

# Treatment of PJI in centers The French CRIOAc model

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  @FerryLyon 

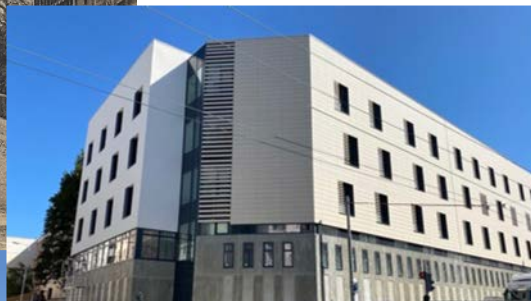
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Member of Executive Committee of the European Bone and Joint Infection Society (EBJIS)

Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

# I am infectious disease physician (with a PhD)



I have conflict of interest with the patients!



# Two major problems

**Implantable  
medical device  
(connected)**



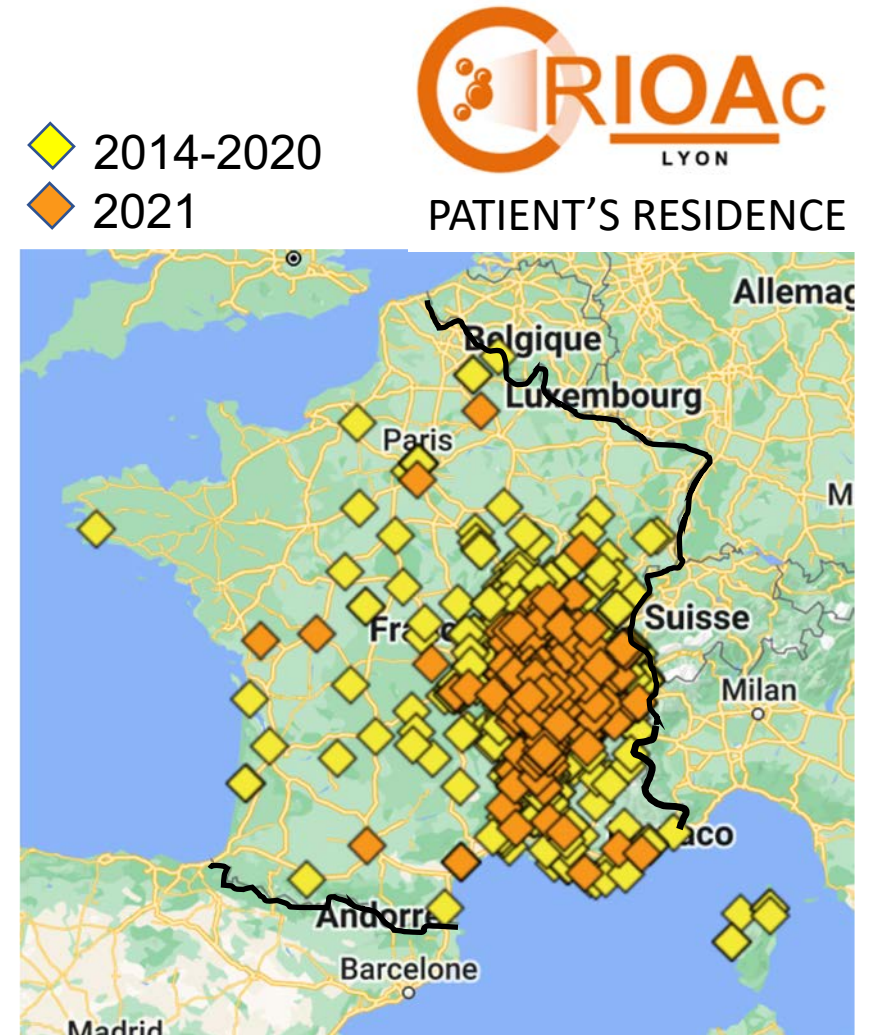
**Implant-associated  
infections**



**Antimicrobial  
resistance**

**Severe bacterial infections**  
(bone and joint, pneumonia, endocarditis, sepsis)

# Referral center for the management of complex bone and joint infections (BJI)

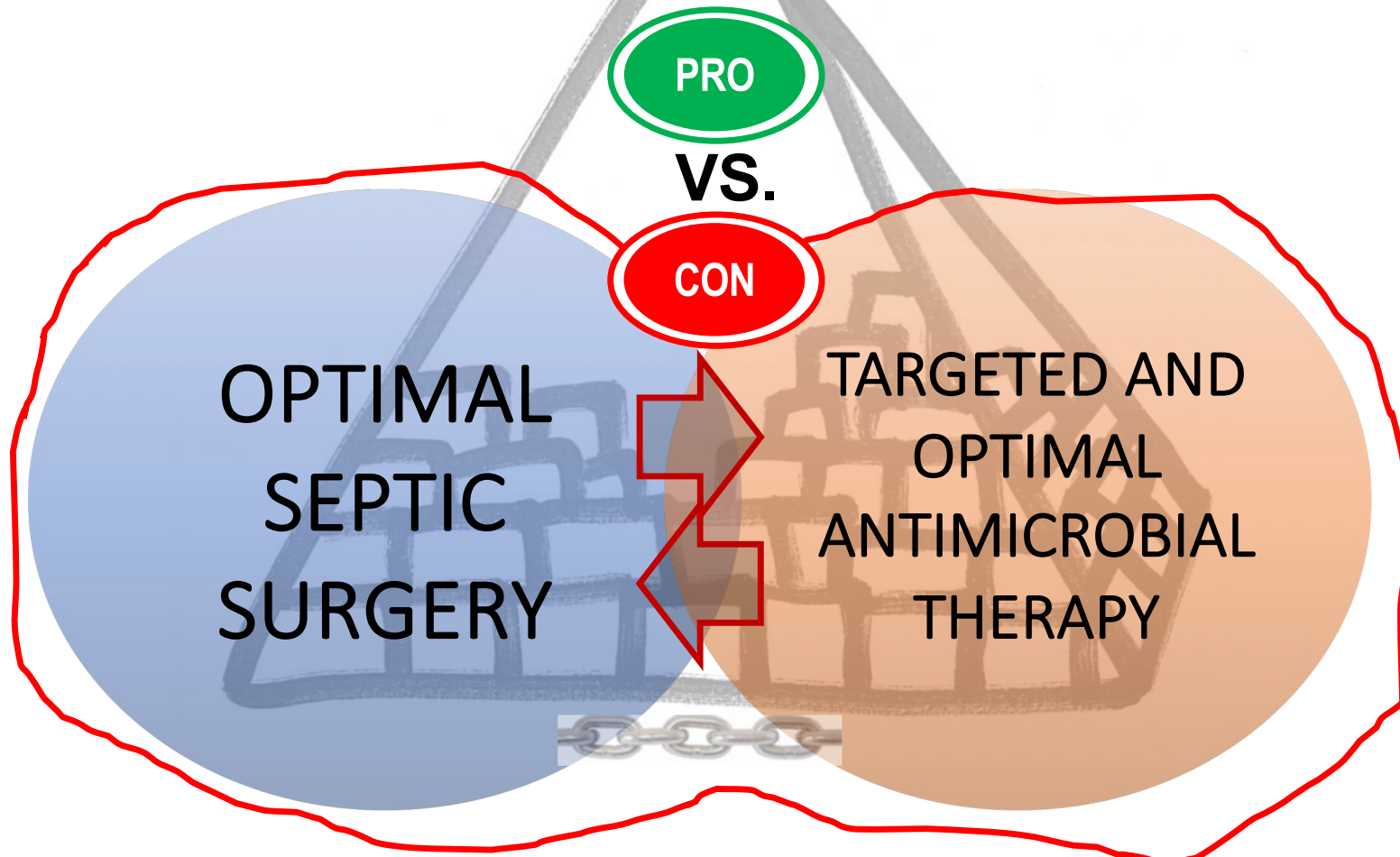




# Personalized medicine for BJI

## MULTIDISCIPLINAR MEETING

THE BEST INDIVIDUALIZED MEDICOSURGICAL STRATEGY



# Referral center for the management of complex bone and joint infections (BJI)

*Centre de Référence des Infections osteoarticulaires complexes*

Established by the French health ministry (DGOS) since 2009

## Why?

- Several plans against nosocomial infections in France
- Incidence of complex BJI is higher than expected
- It is associated with high morbidity, motor disability, cost and mortality
- Complete separation of the management (surgery, and then antibiotics)
- Wandering patients undergoing numerous suboptimal surgeries
- Need to concentrate complex patients to improve the knowledge and the care



# Referral center for the management of complex bone and joint infections (BJI)

*Centre de Référence des Infections osteoarticulaires complexes*

Established by the French health ministry (DGOS) since 2009

## How?

- Establishment of a call, each 5 years, to label expert hospitals
- The number is balanced between territorial coverage and expertise
- CRIOAc and « associated centers »
- Funding of a dedicated secured national website to perform multidisciplinary meetings
- Provision of a secretary and a study nurse to organize the performance of multidisciplinary meetings and to communicate

# Referral center for the management of complex bone and joint infections (BJI)

*Centre de Référence des Infections osteoarticulaires complexes*

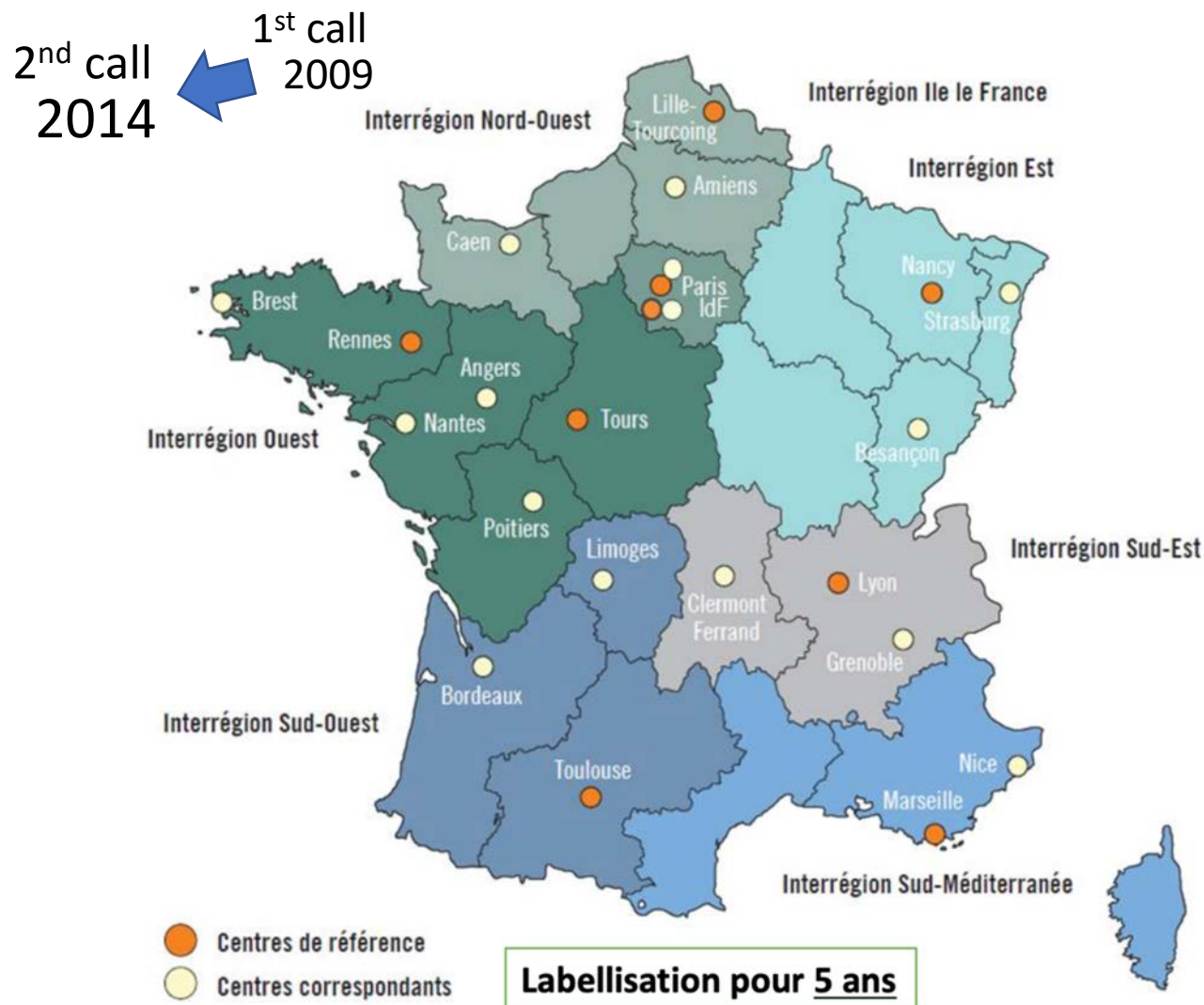
Established by the French health ministry (DGOS) since 2009

