ACTIV
Association à but non lucratif

ACTIV (Association Clinique et Thérapeutique Infantile du Val-de-Marne) est une association fondée en février 1988 et régie par la loi du 1-7-1901 dont le but est de promouvoir les **études cliniques et épidémiologiques, la recherche diagnostique et thérapeutique en pathologie pédiatrique.**

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La Recherche

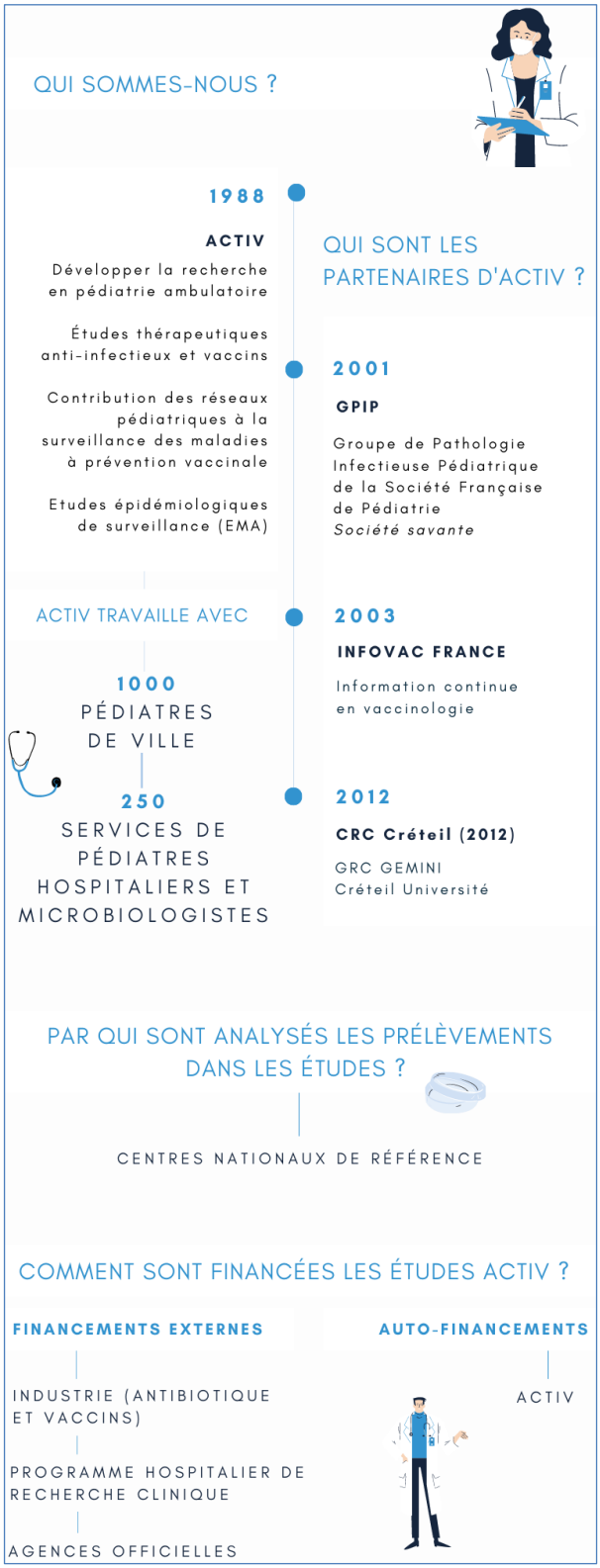
ACTIV dispose de l'**expérience**, des moyens structurels, humains et méthodologiques pour réaliser des études cliniques, de la **conception du protocole à la publication** nationale et internationale.

Ces études sont à l'initiative d'ACTIV, de pédiatres de terrain, de l'université, d'agences officielles, de l'industrie pharmaceutique. Elles couvrent essentiellement le **champ infectieux** (observatoires, épidémiologie, méthodes diagnostiques, thérapeutiques, vaccinologie) et ont pour objectif de contribuer à la pratique d'une médecine fondée sur des preuves (**"evidence based medicine"**).

Si la majorité des travaux est **ambulatoire**, certains se déroulent en **milieu hospitalier**, à l'échelon régional ou national.

