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**Original article**

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

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## **Abstract**

### Background:

Bone and joint infections (BJIs) have a major clinical and economic impact in industrialized countries. Its management requires a multidisciplinary approach, and a great experience for the most complicated cases to limit treatment failure, motor disability and amputation risk. To our best knowledge there is not currently national specific organization dedicated to manage BJI. Is it possible to build at a national level, a network involving orthopaedic surgeons, infectiologists and microbiologists performing locally multidisciplinary meetings to facilitate the recruitment and the management of patients with complex bone and joint infection in regional centers?

### Hypothesis:

A national healthcare network with regional labeled centers creates a dynamic that improves the recruitment, the management, the education, and the clinical research in the field of complex BJI

### Patients and Methods:

We describe the history of this unique national healthcare network and how it works, specify the missions confided to the CRIOAc, evaluate the activity of the network over the first decade, and finally discuss perspectives.

### Results:

The labelling of 24 centers in the CRIOAc network allowed for a meshing of the territory, with the possibility of management of complex BJI in each region of France. A dedicated secure national online information system was designed and used to facilitate decision-making during multidisciplinary consultation meetings. Since October 2012 to June 2017, 4,553 multidisciplinary consultation meetings have been performed in the structures belonging to the network, with 34,607 cases discussed in 19,961 individual. Prosthetic joint infections represented 38% (7,585/19,961) of all BJIs. Among all the cases discussed, the rate of complexity was of 61% (21,110/34,607) (related

to antibiotic resistance, infection recurrence, patient co morbidities). A national scientific meeting was created and a national postgraduate diploma in the field of BJI was launched in 2014. The promotion of education, clinical research and interactivity between each academic discipline and between each labeled centers across the country has synergized the strengths and have greatly facilitated the management of patients with BJI.

Discussion:

The setting up of the CRIOAc network in France took time, and has a cost for the French Ministry of Health. However, this network has greatly facilitated the management of BJI in France, and allowed to concentrate the management of complex BJI in centers that have significantly gained skills. There is, to our knowledge, no other exemple of such nation-wide network in the field of BJI.

Level of Evidence : IV, case series without control group

Key Words: Bone and joint infection; Osteomyelitis; Reference center; Network; Antibiotherapy

## 1. Introduction

Different kinds of bone and joint infection (BJI) have been described, with correspondingly different therapeutic strategies and prognoses. Some of them, such as uncomplicated childhood osteomyelitis, are easy to treat, requiring short-course antimicrobial therapy without surgery. Others, such as implant-associated BJI, a very heterogeneous group of BJIs, are more complex to treat, as eradication of the pathogen is challenging [1-6]. It has been proven that the implementation of a surgical site infection surveillance protocol reduces the incidence of surgical site infection such as post-operative prosthetic joint infections [7]. However, the risk of post-operative infection still persists, especially in patients that cumulate several risk factors for infection such as age, obesity, diabetes, smoking and iterative prosthesis replacement [8]. In such infected patients, it is widely recognized in the literature that team-work is required to personalize disease management, determine optimal medico-surgical strategy, and limit treatment failure, motor disability and amputation risk [9]. Several multidisciplinary groups have formed in the major hospital-university hospitals in Europe, but no national network structuring has been implemented, except in France. As a result, the management of BJI was included in the 2<sup>nd</sup> (2005-2008) French national plan to combat nosocomial infection. It is a question of improving management by bringing together in a single reference center the competencies of the various specialties concerned, inspired by the reference centers on rare disease that have been in operation in France for several years. Care quality is basically founded on an organizational set-up ensuring rapid access to diagnosis and appropriate treatment. This involves coordination between the main specialties: surgery, infectious diseases, microbiology, radiology and the general practitioner. Thus, in 2008, the General Directorate for Provision of healthcare (*Direction Générale de l'Offre de Soins: DGOS*) of the French Health Ministry (*Ministère des Affaires Sociales et de la Santé*) founded a network of regional centers, with particular rules and funding, to determine which BJI are complex and to facilitate their management: the CRIOAcs (*Centres de Référence des Infections Ostéoarticulaires complexes*). It first approved first eight (and soon nine) CRIOAcs, as well as approval of

“corresponding centers” (CCs), in order to provide the most appropriate care possible throughout the national territory.

The aims of the article were: 1) to describe the history of this unique national network and how it works; 2) to specify the missions confided to the CRIOAcs; 3) to evaluate the activity of the network over the first decade; 4) to discuss perspectives; to finally answer the question: is it possible to build at a national level, a network involving orthopaedic surgeons, infectiologists and microbiologists performing locally multidisciplinary meetings to facilitate the recruitment and the management of patients with complex bone and joint infection in regional centers?

