extending Three-Arm Study in the Treatment of Superficial Bladder Cancer

P8108 Final Project, Fall 2022

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2022-12-05

## Background

# Superficial Bladder Cancer

- ▶ Also known as Stage 1 bladder cancer
- ▶ Common diagnosis (75% of bladder cancer cases<sup>1</sup>) and rarely life-threatening on its own.
- ▶ Thought to arise due to urinary issues<sup>1</sup> or through “abnormalities of tryptophan metabolism”<sup>2</sup>
- ▶ Particular interest in preventing recurrence of disease
  - ▶ Natural history study conducted in Sweden saw that “death was directly related to tumor grade, number of tumors, and volume of recurrences.”<sup>3</sup>

## Pyridoxine and Thiotepa

- ▶ *Pyridoxine* (vitamin  $B_6$ ) thought to reduce “abnormalities of tryptophan metabolism”
- ▶ *Thiotepa* has been the standard of care for the treatment of superficial bladder cancers.
- ▶ Effects of these two therapies compared in randomized clinical trial conducted by Byar and Blackard in 1977

## Byar and Blackard (1977)

- ▶ Primary clinical interest: prevent and reduce recurrence of Stage 1 bladder cancer.
- ▶ Event time agnostic analysis conducted included comparing overall rates and percentages of occurrence between groups
  - ▶ Pairwise difference detected in rate of recurrence between thiotepa and placebo, and thiotepa and pyridoxine
  - ▶ No other differences in event incidence between groups detected
- ▶ Survival analysis conducted involved the construction of life-table estimates.
  - ▶ Life-table analysis indicate that the time to first recurrence was significantly different between pyridoxine and placebo groups.
  - ▶ Analysis restricted to subjects who experienced recurrence after at least 10 months of follow-up

## Proposed Project

# Motivation

- ▶ Research ought to be reproducible, especially if data has become open-source
- ▶ Different models may be more informative than just the actuarial curves constructed

# Analysis Plan

1. Reproduce analysis conducted in original study to see if results are reproducible
2. Construct models that differ from original study to see if they can be more informative



## Reproduce Analysis

## Study Design

It was a randomized clinical trial. 121 patients from ten Veterans Administration hospitals were admitted to this study between November, 1971, and August, 1976. All patients had superficial bladder tumors (Stage I) when they entered the trial. Patients were assigned at random to one of three treatment groups: placebo, 1 tablet per day; oral pyridoxine, one 25 mg. tablet per day; or thiotepa, 60 mg. in 60 ml. of water instilled in the bladder for two hours once a week for four weeks and then once a month.

# Study Design

The goal of the study should be to determine the effect of treatment on the frequency of tumor recurrence.

The endpoint can be seen as the recurrence of bladder cancer, which is defined by a visit at which one or more tumors have reappeared in the bladder after having been removed previously.

The average follow-up information available for study was about thirty-one months in all three treatment groups, but some patients have been followed up as long as five years.

## Exploratory Data Analysis

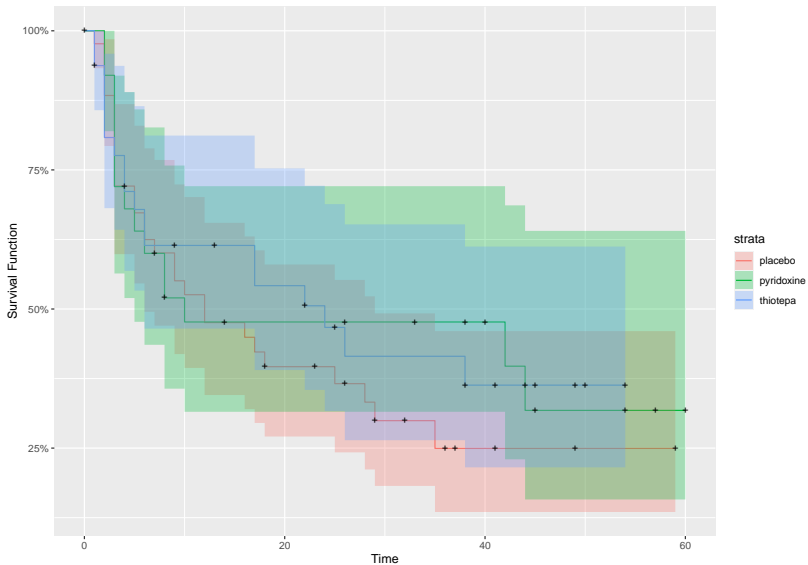
id	treatment	numbesize	recur	start	stop	status	rtumor	size	enum
1	placebo	1	1	0	0	0	3	.	1
2	placebo	1	3	0	0	1	3	.	1
3	placebo	2	1	0	0	4	0	.	1
4	placebo	1	1	0	0	7	0	.	1
5	placebo	5	1	0	0	10	3	.	1
6	placebo	4	1	1	0	6	1	1	1

- ▶ id: Patient id
- ▶ treatment: Placebo, pyridoxine (vitamin B6), or thiotepa
- ▶ recur: Number of recurrences
- ▶ start,stop: The start and end time of each time interval
- ▶ status: End of interval code, 0=censored, 1=recurrence, 2=death from bladder disease, 3=death other/unknown cause

## Exploratory Data Analysis

name	Placebo	Pyridoxine	Thiotepa
evaluable_patients	48.00	32.00	38.00
num_without_recur	19.00	17.00	20.00
num_with_recur	29.00	15.00	18.00
total_recur	87.00	57.00	44.00
total_month_follow	1528.00	993.00	1183.00
percent_recur	60.42	46.88	47.37
recur_rate	5.69	5.74	3.72

# Exploratory Data Analysis



## References

1. Superficial bladder cancer. Division of Urologic Surgery. (n.d.). Retrieved from <https://urology.wustl.edu/urologic-cancers/bladder-cancer/surgery-for-superficial-b/>
2. C;., B. D. B. (n.d.). Comparisons of placebo, pyridoxine, and topical thiotepa in preventing recurrence of stage I bladder cancer. Urology. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/414402/>
3. Pasin, E., Josephson, D. Y., Mitra, A. P., Cote, R. J., & Stein, J. P. (2008). Superficial bladder cancer: An update on etiology, molecular development, classification, and natural history. Reviews in urology. Retrieved December 3, 2022, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2312342/>