



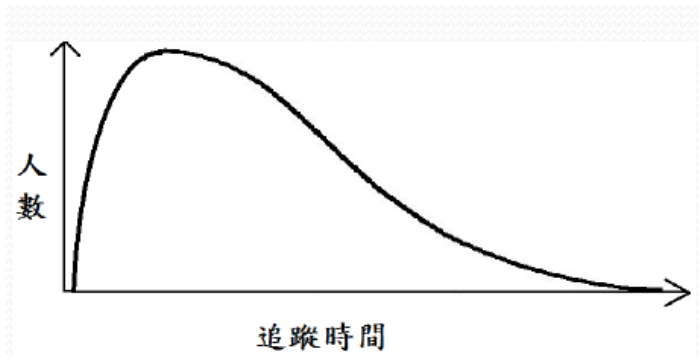
# 存活分析 (1)

醫學研究部生統小組

陳俊朋

# 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- 研究結束時間/疾病發生時間/死亡時間
- 資料特性：資料通常不是常態分配



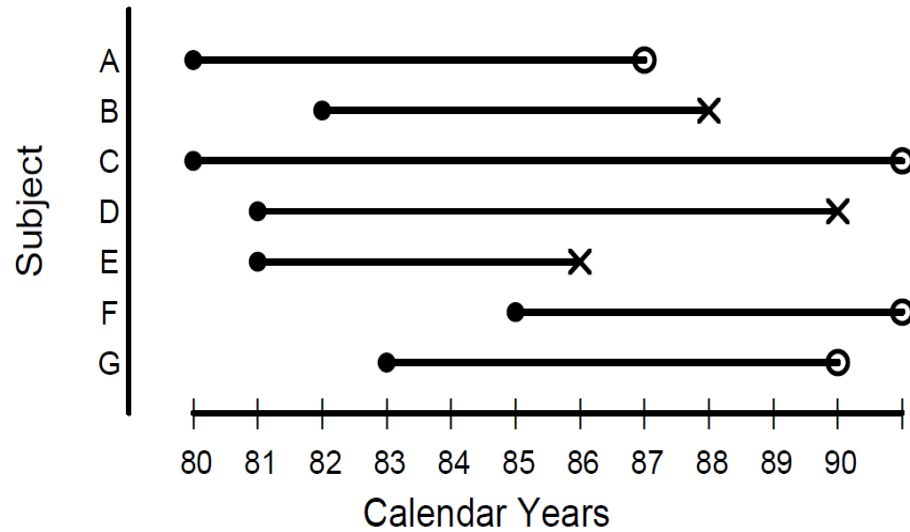
# 資料分類

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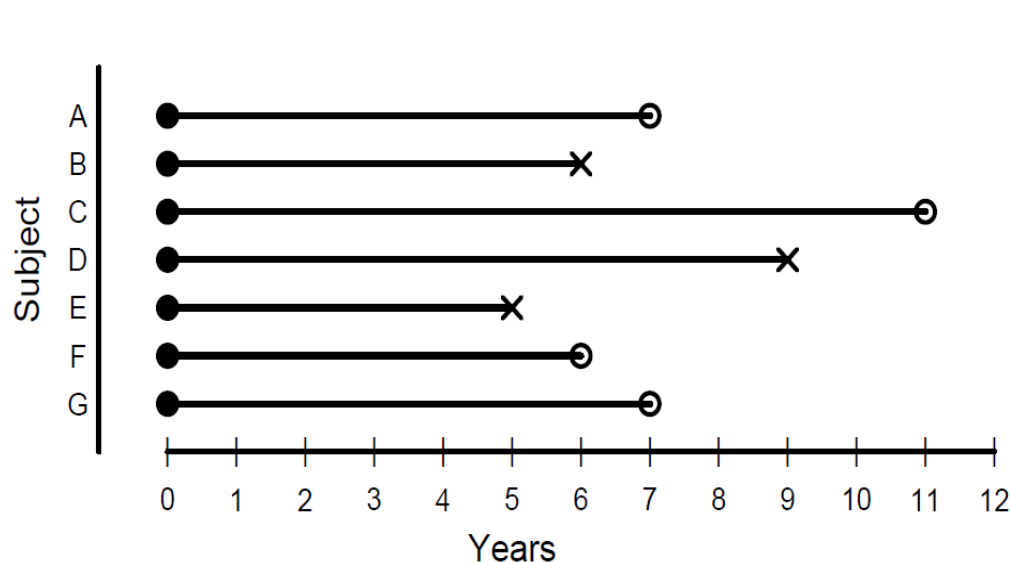
- 完整資料(complete data)
  - 觀察期間提供事件發生的時間點
- 設限資料(censored data)
  - 觀察期間失去聯絡或觀察結束時仍未發生事件
- 競爭死因資料(Competing cause of deaths)
  - 觀察期間死於其他死因之時間

# Survival time

(● initial follow-up, × death, ○ alive.)



- 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

# 存活分析－統計方法

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

## 2.2. Statistical Analysis

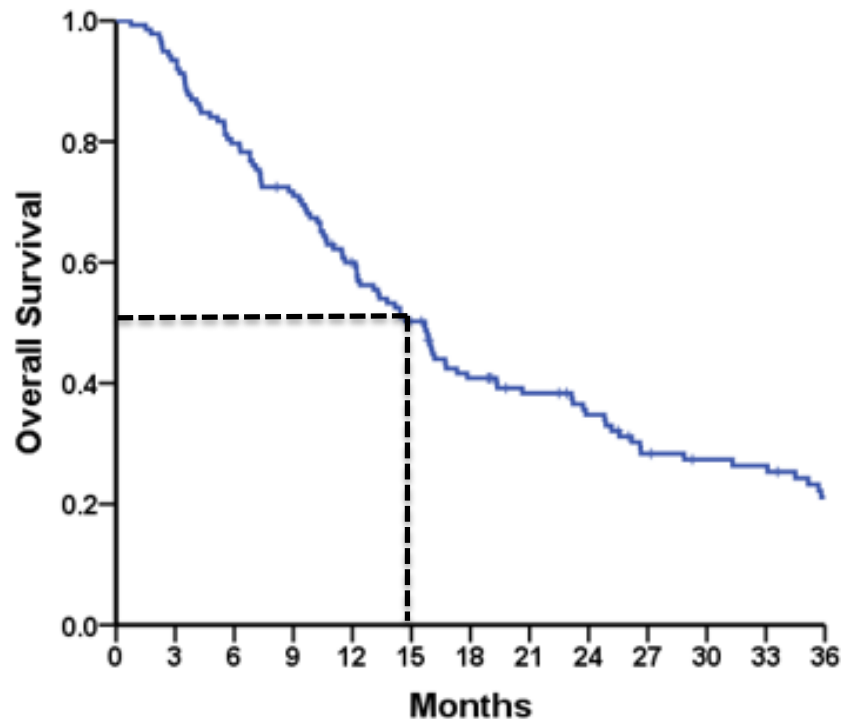
The most important censored point of this study was the first episode of UBR. UBR-free survival was defined as the interval between the date of NUx and the date of the first episode of UBR. Survival data was analyzed using both the Kaplan–Meier method and the logrank test. Univariate and multivariate analyses by Cox’s proportional hazards model were used to determine the relevance between each of the clinicopathological factors and UBR. P-values less than 0.05 were defined as statistically significant. All statistical analyses were performed with SPSS (Statistical Package for the Social Sciences, version 22.0, IBM, NY, USA).

Chen, Chuan-Shu, et al. *Diagnostics* 10.4 (2020): 201.

