Preparedness and Clinical Management of HCIDs in Europe

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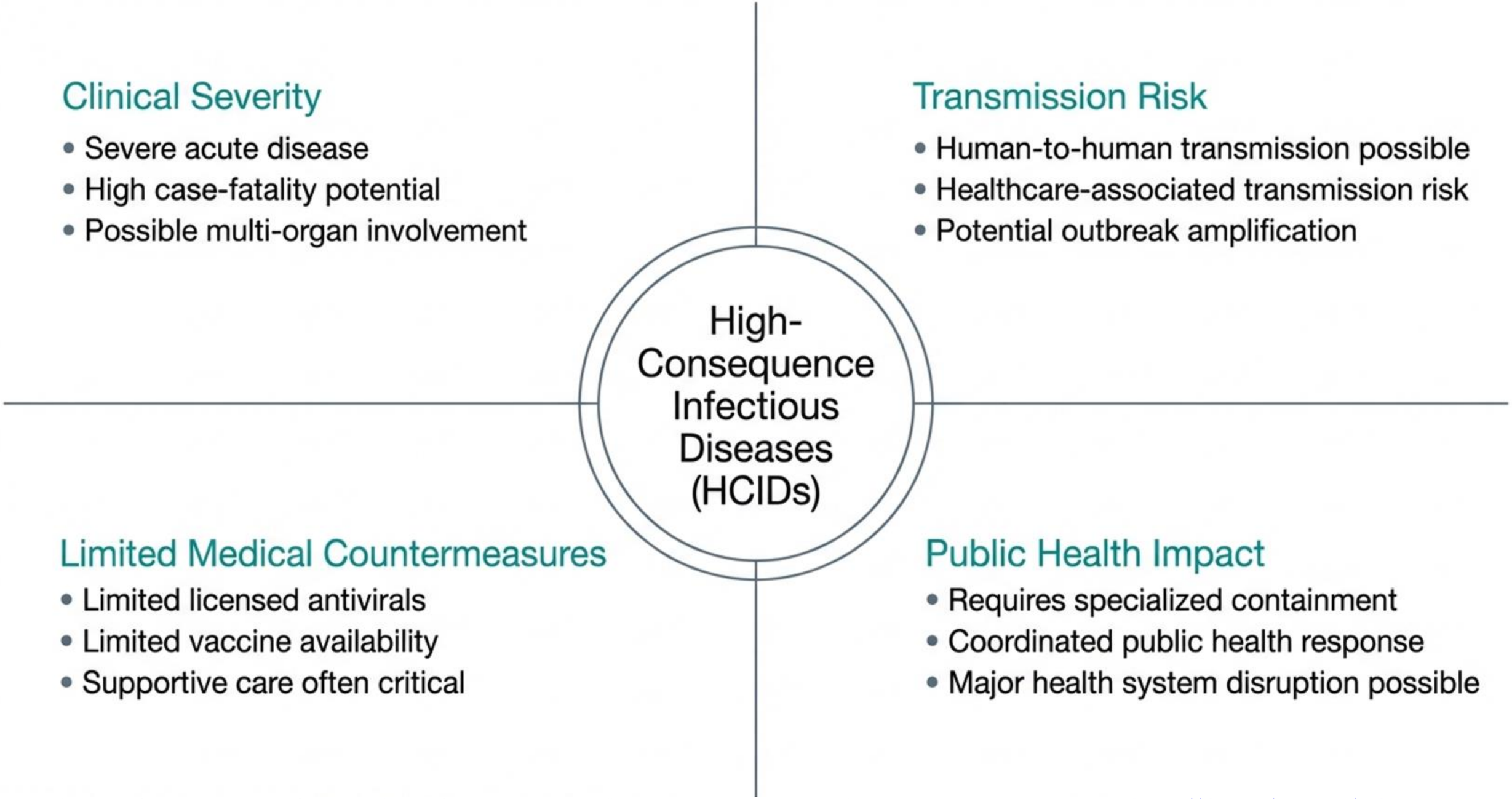


Preparedness and Response Considerations for High-Consequence Infectious Disease. Emerg Infect Dis. 2025;31(8):1507-1515. https://doi.org/10.3201/eid3108.250313. A Methodology for Determining Which Diseases Warrant Care in a High-Level Containment Care Unit. Viruses. 2019 Aug 22;11(9):773. doi: 10.3390/v11090773.

Classification and Management of High-Consequence Infectious Diseases (HCIDs)

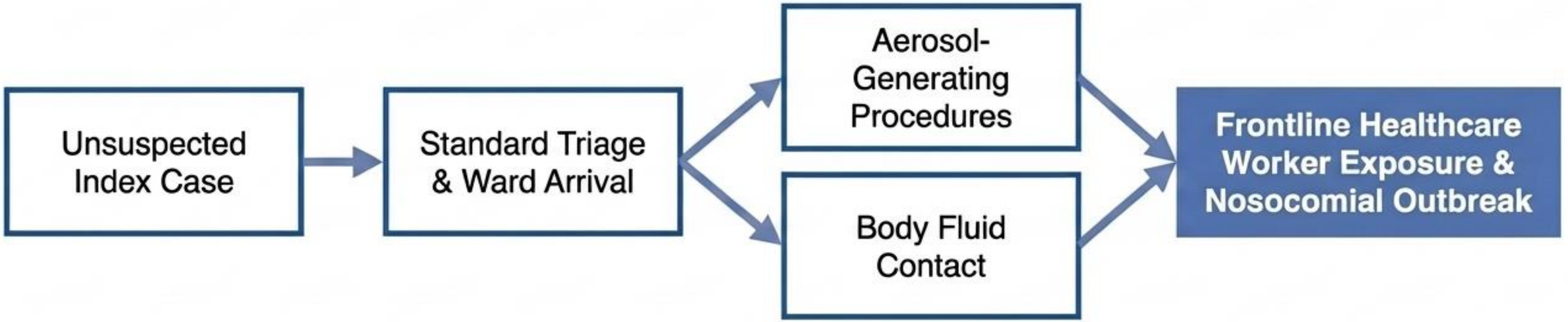
According to UKHSA and EUNID frameworks, HCIDs are life-threatening diseases with high case-fatality rates and potential for community spread. They are classified by their primary transmission route to determine the specific engineering and infection prevention and control (IPC) measures required for safe patient management.

CONTACT-TRANSMITTED HCIDs	AIRBORNE HCIDs
Transmission-Based Categories	**Transmission-Based Categories**
 • Ebola Virus Disease (EVD) • Crimean-Congo Hemorrhagic Fever (CCHF) • Marburg Virus Disease • Lassa Fever • Lujo Virus Disease	 • Middle East Respiratory Syndrome (MERS) • Severe Acute Respiratory Syndrome (SARS) • Avian Influenza (e.g., H5N1, H7N9) • Pneumonic Plague (*Yersinia pestis*) • Mpox (Clade I only)
Contact HCID Strategy	**Airborne HCID Strategy**
 • Focuses on preventing transmission via blood and body fluids through defined PPE and ward-based systems.	 • Requires negative pressure isolation rooms and enhanced respiratory protection (e.g., N95/FFP3 masks).

Cases of high-consequence infectious diseases identified in the UK, 1962-2023. J Med Microbiol. 2025 Mar;74(3):001982. doi: 10.1099/jmm.0.001982.

Risk of Nosocomial Transmission

- Standard healthcare facilities frequently act as major amplifiers of HCID transmission.
- Unprotected exposure typically occurs before clinical suspicion of an HCID arises.
- Transmission is primarily driven by body fluid contact and aerosol-generating procedures.



Infection control in the management of highly pathogenic infectious diseases: consensus of the European Network of Infectious Disease. Lancet Infect Dis. 2009 May;9(5):301-11. doi: 10.1016/S1473-3099(09)70070-2. Nosocomial infections caused by Crimean-Congo haemorrhagic fever virus. J Hosp Infect. 2020 May;105(1):43-52. doi: 10.1016/j.jhin.2019.12.001.

Burden of Ebola on Healthcare Workers

- Healthcare workers face drastically increased infection risks during Ebola virus outbreaks.
- Many secondary infections occurred within standard, unequipped healthcare facilities.
- Robust infection prevention and control infrastructure is absolutely essential for occupational safety.

