

存活分析 (1)

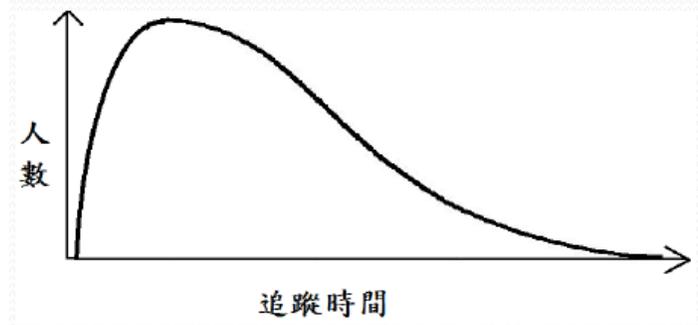
醫學研究部生統小組

陳俊朋

2025/12/16

Survival Analysis

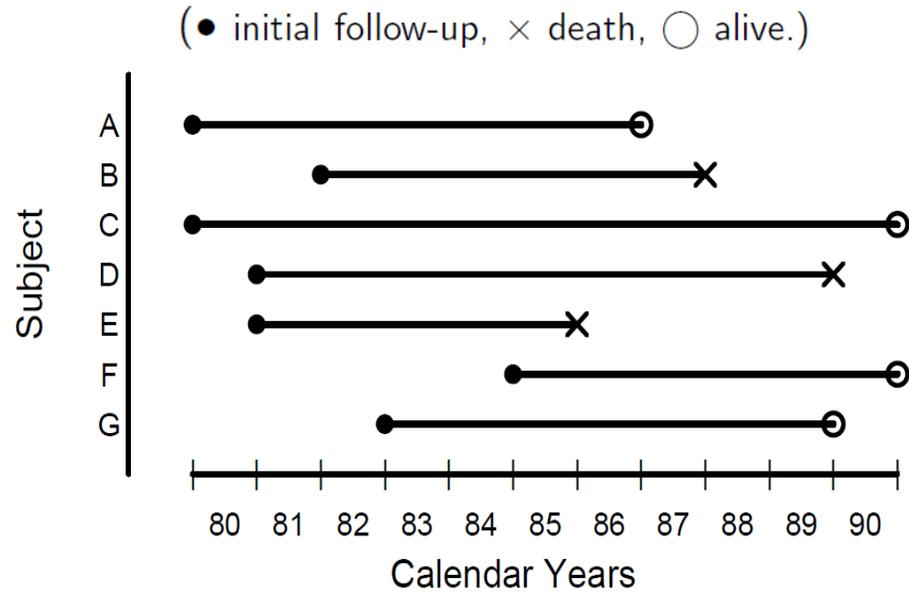
- 將『時間』變項列入分析的統計方法
- 從一時間點至事件(event)發生的時間(time to event)，稱為survival time
 - Start time- 研究起始時間/確診癌症時間
 - End time- 疾病發生時間/死亡時間
- 資料特性：資料通常不是常態分配



資料分類

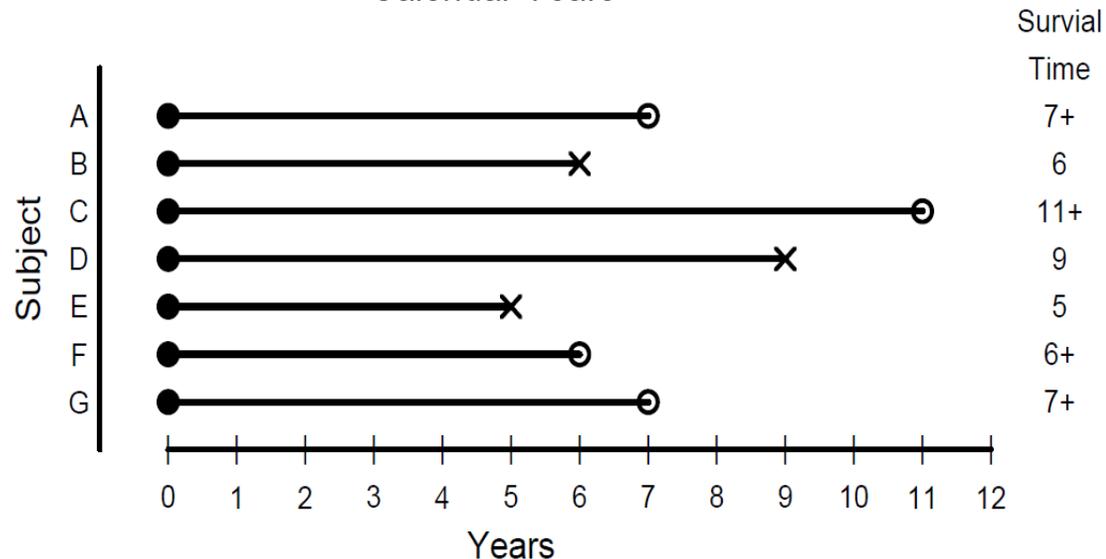
- 完整資料(complete data)
 - 觀察期間提供事件發生的時間點
- 設限資料(censored data)
 - 觀察期間失去聯絡或觀察結束時仍未發生事件
- 競爭死因資料(Competing cause of deaths)
 - 觀察期間死於其他死因之時間

Survival Time



➤ Survival time= 事件發生時間 - 追蹤的起始時間
(需大於0)

➤ 個案BDE是完整資料；
個案ACFG為設限資料



存活資料建檔

基本資料

存活狀態

起訖時間

分析整理

ID	Sex	Age	Tx	event (death)	Start date	Death date	follow date	End date	follow year
Case1	0	45	0	0	2012/5/8		2016/7/15	2016/7/15	4.19
Case2	1	55	0	1	2013/12/9	2015/1/16		2015/1/16	1.10
Case3	0	56	0	0	2012/5/10		2014/3/12	2014/3/12	1.84
Case4	1	51	1	1	2014/9/11	2016/7/18		2016/7/18	1.85
Case5	0	62	1	1	2012/8/12	2016/12/19		2016/12/19	4.35
Case6	1	70	0	1	2018/7/13	2019/7/20		2019/7/20	1.02
Case7	1	58	0	0	2015/5/14		2016/8/21	2016/8/21	1.27
Case8	0	66	0	0	2018/8/15		2019/7/22	2019/7/22	0.93
Case9	0	60	1	0	2019/5/16		2019/7/23	2019/7/23	0.19
Case10	0	63	1	0	2017/10/17		2018/7/24	2018/7/24	0.77
Case11	0	66	1	0	2016/3/20		2017/7/25	2017/7/25	1.35
Case12	0	69	1	0	2014/8/22		2016/7/26	2016/7/26	1.93

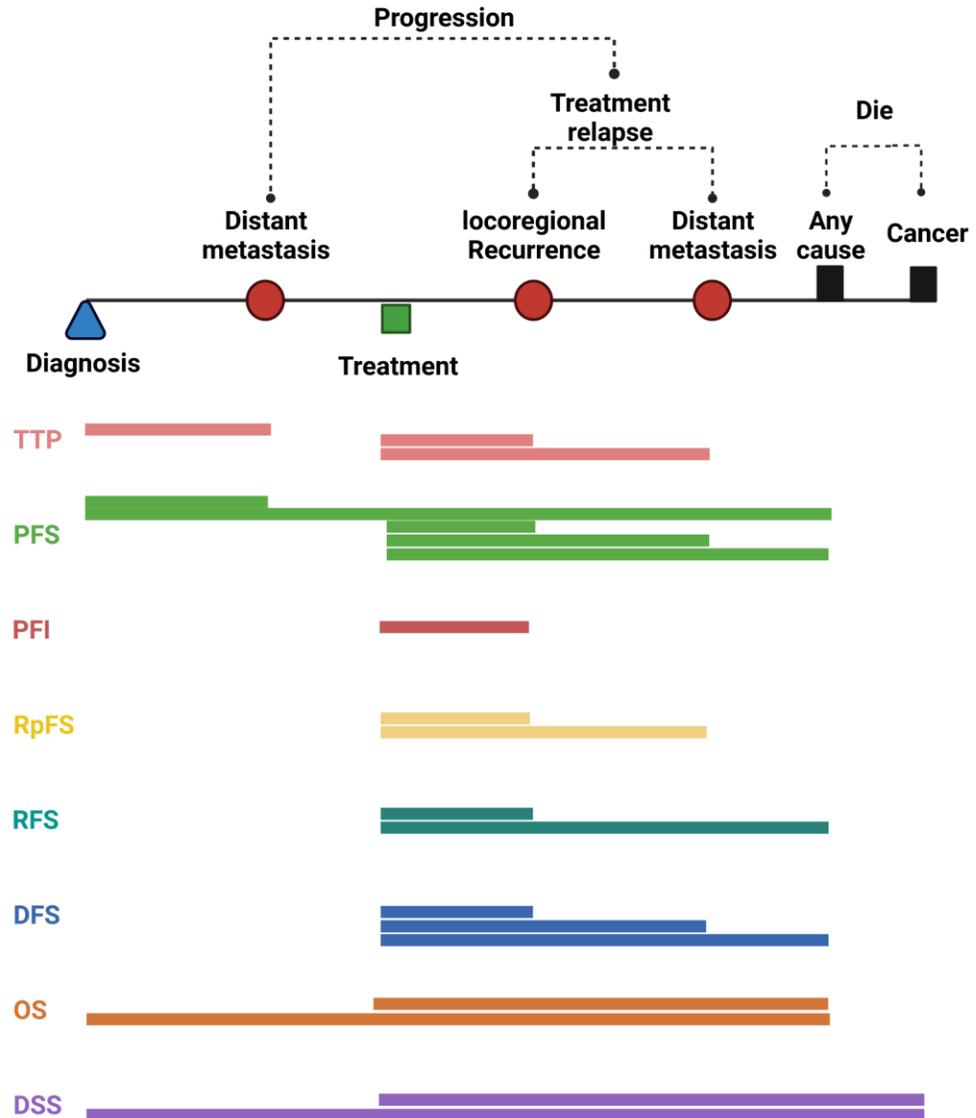
- 日期格式統一西元年
- 可分組比較存活曲線差異，如Sex (F vs M), Age (<60 vs >=60)
- 事件(event): 0=存活; 1=死亡
- 未死亡個案End_date，研究者需設定結束時間(建議可用最後看診日期)

