ANALYSIS AND INTERPRETATION OF CENSORED COST DATA USING REAL-WORLD EVIDENCE: A STEP-BY-STEP APPROACH

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INTRODUCTION TO CENSORING

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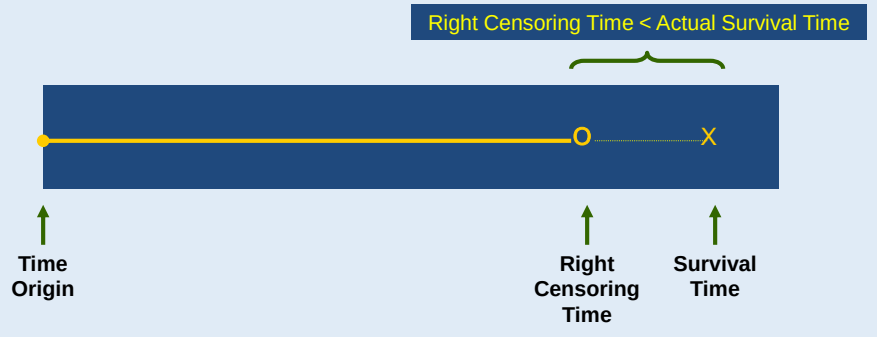
WHAT IS CENSORING?

- An observation is said to be *censored* if we have only partial information about a particular variable of interest.
- There are many different types of censoring:
  - Left / Right / Interval Censoring
  - Type I / Type II Censoring
  - Informative / Non-informative Censoring

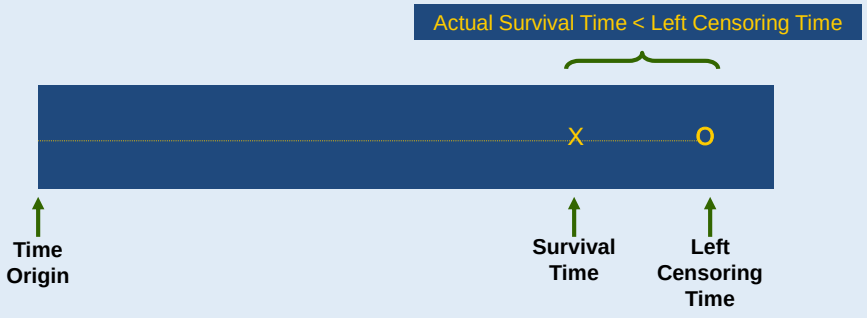
TYPES OF CENSORING

- An observation is said to be *right* censored if all we know is that an event did not occur until after an observed point in time.
- This is the most common form of censoring since a study may be terminated before the event occurs.



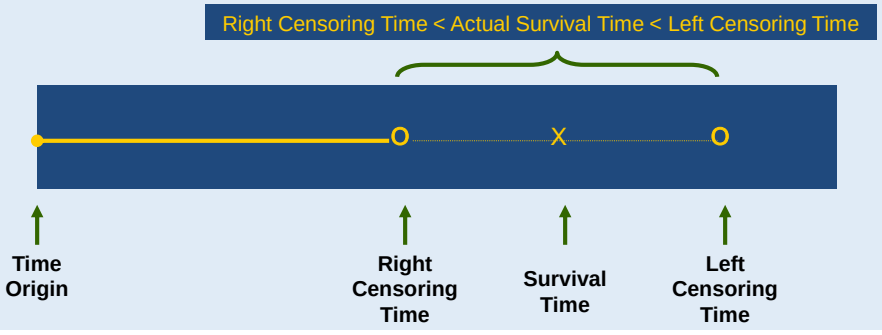
TYPES OF CENSORING

- An observation is said to be *left* censored if all we know is that an event occurred before some observed point in time.
- This occurs when some subjects may have already had the event at the time they enter the study



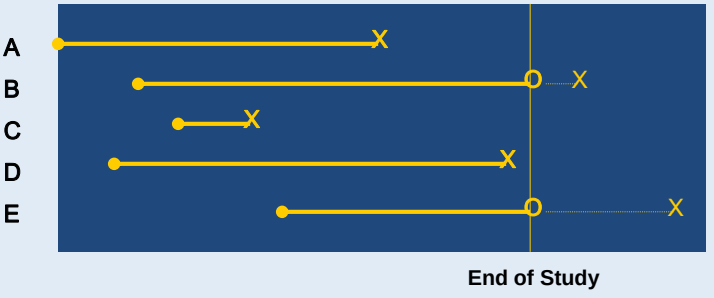
TYPES OF CENSORING

- An observation is said to be *interval* censored if all we know is that an event occurred during some time interval (i.e. between two known points in time).
- Interval censoring can be thought of as a combination of left and right censoring.



TYPES OF CENSORING

Type I censoring also occurs when entry times vary randomly across individuals but the end of the study is pre-determined.

