



Pansements imprégnés

Jean-Christophe Lucet

Unité d'hygiène et de lutte contre l'infection nosocomiale

Hôpital Bichat-Claude Bernard

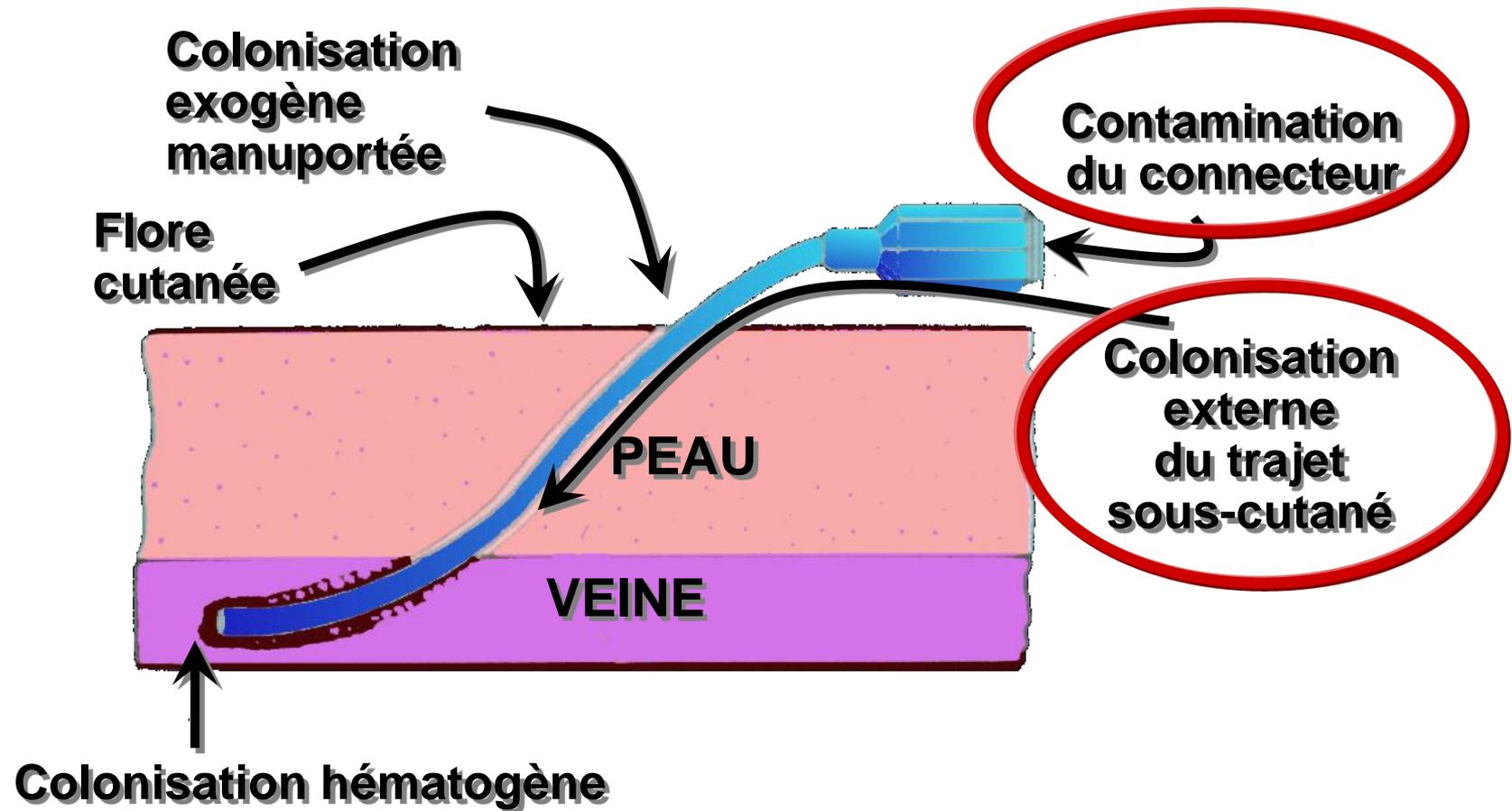
Faculté Paris VII Denis Diderot

Journée Maurice Rapin, 12 octobre 2011

Pourquoi ? Pour qui ?

- Délivrance locale d'antibiotiques
- Concentration :
 - Elevée au site d'implantation
 - Persistante plusieurs jours/semaines
- Réduction de l'impact écologique
- Antiseptique (CHG) ou antibiotiques (gentamicine)
- Pour quelles situations ?
 - Ciments imprégnés en orthopédie
 - **Cathétérisme veineux**
 - **Chirurgie**

Modes de colonisation des cathéters



D'après Maki DG, in "Hospital Infections", Bennett & Brachman, 1992

Eponges imprégnées de chlorhexidine (Biopatch™)



- Pansement tous les **2 jours** transparents vs tous les **7 jours** avec une éponge. Randomisé
 - Apache II 22 idem dans les 2 groupes

	Controle n=736 KT	Biopatch n=665 KT	
--	----------------------	----------------------	--

Maki+	216 (29%)	109 (16%)	<i>HR: 0.62 (0.49-0.78)</i>
Maki + 1	24 (3.3%)	8 (1.2%)	<i>HR: 0.38 (0.16-0.89)</i>
HC periph			

Biopatch™ (meta-analysis)

Catheter Colonization

02 Central venous or arterial catheters

Study	Treatment	Control	Forest Plot	OR	95% CI
Chambers ¹⁷	3/58	13/54		8.24	0.17 [0.05, 0.64]
Garland ¹⁵	47/335	82/370		28.35	0.57 [0.39, 0.85]
Hanazaki ⁹	0/25	7/25		2.03	0.05 [0.00, 0.90]
Levy ¹⁶	11/74	21/71		15.81	0.42 [0.18, 0.94]
Maki ¹⁹	109/665	216/736		32.79	0.47 [0.36, 0.61]
Roberts ¹⁸	4/17	3/16		5.53	1.33 [0.25, 7.17]
Subtotal (95% CI)	1174	1272		92.76	0.47 [0.34, 0.65]

Total events: 174 (Treatment), 342 (Control)

Test for heterogeneity: $\chi^2 = 7.04$, $df = 5$ ($P = 0.22$), $I^2 = 29.0\%$

Test for overall effect: $Z = 4.58$ ($P < 0.00001$)

Catheter-related BSI

02 Blood stream infection by central venous or arterial catheters

Study	Treatment	Control	Forest Plot	OR	95% CI
Chambers ¹⁷	2/58	7/54		13.51	0.24 [0.05, 1.21]
Garland ¹⁵	12/335	11/370		31.24	1.21 [0.53, 2.79]
Levy ¹⁶	3/74	4/71		14.67	0.71 [0.15, 3.28]
Maki ¹⁹	8/665	24/736		32.12	0.36 [0.16, 0.81]
Roberts ¹⁸	1/17	0/16		4.00	3.00 [0.11, 79.13]
Subtotal (95% CI)	1149	1247		95.54	0.61 [0.30, 1.26]

Total events: 26 (Treatment), 46 (Control)

Test for heterogeneity: $\chi^2 = 6.48$, $df = 4$ ($P = 0.17$), $I^2 = 38.3\%$

Test for overall effect: $Z = 1.32$ ($P = 0.19$)

Purpose

- To assess the effect of CHG-IS when the baseline CR infection rate is acceptably low
- To evaluate if a 7-day dressing change of arterial and CVCs is sufficient in ICUs

Methods

- Two-by-two factorial, assessor-blind trial
- 7 ICUs/5 hospitals (3 university-2 non university) (2 surgical, 2 medical, 3 mixed)
- By-patient-allocation (block of 8, stratified by ICU):
 - **3- day dressing (standard care)**
 - **3-day dressing + CHG-IS**
 - **7-day dressing**
 - **7-day dressing + CHG-IS**
- Inclusion: CVC and/or arterial catheter > 48 hours

Catheter Insertion and Care

- Catheters
 - Maximal barrier precaution
 - Preferential use of subclavian and radial access
 - Skin deterision (PVI scrub) + alcoholic-PVI (70%-5%)
 - Immediate removal if no longer needed or suspicion of CRI
- Transparent dressings (Tegaderm TM 3M, Saint Paul MN)
 - Alcoholic PVI for skin disinfection
 - Immediate dressing change if leakage or soiling
 - With or without Biopatch TM (Ethicon Inc., Somerville, NJ)