Definition of Time to Event Variables

指標	事件	設限
1. 無疾病進展存活期 (progression free survival, PFS)	疾病進展或死亡	無疾病進展
2. 無疾病存活期 (disease free survival, DFS)	疾病復發或死亡	無疾病復發
3. 治療至疾病進展時間 (time to progression, TTP)	疾病進展	無疾病進展、無疾病狀態死亡(如車禍或不明原因)
4. 治療至治療失敗時間 (time to treatment failure, TTF)	疾病進展、疾病復發、藥物副作用、死亡	無疾病進展或復發
5. 總存活時間 (overall survival, OS)	死亡	存活
6. 疾病特定存活期 (disease specific survival, DSS)	由疾病本身所導致的死亡(車禍或其他原因要歸為設限資料)	存活、因其他原因死亡

Definition for the Assessment of Time-to-event Endpoints in Cancer

Time to progress	The time from diagnosis/treatment to the progression of tumor (in any aspect).
Progression-free survival	The time from diagnosis/treatment to the progression of tumor (in any aspect) or death (for any cause).
Progression-free interval	The time from treatment to locoregional recurrence.
Relapse-free survival	The time from treatment to the relapse (local, regional, distant).
Recurrence-free survival	The time from treatment to locoregional recurrence or death (for any cause)
Disease-free survival	The time from treatment to locoregional recurrence, metastasis or death (for any reason)
Overall survival	The time from diagnosis/treatment to death (for any reason).
Disease-specific survival	The time from diagnosis/treatment to death (cancer-specific).

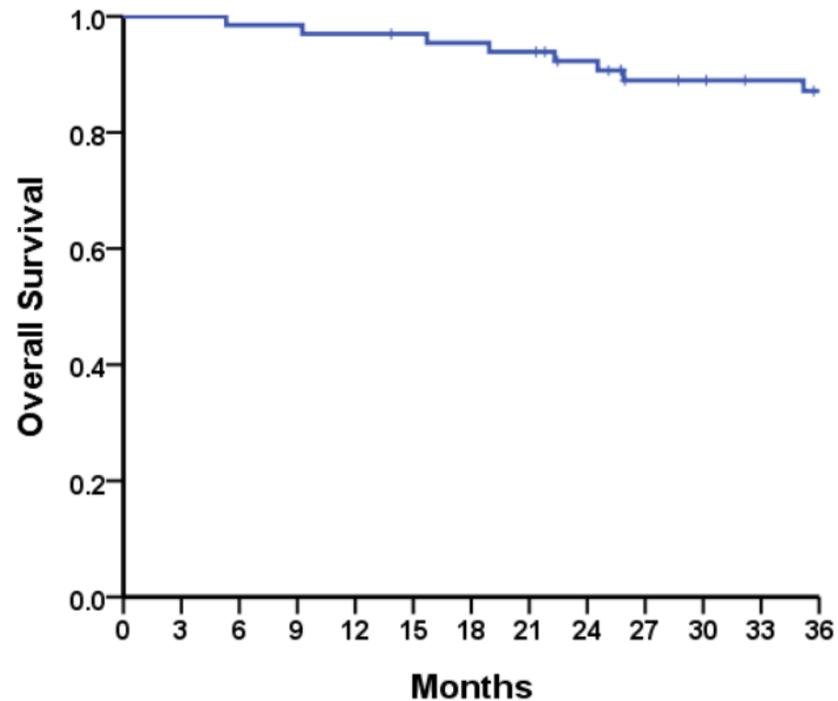
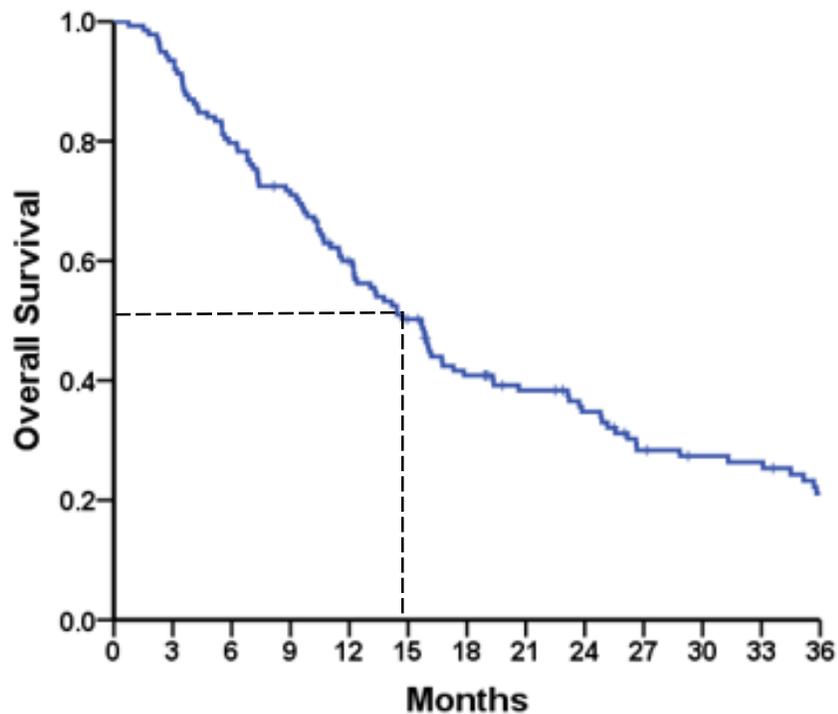


存活分析－統計方法

- 無母數分析
 - Kaplan-Meier
 - Log-rank test
 - Cox Proportional Hazards Model

Kaplan-Meier

- 常用來估計存活曲線的方法，此方法用每一個事件發生時間點及設限點來設定區間
- 可估計存活中位數及不同時間點的存活率



Kaplan-Meier Estimates

ID	fu_time (month)	status
1	2	0
2	2	0
3	2	1
4	3	0
5	3	0
6	4	1
7	4	0
8	5	0
9	6	1
10	6	0

month	Number at risk	Number of events	Number of censored	Conditional Probability	Survival Function
1	10	0	0	$10/10 = 1.00$	1.00
2	10	1	2	$9/10 = 0.90$	$0.90 * 1.00 = 0.90$
3	7	0	2	$7/7 = 1.00$	$1.00 * 0.90 = 0.90$
4	5	1	1	$4/5 = 0.80$	$0.80 * 0.90 = 0.72$
5	3	0	1	$3/3 = 1.00$	$1.00 * 0.72 = 0.72$
6	2	1	1	$1/2 = 0.50$	$0.50 * 0.72 = 0.36$

Log-rank Test

- Kaplan-Meier法僅能了解不同組別的存活曲線分佈
- 比較組別間是否差異
 - H0: 兩條存活曲線相同
 - H1: 兩條存活曲線不相同

Shen et al. *BMC Cancer* (2020) 20:709
<https://doi.org/10.1186/s12885-020-07210-8>