# 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



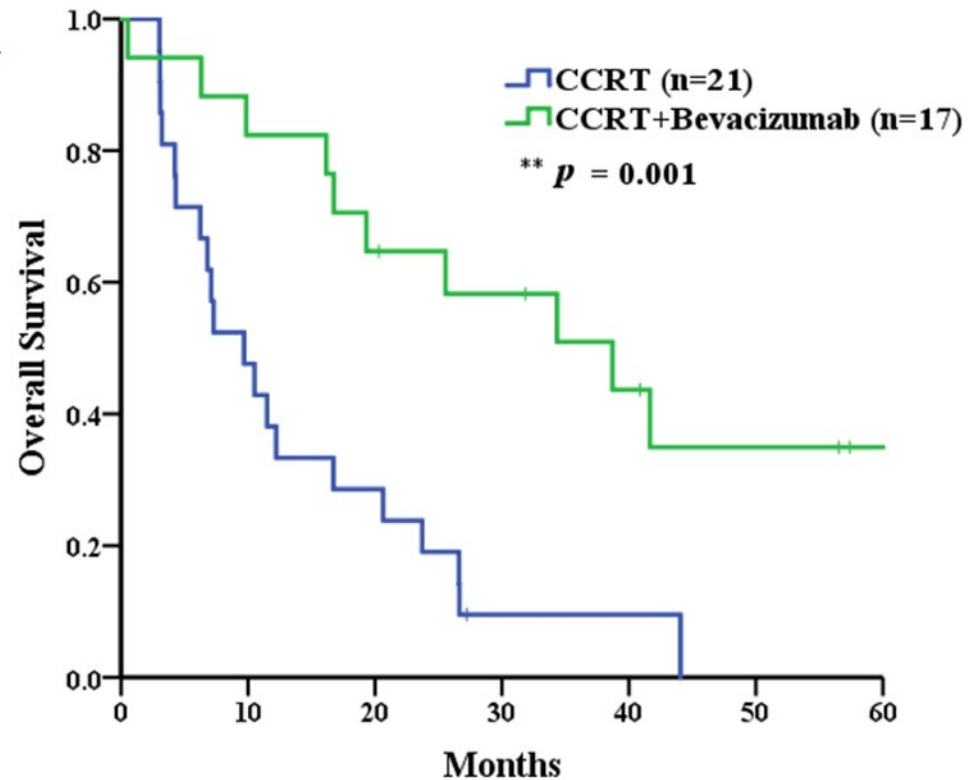
ID	fu_time (month)	status
1	2	0
2	2	0
3	2	1
4	3	0
5	3	0
6	4	1
7	4	0
8	5	0
9	6	1
10	6	0

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	$1/2 = 0.50$	$0.50 * 0.72 = 0.36$

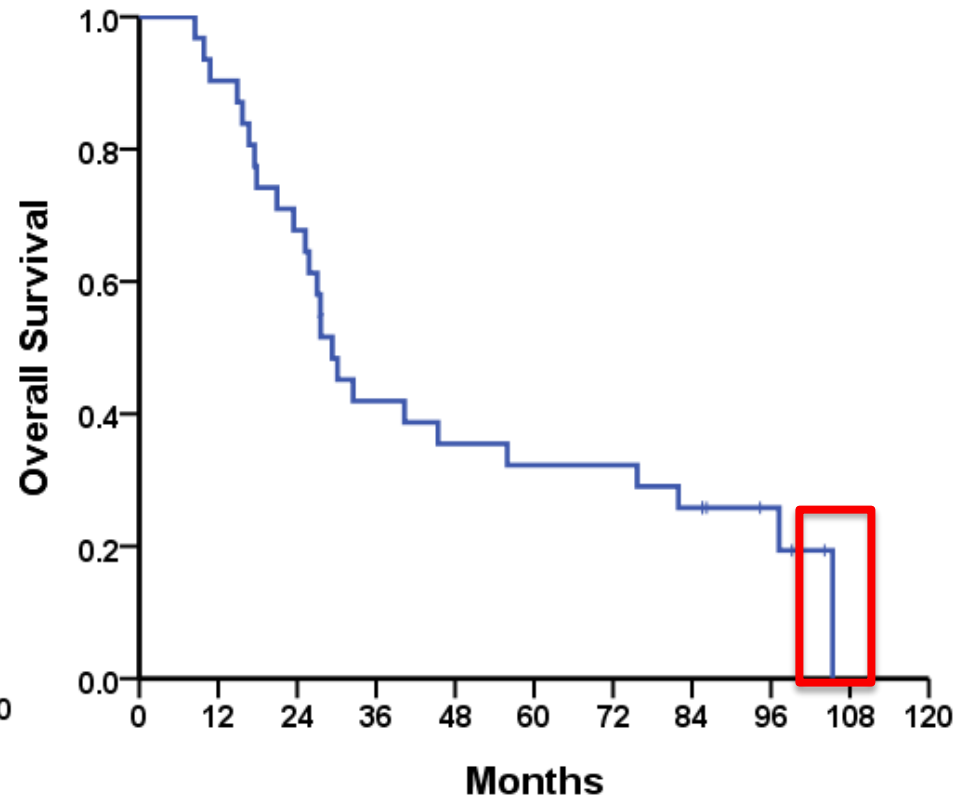
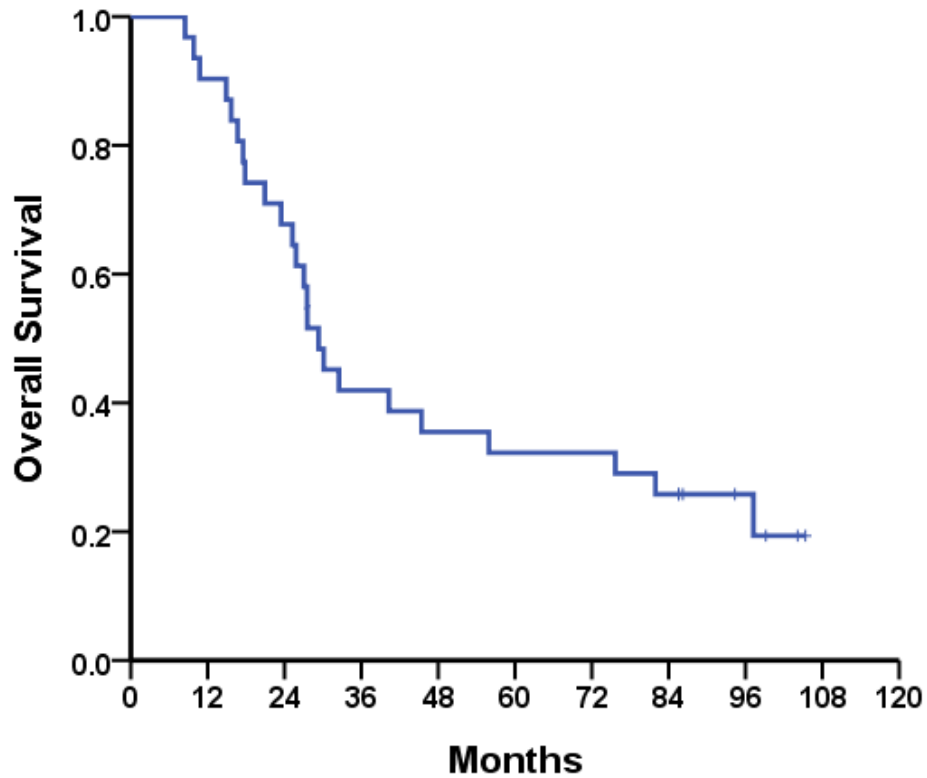
# Log-rank test