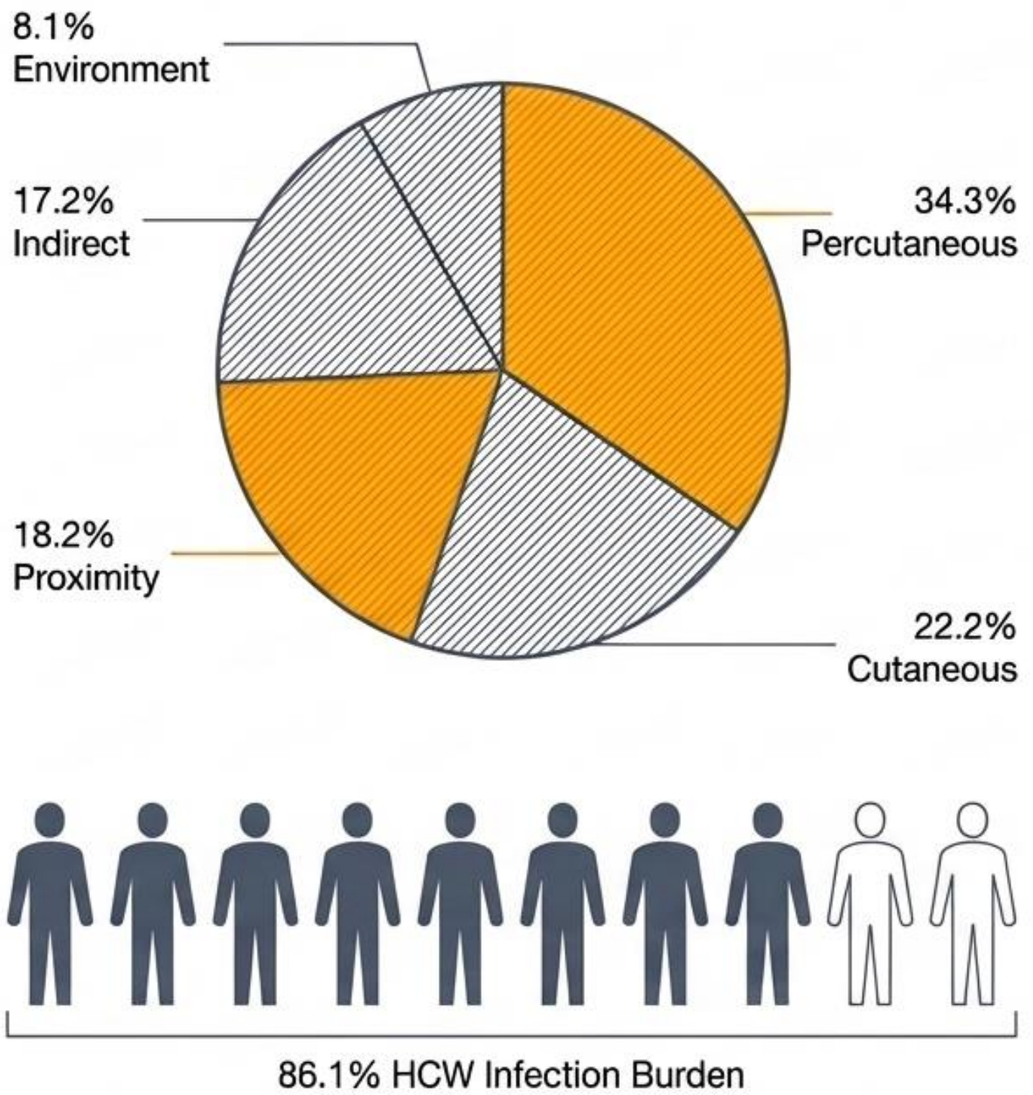
800+
EVD Cases among Healthcare Workers

400+
EVD Deaths among Healthcare Workers

Epidemiology of ebolavirus disease (EVD) and occupational EVD in health care workers in Sub-Saharan Africa: Need for strengthened public health preparedness. J Epidemiol. 2017 Oct;27(10):455-461. doi: 10.1016/j.je.2016.09.010. Ebola Virus Disease in Health Care Workers--Guinea, 2014. MMWR Morb Mortal Wkly Rep. 2015 Oct 2;64(38):1083-7. doi: 10.15585/mmwr.mm6438a6. Ebola virus disease in health care workers--Sierra Leone, 2014. MMWR Morb Mortal Wkly Rep. 2014 Dec 12;63(49):1168-71. Ebola virus disease cases among health care workers not working in Ebola treatment units--Liberia, June-August, 2014. MMWR Morb Mortal Wkly Rep. 2014 Nov 21;63(46):1077-81.

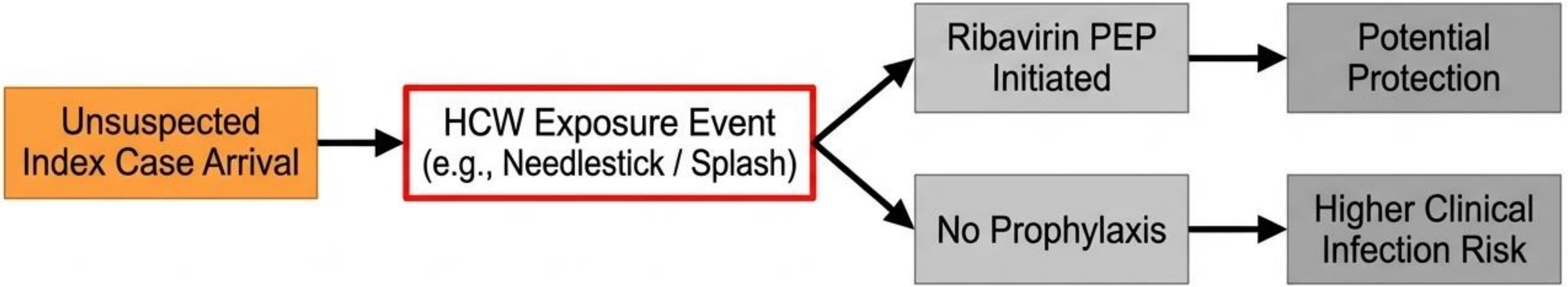
Nosocomial CCHF: Global Scope and Transmission Routes

- Global review (1953–2016) identified 158 nosocomial cases with a 32.4% case-fatality rate.
- Healthcare workers represent 86.1% of nosocomial cases, disproportionately affecting nursing staff and doctors.
- Transmission is primarily percutaneous (34.3%), cutaneous (22.2%), or via aerosol-generating proximity (18.2%).
- Severe IPC lapses in Afghanistan (2023) caused 48 secondary cases from a single index patient.



NotebookLM

Nosocomial infections caused by Crimean-Congo haemorrhagic fever virus. J Hosp Infect. 2020 May;105(1):43-52. doi: 10.1016/j.jhin.2019.12.001. The largest reported outbreak of CCHF in hospital settings: lessons from Kandahar, Afghanistan. Lancet Infect Dis. 2023 Sep;23(9):e330-e331. doi: 10.1016/S1473-3099(23)00478-4.



Turkish cohort (2002–2014) recorded 51 healthcare exposures, causing 49% infection and 16% mortality.

High vulnerability: 25% of occupational exposures occurred before any clinical suspicion of CCHF.

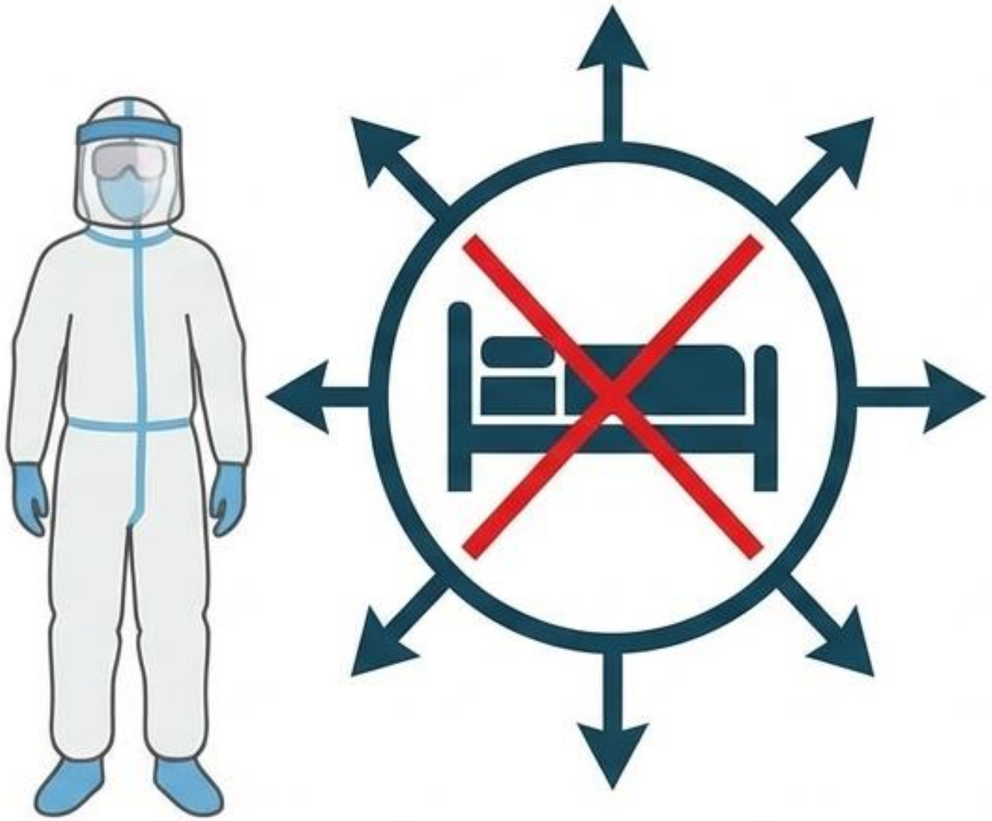
Ribavirin post-exposure prophylaxis following needlestick injuries demonstrated potential protective effects against clinical infection.