Judgment Criteria

- Definitions:
 - (1) **Catheter colonization** (quantitative technique) $> 10^3$ CFU/ml (Brun-Buisson 1987)
 - (2) **Catheter-related BSI**: one or more BC + significant catheter culture + no other infected focus
 - (3) **Systemic CRI without BSI**: catheter colonization + sepsis + (purulence or regression after catheter removal)
- Primary end-points:
 - Dressing frequency: (1) = catheter colonization
 - CHG-IS: (2)+(3) = major catheter-related infection

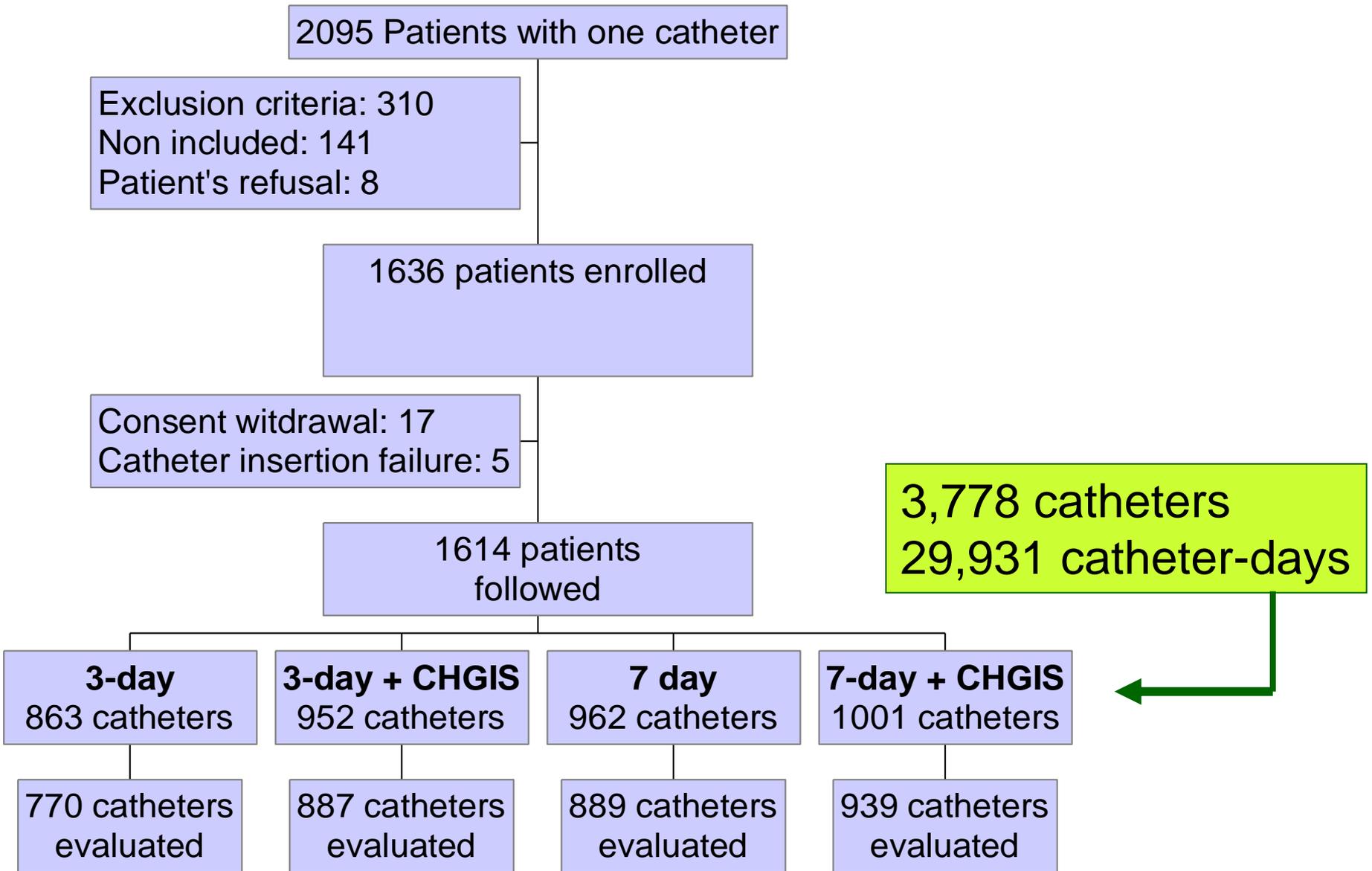
 - Blind assessment by an independent expert committee

Number of Subjects

- At least 2 catheters per patient
- CHG-IS decreases major CRI by 60%
Baseline risk of major CRI, 4%, $\alpha=0.05$, $\beta=.2$, (bilateral)
→ 408 patients (816 catheters) in each arm
- 7-day dressing is non inferior to 3-day dressing (catheter colonization)
Colonization rate 12% in the 3-day arm, upper limit of the 95%CI less than 15% in the 7-day arm, $\alpha=0.05$, $\beta=.2$, (bilateral)
→ 737 patients (1474 catheters) in each arm

1600 patients (3200 catheters)

Flow Chart



Patients

	All (n=1525)	Ctl (n=756)	CHGIS n=769)	3-day (n=741)	7-day (n=772)
• Age (med)	62	63	62	63	62
• Male gender (%)	64	63	65	66	62
• Chronic disease (%)	33	35	30	33	33
• Immune deficiency (%)	6	6	6	6	5
• SAPS2 (med)	53	53	52	52	53
• SOFA (med)	12	12	12	12	12
• Admission category (%)					
– Medical	70	69	70	71	69
– Surgery, scheduled	7	9	5	7	7
– Surgery, emergency	23	22	25	23	23
• Mech. ventilation (%)	87	85	89	85	89
• Length of ICU stay (med)	11	10	12	10	11
• ICU death (%)	34	34	33	32	35