- 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



# Survival curve



# Survival curve



Survival Table

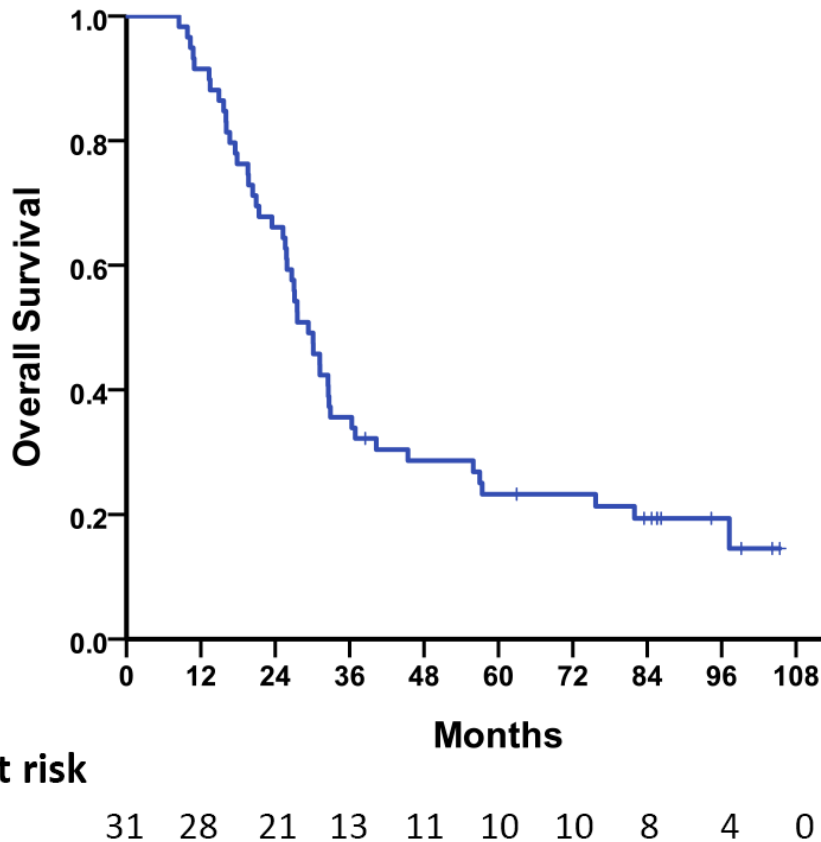
	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
1	8.467	Death	.968	.032	1	30
2	9.833	Death	.935	.044	2	29
3	10.767	Death	.903	.053	3	28
4	14.900	Death	.871	.060	4	27
5	15.667	Death	.839	.066	5	26
6	16.667	Death	.806	.071	6	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

Survival Table

	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
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1	8.467	Death	.968	.032	1	30
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7	17.533	Death	.774	.075	7	24
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29	99.167	Survival	.	.	24	2
30	104.167	Survival	.	.	24	1
31	105.367	Death	.000	.000	25	0

# Survival curve

Survival Table



	Time	Status	Cumulative Proportion Surviving at the Time		N of Cumulative Events	N of Remaining Cases
			Estimate	Std. Error		
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28	97.233	Death	.194	.081	24	3
29	99.167	Survival	.	.	24	2
30	104.167	Survival	.	.	24	1
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# 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

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

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

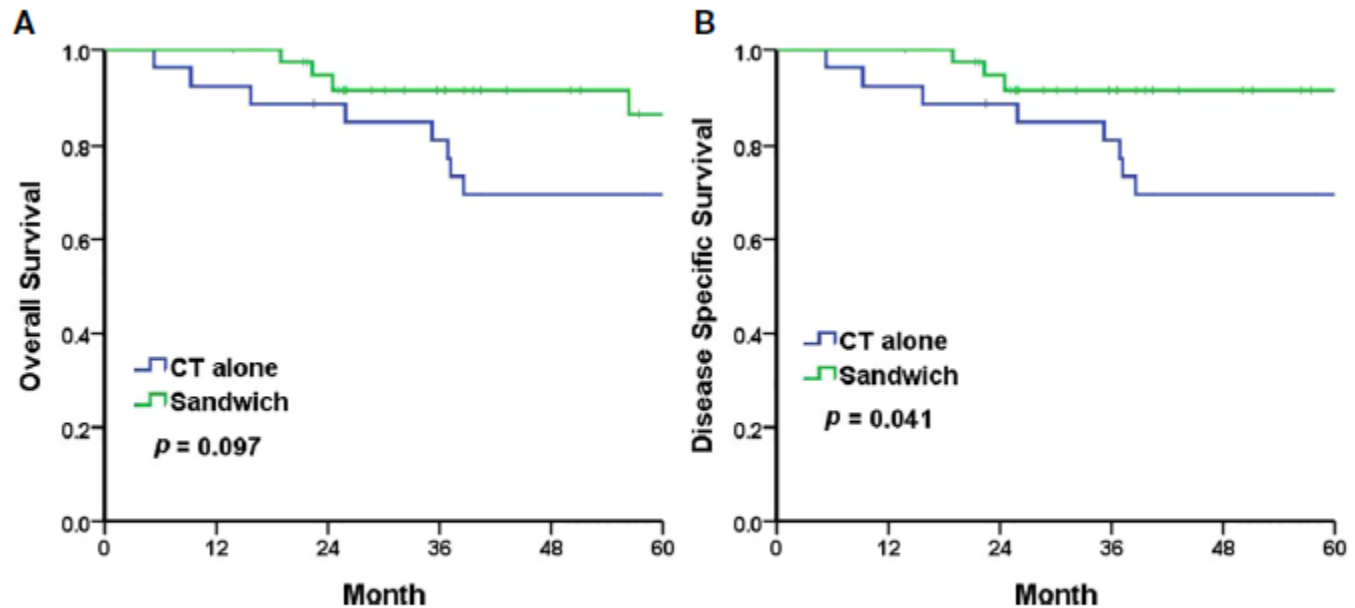


FIGURE 2  
The Kaplan–Meier survival curves for 5-year overall survival (A) and 5-year disease-specific survival (B). CT chemotherapy.

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*
LVI						
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*

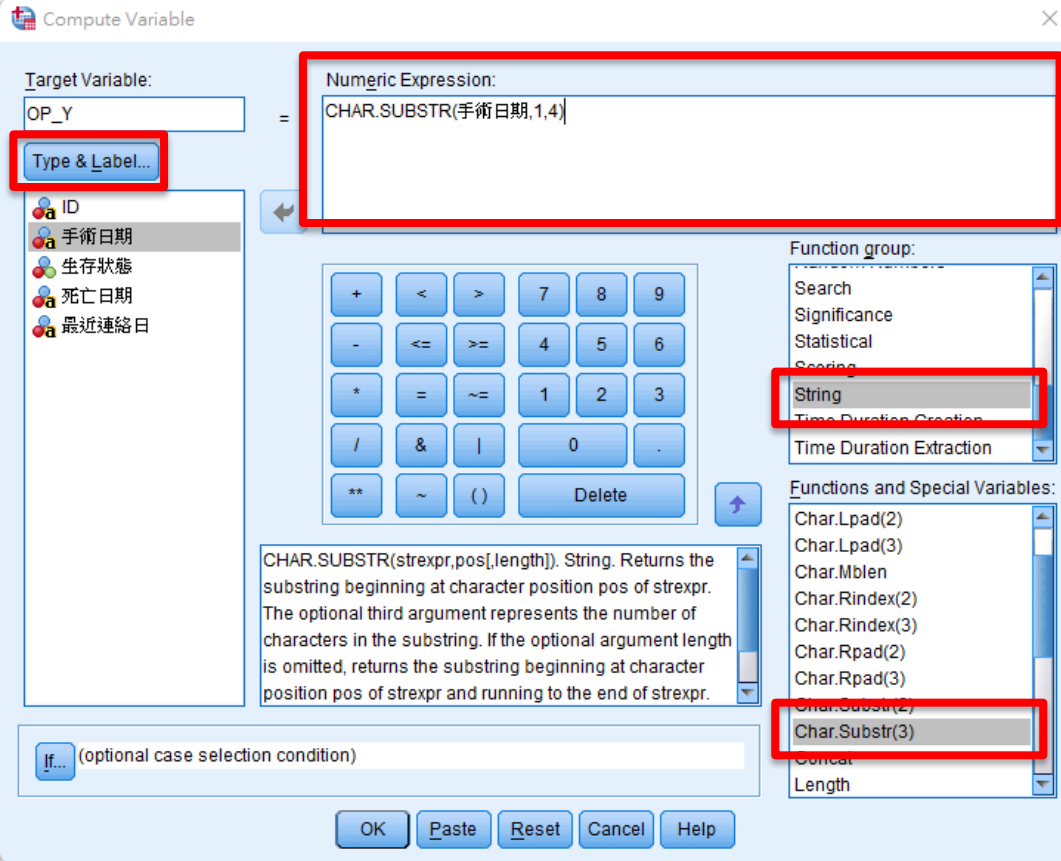
Outcomes of "sandwich" chemoradiotherapy compared with chemotherapy alone for the adjuvant treatment of FIGO stage III endometrial cancer. *Frontiers in oncology*, 12 (2022) , 946113-946113.



