BASEL, SWITZERLAND

Clinnova

REPORT

2024–2025

www.clinnova.eu

Outline

Clinnova European Consortium

Clinnova: Federating Medicine in Europe aims to drive the digitalization of healthcare and advance precision medicine by building a robust, data-enabling environment. The goal is to deliver high-quality, interoperable health data that is accessible, shareable, and ready for meaningful analysis, ultimately improving patient care and accelerating biomedical research through patient-oriented applications. Clinnova focuses on three major use cases of chronic diseases: 1) Rheumatoid Arthritis (RA), 2) Multiple Sclerosis (MS), 3) Inflammatory Bowel Disease (IBD), and showcasing the potential of its platform in diverse clinical contexts.

By establishing a high-performance, interoperable data infrastructure, Clinnova aspires to catalyze the emergence of a vibrant digital health industry in region , laying the groundwork for a European development platform. We are actively exploring public and private investment opportunities to attract start-ups and solution providers into this growing ecosystem. Together, these efforts create the conditions, momentum, and opportunity for the European digital health industry to achieve international leadership.

Rheumatoid Arthritis (RA)

Multiple Sclerosis (MS)

Inflammatory Bowel Diseases (IBD)

In January 2024, over 70 collaborators came together in Strasbourg (France) for the consortium meeting, marking a milestone in our shared journey. The next gathering is already on the horizon, scheduled for October 2025, a testament to the Clinnova collective's ambition in shaping the future of healthcare.

Scan to Learn More

Clinnova Basel

RC2NB Basel

Clinnova Consortium

Clinnova Consortium Partners

Basel, Switzerland: University of Basel, Universitätsspital Basel, RC2NB (Research Center for Clinical Neuroimmunology and Neuroscience Basel), Clarunis (Universitäres Bauchzentrum Basel), Indivi; Neurostatus-UHB; **Baden-Württemberg, Germany**: Miracum, Universitäts Klinikum Freiburg, BDIH (Bosch Digital Innovation Hub), UMM (Universitatsmedizin Mannheim), Medizinische Fakultät Mannheim der Universität Heidelberg, Universitätsklinikum Mannheim, KTBW (Koordinierungsstelle Baden-Württemberg); **Luxembourg**: LCSB (Luxembourg Center for Systems Biomedicine), LIH (Luxembourg Institute of Health), Université du Luxembourg, Hôpitaux Robert Schuman, CHL (Centre Hospitalier de Luxembourg);

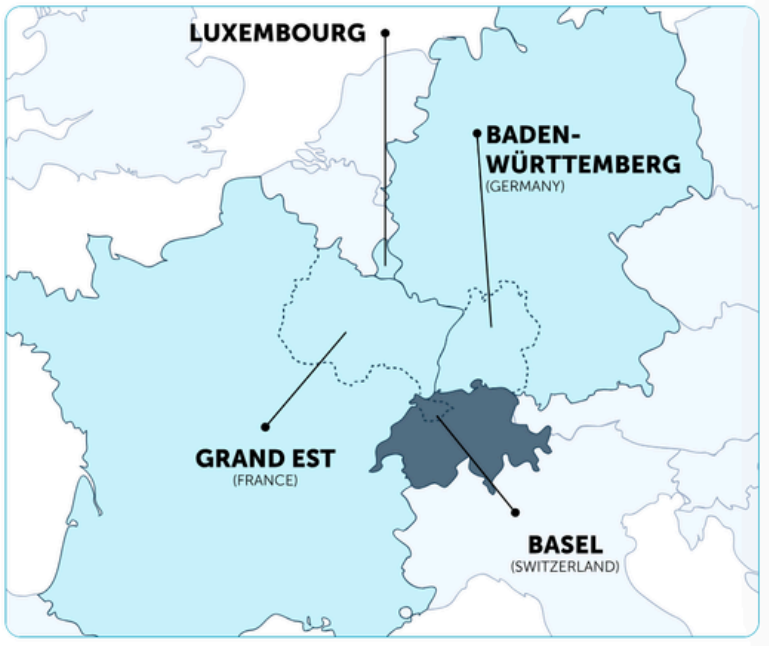
Grand Est, France: La Région Grand Est, IPHC (Institut pluridisciplinaire Hubert Curien), Université de Strasbourg, Université de Reims Champagne-Ardenne, BioValley France, IHU (L'Institut hospitalo-universitaire de Strasbourg, Institute of Image-Guided Surgery), CHRU Nancy (Centre Hospitalier Régional Universitaire de Nancy), Université de Lorraine, CHRU Reims (Centre Hospitalier Régional Universitaire de Reims), INESIA (innovation en e-santé et intelligence artificielle), Hôpitaux Universitaires de Strasbourg, IHU Infiny (Maladies Inflammatoires Chroniques de l'Intestin), INSERM (Institut national de la santé et de la recherche médicale), PRIeSM (Plateforme régionale d'innovation en e-santé mutualisée).

Basel, Switzerland

Baden-Württemberg, Germany

Luxembourg

Grand Est, France



Editorial

Clinnova
Federating Digital Medicine in Europe

Prof. Cristina Granziera, MD, PhD
Principal Investigator, Clinnova Basel

> ***"Clinnova shows that we no longer have to choose between privacy and progress. From building federated infrastructure to launching innovative tools, recruiting patients, and breaking silos across disciplines and borders, we are proving that collaboration and trust can drive true innovation."*** *Prof. Cristina Granziera, Principal Investigator, Clinnova Basel*

Clinnova was ideated from the start as way more than just a project, but rather as a platform to federate digital medicine in Europe. Its mission is to redefine how we approach complex, chronic diseases by merging clinical care, innovative molecular analyses, advanced imaging, and secure data-driven research powered by patients for patients. Digitalization of healthcare and precision medicine by creating a data-enabling environment for accessing, sharing and analyzing interoperable, high-quality health data across Europe.

This report captures the momentum behind Clinnova Basel (Switzerland). To make this vision a reality we have dismantled silos not only between disciplines but between institutions, countries, and systems. At the core of Clinnova is a simple but profound belief: data should work for people. In multiple sclerosis (MS), inflammatory bowel disease (IBD), and rheumatoid arthritis (RA), all chronic diseases, where patients deserve more than fragmented care and generalized treatment paths. They deserve precise answers, grounded in the richness of their own clinical, biological, and digital data. They deserve systems that learn with them, and for them, in short; personalized medicine.

Clinnova means embracing a new technological architecture where data remains protected and private, yet becomes part of a collective intelligence.

This is the power of federated learning, an approach that allows us to build shared AI models, while data never leaves its home institution. In Basel, we are proud to be at the heart of this transformation. Together with our partners, we are proving that cross-border, privacy-preserving research can be a working reality.

All of this started with the trust and support from Canton Basel-Stadt, with an investment of CHF 4 million, which was pivotal in making this vision real. This critical support enabled us to lead the technical infrastructure for federated learning across the entire Clinnova consortium, launch Clinnova-MS and expand into Clinnova-IBD in Basel.

Equally essential has been the support of Basel University Hospital and the unwavering dedication of Prof. Andrea Schenker-Wicki, President of the University of Basel, whose steadfast commitment to pioneering research and international collaboration has been a cornerstone of Clinnova's success. The coordination and program leadership of Dr Bebeka Cosandey has further ensured that the ambitious vision of Clinnova Basel is translated into concrete, measurable progress and impact.

Basel today stands as one of the top global life science and innovation hubs, top-notch research, healthcare, and infrastructure that benefit the whole consortium. Here in Basel, we are leading the way in the Multiple Sclerosis (MS) use case and have implemented the Neurostatus-UHB tool, which enables the electronic assessment of the internationally recognized gold standard, the Expanded Disability Status Scale (EDSS), for assessing and quantifying disability in multiple sclerosis. Additionally, the dreaMS app, developed in Basel by the Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB) and the medical technology company "INDIVI", turns smartphones into clinical monitoring tools. It captures digital biomarkers of balance, motor skills, vision, and cognition, enabling precise, real-world tracking of MS progression with minimal patient burden. dreaMS is poised to become a core digital tool across the consortium, shaping the future of remote monitoring in the MS use case.

Dr Bram Stieltjes, Dr Francesco Santini, and the IT team in Basel are now spearheading Clinnova's Federated Learning efforts, building a secure, cross-border AI framework where patient data stays local, but knowledge is shared. Their pioneering work on the Federated Data Catalogue and Data Integration Centres is laying the foundation for privacy-preserving, scalable, and clinically meaningful AI models. Clinnova-MS is progressing steadily with patient recruitment, while Clinnova-IBD Basel, led by Prof Jan Niess, has just completed site initiation and is ready to enroll its first participants.

Clinnova Basel today stands as a frontrunner in driving data-powered, patient-centered research, having achieved major milestones in clinical recruitment, digital health, and federated data infrastructure.

We are proudly leading the way for other sites as we now scale, expand, and accelerate towards truly personalized healthcare, not just in Switzerland, but across Europe.

