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Sequential analysis of uncommon adverse outcomes

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Summary

- 手術後的部位感染(SSIs)往往被醫療人員所忽略，特別是在出院後
- Deep and organ space (complex) SSIs發生頻率較低且檢測可靠並且適用於監測傷口護理
- 從院內著手改善感染率也是重要的課題，並且針對發病率以及死亡率(Morbidity and mortality； M&M)需特別監控
- 統計表和累計觀察值減去預期（O-E）圖和漏斗圖，能夠明顯的發現AEs變異，使醫療人員能快速處理狀況發生。

Introduction

- SPC可有效監控不良事件發生
- 使用昆士蘭健康中心保健相關感染的監測和預防(Queensland Health Centre for Healthcare Related Infection Surveillance and Prevention；CHRISP)數據，2575筆骨科手術資料蒐集於2001~2006

- 監測涉及的五個部分：

  髖關節部分關節置換術（PHR）

  髖關節全關節置換術（THR）

  全膝關節置換術（TKR）

  人工髖關節置換術（RTHR）

  人工全膝關節換置術（RTKR）
- MRSA bacteraemias之管制

Methods for calculating an expected probability

- 估計機率由136 complex SSIs complicating 12838 orthopaedic procedures performed in 18 hospitals and recorded in the 2001-2006 CHRISP database.
- 12838資料分類：

  1.Initially stratified by procedure type.(最初分類)

  2.US Centers for Disease Control and Prevention Nosocomial Infections Surveillance System (NNIS) risk index.(NNIS分類)

- (NNIS) risk index區分了四個等級，此篇研究只使用了三個等級(labelled 0, 1 and 2)
- 最初有15個分類，將類似以及較小的樣本合併後分成7類，如Table I
- 機率估計=(number of complex SSIs)/(number of records in that category)

例如： 在G類別的364個RTHR在所有的風險指數下，觀察到11個complex SSIs，機率為11/364 =0.03022

Table I

Estimated expected probability of the incidence of a complex SSI for categories based on stratification by procedure type and NNIS risk index

Category	Procedure	Risk index	Complex SSI	Procedures	*P*
A	Partial hip replacement	All	3	158	0.01899
B	Total hip replacement	0	25	3335	0.0075
C	Total hip replacement	1, 2	26	1696	0.01533
D	Revision of total hip replacement	All	14	547	0.02559
E	Total knee replacement	0	36	4518	0.00797
F	Total knee replacement	1, 2	21	2220	0.00946
G	Revision of total knee replacement	All	11	364	0.03022

SSI, surgical site infection; NNIS, National Nosocomial Infection Surveillance System.

- Hospital X performed 2575 procedures and 30 of these resulted in complex SSIs.
- The expected number was estimated by:

$$0 \times (0.018987) + 873 \times (0.007496) + 176 \times (0.01533) + 3 \times (0.025594) + 1311 \times (0.007968) + 212 \times (0.009459) + 0 \times (0.03022) = 21.77,$$

第一個數字為A~G的發生期間，括號則為Table I 中的P值。

在Table I中醫院X沒有進行監測PHR或RTHR程序。

利用邏輯式回歸求估計期望機率

附錄一(1/2)

- 邏輯式回歸提供了一個估計期望機率方法
- 醫院X之估計期望機率為22.48
- 邏輯式回歸時，通常需要兩個以上的解釋變數，之前提到的procedure type以及NNIS risk index
- 公式如下R (S)= g< -glm(complex SSI~group 2 +group 3, family=binomial)

	Estimate	SE	*z*-value	Pr(>|*z*|)
(Intercept)	−4.7822	0.1089	−43.908	<2e-16
Group 2	0.5249	0.2453	2.140	0.0324*
Group 3	1.2052	0.2148	5.611	2.01e-08

Null deviance: 1507.5 on 12 837 degrees of freedom.
Residual deviance: 1480.2 on 12 835 degrees of freedom.