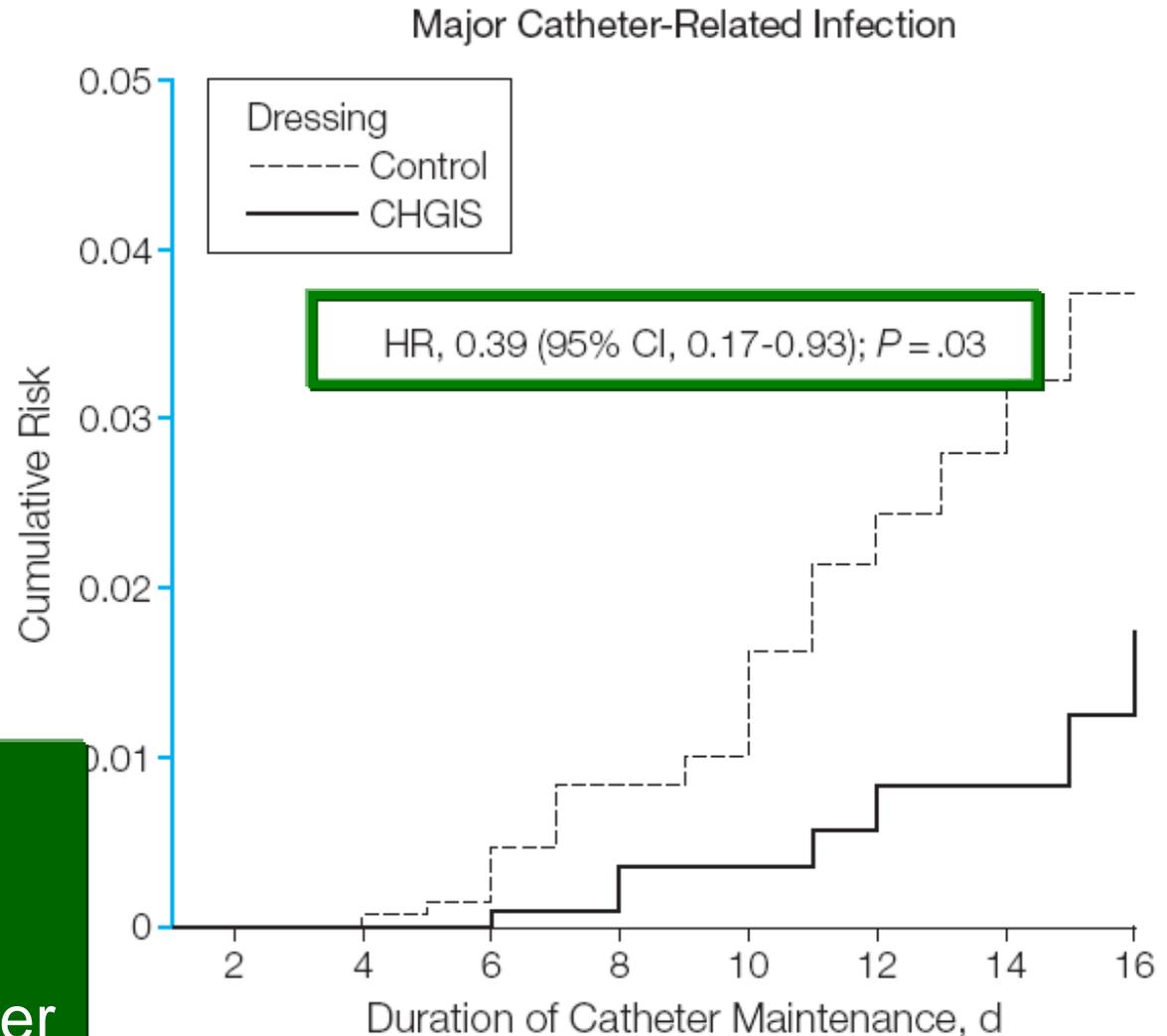
Catheters

	All	Ctl	CHGIS	3-day	7-day
• Time in place (med, d.)	6	6	6	6	6
• Arterial catheter (%)	46	46	46	45	46
– Femoral	41	43	39	42	40
– Radial	59	57	61	58	60
• Venous catheter (%)	54	55	54	54	54
– Jugular	27	25	30	27	27
– Subclavian	40	41	39	40	41
– Femoral	33	34	31	33	33
• GWX (%)	4	3	5	5	4
• Lumens (%)					
– One or two	12	13	11	13	11
– Three	88	87	89	87	89
• AB at insertion (%)	67	66	68	66	68
• Lipids/heparin (%)	38/35	38/34	38/35	39/34	37/35

Eponge imprégnée de CHG



7 réanimations
1653 patients
3,778 cathéters
28,931 jours cathéter



CHG-IS (Biopatch®) vs Control

	All catheters (n= 3532)	Control (n=1685)	CHG-IS (n=1847)
Catheter colonization	310 (8.8%)	213 (12.6%)	97 (5.3%)
- CNS	153	106	47
- <i>S. aureus</i>	16	14	2
- Other Gram pos. cocci	34	28	6
- <i>Pseudomonas sp.</i>	53	38	15
- <i>Enterobacteriaceae</i>	97	65	32
- <i>A. baumannii</i> / Fungi	28	21	7

15.8 vs 6.3/1000 cath.days; HR, 0.36 (95%CI, 0.28-0.46); P< 0.001

Coût global de mise en place d'un pansement

Centre	Coût IDE et AS	Coût du matériel	Coût total	Nb pansements réalisés dans le centre
01	\$1,7	\$2,7	\$13,1	1142
02	\$2,8	\$4,0	\$6,8	4251
03	\$3,8	\$3,8	\$7,6	1121
04	\$4,2	\$4,7	\$8,8	1713
05	\$6,9	\$1,9	\$8,8	1213
06	\$9,1	\$2,5	\$11,5	2973
07	\$6,6	\$3,2	\$9,8	524

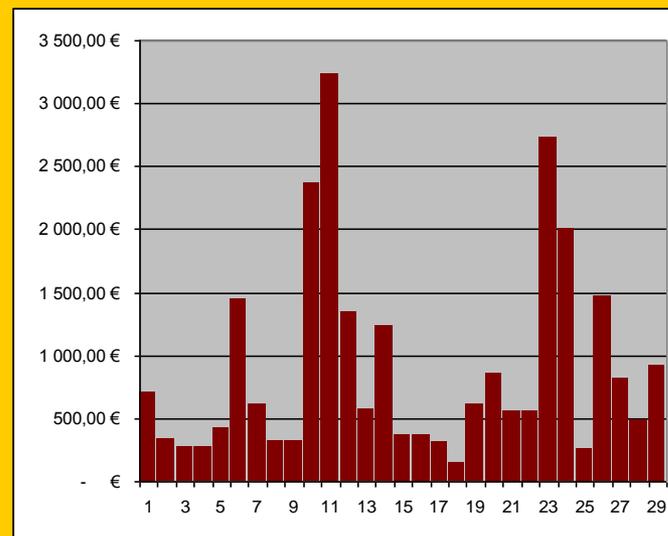
9.08 \$



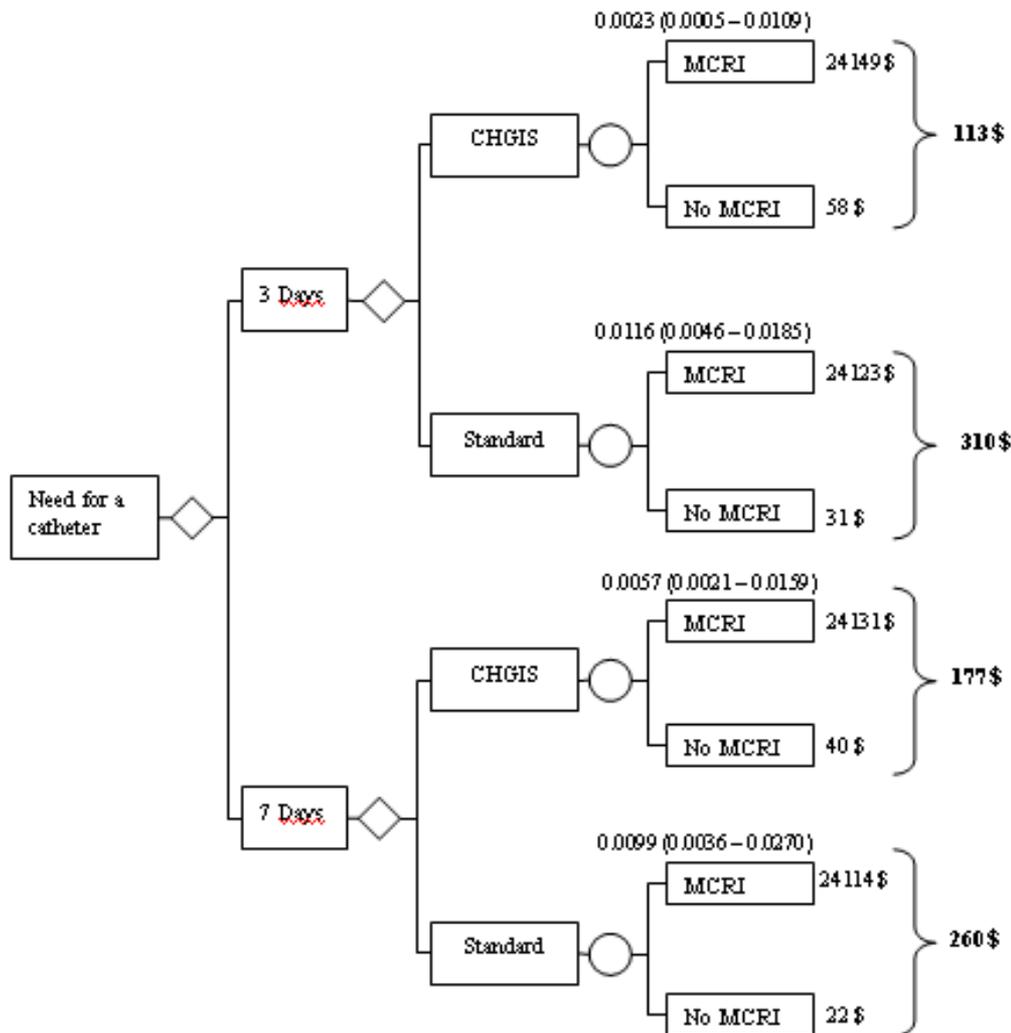
9.73 \$

29 CRIs (Examens, procédures et soins directement liés à l'infection)

Moyenne	\$1 227,47
Ecart Type	\$1 089,63
Médiane	\$792,28
Min	\$201,72
Max	\$4 444,95
Quartile 25%	\$464,46
Quartile 75%	\$1 690,00



Analyse cout - bénéfice



Cout par cathéter (US\$)

Eponge CHG, 3 j. : 113

Standard, 3 j. : 310

Eponge CHG, 7 j. : 177

Standard, 7 j. : 260

Analyse de sensibilité

Paramètre	Condition pour CHG rentable	
	3 jours	7 jours
Éponge CHG vs pansement standard, hazard ratio (HR)	HR < 0.90	HR < 0.79
Taux d'ILC	> 0.14 %	> 0.21 %
Cout d'une ILC	> \$ 2,940	> \$ 4,400

Conclusion

- Les éponges imprégnées de CHG (Biopatch®) diminuent l'incidence des ILC, même si le taux de base est inférieur à 2/1000 jours. cathéter
- Les éponges imprégnées de CHG sont coût-efficaces, même si:
 - La prolongation de la DS induite est < 2 jours
 - Le taux d'ILC est $> 0.21\%$ (0.3 pour 1000 jours-cath.)
 - La diminution vraie du risque est < 0.79

Pour quels cathéters ?

