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ONWARD: A one health, pan-European multidisciplinary network advancing surveillance, research, clinical management and control of zoonotic hepeviruses

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ABSTRACT

Zoonotic hepeviruses, particularly hepatitis E virus (HEV, species *Paslahepevirus balayani*) represent a major yet underestimated public health challenge in Europe. Despite being the leading cause of acute viral hepatitis, surveillance, diagnostic practices and prevention strategies remain heterogeneous across EU/EEA countries, limiting comparability and hindering accurate burden estimates. Underdiagnosis is further compounded by

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extrahepatic manifestations and the growing impact of chronic HEV infection in immunocompromised patients. At the human–animal–environment interface, zoonotic HEV circulates widely in domestic pigs, wildlife and food products, while coordinated surveillance and control measures remain inconsistently implemented. The recent recognition of ratHEV (species *Rocahepevirus ratti)* as a cause of acute and chronic hepatitis in Europe further expands the spectrum of zoonotic hepevirus infections and underscores the need for integrated One Health approaches. To address these challenges, the One Health Zoonotic Hepevirus Network (ONWARD; COST Action CA24140) was launched in 2025 as a pan-European, multidisciplinary collaboration uniting experts across human, veterinary, food safety and environmental health sectors. ONWARD aims to harmonise diagnostic tools, strengthen clinical research, integrate multisectoral surveillance, promote capacity building and support evidence-based policy development. By fostering coordination with European stakeholders ONWARD provides a structured framework to strengthen preparedness, surveillance and response to zoonotic hepevirus threats across Europe.

1. Improving Europe's response to emerging zoonotic hepeviruses

Zoonotic hepeviruses, including species *Paslahepevirus balayani* (hepatitis E virus, HEV), represent a major underestimated public health challenge in Europe [1]. Although HEV is recognised as the leading cause of acute viral hepatitis in the continent [2], most countries lack standardised procedures for its surveillance and control [3]. National surveillance for HEV infections is in place in many EU/EEA countries [4]; however, approaches, case definitions and testing strategies, including blood donation screening, remain heterogeneous, limiting comparability across Member States despite the subsequent development of EU-level operational recommendations [5]. Therefore, the true burden of the disease remains under-recognised and under-reported, with thousands of infections likely undiagnosed due to the lack of harmonised diagnostic algorithms and reference laboratory testing. The problem of underdiagnosis is compounded by the occurrence of extrahepatic clinical manifestations [6], which escape detection by current surveillance systems. In addition, chronic HEV infection has emerged as a significant clinical problem among immunocompromised patients [7], particularly in solid-organ transplant recipients, representing an important cause of hospital admission in this population [8].

At the animal level, HEV is recognised by the European Food Safety Authority (EFSA) as a foodborne zoonotic virus of major relevance for the EU [9]. EFSA has recommended prioritising its control and improving harmonised surveillance across Member States [10], particularly within pig herds and wildlife populations, which constitute the main reservoirs of the virus [11]. Nevertheless, surveillance remains largely uncoordinated, despite the existence of a proposed framework for pig-farm surveillance and the intense trade of live animal and animal products among European countries [12]. Other routes of transmission, including blood transfusion and organ transplantation, have been documented, but systematic donor screening across the EU is still lacking [13].

From a clinical standpoint, no specific antiviral treatments or vaccines are currently approved in Europe. Therapeutic management relies largely on off-label use of existing drugs (e.g. ribavirin), supported by limited and heterogeneous evidence from small retrospective cohorts [14]. The only human vaccine available to date is licensed exclusively in certain Asian countries, and its applicability to European genotypes remains uncertain [15]. Therefore, preventive measures are essentially limited to avoiding the consumption of raw or undercooked animal products; a recommendation that, while effective in theory, is difficult to sustain and insufficient to reduce the overall burden of infection in Europe. From a scientific perspective, there are countless open questions regarding the pathogenesis, the true genetic diversity, the spectrum of animal reservoir, and the modes of transmission of HEV.