Spanish experience (2016) confirms unrecognized cases demand early suspicion, strict IPC, and HLIU transfer.

Healthcare-associated Crimean-Congo haemorrhagic fever in Turkey, 2002-2014: a multicentre retrospective cross-sectional study. Clin Microbiol Infect. 2016 Apr;22(4):387.e1-387.e4. doi: 10.1016/j.cmi.2015.11.024. Autochthonous Crimean-Congo Hemorrhagic Fever in Spain. N Engl J Med. 2017 Jul 13;377(2):154-161. doi: 10.1056/NEJMoa1615162.

Evolution of the Care Paradigm: Overcoming Historical Limitations

The Containment-First Model

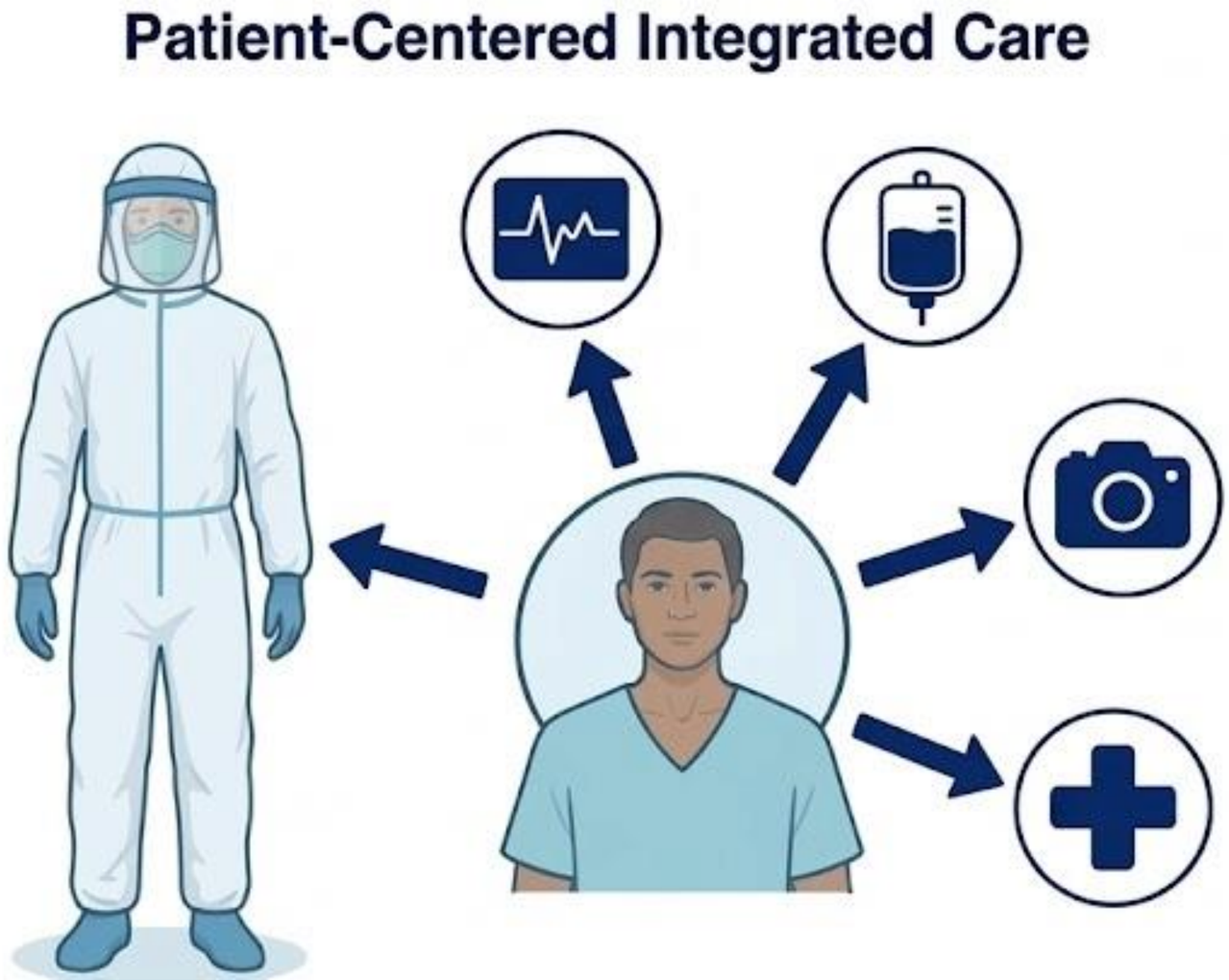


- Historical outbreak responses prioritized strict pathogen containment over individualized, comprehensive clinical care.
- Isolated patients experienced minimal clinical intervention with limited access to advanced supportive therapies.
- Cumbersome PPE and rigid isolation protocols created significant operational barriers to bedside care.
- Passive containment strategies frequently caused **severe patient distress** and resulted in **suboptimal clinical outcomes**.

Embedding treatment in stronger care systems. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Ebola virus disease and critical illness. Crit Care. 2016 Jul 29;20(1):217. doi: 10.1186/s13054-016-1325-2. Infection control in the management of highly pathogenic infectious diseases: consensus of the European Network of Infectious Disease. Lancet Infect Dis. 2009 May;9(5):301-11. doi: 10.1016/S1473-3099(09)70070-2.

The Modern Paradigm: Advanced Supportive Care and Dignity

Patient-Centered Integrated Care



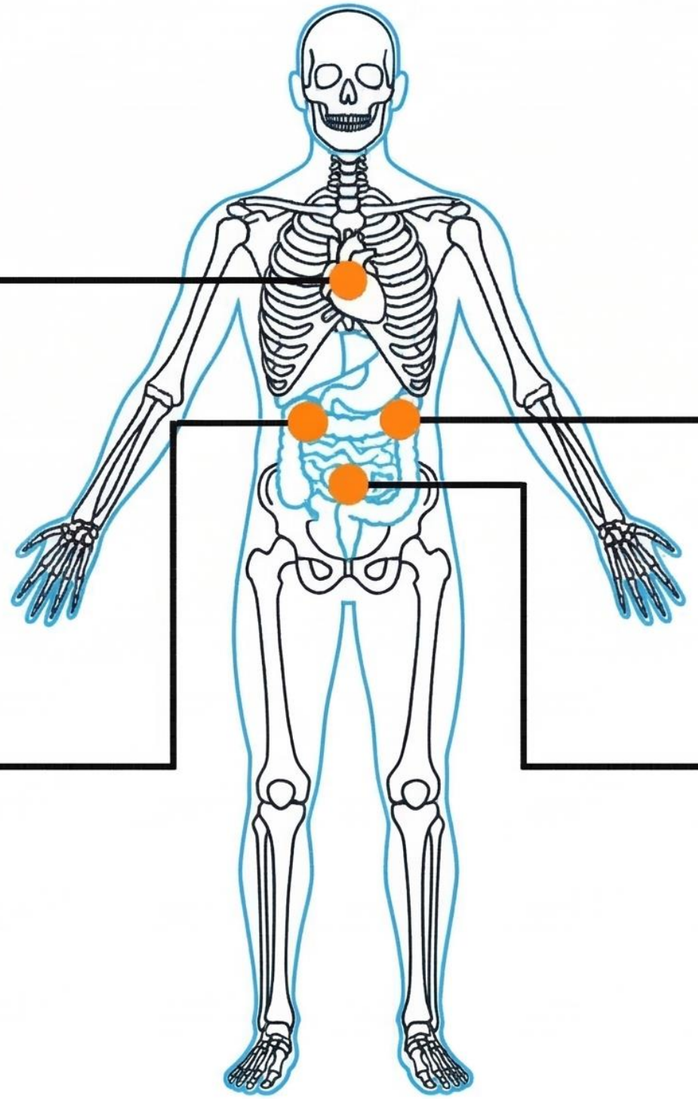
- Modern care integrates early aggressive fluid management, continuous monitoring, and antiviral and other directed therapies.
- Critical care protocols enable mechanical ventilation and transfusion support for severe thrombocytopenia.
- Transparent isolation structures and digital communication tools allow safe interactions, preserving patient dignity.
- Comprehensive disease management incorporates essential symptom control and comfort-focused palliative care.

Embedding treatment in stronger care systems. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Ebola virus disease and critical illness. Crit Care. 2016 Jul 29;20(1):217. doi: 10.1186/s13054-016-1325-2. Clinical Management of Ebola Virus Disease in the US and Europe. N Engl J Med. 2016 Feb 18;374(7):636-46. doi: 10.1056/NEJMoa1504874.

Reversing EVD Pathophysiology

Massive Fluid Loss:
Gastrointestinal losses exceeding 10L daily necessitate aggressive intravenous volume resuscitation.