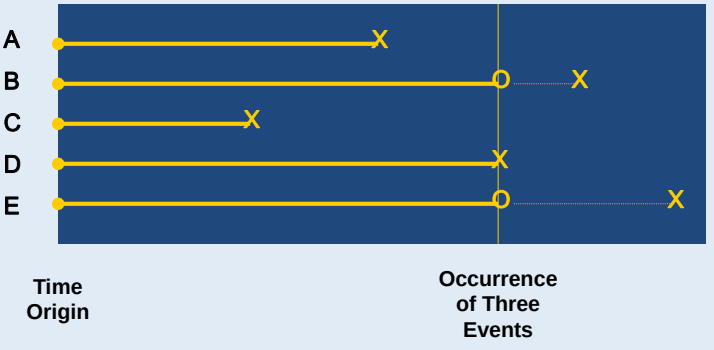


Three patients experience the event and two are censored.

For such studies, entry time should be included as a covariate in any regression models.

TYPES OF CENSORING

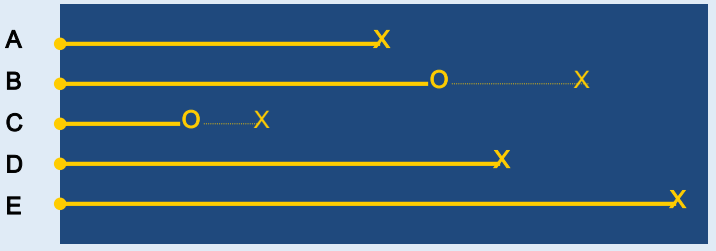
Type II censoring occurs when the study continues until observing some number of events pre-specified by the investigator.



Three patients experience the event and two are censored.

TYPES OF CENSORING

Random censoring occurs when follow-up is terminated for reasons that are not under the control of the investigator.
(e.g. withdrawals, loss to follow-up)



Three patients experience the event and two are censored.

Time Origin

End of Study

TYPES OF CENSORING

- Non-informative censoring (ignorable missing)
  - Missing completely at random (MCAR): the propensity for a data point to be missing is completely random. i.e. The missing data are just a random subset of the data.
  - Missing at random (MAR): the propensity for a data point to be missing is not related to the missing data, but it is related to some of the observed data.
- Informative censoring (non ignorable missing)
  - Missing not at random (MNAR): the propensity for a data point to be missing depends on the unobserved event time.

WHAT HAPPENS IF YOU DON'T ACCOUNT FOR CENSORING?

- Cost data are prone to the following issues:
  - Substantial proportion of the patients having zero costs
  - Distribution of health care costs is usually heavily right skewed
  - Assumption of homoscedasticity is often violated with cost data
  - Incomplete data when health care expenses are not available for all participants for the entire period of interest
- Unfortunately clinical cost data are often subject to censoring, and methodologies applicable to censored cost data have not been well applied.
- The objective of this presentation is to examine this fourth obstacle in detail and present techniques to correctly estimate health care costs after accounting for censoring.

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INVERSE PROBABILITY-WEIGHTED ESTIMATOR

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DATASET EXAMPLE

Patient	t1	t2	t3	t4	t5	t6	t7	t8	t9	t10	Total cost	d/c	survival time (yr)
1	4830	3461	91	627	2978	1788	513	2269	1330	2606	20493	c	10
2	2636	525	3154	374	1481	379	.	.	.	.	8549	c	6
3	4398										4398	d	1
4	2840	2740	3477	440	12	962	1407	2286	942	669	15775	c	10
5	4398	3966	.	.	.	.	.	.	.	.	8364	c	2
6	3512	3122	4288	172	1376	2462	1575	2930	565	2173	22175	c	10
7	2103	4024	1091	1990	2600	1111	193	.	.	.	13112	c	7
8	3088	2414	4881	2671	2290	1071	1474	1882	2740	.	22511	c	9
9	2639	1024	2676	459	2373	165	2484	1776	624	30	14250	c	10
10	2429	1049	3193								6671	d	3
11	3578	3540	1564	2520	1745	2710	791	2255	2979	370	22052	c	10
12	4253	4119	1695	1301	2508	.	.	.	.	.	13876	c	5
13	3153	751	4290	1880	983	541	2707	569	1616	410	16900	c	10
14	2436	777	1488	211	1314	1099	376	98	1301	1120	10220	c	10
15	3898	2359	431	2450	.	.	.	.	.	.	9138	c	4
16	3207	4476									7683	d	2
17	2182	4714									6896	d	2
18	2159	3477	4033	1211	1202	2715	1799	877			17473	d	8
19	3855	2984	234	731	2288	2046	1813	.	.	.	13951	c	7
20	2960	2630	3297	2936	102	1903	2677	1683	841	2458	21487	c	10
Mean	3228	2745	2493	1332	1661	1458	1484	1663	1438	1230	13799		

*d/c, died or censored.

Gray AM, PM Clarke, JL Wolstenholme, S Wordsworth. Applied Methods of Cost-effectiveness Analysis in Health Care. 2011. Oxford University Press, New York.

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WHAT ARE YOUR OPTIONS?

Patient	t1	t2	t3	t4	t5	t6	t7	t8	t9	t10	Total cost	d/c	survival time (yr)
1	4830	3461	91	627	2978	1788	513	2269	1330	2606	20493	c	10
2	2636	525	3154	374	1481	379	.	.	.	.	8549	c	6
3	4398										4398	d	1
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Mean	3228	2745	2493	1332	1661	1458	1484	1663	1438	1230	13799		

*d/c, died or censored.