附錄一(2/2)

- The fitted values were:
  group 1, 0.0083;
  group 2, 0.014;
  group 3, 0.0272.
- 這些群組都不同於其他兩個，包含內容如下
  group 1 included PHR and TKR all NNIS Risk Indices (RI) and THR RI zero,
  group 2 THR RI one,
  group 3 RTHR and RTKR all RI and THR RI two.
- 隨機效應分析，醫院的群組會有不同的預期結果率，例如：菌血症率在大醫院(有較複雜的程序)大於社區醫院。

Sequential analysis

- Tabulations
- Cumulative observed minus expected (O-E) charts with cumulative sum signals
- Cumulative funnel plots

Tabulations

Table II
Observed and expected numbers of complex surgical site infections (SSIs) for hospital X

Year	Half	No. of procedures	Observed no. of complex SSIs	Expected no. of complex SSIs
2001	1	159	2	1.37
	2	194	1	1.63
2002	1	164	2	1.33
	2	183	1	1.51
2003	1	229	0	1.89
	2	238	1	2.08
2004	1	195	5	1.65
	2	224	6	1.90
2005	1	231	1	1.97
	2	270	7	2.31
2006	1	200	2	1.66
	2	288	2	2.46
Total		2575	30	21.77

上半年
下半年

AEs增加

AEs增加

Cumulative observed minus expected (O-E) charts with cumulative sum signals

- 這些圖表類似累積E-O變額壽險調整顯示(variable life-adjusted display ； VLAD)圖，兩個標準差等距控制界線表示在附錄二
- cumulative O-E線是近似水平線時，當rate/count是穩定, 惡化時為上升以及性能提高為下降。

Figure 1.

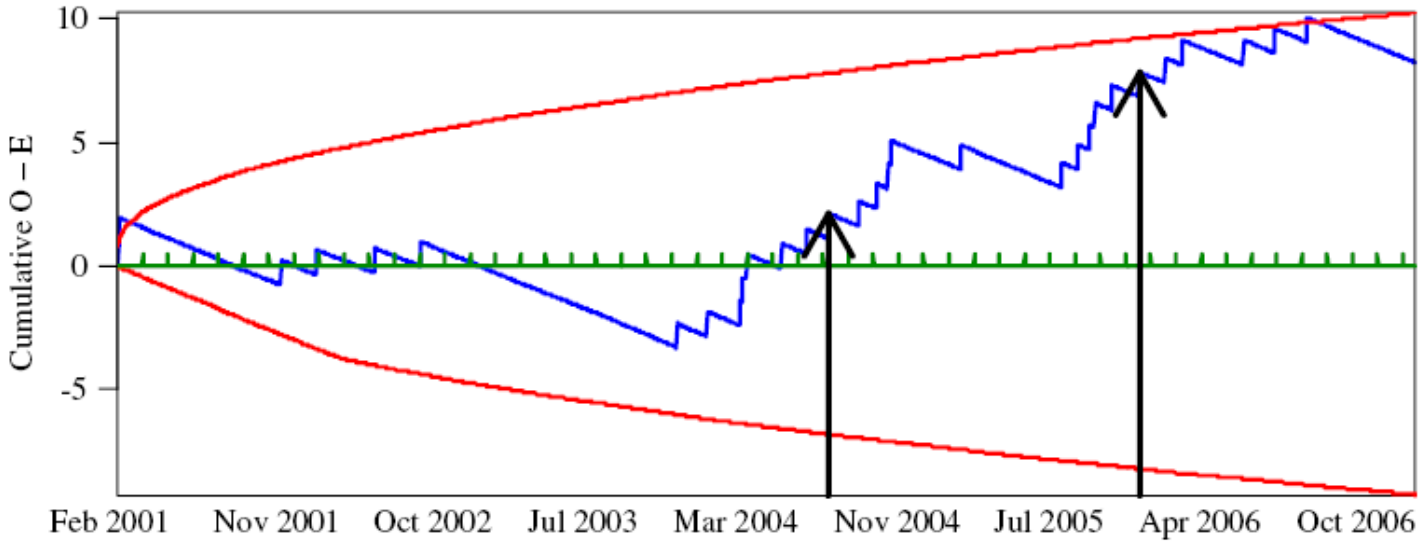

Figure 1. Orthopaedic complex surgical site infection, observed minus expected ($O - E$) plot from February 2001 to December 2006; total: 2575. Blue: observed; red: 95% limits; arrows: cumulative sum signals; tick marks every 50 units. Signals on 12 August 2004, 9 November 2005.