Electrolyte Derangement:
Severe hypokalemia requires continuous laboratory-guided replacement to prevent arrhythmias.



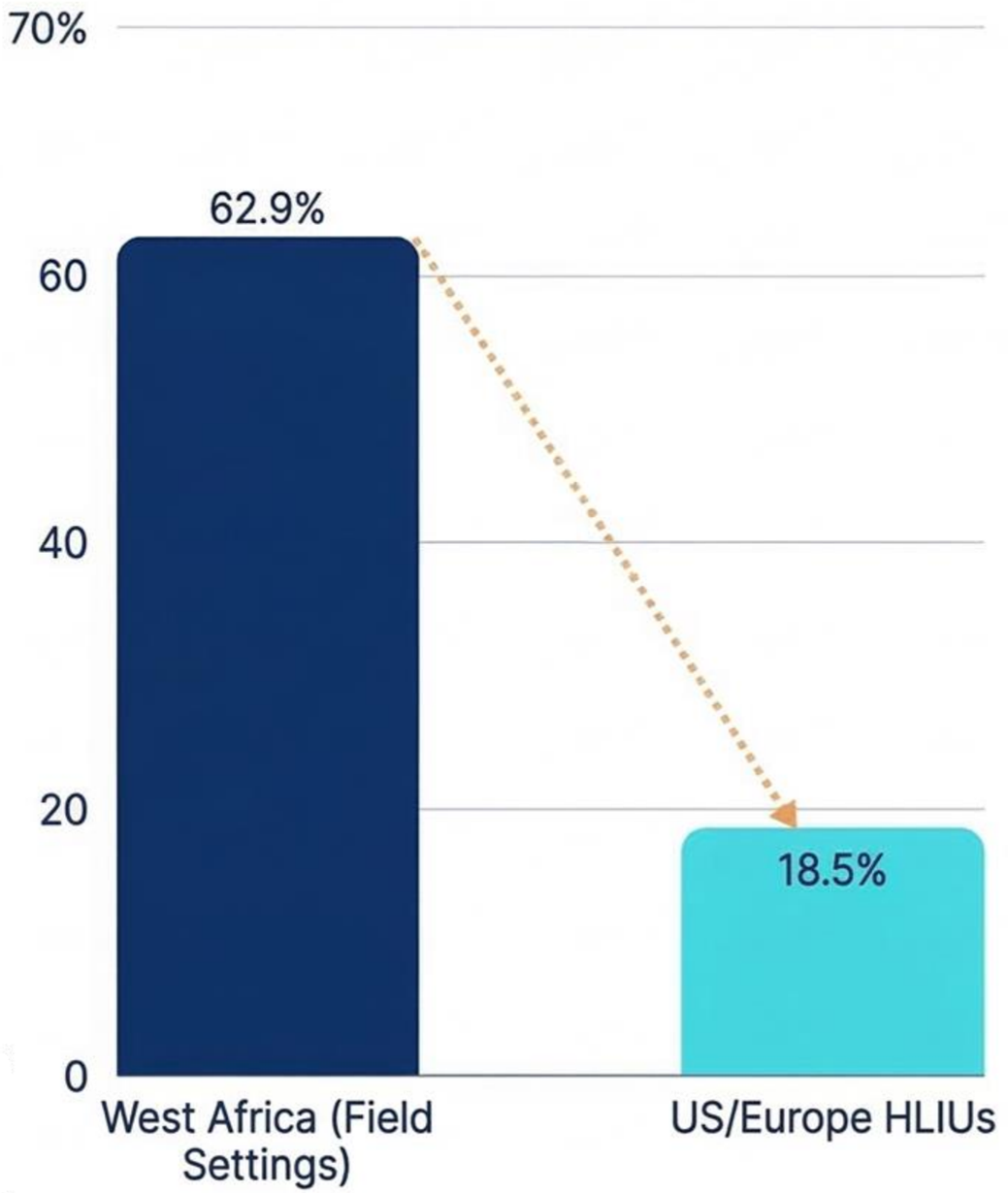
Renal Failure:
Acute kidney injury from hypovolemic shock demands continuous renal replacement therapy.

Respiratory Collapse:
Acute respiratory distress syndrome is countered with invasive mechanical ventilation.

EVD and critical illness. Crit Care. 2016 Jul 29;20(1):217. doi: 10.1186/s13054-016-1325-2. Clinical Management of EVD in the US and Europe. N Engl J Med. 2016 Feb 18;374(7):636-46. doi: 10.1056/NEJMoa1504874. Insights from clinical research completed during the west Africa EVD epidemic. Lancet Infect Dis. 2017 Sep;17(9):e280-e292. doi: 10.1016/S1473-3099(17)30234-7.

Impact of Intensive Care and HLIUs on HCID Mortality

- **Dramatic Survival Benefit:** The provision of advanced critical care in HLIUs significantly reduces HCID mortality compared to austere field settings.
- **The EVD Experience:** During the 2013–2016 epidemic, the case-fatality rate for Ebola virus disease (EVD) in West Africa was 62.9%, compared to 18.5% for patients managed in US and European HLIUs.
- **Reversing Pathophysiology**: Improved survival is directiy linked to aggressive intravenous fluid resuscitation and laboratory-guided electrolyte correction.
- **Advanced Organ Support:** HLIUs provide life-saving rescue therapies, Including mechanical ventilation and continuous renal replacement therapy, for patients who develop multiorgan failure.



Ebola virus disease and critical illness. Crit Care. 2016 Jul 29;20(1):217. doi: 10.1186/s13054-016-1325-2. Clinical Management of Ebola virus disease in the United States and Europe. N Engl J Med. 2016 Feb 18;374(7):636-46. doi: 10.1056/NEJMoa1504874.

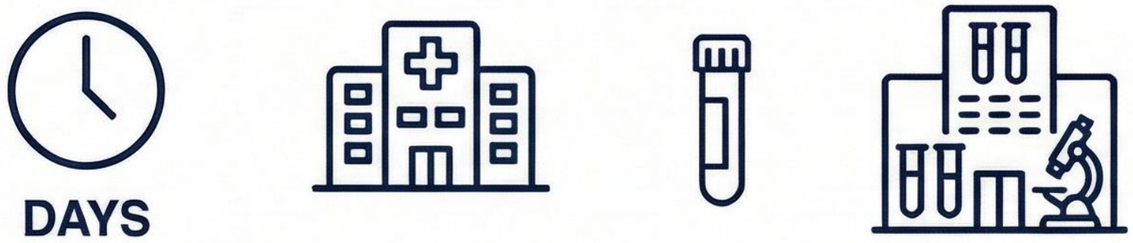
Current Therapeutics and Medical Countermeasures

- **Targeted Countermeasures:** The therapeutic **landscape** is evolving from purely supportive care to pathogen-specific treatments.
- **Ebola Virus Disease:** FDA-approved monoclonal antibodies (e.g., ansuvimab-zykl, Inmazeb) and licensed vaccines.
- **Crimean-Congo Haemorrhagic Fever:** Ribavirin frequently used for early treatment or post-exposure prophylaxis; **favipiravir** is also being investigated.
- **Adaptive Platform Trials:** Trials such as PALM evaluate multiple investigational therapeutics simultaneously during outbreaks.

Pathogen	Approved Countermeasures
Ebola Virus (EVD)	FDA-approved monoclonal antibodies (ansuvimab-zykl, Inmazeb); Licensed vaccines.
Marburg Virus (MVD)	Investigational therapeutics (MBP091); ChAd3-MARV vaccine under trial.
Crimean-Congo HF	Ribavirin (early treatment / post-exposure prophylaxis); Possible role of favipiravir.

Emerg Infect Dis. 2025 Aug;31(8):1507-1515. doi: 10.3201/eid3108.250313. N Engl J Med. 2025 Sep 11;393(10):983-993. doi: 10.1056/NEJMoa2415816. Lancet Infect Dis. 2025 Apr;25(4):e223-e234. doi: 10.1016/S1473-3099(24)00656-X. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Emerg Infect Dis. 2025 Feb;31(2):9-16. doi: 10.3201/eid3102.240251. Clin Microbiol Infect. 2016 Apr;22(4):387.e1-387.e4. doi: 10.1016/j.cmi.2015.11.024. PLoS Pathog. 2024 Mar 15;20(3):e1012038. doi: 10.1371/journal.ppat.1012038.

Bridging the Diagnostic Gap: A Novel CCHF Rapid Diagnostic Test



Traditional Centralized RT-PCR

Long diagnostic delay (days) requiring sample transport to a central reference laboratory.

Hinders Early Triage and Infection Prevention and Control (IPC) Efforts.

Novel Lateral Flow RDT

Rapid results in 10–30 minutes enabling immediate bedside or point-of-care clinical decisions.