## 2. Patients and Methods

### 2.1 Burden of BJI

A national study using the national health administration data-base (*Programme de Médicalisation des Systèmes d'Information: PMSI*) demonstrated that BJIs have a major clinical and economic impact in France. There was overall prevalence of 54 cases per 100000, which is in the range of other studies performed in Europe and in the USA. BJI prevalence was age- and sex-dependent, increasing 6-fold between age <50 years and age >70 years. Most patients had underlying diseases, especially diabetes, and related comorbidities, including ulcer sores and vascular disorders. In 2008, the total direct cost of BJI-related care in France was of €259 million (€7,178 per hospital stay); one of the main contributors to this cost was the rate of hospital readmission (19%). Of note, these figures do not take account of the cost of long-term care and rehabilitation, or the vast array of indirect costs. The authors estimated that only 10% of the total costs were healthcare-related, the remainder being social and occupational costs [10]. Implant-associated BJI, corresponding to one-third of all BJI patients in France, is frequently postoperative and more costly than native BJI: at least one surgery is always required, the prevalence of bacterial resistance is higher, the use of expensive antibiotics greater, the overall length of stay longer, and the rate of relapse higher. For instance, in the USA in 2009, the estimated mean cost associated with methicillin-susceptible *S.*

*aureus* prosthetic joint infection (PJI) was of \$68,053, whereas methicillin-resistant *S. aureus* BJI costs were significantly higher, at a mean \$107,264 per case [11]. In Australia, the median cost per patient of treating PJI was of AU\$34,800 (\$26,000), with a 156% increment in case of treatment failure [12]. Finally, the global cost of BJI will increase in coming decades, especially due an increase in the absolute number of PJI cases, as the need for joint arthroplasty is expected to increase substantially with population demographic ageing. In the USA, the annual cost to hospitals of revision surgery for infection increased from \$320 million in 2001 to \$566 million in 2009, and is projected to exceed \$1.62 billion by 2020 [13].

## **2.2 First step: 2008-2009**

In February 2007, in a first national meeting, (*Premiers Etats Généraux des Infections Nosocomiales*) organized by “*Le Lien*”, an active French patient association for the protection of patients against nosocomial infection, the French Health Ministry said that the fight against nosocomial infection was a priority in France, and proposed to implement a network of CRIOAcs validated by the Higher Public Health Council (*Conseil Supérieur d'Hygiène Publique*) and the Technical committee of nosocomial and health-care associated infections (*Comité Technique des Infections Nosocomiales et des Infections Liées aux Soins*). Specifications for the network were drafted by the six health-care societies representing physicians, scientists and other health-care professionals involved in the management of BJI: *Société de Pathologie Infectieuse de Langue Française* (SPILF), *Société Française de Chirurgie Orthopédique et Traumatologique* (SoFCOT), *Société Française de Microbiologie* (SFM), *Société Française d'Anesthésie et de Réanimation* (SFAR), *Société Française d'Hygiène Hospitalière* (SF2H), and *Société Française de Rhumatologie* (SFR), in collaboration with *Le Lien*. In 2008, each regional health agency identified one hospital with significant BJI activity, based on national health administration data. Thus, eight centers were first selected as CRIOAcs in 2008: Paris, Boulogne-Billancourt (Ile de France), Lille-

Tourcoing (north of France), Reims (north-east), Lyon (east), Marseille, (south-east), Toulouse (south-west), and Tours (center) [14].

### **2.3 Second step: national coordination 2009-2010**

A first national coordination meeting of the 8 CRIOAcS was held in June 2009, and a national coordinator (Pr. Alain Lortat-Jacob) was appointed by the Ministry of Health to ensure that its implementation matched the original orientation, notably as concerns perceived stakes, internal organization, and inter-regional coordination with other health-care establishments. To optimize geographic coverage, a 9<sup>th</sup> CRIOAc was designated in early 2011 (Rennes, west of France). A funding plan for the centers was drawn up, with an already set annual budget plus activity-dependent budget. The budget is of about €150,000 per CRIOAc, for financing 2 officers to facilitate events organization, information and inter-regional coordination. The activity-dependent budget is based on the PMSI data-base, for which a specific code (08C56x) was created and used for each hospital admission for complex BJI. For each surgical stay with this code, the hospital receives an extra 12% funding from the national health insurance system. Criteria for complex BJI were detailed in the “*Journal Officiel de la République Française*” that publishes Laws and Decrees, and are summarized in Table 1 [14].