# 日期變數處理-SPSS

- 日期/時間計算 (函數說明)
  - 月或日為99時，利用計算變數轉換數值。月=99轉為7、日=99轉為15。
  - 保留特定區段的字串(CHAR.SUBSTR)
    - CHAR.SUBSTR(變數,起始位置,保留長度)。
    - EX: CHAR.SUBSTR(20090731,1,4) = 2009
  - 合併各字串變數
    - CONCAT(變數1,變數2,變數3,...)。
    - EX: CONCAT('2003', '/', '09', '/', '21')='2003/09/21'

# 日期變數處理



Target Variable: OP\_Y =

Numeric Expression: CHAR.SUBSTR(手術日期,1,4)

Type & Label...

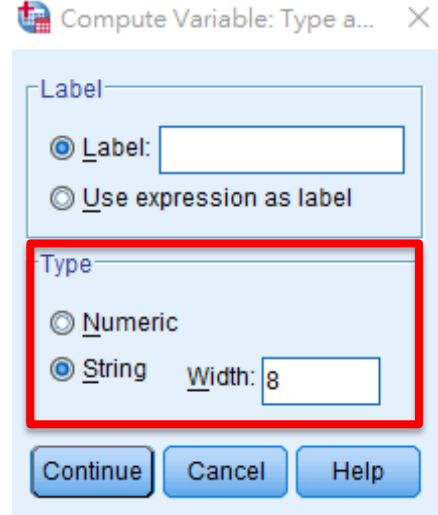
Function group: String

Functions and Special Variables: Char.Substr(3)

CHAR.SUBSTR(strexp, pos[, length]). String. Returns the substring beginning at character position pos of strexp. The optional third argument represents the number of characters in the substring. If the optional argument length is omitted, returns the substring beginning at character position pos of strexp and running to the end of strexp.

If... (optional case selection condition)

OK Paste Reset Cancel Help



Label

Label:

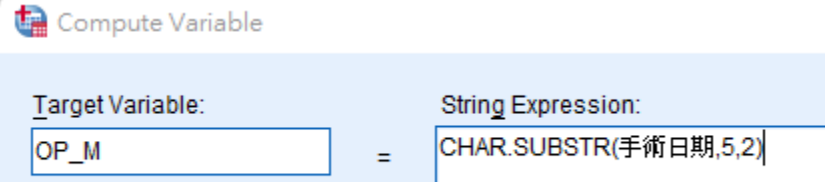
Use expression as label

Type

Numeric

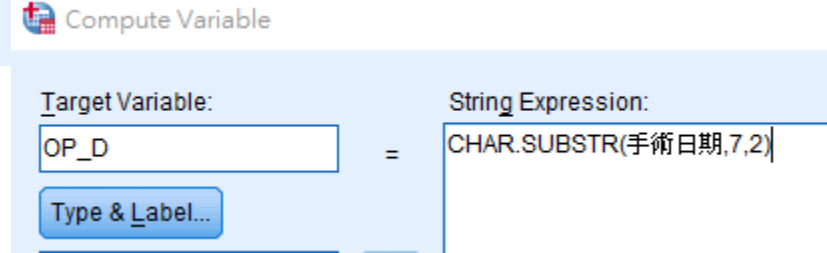
String Width: 8

Continue Cancel Help



Target Variable: OP\_M =

String Expression: CHAR.SUBSTR(手術日期,5,2)



Target Variable: OP\_D =

String Expression: CHAR.SUBSTR(手術日期,7,2)

Type & Label...

# 日期變數處理

ID	手術日期	生存狀態	死亡日期	最近連絡日	OP_Y	OP_M	OP_D
case1	20060303	.0	20080525		2006	03	03
case2	20120517	.0	20121026		2012	05	17
case3	20060503	.0	20090617		2006	05	03
case4	20101112	.0	20160402		2010	11	12
case5	20120803	.0	20130512		2012	08	03
case6	20110224	.0	20140514		2011	02	24
case7	20121199	.0	20141016		2012	11	99
case8	20130821	.0	20141212		2013	08	21
case9	20140523	.0	20160608		2014	05	23
case10	20160113	.0	20170811		2016	01	13
case11	20150303	.0	20180329		2015	03	03
case12	20160905	.0	20190812		2016	09	05
case13	20141219	.0	20200125		2014	12	19
case14	20120420	1.0		20150710	2012	04	20
case15	20151229	1.0		20211004	2015	12	29
case16	20160420	1.0		20210909	2016	04	20
case17	20190827	1.0		20211018	2019	08	27
case18	20050820	1.0		20170831	2005	08	20
case19	20051016	1.0		20180816	2005	10	16
case20	20111224	1.0		20151018	2011	12	24

# 日期變數處理

OP_Y	OP_M	OP_D	OP_D2
2006	03	03	03
2012	05	17	17
2006	05	03	03
2010	11	12	12
2012	08	03	03
2011	02	24	24
2012	11	99	15
2013	08	21	21
2014	05	23	23
2016	01	13	13
2015	03	03	03
2016	09	05	05
2014	12	19	19
2012	04	20	20
2015	12	29	29
2016	04	20	20
2019	08	27	27
2005	08	20	20
2005	10	16	16
2011	12	24	24

Compute Variable

Target Variable: OP\_D2 = String Expression: OP\_D

Type & Label...

---

Compute Variable

Target Variable: OP\_D2 = String Expression: "15"

Type & Label...

ID  
 手術日期  
 生存狀態  
 死亡日期  
 最近連絡日  
 OP\_Y  
 OP\_M  
 OP\_D  
 OP\_D2

If... OP\_D = "99"

OK Paste Reset Cancel Help

# 日期變數處理

OP_Y	OP_M	OP_D	OP_D2	OP_date
2006	03	03	03	2006/03/03
2012	05	17	17	2012/05/17
2006	05	03	03	2006/05/03
2010	11	12	12	2010/11/12
2012	08	03	03	2012/08/03
2011	02	24	24	2011/02/24
2012	11	99	15	2012/11/15
2013	08	21	21	2013/08/21
2014	05	23	23	2014/05/23
2016	01	13	13	2016/01/13
2015	03	03	03	2015/03/03
2016	09	05	05	2016/09/05
2014	12	19	19	2014/12/19
2012	04	20	20	2012/04/20
2015	12	29	29	2015/12/29
2016	04	20	20	2016/04/20
2019	08	27	27	2019/08/27
2005	08	20	20	2005/08/20
2005	10	16	16	2005/10/16
2011	12	24	24	2011/12/24

Compute Variable

Target Variable: OP\_date =

String Expression: CONCAT(OP\_Y,"/",OP\_M,"/",OP\_D2)

Type & Label...

Compute Variable: Type a... X

Label

Label:

Use expression as label

Type

Numeric

String Width: 12

Continue Cancel Help

# 日期變數處理

生存狀態	死亡日期	最近連絡日	FU
.0	20080525		20080525
.0	20121026		20121026
.0	20090617		20090617
.0	20160402		20160402
.0	20130512		20130512
.0	20140514		20140514
.0	20141016		20141016
.0	20141212		20141212
.0	20160608		20160608
.0	20170811		20170811
.0	20180329		20180329
.0	20190812		20190812
.0	20200125		20200125
1.0		20150710	20150710
1.0		20211004	20211004
1.0		20210909	20210909
1.0		20211018	20211018
1.0		20170831	20170831
1.0		20180816	20180816
1.0		20151018	20151018

**Compute Variable**

Target Variable: FU = Numeric Expression: 死亡日期

Type & Label...

---

**Compute Variable**

Target Variable: FU = Numeric Expression: 最近連絡日

Type & Label...