BMC Cancer

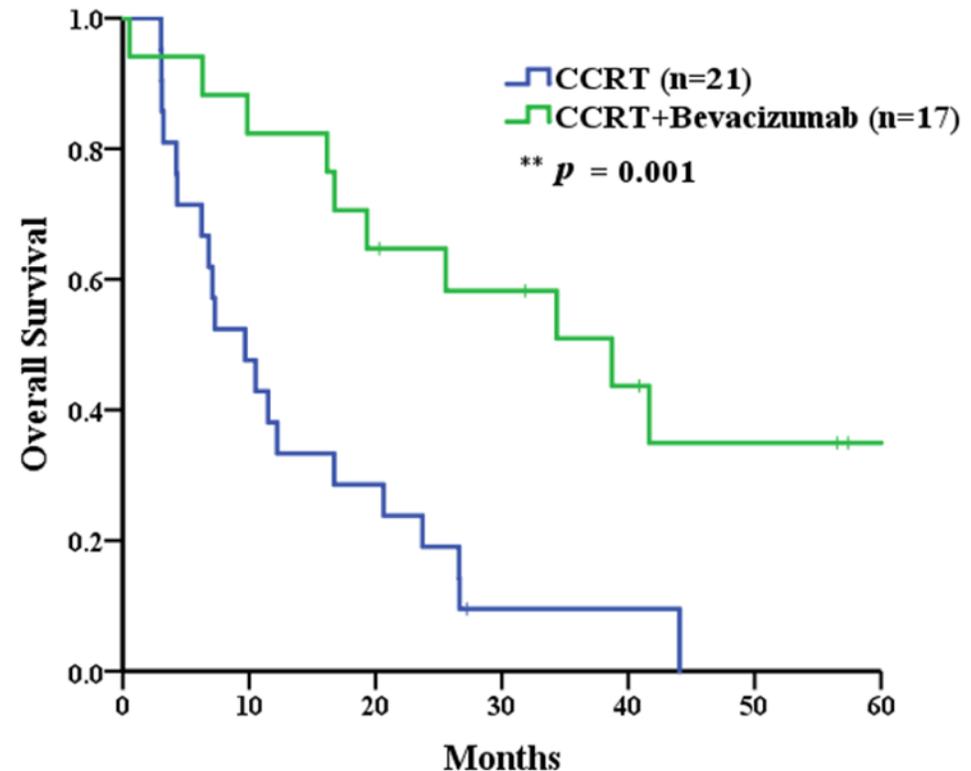
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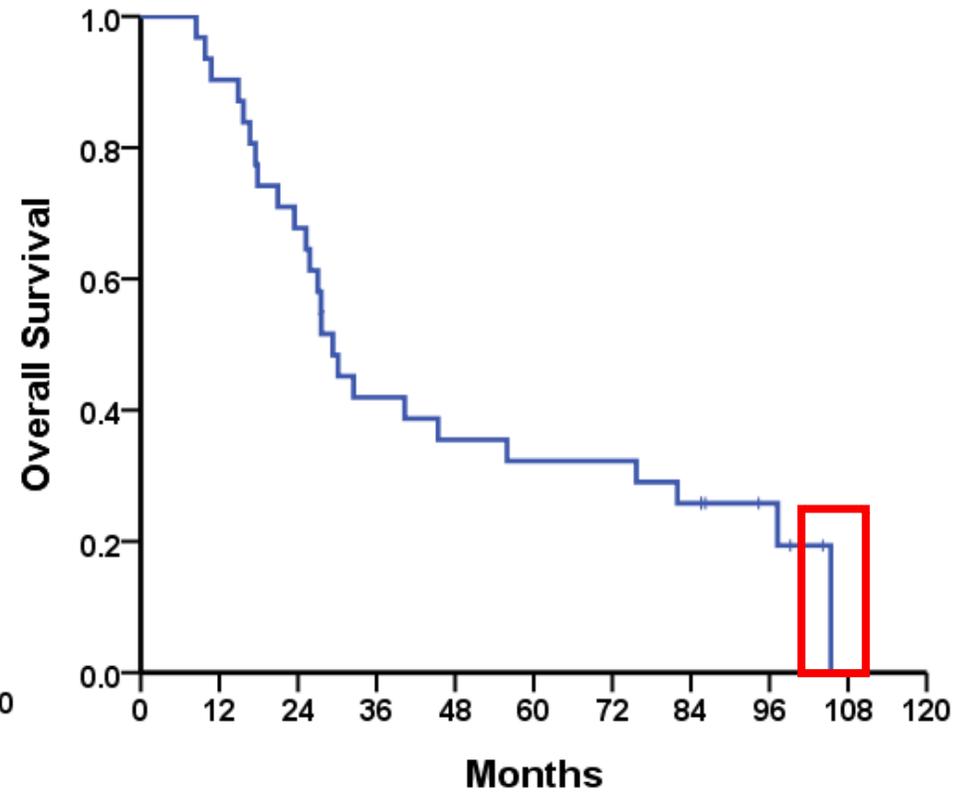
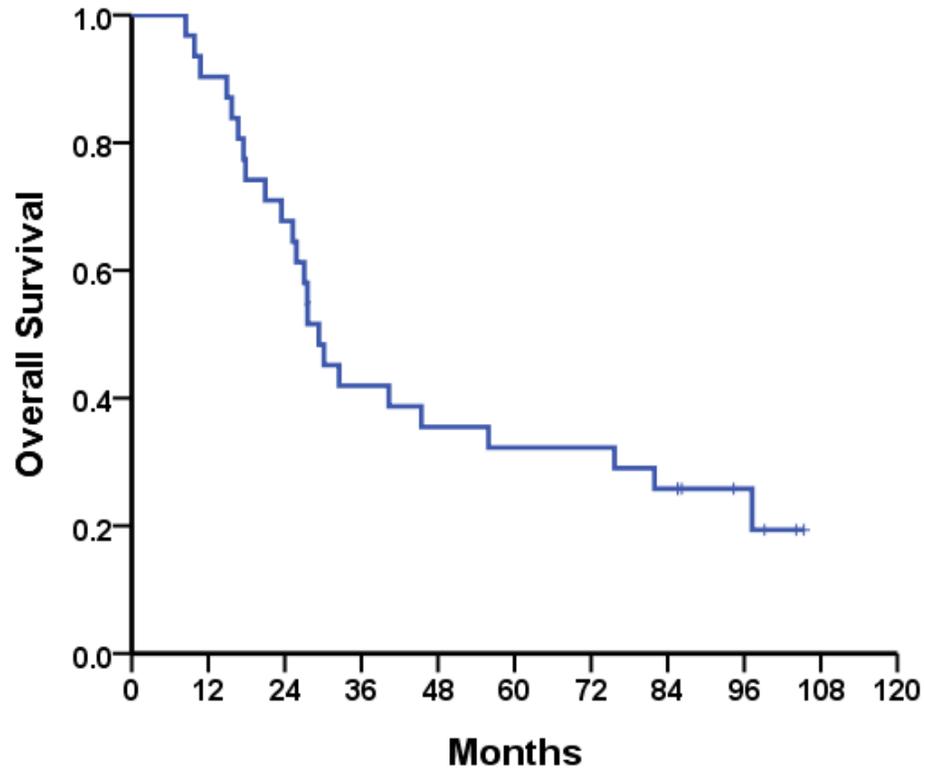
Both p53 codon 72 Arg/Arg and pro/Arg genotypes in glioblastoma multiforme are associated with a better prognosis in bevacizumab treatment



Chiung-Chyi Shen^{1,2,3,4,5,6*}, Wen-Yu Cheng^{1,2,7}, Chung-Hsin Lee^{1,8}, Xue-Jun Dai⁹, Ming-Tsang Chiao¹, Yea-Jiuen Liang¹, Wan-Yu Hsieh¹, Tsuo-Fei Mao⁵, Guo-Shi Lin⁹, Shou-Ren Chen⁹, Bai-Shuan Liu¹⁰ and Jun-Peng Chen¹¹



Survival Curve



Survival Curve

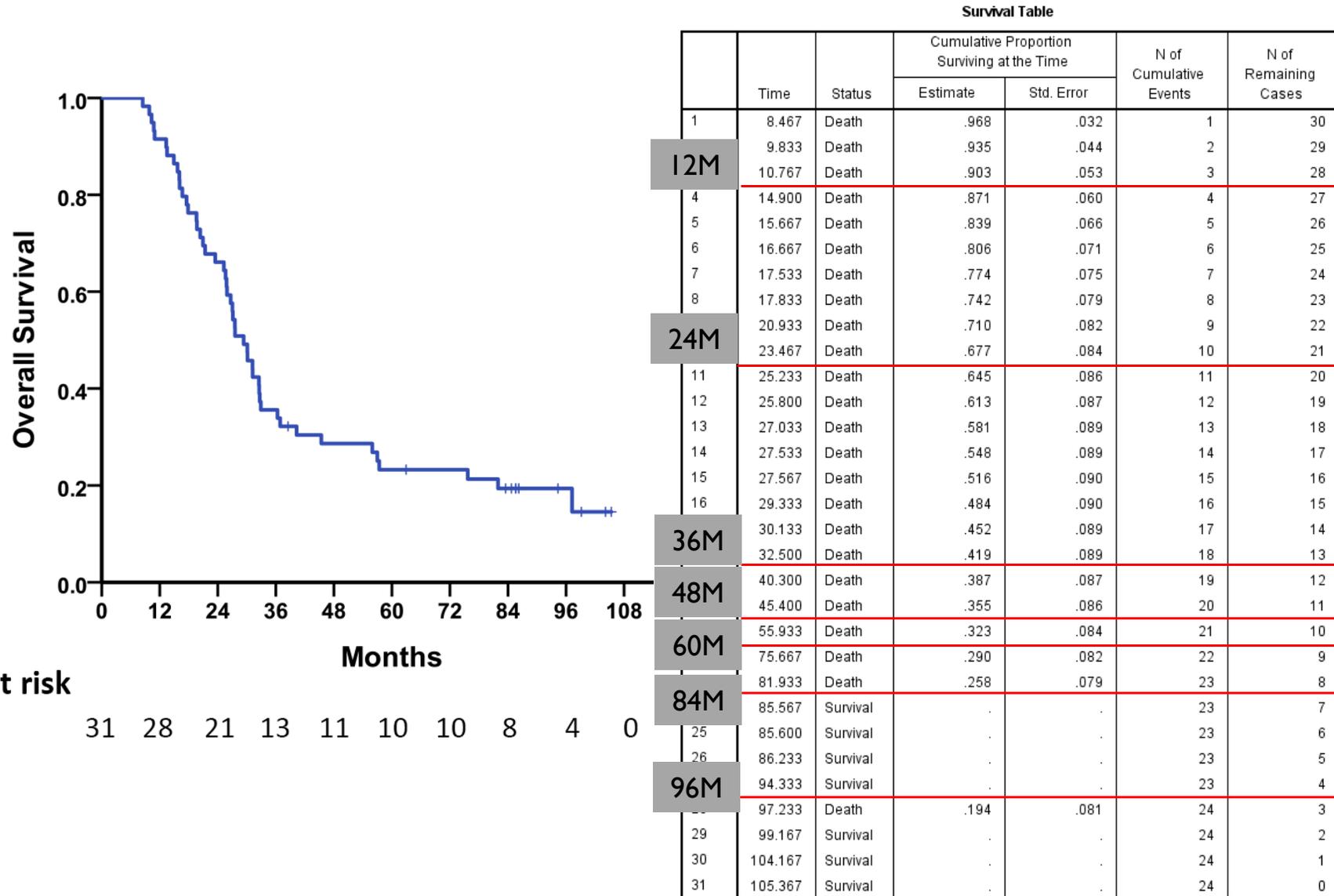
Survival Table

	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
1	8.467	Death	.968	.032	1	30
2	9.833	Death	.935	.044	2	29
3	10.767	Death	.903	.053	3	28
4	14.900	Death	.871	.060	4	27
5	15.667	Death	.839	.066	5	26
6	16.667	Death	.806	.071	6	25
7	17.533	Death	.774	.075	7	24
8	17.833	Death	.742	.079	8	23
9	20.933	Death	.710	.082	9	22
10	23.467	Death	.677	.084	10	21
11	25.233	Death	.645	.086	11	20
12	25.800	Death	.613	.087	12	19
13	27.033	Death	.581	.089	13	18
14	27.533	Death	.548	.089	14	17
15	27.567	Death	.516	.090	15	16
16	29.333	Death	.484	.090	16	15
17	30.133	Death	.452	.089	17	14
18	32.500	Death	.419	.089	18	13
19	40.300	Death	.387	.087	19	12
20	45.400	Death	.355	.086	20	11
21	55.933	Death	.323	.084	21	10
22	75.667	Death	.290	.082	22	9
23	81.933	Death	.258	.079	23	8
24	85.567	Survival	.	.	23	7
25	85.600	Survival	.	.	23	6
26	86.233	Survival	.	.	23	5
27	94.333	Survival	.	.	23	4
28	97.233	Death	.194	.081	24	3
29	99.167	Survival	.	.	24	2
30	104.167	Survival	.	.	24	1
31	105.367	Survival	.	.	24	0

