

LiverTwin AI

A Virtual Human Twin for Chronic Hepatitis B and Liver Disease
Predictive · Preventive · Personalized · Participatory liver care

LiverTwin AI is a proposed European initiative building a continuously updated, AI-powered digital twin of the chronic Hepatitis B (HBV) patient. By integrating clinical, biological, behavioural and environmental data, it aims to make liver care predictive and personalized — supporting earlier intervention, better treatment decisions, continuous monitoring, and improved long-term outcomes. LiverTwin is not a drug-development project; it is the predictive and clinical-intelligence layer around next-generation Hepatitis B care.

1. The Problem: Chronic Liver Disease — A Crisis Without a Compass

257M	1.1M	€18B+	Up to 80%
People living with chronic HBV globally	Deaths per year from HBV complications	Annual economic burden in Europe	Diagnosed only at advanced fibrosis stages

Chronic HBV management remains difficult on several fronts:

- **Late detection.** Up to 80% of patients are diagnosed at advanced fibrosis stages, when intervention options are limited.
- **No functional cure.** Existing antivirals suppress HBV replication but rarely achieve HBsAg clearance — the goal remains elusive.
- **Fragmented data.** Clinical decisions rely on episodic lab values, missing behavioural, imaging and lifestyle signals that shape progression.
- **One-size-fits-all care.** Treatment protocols lack personalization; response prediction depends on physician intuition rather than evidence-based AI.
- **Monitoring gaps.** Patients are lost to follow-up and early warning signals are missed between clinic visits.

2. Why Now — A Convergence of Technology, Policy & Unmet Need

- **Multimodal AI maturity.** Foundation models now integrate imaging, genomics, wearables and EHR data at clinical scale, making comprehensive liver twins technically feasible.
- **Biomarker breakthroughs.** Novel HBV biomarkers (HBcrAg, HBV RNA, cccDNA surrogates) offer real-time viral-activity insight for predictive modelling.
- **Digital health infrastructure.** The European Health Data Space (EHDS) and GDPR-compliant federated learning enable cross-border data flows at scale.
- **EU regulatory alignment.** The EU AI Act and EMA AI guidelines create a clear pathway for CE-marked, explainable clinical decision support.
- **Horizon Europe momentum.** The Virtual Human Twin flagship makes 2027 the optimal window for hepatology applications.

3. The LiverTwin Vision & Architecture

LiverTwin AI creates a living digital mirror of each patient across four pillars: **Predictive** (progression models forecasting outcomes 6–24 months ahead), **Preventive** (personalized strategies targeting modifiable risk before irreversible damage), **Personalized** (treatment-response prediction tailored to biomarker and genetic profiles), and **Participatory** (a patient AI companion keeping patients engaged and

adherent).

LAYER 1 — Multimodal Data Ingestion	Labs & biomarkers · medical imaging · wearable sensors · lifestyle & behaviour · emotional indicators · genomics & proteomics · treatment history
LAYER 2 — AI & Digital Twin Core	Federated learning engine · multimodal fusion model · digital liver simulation · progression predictor · explainable AI (XAI) layer
LAYER 3 — Clinical & Patient Outputs	Clinical decision support · risk scores & alerts · patient dashboard · prevention plan · treatment-response prediction · regulatory reporting

Cross-cutting by design: Privacy-by-Design · GDPR-compliant · HL7 FHIR integration · CE-mark pathway ready.

4. Biomarkers & Predictive Performance

LiverTwin fuses viral-activity markers (HBV RNA, HBsAg quantification, HBcrAg, cccDNA surrogates), liver-function dynamics (ALT/AST, FibroScan LSM, MRI stiffness, albumin/bilirubin), immune-landscape signals (T-cell exhaustion, PD-1/PD-L1, NK activation, cytokines) and novel metabolic markers (gut microbiome, metabolomics, epigenetic methylation).

Prediction target	What it does	Target AUC*
6-month progression risk	Fibrosis-stage transition probability with confidence intervals	87%
HCC development score	Hepatocellular carcinoma risk within 3 years for cirrhotic patients	91%
Treatment-response prediction	Likelihood of functional-cure response under novel antiviral regimens	84%
Decompensation alert	Early-warning system for acute-on-chronic liver failure events	93%

** Indicative target performance benchmarks based on published literature and consortium pilot data.*

5. AI-Supported Clinical Decision Support

The clinical workflow is a closed loop: patient data is aggregated from EHR, wearables and labs; the LiverTwin is updated in near real-time; a risk-stratification score is generated with an XAI explanation; the clinician receives a prioritized alert and recommended action; and the logged clinical decision is fed back into the model. Explainability sits at the core — SHAP/LIME explanations, uncertainty quantification, and an evidence trail linking every recommendation to specific patient signals.

- **Human-in-the-loop by design** — AI augments, never replaces, the clinician.
- EU AI Act Article 13 transparency requirements fully addressed; audit log aligned with MDR 2017/745.
- Validated against EASL HBV guidelines and the EMA AI/ML Software-as-a-Medical-Device pathway.

6. Consortium Structure

An interdisciplinary international partnership targeting 10–14 members across 6+ EU Member States and Associated Countries, on a TRL 4–7 pathway. Roles being assembled:

In place	Role
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Partners we are seeking — including the academic in-silico modelling and validation role we hope Insigneo could anchor:

- **AI / Digital Health partner** — Virtual Human Twin methodology, machine learning, predictive analytics, clinical decision support, explainable AI.
- **Academic / research organization** — in-silico & computational medicine, health data science, biomarker research, VHT modelling and validation.
- Complementary roles: digital-health SMEs, patient associations, clinical-trial infrastructure, and health-economics/policy partners.

7. Innovation, Impact & Horizon Europe Alignment

Three European firsts: the first multimodal AI virtual twin designed specifically for chronic HBV at European scale; the first real-time integration of HBV-specific biomarkers with behavioural and emotional-health data in a unified predictive model; and the first XAI-driven hepatology CDS tool built from the ground up for EU AI Act compliance and MDR certification.

Expected impact: early detection of fibrosis progression in ~40% more patients, ~30% fewer liver-related hospitalizations, improved treatment personalization for 50,000+ EU patients/year, and acceleration of functional-cure trial design and recruitment — with a replicable architecture for hepatitis C, MASLD and other chronic liver diseases.

Direct alignment with HORIZON-HLTH-2027-03-TOOL-04 and the VHT flagship, the EU Cancer Mission (HCC early detection), the European Health Data Space, the EU AI Act, and SDG 3. LiverTwin is committed to FAIR data, open-science components, and sex-disaggregated, diversity-inclusive cohort design.

8. Scalability Beyond HBV

HBV is the starting point; the architecture is universal. **Phase 1 (2027–2028):** chronic Hepatitis B core development. **Phase 2 (2029–2030):** expansion to Hepatitis C (post-SVR monitoring) and MASLD/NASH. **Phase 3 (2031+):** a pan-liver platform covering PBC, PSC, autoimmune hepatitis and hereditary conditions. **Beyond 2033:** a multi-organ VHT integrating cardiac, metabolic and renal twins. Reusable assets: federated learning framework, XAI engine, patient companion app, EHR integration layer, and regulatory dossier templates.

PROPOSED NEXT STEP

We would welcome a short introductory call to walk your team through the concept and explore where your group's in-silico modelling and validation expertise would best fit. LiverTwin AI represents a once-in-a-decade opportunity to lead the transformation of chronic liver disease care through AI.