### **2.4 Third step: Network finalization, including corresponding centers (CCs), and implementation of an online information system (2011-2016)**

To finalize the network, 15 “corresponding centers” (CCs) were labeled in 2011 (1 or 2 per CRIOAc), totaling 24 CRIOAcS and CCs (figure 1). In 2012, the Nancy university hospital replaced Reims, as the CRIOAc of the north-east region. Missions attributed to CRIOAc and CCs were clarified at this step. CRIOAcS and CCs share certain missions: (1) information and orientation: organization of response to calls from health-care professionals and also patients; (2) referral: responses to requests for advice on treatment for patients with easy-to-treat or complex BJI; (3)

organization and centralization of multidisciplinary consultation meetings with quorum (at least one infectious disease physician, one orthopedic surgeon, and one microbiologist), to determine the optimal medico-surgical strategy for each patient, and determine whether the BJI is complex or not. CRIOAc have national, regional and local level teaching missions, and also promote clinical research in BJI. All of the CRIOAc and CC have to draft an annual report describing their activities, the reports are yearly presented by the General Directorate for Provision of healthcare to the community and discussed. For use by all of the labeled centers, a dedicated secure national online information system was designed to collect several data such as medical history, clinical characteristics, the type of BJI, pathogen and surgery and antibiotics proposed. The objectives of this online information system are to: (1) facilitate decision-making during multidisciplinary consultation meetings; (2) draw up a summary of the patient's clinical history, the BJI's complexity status, and decisions taken; (3) share the medical synthesis in pdf format within the approved structures and with the concerned physicians; (4) facilitate patient follow-up; (5) produce activity data for assessment of the centers' missions; and (6) undertake epidemiological research. The system allows for real-time knowledge of the activity of the centers (number of multidisciplinary consultation meetings, number of cases discussed, complexity rate, etc.). In 2011, it has been proposed that the CRIOAc should alternatively organize national scientific meeting on BJI every 2 years. In 2014, the *Société de Pathologie Infectieuse de Langue Française* (SPILF), and the *Société Française de Chirurgie Orthopédique et Traumatologique* (SOFECOT) decided to create a postgraduate national diploma in the field of BJI in which residents in medicine or surgery can be enrolled every 2 years. In 2016, a scientific committee was set up among health professionals from the CRIOAc to organize access to and use of medical data for epidemiological studies.

### **3. Results**

The labelling of 24 centers in the CRIOAc network allowed for a meshing of the territory, with the possibility of management of complex BJI in each region of France. Since October 2012 to June

2017, 4,553 multidisciplinary consultation meetings have been performed in the structures belonging to the network, with 34,607 cases discussed in 19,961 individual patients (figure 2). The mean age of the patient was 61 years ( $\pm 8$ ). Among all the cases discussed, the rate of complexity was of 61% (21,110/34,607), without significant change over time. Only one discussion in multidisciplinary consultation meetings was required for 53% (10,579/19,961) of the patients, two for 24% (4,791/19,961), 3 for 12% (2,395/19,961) and 4 or more for 11% (2,196/19,961). Among individual cases, prosthetic joint infections represented 38% (7,585/19,961) of BJIs, and 42% of them (3,186/7,585) had at least one criteria for complexity. The national postgraduate diploma in the field of BJI was launched in 2014, and is now facilitated by the 8 universities with which the CRIOAc are linked, with national and regional coordinators. Theoretical and practical (internship) formation is proposed, and students are evaluated on the basis of a written examination and a written dissertation. More than 50 fellows in infectiology, microbiology or orthopaedics residents or physicians participated in 2014-2015 and 2016-2017. The first national scientific meeting of the CRIOAc network was located in Toulouse in 2013, followed by Lille in 2015, and Tours in 2017. This scientific meeting brings together 300 to 500 professionals involved in the management of BJI. In the field of the clinical research, several regional and national projects have been completed and published. Of note, some national projects were funded or supported by the Health Ministry such as DATIPO in 2009 (comparison of different duration of antibiotics in patients with PJI; Prospective open randomized multicentre non-inferiority phase 3 trial NCT01816009), EVRIOS in 2015 (comparison of different dosages of rifampin; Prospective open randomized multicentre non-inferiority phase 3 trial; NCT02599493), and PHAGOS and PHAGOPIED in 2016 (safety of bacteriophages targeting *S. aureus* in patients with PJI and diabetic foot osteomyelitis; NCT02664740). Indeed, these multiple interactions in the CRIOAc network facilitate the emergence and the feasibility of multicentric studies with high level of evidence. Finally, to optimize the management of acute prosthetic joint infection, and to avoid its complication, some experts from the CRIOAc network directly participated to the literature review and the drafting of

the French guidelines hosted by the “*Haute Autorité de Santé*” (HAS) for the management of prosthetic joint infection occurring during the month following the implantation. The methodology used followed the “best practice recommendations” of the HAS. Accordingly, the first step was a review of the literature and a critical analysis of the data. Once enough evidence was gathered, an evidence report was drafted. Secondly a multidisciplinary and multiprofessional group, of 15 to 20 professionals and representatives of patients and users of the Healthcare system, drafted the recommendations that were submitted to a peer review group, before publication of the guidelines.