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IGNORE CENSORING

Patient	t1	t2	t3	t4	t5	t6	t7	t8	t9	t10	Total cost	d/c	survival time (yr)
1	4830	3461	91	627	2978	1788	513	2269	1330	2606	20493	c	10
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16	3207	4476									7683	d	2
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Mean	3228	2745	2493	1332	1661	1458	1484	1663	1438	1230	13799		

*d/c, died or censored.

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CALCULATION OPTIONS

- Complete cases: $11,843
- All cases (ignore censoring): $13,799
- Annualized costs: $17,841
- Adjust for censoring:
  - KMSA: $15,219
  - IPW: $15,888

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NOTATION

- T = ascertainment time
- T_0 = time of study entry
- a_i = generic measurement time
- C = censoring time
- Y = costs
- k = interval (e.g. month)
- S(.) = survival function

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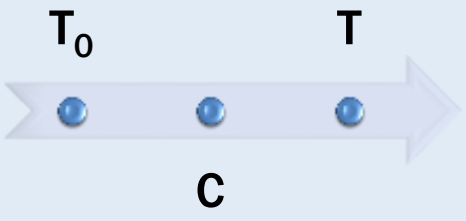
RIGHT CENSORING

- T > C



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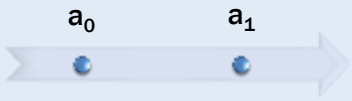
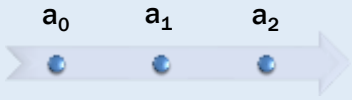
INTUITION BEHIND IPW

- Lower prob of completeness = higher weight
- Simple weight



- Partitioned weight



IPW: inverse probability weight

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INTERVAL ADJUSTMENT USING IPW

- B&T approach
- Cost history
  - monthly data
  - K intervals

B&T: Bang and Tsiatis

Willan and Briggs 2006.

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B&T'S APPROACH - DEFINITION

- Partition (interval)
- Eligible patient
- Weight = inverse censoring probability
  - Censoring probability, not death probability

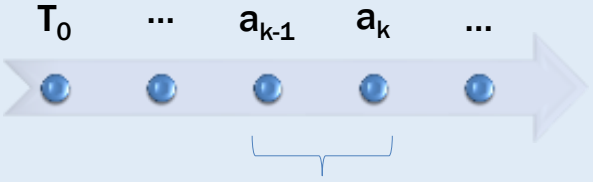
$$S(t) = \prod_{j:a_j<t}\left(1-\frac{d_j}{n_j}\right)$$

d_j: number of censored patients
n_j: number at risk of being censored

Willan AR and AH Briggs. Statistical Analysis of Cost-effectiveness Data. John Wiley & Sons, Ltd. 21

B&T'S APPROACH – STEP 1

- Partition study interval



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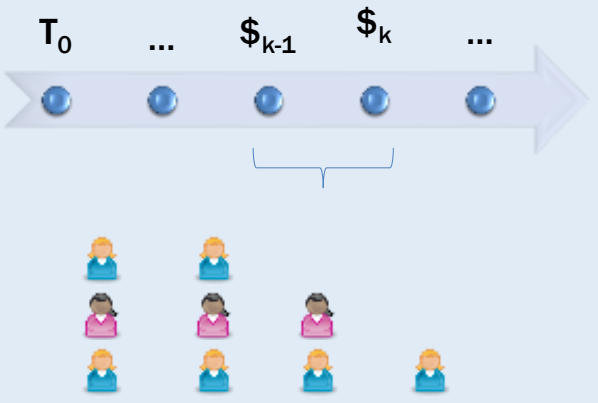
B&T'S APPROACH – STEP 2

- Estimate average interval costs for eligibles



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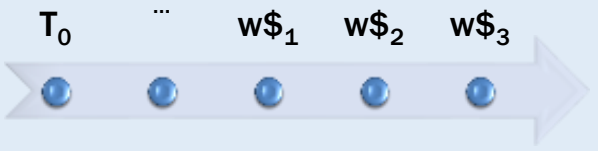
B&T'S APPROACH – STEP 3

- Weight average interval costs using IPW



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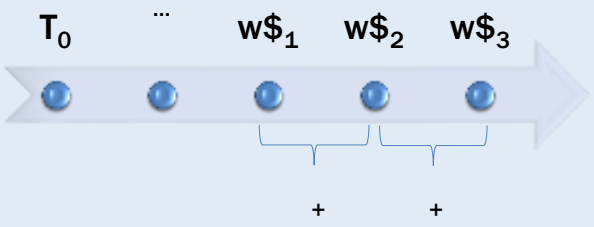
B&T'S APPROACH – STEP 4

- Sum weighted average interval costs



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CENSORING CONCERNS

- Degree of censoring
- 'High' degree – use phase-based costs

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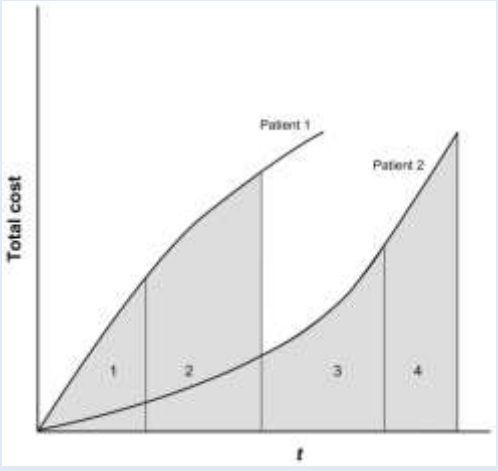
PARTITIONED COST HISTORIES



Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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Table 3 Simulations to evaluate impact of censoring

Censoring	Mean ten-interval cumulative costs ($)[a]	Interquartile range
7% Censoring		
True costs	8.29	8.21–8.38
Full-sample estimator	7.49	7.41–7.56
Uncensored case estimator	7.68	7.61–7.77
Simple IPW	8.06	7.97–8.15
18% Censoring		
True costs	8.29	8.20–8.37
Full-sample estimator	7.03	6.96–7.10
Uncensored case estimator	7.50	7.42–7.58
Simple IPW	8.49	8.39–8.59
21% Censoring		
True costs	9.07	9.00–9.16
Full-sample estimator	7.57	7.49–7.65
Uncensored case estimator	8.20	8.12–8.28
Simple IPW	9.35	9.24–9.45
53% Censoring		
True costs	7.45	7.37–7.53
Full-sample estimator	4.90	4.89–5.04
Uncensored case estimator	5.28	5.18–5.38
Simple IPW	9.87	9.64–10.1

Wijeysundera HC, 2012

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KEY POINTS TO REMEMBER

- There is no perfect model!
- Address primary sources of potential bias
- Deliberation is key.

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LIN'S REGRESSION

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OVERVIEW OF METHOD

- Estimation of cost accumulation
- Efficient use of available data
- Potential confounding
  - Stratification vs. covariate-adjustment

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ADJUSTED COST ESTIMATION

- Weighted conditional mean estimation i.e., regression analysis
- With or w/o history

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COVARIATE ADJUSTMENT

- Censoring distribution: covariate-dependent censoring
- Cost distribution:

Partition?	Crude	Adjusted
No	A	C
Yes	B	D

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FIRST, SOME NOTATION

j = study arm
k = interval
i = patient
Y = cost
S = survival function
G= IPW

$$Z_{ji} = \min\left(T_{ji}, C_{ji}\right)$$
$$Z^{*}_{jki} = \min\left(Z_{ji}, a_{k+1}\right)$$
$$\delta_{ji} = I\left\{T_{ji} < C_{ji}\right\}$$
$$\bar{\delta}_{ji} = 1 - \delta_{ji}$$
$$\delta^{*}_{jki} = \delta_{ji} + \bar{\delta}_{ji} I\left\{X_{ji} \geq a_{k+1}\right\}$$

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A: CRUDE ESTIMATE WITHOUT PARTITION

$$\hat{v}_j = \left(\sum_{i=1}^{n_j} \frac{\delta^*_{ji}}{\hat{G}\left(Z^*_{ji}\right)} \right)^{-1} \sum_{i=1}^{n_j} \frac{\delta^*_{ji} \hat{Y}_{ji}}{\hat{G}\left(Z^*_{ji}\right)}$$

Willan and Briggs 2006.

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B: CRUDE ESTIMATE WITH PARTITION

$$\hat{v}_j = \sum_{k=1}^{K} \hat{v}_{jk}$$

$$\hat{v}_{jk} = \left(\sum_{i=1}^{n_j} \frac{\delta^*_{jki}}{\hat{G}\left(Z^*_{jki}\right)} \right)^{-1} \sum_{i=1}^{n_j} \frac{\delta^*_{jki} \hat{Y}_{jki}}{\hat{G}\left(Z^*_{jki}\right)}$$

Willan and Briggs 2006.

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C: COVARIATE-ADJUSTED ESTIMATE WITHOUT PARTITION

$$\hat{\beta} = \left(\sum_{i=1}^{n} \frac{\delta_i^*}{\hat{G}\left(T_i^*\right)} X_i X_i' \right)^{-1} \sum_{i=1}^{n} \frac{\delta_i^* Y_i X_i}{\hat{G}\left(T_i^*\right)}$$

Lin DY. Linear regression analysis of censored medical costs. Biostatistics (2000), 1, 1, pp 35-47.

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D: COVARIATE-ADJUSTED ESTIMATE WITH PARTITION

$$\hat{\beta} = \sum_{k=1}^{K} \left[\left(\sum_{i=1}^{n} \frac{\delta_{ki}^*}{\hat{G}\left(T_{ki}^*\right)} X_i X_i' \right)^{-1} \sum_{i=1}^{n} \frac{\delta_{ki}^* Y_{ki} X_i}{\hat{G}\left(T_{ki}^*\right)} \right]$$

Lin DY. Linear regression analysis of censored medical costs. Biostatistics (2000), 1, 1, pp 35-47.

