



Newsletter

NOVEMBER 2025

Dear MISTRAL colleagues,

Thank you all for your continued dedication and hard work in these last months of MISTRAL visits — your efforts are truly appreciated.

In this seventh MISTRAL Study Newsletter, we share updates on our study, provide insights from ongoing analyses, and put a spotlight on recent research related to the gut microbiome. We hope these updates keep you informed and engaged with the exciting progress in our work.

As always, we welcome your feedback, insights, or any good ideas you'd like to share — just reach out, and we'll be happy to include them in future updates to benefit the wider network.

Warm regards,

The MISTRAL Team at CHIP

Study updates



Visit 2 update

As of 17th November 2025, 786 participants have returned to their clinic and completed their second visit.

Please remember that since EU funding concludes at the end of 2025, **no further MISTRAL visits should be conducted after 1 December**. Any study visits not completed before this date will be considered *lost to follow-up*.



Status of visit 2 per clinical site

Last scheduled shipment of samples

In order to ensure that all remaining Visit 2 samples can be shipped to IrsiCaixa in Spain by the end of 2025, we kindly ask that you send all outstanding samples to us no later than **Monday, 1 December 2025**. Please reach out to our laboratory technician Annette Hauberg Fischer (annette.hauberg.fischer@regionh.dk) to organize the shipment.

MISTRAL Follow-up (FU3 Autumn 2025)

As of 1st October 2025, the MISTRAL follow-up dataset (FU3 Autumn 2025) is open for data entry in REDCap. This includes all participants that completed Follow-up 2 last Autumn, as well as participants with enrolment forms checked and locked (validated) in REDCap before 1st May 2025. This is a kind reminder to complete Follow-up 3 by **1st December 2025**. Should you encounter any challenges, please inform us promptly. We are happy to assist you with any support to facilitate the process.

We hope this will not be the last follow-up dataset! If funding allows, we will continue until 2030.

Analysis update

As part of the MISTRAL project, shotgun metagenomic sequencing has now been completed for 958 participants. High data quality across the full dataset has allowed for comprehensive and statistically robust downstream analyses.

Since the last update, bioinformatic and statistical analyses have progressed substantially. Using the complete metagenomic dataset, we have integrated microbiome, clinical, lifestyle, and laboratory information into a unified analysis framework. Statistical modelling and bioinformatic analyses demonstrate that gut microbiome composition is significantly associated with both systemic inflammation and cardiovascular disease (CVD) risk scores, with each exerting independent effects on microbial community structure. Measures of microbiome markers show consistent relationships with