#### **4. Discussion**

The management of BJIs requires a multidisciplinary approach, and a great experience for the most complicated cases to limit treatment failure, motor disability and amputation risk. The French Health Ministry hypothesized that a nationwide healthcare network with regional labeled centers could create a dynamic that improves the recruitment, the management, the education, and the clinical research in the field of complex BJI. The setting up of the CRIOAc network in France took time, and has a cost for the French Ministry of Health. However, this network has greatly facilitated the management of BJI in France, and allowed to concentrate the management of complex BJI in centers that have significantly gained skills. There is, to our knowledge, no other example of such nation-wide network in the field of BJI. This dynamic is the first step to obtain a reduction of the burden of CRIOAc in France. To drive this effort, the health ministry has to continue to support the network, and the CRIOAc scientific committee has to identify and support key thematic research for complex BJIs in the following domains: prevention; pathophysiology, diagnosis, biomarker development and monitoring; dedicated pharmacological agents and medical device; quality of care; public awareness and understanding. To evaluate and perpetuate the network, as for all certified and funded structures, and in addition to the annual reports produced, conformity to the specifications is reassessed periodically [15], and CRIOAc certification will be re-assessed for a 5-year period starting in 2017. A national jury representing the CRIOAc, the patient association “*Le*

*Lien*” and BIJ experts from the regional health agencies will advise the DGOS health-care supply office on the selection of candidates put forward by the regional health agencies, and the DGOS will decide in the light of this advice. The specifications have been updated, and now encourage taking into account activity in terms of hospital stays and number of multidisciplinary consultation meetings, with thresholds being set such as (i) effective patient satisfaction assessment; (ii) effective geographic coverage, without blank areas; and (iii) effective implementation of CRIOAc missions in terms of coordinating the expertise, orientation and information of other agents (community practices, patients, private-sector structures, etc.). During the 5-year period aforementioned, the national database collecting the data of each multidisciplinary consultation meetings will be used for epidemiological studies and report purposes. A national website for patients and the various health professionals will be created to publicize the system, and optimize referrals and timely treatment before simple situations become complex. As this networking structure greatly facilitates the synergy between the representatives of each academic disciplines involved, it will also continue to promote research, with clinical trials assessing new diagnostic tools, surgical procedures for a given BJI, specific antibiotics, or overall medical/surgical strategy. Epidemiological data will allow feasibility studies and also partnerships with the industry, in the fields of diagnostic, implants, bone cements, bone substitutes, antibiotics and all the various therapeutic alternatives such as bacteriophages. To answer the question, it was possible to build at a national level in France, a network involving orthopaedic surgeons, infectiologists and microbiologists performing locally multidisciplinary meetings. This dynamic facilitates the recruitment and the management of patients with complex bone and joint infection in regional centers. The promotion of education, clinical research and interactivity between each academic discipline and between each labeled centers across the country has synergized the strengths and optimized the management of patients with BJI. By drawing upon the strengths of academic and health ministry expertise, the CRIOAc network represents a potential new model at a national level, for filling knowledge gaps, and enhancing management and innovation in complex diseases.

Our study has some limitations: 1) we are not aware of BJI not implemented in the database and the extra cost related when those patients are managed in centers outside the CRIOAc network.

However, every cases discussed in multidisciplinary meetings are recorded in the system, centers outside the network more and more facilitate the recruitment of their patients by centers belonging the network, and based on the PMSI database, most of BJI in France are managed in the CRIOAc network; 2) we did not compare the cost and rate of success of BJI managed inside vs. outside this network, but the patients outside the network probably have the most easy-to-treat BJI. Finally comparison of BJI healing of patients inside the network could be monitored over the time in future dedicated investigation.

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## Figure legends

**Figure 1.** Distribution of CRIOAc (orange) and their CCs (yellow) in the various regions of France in 2011-2016. CRIOAc: Complex Bone and Joint Infection reference Center (*Centre de Référence des Infections Ostéoarticulaires complexes*); CC: Corresponding Center

**Figure 1.** Distribution régionale des Centre de Référence des Infections Ostéoarticulaires complexes (CRIOAc) (en orange) et de leurs Centres Correspondants (en jaune) sur la période 2011-2016.