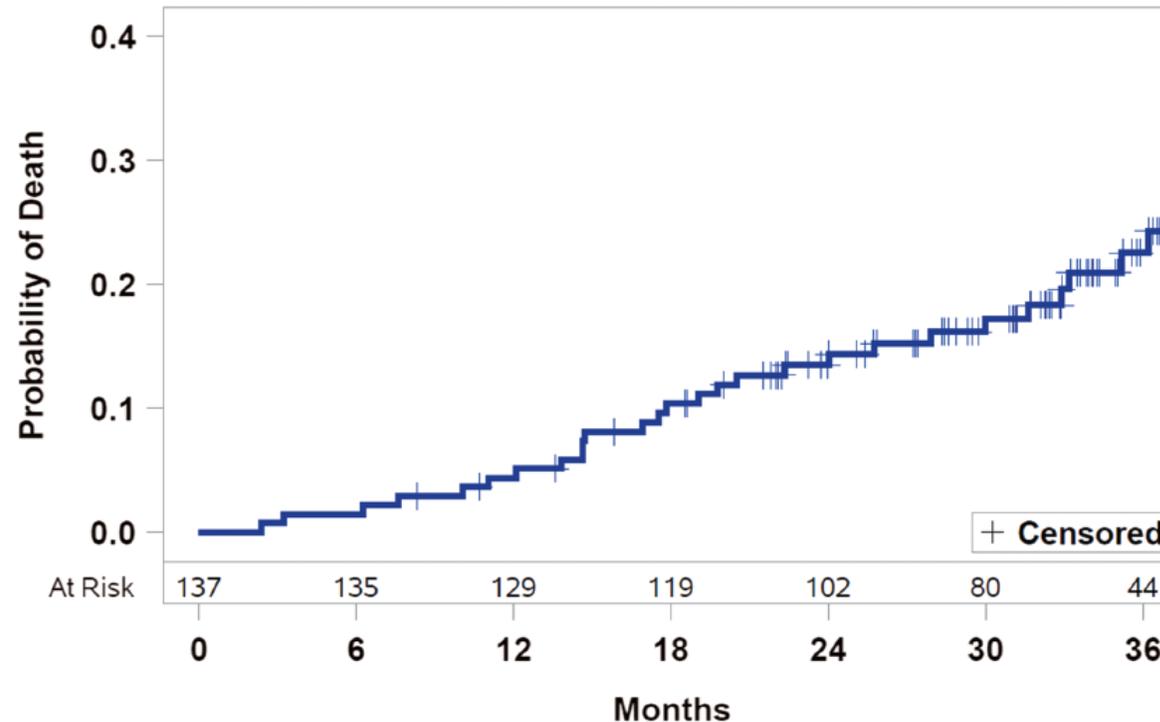
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8	17.833	Death	.742	.079	8	23
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28	97.233	Death	.194	.081	24	3
29	99.167	Survival	.	.	24	2
30	104.167	Survival	.	.	24	1
31	105.367	Death	.000	.000	25	0

Presentation of Survival Curve



Presentation of Survival Curve



Months represent months from the date of therapy activation.

Figure 5. Kaplan–Meier curve of mortality. Kaplan–Meier curve showing estimated mortality through 36 months of active therapy using the pooled treatment and former control groups. Patients who did not die were censored at last contact if they did not reach 36 months of active therapy.

Cox Proportional Hazards Model

- 評估多個變數對存活(Time to event)的影響
- 可使用類別/連續變數呈現危險因子，並估算出這些危險因子對outcome的影響

$$\log \frac{h(t)}{h_0(t)} = \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k$$

Hazard ratio (HR)	Explanation
HR=1	Two groups have the same survival experience
HR>1	Survival is better in the control group
HR<1	Survival is better in the treatment group

Kaplan-Meier Example

- 比較在第三期子宮內膜癌術後治療，Sandwich組和CT alone兩組治療預後的差異

Outcomes of "sandwich" chemoradiotherapy compared with chemotherapy alone for the adjuvant treatment of FIGO stage III endometrial cancer

Shao-Jing Wang¹, Lily Wang², Lou Sun¹, Yu-Hsiang Shih¹, Shih-Tien Hsu^{1,3,4}, Chin-Ku Liu¹, Sheau-Feng Hwang^{1,5} and Chien-Hsing Lu^{1,6*}

¹Department of Gynecology and Obstetrics, Taichung Veterans General Hospital, Taichung, Taiwan, ²Department of Radiation Oncology, Taichung Veterans General Hospital, Taichung, Taiwan, ³Center for General Education, Ling Tung University, Taichung, Taiwan, ⁴School of Medicine, China Medical University, Taichung, Taiwan, ⁵Department of Palliative Care Unit, Taichung Veterans General Hospital, Taichung, Taiwan, ⁶Institute of Biomedical Sciences, Ph.D. Program in Translational Medicine, and Rong-Hsing Research Center for Translational Medicine, National Chung-Hsing University, Taichung, Taiwan

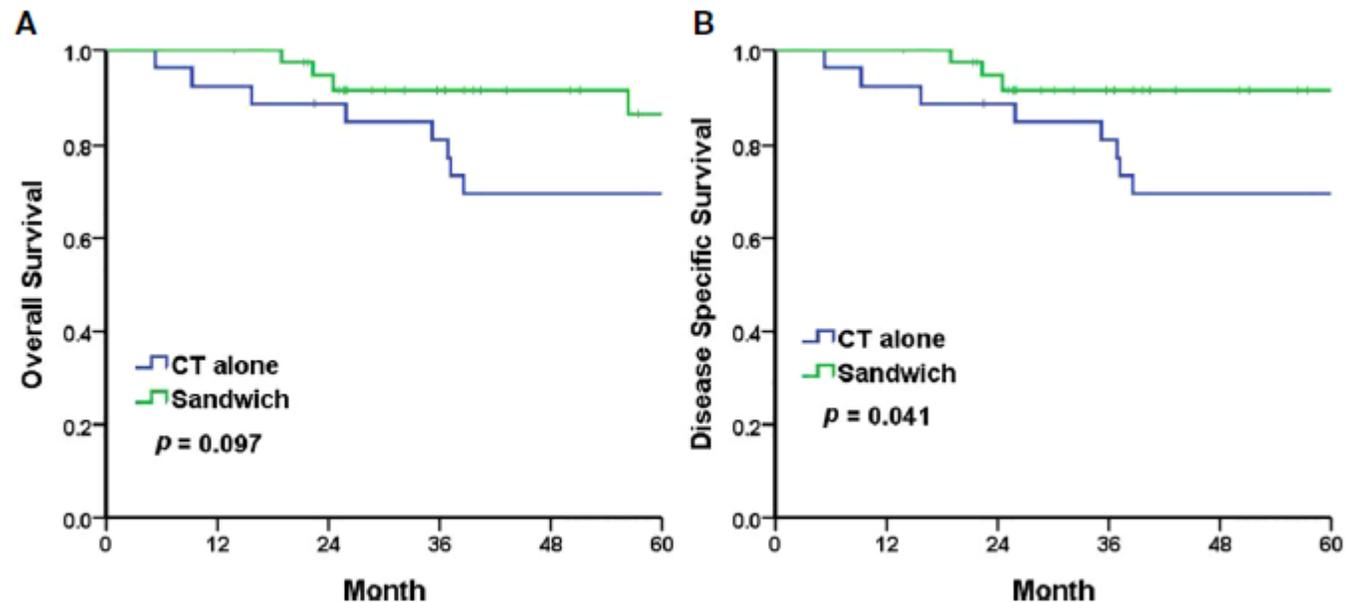


FIGURE 2

The Kaplan-Meier survival curves for 5-year overall survival (A) and 5-year disease-specific survival (B). CT chemotherapy.

Outcomes of "sandwich" chemoradiotherapy compared with chemotherapy alone for the adjuvant treatment of FIGO stage III endometrial cancer. *Frontiers in oncology*, 12 (2022), 946113-946113.

Cox Regression Example

5-year disease-specific survival

	Univariate			Multivariable		
	HR	95% CI	<i>p</i> -value	HR	95% CI	<i>p</i> -value
Age group						
<60	Reference					
≥60	1.34	(0.36-5.07)	0.665			
FIGO stage						
IIIA and IIIB and IIIC1	Reference					
IIIC2	1.45	(0.44-4.75)	0.541			
Histology grading						
Grades 1 and 2	Reference			Reference		
Grade 3	8.70	(1.11-68.01)	0.039*	9.16	(1.17-71.70)	0.035*
Treatment						
CT alone	Reference			Reference		
Sandwich	0.27	(0.07-1.04)	0.056	0.23	(0.06-0.87)	0.030*
LVSI						
Absent	Reference					
Present	3.82	(0.49-29.89)	0.201			
Deep myometrial invasion						
Absent	Reference			Reference		
Present	7.85	(1.00-61.34)	0.050	9.44	(1.20-74.15)	0.033*

Outcomes of " sandwich" chemoradiotherapy compared with chemotherapy alone for the adjuvant treatment of FIGO stage III endometrial cancer. *Frontiers in oncology*, 12 (2022), 946113-946113.

