



實證醫學病例討論報告

Loop diuretics infusion following
cardiac surgery

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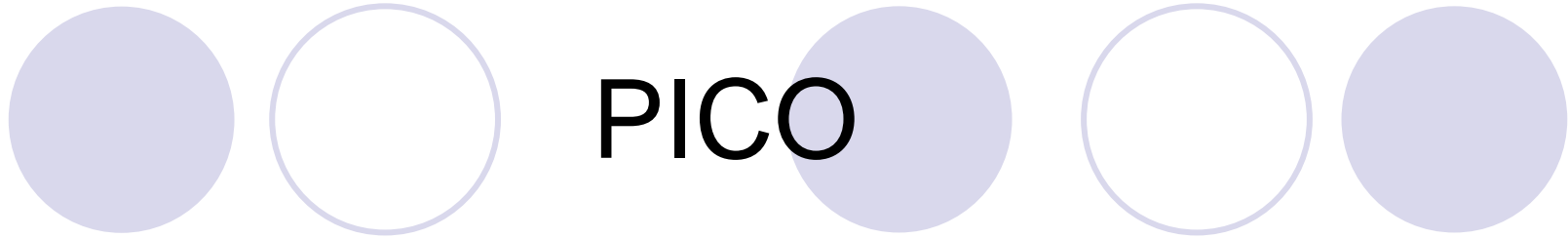


臨床場景 (clinical scenario)

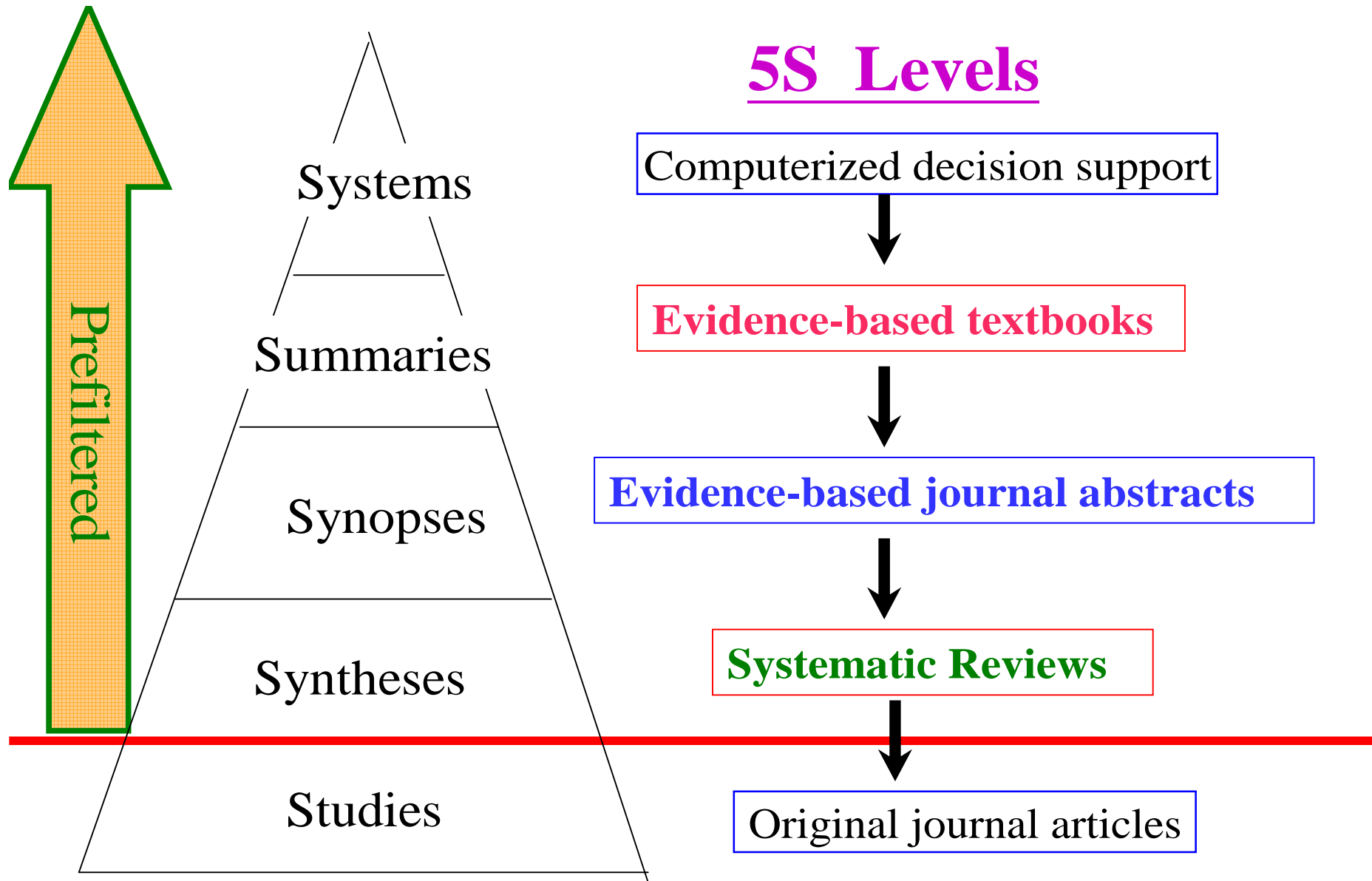
- A 65 years old male underlying with diabetes.
- He was diagnosed of stable angina recently
- Coronary angiography revealed 3 vessel disease with proximal LAD stenosis
- Coronary artery bypass grafting was indicated.
- Pre-op showed preserve LV systolic function (EF: 55%).
- Creatinine level was within normal (0.9mg/dl).