## In order to

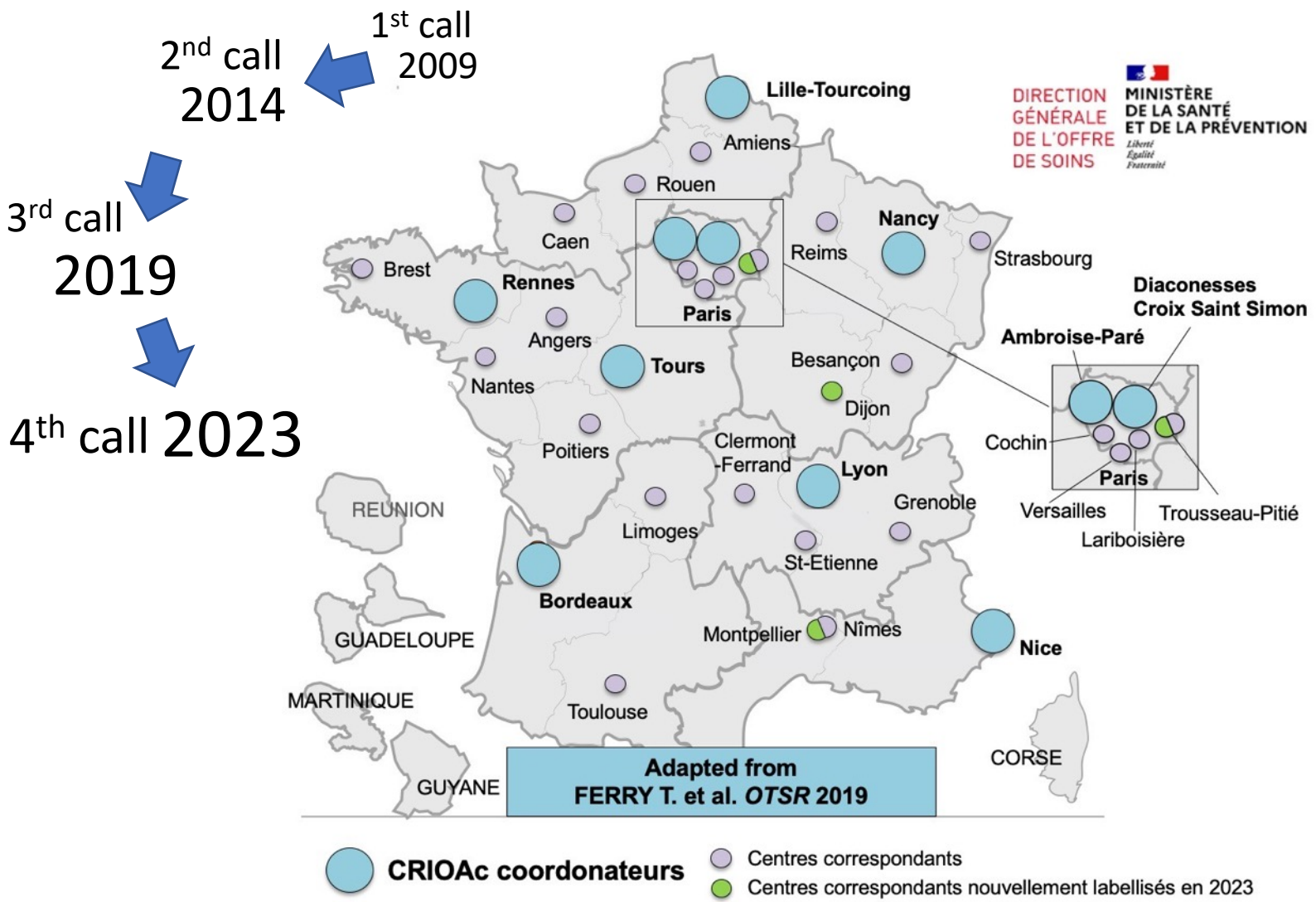
- Facilitate the multidisciplinary management of BJI
- Start the discussions before surgery
- Perform multidisciplinary meetings to define if the BJI is complex or not
- Concentrate the most difficult-to-treat patients and create expert teams
- Promote the research, innovations and their evaluations, and education in the field of BJI



# Referral center for the management of complex bone and joint infections (BJI)



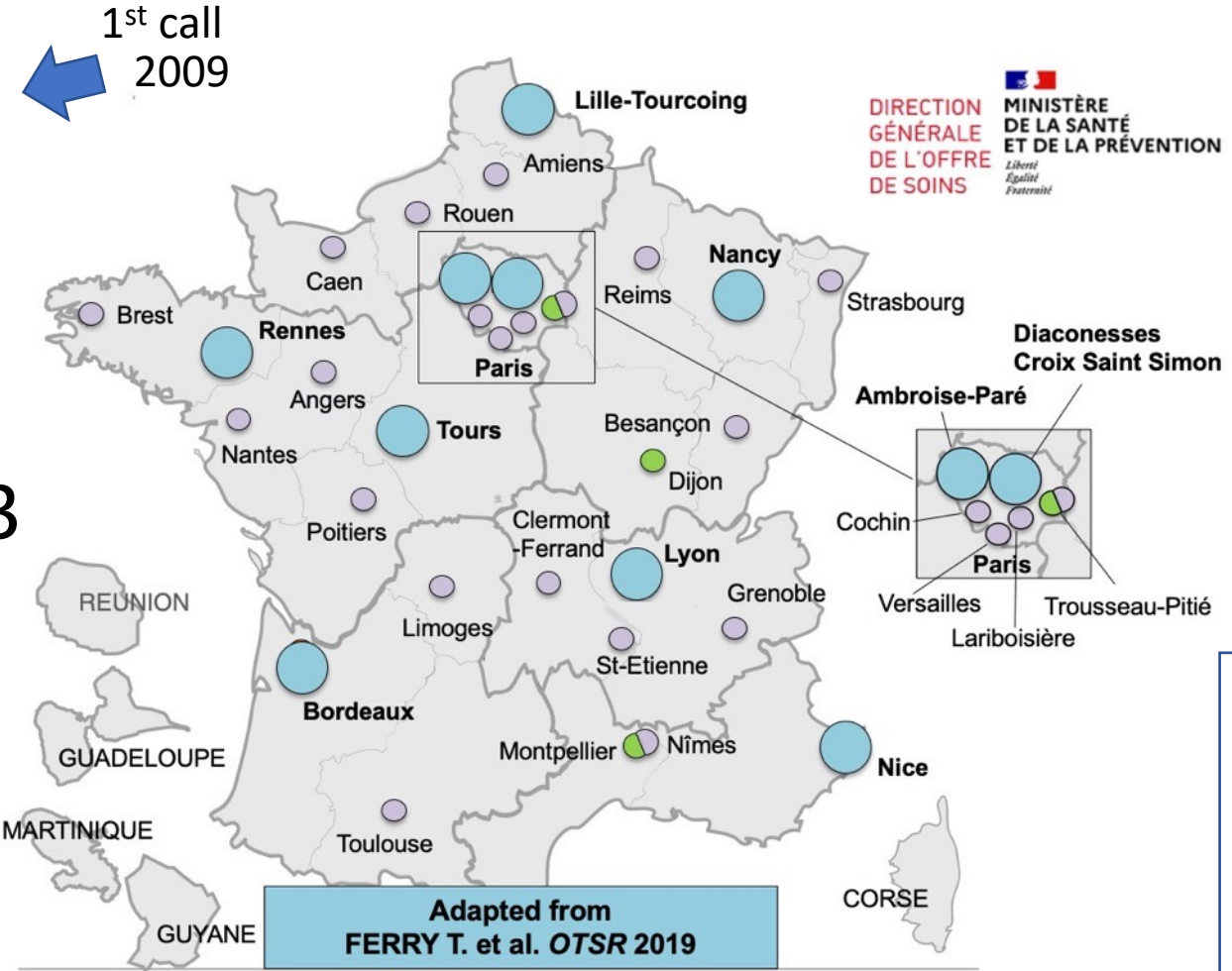
# Referral center for the management of complex bone and joint infections (BJI)





# Referral center for the management of complex bone and joint infections (BJI)

1<sup>st</sup> call 2009  
2<sup>nd</sup> call 2014  
3<sup>rd</sup> call 2019  
4<sup>th</sup> call 2023



Adapted from  
FERRY T. et al. OTSR 2019

● CRIOAc coordonateurs  
● Centres correspondants  
● Centres correspondants nouvellement labellisés en 2023



Health  
Ministry

**REFERRAL CRIOAc, n=9**  
**115 k€/year**

**ASSOCIATED CRIOAc, n=21**  
**45 k€/year**

**TOTAL BUDGET**  
**2 Million €/year**



**+ Hospital stay in surgery  
paid +12% more\***

\*if the BJI is considered to be complex by the multidisciplinary team before surgery



Healthcare  
Insurance

<https://si-ioa.sante.gouv.fr>

## A secured national website

- Design the website
- Secure the access (professional card)
- Secure the hosting of the data (medical data)
- Permit extractions (RGPD)
- Maintain, protect and update the system