KM and Cox Regression SPSS dataset

ID	group	OP_date	End_Date	STATUS_5y	STATUS_DSS_5y	Month_OS	Age_gp	Hist_grading
1	1	2016/04/20	2021/09/09	1	0	64.66	0	2
2	1	2012/04/27	2020/02/20	1	0	93.80	1	1
3	1	2015/12/30	2021/01/19	1	0	60.68	0	1
4	0	2010/11/12	2016/04/02	1	0	64.66	0	2
5	1	2012/11/21	2014/10/01	0	1	22.31	0	2
6	1	2013/10/08	2020/02/12	1	0	76.16	0	1
7	0	2006/03/29	2008/05/25	0	1	25.89	0	1
8	1	2012/06/19	2020/12/23	1	0	102.14	1	2
9	1	2018/10/29	2021/10/20	1	0	35.71	1	1
10	1	2019/08/27	2021/10/18	1	0	25.72	0	2
11	0	2010/02/05	2017/11/24	1	0	93.60	0	2
12	0	2011/02/24	2014/05/14	0	1	38.60	0	2
13	1	2017/08/25	2021/01/05	1	0	40.38	1	1
14	1	2012/04/20	2015/07/10	1	0	38.64	0	2
15	0	2005/10/06	2015/02/18	1	0	112.43	0	2
16	1	2018/06/25	2021/10/14	1	0	39.66	0	2
17	1	2015/04/08	2021/09/28	1	0	77.70	1	1
18	1	2014/10/17	2021/10/27	1	0	84.34	0	1
19	0	2012/08/03	2013/05/12	0	1	9.26	0	2
20	1	2013/01/14	2017/09/26	0	0	56.38	0	2

Kaplan-Meier 分析操作

The image shows the SPSS Kaplan-Meier analysis workflow with three dialog boxes highlighted by red boxes and arrows:

- Main Dialog:** The 'Time' variable is 'Month_OS' and the 'Status' variable is 'STATUS_DSS_5y(1)'. The 'Define Event...' button is highlighted.
- Kaplan-Meier: Define Event For Status ...:** The 'Value(s) indicating event has occurred' is set to 'Single value: 1'. This dialog is highlighted.
- Kaplan-Meier: Compare Factor Levels:** The 'Log rank' test statistic is selected. This dialog is highlighted.
- Kaplan-Meier: Options:** The 'Survival' plot is selected. This dialog is highlighted.

Other visible elements include a list of variables on the left (ID, OP_date, End_Date, STATUS_5y, Age_gp, Hist_grading, FIGO_stage, LVSI, Deep myometrium invasion [...], BMI25_gp, Cx involvement [Cxinvolveme...], 病歷號碼) and buttons for 'OK', 'Paste', 'Reset', 'Cancel', 'Continue', 'Cancel', and 'Help'.

Kaplan-Meier Output

Case Processing Summary

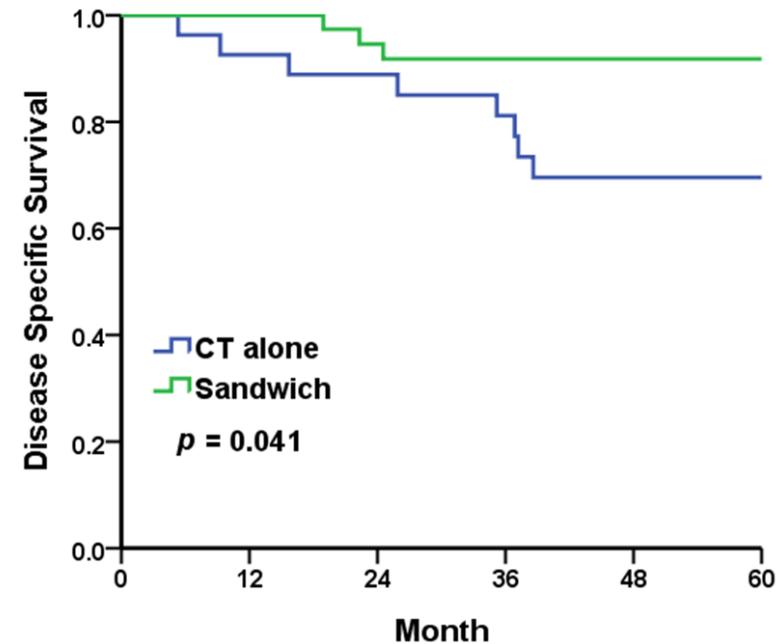
group	Total N	N of Events	Censored	
			N	Percent
CT alone	27	8	19	70.4%
Sandwich	39	3	36	92.3%
Overall	66	11	55	83.3%

Disease specific survival

Treatment	Total	DSS	Censored		Survival rate (%)			p for log rank
			n	%	1y	3y	5y	
CT alone	27	8	19	70.4%	92.6%	81.2%	69.6%	0.041
Sandwich	39	3	36	92.3%	100.0%	97.4%	91.8%	

Survival Table

group	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases	
			Estimate	Std. Error			
CT alone	1	5.322	DSS	.963	.036	1	26
	2	9.265	DSS	.926	.050	2	25
	3	15.704	DSS	.889	.060	3	24
	4	22.472	no-DSS	.	.	3	23
	5	25.889	DSS	.850	.069	4	22
	6	35.187	DSS	.812	.076	5	21
	7	36.862	DSS	.773	.082	6	20
	8	37.191	DSS	.734	.086	7	19
	9	38.604	DSS	.696	.090	8	18
	10	63.639	no-DSS	.	.	8	17
	11	64.526	no-DSS	.	.	8	16
	12	64.657	no-DSS	.	.	8	15
	13	72.279	no-DSS	.	.	8	14
	14	85.290	no-DSS	.	.	8	13
	15	89.823	no-DSS	.	.	8	12



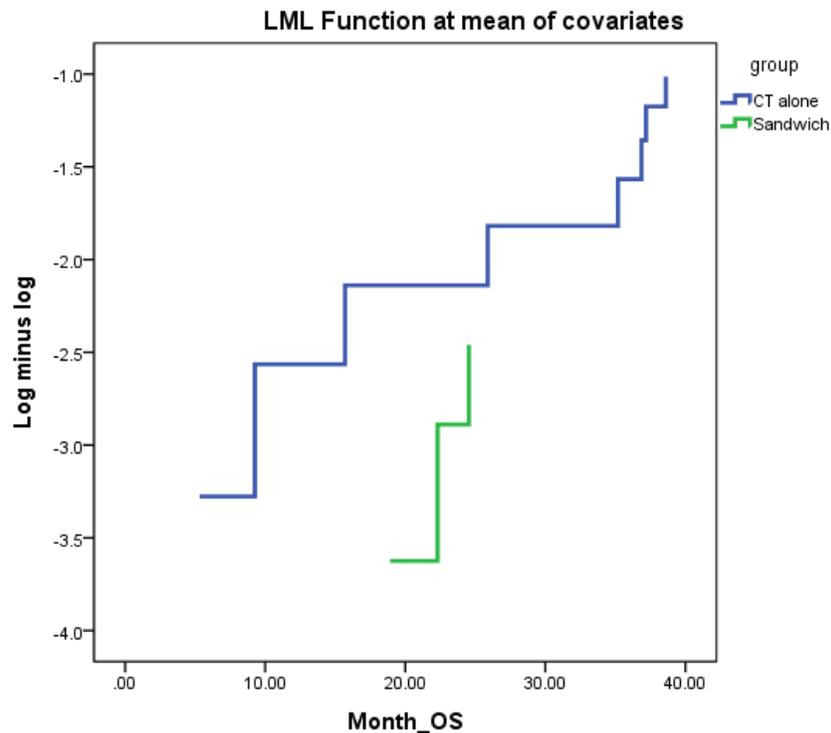
Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	4.169	1	.041

Test of equality of survival distributions for the different levels of group.

Cox PH assumption

- 透過Cox model LML圖形判定是否符合假設
 - 交叉代表未符合
 - 平行代表符合



- 在Cox model加入time-dependent變數的交互作用項判定是否符合假設
 - 顯著代表未符合
 - 未顯著代表符合

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)
T_COV_	-.022	.062	.120	1	.729	.979
group	-.786	1.581	.247	1	.619	.456