> ***With Clinnova, we are demonstrating how federated learning can transcend institutional and national boundaries, enabling secure, collaborative medical AI. From Basel, we proudly lead the development of this comprehensive ecosystem, starting with a use case in multiple sclerosis lesion detection in brain MRI scans, and ultimately advancing the development and adoption of AI-powered diagnostic tools."*** *Prof. Andrea Schenker-Wicki, President of the University of Basel*

Prof. Andrea Schenker-Wicki, Dr. Dr. h.c. mult.
President of University of Basel

Clinnova Basel Organizational Chart

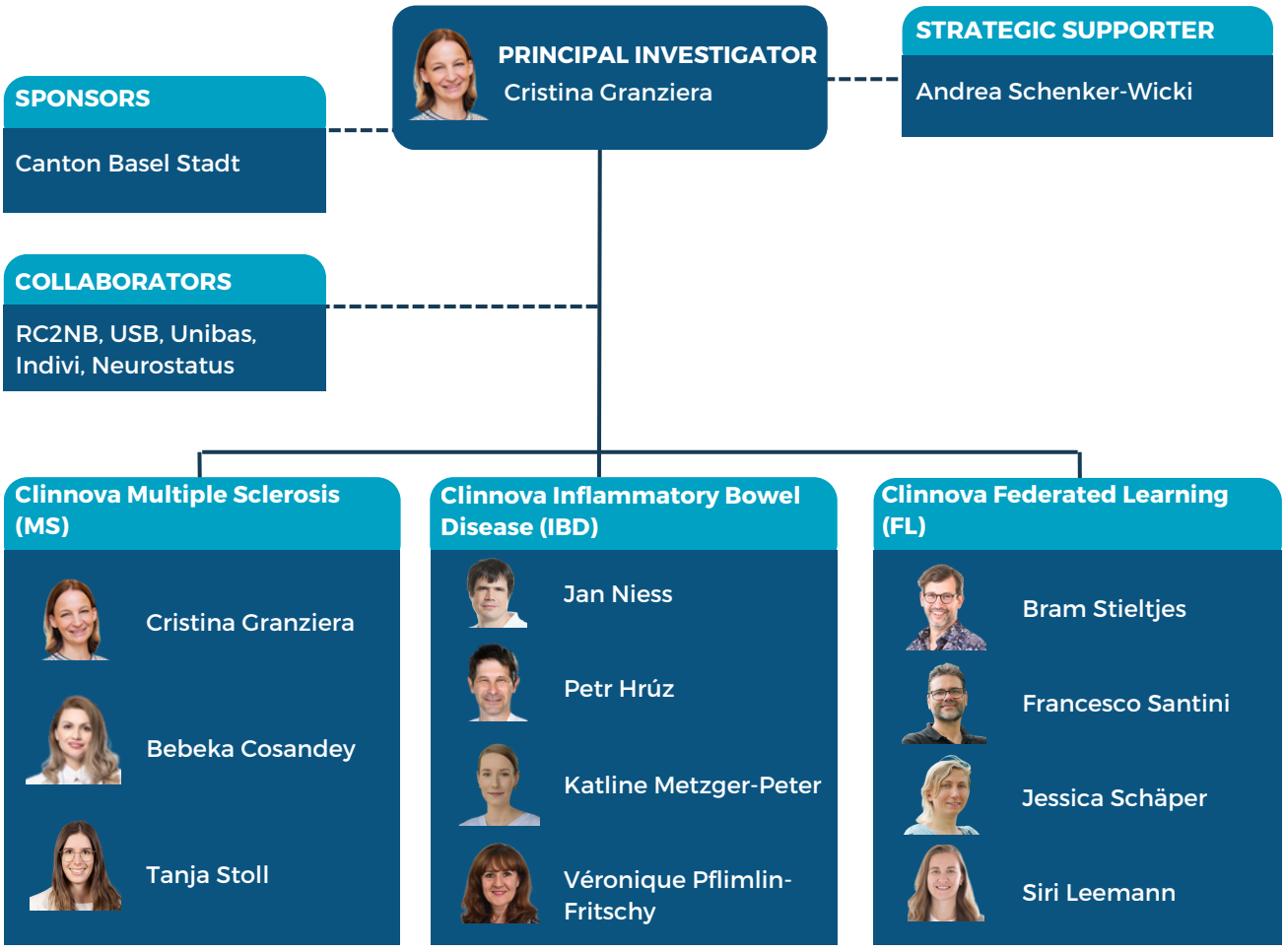
Clinnova Basel is at the frontline of a European effort to transform healthcare through data-driven, patient-centered innovation. Creating a secure, interoperable environment for high-quality health data enables precision medicine that delivers tailored care for chronic diseases.

The initiative merges clinical excellence, advanced imaging, and cutting-edge digital tools such as the dreaMS app for remote monitoring, while pioneering a federated learning framework that protects privacy and fosters cross-border collaboration.

With a well-rounded support and deep regional expertise, Clinnova Basel is setting the standard for how clinical research, healthcare, and digital infrastructure can converge to improve outcomes and accelerate biomedical discovery.

Its work is laying the foundation for a scalable, internationally competitive digital health industry in Europe, proving that data can work for patients while driving innovation with them.

At the heart of Clinnova Basel's success are the people (see below) driving its mission forward fostering cross-border collaboration and setting the pace in digital health. With Multiple Sclerosis as its most advanced and leading use case in Basel, this team proves how patient-centered innovation can scale.



RC2NB - Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB)
USB - University Hospital Basel
Unibas - University of Basel

Clinnova Multiple Sclerosis (MS): Milestones and Momentum in Basel

Number of Patients Enrolled

As of August 2025, 20 patients are enrolled .

Comprehensive Study Infrastructure Finalized

Q3 2024, a pivotal milestone, marking the completion of technical, regulatory, and clinical preparations.

Team Expansion

Q2 2024, we welcomed Tanja Stoll, our dedicated study nurse, whose contributions have been instrumental to the project's success.

First Patient In (FPI)

Q4 2024, the official launch of patient enrollment, bringing Clinnova-MS Basel to life and advancing our mission.

MS Info Day Success

Clinnova-MS Basel had a strong presence during the Multiple Sclerosis Info Day on December 7, 2024, where we had the opportunity to connect with people living with MS.

First 6-month Follow-Up

In June 2025, the first Clinnova MS Basel participant completed the 6-month follow-up, reinforcing engagement and data quality in this patient-centered study.

Dr Bebeka Cosandey

This year in Basel was defined by growth, preparation, and connection. Behind the scenes, essential groundwork was completed, enabling a smooth transition into the clinical phase. Our team grew stronger, and community ties deepened reflecting a shared commitment to advancing MS research with purpose and care.

Clinnova Multiple Sclerosis (MS) Team

Prof. Cristina Granziera
Principal Investigator, Clinnova Basel and co-CEO of RC2NB

Dr. Bebeka Cosandey
Lead Scientific Project Manager

Tanja Stoll
Study Nurse

Between 2024 and 2025, the Clinnova-MS study team achieved key milestones that set the stage for its longitudinal research. In June 2024, the Clinnova-MS study received the Swiss ethics approval, unlocking the start of clinical site setup and patient enrolment preparations. Just one month later, the study was officially registered on ClinicalTrials.gov (Identifier: NCT06526364).

At the same time, the cutting-edge digital dreaMS app was integrated into the study framework; a gamified, remote, and highly personalized tool to monitor cognitive and functional changes in people living with MS. This digital backbone not only empowers patients to actively engage with their health but also advances the vision of decentralized, real-world data collection at scale.

To operationalize this ambitious protocol, the team was strengthened in August 2024 with the addition of a dedicated Clinnova MS Basel study nurse. This pivotal role ensures seamless implementation of Standard Operating Procedures (SOPs), high-quality execution of study visits, meticulous documentation, and participant management. Rigorous laboratory dry runs validated all experimental and logistical processes, ensuring that every detail met the highest standards before the first participant entered the study.

By October 2024, a targeted recruitment strategy was in place, paving the way for patient screening and culminating in the landmark First Patient In (FPI) in December 2024 at the University Hospital Basel - a defining moment for the project.

From left to right: Dr. Bebeka Cosandey, Prof. Cristina Granziera and Tanja Stoll

To amplify its presence and foster collaboration across stakeholders, the official Clinnova consortium website (www.clinnova.eu) went live in February 2025, showcasing the vision, progress, and opportunities of this transformative initiative. These milestones collectively lay the groundwork for longitudinal, personalized monitoring of MS progression, blending digital innovation with clinical-grade precision.

Since the start of recruitment, it has steadily progressed, with 20 participants enrolled by August 2025, resulting in an average recruitment rate of 2–3 participants per month. This deliberate, high-standard screening process ensures a well-defined, high-quality cohort, poised to yield meaningful and reliable findings that can set new benchmarks in MS research.

Early metrics already signal success: preliminary data on app adherence indicate remarkable participant engagement (adherence rate: 67%), underscoring the appeal and usability of the digital dreaMS app. Along with this high adherence rate, the majority of participants have volunteered to donate additional optional biological samples, thereby broadening the research potential for identifying new biomarkers that could indicate a change in the clinical course of multiple sclerosis. Together, these are powerful testaments to participants' motivation and shared hope to accelerate progress in understanding and treating MS.

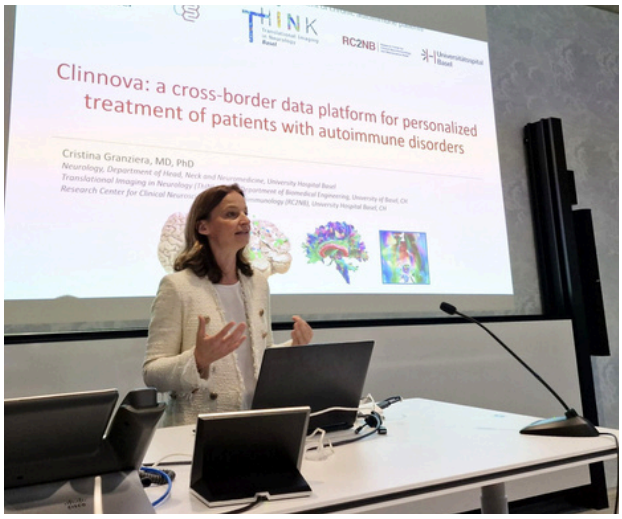
> ***I joined this study because I believe in the future of personalized medicine. If my participation helps others with MS live better lives, it's worth it.*** *Study participant*

Advancing Research Excellence: Imaging and Biomarker Work Packages

The study's ambition extends beyond patient care into scientific innovation. In the imaging workpackage, funds in year one are allocated to 1.5 full-time collaborators dedicated to setting up centralized data collection, planning advanced analyses of standardized imaging data across sites, and contributing to the federated learning platform's development.