- Figure 1 suggests that there were two runs of SSIs.
- 此圖為複雜的骨科手術部位感染，藍色為觀察值，紅色為95%界線，箭頭為累積總和信號(50個為單位)，信號在2004年8月12日以及2005年11月9日

- The first started on 3 November 2003 at 2.3 fewer SSIs than expected and ended on 12 November 2004 with 5.1 excess SSIs.
- The second run started on 8 August 2005 (4.2 excess SSIs) and ended on 13 March 2006 (9.1 excess SSIs).
- The upper limit was reached on 13 August 2006.

Figure 2

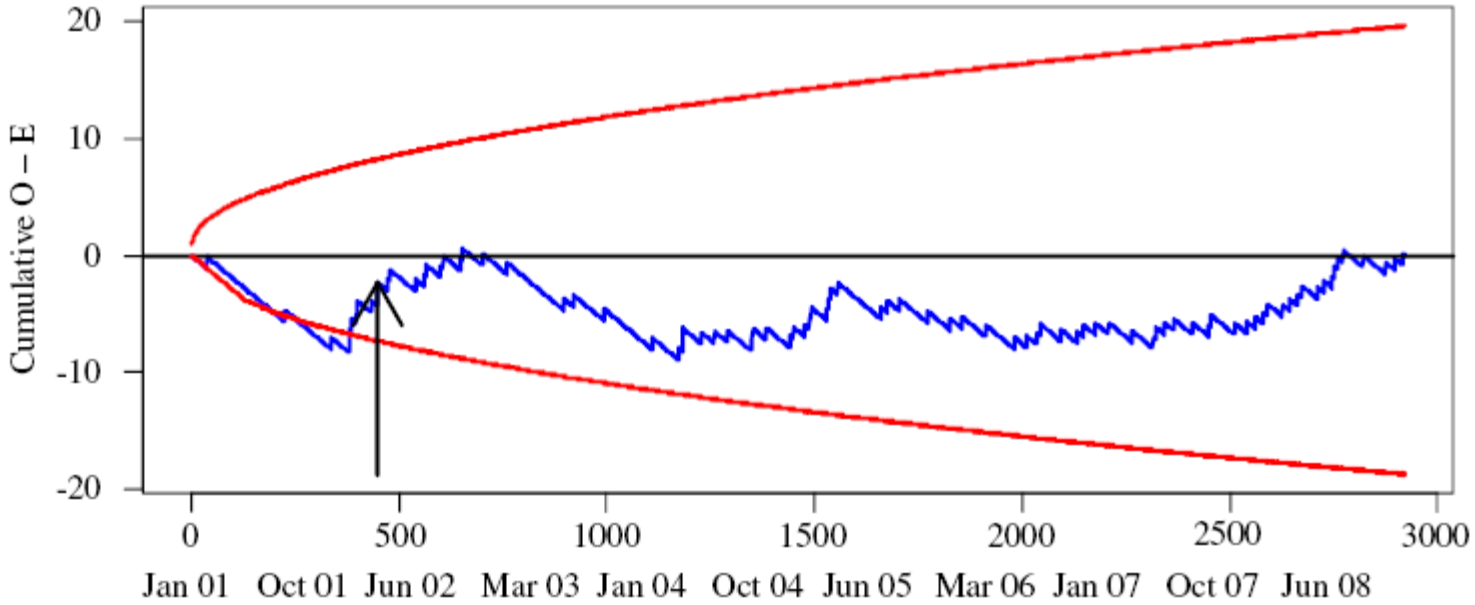

Figure 2. MRSA bacteraemias, observed minus expected ($O - E$) chart from January 2001 to December 2008; $N = 2922$ days. Signals on 26 March 2002.