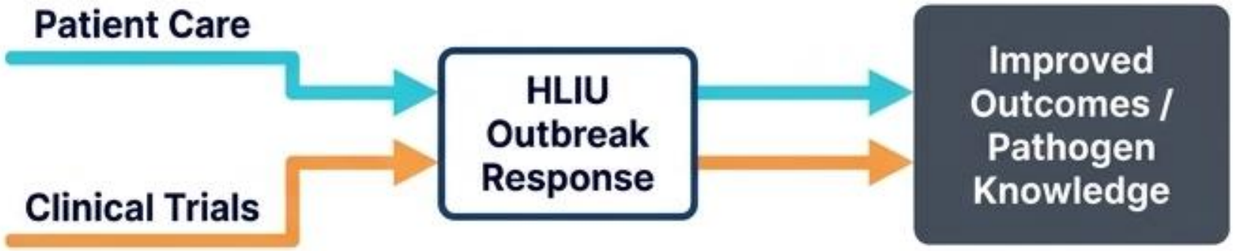
Improved Early Decision-Making, Accelerates **Supportive** Care, Strict Isolation Protocols, and Decentralized Clinical Impact.

Sensitivity: 90.4% **Specificity: 96.2%** **Sensitivity Ct ≤ 30: 92.9%**

Development and evaluation of an antigen targeting lateral flow test for Crimean-Congo Haemorrhagic Fever. EBioMedicine. 2024 Dec;110:105460. doi: 10.1016/j.ebiom.2024.105460.

Integrating Clinical Research into Outbreak Management

- **Research as a Core Pillar:** Clinical research integrated into outbreak response and HLIU workflows.

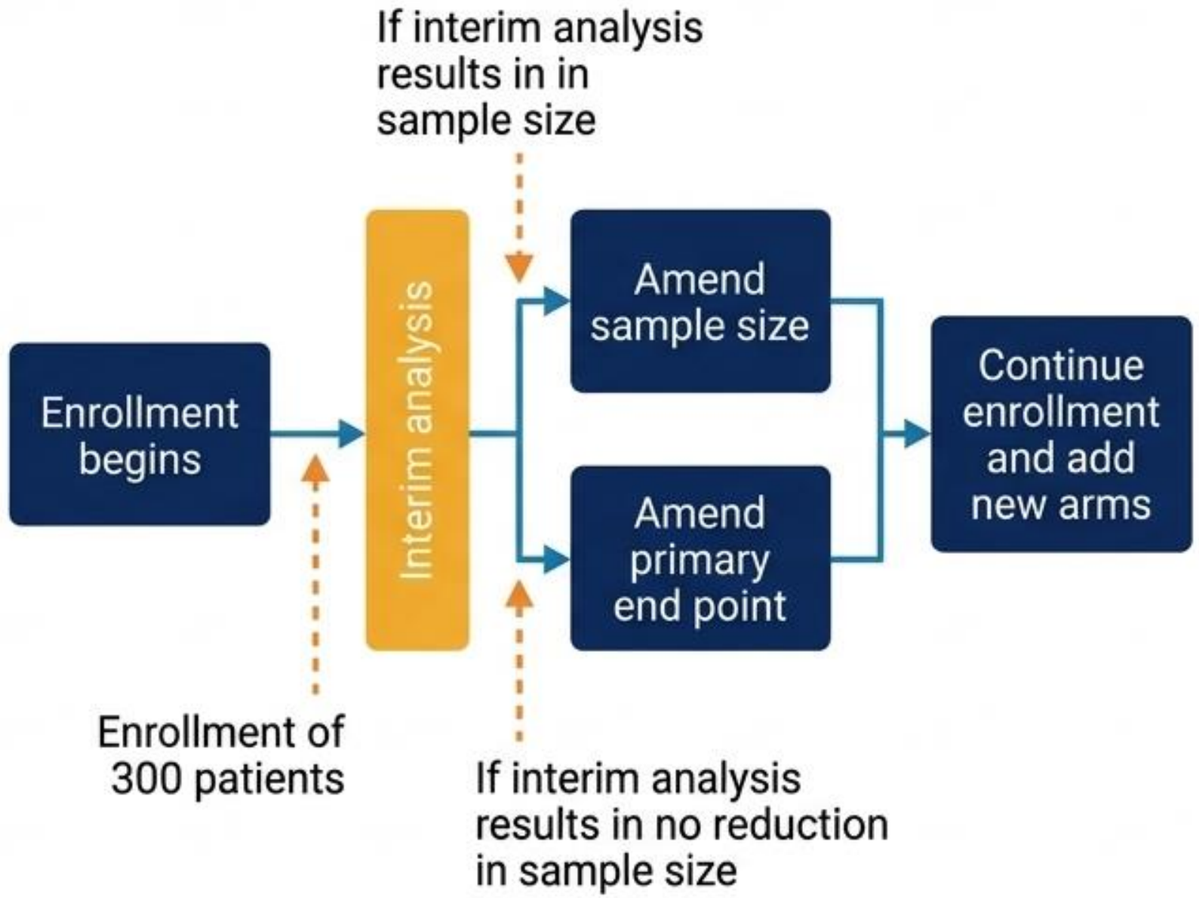


- **Adaptive Platform Trials:** Phase II/III randomized trials evaluating multiple therapeutics simultaneously.
- **Harmonized Protocols:** Pre-positioned international protocols enabling rapid, standardized outbreak research.
- **Equitable Access:** Research frameworks include special populations and equitable access to experimental treatments.
- **One Health Approaches:** R&D expands to veterinary vaccines and vector control strategies.

Embedding treatment in stronger care systems. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Adaptive Design for Phase II/III Platform Trial of Lassa Fever Therapeutics. Emerg Infect Dis. 2025 Feb;31(2):9-16. doi: 10.3201/eid3102.240251. Research and product development for Crimean-Congo haemorrhagic fever: priorities for 2024-30. Lancet Infect Dis. 2025 Apr;25(4):e223-e234. doi: 10.1016/S1473-3099(24)00656-X.

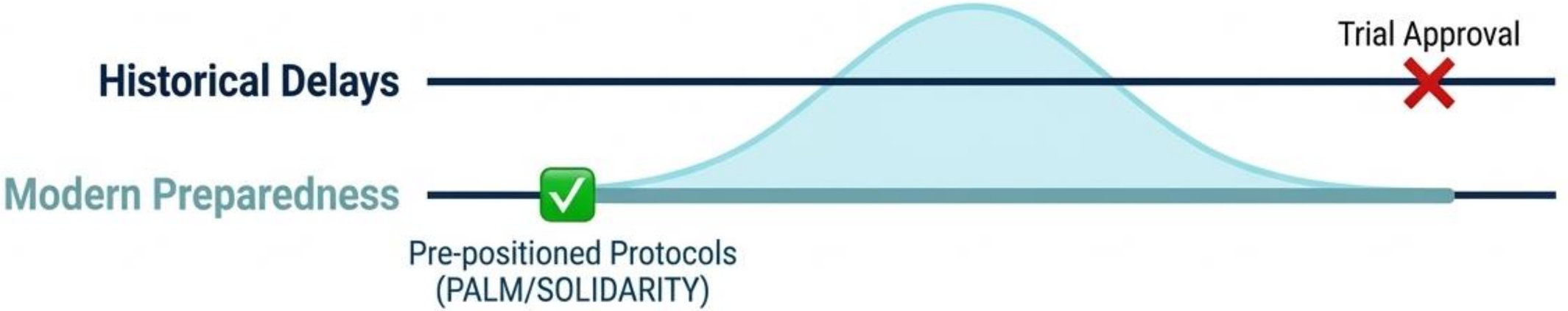
Adaptive Platform Trials: The Lassa Fever Blueprint

- **Methodological Innovation:** The WALC Phase II/III trial evaluates multiple therapeutics through unified protocols.
- **Interim Analysis:** After 300 patients, monitoring boards safely re-estimate target sample sizes.
- **Composite Endpoints:** The trial uses a composite endpoint including death, shock, ARDS, and AKI.
- **Flexible Adaptation:** Ineffective arms are dropped and new candidates added without halting trials.



Adaptive Design for Phase II/III Platform Trial of Lassa Fever Therapeutics. Emerg Infect Dis. 2025 Feb;31(2):9-16. doi: 10.3201/eid3102.240251.