In years two and three, a full-time scientific staff member will continue this analytical work, translating raw imaging into actionable insights.

Meanwhile, the first batch of biological samples have been sent to our collaborating laboratory, Luxembourg Institute of Health (LIH) looking into genetic factors associated with early MS, transition phases to progressive MS or response to treatment from blood, saliva, and cerebrospinal fluid (CSF) samples. Furthermore, we investigate the composition of gut microbiota in multiple sclerosis patients from stool samples, and assess the influence of environmental factors on disease onset and progression using hair samples.



Prof. Cristina Granziera, Principal Investigator Clinnova Basel

Clinnova-MS Study Visit

Each Clinnova-MS study visit is a coordinated effort, built on close interdisciplinary collaboration between physicians, neuropsychologists, research and clinical staff, and laboratory teams. Together, they ensure smooth execution and high-quality data collection across a broad spectrum of biomarkers:

- Clinical Biomarkers (e.g., eEDSS)
- Imaging Biomarkers (MRI)
- Digital Biomarkers (dreaMS app)
- Biological Biomarkers (Sample collection)

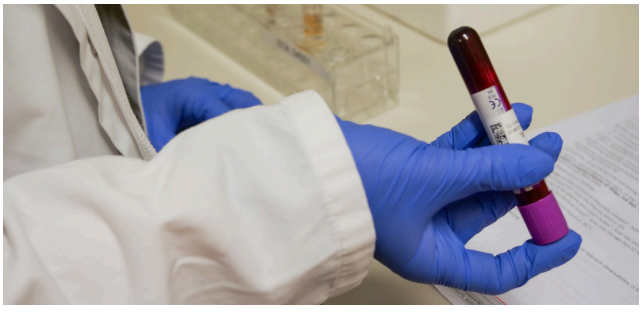
This comprehensive approach forms the core of Clinnova's mission: integrating multi-dimensional data to transform personalized healthcare.

Clinical biomarkers are collected by the treating physician and documented by the study nurse in close cooperation, ensuring accuracy and relevance.

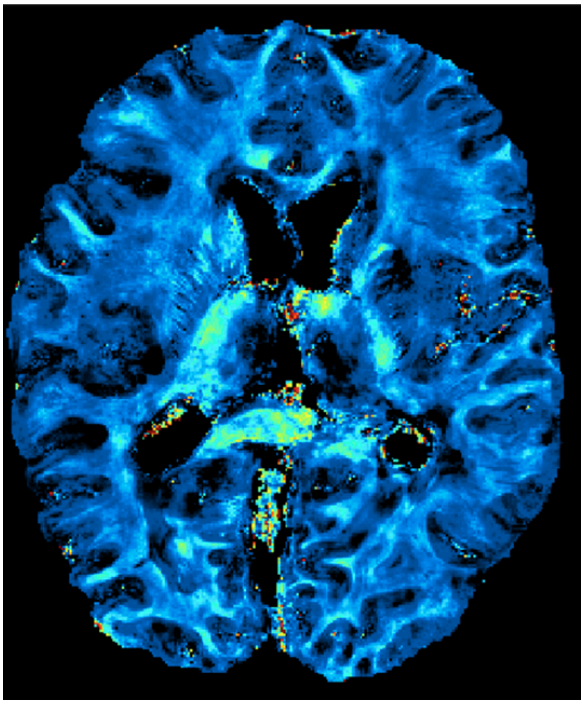
Imaging biomarkers are represented by routine clinical MRI scans, which are seamlessly integrated into the study database.

Digital biomarkers are collected using the dreaMS app. Introduced by the study nurse during the visit, the app is explained in detail, and participants are guided through all exercises. To validate the data, neuropsychologists and study nurses also conduct gold-standard reference tests across corresponding functional domains.

Biological biomarkers are obtained through both mandatory and optional sample collection. In addition to a standard blood draw, participants can choose to contribute hair, saliva, and stool samples. Hair and saliva are collected on-site; stool samples are collected at home using a kit provided during the visit.

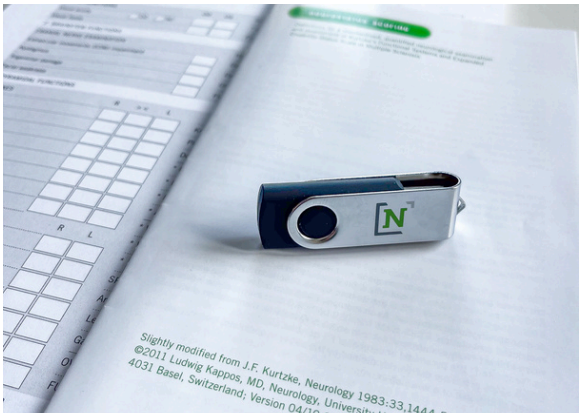


Blood Sample Processing After Study Visit



MHigh-Resolution Magnetic Resonance Imaging Brain Scan

Following collection, samples are immediately processed, stored, or shipped. Blood is drawn into serum, EDTA, PAXgene, and ACD tubes. While PAXgene and ACD samples are shipped the same day, serum and EDTA samples are processed on-site and stored at –80°C. Plasma undergoes DNA stabilization to preserve nucleic acid integrity before long-term storage.
When available, CSF samples from the biobank are also processed on-site and sent to our partner laboratory for advanced analysis.



Training Material for EDSS assessment

Clinnova

Federating Digital Medicine in Europe

Clinnova-MS study visit: Structured patient interview, walkthrough of the dreaMS app, conduction of reference tests as well as collection and processing of biological samples.

dreaMS App for Clinnova MS

dreaMS App: Transforms any smartphone into a measurement laboratory for precision medicine development.

Through end-to-end collaboration with Indivi we are spearheading the use of advanced computational and statistical modelling methods to potentialy yield more precise measures of progression of Multiple Sclerosis with improved signal-to-noise properties.

6+ Sources of Digital Data

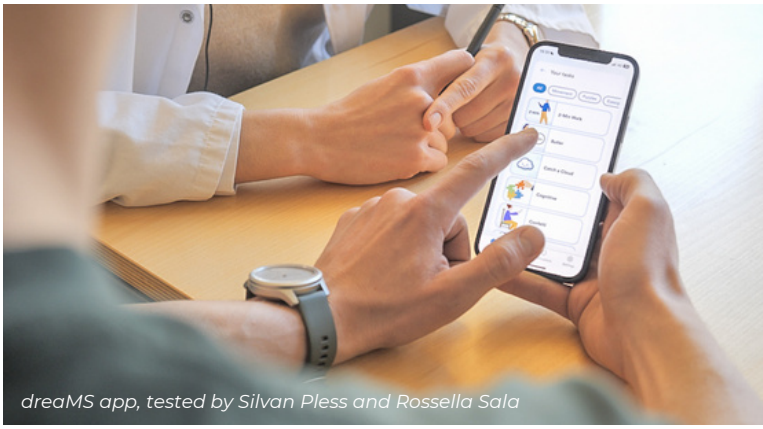
- Movement
- Balance
- Dexterity
- Vision
- Cognition
- Patient-Related Outcomes

Digital Endpoint Development

- Comprehensive neurological functions coverage
- Continuous data monitoring
- Use in everyday setting
- Regulatory processes
- Multilingual, international deployment
- Data transfer, processing and statistical analysis

Clinnova's role in dreaMS

Following dreaMS Study VS1, we are currently conducting dreaMS Clinnova study. This study is an international research project designed to validate the digital biomarkers generated through the dreaMS software. It builds on the previous dreaMS VS1 study, which included 300-400 patients with multiple sclerosis and assessed the clinical validity of candidate digital biomarkers (cDB) related to movement, balance, dexterity, vision, and cognition. Clinnova involves a larger international population, systematically replicating the results of VS1 while extending the evaluation to additional patient-relevant outcomes such as hospitalizations and quality of life. Sub-studies and deep phenotyping are included for more detailed analysis, and patients are actively involved in the study's design and dissemination activities.



dreaMS app, tested by Silvan Pless and Rossella Sala

The main objective of the dreaMS Clinnova study is to provide validated digital biomarkers that can be used for patient care, research, and regulatory decisions related to MS treatment. Beyond validation, the study aims to create a collaborative research platform for future studies and international academic partnerships. This research will contribute to more precise MS monitoring and treatment, improving the quality of life for people with MS by leveraging advanced digital health technologies.