- Cathéters de courte durée, CVC ou KTA
- Données insuffisantes pour les CVC de durée intermédiaire (et rationnel faible)
- Cathéter d'hémodialyse ou Swan-Ganz ?
- A la condition que les autres mesures de prévention soient respectées
- A partir de quel taux d'ILC ?

CHG sponge or CHG gel?



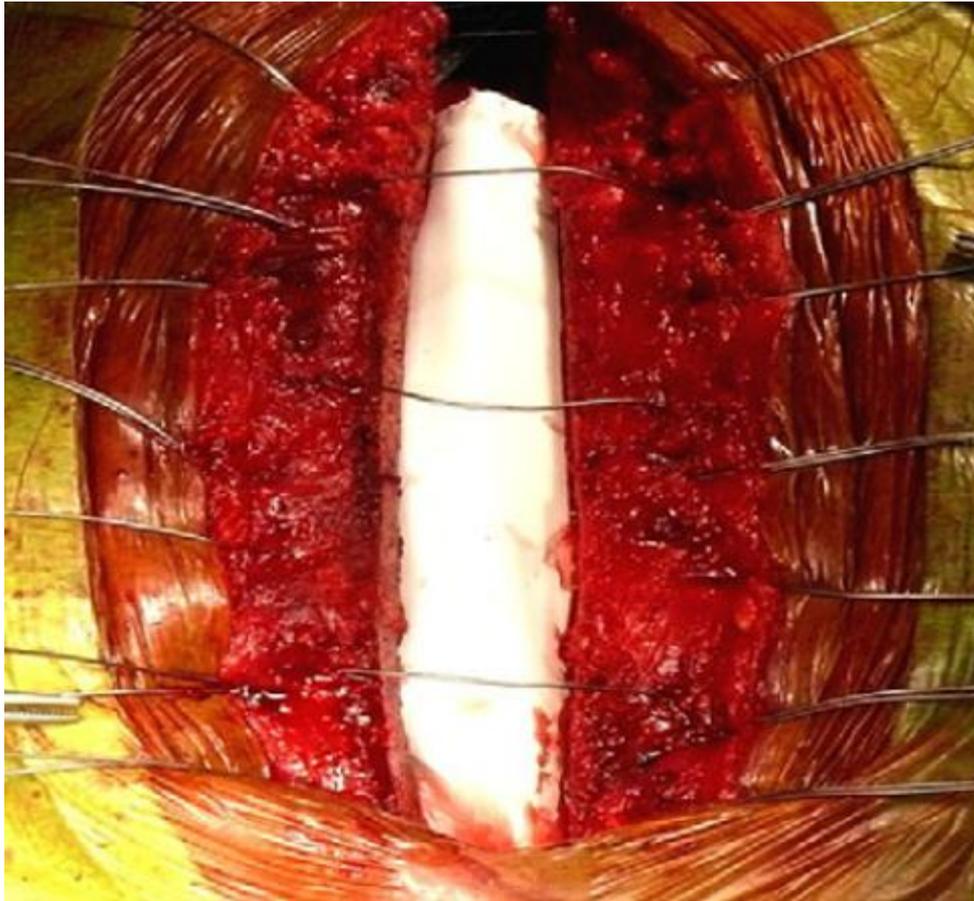
CHG sponge or CHG gel?

Biopatch®

- 92 mg of CHG per disk
- Reduce bacterial count over time and suppress regrowth during at least 7 days
- **Continuous inspection of the insertion site not possible**
- Absorption of 8-fold sponge-weight of exsudate
- Better release of CHG due to better skin contact if properly placed (discordant results)
- Learning curve for application, Perfect application difficult (jugular) and sometimes impossible
- **Clinical studies available**

Tegaderm CHG®

- 45 mg of CHG (3 X 4 cm)
- Identical or slightly better *in vivo* time-kill of flora on unprepped skin (> 7 days) and prepped skin
- **Continuous inspection possible although inf. to transparent dressings**
- Absorption possible but slower than the sponge
- Dressing under the catheter is not in contact with CHG (discordant results)
- Easy application and removal
- **No clinical studies supporting efficacy**



Collagène – gentamicine en Ch. cardiaque

- Inocoll® : 2 pansements collagène (5x20 cm) + 120 mg gentamicine, insérés entre les berges sternales lors de de la fermeture
- En 2010 : une seule étude prospective, bicentrique, randomisée, contrôlée, en simple aveugle
- 2000 patients inclus, Ch. coronaire
- Infection sternale :
 - Inf. sternale : 9.0% vs 4.3% (0.45, 0.37-0.68, P< 0.0001)
 - Reprise op. : 3.9% vs 2.1% (0.54, 0.32-0.92, P=0.02)
- Reprise pour saignement : 2.3% vs 4.0%, P= 0.03

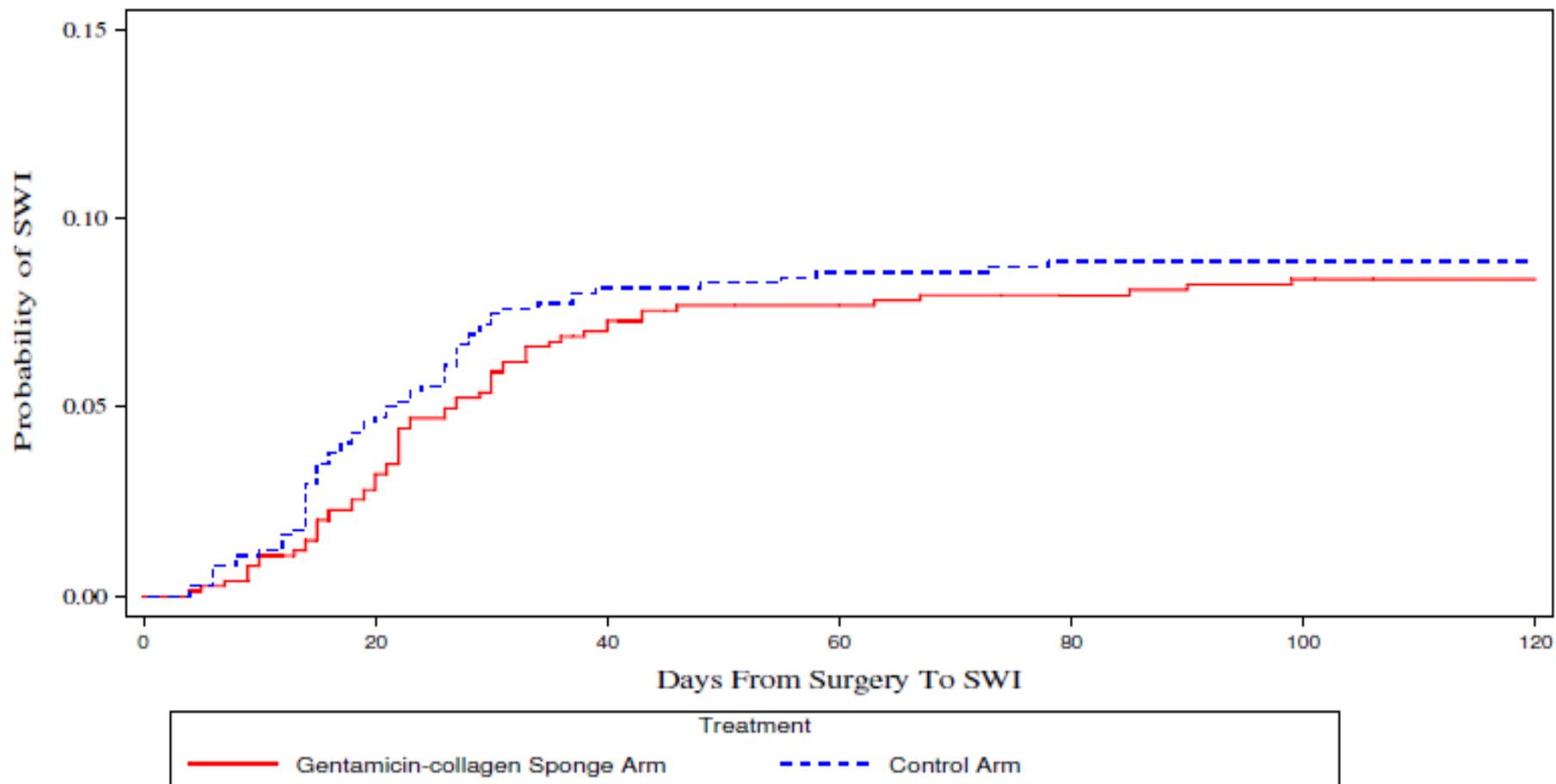
Effect of an Implantable Gentamicin-Collagen Sponge on Sternal Wound Infections Following Cardiac Surgery