<https://si-ioa.sante.gouv.fr>

# A secured national website



Sud-Est - CR - Hospices civils de Lyon - RCP Chirurgie Septique

MO  E, 72 ans





**Contexte de la RCP** Synthèse clinique Localisation/Microbiologie/Chirurgie

Episode : ☐ Premier épisode ☒ Rechute

Motif : ☐ Stratégie médico-chirurgicale  
☐ Bilan pré-thérapeutique  
☒ Réévaluation en cours de traitement  
☐ Deuxième temps de chirurgie après infection

Passage en recours/deuxième avis : ☒ Oui ☐ Non

**Précédentes fiches RCP**

Intitulé RCP	Date de passage	CR PDF
<input checked="" type="checkbox"/> HCL	15/05/2014	
<input checked="" type="checkbox"/> HCL	20/03/2014	
<input checked="" type="checkbox"/> HCL	16/01/2014	
<input checked="" type="checkbox"/> HCL	05/12/2013	

Page 1 sur 1

Page courante 1 - 5 sur 5

INFECTIOUS  
DISEASE  
PHYSICIAN

ORTHOPAEDIC  
SURGEON

**QUORUM**

MICROBIOLOGIST



M0 [redacted], 72 ans

Contexte de la RCP Synthèse clinique Localisation/Microbiologie/Chirurgie Antibiothérapie Finalisation et validation de la RCP

Age : 72 Poids actuel : 89 kg Taille : 175 cm IMC : 29.06

Dosage CRP : 25 mg/L

Score ASA : 3 - Patient avec anomalie systémique sévère

Créatininémie : 120 µmol/L Clairance de la créatinine : 52,5 mL/min/1,73m²

Comorbidités ou terrains interférents :

☒ Insuffisance rénale ☐ Insuffisance hépatique ☐ Insuffisance cardiaque

☐ Polypathologie ☐ Immunodépression ☐ Diabète

Justification :

Facteurs de risque :

☒ Traitement immunosupresseur ☐ Infection par le virus VIH ou par les virus des hépatites

☐ Cirrhose ☐ Néoplasie évolutive

☐ Chimiothérapie anti-cancéreuse ☐ Maladies auto-immunes et rhumatismes inflammatoires chroniques

☐ Rhumatisme inflammatoire chronique ☒ Drépanocytose

☒ Hémophile ☐ Transplantation d'organe

☐ Obésité morbide (IMC > 30) ☐ Tabagisme actif

☐ Diabète avec complication(s) ☐ Autre :

Si Autre, préciser :

Allergie connue aux antibiotiques : ☐

Résumé clinique :

Patiente vue à 3 semaines de l'implantation de la prothèse arthrode. Antibiothérapie probabiliste par TAZOCILLINE et LINEZOLIDE. Patiente sous TRIFUCAN au moins jusqu'à l'automne 2014. Cultures positives à Staphylocoque épidermidis multi résistant (2 prélèvements positifs uniquement en milieu liquide). Localement bonne cicatrisation.



M0  72 ans

Contexte de la RCP Synthèse clinique Localisation/Microbiologie/Chirurgie Antibiothérapie Finalisation et validation de la RCP

**Microbiologie**

Ajouter

Site

Genou

**Document site' créé le 09/12/2013 à 11:04 par Tristan FERRY**

Site : Genou Côté : ☐ Gauche ☒ Droit

Cadre nosologique : ☒ Prothèse ☐ Ostéite  
☐ Pseudarthrose ☐ Arthrite  
☐ Matériel d'ostéosynthèse ☐ Autres

**Microbiologie**

Microbiologie : ☒ Documenté fiable ☐ Non documenté ☐ Non contributif

Germe(s)

Staphylococcus epidermidis ☒ Avec résistance

Commentaire :

**PEC Chirurgicale**

Acte : -- Sélectionner --

Remarques : -- Sélectionner --

- Ablation de matériel
- Abstention chirurgicale contre indication
- Abstention chirurgicale non-indication
- Abstention chirurgicale refus du patient
- Amputation
- Arthrodèse
- Biopsie
- Changement prothèse 1 temps
- Changement prothèse 2 temps
- Changement prothèse partiel
- Espaceur

Fermer Enregistrer



M0  72 ans

Contexte de la RCP

Synthèse clinique

Localisation/Microbiologie/Chirurgie

Antibiothérapie

Finalisation et validation de la RCP

## Antibiothérapie

Abord veineux : ☐ Périphérique ☐ Cathéter central  
☐ Chambre implantable ☒ Picc Line  
☐ Absence d'abord veineux

## Prescription antibiothérapie pré-opératoire

☒ Non ☐ Oui

## Prescription antibiothérapie post-opératoire

☐ Non ☒ Oui

Molécule

Posologie

Durée prévisible

Voie d'administration

Daptomycine

850mg 1j sur 2

3 mois

☒ iv ☐ po ☐ sc

+

Tigécycline

50mg/12h

3 mois

☒ iv ☐ po ☐ sc

+

-

Péfloxacin

Pénicillines G

Pénicillines V

Pipéracilline

Pipéracilline tazobactam

Pristinamycine

Quinolone autre

Quinupristine +dalfopriline

Rifampicine

Sulfadiazine

Sulfaméthoxazole Triméthoprim

Teicoplanine

Ticarcline

Ticarcline ac clavulanique

Tigécycline





Sud-Est - CR - Hospices civils de Lyon - RCP Chirurgie Septique

MOR  72 ans

Contexte de la RCP Synthèse clinique Localisation/Microbiologie/Chirurgie Antibiothérapie Finalisation et validation de la RCP

IOA complexe : ☐ Non ☒ Oui

Critères de complexité

Critères : ☒ Echec de traitement antérieur ☒ Programme chirurgical  
☒ Terrain ☒ Microbiologie

Etablissement de prise en charge :

## Criteria of complexity

- Host :
  - Patients with severe comorbidities that limit the therapeutic program
- If the BJI is COMPLEX  
SURGICAL HOSPITAL STAY € +12%
- Surgical criteria :
  - BJI requiring bone resection and bone and/or soft-tissue reconstruction
- Relapse

# Referral center for the management of complex bone and joint infections (BJI)

## Does it work?



# Referral center for the management of complex bone and joint infections (BJI)





# Referral center for the management of complex bone and joint infections (BJI)

**Bedside multidisciplinary meetings during 1-day hospital stay**



# Referral center for the management of complex bone and joint infections (BJI)

Bedside multidisciplinary meetings during 1-day hospital stay



Orthopaedic surgeon



Plastic surgeon

Infectious diseases physician

Microbiologist

Blood test

Pharmacist

PK of antibiotics

Pharmacologist

Puncture

Psychologist

X-RAY

MRI

Anesthesiologist

CT-SCAN

Complex Bandage



# Referral center for the management of complex bone and joint infections (BJI)



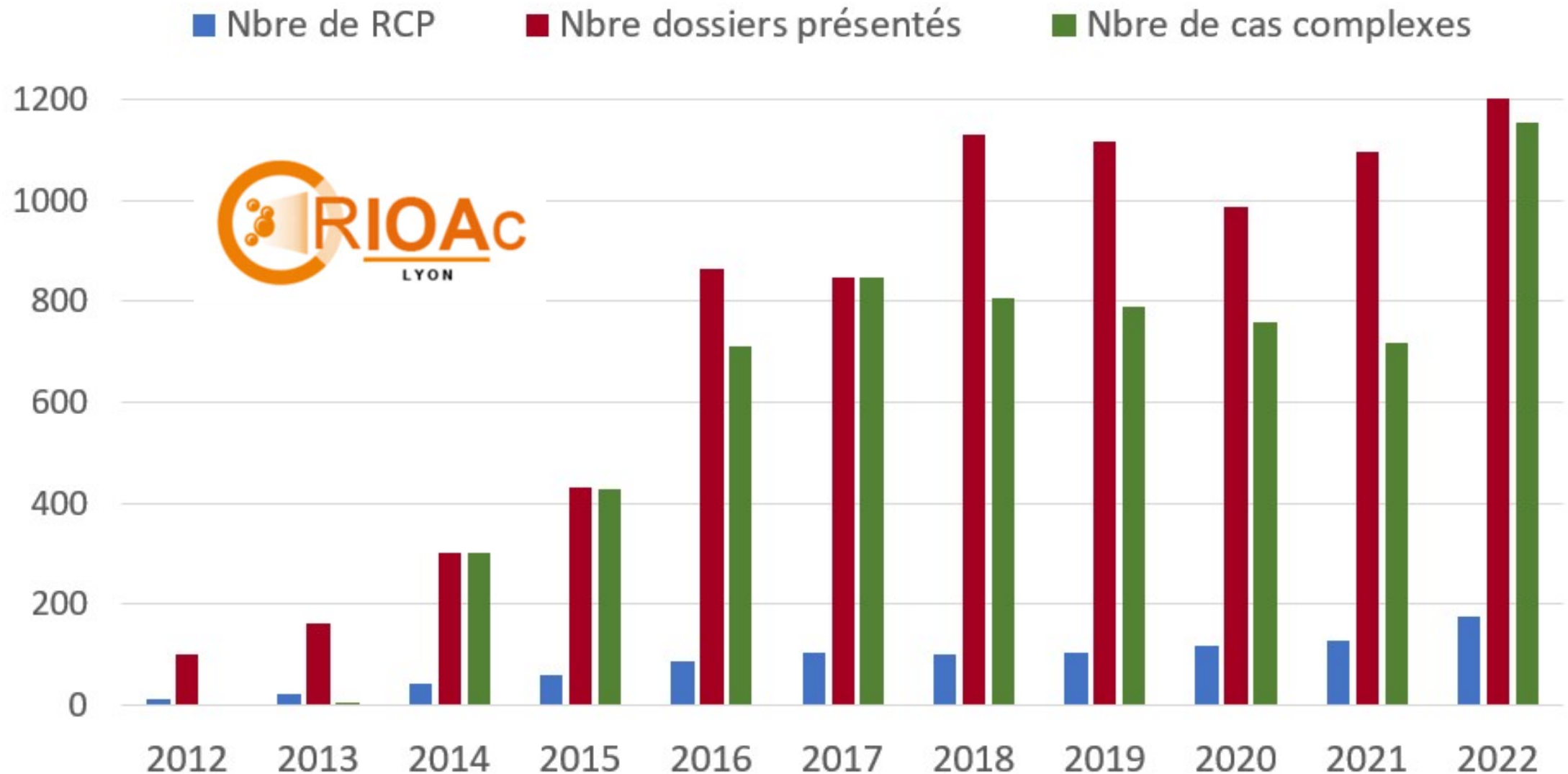
LE CENTRE ESPACE PATIENT ESPACE PRO RECHERCHE ENSEIGNEMENT

Aujourd'hui ◀ ▶ décembre 2023 Imprimer Semaine Mois Planning

lun.	mar.	mer.	jeu.	ven.	sam.	dim.
27	28	29	30	1 déc.	2	3
RCP Crâne VisioRCP GHN VisioRCP Thérap	RCP HEH	IMDT Armenia	RCP HDJ VisioRCP CHLS			
4	5	6	7	8	9	10
RCP Rachis VisioRCP GHN VisioRCP Thérap	RCP HEH RCP Massif Facia		RCP HDJ			
11	12	13	14	15	16	17
RCP Crâne VisioRCP GHN VisioRCP Thérap	RCP HEH	IMDT Armenia	RCP HDJ VisioRCP CHLS			
18	19	20	21	22	23	24
RCP Rachis VisioRCP GHN VisioRCP Thérap	RCP HEH		RCP HDJ			
25	26	27	28	29	30	31
	RCP HEH		RCP HDJ			