Clinnova and eEDSS-Neurostatus

Empowering Global MS Research with Precision and Expertise

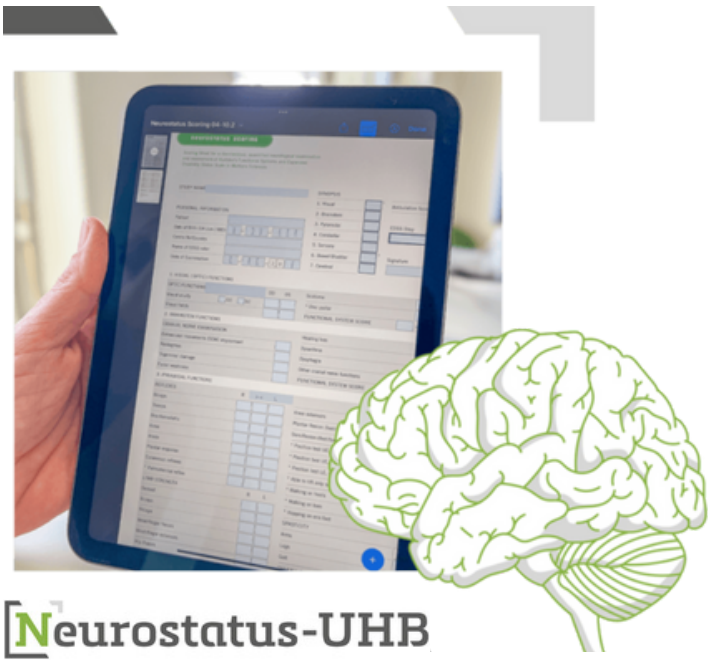
At the forefront of Clinnova-MS's commitment to world-class clinical data quality is the Neurostatus-Expanded Disability Status Scale (EDSS), the internationally recognized gold standard for assessing disability in MS. Developed to deliver standardized, reproducible, and globally comparable measurements, the EDSS enables standardized and reliable tracking of disease progression in both clinical trials and routine care, ensuring that patient outcomes can be meaningfully compared across studies, regions, and populations.

To fully leverage the potential of this test, Clinnova uses the Neurostatus-eEDSS Scoring Tool , which brings clinical data collection into the digital era. With integrated consistency checks and real-time validation, it enables data reliability and comparability to be elevated across all participating sites. Together, these measures position Clinnova MS at the cutting edge of international observational studies, delivering standardized, high-fidelity clinical data that drives innovation, accelerates discoveries, and benefits patients worldwide.

To operationalize this standard across the entire Clinnova European network, a suite of innovative tools and services has been deployed, developed and proven in Basel, now adopted consortium-wide.

- The E-Test Online Certification Tool, enabling centralized, consistent certification of clinical raters worldwide.
- Tailored Training Services, equipping clinical and research teams with the specialized expertise needed to deliver high-quality, reproducible assessments.
- Comprehensive Scoring and Training Materials, ensuring alignment with global reference standards and best practices.

By embedding the eEDSS-Neurostatus at the heart of its clinical data framework, Clinnova-MS sets a benchmark in data accuracy and harmonization, unlocking the full potential of its multi-center, multinational research. This standardized approach not only enhances the validity of biomarker discovery and treatment evaluation, but also provides high-quality, structured datasets essential for training robust AI models and predictive analytics.



Behind the Data: Luh's Story with Clinnova-Multiple Sclerosis (MS)

At Clinnova-MS, we often say that research is not just about numbers, scans, and scores, it's about people. About every single person who walks through our doors and chooses to share a piece of their journey with us. Luh Simpen is one of those people.

From her very first visit to the clinic, Luh radiated something rare, a combination of curiosity, courage, and contagious positivity. When she arrived, she stopped mid-step, eyes lighting up at the bold Clinnova-MS poster hanging in our hallway. With a big, beaming smile, she turned to us and asked: "*Could you take a picture of me and the poster*?"

It might seem like a small gesture. But for us (Clinnova MS team) and for her, it meant something far greater. That photo wasn't just a memento. It was a personal declaration: "*I believe in this. I am part of this.*"

To Luh, joining Clinnova-MS wasn't just about contributing data; it was about creating visibility for multiple sclerosis, supporting future patients, and placing her trust in the vision of the University Hospital Basel. That photo marked her pride in being part of something bigger, a movement toward better treatments, better outcomes, and a deeper understanding of life with MS.

And her commitment didn't stop there.

Luh has been an enthusiastic participant in our continuous testing of the dreaMS app, our digital companion designed to measure subtle changes in MS through playful, science-based tasks.

She checks in regularly, completes tasks with remarkable consistency, and has helped us reach great adherence. When we asked her what kept her so engaged, she said: "*Because I see what it could mean for someone like me, today and tomorrow.*"

This level of dedication isn't something we take for granted. Behind every successful test, every dataset, and every insight are real people like Luh and the study nurses who support them with equal care and compassion. They create a space where science meets humanity, where patients feel seen, heard, and empowered to contribute beyond the clinic.

Luh's story reminds us that research can be joyful. That trust can be tangible. And that when patients and researchers walk side by side, real progress becomes possible.

It's a reminder. A reminder that while we build data models and collect clinical metrics, we are also building something else: a community rooted in trust, purpose, and progress.

And that's what Clinnova is really all about.

> *When we asked her what kept her so engaged, she said:* ***"Because I see what it could mean for someone like me, today and tomorrow."***

Clinnova participant: Luh Simpen
Image credit: Tanja Stoll (Clinnova-MS study nurse)

Clinnova Federated Learning (FL) Team

Dr. Bram Stieltjes
Principal Investigator, Data Architecture Lead, Clinnova Basel

Dr. Francesco Santini
Development Lead Engineer for Federated Learning - Medical Imaging

Jessica Schäper
Development Engineer for Federated Learning - Medical Imaging

Dr. Siri Leemann
Project Manager Personalized Health Basel

Shaping the Future of Collaborative Medical AI

Clinnova Federated Learning (Clinnova-FL) is developing a comprehensive framework for federated learning to enable secure, collaborative data analysis across diverse sites, countries, and diseases. here we outline the conceptual framework, technical developments, current implementation status, and future directions of the project.

Led by the Basel team, Clinnova-FL builds upon the existing Dafne ecosystem to create an interoperable modular, and user-friendly platform that facilitates collaborative model training across multiple institutions while preserving data privacy and security. The project initially pilots this approach using medical imaging data, focusing on multiple sclerosis (MS) lesion segmentation.

From left to right: Jessica Schäper, Francesco Santini and Siri Leemann

At its core, Clinnova-Federated Learning (FL) is designed to enable hospitals and research institutions to collaborate on training AI models without ever sharing sensitive patient data. Instead, data stays securely within each institution, while only the learnings from the data and the mathematical models are shared and combined. This approach is particularly important in healthcare, where privacy, security, and trust are paramount.

Vision and Strategic Approach

Clinnova Data Architecture is a simple yet powerful idea: medical institutions can collaborate to improve healthcare without ever sharing their most sensitive data. Instead of moving data, we move the algorithms. The AI learns from data locally, within each institution's secure environment, while the knowledge it gains is shared across the network, which, is referred to as Federated Learning.

This is a paradigm shift in how we think about data, privacy, and collaboration in medicine. As the lead institution for this effort, the Basel team has embraced the challenge of designing a system that meets the real-world needs of both clinicians and researchers. This means balancing cutting-edge AI technology with the highest standards of data protection, regulatory compliance, and operational usability.

This initiative has focused on a concrete, high-impact use case: helping doctors and researchers detect and analyze brain lesions in people living with MS. But the potential applications go far beyond MS, with the long-term goal of supporting many other diseases and imaging challenges.

The vision driving this work goes beyond developing a tool for federated AI. It is about building a Federated Network of Data Integration Centres, a sustainable, interoperable infrastructure that empowers hospitals and research institutions to collaborate without compromising patient confidentiality.

Each centre remains fully in control of its data while contributing to a shared effort to develop and validate AI models that are robust, clinically useful, and generalizable across populations.

The Basel team, leveraging years of expertise in digital health, medical imaging, and data science, has taken the lead in designing an architecture that is:

- Scalable *across countries and healthcare systems*

- Modular and adaptable *to different diseases beyond multiple sclerosis*

- Intuitive *enough for clinicians and researchers without deep technical backgrounds*

- Rigorously compliant *with data protection laws and clinical standards*

Building on the foundation of the Dafne ecosystem, a platform originally designed for distributed AI in radiology, Basel has expanded the system's capabilities to meet the broader ambitions of Clinnova. This includes not only technical frameworks for federated machine learning but also governance models, documentation, deployment strategies, and community building among partners.

This leadership role is about driving both technology development and a cultural shift in how we approach data-driven healthcare. The goal is to enable every participating institution to become a node in a learning healthcare system, one where insights are continuously refined, models are improved collaboratively, and the benefits reach patients faster. This will make Clinnova Federated Learning the backbone of a future where healthcare innovation respects privacy, empowers institutions, and accelerates the impact of AI for patients across borders.

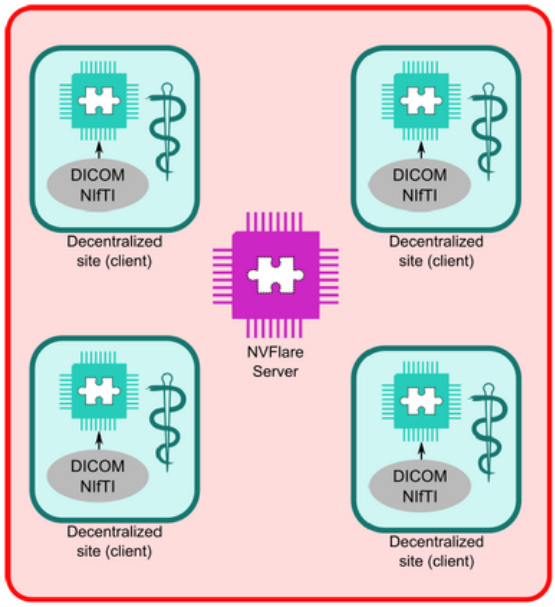
Francesco Santini, Development Lead Engineer for Federated Learning, Basel

> ***Clinnova-FL delivers a modular, privacy-by-design federated learning platform tailored to medical imaging, enabling distributed training of high-performance diagnostic models directly on-site, across diverse institutions and infrastructures"*** *says Francesco Santini, Development Lead Engineer for Federated Learning (Basel).*

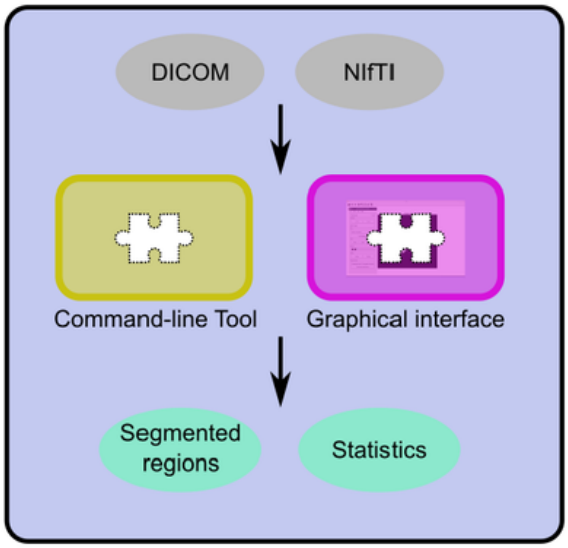
Building the Technical Framework: How It Works

Clinnova-FL is built on an innovative technical framework that balances advanced AI capabilities with privacy protection. At a high level, the system allows multiple hospitals or research centers to train AI models together.