Pre-positioning Protocols and Harmonizing Research

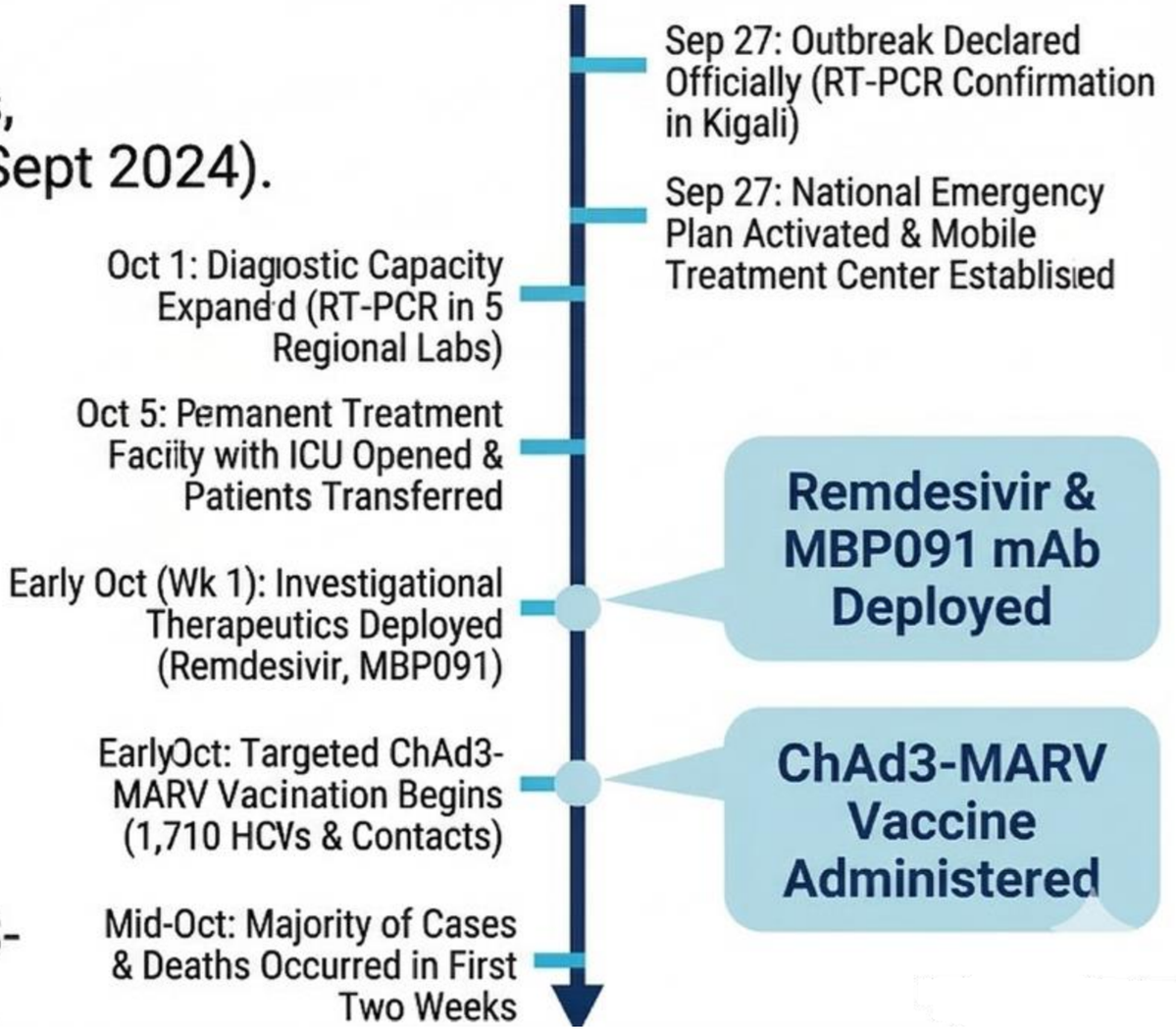


- **Historical Delays:** Traditional sequential trial approvals missed the peak of previous outbreak curves.
- **Pre-positioned Readiness:** Modern adaptive trials secure regulatory and operational frameworks before outbreaks occur.
- **Regional Harmonization:** Initiatives like the African Vaccine Regulatory Forum share capacity to increase efficiency.
- **Multi-Outbreak Enrollment:** Conserved master protocols allow continuous patient enrollment across distinct sporadic outbreaks.

Embedding treatment in stronger care systems. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Adaptive Design for Phase II/III Platform Trial of Lassa Fever Therapeutics. Emerg Infect Dis. 2025 Feb;31(2):9-16. doi: 10.3201/eid3102.240251.

Marburg Virus Disease in Rwanda (2024): An Updated Timeline & Context

- **Urban Emergence:** Rwanda's first Marburg outbreak began with clusters in Kigali hospitals, officially declared after RT-PCR confirmation (Sept 2024).
- **Heavy Toll on HCWs:** 77% (51/66) of confirmed cases occurred among healthcare workers.
- **Reduced Mortality:** Overall case-fatality rate was 23%, far below historical MVD outbreaks.
- **Rapid Countermeasure Deployment:** Investigational therapeutics and targeted vaccination were initiated within the first week of declaration.
- **Targeted Vaccination:** Over 1,700 frontline workers and high-risk contacts received ChAd3-MARV vaccine under emergency authorization.



Marburg Virus Disease in Rwanda, 2024 - Public Health and Clinical Responses. N Engl J Med. 2025 Sep 11;393(10):983-993. doi: 10.1056/NEJMoa2415816.

Safe Delivery of Intensive Care for MVD

9 Patients safely mechanically ventilated	**2** Patients initiated on hemodialysis for AKI
1-to-1 Staffing by dedicated ICU physicians	**0** Nosocomial transmissions during critical care

Advanced Interventions: Critically ill MVD patients safely received mechanical ventilation and fluid resuscitation.

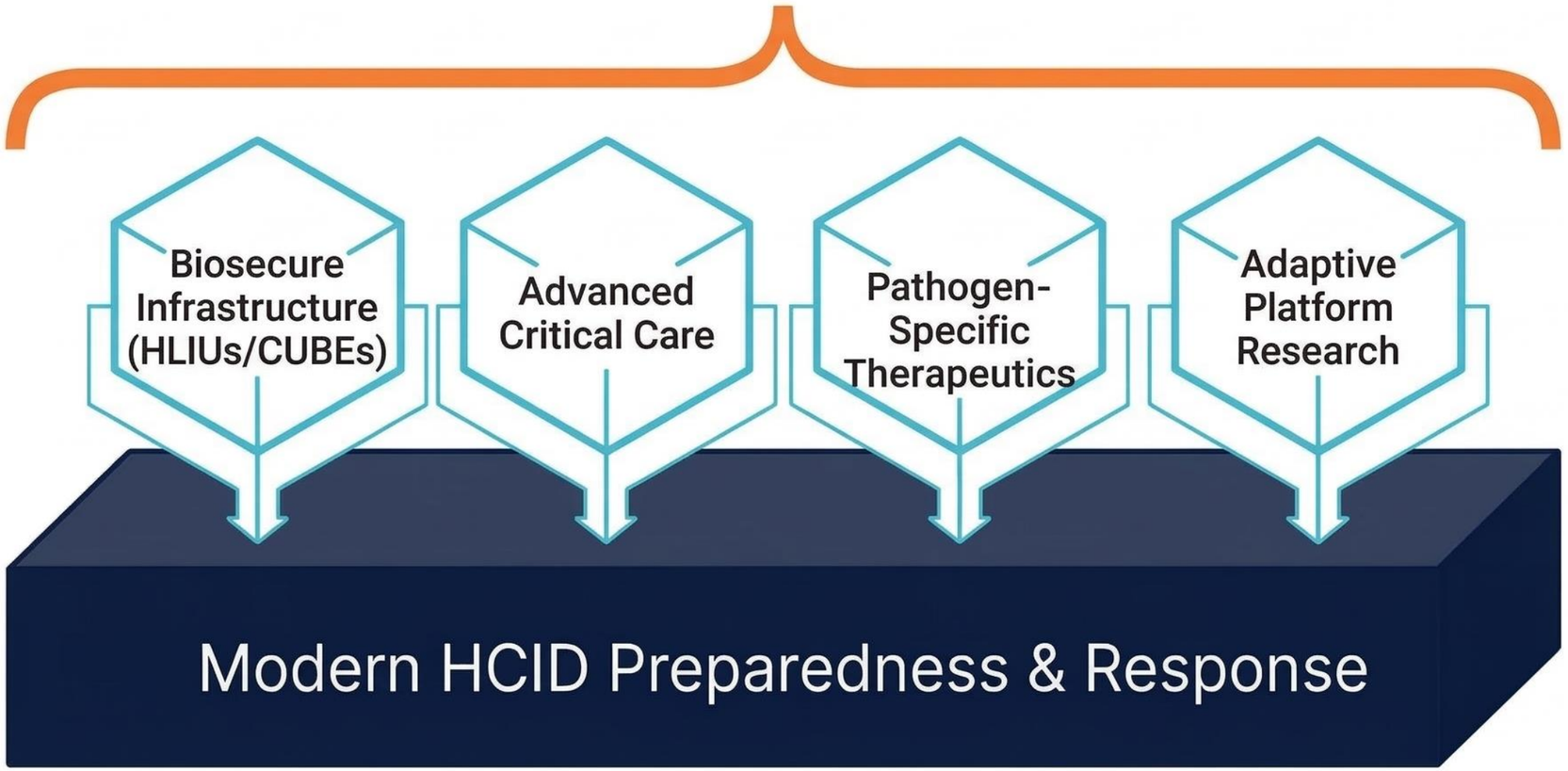
Organ Support: Hemodialysis was successfully initiated under high-level biosafety conditions for severe AKI.

Continuous Monitoring: Dedicated treatment centers utilized one-to-one staffing by in-house ICU physicians.