- ID
- 手術日期
- 生存狀態
- 死亡日期
- 最近連絡日
- FU
- OP\_Y
- OP\_M
- OP\_D
- OP\_D2
- OP\_date

Calculator interface with buttons: +, <, >, 7, 8, 9, -, <=, >=, 4, 5, 6, \*, =, ~=, 1, 2, 3, /, &, |, 0, ., \*\*, ~, (), Delete

If... 生存狀態 = 1

OK Paste Reset Cancel Help

# 日期變數處理

OP_date	FU_date
2006/03/03	2008/05/25
2012/05/17	2012/10/26
2006/05/03	2009/06/17
2010/11/12	2016/04/02
2012/08/03	2013/05/12
2011/02/24	2014/05/14
2012/11/15	2014/10/16
2013/08/21	2014/12/12
2014/05/23	2016/06/08

Variable Type

- Numeric
- Comma
- Dot
- Scientific notation
- Date
- Dollar
- Custom currency
- String
- Restricted Numeric (integer with leading zeros)

dd-mmm-yyyy  
 dd-mmm-yy  
 mm/dd/yyyy  
 mm/dd/yy  
 dd.mm.yyyy  
 dd.mm.yy  
 yyyy/mm/dd  
 yy/mm/dd  
 yyddd  
 yyyyddd  
 q Q yyyy

Compute Variable

Target Variable: FU\_Y = String Expression: CHAR.SUBSTR(FU,1,4)

Typ Compute Variable

Target Variable: FU\_M = String Expression: CHAR.SUBSTR(FU,5,2)

Typ Compute Variable

Target Variable: FU\_D = String Expression: CHAR.SUBSTR(FU,7,2)

Type & Label...

↓

Compute Variable

Target Variable: FU\_date = String Expression: CONCAT(FU\_Y,"/",FU\_M,"/",FU\_D)

Type & Label...

※合併後的日期需於變數檢視中，更改為日期型式，才能進行日期/時間計算

# 計算追蹤時間

轉換>日期和時間精靈>以日期和時間計算>計算介於兩個日期之間的時間單位數

Transform Analyze Direct Marketing Graphs

- Compute Variable...
  - Programmability Transformation...
- Count Values within Cases...
  - Shift Values...
- Recode into Same Variables...
- Recode into Different Variables...
- Automatic Recode...
  - Create Dummy Variables
- Visual Binning...
  - Optimal Binning...
    - Prepare Data for Modeling
- Rank Cases...
- Date and Time Wizard...**
- Create Time Series...
- Replace Missing Values...
- Random Number Generators...

Date and Time Wizard - Step 2 of 3

Calculate the number of time units between two date or date/time variables.

The result will be an integer variable. Any fractional part of a unit will be discarded. The result will be a duration variable. Only duration variables are shown in the variables list below.

Variables:

- Current date and ti...

Date1:

- FU\_date

minus Date2:

- OP\_date

Unit:

- Years

Result Treatment:

- Truncate to integer
- Round to integer
- Retain fractional part

For month and year units, the result is based on average unit length unless truncation is used.

STIME is the current date and time.

Date and Time Wizard - Step 3 of 3

Calculation: FU\_date - OP\_date

Result Variable: OS\_year Units: Years

Variable Label:

Execution:

- Create the variable now
- Paste the syntax into the syntax window



# 計算追蹤時間

- 日期格式靠右
- $OS\_year = FU\_date - OP\_date$

OP_date	FU_date	OS_year
2006/03/03	2008/05/25	2.23
2012/05/17	2012/10/26	.44
2006/05/03	2009/06/17	3.12
2010/11/12	2016/04/02	5.39
2012/08/03	2013/05/12	.77
2011/02/24	2014/05/14	3.22
2012/11/15	2014/10/16	1.92
2013/08/21	2014/12/12	1.31
2014/05/23	2016/06/08	2.05
2016/01/13	2017/08/11	1.58
2015/03/03	2018/03/29	3.07
2016/09/05	2019/08/12	2.93
2014/12/19	2020/01/25	5.10
2012/04/20	2015/07/10	3.22
2015/12/29	2021/10/04	5.77
2016/04/20	2021/09/09	5.39
2019/08/27	2021/10/18	2.14
2005/08/20	2017/08/31	12.03
2005/10/16	2018/08/16	12.83
2011/12/24	2015/10/18	3.82

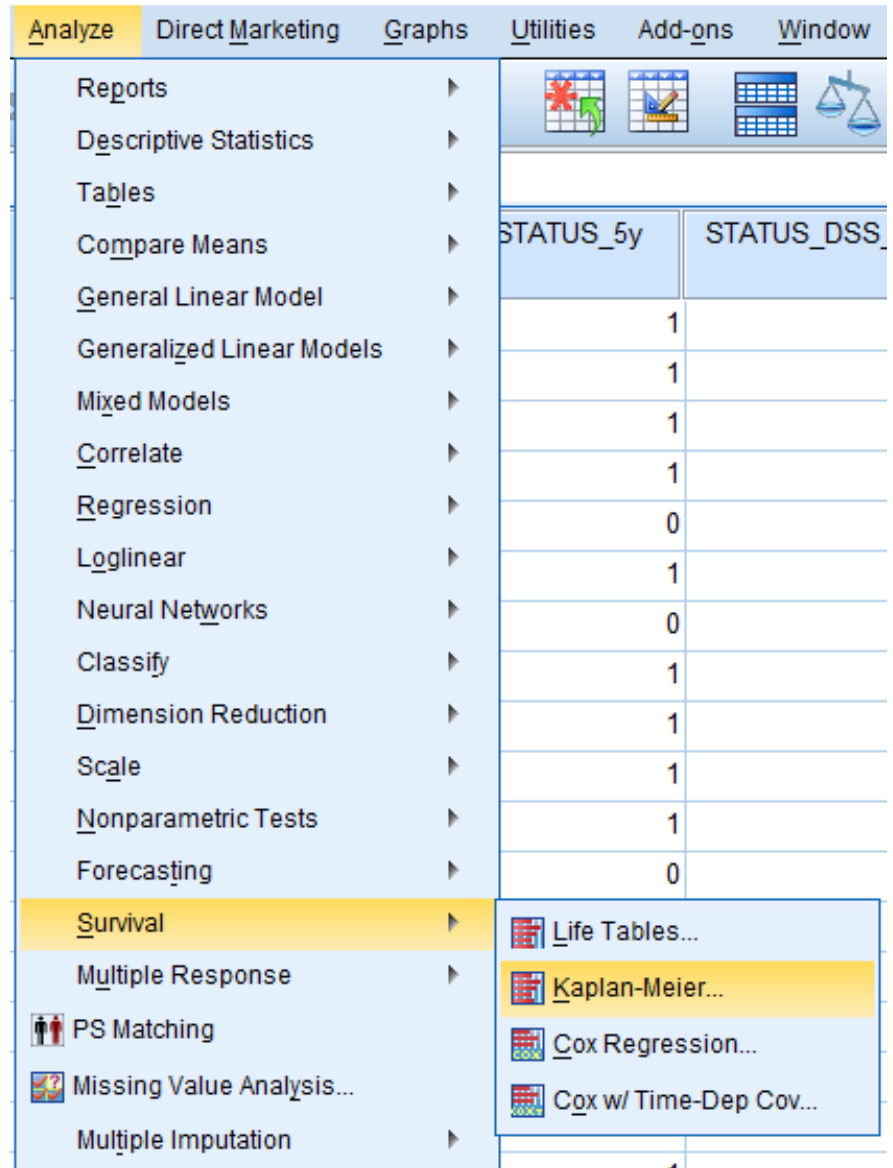
# KM and Cox regression SPSS dataset



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

分析 > 存活分析  
> Kaplan-Meier 統計



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

# Kaplan-Meier 分析操作



Kaplan-Meier

- ID
- OP\_date
- End\_Date
- STATUS\_5y
- Age\_gp
- Hist\_grading
- FIGO\_stage
- LVSI
- Deep myometrium invasion [...]
- BMI25\_gp
- Cx involvement [Cxinvolvement...]
- 病歷號碼

Time:

Status:

**Define Event...**

**Compare Factor...**

Save...