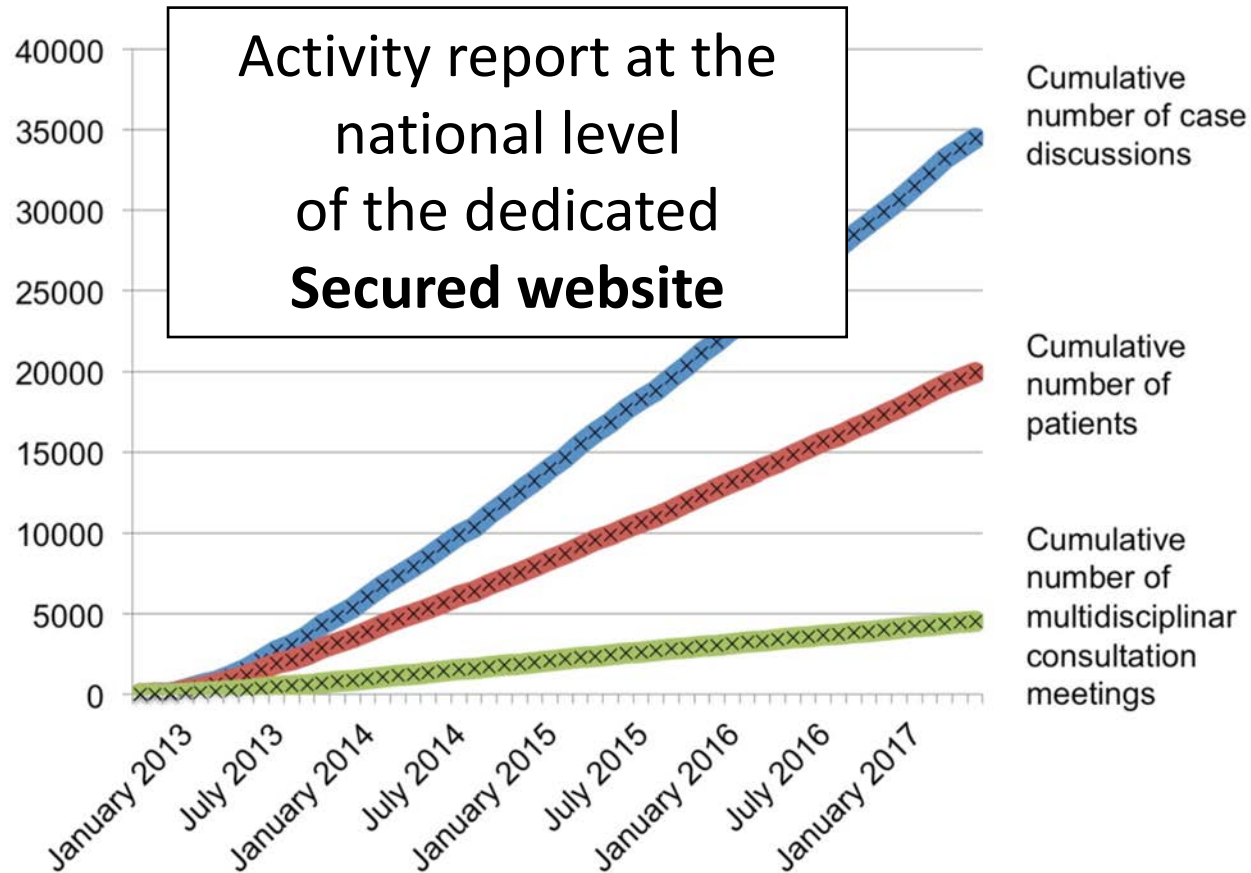
+ Google Agenda

# Referral center for the management of complex bone and joint infections (BJI)





Original article

## The CRIOAc healthcare network in France: A nationwide Health Ministry program to improve the management of bone and joint infection



### Network presented:

National Orthopaedic  
SIOT meeting in 2018 

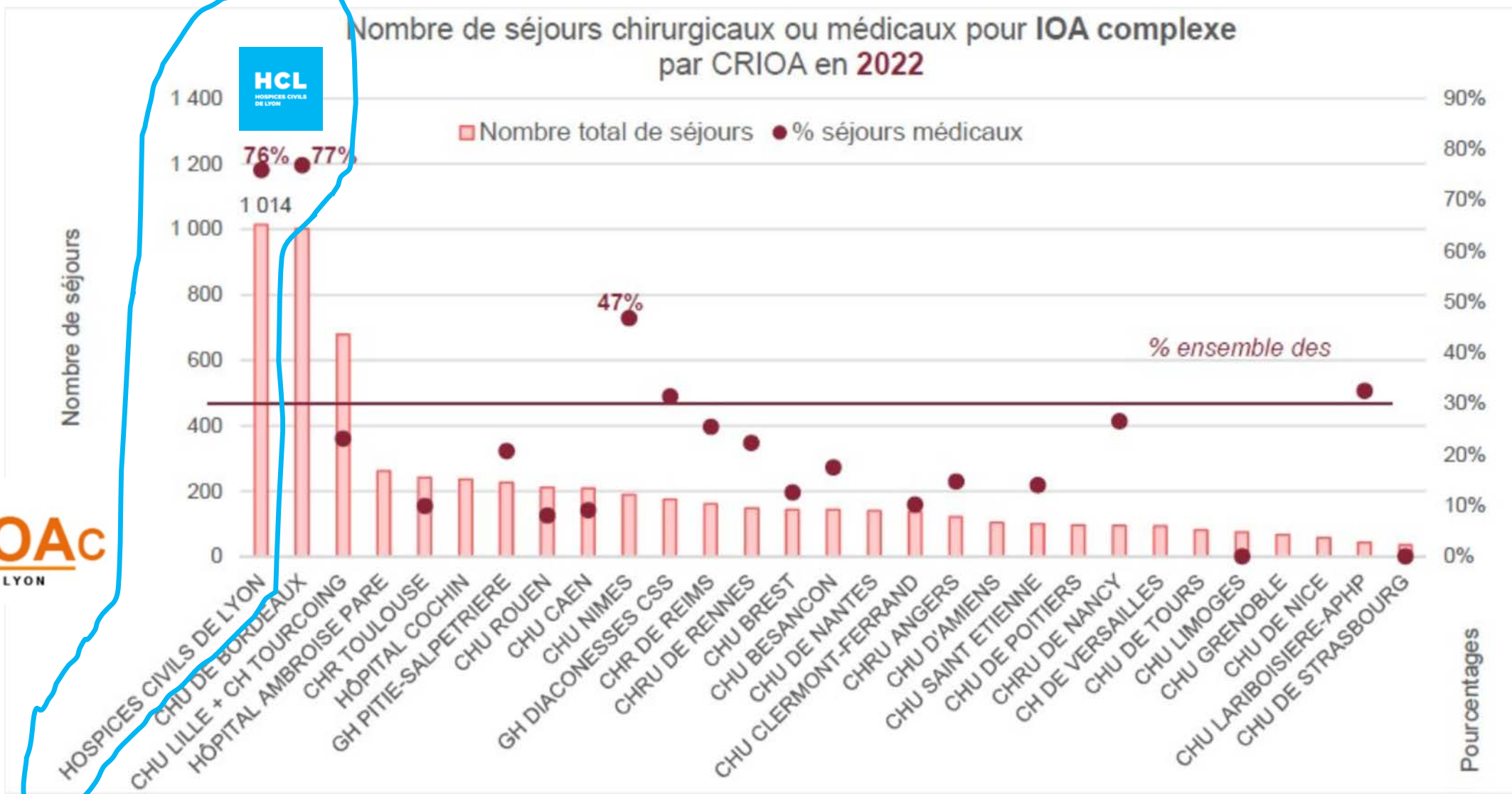
National Swiss ID   
SSI-SSHH meeting in 2020