Zero Transmission: Unprecedented critical care was delivered safely without nosocomial transmission among healthcare workers.

Marburg Virus Disease in Rwanda, 2024 - Public Health and Clinical Responses. N Engl J Med. 2025 Sep 11;393(10):983-993. doi: 10.1056/NEJMoa2415816. Safe delivery of intensive care for Marburg virus disease in Rwanda. Lancet Infect Dis. 2025 Oct 29:S1473-3099(25)00466-9. doi: 10.1016/S1473-3099(25)00466-9.

The New Standard of HCID Care



Unified Response: Advanced critical care and integrated clinical research concurrently replace isolation-only paradigms.

Architectural Precision: Biosecure engineering enables aggressive organ support while ensuring healthcare worker safety.

Continuous R&D: Pre-positioned adaptive platform trials ensure rapid generation of robust therapeutic efficacy data.

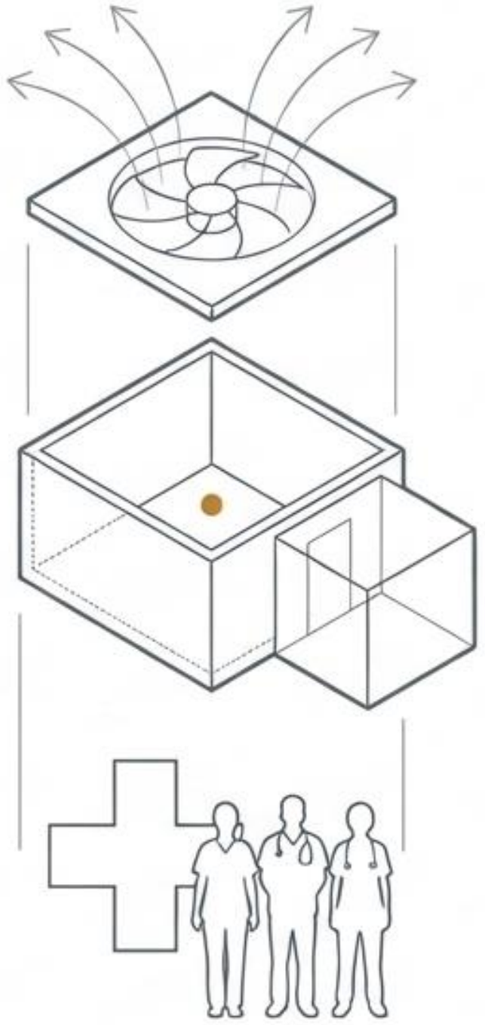
Global Equity: Modern frameworks deploy intensive care capabilities directly to resource-limited outbreak epicenters.

Lancet Infect Dis. 2025 Oct 29:S1473-3099(25)00466-9. doi: 10.1016/S1473-3099(25)00466-9. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8. Emerg Infect Dis. 2025 Feb;31(2):9-16. doi: 10.3201/eid3102.240251. Lancet Infect Dis. 2009 Jan;9(1):45-56. doi: 10.1016/S1473-3099(08)70304-9.

The Biosafety Barrier

Scaling HCID Containment from Point-of-Care to Global Infrastructure

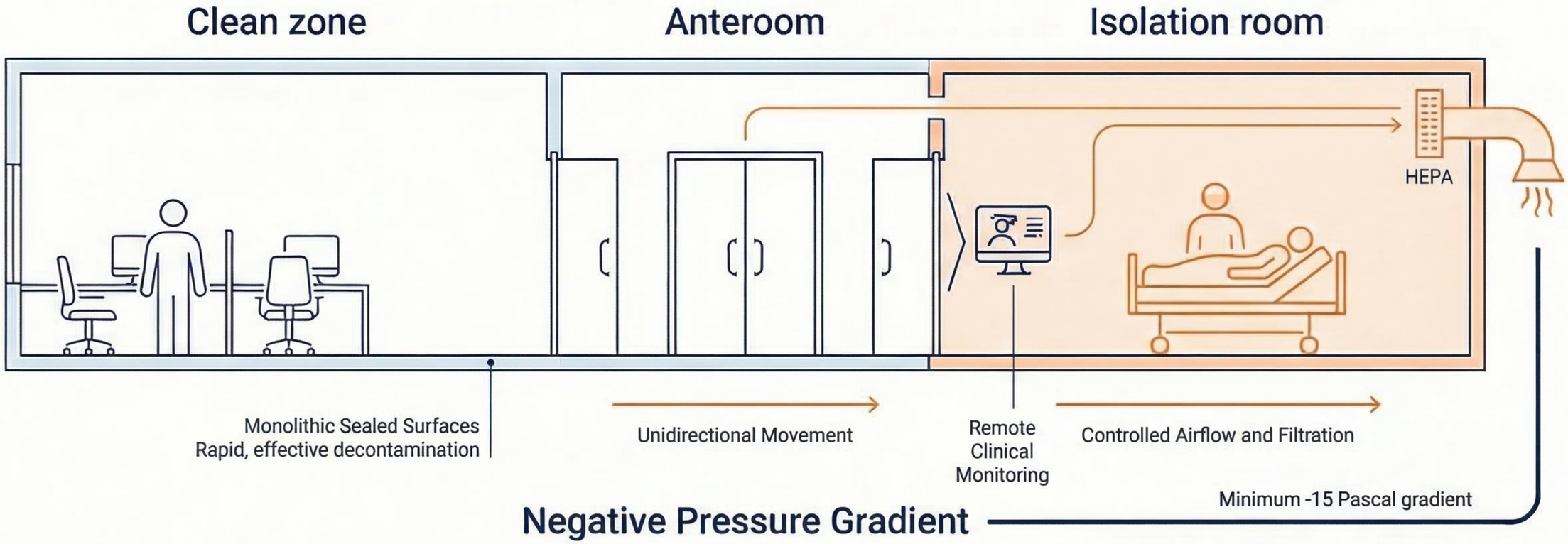
High-Level Isolation Units (HLIUs): The Gold Standard



- Specialized biocontainment facilities are designed for safe pathogen containment and high-quality clinical care.
- Infrastructure mandates negative pressure (>15 Pa), continuous HEPA filtration, and dedicated PPE anterooms.
- Units feature integrated decontamination systems and immediate access to advanced diagnostic capabilities.
- Safe operations rely on highly trained multidisciplinary teams conducting continuous simulation training.

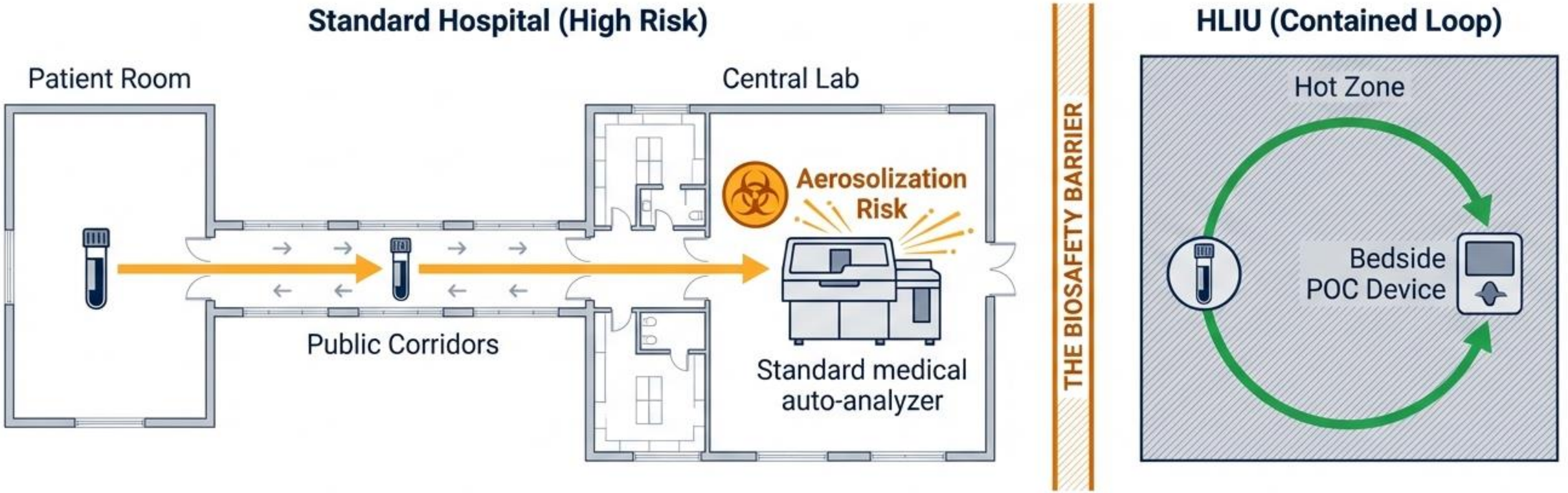
Framework for the design and operation of high-level isolation units: consensus of the European Network of Infectious Diseases. Lancet Infect Dis. 2009 Jan;9(1):45-56. doi: 10.1016/S1473-3099(08)70304-9. Preparing for patients with high-consequence infectious diseases: Example of a high-level isolation unit. PLoS One. 2022 Mar 3;17(3):e0264644. doi: 10.1371/journal.pone.0264644. EuroNHID checklists for the assessment of high-level isolation units and referral centres for highly infectious diseases: results from the pilot phase of a European survey. Clin Microbiol Infect. 2009 Aug;15(8):711-9. doi: 10.1111/j.1469-0691.2009.02874.x.