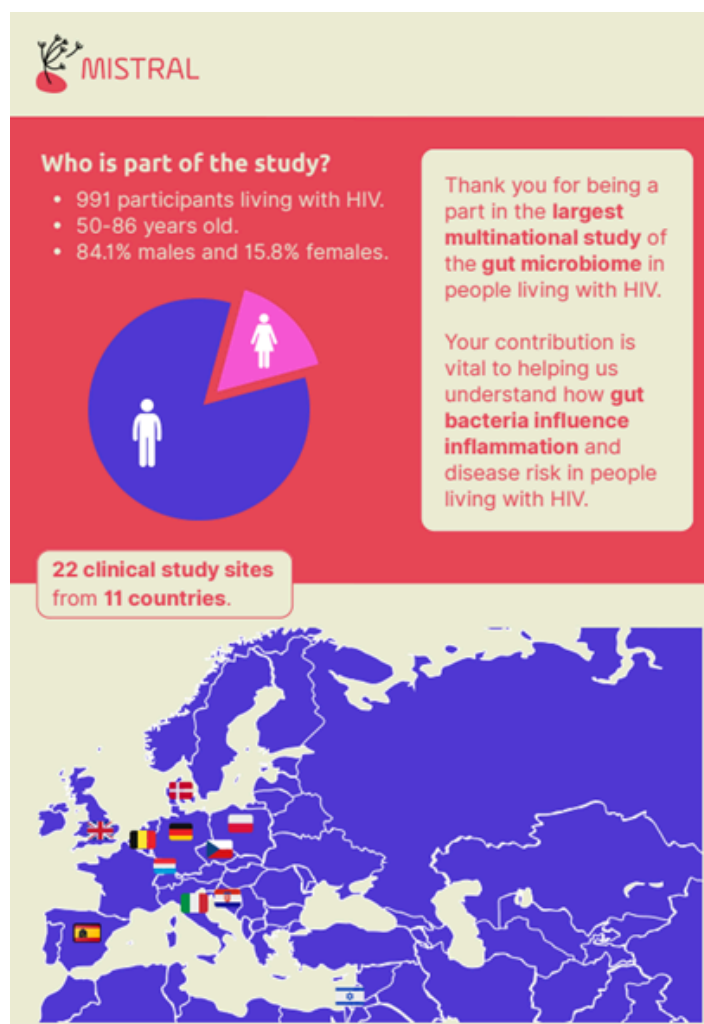
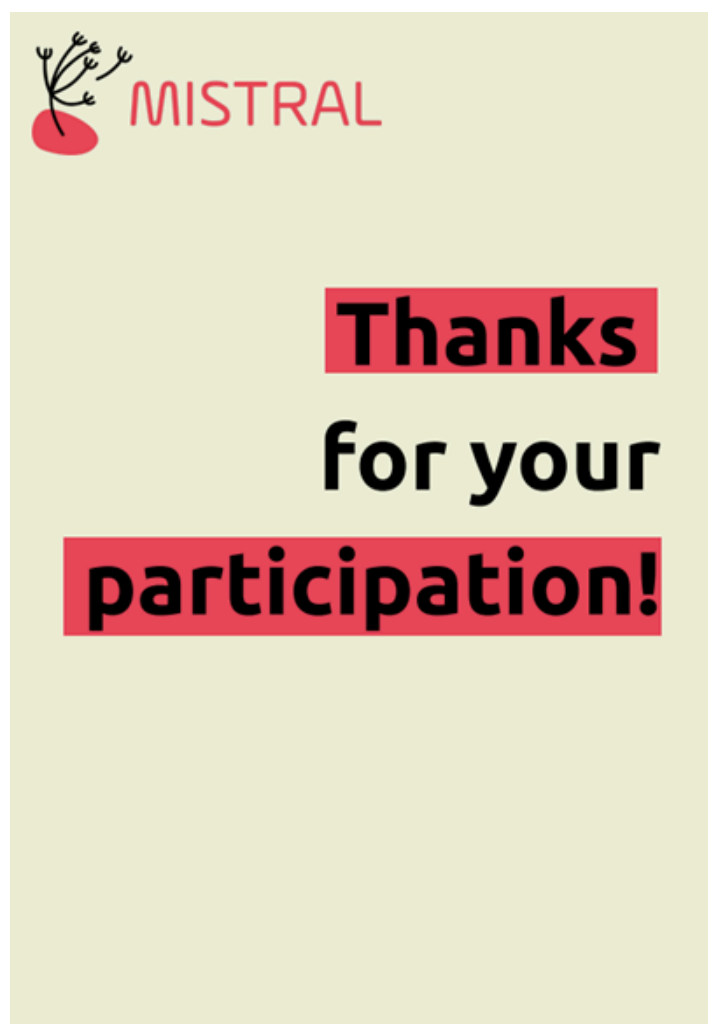
inflammatory and cardiovascular markers, strengthening the evidence for microbiome involvement in cardiometabolic pathways among people living with HIV.

The extended analyses further highlight strong influences of sex, country, HIV transmission mode, and sexual practices on microbiome variation within the cohort. Notably, sex-stratified analyses indicate that the associations between microbiome features and CVD risk are more pronounced in men, suggesting potential gender-specific microbiome–host interactions. The MISTRAL WP4 team is now focusing on functional analyses to explore mechanistic links between inflammation, cardiovascular health, and microbial metabolism, aiming to identify microbial metabolism-derived signatures relevant to cardiometabolic risk in people living with HIV.