- 14 mois, 48 centres US, 1502 patients
- Inclusion :
 - Toute chirurgie cardiaque non urgente
 - DIR ou DNIR ou IMC > 30
- Mesures de prévention classiques
- Surveillance :
 - Chirurgiens non aveugles, pas de placebo
 - Mais comité d'adjudication indépendant, aveugle du bras de randomisation
- Critères de jugement :
 - ITT
 - Iaire : inf. sternale J90 (II : inf prof et sup., reprise, durée de séjour

Characteristic	No. (%) of Patients ^a	
	Gentamicin-Collagen Sponge (n = 753)	Control (n = 749)
Patient demographics		
Age, median (IQR), y	64.2 (58.0-71.5)	64.9 (57.2-72.1)
White race	688 (91.4)	683 (91.2)
Weight, median (IQR), kg	98.0 (86.1-113.0)	98.8 (85.0-111.1)
Body mass index, median (IQR)	33.1 (30.2-37.2)	32.8 (30.0-36.2)
Body mass index >30	574 (76.2)	563 (75.2)
Male sex	530 (70.4)	530 (70.8)
Medical history		
History of hypertension	659 (87.5)	659 (88.0)
History of diabetes	493 (65.5)	513 (68.5)
Current or history of smoking	458 (60.8)	450 (60.1)
Current smoking	136 (29.7)	123 (27.3)
History of chronic obstructive pulmonary disease	117 (15.5)	107 (14.3)
History of peripheral vascular disease	105 (13.9)	89 (11.9)
Previous median sternotomy	52 (6.9)	42 (5.6)
History of TIA or stroke	77 (10.2)	81 (10.8)
History of myocardial infarction	233 (31.0)	245 (32.7)
History of congestive heart failure	89 (11.8)	90 (12.0)
History of hyperlipidemia	619 (82.2)	607 (81.0)
Steroid use ≤1 mo prior to surgery	28 (3.7)	33 (4.4)
Receiving dialysis preoperatively	4 (0.5)	2 (0.3)
Preoperative diagnostic values		
Left ventricular ejection fraction, median (IQR), %	55 (45-60)	55 (45-60)
Serum glucose, median (IQR), mg/dL	125 (101-160)	124 (103-167)
Serum hemoglobin A _{1c} , median (IQR), %	6.5 (5.9-7.6)	6.6 (5.9-7.7)
Hematocrit, median (IQR), %	39 (36-42)	39 (36-42)
Serum creatinine, median (IQR), mg/dL	1.0 (0.9-1.3)	1.0 (0.9-1.2)
Preoperative core temperature, median (IQR), °C	97.6 (97.0-98.2)	97.7 (97.0-98.2)
Preoperative hospital stay, median (IQR), d	1.0 (0-3.0)	1.0 (0-3.0)
Parsonnet risk score, median (IQR) ^b	9.0 (6.0-14.5)	9.0 (6.0-16.0)

^aValues are median (interquartile range) unless otherwise indicated.

^bValues are median (interquartile range) unless otherwise indicated.



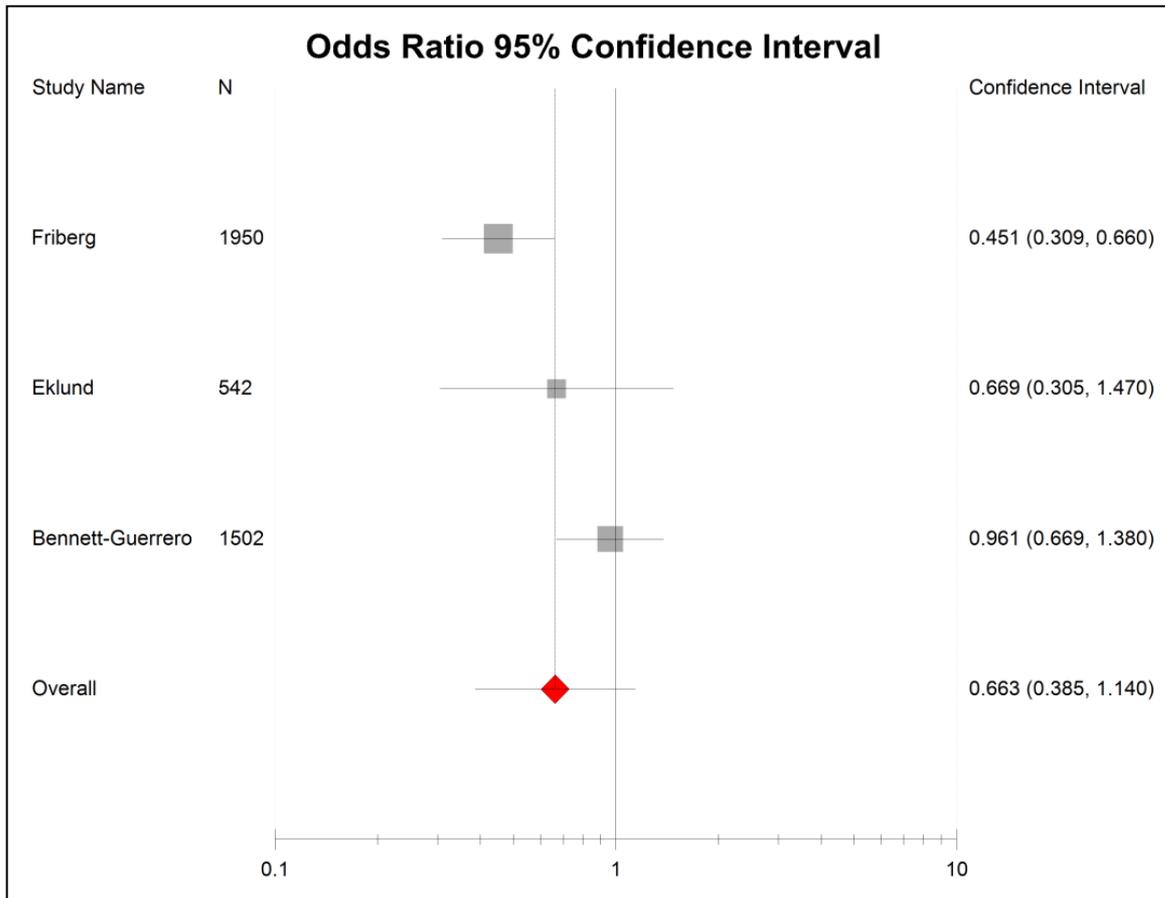
Gentamicin-Collagen			
	Sponge Arm	Control Arm	P-value
Number of subjects with positive culture	27	32	NA
<i>Acinetobacter calcoaceticus</i>	1 (3.7%)	0 (0.0%)	0.458
Coagulase-neg staphylococci	3 (11.1%)	10 (31.3%)	0.063
<i>Enterobacter cloacae</i>	2 (7.4%)	1 (3.1%)	0.588
<i>Enterococcus faecalis</i>	1 (3.7%)	1 (3.1%)	>.99
<i>Escherichia coli</i>	3 (11.1%)	3 (9.4%)	>.99
Group B species streptococcus	1 (3.7%)	0 (0.0%)	0.458
<i>Klebsiella pneumoniae</i>	0 (0.0%)	2 (6.3%)	0.495
<i>Klebsiella</i> spp	1 (3.7%)	2 (6.3%)	>.99
Methicillin-resistant <i>staphylococcus aureus</i>	4 (14.8%)	2 (6.3%)	0.398
Methicillin-sensitive <i>staphylococcus aureus</i>	9 (33.3%)	7 (21.9%)	0.324
<i>Proteus mirabilis</i>	4 (14.8%)	5 (15.6%)	>.99
<i>Providencia stuartii</i>	1 (3.7%)	0 (0.0%)	0.458
<i>Pseudomonas aeruginosa</i>	3 (11.1%)	3 (9.4%)	>.99
<i>Serratia marcescens</i>	2 (7.4%)	4 (12.5%)	0.678
<i>Streptococcus agalactiae</i>	1 (3.7%)	0 (0.0%)	0.458
Other	3 (11.1%)	3 (9.4%)	>.99