臨床場景 (clinical scenario)

- After CABG performed smoothly, the patient received intensive care in ICU
- However, inadequate urine output was noted in the initial 4 hours (80ml in 4 hours, patient BW 70kg)
 - BP 130/80mmHg, HR 75bpm
 - PAP: 30/15mmHg
 - Albumin transfusion in post-op
 - Lab: Cr 2.5mg/dl(pre-op 0.9)
K: 5.5 mEq/l



P	Patient following cardiac surgery, with inadequate urine output
I	Continuous furosemide infusion
C	Intermittent furosemide infusion
O	Effectiveness and side effect



Modified from R Brain Haynes et al.: ACP Journal Club Nov/Dec 2006 | Vol 145 • Number 34;A8-A9.

搜尋 Systems



- Data base : UpToDate
- Key word : Cardiac surgery, loop diuretics, furosemide, continuous infusion
- Result: nil

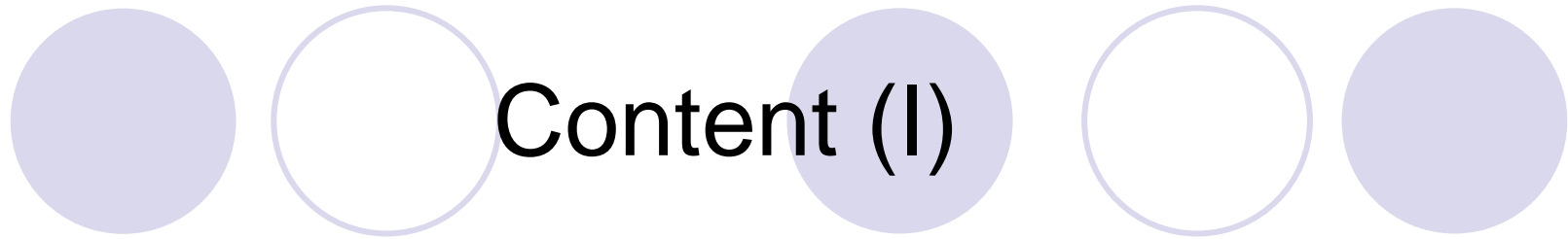


搜尋 Synopses

- Data base : ACP Journal Club
- Key word : Cardiac surgery, loop diuretics, furosemide, continous infusion
- Result: nil

搜尋 Syntheses

- Data base: Cochrane Library
- Key word : (Cardiac surgery), loop diuretics, furosemide, continous infusion
- Result: one
 - ***Continuous infusion versus bolus injection of loop diuretics in congestive heart failure***
DRK Salvador, NR Rey, GC Ramos, FER Punzalan
Cochrane Database of Systematic Reviews 2008 Issue 4



- Method :

- **eight RCT involving 254 patients were included**
- comparing the efficacy of continuous intravenous infusion versus bolus intravenous administration of loop diuretics in congestive heart failure



Content (II)

- Main result:
 - In seven studies, **urine output** (as measured in cc/24 hours) was greater in continuous infusion group
 - with a weighted mean difference (WMD) of 271 cc/24 hour (95%CI 93.1 to 449; $p < 0.01$).
 - In two studies, Electrolyte disturbances (hypokalemia, hypomagnesemia) were not significantly different
 - with a relative risk (RR) of 1.47 (95%CI 0.52 to 4.15; $p = 0.5$).
 - In two studies, **less adverse effects (tinnitus and hearing loss)** were noted when continuous infusion was given
 - RR 0.06 (95%CI 0.01 to 0.44; $p = 0.005$).
 - In one study, **the duration of hospital stay** was significantly shortened by 3.1 days with continuous infusion
 - WMD -3.1 (95%CI -4.06 to -2.20; $p < 0.0001$) while cardiac mortality was significantly different, RR 0.47 (95% CI 0.33 to 0.69; $p < 0.0001$).
 - In two studies, **all cause mortality** was significantly different in the two treatment groups, RR 0.52 (95%CI 0.38 to 0.71; $p < 0.0001$).