National Orthopaedic   
British Orthopaedic association in 2021

National Orthopaedic   
AE-Kongress in 2023

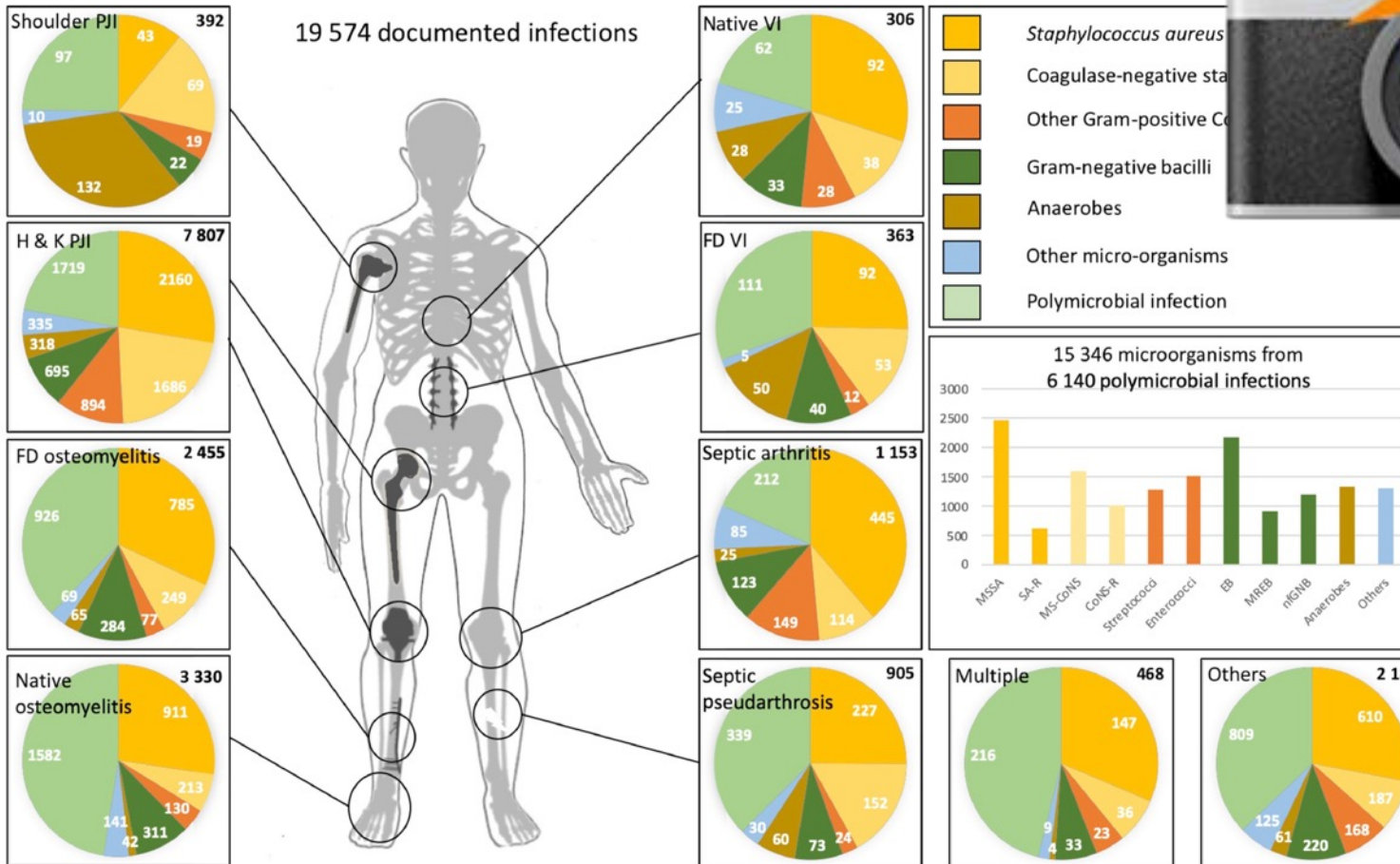


# Referral center for the management of complex bone and joint infections (BJI)



# Referral center for the management of complex bone and joint infections (BJI)

Lemaignen et al. J Infect 2021




 G4 HOPITAUX UNIVERSITAIRES  
 AMIENS  
CAEN  
LILLE  
ROUEN


 CRIOAC  
 Grand Est

CENTRES DE RÉFÉRENCE DES INFECTIONS  
OSTÉO-ARTICULAIRES COMPLEXES  

 CRIOAC  
 ILE DE FRANCE

CENTRES DE RÉFÉRENCE  
POUR LES INFECTIONS OSTÉO-ARTICULAIRES COMPLEXES  
DU GRAND OUEST  

 CRIOGO


 CRIOAC  
 LYON


 Crioac  
 GSO

# Referral center for the management of complex bone and joint infections (BJI)

## National scientific committee

**T. FERRY (Infectiologist Lyon), President**

J. COURJON (Infectiologist, Nice)

G. LE MOAL (Infectiologist, Poitiers)

S. MARMOR (Orthopaedic surgeon, Paris)

J.-Y. JENNY (Orthopaedic surgeon, Strasbourg)

H. COMMON (Orthopaedic surgeon, Rennes)

V. DUBOIS (Microbiologist, Bordeaux)

A.-L. ROUX (Microbiologist, Paris)

Promotion of the  
research and  
innovation

Multidisciplinary  
expertise

Specialists from  
each region

Improve the  
network

Update of the  
secured web system

Evolution of  
the system

Requested for  
the next call

Database  
management

Promotion of  
education

Congress  
every 2 years

Post graduate  
national diploma

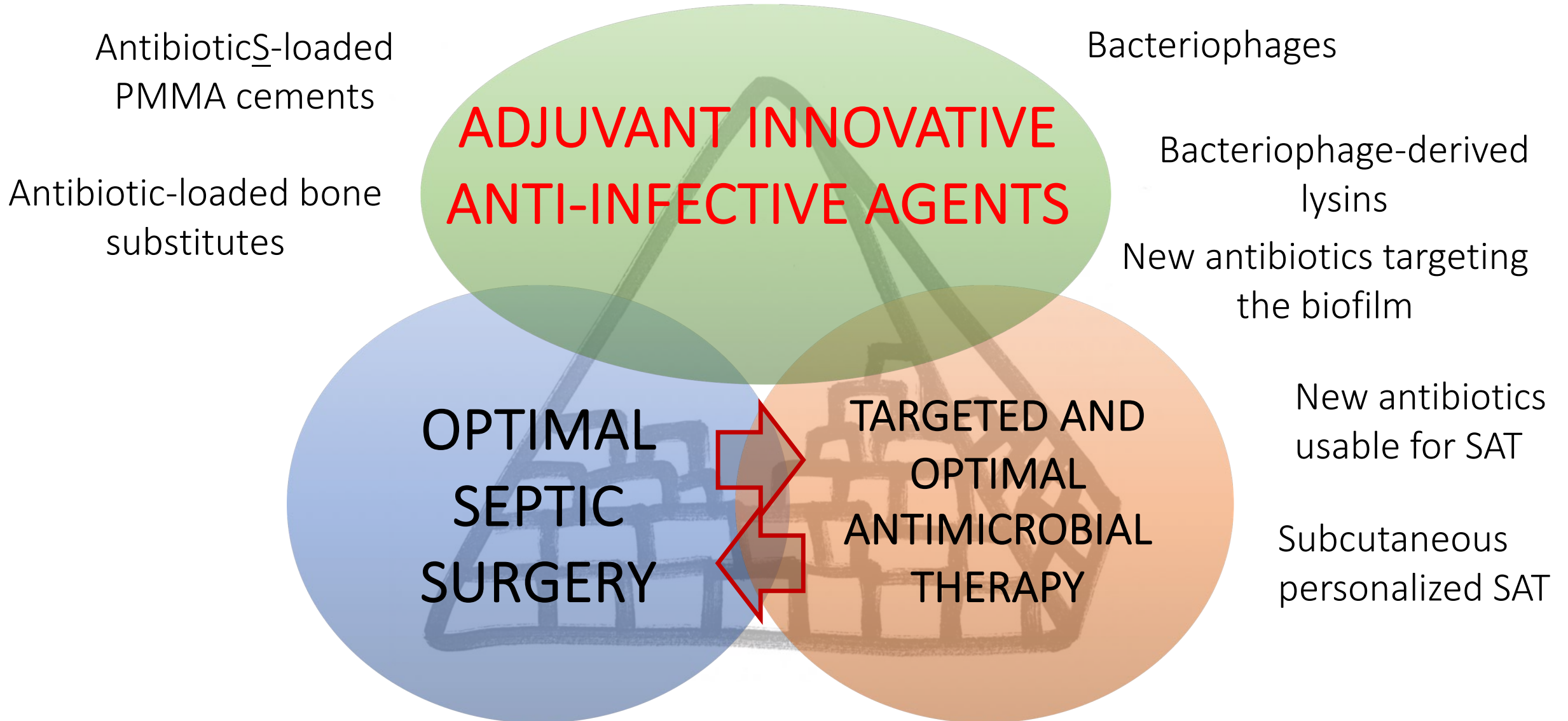
Feasibility  
analysis

Epidemiology  
analysis

Academic  
research project

Clinical trials

# Personalized medicine for BJI



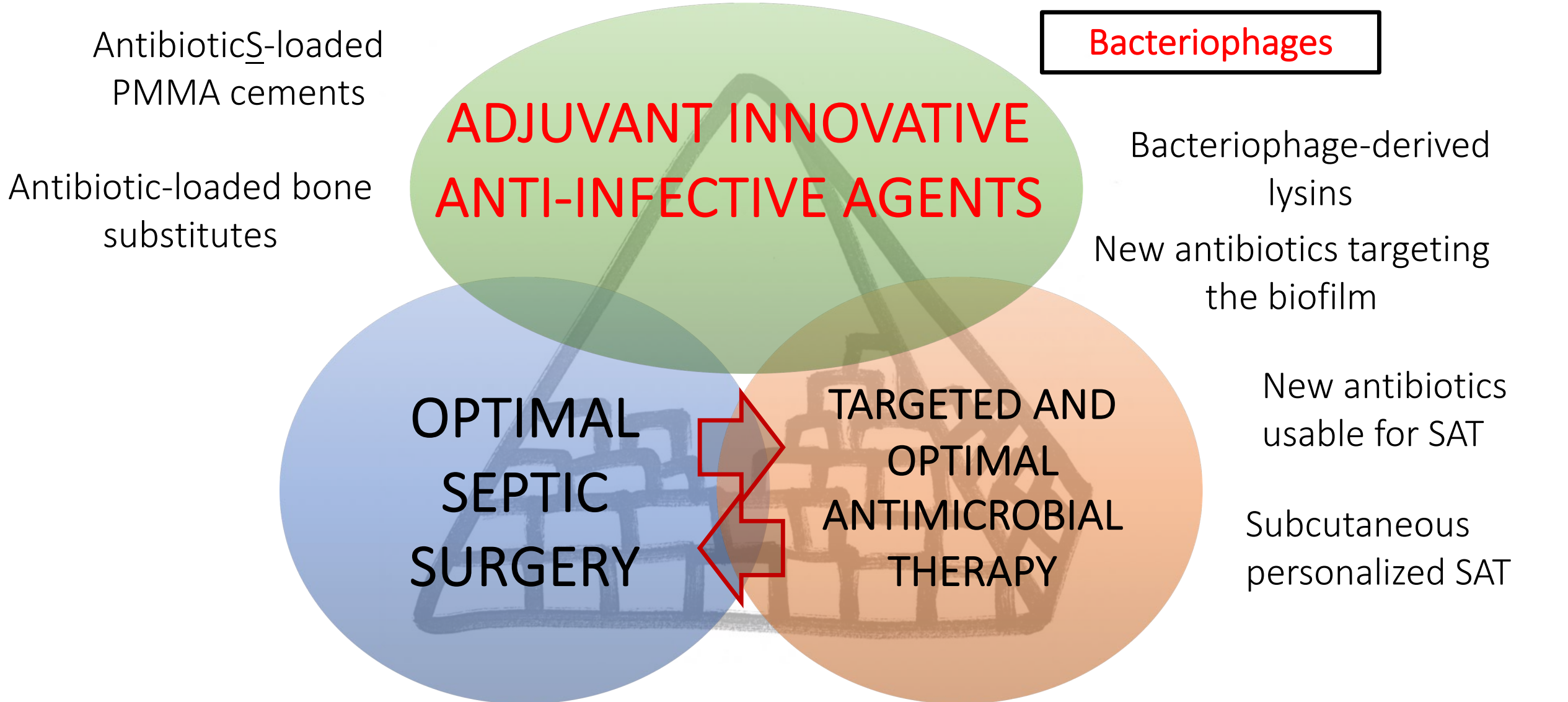


# Referral center for the management of complex bone and joint infections (BJI)

## Ongoing Randomized Clinical trials in the CRIOAc network :

- **PhagoDAIR I**, Phages in patients with PJI
- **CONVICTION** Study (CERAMENT® G), Stage III long-bone osteomyelitis
- **RIFAMAB** Study, rifabutin versus rifampin in patients with staphylococcal PJI
- **RIFACUTE** Study, addition of rifampin in *C. acnes* PJI
- **SYNBIOSE-H** Study, 1-stage with DAC® gel versus 2-stage in PJI