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COVARIATE-ADJUSTED, W/PARTITION, COVARIATE-DEPENDENT CENSORING

$$\hat{\beta} = \sum_{k=1}^{K} \left[\left(\sum_{i=1}^{n} \frac{\delta_{ki}^{*}}{\hat{G}\left(T_{ki}^{*} \mid V_i, W_i\right)} X_i X_i' \right)^{-1} \sum_{i=1}^{n} \frac{\delta_{ki}^{*} Y_{ki} X_i}{\hat{G}\left(T_{ki}^{*} \mid V_i, W_i\right)} \right]$$

Lin DY. Linear regression analysis of censored medical costs. Biostatistics (2000), 1, 1, pp 35-47.

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SUMMARY

- Censoring proportion still important to consider
- Decide at the start whether to partition or not to partition
- Consider options for covariate-adjustment

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PHASE-BASED COSTING

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WHAT IS PHASE-BASED COSTING?

- A method used for estimating lifetime costs or estimating costs in the presence of heavy censoring.
- Does not use a reweighting method
- Steps:
  1. Define a priori clinically important phases of disease.
  2. Determine inflection points in cumulative cost.
  3. Allocate observation time and costs for each patient to the phases.
  4. Once the costs for all patients have been assigned, determine the mean cost per phase.
  5. Using both the data on cost per phase and time to death, determine the cumulative lifetime costs.

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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DEFINE A PRIORI CLINICALLY IMPORTANT PHASES OF DISEASE

- The total time period for each patient (before and after the index date) will be divided into 3 phases of care namely:
  - initial phase (3 months post-diagnosis),
  - continuation phase (time frame between initial and terminal phase), and
  - terminal phase (6 months pre-death).

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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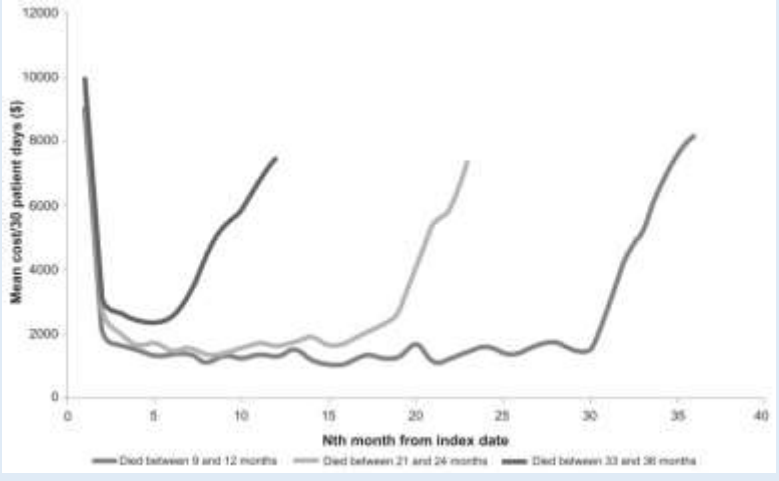
DETERMINE INFLECTION POINTS IN CUMULATIVE COST



Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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ALLOCATE OBSERVATION TIME AND COSTS FOR EACH PATIENT TO THE PHASES

- Patients who do not die would have their post diagnosis time and associated costs first assigned to the initial phase. Any remaining time would be assigned to the continuation phase.
- Patients who die would have their post diagnosis time and associated costs first assigned to the terminal phase. Any remaining time would be assigned to the initial phase followed by the continuation phase.
- Example

ID	m1	m2	m3	m4	m5	m6	m7	m8	m9	m10	m11	m12	m13	mDeath
1	4000	4600	4600	42	80	34	54	62	62	54	62	62	62	.
2	4600	3672	3528	68	59	50	4632	4999	4567	4215	4132	5437		m12

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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DETERMINE THE MEAN COST PER PHASE

- Take the mean cost per phase
- Sum costs for all patients per phase divided by the number of patients who entered the phase.

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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USING BOTH THE DATA ON COST PER PHASE AND TIME TO DEATH, DETERMINE THE CUMULATIVE LIFETIME COSTS

$$\text{Total cost}(60) = \sum_{t=1}^{60} \overline{C}_t$$

- This expression assumes that the patient is alive for the entire period so it should appropriately be described as the five year costs conditional on survival to five years.
- To estimate expected five year costs for all patients allowing for deaths

$$\text{Total cost}(60) = \sum_{t=1}^{60} \widehat{S}(t)\,\overline{C}_t$$

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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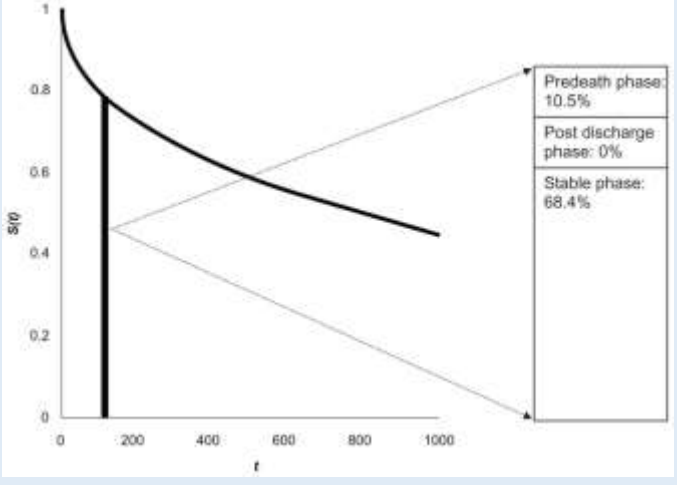
USING BOTH THE DATA ON COST PER PHASE AND TIME TO DEATH, DETERMINE THE CUMULATIVE LIFETIME COSTS



Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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SUMMARY

- Phase-based costing is an attempt to provide meaningful cost estimates that are clinically appealing.
- The idea is to admit that high censoring rate (>50%) results in biased estimates on reweighting
- Creates "synthetic" patients with complete costs by allowing patients to contribute as much information as possible yo as many phases as possible.