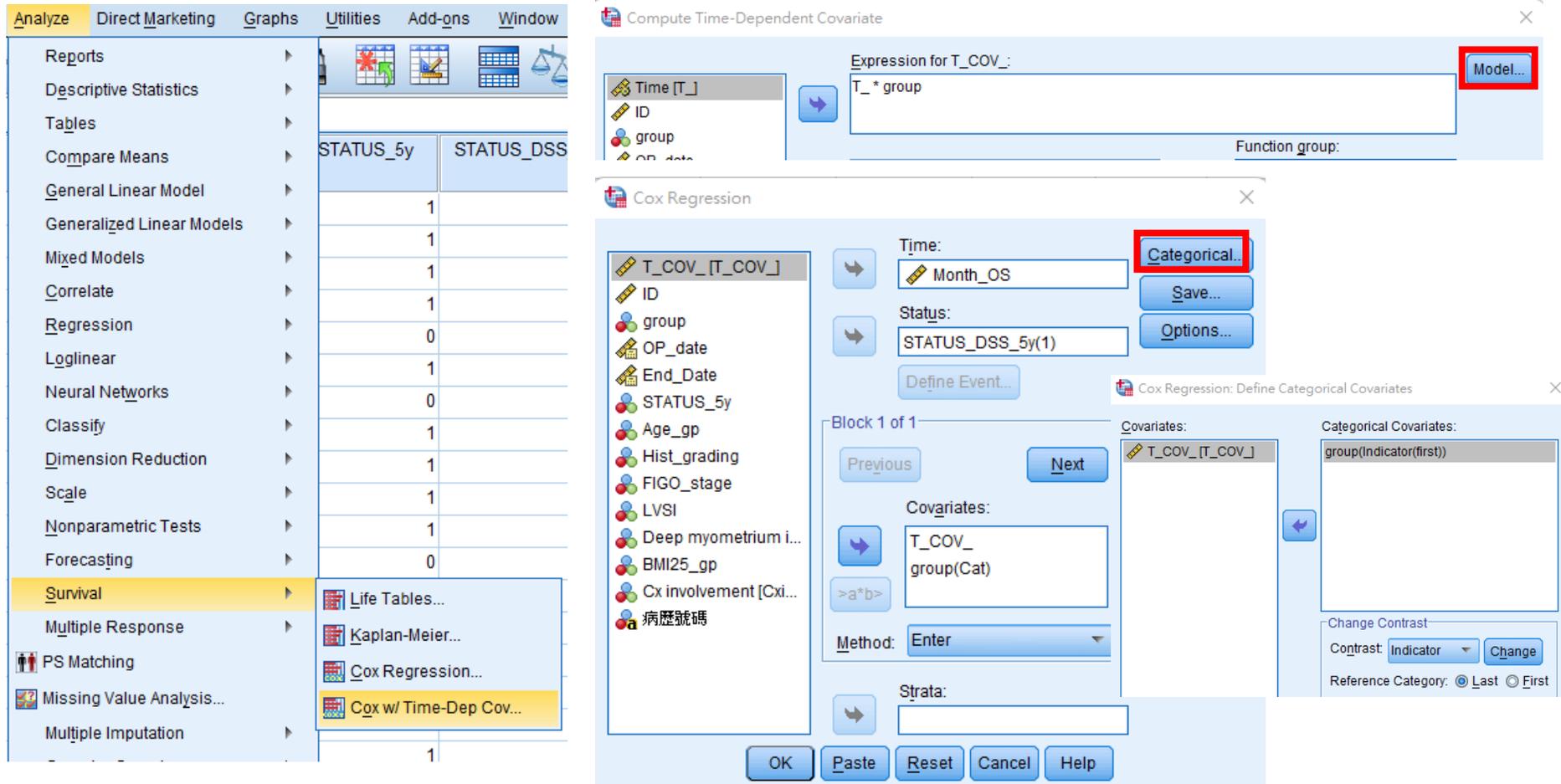
Cox PH assumption

- Log minus log (LML) 圖形

The image shows two screenshots of the SPSS software interface. The left window is titled "Cox Regression" and displays a list of variables on the left, including ID, OP_date, End_Date, STATUS_5y, Age_gp, Hist_grading, FIGO_stage, LVSI, Deep myometrium i..., BMI25_gp, Cx involvement [Cxi..., and 病歷號碼. The "Time:" field is set to "Month_OS", the "Status:" field is set to "STATUS_DSS_5y(1)", and the "Strata:" field is set to "group". The "Method:" dropdown is set to "Enter". The right window is titled "Cox Regression: Plots" and shows the "Plot Type" section with the "Log minus log" checkbox checked. The "Covariate Values Plotted at:" section is empty, and the "Change Value" section has the "Mean" radio button selected.

Cox PH assumption

- Cox time-dependent變數的交互作用項



The image displays the SPSS software interface for configuring a Cox regression model with time-dependent covariates. The 'Analyze' menu is open, showing the path: Analyze > Survival > Cox w/ Time-Dep Cov... The 'Compute Time-Dependent Covariate' dialog box is open, showing the expression for T_COV_ as T_* group. The 'Cox Regression' dialog box is open, showing the Time variable as Month_OS, the Status variable as STATUS_DSS_5y(1), and the Covariates as T_COV_group(Cat). The 'Cox Regression: Define Categorical Covariates' dialog box is open, showing the Covariates as T_COV_[T_COV_] and the Categorical Covariates as group(Indicator(first)).

Model	STATUS_5y	STATUS_DSS
General Linear Model	1	
Generalized Linear Models	1	
Mixed Models	1	
Correlate	1	
Regression	0	
Loglinear	1	
Neural Networks	0	
Classify	1	
Dimension Reduction	1	
Scale	1	
Nonparametric Tests	1	
Forecasting	0	
Survival		
Multiple Response		
PS Matching		
Missing Value Analysis...		
Multiple Imputation		

Cox model-分析操作

分析>存活分析>Cox迴歸

The screenshot shows the SPSS software interface. The 'Analyze' menu is open, and the 'Survival' option is selected. The 'Survival' submenu is also open, showing 'Cox Regression...' as the selected option. The background shows a data view with columns 'STATUS_5y' and 'STATUS_DSS'.

STATUS_5y	STATUS_DSS
1	
1	
1	
1	
0	
1	
0	
1	
1	
1	
1	
0	
1	
1	
1	
0	
1	
0	
0	

Cox model-分析操作

The image displays three sequential screenshots of the SPSS Cox Regression dialog boxes, illustrating the configuration of categorical covariates and model options.

1. Cox Regression (Main Dialog): This dialog shows the selection of variables for the model. The **Time** variable is set to `Month_OS` and the **Status** variable is set to `STATUS_DSS_5y(1)`. The **Covariates** list includes `Hist_grading(Cat)`, `group(Cat)`, and `Deepmyometriuminvasion...`. The **Method** is set to `Enter`. The **Options...** button is highlighted with a red box.

2. Cox Regression: Define Categorical Covariates: This dialog shows the configuration for the categorical covariates. The **Categorical Covariates** list includes `Hist_grading(Indicator(first))`, `group(Indicator(first))`, and `Deepmyometriuminvasion(Indicator(first))`. The **Change Contrast** section shows the **Contrast** set to `Indicator` and the **Reference Category** set to `First`. The **Options...** button from the main dialog is highlighted with a red box and an arrow pointing to this dialog.

3. Cox Regression: Options: This dialog shows the configuration for the model options. The **Model Statistics** section shows the **CI for exp(B)** checked and set to `95 %`. The **Probability for Stepwise** section shows the **Entry** probability set to `.05` and the **Removal** probability set to `.10`. The **Maximum Iterations** is set to `20`. The **Options...** button from the main dialog is highlighted with a red box and an arrow pointing to this dialog.

Cox model-Output

Categorical Variable Codings^{a,c,d}

		Frequency	(1)
group ^b	0=CT alone	27	0
	1=Sandwich	39	1
Hist_grading ^b	1=Grade 1 and 2	29	0
	2=Grade 3	37	1
Deepmyometriuminvasio n ^b	0=Absent	27	0
	1=Present	39	1

a. Category variable: group

b. Indicator Parameter Coding

c. Category variable: Hist_grading

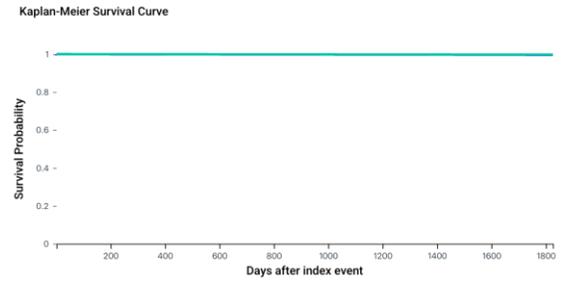
d. Category variable: Deepmyometriuminvasion (Deep myometrium invasion)

經多變項調整後, Sandwich相較於CT alone降低0.23倍的風險死於子宮內膜癌且有統計差異(p= 0.037)

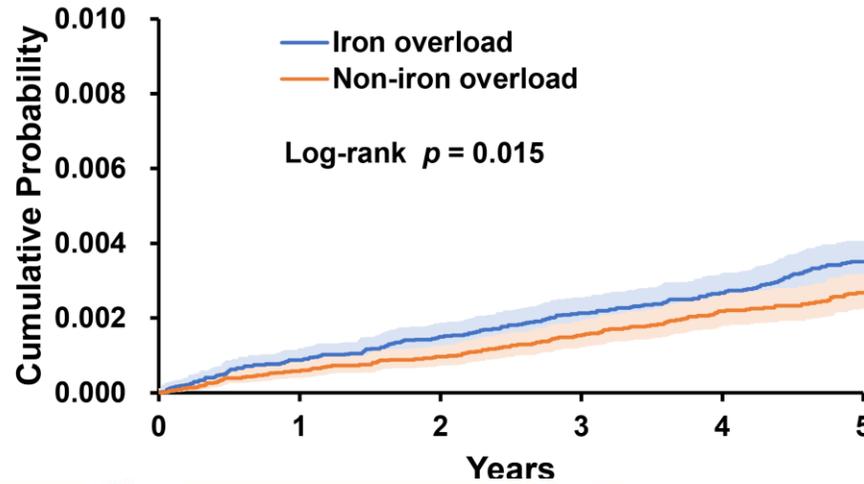
Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Hist_grading	2.215	1.050	4.452	1	.035	9.161	1.170	71.701
group	-1.474	.679	4.711	1	.030	.229	.060	.867
Deepmyometriuminvasio n	2.245	1.051	4.559	1	.033	9.442	1.202	74.150