In addition, the recent emergence of rat-origin HEV species *Rocahepevirus ratti* (ratHEV) as a cause of both acute and chronic hepatitis challenges the traditional paradigm of HEV as the sole zoonotic hepevirus [16]. The detection of ratHEV in patients with acute and chronic hepatitis across several European countries highlights new potential transmission routes and the need to broaden current therapeutic and preventive strategies beyond HEV [17–19]. Given that ratHEV has been identified in rodent populations from nearly all European countries [20], the likelihood of undetected or misdiagnosed human cases is high. This evolving scenario underscores the critical importance of establishing coordinated European action to integrate clinical, veterinary and environmental surveillance within a unified One Health framework.

2. Building a pan-European One Health network

ONWARD (One Health Zoonotic Hepevirus Network) was launched in September 2025 under the European Cooperation in Science and Technology (COST-CA24140) framework to address the scientific, clinical and policy gaps that hinder Europe's capacity to respond to zoonotic hepeviruses (Table 1). Bringing together experts from 32 European countries in virology, hepatology, infectious diseases, clinical microbiology, veterinary medicine, food safety, epidemiology, ecology and public health, ONWARD establishes the first pan-European multidisciplinary framework uniting human, animal and environmental health sectors under a coherent One Health approach (Table 2). Its overarching aim is to build a sustainable European system for the prevention, diagnosis, research and control of zoonotic hepevirus infections. Among the 164 active participants, approximately two-thirds are affiliated with academic institutions (universities and university-linked research centres), while the remaining one-third represent non-academic sectors, including national public health institutes, veterinary authorities, governmental agencies, clinical laboratories and international organisations. This balanced composition ensures that ONWARD integrates both fundamental research excellence and applied, policy-relevant perspectives across the One Health spectrum.

Young researchers (YRs) are positioned at the core of ONWARD; not as passive participants, but as active contributors and emerging leaders shaping the network's scientific and strategic direction. They are systematically empowered through priority access to mobility grants (e.g. STSMs), targeted training schools and workshops, and structured mentorship programmes pairing them with senior investigators. Crucially, YRs are embedded in leadership and decision-making processes: they are encouraged to coordinate working group tasks, lead dissemination activities, and contribute directly to key outputs. Through this integrated approach, ONWARD not only supports capacity building but actively cultivates the next generation of leaders in hepevirus research.

The Action pursues five main objectives:

i. Harmonise diagnostic and molecular tools for HEV and ratHEV detection and typing across laboratories in Europe.
ii. Strengthen clinical research and evidence-based management of zoonotic hepevirus infections.
iii. Integrate human, animal, food and environmental molecular surveillance to improve source attribution and risk assessment.
iv. Promote data sharing, capacity building and inclusiveness within the European scientific community.

v. Support evidence-based policy development and strengthen Europe's preparedness for emerging zoonotic threats.

To achieve these goals, ONWARD is organised into five interconnected Working Groups (WGs) supported by three cross-cutting Task Forces that foster coordination, innovation and inclusiveness across disciplines. The first three WGs address the scientific and technical core of the Action, namely WG1 focuses on the harmonisation of diagnostic and molecular characterisation methods for HEV and ratHEV; WG2 addresses advancing clinical research, defining therapeutic algorithms, and assessing disease burden; and WG3 centres on integrating animal, food and environmental data to better understand transmission pathways and improve food safety. Two additional WGs reinforce the translational and strategic dimensions of the network WG4 dedicated to communication, dissemination and training activities andWG5 establishes synergies with European and global initiatives and stakeholders, ensuring policy relevance and outreach. Through this integrated structure, ONWARD seeks to generate the knowledge, technical capacity and

Table 2
Composition and diversity of the ONWARD network.