Eb : 51%, Sa : 37%, SCN : 22%

Genta-R : 3 dans chaque groupe (4/6 SCN)

Collagène-gentamicine

Méta-analyse des essais randomisés en chirurgie cardiaque



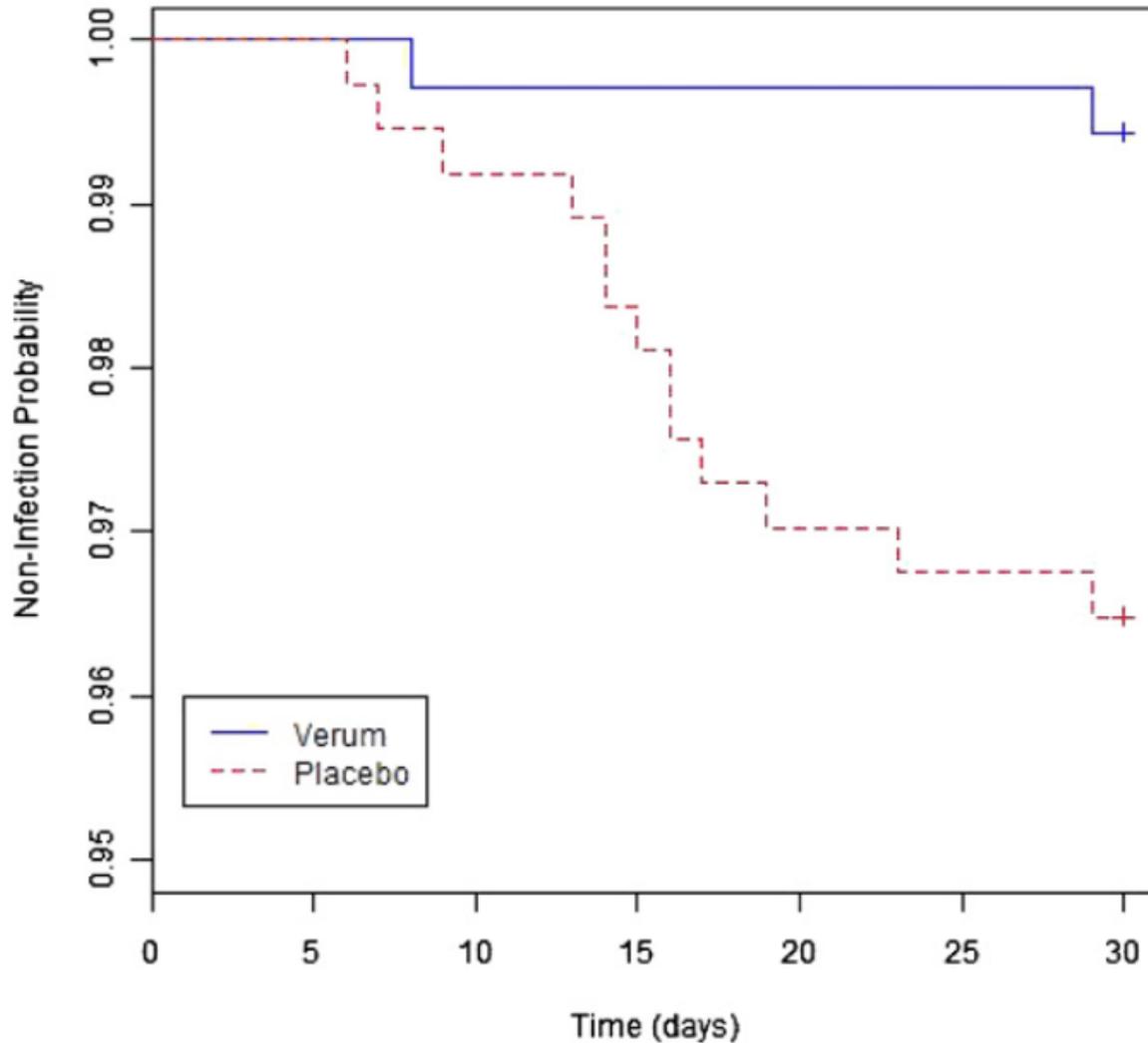
Heterogeneity: $I^2 = 0.75$;
 $Q = 7.96$; $p=0.019$

Collagène – gentamicine en Ch. cardiaque

Etude récente

- Monocentrique, un an, toutes chirurgies cardiaques, double aveugle
- Critères de jugement principal : infection profonde à J30
- 800 inclus, 720 suivis
- Infection sternale :
 - Inf. profonde : 3.5% vs 0.6% (0.15, 0.02-0.69, P= 0.014)
 - Toutes ISO : 6.5 vs 2.5% (0.37, 0.15-0.54, P=0.012)

Collagène – gentamicine en Ch. cardiaque



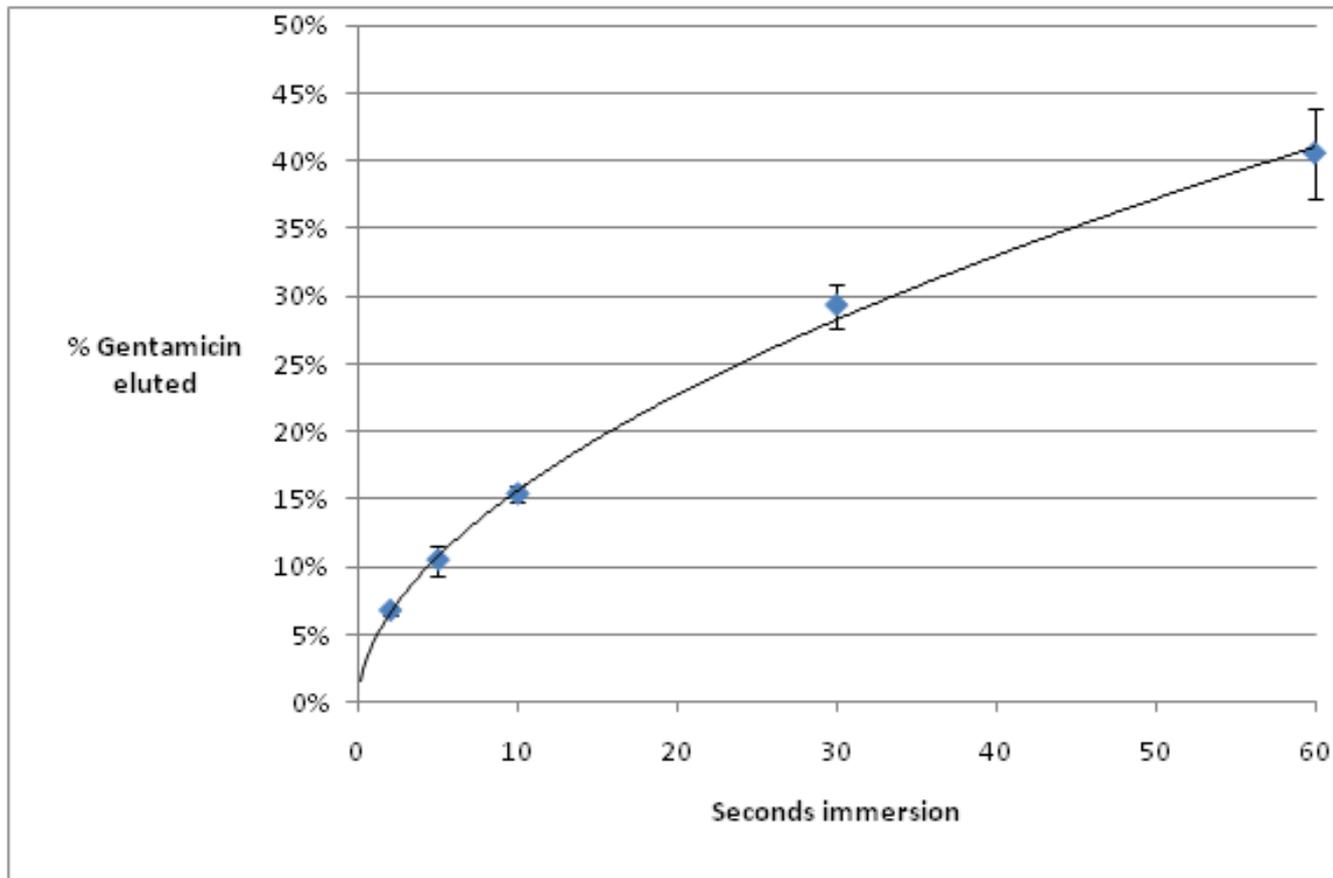
Collagène – gentamicine en Ch. cardiaque