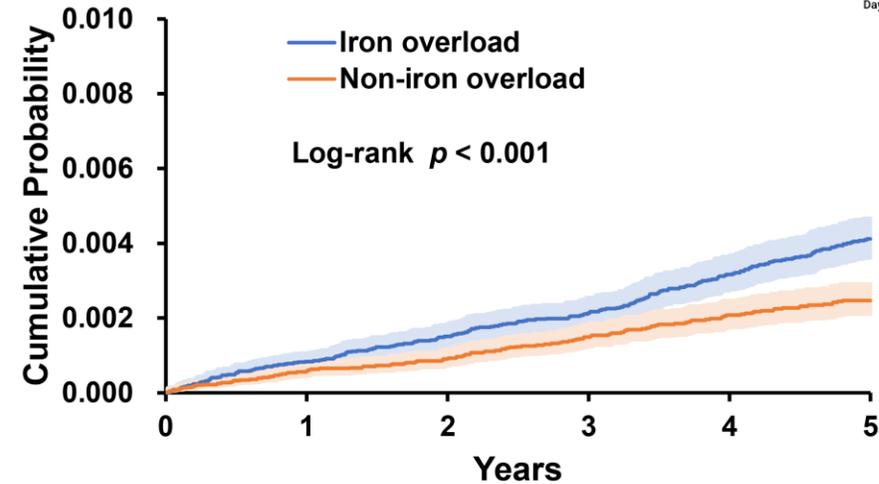
TriNetX Survival curve



(A) OHT



(B) POAG

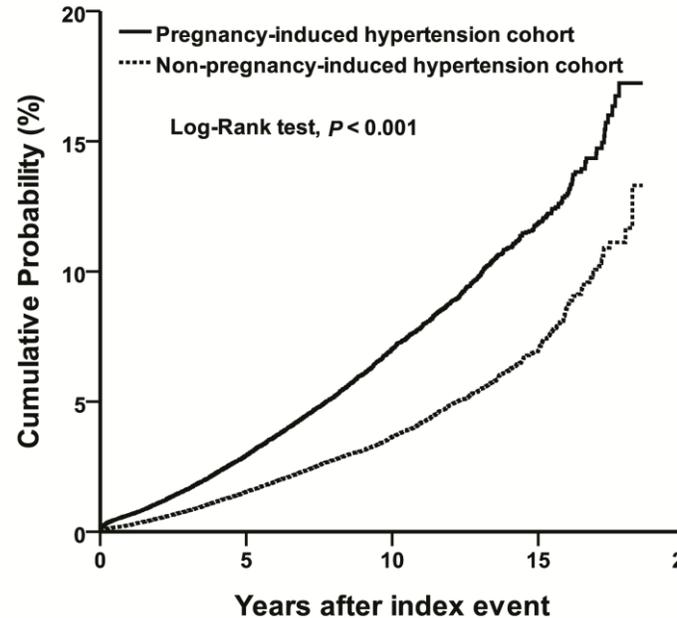


Cohort	Patients in Cohort	Patients with Outcome	Cohort Statistics		Log-Rank Test		
			Median Survival (Days)	Survival Probability at End of Time Window	χ^2	df	p
1 NEW/E83.1-E61.1	63,577	181	-	99.649%	5.95	1	0.0147
2 NEW/ferritin<200	63,577	129	-	99.732%			

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Hazard Ratio		Proportionality		
Hazard Ratio	95% CI	χ^2	df	p
1.323	(1.056, 1.659)	0.378	1	0.5386

Cox PH assumption
 $p > 0.05$



Shih, Y. H., Yang, C. Y., & Lung, C. C. (2025). Pregnancy-Induced Hypertension and Association With Future Autoimmune Diseases. *Obstetrics and gynecology*, 145(4), 426–434.

Cox model with time-dependent covariates

- 稱為隨時間變動的共變數(Time-varying covariate)
- 自變項會隨著追蹤時間所變化(短時間效應)
 - 藥物劑量、血壓、年齡
 - 出血狀態、中風

$$h(t|X(t)) = h_0(t) \exp(\beta_1 X_1(t) + \beta_2 X_2(t) + \dots + \beta_p X_p(t))$$

Cox model with time-dependent covariates

- 在短期內體重不足是洗腎患者死亡率的重要風險因素，但長期反而是體重過重更為明顯

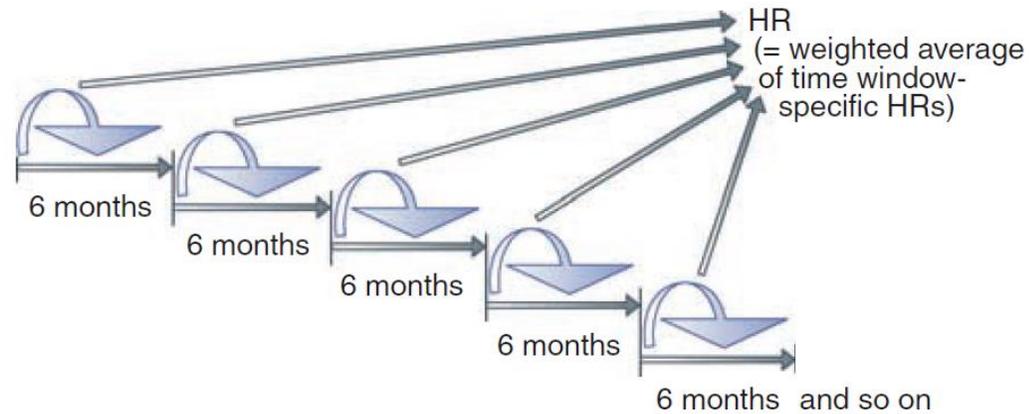


Figure 3 | Effect of time-varying risk on mortality.



Cox model with time-dependent covariates

- External Time-Dependent Covariates (外在時間變數)
 - 這類變數不受個體影響，僅與時間有關
 - 年齡
 - 空氣污染指數
 - 經濟狀況變化
- Internal Time-Dependent Covariates (內在時間變數)
 - 這類變數與個體特徵有關且隨個體狀態變化
 - 體重變化
 - 血壓變化
 - 服藥狀態/藥品劑量

Cox model with time-dependent covariates

- 情境
 - 追蹤期間才可能會發生的變項
 - 不斷改變
- 注意事項
 - 干擾因子不可為中介變數
 - Time-dependent covariates 不可為中介變數

Time-dependent covariates-example

- 寬資料(wide format) 需轉換長資料(long format)

id	entry_time	transplant_time	death_time	status	age
1	0	50	70	1	45
2	0	30	90	1	60
3	0	NA	40	1	50
4	0	20	60	1	55
5	0	30	50	0	35
6	0	15	40	0	45
7	0	35	60	0	50
8	0	NA	40	1	55
9	0	25	50	1	65
10	0	NA	30	0	60

Time-dependent covariates-example

- 長資料(long format)

id	Start	Stop	transplant	status	age
1	0	50	0	0	45
1	50	70	1	1	45
2	0	30	0	0	60
2	30	90	1	1	60
3	0	40	0	1	50
4	0	20	0	0	55
4	20	60	1	1	55
5	0	30	0	0	35
5	30	50	1	0	35
6	0	15	0	0	45
6	15	40	1	0	45
7	0	35	0	0	50
7	35	60	1	0	50

Time-dependent covariates-R操作

安裝套件並載入

匯入原始數據

轉換資料格式

狀態設定

執行分析

id	entry_time	transplant_time	death_time	status	age
1	0	50	70	1	45
2	0	30	90	1	60
3	0	NA	40	1	50
4	0	20	60	1	55
5	0	30	50	0	35
6	0	15	40	0	45
7	0	35	60	0	50
8	0	NA	40	1	55
9	0	25	50	1	65
10	0	NA	30	0	60

```
#安裝套件並載入
```

```
install.packages("dplyr")
```

```
install.packages("tidyr")
```

```
install.packages("survival")
```

```
library(dplyr)
```

```
library(tidyr)
```

```
library(survival)
```

```
#原始數據(wide format)
```

```
data <- data.frame(
```

```
  id = c(1, 2, 3, 4, 5, 6, 7, 8, 9, 10),
```

```
  entry_time = c(0, 0, 0, 0, 0, 0, 0, 0, 0, 0),
```

```
  transplant_time = c(50, 30, NA, 20, 30, 15,
```

```
  35, NA, 25, NA),
```

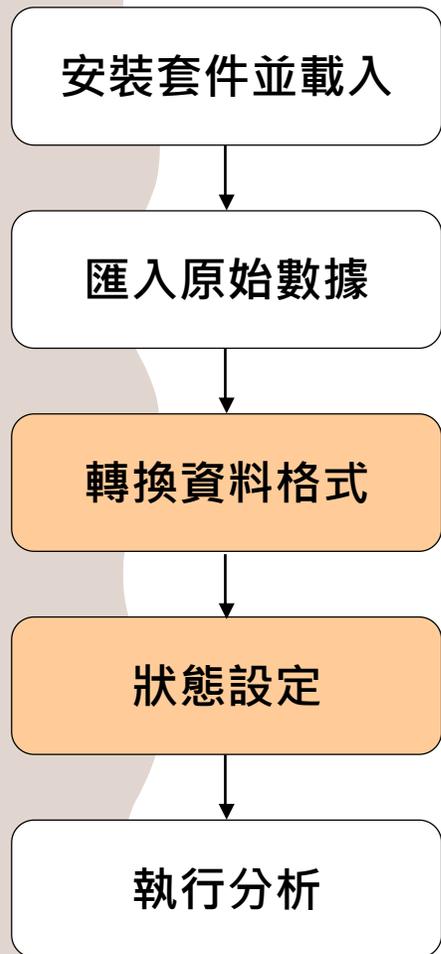
```
  death_time = c(70, 90, 40, 60, 50, 40, 60,
```

```
  40, 50, 30),
```

```
  status = c(1, 1, 1, 1, 0, 0, 0, 1, 1, 0),
```

```
  age = c(45, 60, 50, 55, 35, 45, 50, 55, 65,
```

```
  60)
```



	id	Start	Stop	transplant	age	status
1	1	0	50	0	45	0
2	1	50	70	1	45	1
3	2	0	30	0	60	0
4	2	30	90	1	60	1
5	3	0	40	0	50	1
6	4	0	20	0	55	0
7	4	20	60	1	55	1
8	5	0	30	0	35	0
9	5	30	50	1	35	0
10	6	0	15	0	45	0