**Options...**

Kaplan-Meier: Compare Factor Levels

Test Statistics

Log rank  Breslow  Tarone-Ware

Linear trend for factor levels

Pooled over strata  Pairwise over strata

For each stratum  Pairwise for each stratum

Continue Cancel Help

Kaplan-Meier: Define Event For Status ...

Value(s) indicating event has occurred

Single value:

Range of values:  through

List of values:

Add Change Remove

Continue Cancel Help

Kaplan-Meier: Options

Statistics

Survival table(s)

Mean and median survival

Quartiles

Plots

Survival

One minus survival

Hazard

Log Survival

Continue Cancel Help

OK Paste Reset Cancel

# Kaplan-Meier Output



Case Processing Summary

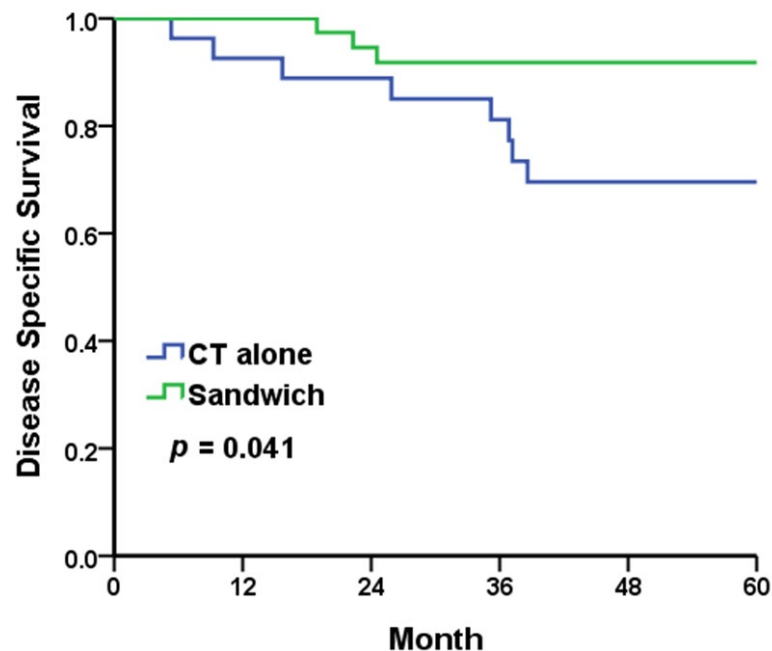
group	Total N	N of Events	Censored	
			N	Percent
CT alone	27	8	19	70.4%
Sandwich	39	3	36	92.3%
Overall	66	11	55	83.3%

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



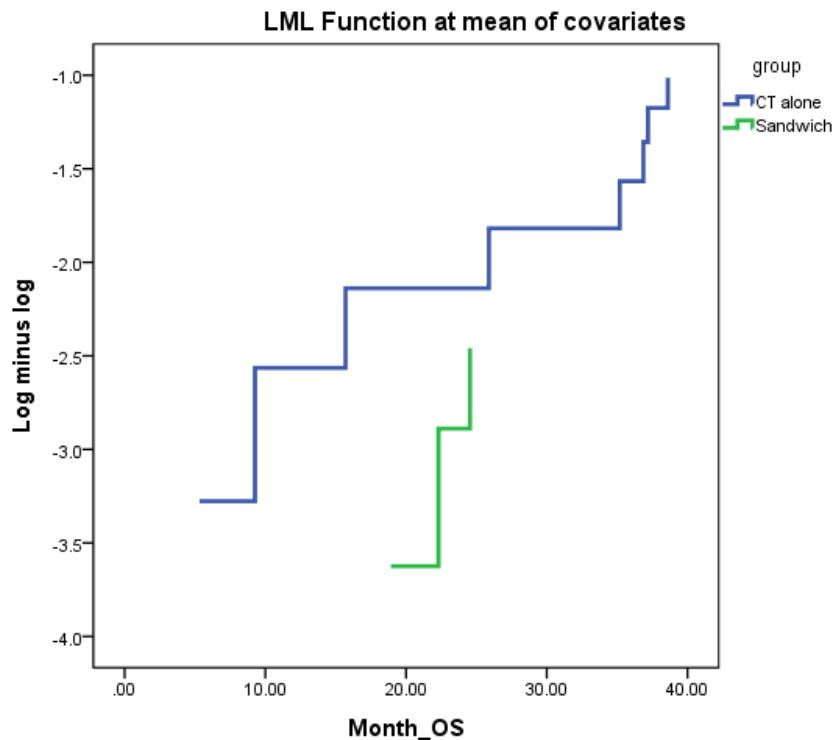
Overall Comparisons

	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



- LML圖形

The image shows two overlapping dialog boxes from the SPSS software interface. The left dialog is titled "Cox Regression" and contains the following fields and options:

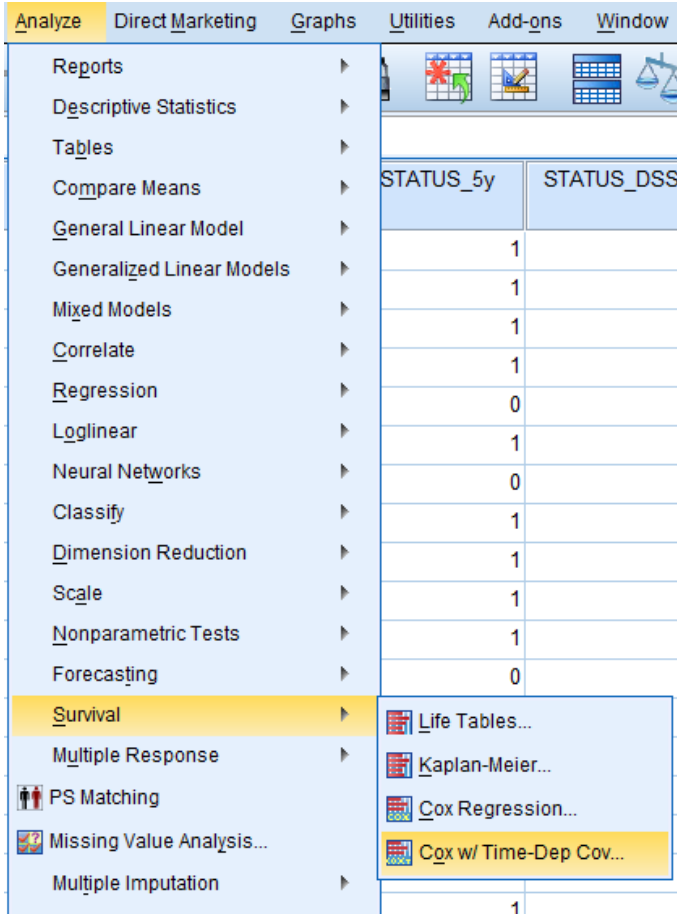
- Time:** Month\_OS
- Status:** STATUS\_DSS\_5y(1)
- Block 1 of 1:** Includes "Previous" and "Next" buttons.
- Covariates:** An empty text box.
- Method:** Enter
- Strata:** group
- Buttons:** OK, Paste, Reset, Cancel, Help

The right dialog is titled "Cox Regression: Plots" and contains the following options:

