CArdiovascular Risk Assessment via multimodal data analysis enabling personalised prevention strategies targeting MEnopausaL women

CARAMEL 4th Project Brief

Two years after its official launch in December 2024, the CARAMEL project continues to advance its research agenda, with growing emphasis on translating multimodal AI research into clinically relevant, trustworthy digital tools and personalised cardiovascular prevention strategies for menopausal women. Following the Athens Plenary Meeting held on November 2026, this fourth Project Brief summarises the main achievements of the last six months across the active Work Packages (WPs) and outlines priorities for the next semester, including clinical study implementation, model validation, digital integration, end-user engagement and impact.



WP2 - Project management & coordination II

Achievements

- The project coordination and management framework remained fully operational throughout the semester, ensuring continuous monitoring of activities, deliverables, milestones and risks across all WPs. The 4th Semester Work Plan was implemented, with no project risks materialising during the reporting period;
- The third consortium-wide 360° self-assessment was conducted in July 2026, followed by the definition of an Action Plan to strengthen internal collaboration and project implementation;
- Periodic Report 1, covering M01–M20, was successfully coordinated and submitted to the European Commission in September 2026, followed by the organisation of the first EC Review Meeting. The review provided valuable feedback on the project's technical and clinical progress, highlighting key priorities for the next implementation phase;

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- Monthly GLED meetings continued to oversee ethical, legal, privacy and data protection matters, including ongoing oversight of CARAMEL-OS and the management of protocol changes requiring ethical review;
- A dedicated Data & Samples Task Force was created, a sub-group of GLED Committee, mandate by CARAMEL's Steering Committee to design and agree on a policy, governance and procedure for the re-use of data and samples within and beyond the project research community. The policy and governance model will be available by November 2027;
- The Gender in Research Training Programme progressed across the consortium, with all seven training modules and the evaluation component delivered and completed by new researchers engaged in the project;
- The 5th Project Meeting was successfully organised in Athens (Greece) hosted by NKUA at M24, November 2026, to review project progress and align priorities for the next implementation phase.

Goals for the next 6 months

- Address the EC's recommendations following the first Review Meeting, coordinating the necessary follow-up actions across WPs, particularly regarding AI model validation, clinical applicability, data integration and clinical study implementation;
- Implement the 5th Semester Work Plan (M25–M30) and finalise the 4th Monitoring Report (M19–M24), maintaining regular oversight of project progress, risks, deliverables and milestones;
- Launch the next consortium-wide 360° self-assessment in April 2027, followed by the corresponding evaluation in May, to further strengthen project management and collaboration;
- Reinforce engagement with the External Advisory Board (EAB), seeking targeted expert feedback on the clinical utility of AI models, the CARAMEL Personalised Prevention Programme (PPP) and potential refinements to the CARAMEL-Observational Study (OS) design;
- Advance the legal and operational framework governing collaboration between CARAMEL and CoroPrevention, including the relevant collaboration and material transfer agreements, to support secure access to biological samples and their use in future joint research activities;
- Advance the work of the Data and Samples Sharing Task Force, including the development of data access policies, preparation of dataset metadata for the European Health Data Space (EHDS) HealthDCAT-AP catalogue sandbox, and arrangements for the long-term storage and reuse of clinical samples;
- Maintain monthly GLED meetings and ensure the formal tracking of ethical amendments across clinical sites.

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WP7- Prospective AI Modelling and Multi-source Integration