Voici quelques-unes des thématiques des études menées par Activ :

- Portage nasopharyngé
- Méningites bactériennes
- Infections invasives à pneumocoque
- Comportement de l'enfant malade
- Pneumonies
- Varicelles hospitalisées en Ile de France
- Coqueluche « ambulatoire » en pédiatrie



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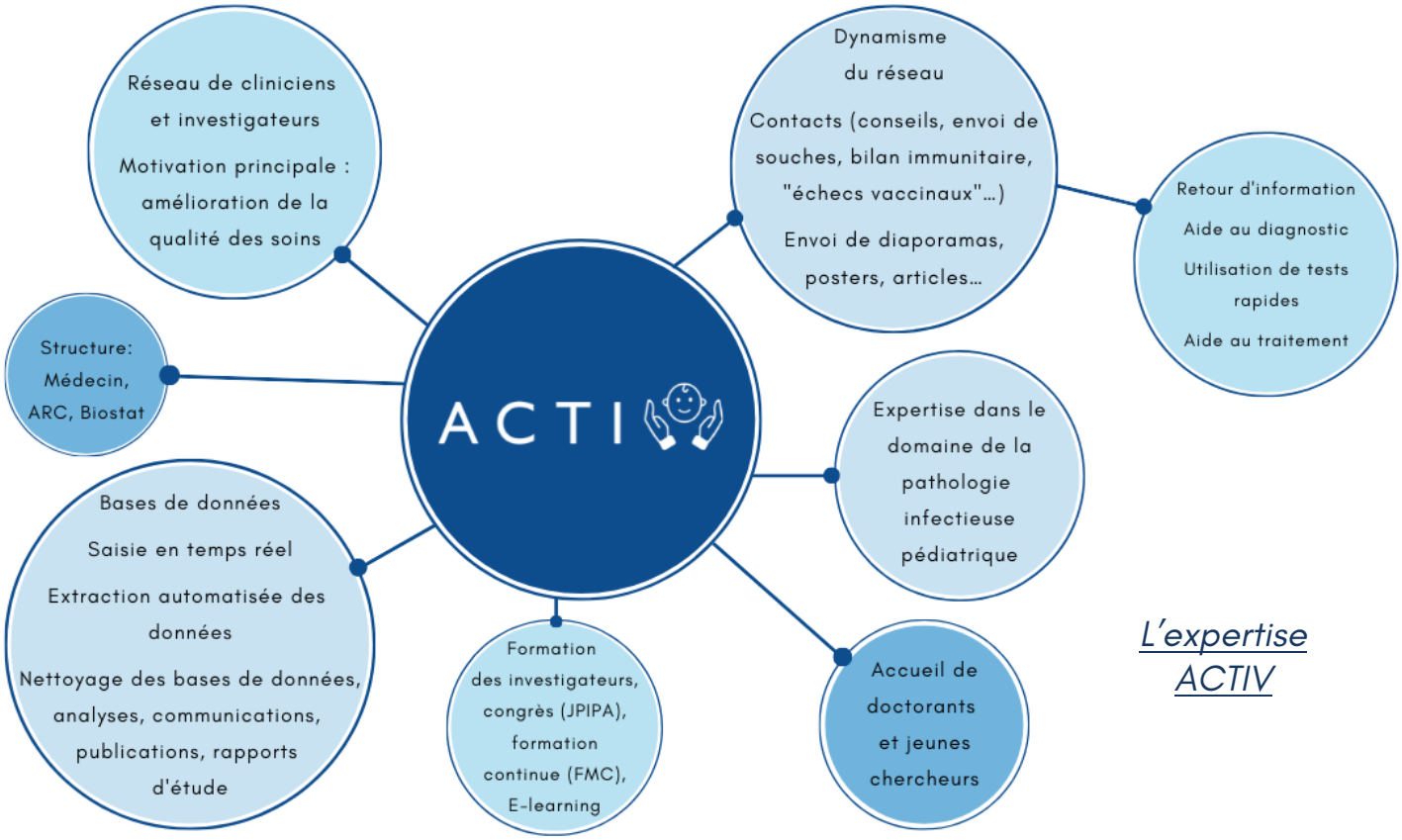