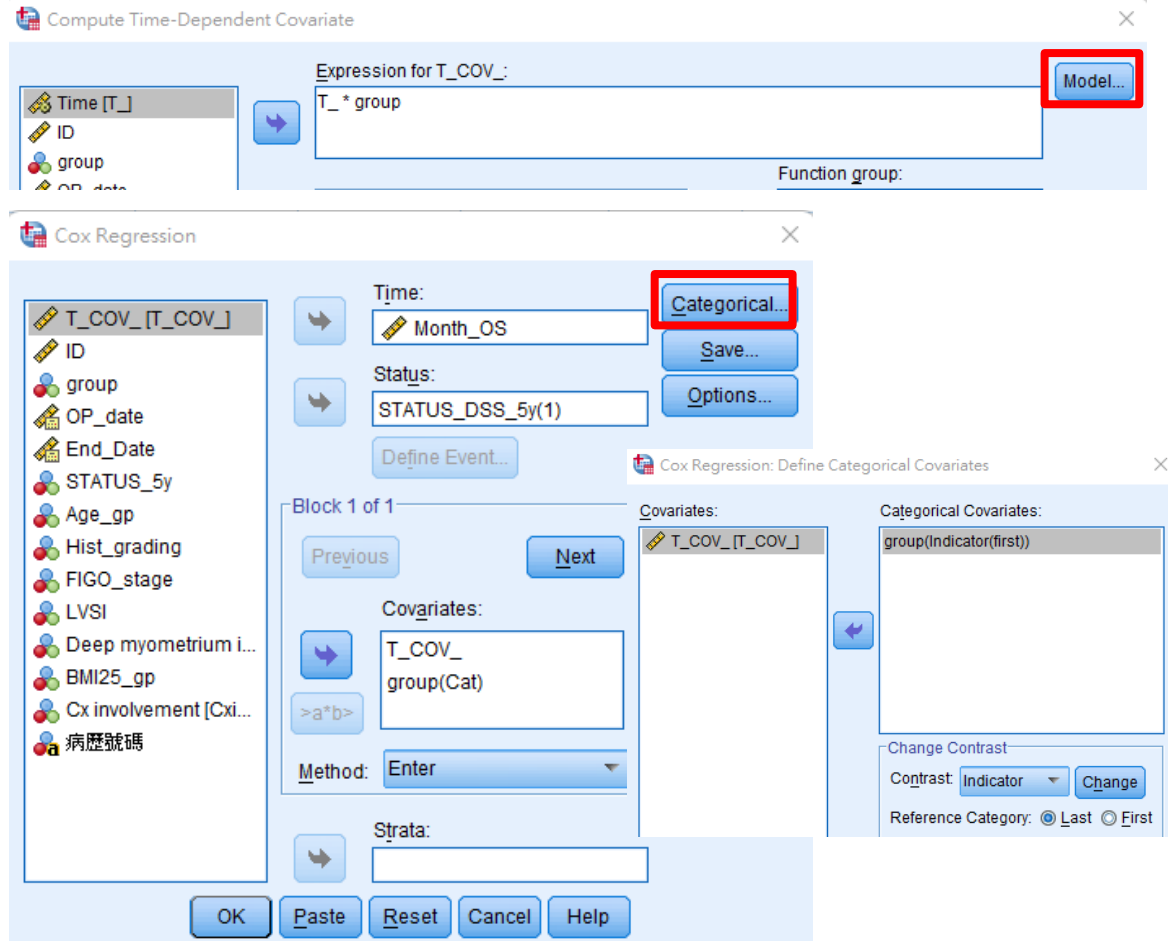
- Plot Type:**  Survival,  Hazard,  Log minus log,  One minus survival
- Covariate Values Plotted at:** An empty text box.
- Separate Lines for:** A button with a right-pointing arrow and an empty text box.
- Change Value:**  Mean,  Value: [empty text box],
- Buttons:** Continue, Cancel, Help

# Cox PH assumption

- Cox time-dependent變數的交互作用項



	STATUS_5y	STATUS_DSS
Reports		
Descriptive Statistics		
Tables		
Compare Means		
General Linear Model		
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	
<b>Survival</b>		
Life Tables...		
Kaplan-Meier...		
Cox Regression...		
<b>Cox w/ Time-Dep Cov...</b>		
Multiple Response		
PS Matching		
Missing Value Analysis...		
Multiple Imputation		



**Compute Time-Dependent Covariate**

Expression for T\_COV\_: T\_\* group

Function group:

**Cox Regression**

Time: Month\_OS

Status: STATUS\_DSS\_5y(1)

Covariates: T\_COV\_ [T\_COV\_] group(Cat)

Method: Enter

**Cox Regression: Define Categorical Covariates**

Covariates: T\_COV\_ [T\_COV\_] group(Cat)

Categorical Covariates: group(Indicator(first))

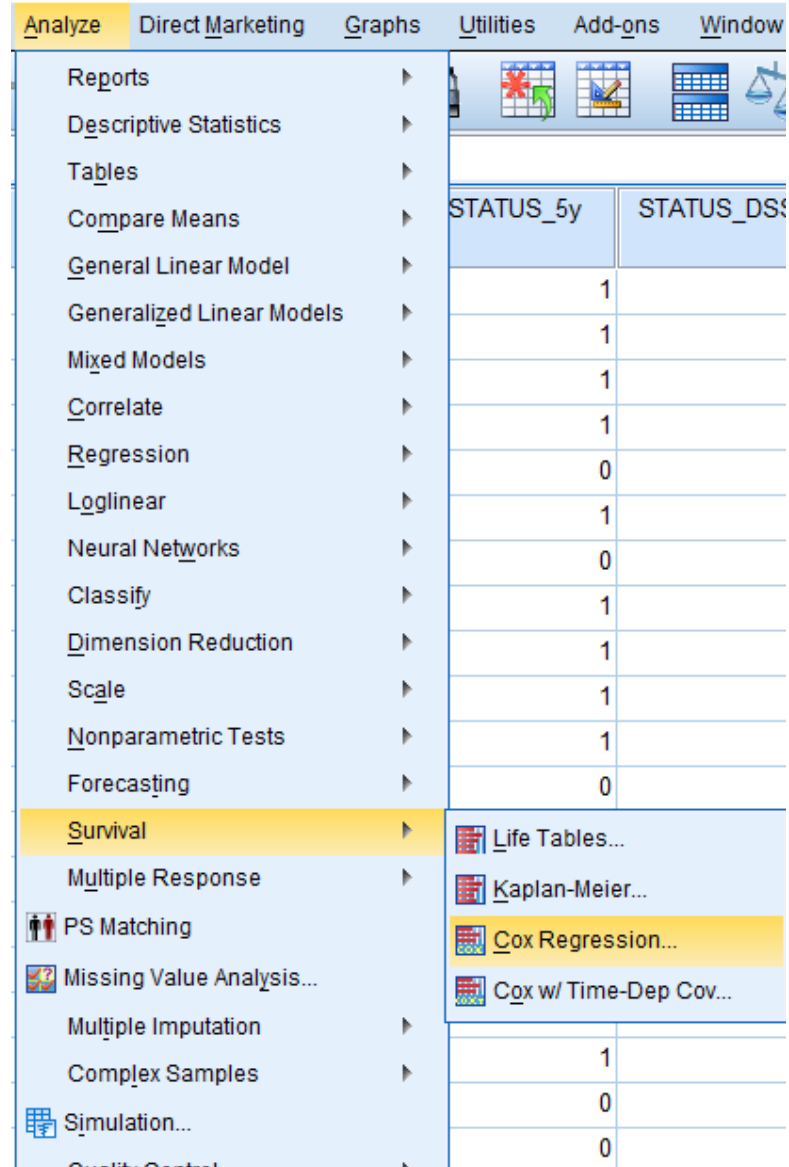
Change Contrast: Contrast: Indicator Change