Achievements

- WP7 progressed from the initial retrospective model portfolio towards the next modelling phase, identifying priorities for model refinement, multi-source integration and future use of CARAMEL-OS data;
- Initial external validation of EHR-based predictive models highlighted limitations in their generalisability across different populations and healthcare settings. To address these challenges, the available data resources were expanded to approximately 1.54 million records, combining datasets from Keralty, SAS and UK Biobank (in the near future) to support subsequent model retraining and validation;
- Preliminary imaging-based modelling activities progressed, including a proof-of-concept analysis investigating the contribution of DXA imaging to cardiovascular risk prediction;
- Development pathways were defined for the next generation of imaging and signal-based AI models, covering retinography, carotid ultrasound, wearable devices, implantable cardiac devices and skin patch recordings, with further development dependent on the availability of appropriate datasets. A multi-source modelling strategy was also outlined to explore the integration of clinical, imaging and physiological data;
- Methodological planning progressed for the integration of explainable AI models into cardiovascular risk assessment and clinical decision support, including approaches for assessing adherence to clinical guidelines and generating personalised recommendations;
- A dedicated clinical utility workshop was organised during the Athens Plenary Meeting, bringing together clinicians and technical partners to explore six promising AI model prototypes covering clinical records, patient trajectories, cardiovascular risk factors, medical imaging, skin patch signals and wearable data. Model demonstrations, multidisciplinary discussions and individual questionnaires were used to seek feedback on clinical relevance, interpretability and potential use within healthcare workflows.

Goals for the next 6 months

- Refine and further develop the most promising imaging AI models, including retinography and carotid ultrasound models, as relevant datasets become available, and advance their integration into image-processing pipelines with visual outputs for future clinical decision support;
- Advance signal-based AI modelling, including implantable cardiac device models for atrial fibrillation detection, wearable-based cardiovascular risk prediction and anomaly detection, and skin patch models as suitable clinical recordings become

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available. Define common interfaces, output formats and visualisations to support their future integration into the CARAMEL ecosystem;

- Retrain and validate EHR-based predictive models using the expanded multi-source datasets, assessing their performance and generalisability across different populations, while developing and benchmarking multimodal approaches that combine clinical risk factors, imaging and physiological signals;
- Progress the integration of AI outputs into the CARAMEL cardiovascular risk assessment and stratification framework, including explainable risk predictions, guideline-adherence assessment and AI-supported recommendations. Define how these outputs will be presented within the Clinical Decision Support System (CDSS);
- Develop AI-enabled personalisation and engagement strategies in collaboration with clinical partners and Patient and Public Involvement (PPI) Committees, exploring lifestyle-based recommendations, personalised goals, behavioural change techniques and their future integration into the CARAMEL self-management tools and Virtual Health Coach;
- Collect further feedback from clinical sites about the clinical utility of the target AI models, based upon the survey used in Athens workshop, to identify priority models, improve the interpretability of AI outputs and ensure their alignment with healthcare professionals' needs and clinical workflows;
- Define and initiate the implementation of the AI lifecycle management strategy, addressing model evaluation, explainability, monitoring and trustworthiness throughout the development and validation process.

WP10 - Digital platform & ecosystem II

Achievements

- A Grafana-based public-health visual analytics dashboard prototype was deployed on VICOM infrastructure, incorporating Keycloak authentication and illustrative views for cohort exploration, cardiovascular risk indicators and geographical information, using representative mock data;
- A draft event-driven architecture and common event schema were prepared for the platform's self-management functionalities, alongside a mock event producer and synthetic examples to support initial technical testing;
- Development of the CDSS progressed through the identification of AI model outputs, clinical data and guideline-based knowledge required for integration. Work began on an initial user interface mock-up, with VICOM and BGU coordinating requirements for future guideline-based decision support functionalities;
- Requirements for the CARAMEL Self-management App (smApp) were consolidated. The existing Data Capture App (datApp) and Self-Assessment App (asApp) modules were integrated as a foundation for the future smApp, while the MEGI Virtual Health

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Coach technology and safety framework were reviewed to inform its CARAMEL-specific adaptation;

- The existing platform security baseline was reviewed, a draft role-based access control (RBAC) scope was prepared, and maintenance activities were carried out to address identified software vulnerabilities;
- The WP10 Integration Matrix and Test Plan were established, identifying 11 interfaces across platform components. Nine local mock, API and interface-contract tests were successfully completed, while cross-component staging scenarios remained to be agreed.