Etude récente

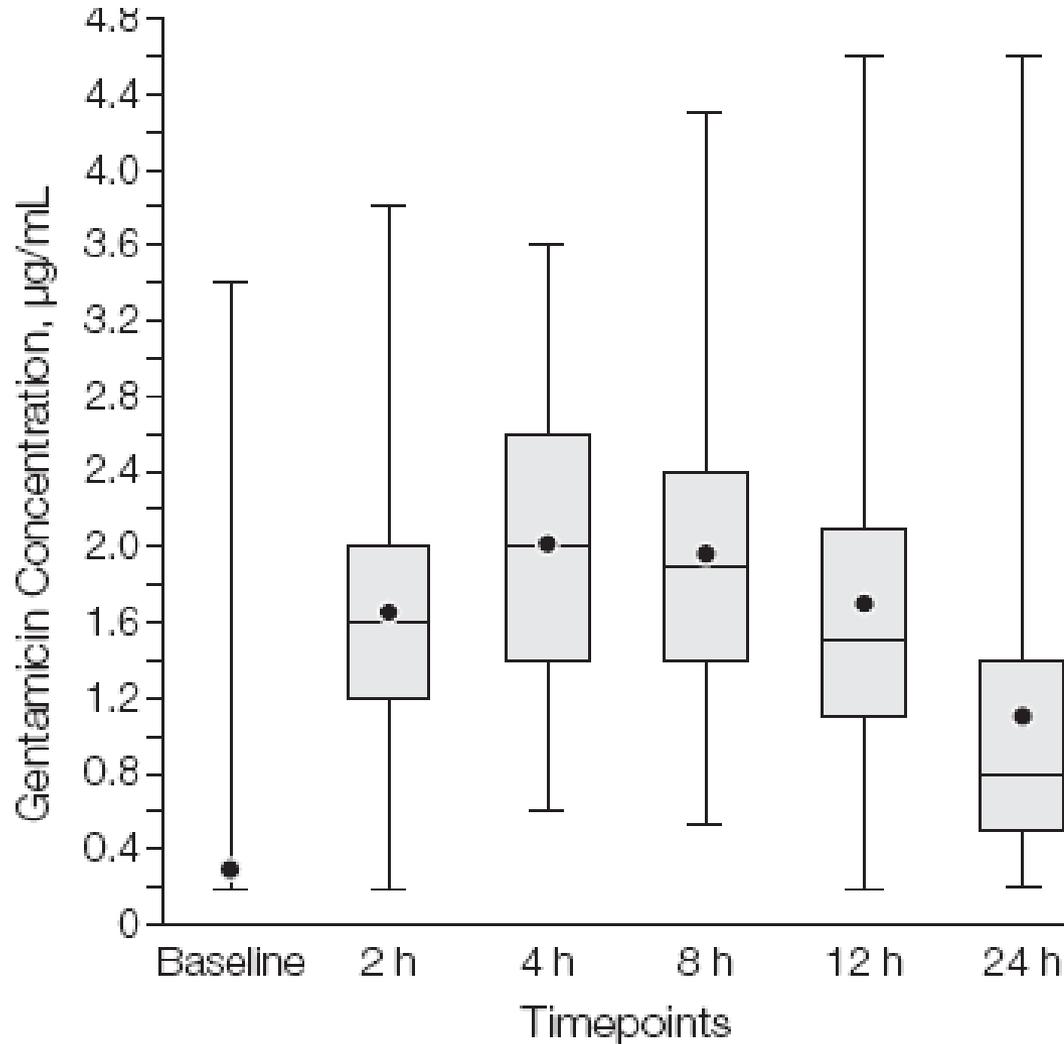
- Monocentrique, un an, toutes chirurgies cardiaques, double aveugle
- Critères de jugement principal : infection profonde à J30
- 800 inclus, 720 suivis
- Infection sternale :
 - Inf. profonde : 3.5% vs 0.6% (0.15, 0.02-0.69, P= 0.014)
 - Toutes ISO : 6.5 vs 2.5% (0.37, 0.15-0.54, P=0.012)
- Biais possibles :
 - Surveillance limitée à J30
 - Pas en ITT

Préparation du pansement ?

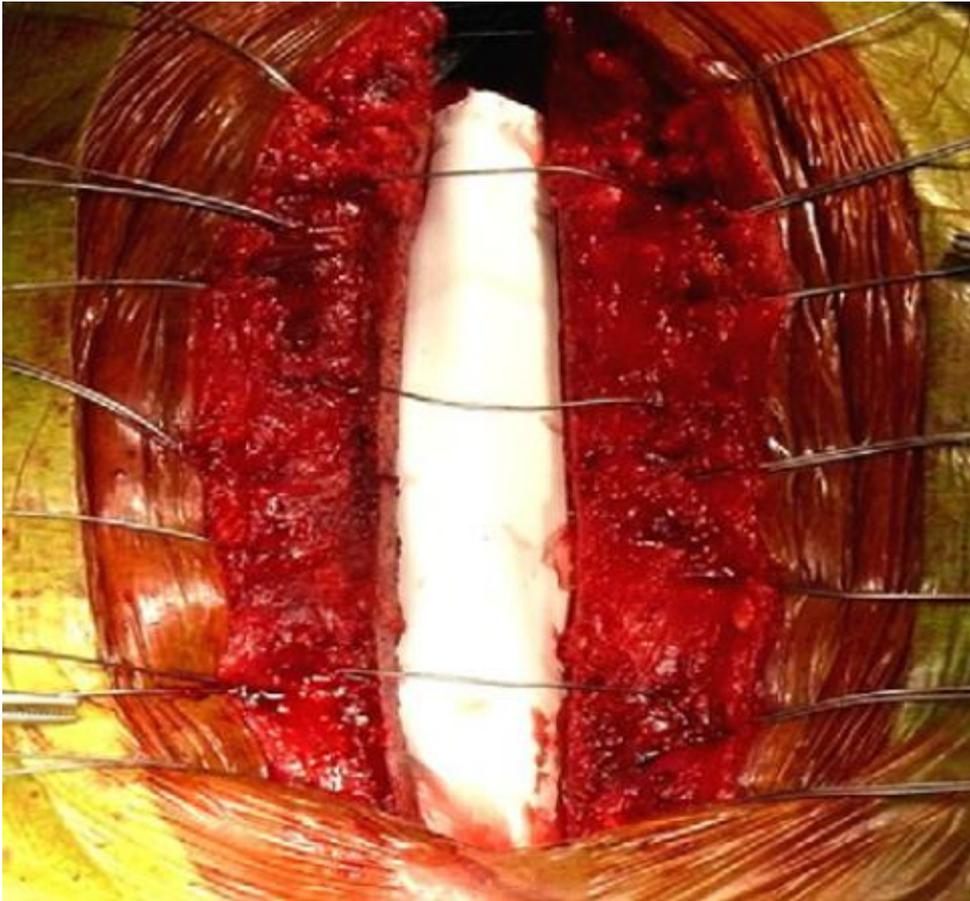
Pourcentage de relargage de gentamicine après immersion



Préparation du pansement ?



Insertion du pansement



Diagnostic de l'ISO

Intra-speciality correlation	N	SSI diagnosis scoring, 7-point Likert scale Intra-correlation coefficient ICC	
		Spontaneous scoring	Scoring with the SSI definition
Anesthesiologists	20	0.15	0.35
Infection control nurses	20	0.19	0.56
Infection control physicians	20	0.30	0.01
Surgeons	16	0.45	0.42
Public health specialists	20	0.56	0.29
Microbiologists	20	0.56	0.42
Infectious diseases specialists	20	0.73	0.66