An email with details about the first writing group meeting will be distributed soon.

MISTRAL participant brochure

As you know, we have developed a participant study brochure to thank participants for their participation in MISTRAL, as well as to provide them with some information on the cohort that they are part of. Please share it with your participants. You can find the English version and in other languages [here](#).



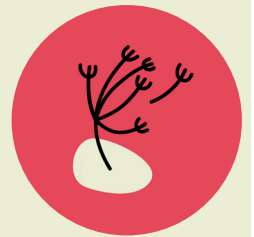
Data catalogue

We're currently developing a data catalogue to give researchers a clearer overview of the types of data being collected within the MISTRAL study. This resource will support external researchers in preparing and submitting study proposals. The catalogue will be available on our website very soon.

20th European AIDS Conference (EACS), Paris, France. 15-18 October 2025

In connection with the EACS Conference in Paris this October, we hosted a joint EuroSIDA and MISTRAL investigator meeting. Thank you to those who joined us in Paris, it was great to see you in person!

MISTRAL beyond 2025



As a reminder, the MISTRAL study is scheduled to conclude in December 2025, when our funding from the European Commission also comes to an end. As we enter this final phase, your continued engagement is key to ensuring we complete the study successfully. If funding allows, we do plan to continue clinical follow-up annually until 2030. We will of course keep you informed along the way.

The MISTRAL consortium



MISTRAL is a large international consortium funded by EU. Research groups from all over Europe are engaged in the work, which has been split into several work packages each with their own aim. Information about all the work packages included in MISTRAL can be found at www.mistral-hiv.eu.

The primary objective of the work led by CHIP is to strengthen and evaluate the understanding of the association between the gut microbiome composition and the risk of developing serious AIDS and non-AIDS events (SNAEs), including cardiovascular events.

MISTRAL cohort characteristics

Twenty-two sites from countries in Europe are part of our MISTRAL work package. A total of 991 participants completed their first visit, of which 334 were already part of EuroSIDA.

The group consists predominantly of white men who have sex with men (MSM). Their diet is mainly omnivorous, and the stool samples collected have mostly been of Type 4 of the Bristol Stool Chart.

We have a richly characterised cohort in relation to factors that may influence the microbiome and the risk of serious non-AIDS events. Preliminary assessments also highlight the need to treat these variables carefully given the observed correlations and small numbers of certain subgroups (e.g., women and non-white ethnicities).



Countries in Europe and Israel part of the MISTRAL cohort

Interesting research on the gut microbiome



Borgognone et al., "Interactions between gut microbiota, plasma metabolome and brain function in the setting of a HIV cure trial", *Frontiers in Cellular and Infection Microbiology* (2025)

A new study from MISTRAL shows connections between gut bacteria and brain health in people living with HIV. The study has been developed in the framework of the BCNO2 clinical trial and suggests that certain intestinal microbes and the compounds they produce may be linked to changes in brain functioning.

The article is available here: <https://doi.org/10.3389/fcimb.2025.1629901>.

Learn more about MISTRAL

Previous MISTRAL newsletters can be found at:

<https://chip.dk/Research/Studies/MISTRAL/MISTRAL-Newsletters>

You can find all the study documents related to the MISTRAL project at

<https://chip.dk/Research/Studies/MISTRAL/Study-documents>

General information about MISTRAL can be found on this website

<https://chip.dk/Research/Studies/MISTRAL>

Information about all the work packages included in MISTRAL can be found at

www.mistral-hiv.eu

Finally, you can follow the MISTRAL consortium on X: <https://x.com/mistralhiv>

This was all we had for now. We look forward to sharing more updates with you in half a year.

Sincerely,

The MISTRAL team at CHIP



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