Category	Details
Participating countries	Albania, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Kosovo, Lithuania, Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tunisia, Türkiye, Ukraine and United Kingdom.
Scientific expertise	Virology & Microbiology (27%) Veterinary Medicine (23%) Infectious Diseases & Hepatology (19%) Epidemiology & Public Health (13%) Food Safety & Environmental Science (10%) Bioinformatics & Modelling (5%) Policy & Communication (3%).
Gender balance	55% female / 45% male
Young researchers	37%

Legend: Young researchers are considered in COST members under 40 years old at the kick-off of the network.

Table 1
Key challenges and gaps in the European response to zoonotic hepeviruses.

Area	Current situation in Europe	Challenge and gaps	ONWARD response
Epidemiology	HEV is the leading cause of acute viral hepatitis in Europe. Human infections are linked to animal reservoirs, food and blood products and environmental exposure, but their relative contribution to transmission remains poorly quantified. Cases of ratHEV infection have already been documented in Europe	True human burden underestimated; risk factors and transmission dynamics at the human–animal–environment interface remain insufficiently characterised, limiting source attribution and targeted control	ONWARD will integrate multisectoral data to improve burden estimation and source attribution.
Surveillance	HEV is notifiable only in a minority of EU countries, while ratHEV is absent from official reporting. Animal and food-chain surveillance is recommended by EFSA but sparsely / inconsistently implemented, with limited integration between veterinary, food-safety and public-health sectors.	No EU-wide harmonised surveillance or reference network. Lack of harmonised and operational protocols for coordinated human–animal–food surveillance.	ONWARD will develop harmonised surveillance frameworks and indicators and promote implementation through collaboration with public health and veterinary authorities.
Diagnostic	Fragmented serological and molecular assays across human, animal and environmental sectors; lack of consensus protocols, limiting reliable diagnosis and comparative analysis. Fragmented molecular and serological assays across human, animal and environmental sectors; lack of consensus protocols, limiting reliable diagnosis and comparative analysis.	Absence of validated inter-laboratory standards and consensus serological/molecular assays; no harmonised serological or PCR-based methods for ratHEV; limited capacity for typing and data sharing across sectors.Absence of validated inter-laboratory consensus molecular assays for canonical and non-canonical samples; no harmonised PCR or serology for ratHEV; limited capacity for typing and data sharing across sectors.	Dedicated ONWARD WGs will develop, validate and disseminate standardised molecular and serological protocols, including for rathev.
Clinical Management	No approved antivirals; ribavirin only partly effective and the therapy is not standardized; chronic and extrahepatic HEV infections under-recognised.	Need for harmonised guidelines, therapeutic innovation and clinical-trial frameworks.	WG2 will define harmonised clinical guidelines, support multicentre studies and promote therapeutic evaluation.
Prevention	No HEV vaccine approved in Europe. Blood-donor screening is inconsistent and unstandardised; screening of plasma-derived products varies across countries. Preventive measures at the animal-production and food-processing levels are inconsistently implemented, with limited guidance on farm biosecurity, feed control and slaughterhouse management.	Lack of robust evidence on vaccine effectiveness for HEV genotype 3, and potential cross-protection, in a European context; absence EU-level recommendations and standard protocols for blood-donor and plasma-derivative screening; absence of coordinated preventive strategies across animal production, food industry and public-health sectors.	ONWARD will generate evidence for vaccination and screening strategies and support development of EU-level recommendations.
Food & Environment	The EU is home to over 150 million domestic pigs; HEV genotypes 3 and 4 detected in pork, game (wild deer, wild boar, rabbit) meat and environmental matrices (water, sludge). Risk of food-borne and environmental transmission persists due to variable control measures across Member States. No evaluation of the potential for HEV transmission by foods of non-animal origin (e.g. fresh produce).	No validated protocols to inactivate HEV in food or environmental matrices; insufficient assessment of contamination routes along the farm-to-fork continuum.	WG3 will identify risk factors and develop practical guidelines for farm, food-chain and environmental control measures.
Societal awareness	Limited public and policymaker knowledge of zoonotic hepevirus infections and transmission routes; fragmented communication among scientific, veterinary, food-safety and health sectors.	Inefficient communication and knowledge transfer between scientists, public-health, veterinary and food-safety authorities and stakeholders, and the general public including risk groups; limited stakeholder engagement in prevention, risk communication and policy translation.	WG4 will implement targeted communication, stakeholder engagement and risk awareness strategies.