Wijeysundera HC, Techniques for estimating health care costs with censored data. Clinicoecon Outcomes Res. 2012; 4: 145–155.

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TRANSLATION: WHO CARES?

Shuo Yang
Bristol-Myers Squibb

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STAKEHOLDER PERSPECTIVES

Evolving role of Real World Evidence (RWE) in decision making

Industry Researchers	• Demonstrate economic value with scientifically sound and rigorous studies • Inform pricing and contracting strategies and performance measurement based on real-world data
Regulatory Agencies	• Cost-Effectiveness and product value in regulatory and pricing decisions • RWE on economic impact of novel health technologies
Access Decision Makers	• Get the "real-world" look at how health technologies compare on cost and effectiveness • Trends in value-based pricing and contracting based on RWE
Providers	• OCM and Clinical pathway evaluation for cost management • Cost burden to patients and treatment affordability

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CASE STUDY #1: A DISEASE BURDEN STUDY

RESEARCH

Determinants of Medicare All-Cause Costs Among Elderly Patients with Renal Cell Carcinoma

Christopher S. Hollenbeak, PhD; Lucas E. Nikkel, BA; Eric W. Schaefer, MS; Evo Alemao, MS; Nasrollah Ghahramani, MD, MS; and Jay D. Raman, MD

ABSTRACT

BACKGROUND: Renal cell carcinoma (RCC) is the third most common genitourinary cancer and the most common primary renal neoplasm. Estimates of the economic burden of RCC in the United States range from approximately $402 million (in year 2000 dollars) to $4.4 billion (in year 2005 dollars). Actual costs associated with RCC, particularly for elderly Medicare patients who account for 46% of U.S. patients hospitalized for RCC, are poorly understood.

OBJECTIVE: To estimate all-cause health care costs associated with RCC using the combined Surveillance Epidemiology and End Results (SEER)-Medicare database.

METHODS: The sample was limited to non-HMO patients aged 65 years or older who were diagnosed with a first primary RCC (SEER site recode 56, kidney and renal pelvis) between 1995 and 2002. Our final sample included

costs in multivariate analyses, including age, race/ethnicity, and comorbidities. Among RCC patients, treatment with surgery and radiation was associated with higher costs per patient than treatment with surgery alone at 1 year ($24,556, 95% CI = $16,673–$32,940) and 5 years ($30,540, 95% CI = $17,853–$43,648). RCC patients who received chemotherapy as part of their treatment regimen also had significantly higher costs per patient than those who received surgery alone at 1 year ($15,144, 95% CI = $9,979–$20,344) and 5 years ($13,440, 95% CI = $1,287–$27,572).

CONCLUSIONS: Newly diagnosed RCC is associated with a significant economic burden, which is largely determined by several patient characteristics, disease stage, and treatment choice.

J Manag Care Pharm. 2011;17(8):610-20

Christopher S. Hollenbeak et al. Determinants of Medicare All-Cause Costs Among Elderly Patients with Renal Cell Carcinoma. J Manag Care Pharm. 2011 Oct; 17(8): 610–620.

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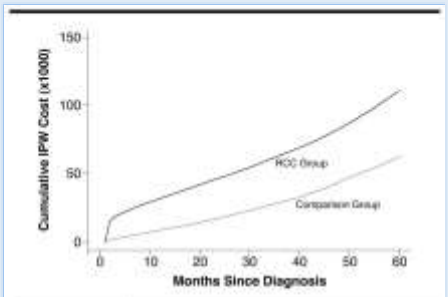
CASE STUDY #1: A DISEASE BURDEN STUDY

- Disease burden is important to inform decision makings (e.g. pipeline and early asset strategies) and more accurate cost estimate from real-world data is critical
- Patient censoring due to variable follow-up time was addressed for estimating the cumulative unadjusted costs:



	Year					
Uncensored cases	0[a]	1	2	3	4	5
RCC group	4,938	3,146	2,288	1,615	1,028	708
Comparison group	9,876	8,861	7,032	5,247	3,420	2,744

[a]Year 0 represents the date of diagnosis. The first year of observation (Table 3) began on the diagnosis date (RCC group) or pseudo-diagnosis date (comparison group).
IPW = inverse probability-weighted; RCC = renal cell carcinoma.

Christopher S. Hollenbeak et al. Determinants of Medicare All-Cause Costs Among Elderly Patients with Renal Cell Carcinoma. J Manag Care Pharm. 2011 Oct; 17(8): 610–620.