Goals for the next 6 months

- Further develop the public-health visual analytics dashboard by completing the REDCap-to-Data Lake statistics workflow, connecting validated data sources and agreeing the OpenGeoHealth exchange mechanism, while refining visualisations based on partner feedback on indicators, filters and privacy constraints;
- Advance the implementation of the platform's event-driven self-management functionalities by selecting the initial event broker, agreeing the first platform-to-smApp interface contract and initiating staging tests for event ingestion and dispatch;
- Finalise the initial CDSS user interface mock-up, gather feedback from healthcare professionals and develop the dedicated platform module. Assess the integration of guideline-based decision support functionalities into the CDSS;
- Progress the development of the CARAMEL smApp, documenting dependencies and defining initial interfaces with the platform and monitoring services. Agree the Virtual Health Coach's inputs, outputs and integration requirements with MAG-MEGI, and prepare initial CARAMEL-specific test scenarios;
- Strengthen platform privacy and cybersecurity by finalising role-based access permissions, agreeing data exposure rules and testing secure service-to-service communication in staging;
- Update the WP10 Integration Matrix, agree component ownership and interface contracts, and initiate the first authorised staging and end-to-end integration tests involving the platform, CDSS, smApps and Virtual Health Coach.

WP12 - Prospective clinical studies (CARAMEL-OS) II

Achievements

- The CARAMEL-OS continued across the six participating clinical sites, reaching a total of 1,085 recruited women by early November 2026, with enrolment rates varying across centres;
- Recruitment progress was systematically reviewed across clinical sites, and potential adjustments to recruitment targets and follow-up duration were discussed in response to implementation challenges;

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- A draft standardised carotid ultrasound acquisition protocol was presented and discussed;
- Clinical and technical discussions addressed key operational aspects of CARAMEL-OS, including blood sample shipment to CIC bioGUNE, the assessment of lipoprotein(a) [Lp(a)] and the harmonisation of procedures across clinical sites;
- A dedicated CARAMEL-OS home monitoring training session was conducted during the Athens meeting, led by PARTICLE and iBreve, providing clinical partners with practical guidance on datApp installation, wearable connectivity, remote monitoring and data synchronisation;
- A dedicated workshop on the CARAMEL PPP was held during the Plenary Meeting, outlining a structured, evidence-based methodology for developing personalised cardiovascular prevention recommendations. The proposed approach applies the GRADE-ADOLOPMENT framework and sets out a multidisciplinary development process for PPP V1, involving clinical and methodological expertise and women's participation;
- Biobanking activities progressed through the collaboration with the CoroPrevention project, supporting the collection and long-term preservation of biological samples for future cardiovascular research.

Goals for the next 6 months

- Accelerate CARAMEL-OS recruitment across clinical sites, prioritising support for sites experiencing slower enrolment and strengthening the monitoring of recruitment rates and study progress;
- Assess the feasibility and approval requirements of potential adjustments to recruitment targets and follow-up duration, ensuring scientific robustness, operational feasibility and compliance with applicable ethical and regulatory requirements;
- Finalise and harmonise the carotid ultrasound acquisition protocol across clinical sites, supporting standardised image collection and centralised assessment of cardiovascular risk markers; training of practitioners from the six clinical sites in the protocol to be completed in this period;
- Harmonise procedures for blood sample collection, shipment and storage across clinical sites, and clarify the arrangements for biomarker analyses, including lipoprotein(a), in collaboration with CIC bioGUNE;
- Advance the CoroPrevention biobanking activities coordinated by TAU, including sample collection, preparation for automated aliquoting and planning for future transfers to CIC bioGUNE, subject to the applicable legal, ethical and data-sharing arrangements;
- Strengthen home monitoring procedures across CARAMEL-OS clinical sites through harmonised participant onboarding, technical support and systematic verification of

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data synchronisation, ensuring consistent use of the datApp and connected devices and minimising data loss during participant follow-up;

- Define the scope and structure of the CARAMEL PPP V1, establish the multidisciplinary development group and identify priority clinical questions covering cardiovascular risk assessment, stratification, preventive interventions and follow-up, taking into account women's individual characteristics and risk profiles;
- Initiate the systematic review and methodological appraisal of existing clinical practice guidelines, applying AGREE II and GRADE-ADOLOPMENT approaches to identify recommendations that can be adopted, adapted or developed specifically for CARAMEL, supporting the progressive development of the updated CVD risk stratification and personalised prevention framework.