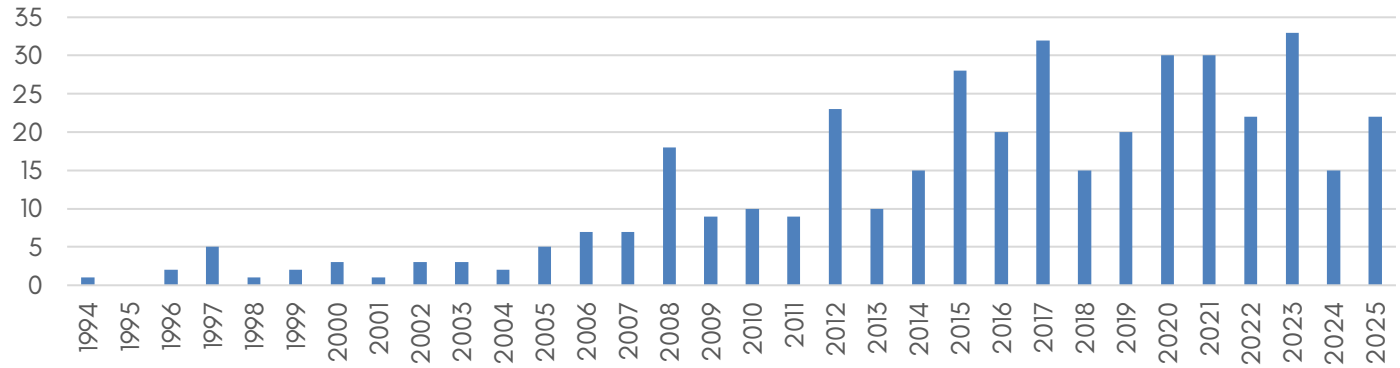
L'expertise ACTIV

Le Réseau ACTIV

ACTIV s'appuie sur un réseau d'investigateurs en ville constitué d'**un noyau dur d'une centaine de pédiatres**, mais qui, pour certaines études, **peut atteindre le millier**. Le réseau hospitalier se compose de **250 services de pédiatrie** et **168 services de microbiologie.**

Les Publications

ACTIV publie **annuellement** entre 20 et 30 articles dans des journaux avec comité de lecture. Retrouvez toutes nos publications *sur notre site*, dans la rubrique « Publications »



Evolution des publications ACTIV depuis sa création en 1988

Pediatric Ambulatory and Hospital Networks for Surveillance and Clinical Epidemiology of Community-Acquired Infections

Corinne Levy, MD[1,2,3,4,5], François Vie le Sage, MD[4,5], Emmanuelle Varon, MD[6], Martin Chalumeau, MD[4,7,8], Emmanuel Grimprel, MD[4,9], and Robert Cohen, MD[1,2,3,4,5,10]

Care of infectious diseases (prevention, diagnosis, and treatment) represents a large part of the activity of pediatric practices as well as primary care, emergency departments, and hospitals. The bacterial and viral species involved in pediatric community-acquired infections (CAIs) can induce severe, moderate, or mild diseases, which require care by hospitalization, emergency departments, or first-line clinicians. For example, pneumococcus manifests as a spectrum of diseases ranging from severe invasive diseases, such as meningitis, bacteremic pneumonia, and bacteremia, to less severe but more frequent diseases, such as acute otitis media (AOM), sinusitis, and pneumonia (**Figure**; available at www.jpeds.com).[1,2] Therefore, outpatient use of antibiotics also involves antibiotic resistance for CAIs; hence, infection management becomes even more complex, often leading to hospitalizations. Moreover, some vaccines, for which the main objective is reducing invasive and severe diseases, have an additional impact on less severe diseases and also change the carriage.[3] Trying to study the bacterial and clinical epidemiology of organisms such as Pneumococcus, Group A *Streptococcus*, or *Escherichia coli*, involved in a large spectrum of CAIs, requires a focus on both the ambulatory setting and on the hospital.

We review the efforts to build a French pediatric research network that focused on CAIs.

Before the 1990s, in France, first-line clinicians and notably ambulatory pediatricians were not involved in clinical research, which was performed mainly by universities and hospitals. Because of a lack of surveillance systems in ambulatory settings, we created a nonprofit ambulatory-pediatric research network, Pediatric Clinical and Therapeutic Association of Val de Marne (ACTIV). This regional network (Paris area) was extended at the national level via a strong collaboration with the Association of French Ambulatory Pediatricians. A link with a preexisting hospital network, the Pathology Pediatric Infectious Disease Group of the French Pediatrics Society, was established several years later. The network has complied with the high-quality standards required by good clinical practice for industrial trials by European and North American drug regulators and the "feasibility in real life," taking into account medical practice with ambulatory care and hospital constraints. With ACTIV, we have designed study protocols aimed at simplifying the procedures, while maintaining a high standard of quality. This approach facilitated the publication of scientific data that were widely used by the European and American medical markets.