CASE STUDY #1: A DISEASE BURDEN STUDY

TABLE 4 Inverse Probability-Weighted Regression of 1-Year and 5-Year Costs, All Study Patients[a]

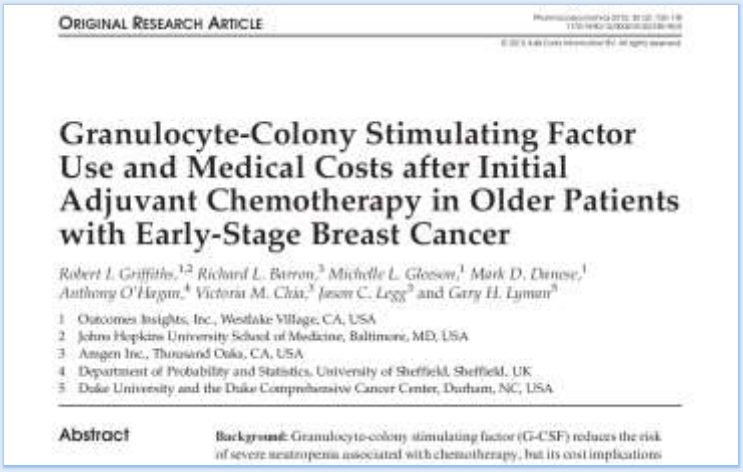
	1-Year Costs		5-Year Costs	
Variable	Coefficient ($)	95% CI ($)	Coefficient ($)	95% CI ($)
Intercept	5,370	4,811-6,070	26,602	24,755-28,451
Age (years)				
65-69	Reference			
70-74	4,218	1,855-6,647	7,098	1,737-12,434
75-79	5,049	2,602-7,514	4,718	−397-9,959
80-84	2,037	−661-4,819	270	−8,269-8,800
85 or older	−2,095	−4,993-988	−10,720	−16,802-−3,811
Sex				
Male	17	−725-738	−205	−2,144-1,684
Female	Reference		0	
Race/Ethnicity				
White	Reference		0	
Black	2,887	848-4,922	11,950	7,211-17,121
Asian	−1,349	−3,525-2,457	2,610	−4,558-10,035
Hispanic	−3,872	−5,662-−2,015	−2,503	−8,304-3,207
Other	−2,779	−3,287-416	−150	−7,304-7,591
Anemia[b]	3,441	1,616-5,248	6,626	2,212-11,064
Hyperlipidemia[b]	88	−794-987	4,245	1,390-7,039
Charlson Comorbidity Index[b]	4,888	4,351-5,450	10,850	9,547-12,188
RCC	22,340	20,835-24,027	20,676	17,594-24,372

[b]All comorbidities were identified from codes during the year prior to RCC diagnosis (RCC cohort) or the assigned pseudo-diagnosis date (comparison cohort).
CI = confidence interval; RCC = renal cell carcinoma.

- Lin's regression was applied to estimate the incremental effect of RCC to costs.
- Each of the 60 monthly costs was fit to a multivariate model. Coefficients for months 1 through 60 were summed to give marginal effects on 5-year costs.

Christopher S. Hollenbeak et al. Determinants of Medicare All-Cause Costs Among Elderly Patients with Renal Cell Carcinoma. J Manag Care Pharm. 2011 Oct; 17(8): 610–620.

CASE STUDY #2: UNDERSTAND LONG-TERM COST TO PAYER



ORIGINAL RESEARCH ARTICLE

Granulocyte-Colony Stimulating Factor Use and Medical Costs after Initial Adjuvant Chemotherapy in Older Patients with Early-Stage Breast Cancer

Robert I. Griffiths,[1,2] Richard L. Barron,[3] Michelle L. Gleeson,[1] Mark D. Danese,[1] Anthony O'Hagan,[4] Victoria M. Chia,[3] Jason C. Legg[3] and Gary H. Lyman[5]

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Abstract **Background:** Granulocyte-colony stimulating factor (G-CSF) reduces the risk of severe neutropenia associated with chemotherapy, but its cost implications

Griffiths RI. et al. Granulocyte-colony stimulating factor use and medical costs after initial adjuvant chemotherapy in older patients with early-stage breast cancer. Pharmacoeconomics. 2012 Feb 1;30(2):103-18.

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CASE STUDY #2: UNDERSTAND LONG-TERM COST TO PAYER

- Examined the association between G-CSF use and long-term direct medical costs to Medicare after initial adjuvant chemotherapy in ESBC.
- Assessed unadjusted (on the left) and adjusted (next page) cumulative costs related to each group with IPW-based approach to address censored cost data

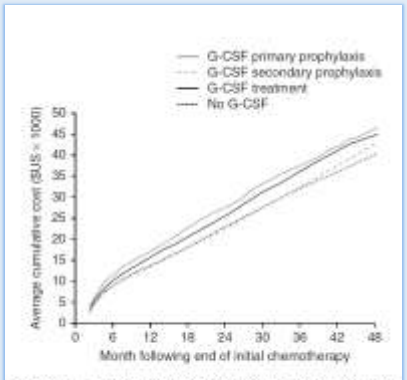

Fig. 5. Cumulative inverse probability weighted cost per month following the end of initial chemotherapy, by study group, unadjusted for other patient demographic, clinical and treatment factors. **G-CSF** = granulocyte-colony stimulating factor.