Legend: HEV, hepatitis E virus (species *Paslahepevirus balayani*); ratHEV, rat hepatitis E virus (species *Rocahepevirus ratti*); EFSA, European Food Safety Authority; EU, European Union; WG, Working Group

collaborative infrastructure required for a unified European response to zoonotic hepevirus infections. Its activities are also designed to generate impact beyond Europe, fostering collaboration and knowledge exchange with partners worldwide. To ensure this global dimension, the Action relies on an External Scientific Advisory Committee composed of leading experts from Africa, Asia and the Americas, who provide strategic insight and help align ONWARD's outcomes with international research and policy priorities. This global perspective strengthens the network's ability to position Europe as a proactive and collaborative actor in the worldwide response to zoonotic hepevirus infections. A core principle of ONWARD is the active diffusion of expertise across the network. Each WG is composed of a balanced mix of senior experts and early-career researchers from multiple countries and sectors, ensuring diverse participation. Cross-WG collaboration is encouraged through joint tasks and shared deliverables, promoting interdisciplinary knowledge exchange. Capacity building is further supported through STSMs, training schools, workshops and laboratory exchanges, which enable hands-on transfer of skills and methodologies. Additionally, ONWARD promotes open sharing of protocols, data and analytical tools, ensuring accessibility and reproducibility across participating institutions. This distributed and inclusive model is designed to broaden expertise across Europe and reduce dependence on a limited number of leading groups.

3. Advancing One Health action across Europe

Over the coming years, ONWARD will translate its objectives into coordinated scientific, clinical and policy actions spanning five interconnected areas of work. Together, these activities are establishing the foundations for a coherent European strategy against zoonotic hepevirus infections.

With the first area covered, ONWARD is standardising and enhancing diagnostic and surveillance practices across Europe. The network is harmonising serological, molecular, partial and whole-genome sequencing and non-canonical sampling protocols to ensure consistency and comparability of results across laboratories. ONWARD is also evaluating emerging technologies, including biosensors, CRISPR-based assays, next-generation sequencing and point-of-care tools, and assessing the use of artificial intelligence to strengthen surveillance capacity. In parallel, ONWARD is reviewing and optimising existing national and regional surveillance frameworks, identifying best practices and shared indicators for active monitoring. The second area advances clinical and therapeutic strategies for zoonotic hepevirus infections, developing common standards for clinical trials and harmonised outcome measurements to enable comparison across studies and patient cohorts. ONWARD reviews existing pharmaceutical data to identify and prioritise promising antiviral candidates, while also working to define and validate biomarkers that can improve diagnosis, monitoring and assessment of treatment response. The third area focuses on developing and implementing control measures at farm, food-chain and environmental levels. ONWARD is identifying risk factors associated with pig farming practices, wildlife interactions, hunting activities and environmental contamination, with the aim of developing practical guidelines for risk reduction. ONWARD also evaluates risks linked to animal products and food handling, reviewing culinary and processing practices to strengthen food safety. Parallel efforts are examining vaccine safety and efficacy, while standardising cell-culture systems and alternative inactivation protocols to support studies on viral infectivity. Together, these three pillars represent the core of ONWARD's One Health approach, linking diagnostic innovation, clinical research and field-based prevention to generate the evidence, tools and coordination needed to reduce zoonotic transmission risks across Europe.