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Total urine output (cc in 24 hour) excluding Aaser 1997	6	213	Weighted Mean Difference (Fixed) 95% CI	410.16 [220.82, 599.50]
02 Total urine output (cc in 24 hour) 7 studies	7	221	Weighted Mean Difference (Fixed) 95% CI	271.01 [93.07, 448.96]
03 Duration of Hospitalization (in days)	1	107	Weighted Mean Difference (Fixed) 95% CI	-3.13 [-4.06, -2.20]
04 All Cause Mortality	2	140	Relative Risk (Fixed) 95% CI	0.52 [0.38, 0.71]
05 Cardiac Mortality	1	107	Relative Risk (Fixed) 95% CI	0.47 [0.33, 0.69]
06 Clinically relevant changes in Blood Chemistry Hypokalemia and Hypomagnemesia	3	71	Relative Risk (Fixed) 95% CI	1.47 [0.52, 4.15]
07 Adverse Effects Tinnitus and Hearing Loss	5	218	Relative Risk (Fixed) 95% CI	0.06 [0.01, 0.44]
08 Increase in Serum Creatinine Levels	3	180	Weighted Mean Difference (Fixed) 95% CI	-0.54 [-0.57, -0.51]
09 Total urine output (cc in 24 hour) 5 studies excluding Aaser, Licata,	5	106	Weighted Mean Difference (Fixed) 95% CI	296.38 [-75.40, 668.16]
10 Total urine output (cc in 24 hour) excluding Licata	6	114	Weighted Mean Difference (Fixed) 95% CI	-67.60 [-370.21, 235.01]



Content (III)

- Conclusion:
 - Currently available data are insufficient to confidently assess the merits of the two methods of giving intravenous diuretics.

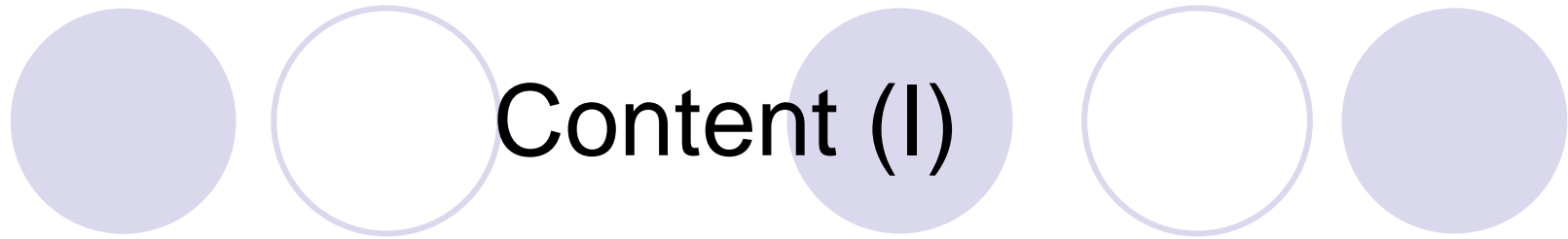


搜尋 Studies

- Data base: PubMed
- Key word : Cardiac surgery, loop diuretics, furosemide, continuous infusion
- Result: one
 - ***Efficacy and safety of a furosemide continuous infusion following cardiac surgery***

[Gulbis BE, Spencer AP](#)

Ann Pharmacother. 2006 Oct;40(10):1797-803



- Method:

- All clinical trials and observational reports identified that evaluated or described the efficacy and/or safety of a continuous infusion of a loop diuretic in adult or pediatric patients who had undergone cardiac surgery were included in this review.