# Personalized medicine for BJI



SAT, Suppressive Antimicrobial Therapy

# Bacteria have also their pandemic!



World Health  
Organization

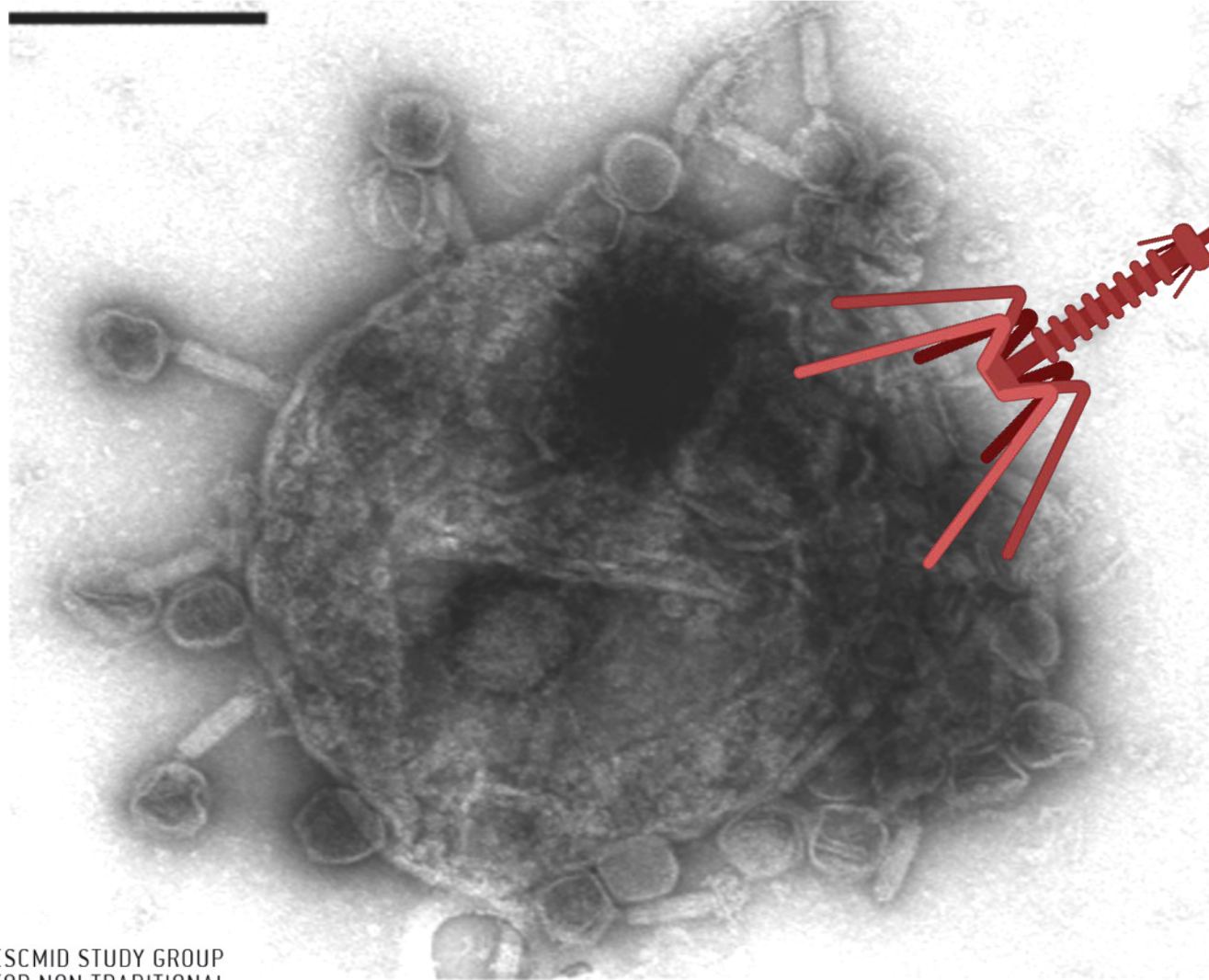
**N**on-**T**raditional  
**A**ntibacterial  
therapy



ESGNTA

European Society of Clinical Microbiology and Infectious Diseases

ESCMID STUDY GROUP  
FOR NON-TRADITIONAL  
ANTIBACTERIAL THERAPY



PHAGE<sub>in</sub>**LYON**  
*Clinic*

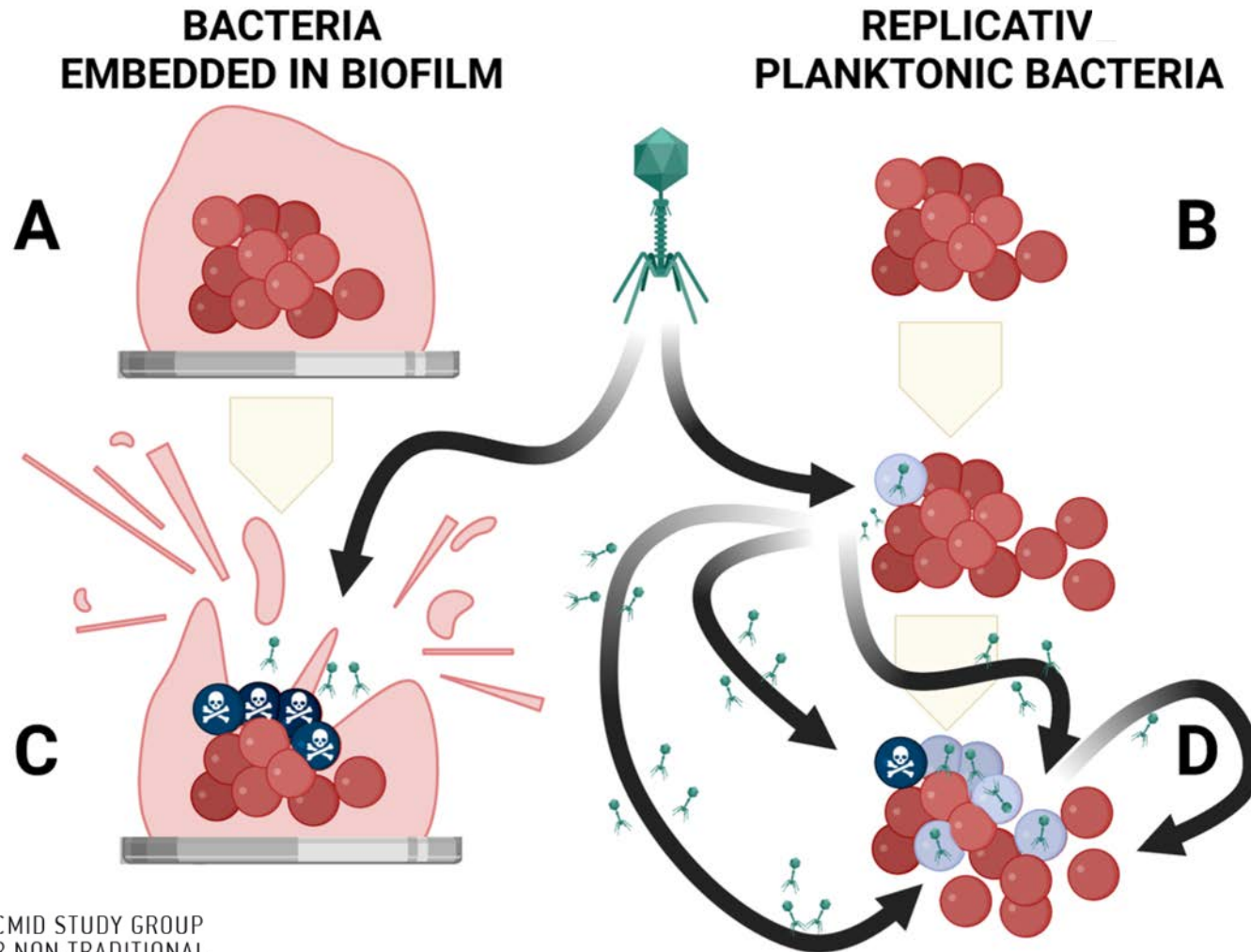
Merabishvili et al. *PloS ONE* 2009

# Bacteria have also their pandemic!



World Health Organization

**N**on-**T**raditional  
**A**ntibacterial  
therapy



PHAGE<sub>in</sub>**LYON**  
*Clinic*



ESGNTA

ESCMID STUDY GROUP  
FOR NON-TRADITIONAL  
ANTIBACTERIAL THERAPY

European Society of Clinical Microbiology and Infectious Diseases

*T. Ferry. Springer 2023 In press*



# Clinical case (not published; 21<sup>th</sup> treated patients)



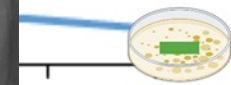
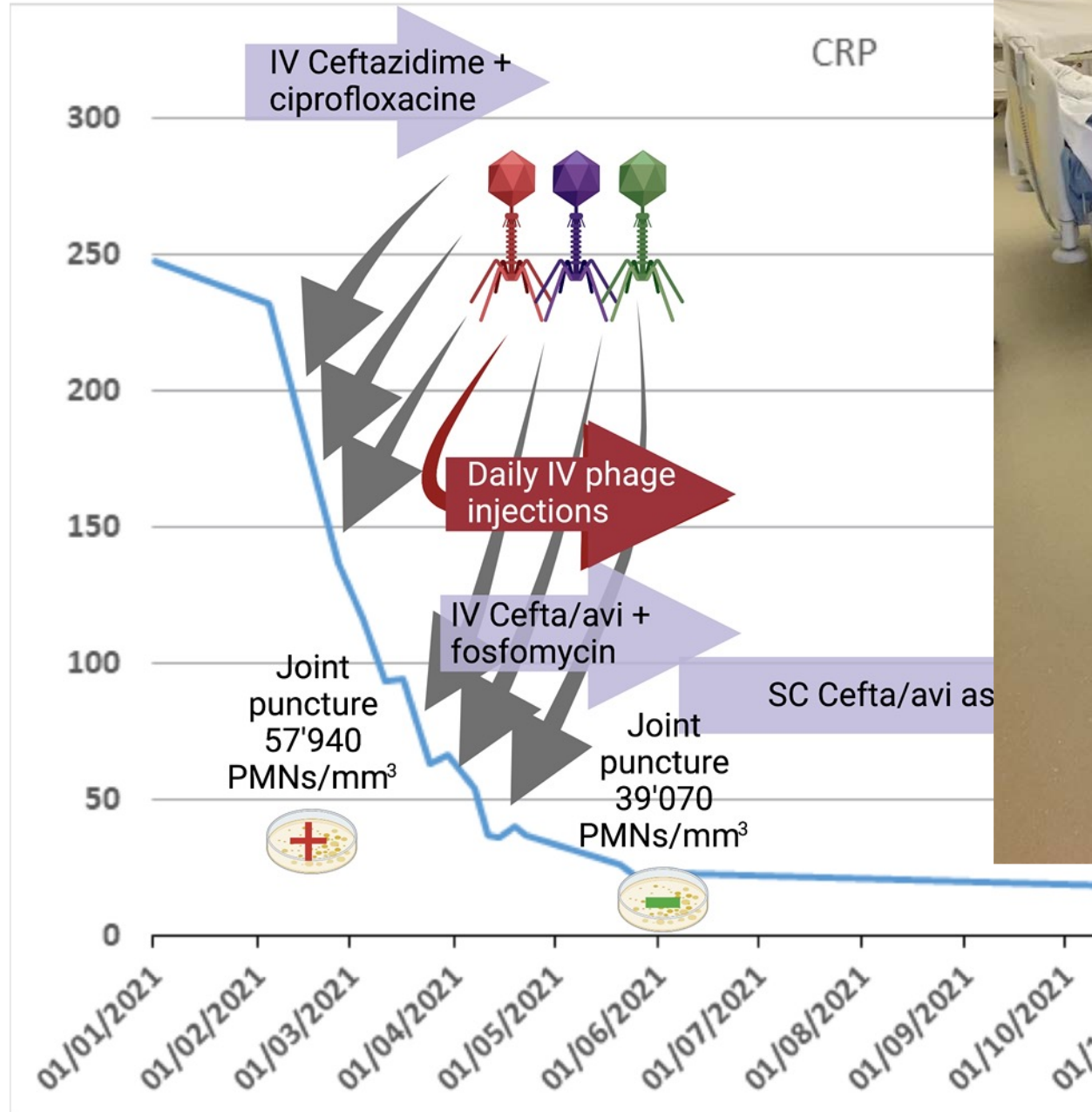
72-year-old man