Beyond these scientific and technical pillars, ONWARD is also building the communication, training and policy bridges needed to ensure that its results have a lasting impact across sectors. In this sense, the fourth area ensures the visibility, stakeholder engagement and communication of ONWARD's outputs. The network is implementing a comprehensive communication and dissemination strategy and coordinating outreach through scientific publications, social media and open-access and on-line resources. Regular reports and stakeholder agreements guide cooperation with national authorities, professional societies and research networks. Finally, the fifth area aligns ONWARD with active European initiatives and agencies to avoid duplication and maximise impact. This includes mapping ongoing projects and networks relevant to hepevirus research and establishing joint activities with complementary programmes under the One Health umbrella. Coordination with European partnerships on health, food safety, water quality, environmental monitoring and zoonotic disease surveillance and control ensures coherence with wider EU priorities and strengthens integration across disciplines. Together, the last two areas translate scientific progress into practical and policy-relevant outcomes. By connecting researchers, clinicians, veterinarians, public health authorities and stakeholders, ONWARD ensures that advances in diagnostics, clinical management and prevention are communicated, adopted and sustained beyond the lifetime of the Action, laying the groundwork for a lasting European framework on zoonotic hepevirus preparedness and response.

4. A collaborative call to action

ONWARD was born from the belief that Europe can only face emerging zoonotic threats by acting together and bridging disciplines, countries, and generations of scientists. As part of the COST framework, it translates this vision into action: promoting equality of opportunity, open collaboration and the free circulation of ideas and expertise across Europe. To ensure that scientific outputs translate into real-world impact, ONWARD integrates policy engagement as a core component of its structure rather than operating as an academic silo. Working Group 5 (WG5) is specifically mandated to establish and maintain formal links with European and international agencies, standardisation bodies, professional societies, and sectoral stakeholders. In addition to ongoing contacts with ECDC, EFSA, and national public health and veterinary authorities, ONWARD is actively engaging with WHO, FAO, WOAH, ISO, ESCMID, ESCV, FVE and others. These partnerships provide embedded policy interfaces that allow ONWARD to align research priorities with regulatory and operational needs across the One Health spectrum. Through this WG, ONWARD will coordinate the development of policy briefs, technical guidelines, and stakeholder-oriented reports, and will organise joint workshops and consultation events to facilitate structured dialogue between scientists, policymakers, industry representatives, and farming unions. This bidirectional engagement ensures that policy needs inform research activities, while scientific evidence is translated into actionable recommendations that can be adopted by competent authorities, professional bodies, and industry. Through these mechanisms, ONWARD is deliberately designed to support real-world policy uptake and harmonised European approaches to the prevention, diagnosis and control of zoonotic hepevirus infections.

Through its coordinated activities, ONWARD is transforming how Europe understands, monitors and controls zoonotic hepevirus infections. By harmonising diagnostic and surveillance protocols, advancing clinical management, and developing preventive and control measures from farm to environment, the network is building an integrated evidence base to support public-health decision making. This collective effort bridges long-standing gaps between human, animal and environmental health sectors and ensures that scientific progress is rapidly translated into policy and practice. The tools, guidelines and collaborative platforms emerging from ONWARD will not only enhance Europe's preparedness for hepevirus infections but also strengthen its resilience against future zoonotic and foodborne diseases within a truly One Health framework.

The success of ONWARD ultimately depends on collective engagement. The network remains open to researchers, clinicians, veterinarians, public-health professionals, agencies and citizens who share the goal of a healthier and safer Europe. By joining forces, we can transform

fragmented initiatives into a coherent European response that connects research, surveillance and policy under a single One Health vision. The outcomes of ONWARD will inform future European surveillance standards and contribute to European Centre for Disease Control and Prevention (ECDC) and EFSA strategic roadmaps on emerging zoonotic viruses. Every contribution will help consolidate the knowledge base and infrastructure needed to sustain Europe's preparedness for zoonotic threats well beyond the lifetime of the Action. Together, we move ONWARD towards a safer, healthier, and better-prepared Europe.

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Author contributions

ARJ and JRM coordinated the conception and development of the manuscript. All named authors contributed to the conceptual design, critical discussion and refinement of the content, and approved the final version of the manuscript.

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Data availability

Not applicable

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