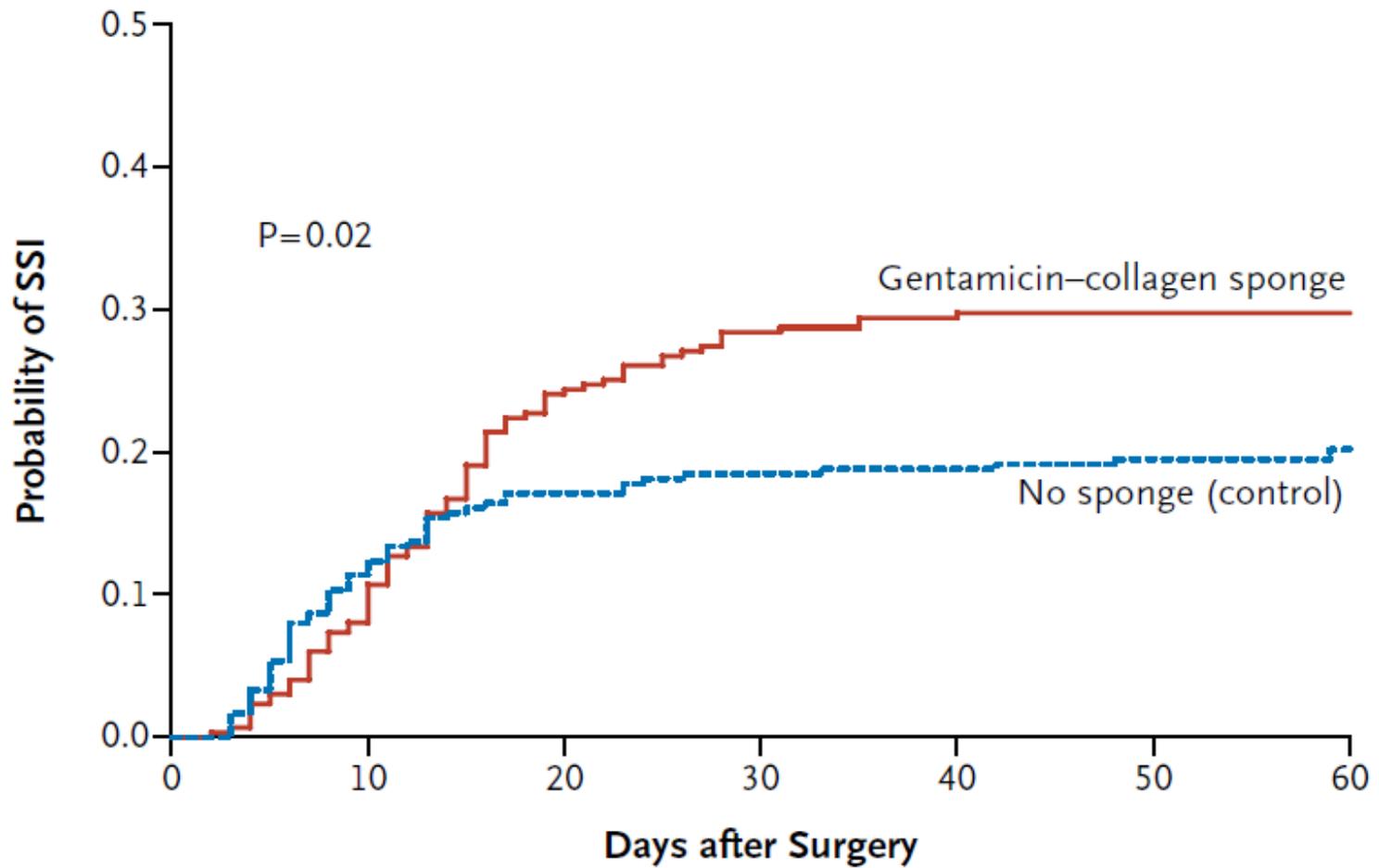
Pourquoi ces discordances ?

- Préparation du pansement
- Mise en place et nombre de pansements
- Méthodes, Critère de jugement
- Physiopathologie de l'ISO ?

Gentamicin–Collagen Sponge for Infection Prophylaxis in Colorectal Surgery

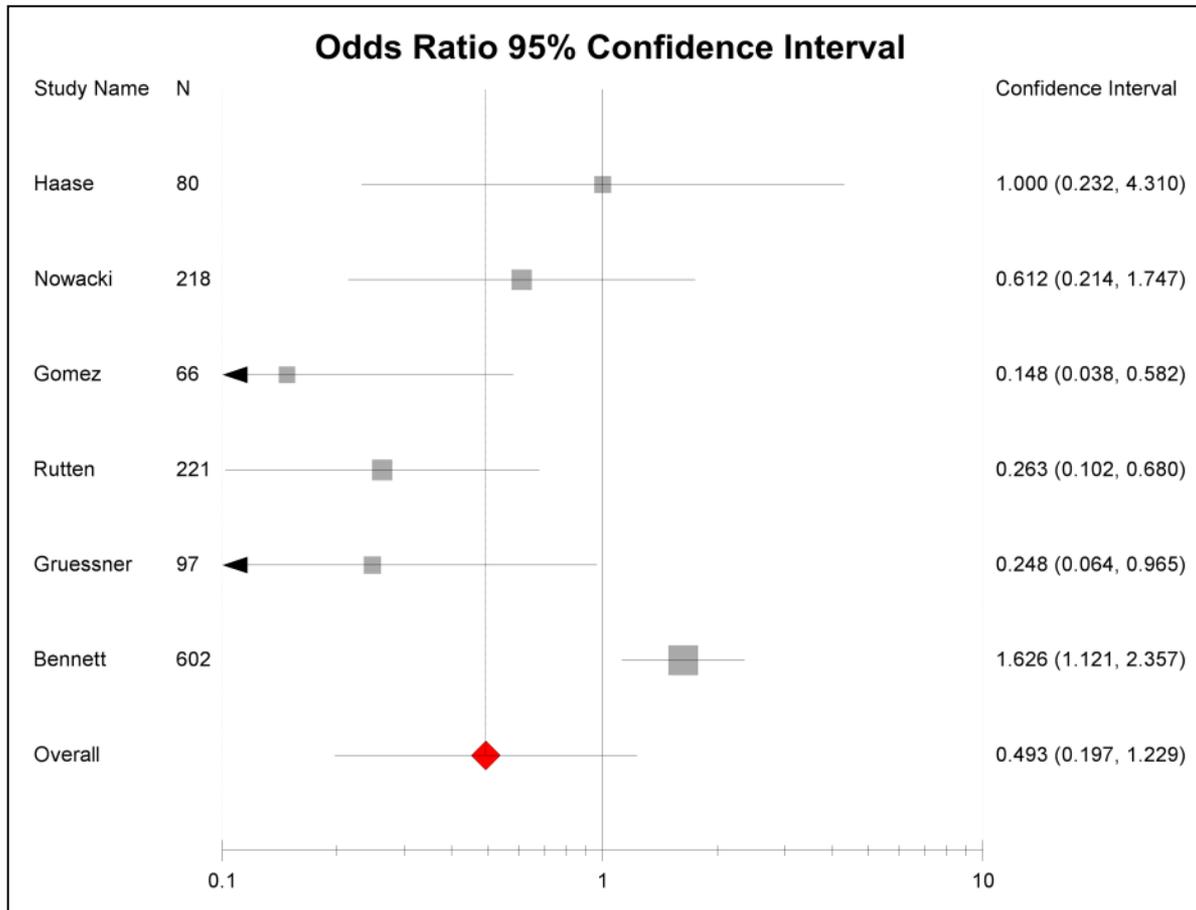
Characteristic	Gentamicin–Collagen Sponge (N=300)	Control (N=302)	P Value
Intention-to-treat analysis			
SSI — no. of patients (%)			
Any (primary end point)	90 (30.0)	63 (20.9)	0.01
Surgically treated	71 (23.7)	49 (16.2)	0.02
Superficial	61 (20.3)	41 (13.6)	0.03
Deep	25 (8.3)	18 (6.0)	0.26
Organ space	4 (1.3)	4 (1.3)	1.00
ASEPSIS score†			
Median	0.0	0.0	
IQR	0.0–10.0	0.0–4.0	
Rehospitalization for SSI — no. of patients (%)	21 (7.0)	13 (4.3)	0.15
Visit to ER or physician for wound-related sign or symptom — no. of patients/total no. (%)	57 (19.7)	31 (11.0)	0.004
Postoperative hospital length of stay — days			
Median	6.0 (5.0–8.0)	6.0 (4.0–8.0)	0.44
IQR			

E Bennet-Guerrero et al , NEJM 2010,



Collagène-gentamicine

Méta-analyse des essais randomisés en chirurgie colo-rectale



Heterogeneity: $I^2 = 0.81$;
 $Q = 26.51$; $p < 0.0001$

Conclusions

- Pansements de cathéters imprégnés de CHG :
 - Cathéters centraux de courte durée
 - Quel (Y a-t-il un) taux d'ILC acceptable ?
- Pansement à la gentamicine pour la prévention des ISO :
 - A réserver à l'infection où la contamination est per-opératoire ou postopératoire immédiate (chirurgie propre)
 - Etudes divergentes,
 - Mais principe séduisant
 - La technique d'insertion peut jouer un rôle
 - Ainsi que la physiopathologie de l'ISO
- Nécessité de l'évaluation des nouveaux DM, au même titre que les autres médicaments