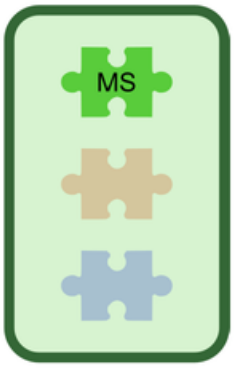
Instead of moving data to a central server, each institution keeps its data locally. The AI model travels to the data, learns from it, and then returns only updated model.



Federated learning workflow



Deployment workflow



Model library

Figure 1: *Clinnova Federated Learning Architecture Overview - This figure illustrates the comprehensive architecture of the Clinnova-FL system with three main components. The top section (red background) depicts the federated learning workflow, showing the NVFlare Server at the center coordinating model training across four decentralized client sites. Each client processes local DICOM/NIfTI medical images while maintaining data privacy. The bottom-left section (blue background) shows the deployment workflow, where trained models are utilized through either command-line tools or graphical interfaces to generate segmented regions and statistics from medical images. The bottom-right section (green background) represents the model library, with the MS (Multiple Sclerosis) lesion segmentation model highlighted as the primary implementation, alongside placeholder models for future expansion. This architecture demonstrates how Clinnova-FL combines federated learning capabilities with practical clinical deployment options.*

Dr. Bram Stieltjes, Data Architecture Lead, Clinnova Basel

The technical foundation combines two complementary platforms. The first is Dafne, an ecosystem developed by the Basel team that provides the infrastructure for deploying AI models in clinical settings. The second is NVIDIA FLARE, a state-of-the-art federated learning engine that handles the secure exchange and aggregation of models across sites.

The current focus is on developing and refining an AI model that can automatically detect MS lesions on brain MRI scans. These lesions are a critical marker of disease activity, helping clinicians monitor progression and treatment response. Behind the scenes, the AI model does much more than just learn from images. It includes sophisticated preprocessing steps such as brain extraction and image correction to ensure the inputs are standardized. Once the model produces results, it applies post-processing filters to improve accuracy and remove irrelevant artifacts. All these steps are encapsulated in a single package, making it straightforward for users to apply the model without needing to manage complex pipelines themselves.

> ***We're building a federated learning framework that is scalable, modular, and privacy-preserving by design. It's a technical backbone that allows AI models to be trained collaboratively without ever moving sensitive data."*** *Dr. Bram Stieltjes, Data Architecture Lead, Clinnova Basel*

Model Architecture

At the core of the system is a dynamic model architecture that encapsulates not just the neural network weights, but also the complete processing pipeline:

- Input/Output Handling: *Flexible interfaces for various medical image formats (DICOM, NIfTI, etc.)*

- Preprocessing: *Brain extraction, bias field correction, registration, and normalization*

- Model Core: *UNet architecture implemented in MONAI/PyTorch with dual-channel input for MPRAGE and FLAIR images*

- Postprocessing: *Threshold-based segmentation and small lesion filtering*

- Interface Layer: *Command-line and GUI access points*

This comprehensive approach ensures that models trained through the federated system can be immediately deployed in clinical settings without additional integration work.

Federated Learning Implementation

The federated learning infrastructure combines elements from two powerful frameworks:

Dafne Ecosystem: *Provides the model structure, deployment mechanisms, and user interfaces*

NVIDIA FLARE: *Handles the coordination of federated training, model aggregation, and secure communication*

This hybrid approach allows us to leverage the strengths of both systems: Dafne's user-friendly interfaces and plugin architecture, and NVIDIA FLARE's robust federated training capabilities.

Importantly, only model weights are exchanged between sites, with all patient data remaining securely within their respective institutions.

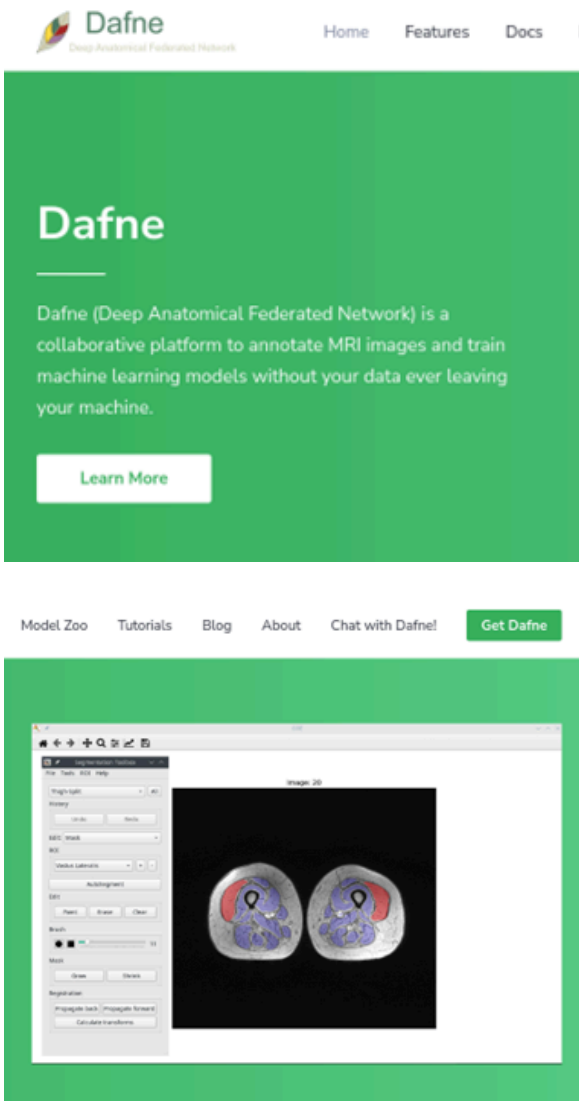


Figure 2*: Screenshot of the existing Dafne (Deep Anatomical Network) ecosystem.*

Federated Communication Workflow

The current implementation follows this workflow:

1. ***A central server*** *(hosted on sciCORE) initiates the training by distributing the base model*
2. ***Client nodes*** *(at participating institutions) receive the model and perform local training on their datasets*
3. ***Only model weight*** *updates are transmitted back to the server*
4. ***The server*** *aggregates the updates using the FedAvg algorithm and creates an improved global model*
5. ***The updated global model*** *is redistributed to clients for further training rounds*
6. ***After training completion****, the final model is made available for deployment through the Dafne infrastructure*

Several technical innovations have been implemented to enhance the system's usability and security:

Technical Innovations and Model Serialization

A key innovation is the approach to model serialization.

The entire model object, including preprocessing and postprocessing logic, is serialized and distributed to clients during the initial round. Ensures the following:

Clients can work with a complete model *without requiring separate installation of preprocessing components*

Models maintain *consistent behavior across different deployment environments*

The system can operate *even in environments with restricted filesystem access*

Privacy-Preserving Preprocessing

The system implements privacy-preserving preprocessing steps such as:

Brain extraction using HD-BET to remove identifiable facial features before any model training

Local metadata processing that ensures sensitive information never leaves the institution

Bias field correction and registration performed locally within each institution

Interoperability with Existing Systems

The system has been designed to interoperate with existing clinical systems through:

Support *for standard medical imaging formats (DICOM, NIfTI)*

Command-line interfaces *for batch processing*

Potential *for PACS/database integration*

Turning Vision into Reality

Over the past year, Clinnova Federated Learning has moved from concept to a working infrastructure. One of the major milestones was the successful integration of the ThINk-MS lesion segmentation model into the Dafne ecosystem. This means that clinicians can now input standard brain MRI scans, whether in DICOM or NIfTI format and receive automated lesion segmentation outputs. Importantly, the system works with a wide range of image resolutions and orientations, reducing barriers to adoption.

In parallel, the team developed a generic federated training module using NVIDIA FLARE. This trainer works hand-in-hand with the Dafne system, enabling collaborative model training while maintaining the privacy safeguards inherent to federated learning.

The central infrastructure hosted at sciCORE, University of Basel's high-performance computing center which is now fully operational. It manages communication between sites, coordinates training, and aggregates models. Local nodes at partner institutions are also being prepared, with clear guidelines for hardware, data and security.

Data must be organized consistently, with separate folders for training and validation, and standardized naming for images and lesion masks. This consistency is crucial for seamless collaboration and reliable model performance.

> ***Clinnova-FL is laying the foundation for secure, cross-border collaboration in health data. It enables institutions to contribute to innovation while keeping full control over their sensitive data."***
> *Prof. Cristina Granziera, MD, PhD, Principal Investigator, Clinnova Basel*

Completed Milestones

As of Q2 2025 Clinnova Federated Learning has achieved several significant milestones:

Integration of ThINk-MS Model: The MS lesion segmentation model developed by the ThINk group has been successfully integrated into the Dafne ecosystem (Dafne-ThINk). This integration provides a command-line interface that accepts images in NIfTI or DICOM format, without specific requirements for resolution or orientation.