WP15 - Communication, dissemination and exploitation II

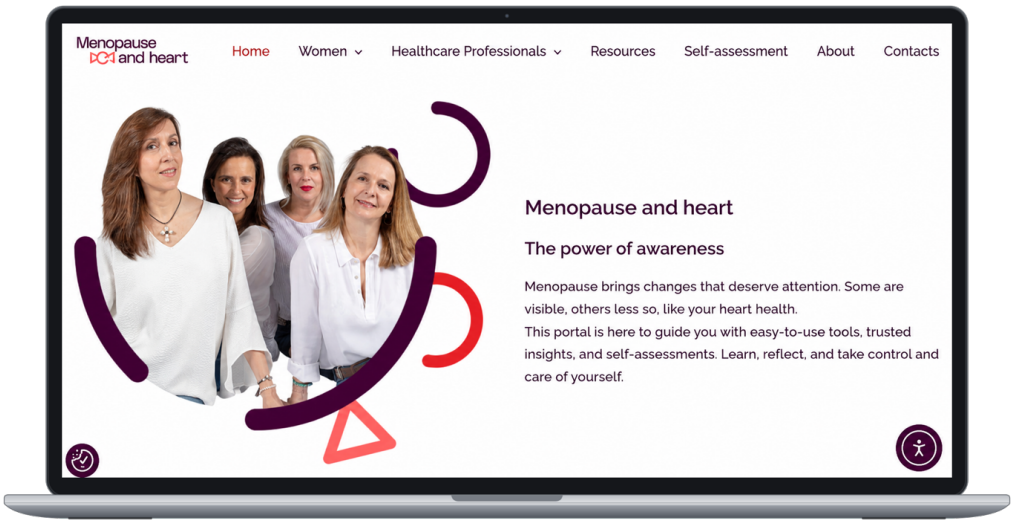
Achievements

- Communication and dissemination activities continued across the consortium, strengthening CARAMEL's visibility through its website, social media channels, newsletters, scientific publications and stakeholder engagement initiatives;
- The *Menopause and Heart* CVD Prevention Portal, accompanying awareness materials were made available online at M20, while the web-based asApp was available at M24, providing accessible information and self-assessment resources for women and healthcare professionals. Translation activities were initiated to support wider accessibility across participating countries;
- A preliminary analysis of evaluation frameworks was conducted to support the future assessment of the Portal's effectiveness, usability, implementation and potential public health adoption, considering Health Technology Assessment (HTA), GRADE, Social Sciences and Humanities (SSH) approaches and complementary evaluation methodologies;
- The first consortium-wide Intellectual Property Rights (IPR) Audit was consolidated, supporting the identification and updating of partners' background knowledge. A market analysis survey was developed and distributed across the consortium to inform the project's exploitation and sustainability strategy;
- Patient and Public Involvement (PPI) activities continued to support the involvement of women, clinicians and researchers in project development;
- Scientific dissemination and networking activities progressed, and clinical sites continued organising awareness and dissemination initiatives, including dedicated women's cardiovascular health events in Croatia and Spain.

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Goals for the next 6 months

- Complete the translation of the *Menopause and Heart* Portal and accompanying awareness materials into the languages of participating clinical sites, followed by coordinated dissemination activities to increase awareness and use of the Portal and web-based asApp;
- Define and initiate the evaluation of the Portal, combining appropriate assessment frameworks to investigate usability, user experience, empowerment, implementation feasibility and potential value for women, healthcare professionals and healthcare systems;
- Complete the CARAMEL market analysis assessing market needs, competitive positioning and the exploitation potential of the project's Key Exploitable Results (KERs). Organise dedicated exploitation workshops to support the development of sustainable exploitation strategies;
- Plan further engagement of PPI Committee in the development of CARAMEL-IS, the CDSS and self-management tools, according to their development timelines;
- Expand networking and clustering activities with relevant European projects, research initiatives, healthcare organisations and stakeholder networks, promoting opportunities for collaboration, knowledge exchange and joint dissemination.

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