Reference Category: Last First



# Cox model-分析操作

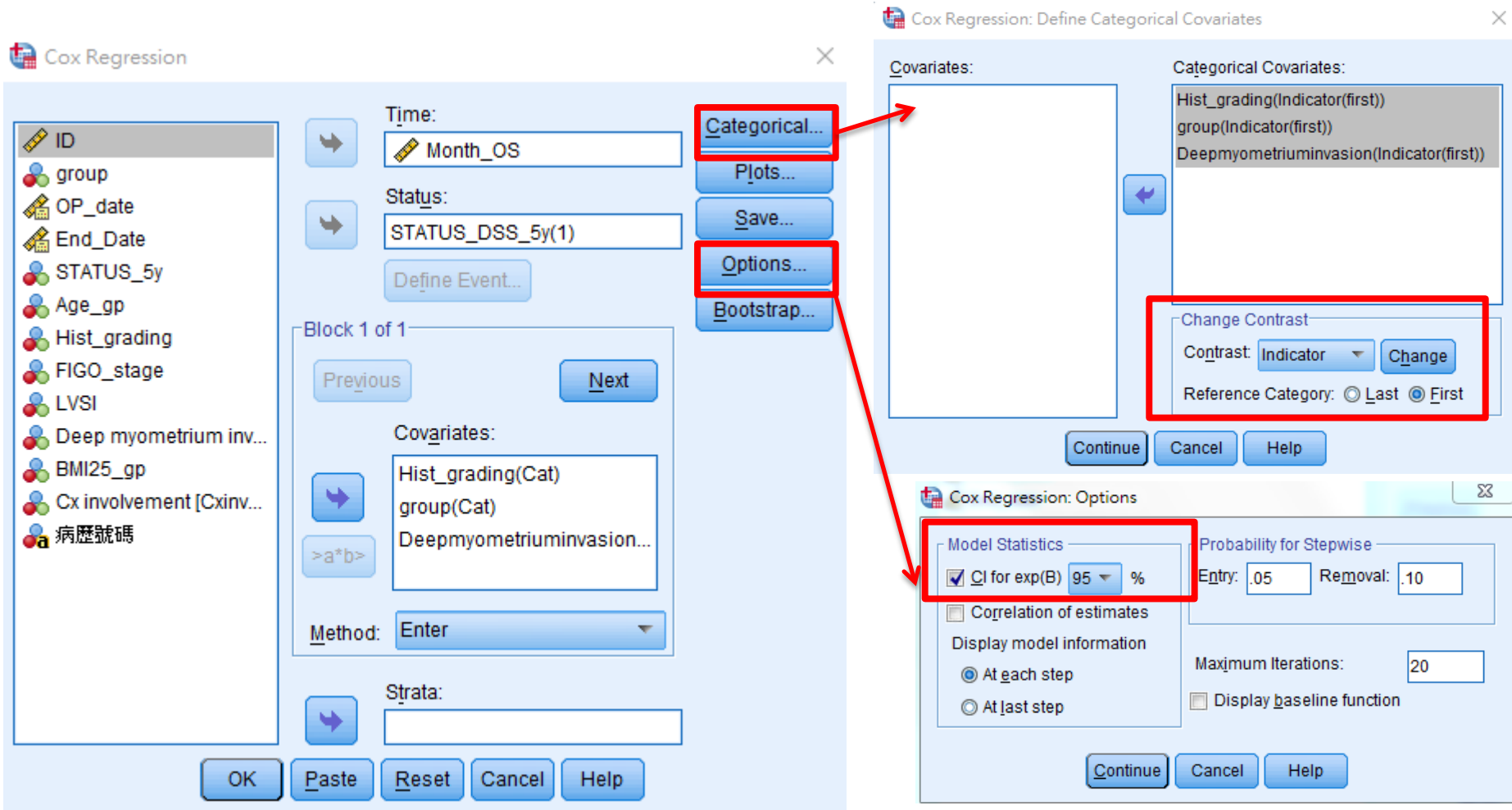
分析>存活分析>Cox迴歸



The screenshot shows the SPSS software interface with the 'Analyze' menu open. The 'Survival' option is selected, and its sub-menu is displayed, highlighting 'Cox Regression...'. The background shows a data table with columns 'STATUS\_5y' and 'STATUS\_DSS'.

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

# Cox model-分析操作



The image shows three overlapping dialog boxes in SPSS for configuring a Cox regression model. Red boxes and arrows highlight specific settings:

- Cox Regression (Main Dialog):**
  - Time:** Month\_OS
  - Status:** STATUS\_DSS\_5y(1)
  - Block 1 of 1:** Previous, Next
  - Covariates:** Hist\_grading(Cat), group(Cat), Deepmyometriuminv...
  - Method:** Enter
  - Strata:** (empty)
  - Buttons:** OK, Paste, Reset, Cancel, Help
- Cox Regression: Define Categorical Covariates:**
  - Covariates:** (empty list)
  - Categorical Covariates:** Hist\_grading(Indicator(first)), group(Indicator(first)), Deepmyometriuminv...
  - Change Contrast:** Contrast: Indicator, Reference Category: Last (selected), First
  - Buttons:** Continue, Cancel, Help
- Cox Regression: Options:**
  - Model Statistics:**  CI for exp(B) 95 %
  - Probability for Stepwise:** Entry: .05, Removal: .10
  - Display model information:**  At each step,  At last step
  - Maximum Iterations:** 20
  - Display baseline function:**
  - Buttons:** Continue, Cancel, Help

# Cox model-Output

**Categorical Variable Codings<sup>a,c,d</sup>**

		Frequency	(1)
group <sup>b</sup>	0=CT alone	27	0
	1=Sandwich	39	1
Hist_grading <sup>b</sup>	1=Grade 1 and 2	29	0
	2=Grade 3	37	1
Deepmyometriuminvasion <sup>b</sup>	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= 0.030)

**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
Deepmyometriuminvasion	2.245	1.051	4.559	1	.033	9.442	1.202	74.150

# 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
  - 藥物劑量、血壓、年齡
  - 出血狀態、中風

# Time-dependent covariates dataset



探討是否服用阿  
斯匹靈對於中風  
的影響

ID	start	stop	Aspirin	SBP	DBP	stroke	Follow_month
1	0	7	1	152	80	0	7
2	0	7	0	166	66	1	9
2	7	9	0	125	50	0	9
3	0	8	1	130	68	0	8
4	0	3	0	139	62	0	3
5	0	1	1	140	80	0	6
5	1	6	0	132	56	0	6
6	0	6	0	121	87	1	12
6	6	12	0	154	90	1	12
7	0	2	0	145	88	1	2
8	0	5	0	120	89	0	5
9	0	6	1	137	76	1	15
9	6	10	0	160	82	0	15
9	10	15	0	134	80	1	15
10	0	1	1	131	72	1	8
10	1	4	1	150	75	0	8
10	4	7	0	136	84	0	8
10	7	8	1	138	82	1	8

# Time-dependent covariates-分析操作



分析>存活分析>Cox迴歸

The image shows the SPSS software interface. The 'Analyze' menu is open, and the 'Survival' option is selected. A sub-menu is displayed, showing 'Cox w/ Time-Dep Cov...' as the chosen option. In the background, a data table is visible with columns 'DBP' and 'stroke'.

	DBP	stroke
2	80	0
6	66	1
5	50	0
0	68	0
9	62	0
0	80	0
2	56	0
1	87	1
4	90	1
5	88	1
0	89	0
7	76	1
0	82	0
1	71	1
1	77	0
2	82	1
5	80	1
5	82	1

# Time-dependent covariates-分析操作



Compute Time-Dependent Covariate

Time [T\_] ID start

Expression for T\_COV\_: T\_ > start

Model...

Cox Regression

Time: Follow\_month

Status: stroke(1)

Define Event...

Block 1 of 1

Previous Next

Covariates: T\_COV\_ Aspirin(Cat)

Method: Enter

Strata:

OK Paste Reset Cancel Help

Cox Regression: Define Categorical Covariates

Covariates: T\_COV\_[T\_COV\_]

Categorical Covariates: Aspirin(Indicator(first))

Change Contrast

Contrast: Indicator Change

Reference Category: Last First

Continue Cancel Help

Cox Regression: Options

Model Statistics

CI for exp(B) 95 %

Correlation of estimates

Display model information

At each step

At last step

Probability for Stepwise

Entry: .05 Removal: .10

Maximum Iterations: 20

Display baseline function

Continue Cancel Help

# 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_	12.641	86.849	.021	1	.884	308999.391	.000	2.608E+79
Aspirin	-.433	.200	4.664	1	.031	.649	.438	.961

服用 Aspirin 有 0.649 倍的 Stroke risk 且有統計差異 ( $p=0.031$ )



# Cox Model v.s Logistic Model

## Cox Regression

- 依變項為時間\*事件
- 加入時間及設限資料
- 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



臺中榮民總醫院  
Taichung Veterans General Hospital



中榮官網



中榮FB

## 滿意度問卷



感謝您的聆聽！

Thank you !