ACTIV	Pediatric Clinical and Therapeutic Association of Val de Marne
AOM	Acute otitis media
CAI	Community-acquired infection
PCV	Pneumococcal Conjugate Vaccine

From Antibiotic Treatment to Prevention with Vaccines

To compare the efficacy of different therapeutic options (type of drug, dosage, duration of antibiotic treatments, etc), in AOM we have performed several clinical trials using rigorous criteria to standardize the AOM diagnosis along with otoscopy training sessions.[4-6] Our research group evaluated the impact of antibiotics on the composition and antibiotic resistance in nasopharyngeal flora that involved a network of almost 100 primary care pediatricians.[5,6] The bacteriological samples were centralized in the National Reference Center for Pneumococci. The advantage of the expertise acquired in this area (several thousand nasopharyngeal samples collected in 10 years) allowed us to perform our pivotal study on nasopharyngeal carriage after the 7-valent pneumococcal conjugate vaccine (PCV) implementation in France in 2001.[7] This study was performed as a postlicensing commitment requested by the European Medicines Agency to determine the impact of the 7-valent pneumococcal conjugate vaccine. Although other studies reported similar results for the PCV impact, none were comparable with those we have conducted since 2001 in terms of design, duration (>17 years), and number of patients enrolled (>15 000).[7]

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Keys to Success

Several factors could explain the success of this network lasting more than 30 years (**Table**; available at www.jpeds.com). The important outcome of the studies performed by the research network has been the implementation of clinical conclusions and recommendations by pediatricians in their practice. This includes the duration of antibiotic therapy for children with AOM or group A *Streptococcus* pharyngitis as well as the use of biomarkers or rapid diagnostic tests to improve diagnostic performance and use of appropriate antibiotics for different infectious diseases.[8-11] Finally, the best proof of success was that pediatricians' behavior was correlated with the research they conducted. Particularly, our group, which promptly implemented the proposed recommendations, showed less prescription of antibiotics and greater vaccination coverage for their patients than other physicians who applied the recommendations later.[12]

We have recently moved to a new method that allows us to even more easily perform studies by directly obtaining data from pediatricians' computers. With 100 pediatricians using the same software (Infansoft, CompuGroup Medical, Koblenz, Germany), we have automated data capture from electronic medical records for children in ambulatory settings, the Panel in Ambulatory Research Infectiology. The participants benefit in real time from the epidemiology of several infectious diseases on a dedicated Website. They can also improve their diagnosis with e-learning sessions specifically dedicated to each pathology.

Link with the Hospital Network

Linking ambulatory and hospital networks is important. For instance, to determine the multifaceted impact of pneumococcal vaccine implementation on invasive pneumococcal infections, we linked the ambulatory with the hospital-based surveillance systems by reconciling separate databases, and we created a national hospital network for bacterial meningitis with the Pathology Pediatric Infectious Disease Group of the French Pediatrics Society.[13,14] More than 230 pediatricians and 168 microbiologists nationally were involved in this study. Microbiologists agreed to voluntarily send each bacterial species isolated from meningitis samples to the corresponding national reference center, which performed serotyping and genotyping, as well as extensive standardized susceptibility testing. The strong participation and motivation of hospital pediatricians and microbiologists were related to the lack of a prior surveillance system that included clinical, therapeutic, and microbiological data for invasive diseases in France. Moreover, the originality and the relevance of our system lies in the fact that we used our research platform that was initially created for outpatient infectious diseases. We identified a team of pediatricians and microbiologists in each participating center and organized a close collaboration with the experts of the national reference centers for the different bacterial species. The research has improved the quality of care, and the network has been regularly asked to perform ancillary studies and specific analyses for each bacteria involved. The bacterial meningitis study surveillance, with more than 6500 cases enrolled since 2001, allowed for the publication of several articles, also involving the contribution of young pediatricians.[15] Moreover, our ambulatory and hospital network initially built for pneumococcal infections was extended to study other diseases and pathogens, such as the increasing incidence of CAIs owing to extended-spectrum β-lactamase-producing *E coli*. These studies provided useful public health data and recommendations.