轉換為長格式 (long format)

```
long_data <- data %>%  
  mutate(has_transplant = !is.na(transplant_time))  
%>%  
  tidyr::pivot_longer(cols = c(transplant_time,  
  death_time), names_to = "period",  
  values_to = "Time") %>%  
  filter(!is.na(Time)) %>%  
  arrange(id, Time) %>%  
  group_by(id) %>%  
  mutate(Start = dplyr::lag(Time, default =  
  first(entry_time)), Stop = Time) %>%  
  mutate(transplant = ifelse(period ==  
  "transplant_time" & has_transplant == "TRUE" |  
  has_transplant == "FALSE", 0, 1)) %>%  
  select(id, Start, Stop, transplant, age, status)
```

狀態設定只出現在最後一個時間段

```
long_data <- long_data %>%  
  group_by(id) %>%  
  mutate(status = ifelse(Stop == max(Stop), status,  
  0))
```

安裝套件並載入

匯入原始數據

轉換資料格式

狀態設定

執行分析

```
coxph(formula = Surv(Start, Stop, status) ~ transplant + age,  
      data = long_data)
```

```
n= 17, number of events= 6
```

	coef	exp(coef)	se(coef)	z	Pr(> z)
transplant	-2.54704	0.07831	1.54815	-1.645	0.0999 .
age	0.08891	1.09299	0.08323	1.068	0.2854

```
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

	exp(coef)	exp(-coef)	lower .95	upper .95
transplant	0.07831	12.7693	0.003767	1.628
age	1.09299	0.9149	0.928478	1.287

```
Concordance= 0.87 (se = 0.097 )
```

```
Likelihood ratio test= 3.73 on 2 df, p=0.2
```

```
Wald test = 2.74 on 2 df, p=0.3
```

```
Score (logrank) test = 3.62 on 2 df, p=0.2
```

```
cox_model <- coxph(Surv(Start, Stop, status)~transplant + age, data= long_data)  
summary(cox_model)
```

Time-dependent covariates-SPSS操作

分析>存活分析>Cox w/
Time-Dep Cov

The screenshot shows the SPSS Analyze menu with the following items listed:

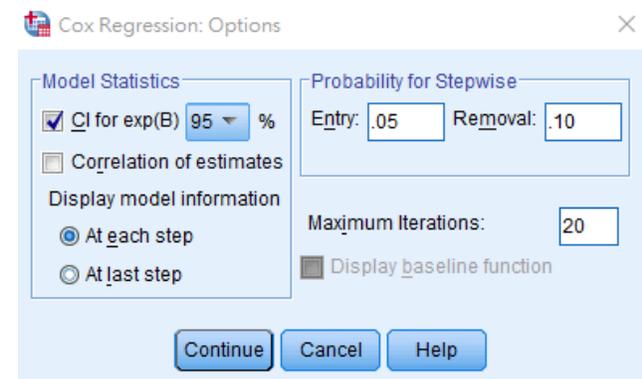
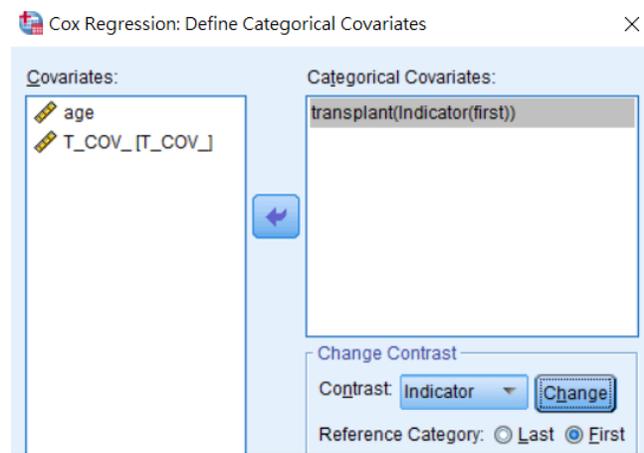
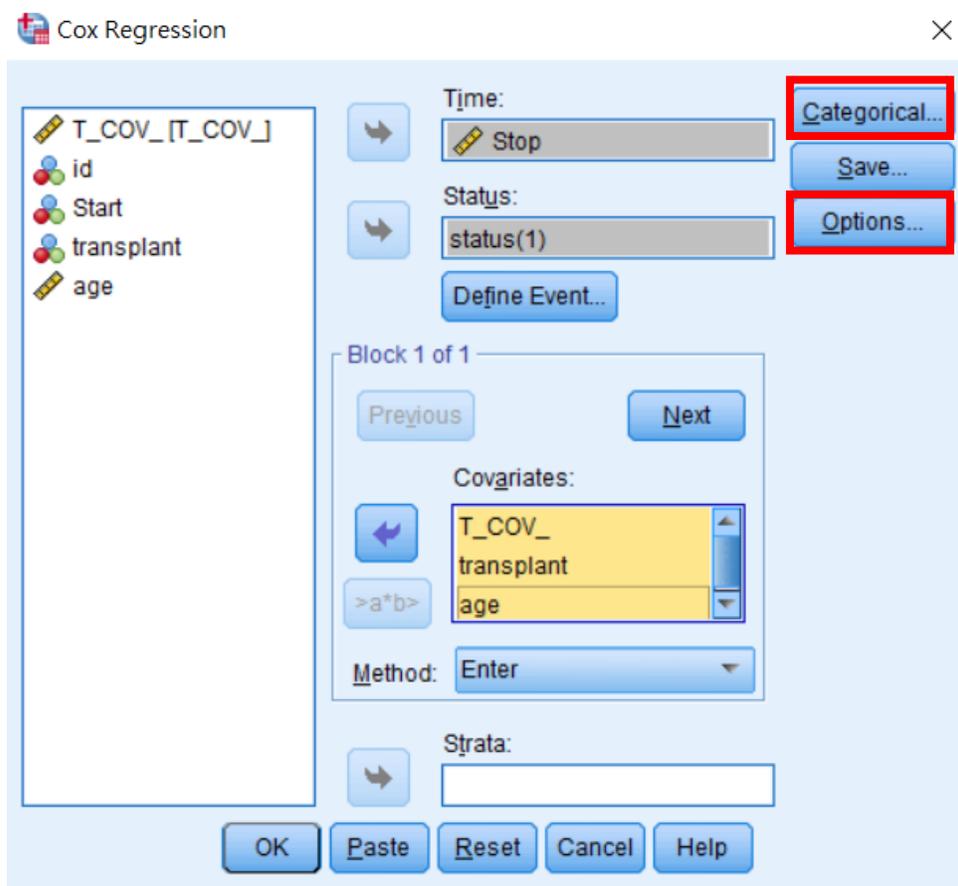
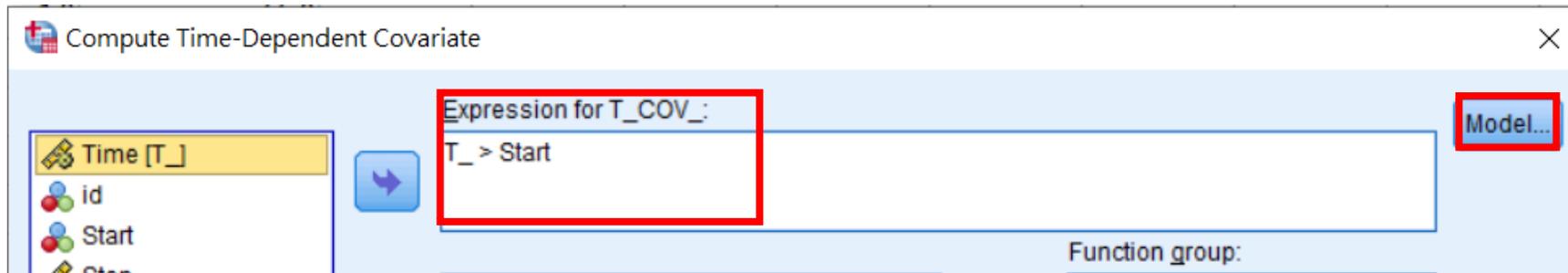
- Reports
- Descriptive Statistics
- Custom Tables
- Compare Means
- General Linear Model
- Generalized Linear Models
- Mixed Models
- Correlate
- Regression
- Loglinear
- Neural Networks
- Classify
- Dimension Reduction
- Scale
- Nonparametric Tests
- Forecasting
- Survival** (highlighted)
- Multiple Response
- PS Matching
- Missing Value Analysis...
- Multiple Imputation
- Complex Samples
- Simulation...
- Quality Control

The Survival submenu is open, showing the following options:

- Life Tables...
- Kaplan-Meier...
- Cox Regression...
- Cox w/ Time-Dep Cov...** (highlighted)
- Parametric Regression
- Cox Regression Extension

In the background, a data table is visible with columns 't' and 'status'.

t	status
.0	.0
1.0	1.0
.0	.0
1.0	1.0
.0	1.0
.0	.0
1.0	1.0
.0	.0
1.0	.0
.0	.0
1.0	.0
.0	.0
1.0	.0



Time-dependent covariates-Output

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
T_COV_	12.099	1537.617	.000	1	.994	179671.761	.000	.
transplant	-2.315	1.526	2.301	1	.129	.099	.005	1.966
age	.082	.082	1.000	1	.317	1.085	.925	1.273

調整年齡後，有腎移植比無腎移植的
死亡風險無統計差異(p= 0.129)

Cox Model vs. Logistic Model

Cox Regression

- 依變項為時間×事件
- 加入追蹤時間及設限資料
- 使用Hazard Ratio (HR)估計

Logistic Regression

- 依變項為類別變數(0 or 1)
- 沒有時間變項
- 使用Odds Ratio (OR)估計

感謝您的聆聽！

Thank you !