Creation of Generic NVIDIA FLARE Trainer: A generic federated model trainer has been developed using NVIDIA FLARE, which works with the Dafne model

structure. This system has been successfully deployed with the Dafne-MS core.

Base Infrastructure Deployment: The server infrastructure has been established, with client configurations that offer flexible data source options

Client Requirements for Participation

For institutions participating in the federated training, the following specifications have been established:

Dataset Requirements: 30-50 subjects with confirmed MS, including 3D MPRAGE and multislice FLAIR acquisitions with whole-brain coverage.

Hardware Requirements: Computing resources with recent CPU, 32GB RAM, NVIDIA GPU with at least 8GB RAM (RTX 30xx series or newer), and secure internet access.

Data Organization: Structured data folders separating training and validation sets, with consistent naming conventions for image contrasts and lesion masks.

Future Directions of Clinnova-FL

The Clinnova-FL roadmap includes the following planned extensions:

Expanded Model Portfolio: Implementation of additional segmentation models for various anatomical structures and pathologies.

Non-imaging Data Integration: Incorporation of federated statistics for non-imaging data and image metadata using approaches like MDClone.

Enhanced User Interfaces: Development of more intuitive interfaces for clinical users, reducing the technical expertise required for model deployment.

Multi-center Validation: Comprehensive validation of models across diverse clinical settings and scanner types.

Long-term Perspective

Clinnova Federated Learning is not an isolated effort. It represents the first building block of a much broader vision: a Federated Network of Data Integration Centres for the Upper Rhine region. This federated infrastructure is designed to go beyond imaging. It will enable researchers and clinicians to securely access a rich, multidimensional patient data space, while ensuring that sensitive patient information never leaves the walls of participating institutions.

In practical terms, the models trained through the federated learning process will serve a dual purpose. On one hand, they will provide clinically meaningful outputs, such as imaging-derived biomarkers. On the other hand, they will contribute to the creation of harmonized data outputs that can be aggregated with other patient data, including clinical records, laboratory results, and genomics, within a secure, privacy-preserving framework.

A key component of this vision is the integration of synthetic data technology through MDClone. This certified tool allows institutions to generate synthetic datasets that preserve the statistical integrity of real-world data while eliminating risks related to patient privacy. Basel brings substantial experience with MDClone and is actively leading the integration of this approach into the Clinnova ecosystem.

Ultimately, this federated network will enable complex, cross-border research queries without the need to centralize sensitive data. It opens the door for large-scale collaborations with external partners, supports the development of next-generation AI models, and drives forward the mission of precision medicine in the region and beyond.

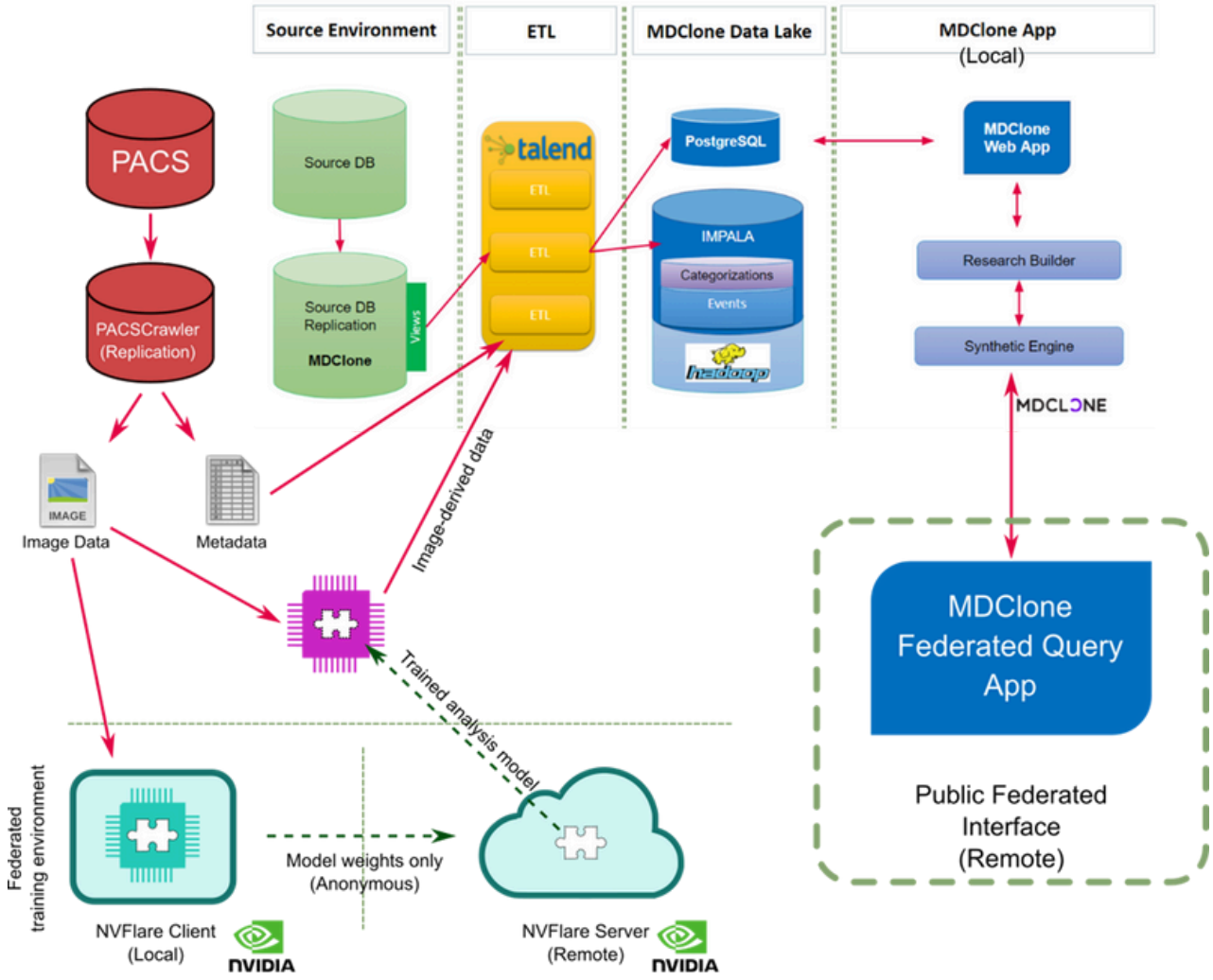


Figure 3: *Future data flow within Clinnova. Imaging models trained through federated learning produce imaging-derived data, which are integrated with clinical and other patient data. This combined dataset passes through an anonymization layer, where synthetic data is generated using MDClone technology. The result is a secure, federated query system that enables large-scale, privacy-preserving research across institutions.*

A New Era for Collaborative AI in Healthcare

The Clinnova Federated Learning initiative represents a major step forward in how medical AI is developed and deployed. By bringing together the strengths of advanced computing, collaborative science, and rigorous privacy protections, Clinnova is helping shape a future where AI can support clinical decision-making without compromising patient trust.

The successful integration of the ThINk-MS model, the establishment of the central infrastructure, and the rollout to partner institutions are tangible demonstrations of what can be achieved through international cooperation and technical innovation.

Through these efforts, Clinnova Federated Learning aims to accelerate the development and adoption of AI-powered diagnostic and analytical tools in clinical practice, ultimately improving patient care through collaborative innovation.

Clinnova Inflammatory Bowel Disease (IBD) Team

Prof. Jan Niess

Principal Investigator

Prof. Petr Hrúz

Principal Investigator

Véronique Pflimlin-Fritschy

Study nurse

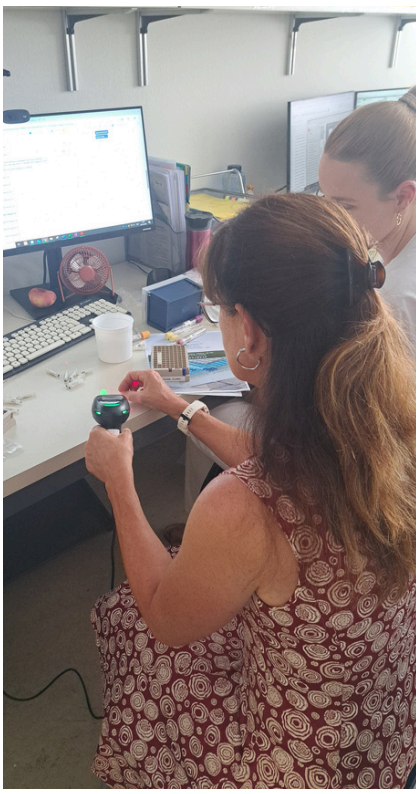
Katline Metzger-Peter

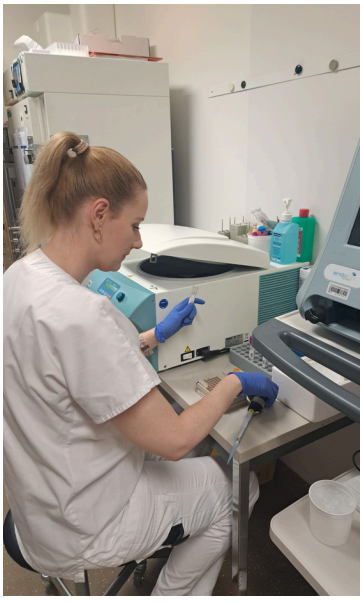
Study nurse

The Inflammatory Bowel Disease (IBD) use case is one of three clinical applications in the Clinnova consortium. It aims to improve the management and stratification of patients with Crohn's disease and ulcerative colitis by aligning clinical documentation, data standards, and digital tools across institutions and national borders. By fostering harmonized protocols and interoperable data infrastructure, the IBD use case supports the development of personalized, data-driven care approaches that address the diverse needs of patients across the region.