**Relapsing *P. aeruginosa* prosthetic right hip PJI with femoral osteomyelitis and large abscess**

Severe chronic inflammation

Disarticulation was proposed





# Clinical case (3<sup>rd</sup> treated patient)

Arthroscopic DAIR with phages to salvage  
*P. aeruginosa* prosthetic knee infection



88-year-old man

Relapsing *P. aeruginosa* prosthetic left knee infection

End-stage cardiac failure

Contraindicated to open DAIR



PHAGE<sup>in</sup>LYON  
Clinic



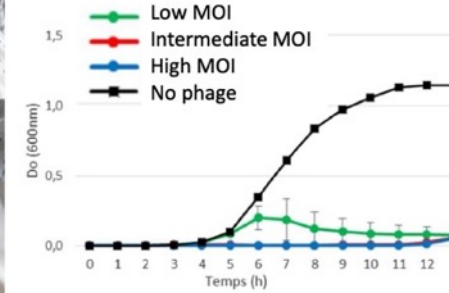
A



Left PKI with purulent joint effusion

B

Phage 1450



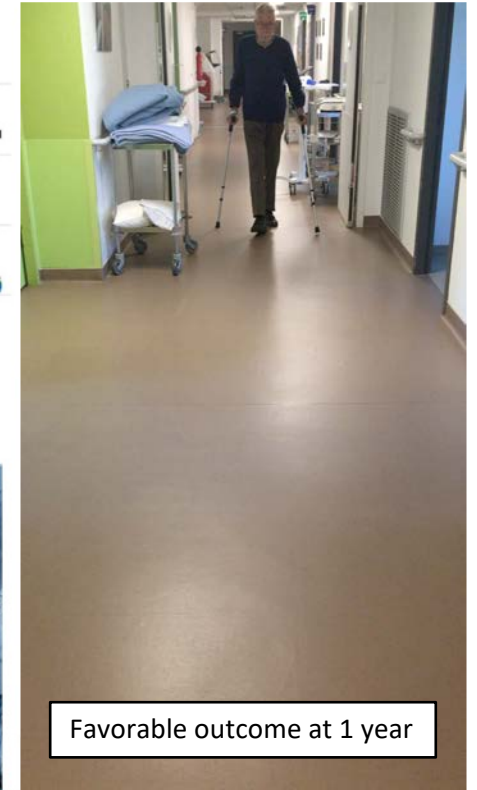
Phagogram (Killing assay)



Arthroscopic DAIR

C

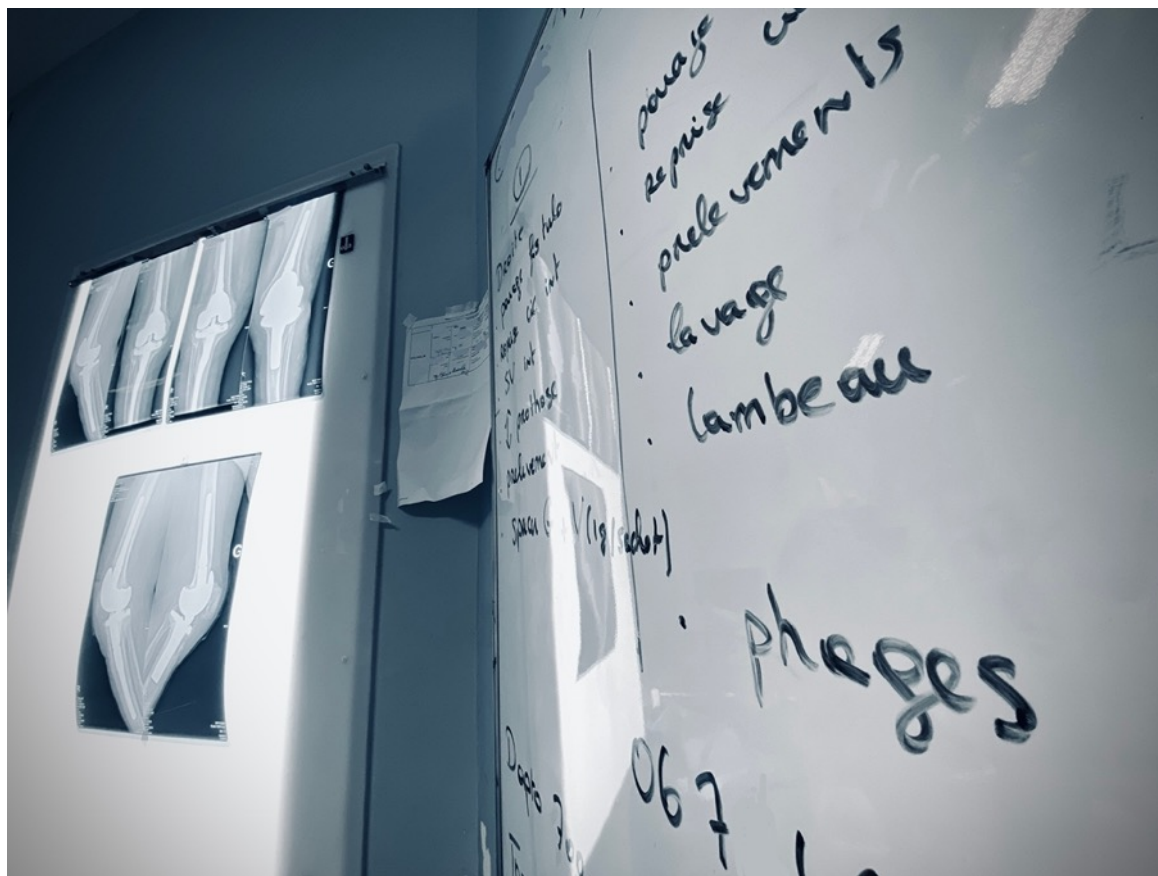
D



Favorable outcome at 1 year



# #PhagoDAIR procedure





# #PhagoDAIR procedure



>1 billion of **active viruses** infecting *S. aureus* in a syringe

# PhagoDAIR I

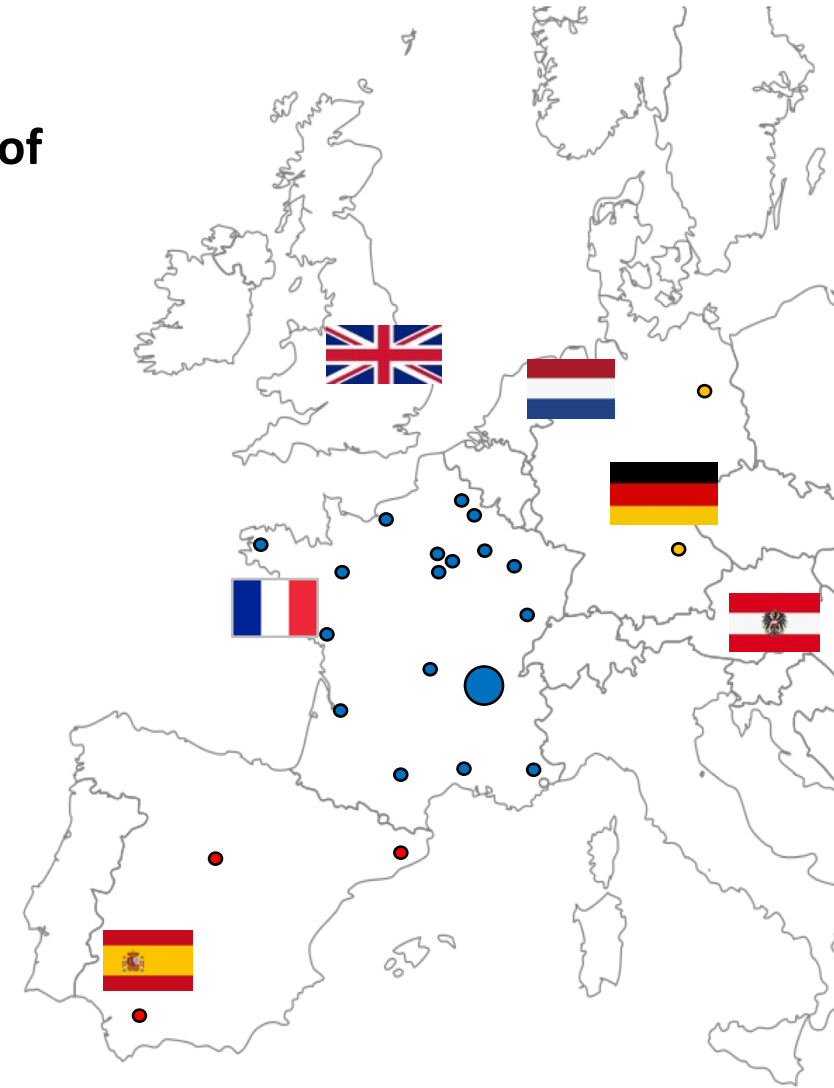
A Pilot, Multicenter, Randomized, Non-Comparative, Double-Blind Study of Phage Therapy in Patients with Hip or Knee PJI due to *S. aureus* Treated with DAIR and Antibiotic Therapy

## Inclusion Criteria

1. *S. aureus* monomicrobial knee or hip PJI with clinical signs of infection with indication of DAIR and Suppressive Antibiotics Therapy (SAT).
2. Phagogram displaying the susceptibility of the strain to at least one of the anti-*Staphylococcus aureus* bacteriophages

## Primary Objective

To estimate the rate of clinical control of infection at Week 12 $\pm$ 2 which will allow to calculate the sample size for future comparative studies.