**Figure 2.** Cumulative number of multidisciplinary consultation meetings, cumulative number of patients and cumulative number of case discussions performed by the 24 centres belonging to the CRIOAc network since the use of the secure national online information system in 2012.

**Figure 2.** Nombre cumulé de Réunion de Concertations Pluridisciplinaires (RCP), nombre cumulé de patients et nombre cumulé de cas discutés dans les 24 centres appartenant au réseau des Centre de Référence des Infections Ostéoarticulaires complexes (CRIOAc) depuis la mise en place du système online d'information sécurisé en 2012.

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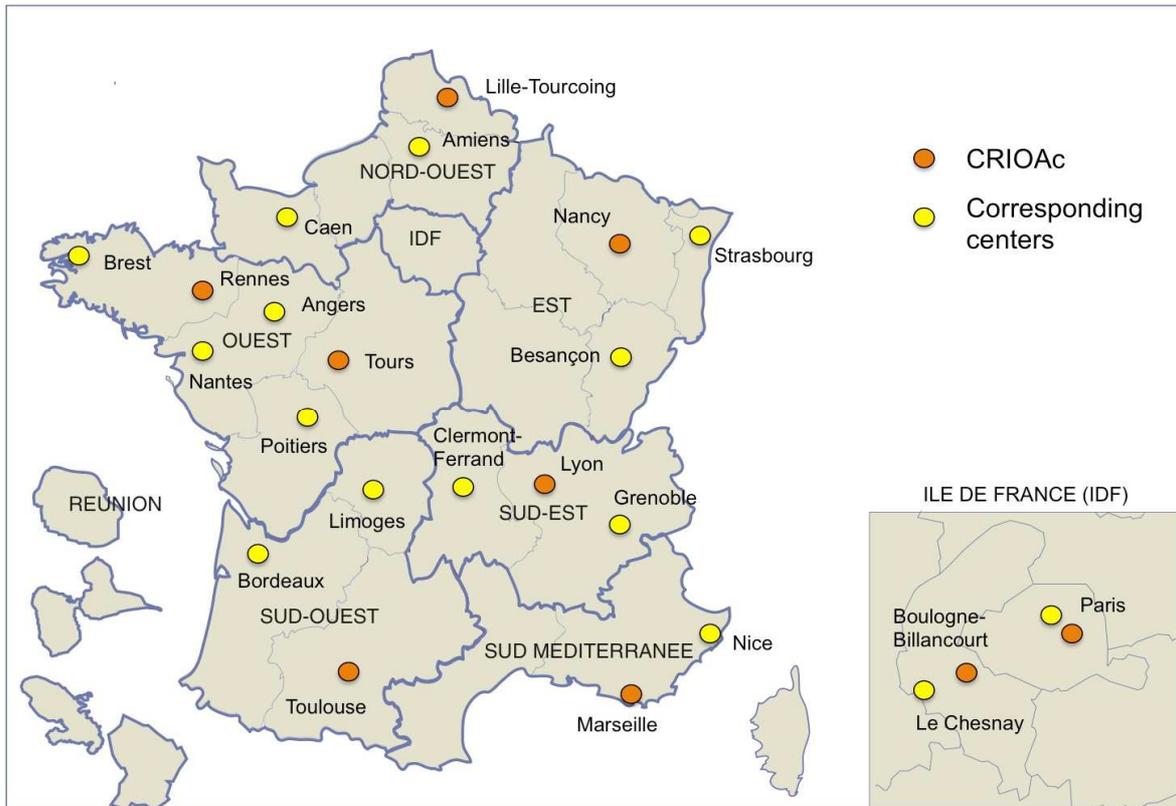
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**Table 1.** Criteria for complexity (summarized from the 2010 publication in “*Journal Officiel de la République Française*”). The presence of at least one criterion provides to the labeled center an extra 12% funding for surgical stays.

|   |
|---|
| <b>Host criteria</b>  |
| Patient with severe comorbidity limiting treatment options                |
| Patient with severe allergy   |
| <b>Microbiological criteria</b>   |
| Difficult-to-treat micro-organism(s) with or without multidrug resistance |
| <b>Surgical criteria</b>  |
| BJI requiring bone resection and bone and/or soft-tissue reconstruction   |
| <b>Relapse</b>  |
| Relapse of a previous episode of BJI                                      |

Figure 1.





**Figure 2.**