The team has worked closely with international partners over the past two years to co-develop standardized clinical protocols, ensuring broad patient access and comprehensive documentation across care settings. This integrated approach enhances the representativeness of the Basel cohort and strengthens its potential to generate meaningful insights for individualized treatment strategies.

Clarunis (University Digestive Health Care Center Basel), a joint competence center of Claraspital and University Hospital Basel, brings together expertise, research activities, and patient care from both hospitals to enhance diagnostic and therapeutic quality. At the Basel site of Clinnova-IBD, led by Prof. Dr. med. Jan Niess from the University Hospital Basel, both Clarunis centers play a pivotal role in implementing the shared vision of the consortium.





Véronique Pflimlin-Fritschy (left) and Katline Metzger-Peter (right) Clinnova - IBD study nurses Image credit: Tanja Stoll

Clinnova-IBD Basel team achieved several important milestones in 2024-2025:

Q3 2024, the team submitted the ethics proposal for local implementation of the IBD protocol.

Q4 2024, they received ethics approval with only minor revisions, fully aligned with protocols already approved and implemented in France, Germany, and Luxembourg.

During the same period, the team contributed to recruitment planning and completed the legal processes required to finalize the bilateral Material and Data Transfer Agreement (MDTA) with the Luxembourg Institute of Health, signed in **Q4 2024.**

In 2025, the team adapted the Clinnova IBD protocols to site-specific and internal processes in Basel, ensuring compliance and operational feasibility while maintaining full alignment with consortium-wide standards.

A site initiation training in Q2 2025 was conducted, including a complete dry run of the sample collection and processing workflow. This exercise, supported by the operational team of the Clinnova-MS use case, allowed the IBD team to test SOPs under real-world conditions, identify logistical challenges, and adjust infrastructure and training to Clinnova's high standards of reproducibility.

This proactive preparation optimized readiness at both Clarunis and Claraspital sites while reinforcing internal expertise and fostering cross-disease collaboration a hallmark of the Clinnova. Such synergies ensure that the multi-disease cohorts operate efficiently, consistently, and at the forefront of innovation.
In addition to Prof. Jan Niess, the Basel effort is spearheaded by Prof. Petr Hrúz, the principal investigator at the Claraspital site, and supported by study nurses Katline Metzger-Peter and Véronique Pfimlin-Fritschy, play a central role in maintaining operational excellence and providing consistent support to patients. Together, the team ensures that the Basel site meets the high expectations of the Clinnova international consortium while tailoring processes to the needs of local patients and staff.

Data recording is a cornerstone of the Clinnova-IBD use case, ensuring that high-quality, interoperable data is collected securely and efficiently. Clinical data are recorded using electronic Case Report Forms (eCRFs) in REDCap, hosted by the University Hospital Basel IT department.

Each patient receives a unique pseudonymized identifier, and only authorized personnel, such as the site project lead and designated delegates, can access or update records. The eCRFs comply with standardized medical terminologies like CDISC and SNOMED CT to ensure full interoperability across all Clinnova sites. The REDCap system is browser-based, secured through password protection and role-based user rights, and backed up regularly to safeguard data integrity and availability throughout the study lifecycle.

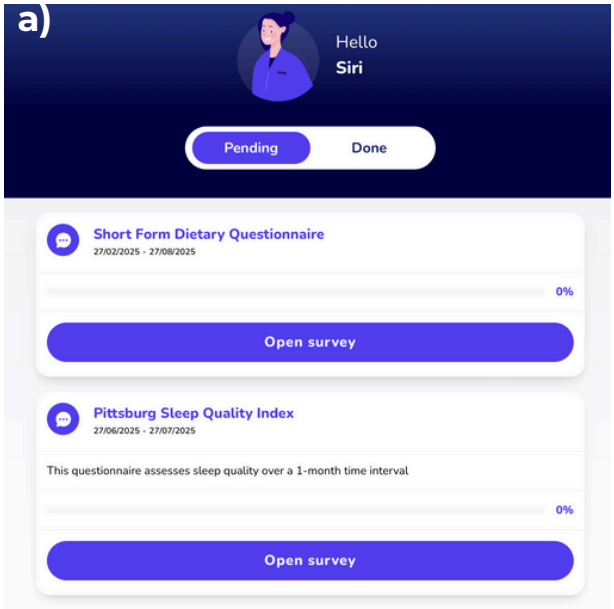
Patient-reported outcomes (PROs), including optional standardized voice recordings, are collected through the Colive app, originally developed by the Luxembourg Institute of Health (LIH) and adapted in Basel to meet local regulatory and operational requirements. Colive evolved from earlier digital health research initiatives into a robust, secure platform for collecting PROs and digital phenotyping data remotely. In the Clinnova-IBD study, participants install the app on their devices and receive individual login credentials at inclusion. They complete monthly questionnaires during the first year and then every six months during follow-up. Automated email reminders help sustain engagement and minimize missing data.

PROs are designed to capture a wide range of parameters, including quality of life, disease activity, psychological distress, medication adherence, and lifestyle risk factors. Participants are instructed to complete the assessments independently and to answer as accurately as possible. All data entered into the Colive app are pseudonymized at the point of collection using a randomized Colive-ID. These data are first stored in the secure Colive database at LIH and subsequently transferred to the local Data Integration Center in Luxembourg. Only pseudonymized data, with no direct or indirect identifiers, are accessible to the study team, while nominative data remain securely stored in separate, restricted-access environments at the clinical site. This setup ensures both long-term usability of the data and full compliance with strict privacy and data protection standards.

Looking ahead, the Basel team will focus on initiating and scaling up patient recruitment while contributing to the first wave of data collection across the Clinnova network. Efforts will also center on integrating data into the federated infrastructure, supporting quality control measures across sites, and beginning exploratory analyses to identify stratification-relevant patient subgroups.

Strengthening collaboration with partner sites remains a priority, particularly in harmonizing outcome documentation and ensuring seamless, interoperable data exchange in line with FAIR principles. These next steps will lay the foundation for innovative decision-support tools and regional learning networks that can transform the care of patients with inflammatory bowel disease and beyond.

> ***Including IBD in Clinnova Basel allows us to explore complex patient subgroups with precision. Inflammatory bowel disease is highly heterogeneous, and by harmonizing clinical protocols and digital infrastructure across sites, we can generate more meaningful insights into disease trajectories. This not only strengthens the Basel contribution to the European consortium but also ensures our patients benefit from cutting-edge, personalized care approaches that emerge from this unique international effort."***
> *Prof Jan Niess, Principal Investigator, Clinnova IBD Basel*



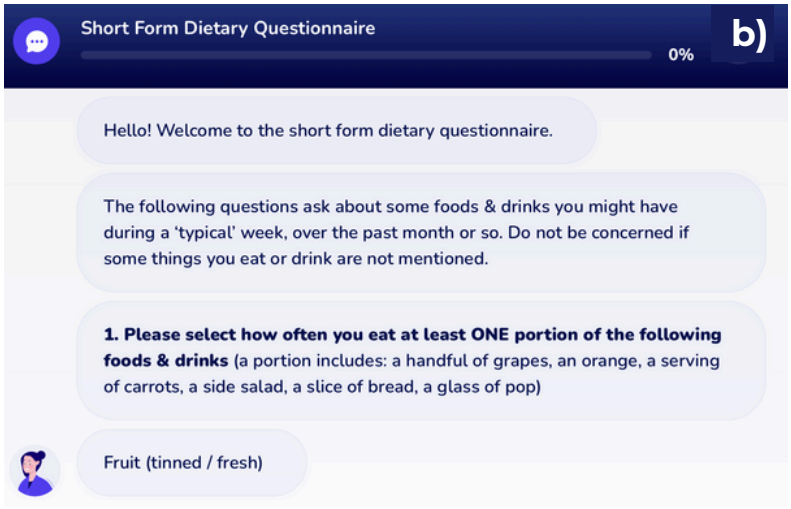


***Figure 4**: Participant Survey Interface and Questionnaire in the Colive App - Colive app is a useful tool for remote diagnosis, prevention, and monitoring of diseases developed by Luxembourg Institute of Health. **a)** The first panel displays the participant survey interface, showing pending surveys with their status, title, date range, and progress, allowing users to access and complete them directly. **b)** The second panel shows an example of the Short Form Dietary Questionnaire, illustrating the questionnaire interface and progress indicator.*

Clinnova Basel Financial Statement

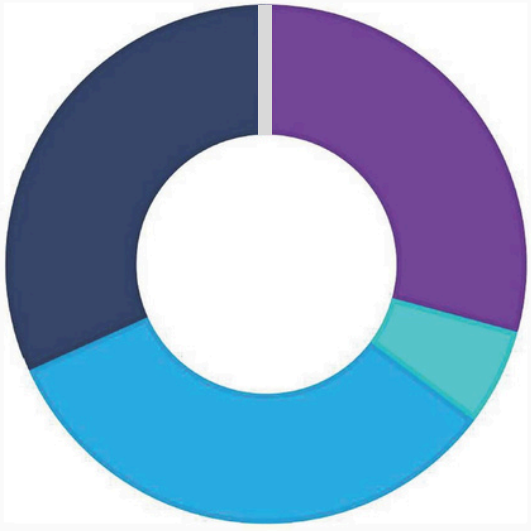
Clinnova Basel continues to transform strategic funding into measurable progress in research and innovation.