**PHAXIAM**

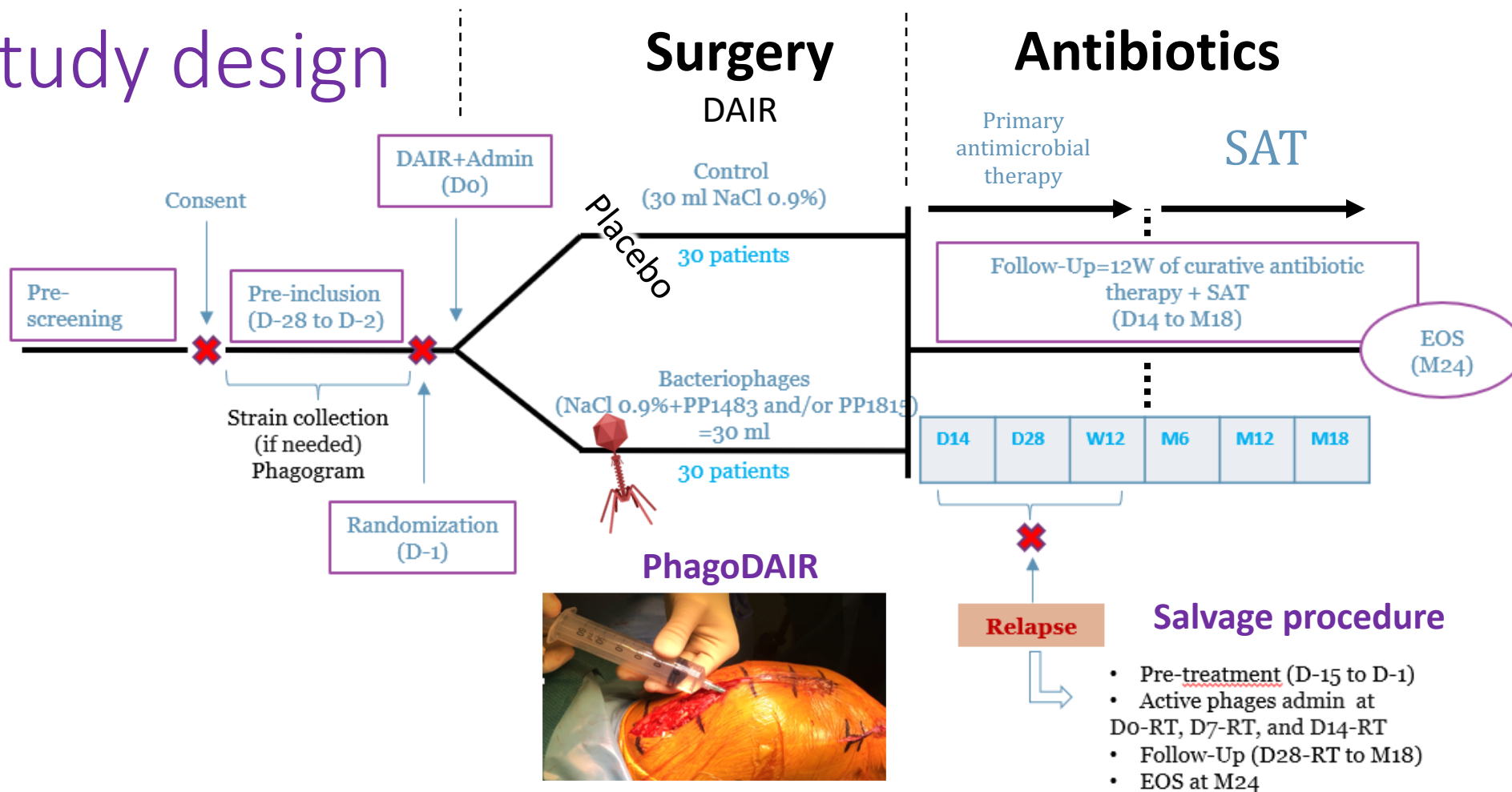
Ex-  **PHERECYDES**  
PHARMA



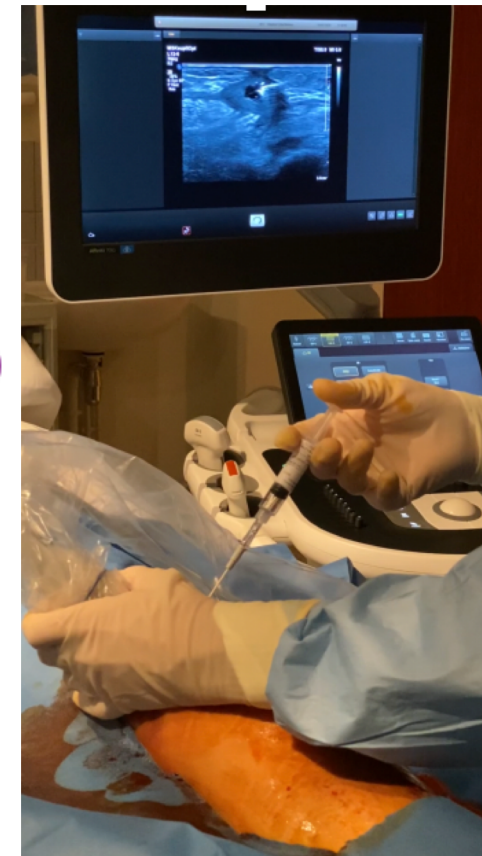
# PhagoDAIR I

A Pilot, Multicenter, Randomized, Non-Comparative, Double-Blind Study of  
Phage Therapy in Patients with Hip or Knee PJI due to *S. aureus*  
Treated with DAIR and Antibiotic Therapy

## Study design



## Salvage procedure





## **P** Bone and joint infections: Lyon becomes the national expert center for phage therapy

The reference center for complex bone and joint infections, based at the Hospices Civils de Lyon, will centralize all requests concerning this last resort treatment, using viruses against resistant bacteria.

Le Progrès – 23 Feb. 2023 at 17:51 | updated 23 Feb. 2023 at 18:08 – Reading time: 2 min



National online  
multidisciplinary meetings



Dedicated to innovative  
anti-infective therapies



**You are thinking about one of your patient who could be a candidate for phage therapy?**

**Online international multidisciplinary meetings each Monday on phage therapy in patients with complex PJI**

Chronic hip or knee PJI  
*S. aureus* or *P. aeruginosa*  
Conservative approach

**Qualifiable for**

- **Compassionate use?**
- **Clinical trial?**



[HCR.REFERENCE-IOA@chu-lyon.fr](mailto:HCR.REFERENCE-IOA@chu-lyon.fr)

# Conclusion



- Creation of regional reference centers in France (funded by health ministry) transformed the patient approach
- Personalized clinical care is the base of the pyramid for the management of complex BJI with bedside multidisciplinary meeting
- Infectious Disease physicians have potential great roles:
  - Can help to keep the function!
  - Have to develop and propose adjuvant personalized innovative anti-infective agents for selected relevant indications
- Phages have a real potential in prosthetic-joint infection
- Need for industrial and academic developement of therapeutic phages (discovery, banking, susceptibility testing) in connection with health care authorities
- Need to perform clinical trials to evaluate the ability of these innovations to improve the outcome





# Lyon BJI Study group



**Coordinator: Tristan Ferry**

**Infectious Diseases Specialists – Tristan Ferry**, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Poudroux, Pierre Chauvelot, Paul Chabert, Johanna Lippman, Evelyne Braun

**Surgeons – Sébastien Lustig**, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schmidt, Elliot Sappey-Marinier, Quentin Ode, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Aram Gazarian, Arnaud Walch, Antoine Bertani, Frédéric Rongieras, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person, Samuel Prive, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal;

**Anesthesiologists – Frédéric Aubrun**, Mikhail Dziadzko, Caroline Macabéo, Dana Patrascu;

**Microbiologists – Laetitia Beraud**, Tiphaine Roussel-Gaillard, Céline Dupieux, Camille Kolenda, Jérôme Josse;

**Imaging – Fabien Craighero**, Loic Boussel, Jean-Baptiste Pialat, Isabelle Morelec;

**PK/PD specialists – Michel Tod**, Marie-Claude Gagnieu, Sylvain Goutelle;

**Clinical research assistant and database manager– Eugénie Mabrut**

## PHAGE<sub>in</sub>LYON Clinic

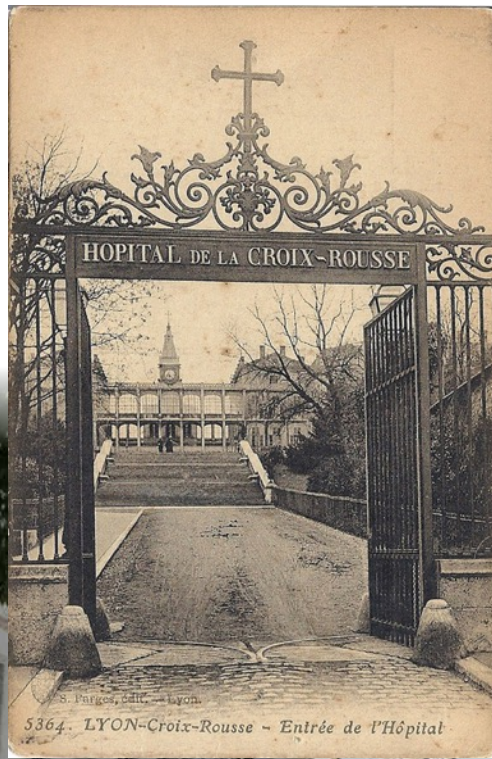
Acknowledgments to ANSM, Phaxiam, and QAMH!

**Coordinator: Tristan Ferry**

Tristan Ferry, Myrtille Le Bouar, Gilles Leboucher, Thomas Briot, Camille Kolenda, Tiphaine Roussel-Gaillard, Karine Dallosto



# Croix-Rousse Hospital







# Join us in Barcelona in 2024!

26-28 SEPTEMBER  
2024

The 42nd Annual meeting of  
the European Bone & Joint  
Infection Society

BARCELONA, SPAIN





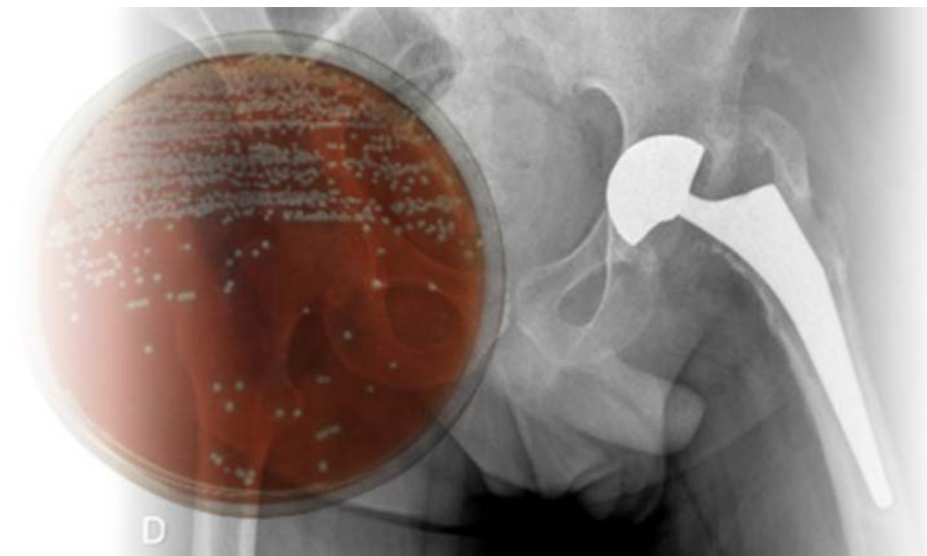
<https://www.crioac-lyon.fr/>



Lyon BJI  
study CrioAc LYON group



- Published cases
- Open acces papers
- All thesis in pdf
- All recommendations
- Newsletter



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