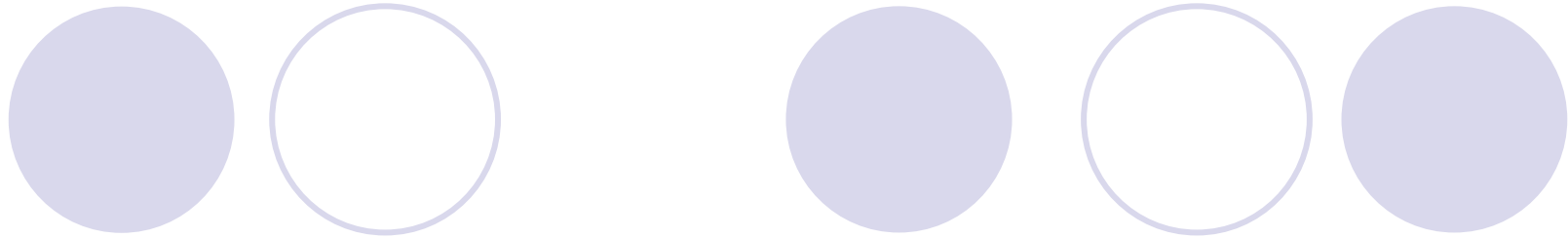


Table 2. Baseline Patient Demographics^a

Reference	Patients (n)		Patient Age (y)		Patient Weight (kg)	
	Continuous Infusion	Bolus	Continuous Infusion	Bolus	Continuous Infusion	Bolus
Adult trials						
Copeland (1983) ¹⁷	9	9	NR	NR	76 ^{b,c}	76 ^{b,d}
Magovern (1990) ¹⁸	6	NA	61 ^b	NA	NR	NA
Lassnigg (2000) ²⁵	41	NA	63 ± 10	NA	75 ± 14	NA
Ad (2002) ²⁶	36	39	52 ^b	51 ^b	NR	NR
Pediatric trials						
Singh (1992) ¹⁸	8	12	1.44 ± 1.4	2.3 ± 2.2	8.23 ± 1.88	10.05 ± 2.7
Luciani (1997) ⁷	11	15	0.31 ± 0.28	0.15 ± 0.21	4.6 ± 0.21	4.3 ± 1.7
Klinge (1997) ¹⁹	23	23	3.4 ± 3.1	2.4 ± 2.1	14.5 ± 9.3	10.8 ± 5.7
van der Vorst (2001) ²⁰	12	NA	0.25 ^b	NA	4.2 ^b	NA

CI = continuous infusion; NA = not applicable; NR = not reported.
^aData reported as mean ± SD where applicable.
^bStandard deviation not reported.
^cMean patient weight calculated from mean total furosemide dose of 45.8 mg (0.6 mg/kg).
^dMean patient weight calculated from mean total furosemide dose of 45.5 mg (0.6 mg/kg).



Content (II)

- Result :
 - Studies in patients who have undergone cardiac surgery have demonstrated that a **more consistent and sustained diuresis** is produced by a continuous infusion of furosemide compared with intermittent bolus doses of furosemide.
 - However, there does **not** appear to be a significant difference in **total urine output or change in serum electrolyte levels** when furosemide is administered as a continuous infusion compared with intermittent bolus doses.



Content (III)

- Conclusion :
 - A continuous infusion of furosemide is an effective and safe method of diuresis in patients undergoing cardiac surgery.



Appraisal

Continuous infusion versus bolus injection of loop diuretics in congestive heart failure

DRK Salvador, NR Rey, GC Ramos, FER Punzalan

Cochrane Database of Systematic Reviews 2008 Issue 4

證據等級

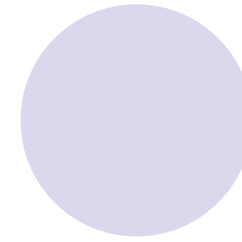
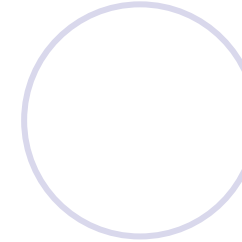
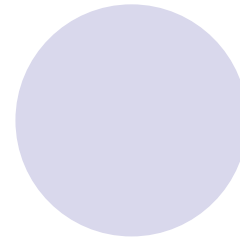
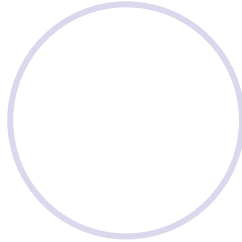
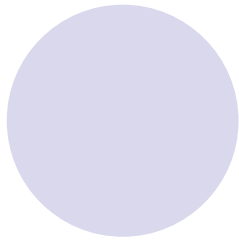
Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with <u>homogeneity*</u>) of RCTs	SR (with <u>homogeneity*</u>) of inception cohort studies; <u>CDR†</u> validated in different populations	SR (with <u>homogeneity*</u>) of Level 1 diagnostic studies; <u>CDR†</u> with 1b studies from different clinical centres	SR (with <u>homogeneity*</u>) of prospective cohort studies	SR (with <u>homogeneity*</u>) of Level 1 economic studies
1b	Individual RCT (with narrow <u>Confidence Interval‡</u>)	Individual inception cohort study with ≥ 80% follow-up; <u>CDR†</u> validated in a single population	Validating** cohort study with good‡‡‡ reference standards; or <u>CDR†</u> tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	<u>All or none§</u>	All or none case-series	Absolute SpPins and SnNouts‡‡	All or none case-series	Absolute better-value or worse-value analyses ‡‡‡
2a	SR (with <u>homogeneity*</u>) of cohort studies	SR (with <u>homogeneity*</u>) of either retrospective cohort studies or untreated control groups in RCTs	SR (with <u>homogeneity*</u>) of Level >2 diagnostic studies	SR (with <u>homogeneity*</u>) of 2b and better studies	SR (with <u>homogeneity*</u>) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of <u>CDR†</u> or validated on split-sample§§§ only	Exploratory** cohort study with good‡‡‡reference standards; <u>CDR†</u> after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with <u>homogeneity*</u>) of case-control studies		SR (with <u>homogeneity*</u>) of 3b and better studies	SR (with <u>homogeneity*</u>) of 3b and better studies	SR (with <u>homogeneity*</u>) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and <u>poor quality cohort and case-control studies§§</u>)	Case-series (and <u>poor quality prognostic cohort studies***</u>)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