Griffiths RI. et al. Granulocyte-colony stimulating factor use and medical costs after initial adjuvant chemotherapy in older patients with early-stage breast cancer. Pharmacoeconomics. 2012 Feb 1;30(2):103-18.

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CASE STUDY #2: UNDERSTAND LONG-TERM COST TO PAYER

Table IV. Inverse probability weighted regression analysis of 48-month direct medical costs (SUS, year 2009 values) following initial chemotherapy

Variable	Type of comparison between study groups [coefficient (95% CI)]	
	G-CSF primary prophylaxis vs no G-CSF primary prophylaxis[a]	four separate study groups
Study group		
No G-CSF [reference category]		
G-CSF-treatment	Reference category	2938 (285, 5590)
G-CSF secondary prophylaxis	Reference category	1145 (−2435, 4535)
G-CSF primary prophylaxis	684 (−3104, 4358)	1600 (−2891, 5759)

Continued next page

Key points for decision makers

- Granulocyte-colony stimulating factor (G-CSF) primary prophylaxis does not affect the long-term medical costs of patients diagnosed with early-stage breast cancer
- G-CSF primary prophylaxis appears to be cost-neutral after completion of initial chemotherapy
- G-CSF treatment is associated with higher long-term costs, suggesting that neutropenia or febrile neutropenia during initial chemotherapy may contribute to higher long-term costs of care

Griffiths RI. et al. Granulocyte-colony stimulating factor use and medical costs after initial adjuvant chemotherapy in older patients with early-stage breast cancer. Pharmacoeconomics. 2012 Feb 1;30(2):103-18.

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CASE STUDY #3: APPLICATION IN COST-EFFECTIVENESS ANALYSIS

BMJ

RESEARCH

Cost effectiveness analysis of larval therapy for leg ulcers

Marta O Soares, research fellow,[1] Cynthia P Iglesias, senior research fellow,[1] Martin Bland, professor of health statistics,[1] Nicky Cullum, professor, deputy head of department,[1] Jo C Dumville, research fellow,[1] E Andrea Nelson, reader in wound healing and director of research,[2] David J Torgerson, professor, director York trials unit,[1] Gill Worthy, trial statistician[1] on behalf of the VenUS II team

ABSTRACT

Objective To assess the cost effectiveness of larval therapy compared with hydrogel in the management of leg ulcers.

Design Cost effectiveness and cost utility analyses carried out alongside a pragmatic multicentre, randomised, open trial with equal randomisation.

Population Intention to treat population comprising 267 patients with a venous or mixed venous and arterial ulcers with at least 25% coverage of slough or necrotic tissue.

Interventions Patients were randomly allocated to debridement with bagged larvae, loose larvae, or

the Healthcare Commission estimated the annual cost of treatment for leg ulcers at £600m (€748m, $838m) to £900m. Nursing time required to manage and treat leg ulcers is the main cost driver in the UK, where patients with leg ulcers often make up a large proportion of community nursing caseloads.[3] Despite the effectiveness of high compression bandaging for the treatment of venous leg ulcers being well established,[4 5] not all patients are suitable or willing to wear compression. Furthermore, the healing process is slow and some ulcers never heal—thus the relevance of investigating the potential value of alternative treat-

Soares MO. et al. Cost effectiveness analysis of larval therapy for leg ulcers. BMJ. 2009 Mar 19;338:b825. doi: 10.1136/bmj.b825.

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CASE STUDY #3: APPLICATION IN COST-EFFECTIVENESS ANALYSIS

Table 3 | Adjusted base case analysis*: annual costs (£), time to healing, and quality adjusted life years (QALYs)

Variables	Mean (95% CI) annual costs	Mean (95% CI) time to healing (days)	QALYs (95% CI)
Hydrogel	1976.4 (1521.4 to 2500.2)	206.5 (202.7 to 260.2)	0.540 (0.489 to 0.589)
Larval therapy	2073.1 (1724.4 to 2433.4)	204.1 (207.9 to 248.3)	0.551 (0.505 to 0.591)
Difference†	96.7 (−491.9 to 685.8)	−2.42 (−41.0 to 31.9)	0.011 (−0.067 to 0.071)

£1.00 (€1.15; $1.45).
*Adjusted for type of ulcer, duration of ulcer (logarithmic), ulcer area (logarithmic), centre (aggregating centres with fewer than 10 elements). Additional adjustment for baseline utility in estimation of QALYs.
†Larval therapy compared with hydrogel.

- Cost-effectiveness model are often used to demonstrate the economic value of health technologies and inform regulatory, pricing, and contracting decisions
- It is critical to address censored costs properly when constructing cost-effectiveness model
- Censoring and how it was adjusted in the study will certainly impact the results

Soares MO. et al. Cost effectiveness analysis of larval therapy for leg ulcers. BMJ. 2009 Mar 19;338:b825. doi: 10.1136/bmj.b825.

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SUMMARY

- Real-world cost data is a key component in many study types
- RWE is playing a more and more important role in decision making process for all different parties involved
- The acceptance and impact of RWD are relied on proper methodology and study practice
- Censored cost is an issue that has to be carefully evaluated and addressed to minimize the bias in study results

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GROUP DISCUSSION

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