- MRSA bacteraemias, observed minus expected (O-E) chart from January 2001 to December 2008; N=2922 days，Signals on 26 March 2002

- Figure 2 shows a run of MRSA bacteraemias between November 2001 (8 fewer than expected) and October 2002 (O and E similar).
- The upper limit was not reached.
- cumulative sum (CUSUM) test into the cumulative O-E chart可即時偵測醫院的不良事件發生

- CUSUM檢定時，將每個數據取代為權重(w)
- 權重順序依次加入。
- 如果總和低於零，則重設為零。
- 若達到了預先設定的控制上限(表示h)，一個信號出現，顯示AEs在運行時達到統計顯著性，h越小越能快速發現問題，即平均運行長度ARL(Ng J ；2008)

- The log-likelihood ratio(對數似然比) CUSUM test可用於確定AE的一個因素增加了一個二進制的機率，當r> 1
- weight for the ith observation is

$$w_i = O_i \times (\log\ r) - \log(1 + (r - 1) \times E_i)$$

O_i =1 ； AE發生
O_i =0 ； otherwise
E_i為估計預期機率

- CUSUM通常設定檢測倍率為(r = 2)
- With h = 2.75我們預計大約每5000程序之間有誤報率。

- For monitoring count data, the weight is

$$w_i = O_i \times \log(r) - (r-1) \times E_i,$$

O_i、E_i分別為觀察值和預期值

- The CUSUM was set to detect a doubling in the MRSA bacteraemia rate (r = 2) 以及每日更新資料
- h=3，the average time between false alarms was approximately 150 months

- CUSUM信號為圖一跟圖二的箭頭指示
- Following a signal, investigation of the relevant systems should occur, the CUSUM value is reset to zero, and monitoring is recommenced.

附錄二

- For the upper and lower control limits for binary data (e.g. complex SSIs)
- Variance= $\Sigma_i(\pi \times (1-\pi))$ ，則上管制界線為2SD= $2\sqrt{\Sigma_i(\pi \times (1-\pi))}$
- 2SD近似界線，X(Xu)= $\sum_{X=Xu \to N} C(N,X)\pi^X(1-\pi)^{(N-X)} \leq 0.02275.$

  實際上，都使用較簡單的beta分配，

  S=$1 - \text{pbeta}(\pi,\ X+1,\ N-X) = 0.02275.$
- Cumulative funnel plots are similar to cumulative *O* − *E* charts except that cumulative rates are displayed.

Cumulative funnel plots

- 累積漏斗圖已被用於經皮冠狀動脈研究數據，通常顯示較低AE率(Kunadian B；2006)
- This chart is similar to the cumulative O-E chart except that the cumulative AE rate is shown (Appendix 2).