French Vaccine Network

In 2003, following the Infovac-Swiss model, we developed InfoVac-France, a website designed by Clair-Anne Siegrist of the University of Geneve, providing physicians with a direct source of information on vaccinations.[16-18] In the context of vaccine hesitancy in the world and particularly in France, here again this network helps provide optimal vaccine support and represents a good opportunity for the release of validated scientific information on vaccines.

Conclusion

Rather than providing guidance for better surveillance of pediatric infectious diseases, herein we present an overview of our surveillance system for diseases and highlight why, in the French context, it was successful beyond our hopes. Owing to different clinical practices and healthcare systems, epidemiology, and vaccination programs worldwide, results from studies performed in other countries cannot always be extracted or transposed to one's own country. This factor has led to each country performing its own clinical research. The strength of our surveillance systems lies in the multiplicity of funding (governmental, university, and pharmaceutical industry). Our challenges are to rigorously maintain several well-established surveillance systems with resources specifically allocated and increase the involvement of young researcher-pediatricians. Our networks are not always representative of all French pediatricians, because our researcher-pediatricians are well-informed and particularly well-trained to follow the latest recommendations. However, we believe in this model, which can easily evolve with themes of research prioritized according to epidemiologic changes. Without competing with the different preexisting research groups in our country, we have federated and involve all the volunteers in our networks. Hence, this "ambulatory/hospital" research network, which is unique in Europe, contributes greatly to answering public health questions, particularly for vaccination strategies and antibiotic resistance.[15] ■

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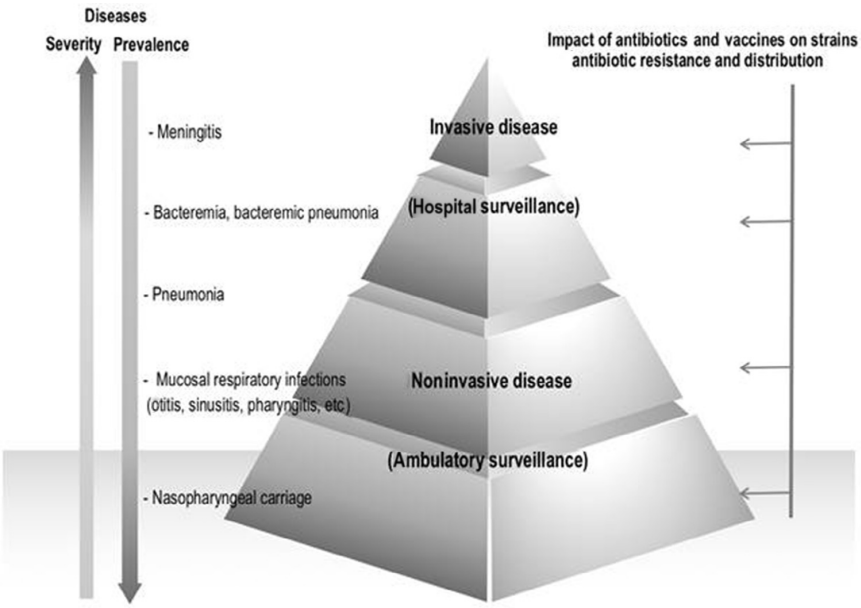

Figure. Spectrum of *Streptococcus pneumoniae* disease.

Table. Factors determining the successful outcome of pediatric ambulatory and hospital networks for surveillance and clinical epidemiology of CAIs

Addressing areas of typical concern for primary care physicians (ie, improvement in diagnosis and/or management of pediatric infectious diseases).
Developing projects aimed at providing answers to common clinical question related to professional practice and promoting pediatric best practice for the benefit of children (ie, studies involving respiratory tract infections, owing to their frequency and easiness in obtaining oropharyngeal or nasopharyngeal samples).
Placing investigators and their training programs at the cornerstone of the research system (investigators easily recognize that contributing to the projects proposed provides a real benefit to their daily practice and professional continuing education).
Building and establishing preliminary relationships between parents and their family pediatricians, which largely favor parental adherence to protocols and facilitate the collection of parental written informed consent to the studies (very few patients are lost to follow-up).