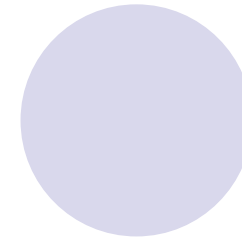
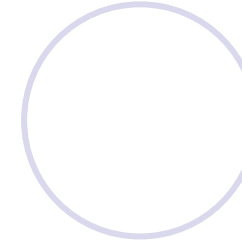
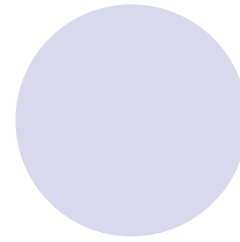
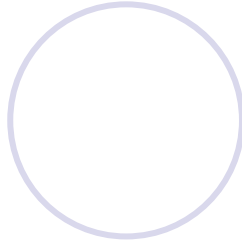
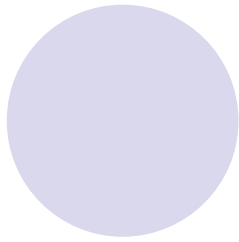
Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998.

證據等級

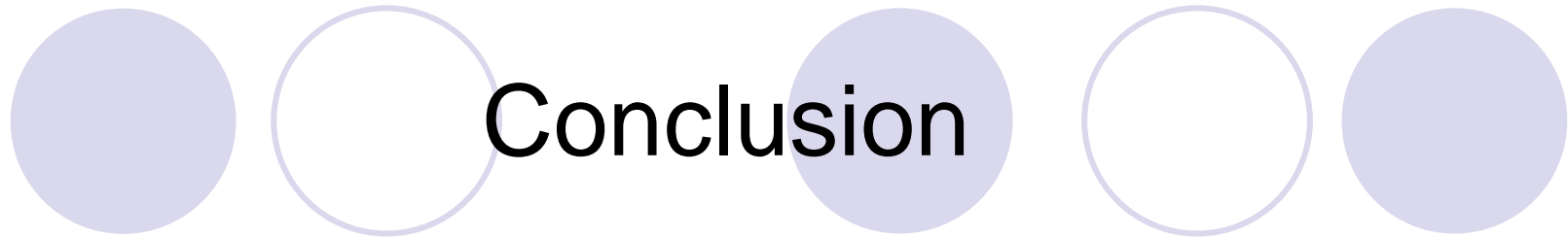
Level	與[治療/預防/病因/危害]有關的文獻
1a	<u>用多篇RCT所做成的綜合性分析(SR of RCTs)</u>
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見



Are the results of this systematic review of therapy valid?	
Is it a systematic review of randomised trials of the treatment you're interested in?	Yes
Does it include a methods section that describes:	Yes
finding and including all the relevant trials?	
assessing their individual validity?	Yes
Were the results consistent from study to study?	No



Can you apply this valid, important evidence from a systematic review in caring for your patient?	
Do these results apply to your patient?	Not fully
Is your patient so different from those in the overview that its results can't help you?	We think it the same
How great would the potential benefit of therapy actually be for your individual patient?	NNT: 3.03 in all cause mortality 2.77 in all cause mortality 2.32 in adverse effect



- After viewing the paper above, continuous loop diuretics infusion was the choiced method in our post-cardiac surgery use, consider about **its efficacy (increase total urine output), shorten hospitalization, low all cause mortality and cardiac mortality, less adverse effect**