With the support of our key funding partner, the Canton of Basel, we strengthened and expanded our activities throughout 2024/2025, ensuring both operational excellence and long-term sustainability. This financial foundation enables us to deliver on Clinnova's vision: advancing personalized, data-driven care for patients with chronic diseases.

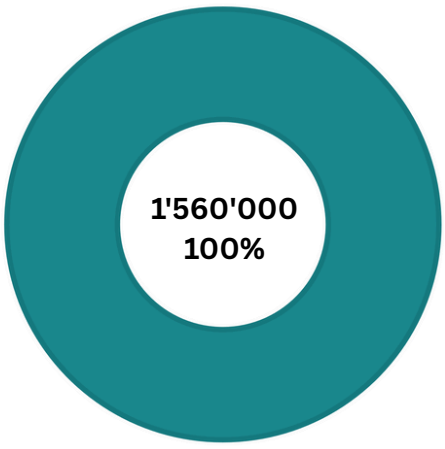
In 2024/2025, funding was strategically allocated to our highly skilled study and data management teams, as well as to cutting-edge imaging, laboratory, and digital infrastructure. Operating expenses totaled CHF 632,368, with a positive balance of CHF 927,632 earmarked for future investments in innovation and cross-border collaboration.

We extend our sincere gratitude to the Canton of Basel-Stadt and all our collaborators and stakeholders. Their commitment to our shared mission ensures that Basel remains a leader in driving meaningful change for patients through research, innovation, and partnership.

- Laboratory Costs -CHF 200'430 -32%
- Administration and other expenses; -CHF 250; 0%
- Study Personnel; -CHF 184'799; -29%
- Data Management Personnel; -CHF 38'281; -6%
- Imaging Costs; -CHF 208'609; -33%



	2024
Income from research contributions	156 000 CHF
Total Operating Income	**1 560 000 CHF**
Study Personnel	-184 799 CHF
Data Management Personnel	-38 281 CHF
Imaging Costs	-208 609 CHF
Laboratory Costs	-200 430 CHF
Administration and other expenses	-250 CHF
Total Operating Expenses	**-632 368 CHF**
Profit/Loss	927 632 CHF



Clinnova Strategic Outlook

Clinnova is entering a decisive phase in its mission to advance precision medicine through responsible data sharing, federated learning, and clinical collaboration across borders. The coming years will focus on scaling up patient cohorts, maturing digital infrastructure, and transitioning from proof-of-concept to real-world application.

Key Milestones

1. Cohort Expansion and Model Development

Building on the early recruitment efforts, Clinnova aims to expand across all partner countries significantly. The goal is to reach more than 100 participants per disease area: multiple sclerosis (MS), inflammatory bowel disease (IBD), and rheumatoid arthritis (RA). This scale will allow more robust training of federated AI models designed to support disease trajectory prediction and treatment response assessments.

2. Digital Infrastructure and Biobanking

A major priority in 2025 will be the launch of a secure, interoperable digital health platform integrating federated learning capabilities, harmonized data pipelines, and biobanking infrastructure. This platform, coordinated in part from Basel, will enable regional centers to contribute data in a standardized, privacy-preserving manner, aligning with FAIR (Findable, Accessible, Interoperable, Reusable) data principles.

3. Clinical Decision Support Pilots

As models mature, Clinnova plans to initiate clinical pilots of AI-driven decision support tools. These tools, tailored for MS, IBD, and RA will be tested in real-world settings to assess their clinical utility, usability, and predictive value. Emphasis will be placed on supporting physicians in stratifying treatments and identifying early digital biomarkers.

4. Ecosystem Expansion and Commercial Activation

To ensure long-term impact, Clinnova will broaden its regional footprint, inviting additional countries, regions and institutions. In parallel, an open innovation platform is planned to foster collaboration with technology startups, research spin-offs, and public-sector stakeholders positioning Clinnova as a reference ecosystem for responsible digital health innovation in Europe.

5. Scientific and Regulatory Validation (2028–2029)

By 2028, Clinnova expects to generate multi-site evidence supporting the clinical validity of its predictive models. These outcomes will form the basis for scientific publications and, where applicable, preparation for regulatory submissions to enable broader clinical use of digital tools developed within the consortium.

Challenges and Opportunities

Clinnova, like any ambitious international consortium, faces challenges — from time-intensive participation and complex recruitment to procedural delays inherent in multinational collaborations. At the same time, digital tools such as Colive and the dreaMS app are being enhanced to deliver a polished, reliable, and user-friendly experience, unlocking their full potential for patients, clinicians, and researchers. These hurdles are also opportunities: they drive stronger collaboration, sharper processes, and greater resilience, positioning Clinnova as a benchmark for how international consortia can thrive in complexity.

Looking Ahead

While challenges remain, from securing sustained funding to navigating complex data governance requirements, Clinnova continues to represent a unique opportunity to prototype the future of digital medicine. As an international consortium operating across borders, Clinnova brings together diverse healthcare systems, regulatory environments, and clinical practices. Naturally, not all countries and disease areas are progressing at the same pace. Differences in infrastructure, cohort readiness, and local implementation frameworks can lead to coordination challenges and uneven development.

Despite these complexities, the consortium remains fully committed to its shared vision. Continued collaboration, transparent communication, and cross-learning between partners remains essential to maintaining alignment and advancing the program as a whole. With a strong foundation now in place, Clinnova is well-positioned to demonstrate how cross-border collaboration, responsible data sharing, and patient-centred innovation can contribute to a more integrated and effective European healthcare landscape.

Clinnova Report

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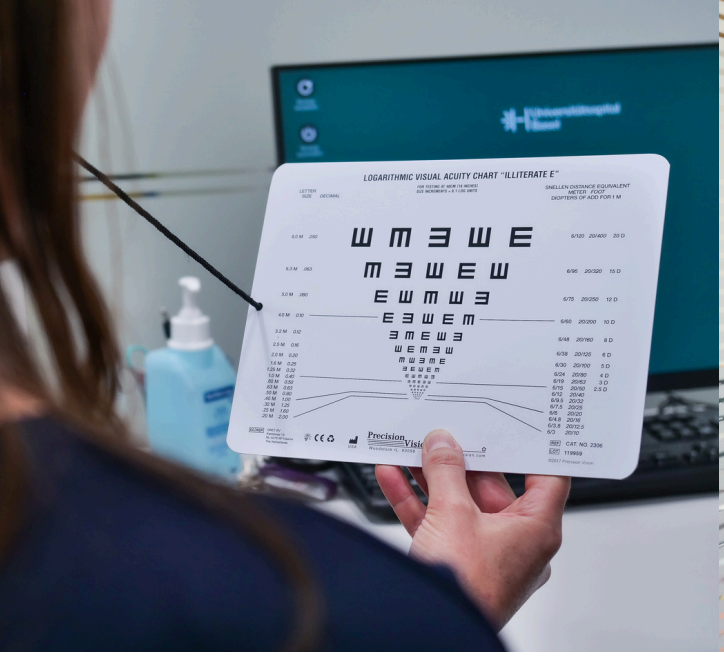
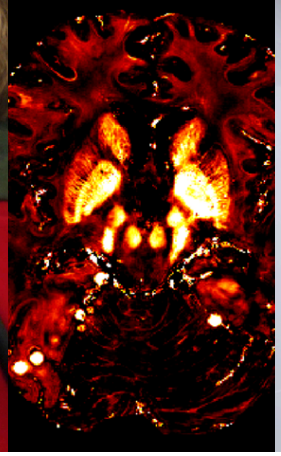


Clinnova

Federating Digital Medicine in Europe

Basel




Clinnova

Federating Digital Medicine in Europe

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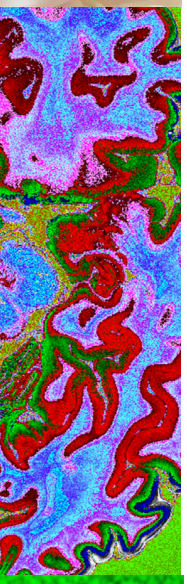
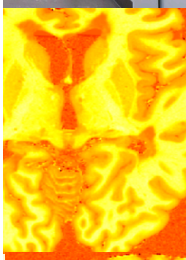
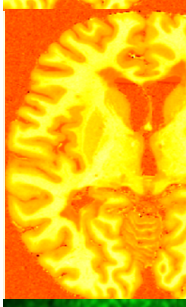
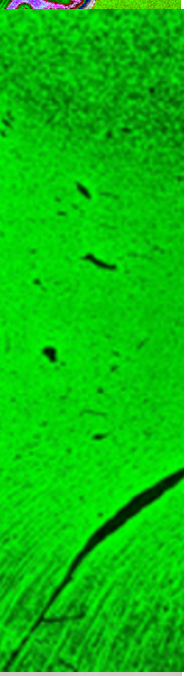
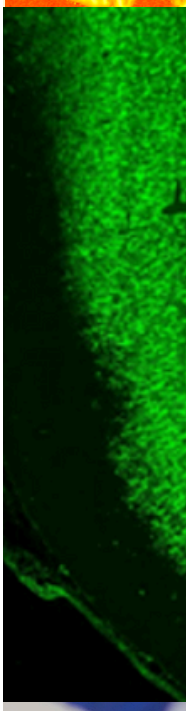


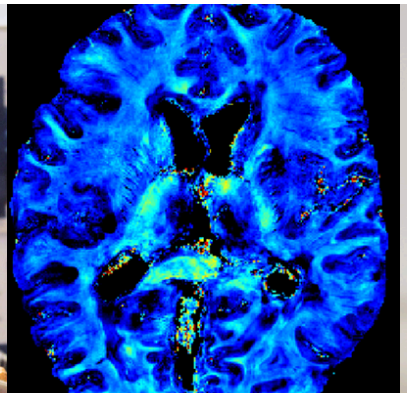



Clinnova