Figure 3

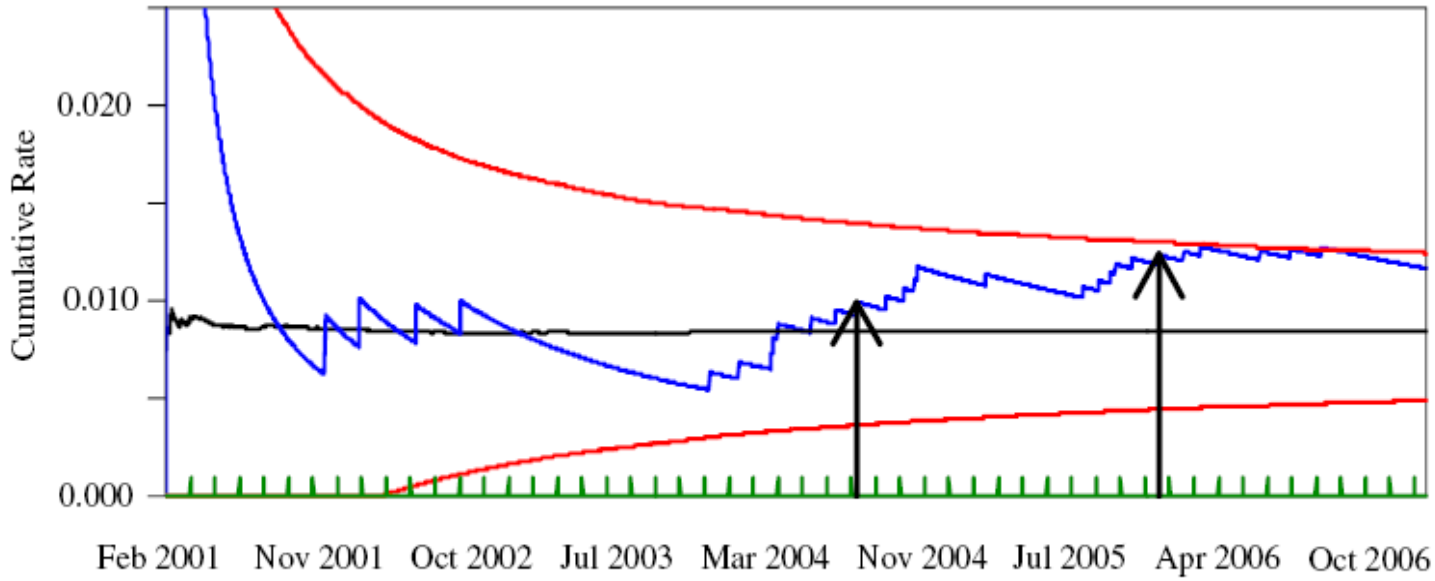

Figure 3. Orthopaedic complex surgical site infection, funnel plot from Februry 2001 to December 2006; total: 2575. Blue: observed; black: expected; red: 95% limits; arrows: CUSUM signals; tick marks every 50 units. Signals on 12 August 2004, 9 November 2005.

- 此圖為複雜的骨科手術部位感染；funnel plot from Februry 2001 to December 2006；2575筆資料；藍色線為觀測值；紅色線為預期值95%區間；箭頭為CUSUM signals；Signals on 12 August 2004, 9 November 2005

Discussion(1/2)

- 標準的CUSUM圖可以檢測運行的重大不良事件，但顯示累積權重，而不是數據值。
- Sherlaw -Johnson納入合併CUSUM信號轉換成VLAD 圖表(Sherlaw-Johnson C；2005)
- cumulative $O - E$ chart可在Aes某時間點看見觀測值以及預測值的相關性
- 如果信號變的雜亂且當序列數據不再相關時，管制圖中必須要選擇一個新的開始點

Discussion(2/2)

- 越早出院，出院後的SSIs正變得越來越重要，光靠CHRISP資源是不夠的，應做宣導...。
- MRSA的傳播通常是良好的控制和歷史平均葡萄球菌菌血症一例發生每月，發生率越低越好。
- M&M審計以cumulative $O - E$,，漏斗圖和CUSUM analysis可以作為預警系統應發生這種情況。
- 最後，必須強調的是，預防不良事件才是最重要的

THE END

名詞

- Sequential analysis
- surgical site infections (SSIs)外科手術部位感染
- lengths of stay (LOS)住院
- Deep and organ space (complex)
- Morbidity and mortality (M&M) 發病率和死亡率
- adverse events (AEs)不良事件
- healthcare-acquired infection (HCAI)衛生感染管制中心
- Nosocomial Infections Surveillance System (NNIS)全國院內感染監測系統
- Queensland Health Centre for Healthcare Related Infection Surveillance and Prevention (CHRISP)昆士蘭衛生中心保健相關感染監測及預防
- variable life-adjusted display (VLAD)變額壽險調整顯示

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