Architectural Design and Advanced Engineering



Framework for the design and operation of high-level isolation units: consensus of the European Network of Infectious Diseases. Lancet Infect Dis. 2009 Jan;9(1):45-56. doi: 10.1016/S1473-3099(08)70304-9. Embedding treatment in stronger care systems. Lancet Infect Dis. 2025 Mar;25(3):e177-e188. doi: 10.1016/S1473-3099(24)00727-8.

Safe Diagnostics and Laboratory Support

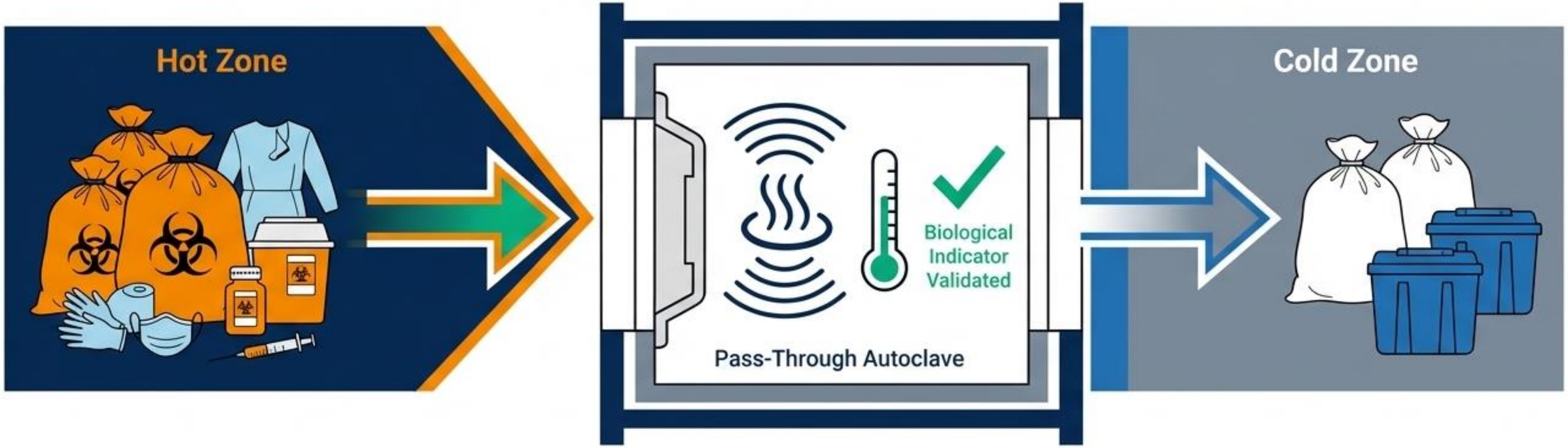


- **The Laboratory Risk:** Routine hospital laboratories face occupational risks processing undiagnosed HCID samples.
- **Dedicated Infrastructure:** HLIUs require BSL-3/BSL-4 laboratories or secure point-of-care testing inside isolation zones.
- **Minimizing Transport:** In-unit point-of-care testing avoids transporting Category A infectious substances through hospital corridors.
- **Critical Care Testing:** Bedside devices enable safe monitoring of blood gases without aerosolizing auto-analyzers.

Lancet Infect Dis. 2009 May;9(5):301-11. doi: 10.1016/S1473-3099(09)70070-2. Lancet Infect Dis. 2009 Jan;9(1):45-56. doi: 10.1016/S1473-3099(08)70304-9. BMJ Glob Health. 2023 Jul;8(7):e012037. doi: 10.1136/bmjgh-2023-012037. Emerg Infect Dis. 2025 Aug;31(8):1507-1515. doi: 10.3201/eid3108.250313.

The Challenge of Waste Management in HLIUs

Waste Inactivation Flow Diagram



High Volume Generation:
HCID care produces massive amounts of Category A waste from single-use PPE.

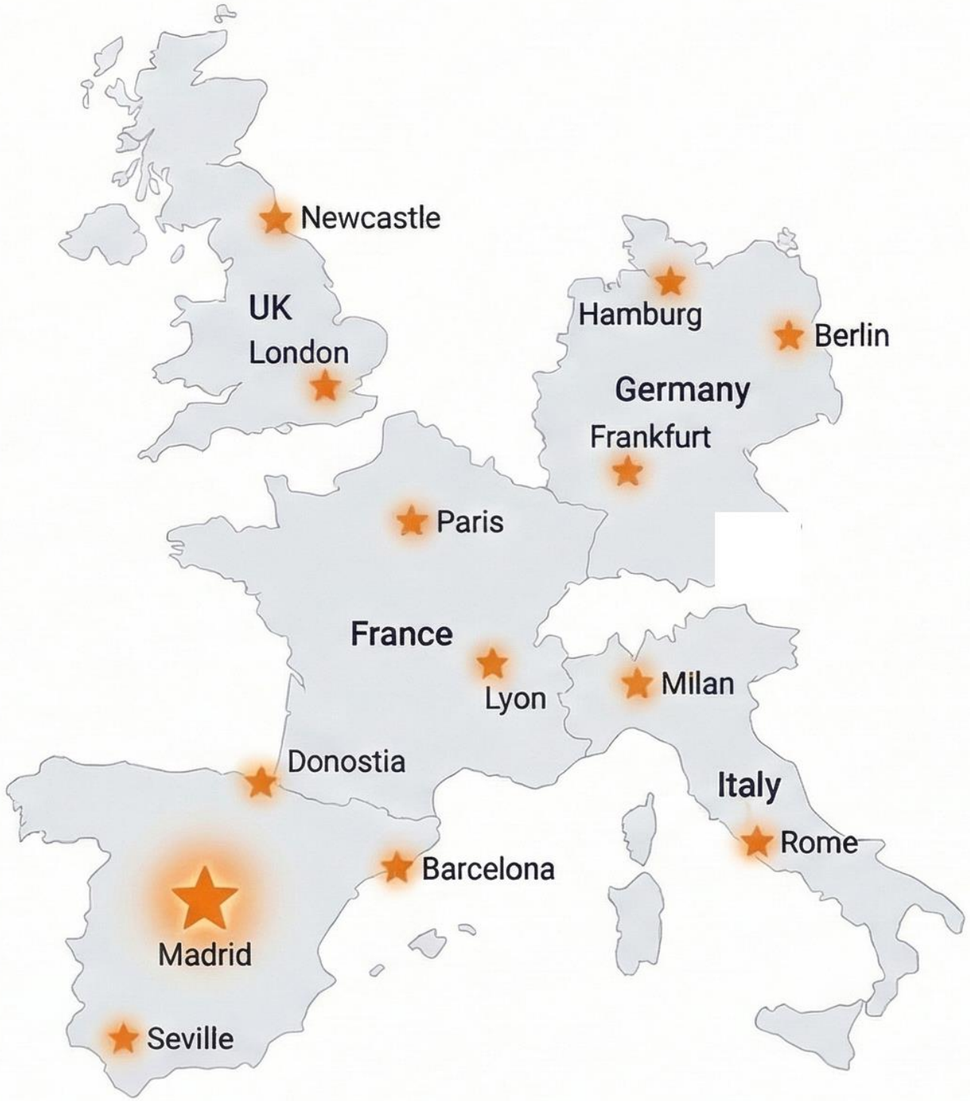
Onsite Autoclaving:
Validated thermal inactivation is the preferred method to safely decontaminate solid biological waste.

Reducing Logistical Burdens:
Onsite sterilization legally converts Category A hazardous materials into routine medical waste.

Liquid Waste Complexity:
Safe disposal strategies require risk assessment, including drain dilution or gel solidification.

PLoS One. 2022 Mar 3;17(3):e0264644. doi: 10.1371/journal.pone.0264644. Lancet Infect Dis. 2009 Jan;9(1):45-56. doi: 10.1016/S1473-3099(08)70304-9. Clin Microbiol Infect. 2009 Aug;15(8):711-9. doi: 10.1111/j.1469-0691.2009.02874.x. BMJ Glob Health. 2023 Jul;8(7):e012037. doi: 10.1136/bmjgh-2023-012037

The European HLIU Landscape: Capacity and Key Nodes



Strategic Geographic Nodes

Strategic Urban Hubs: Primary containment nodes are concentrated in major hubs.

Spanish UATAN Network: Madrid serves as the primary national node, supported by regional units.

Coordinated Infrastructure: The network ensures dynamic response capabilities through distributed high-containment facilities across Western Europe.

Regional Capacity Breakdown

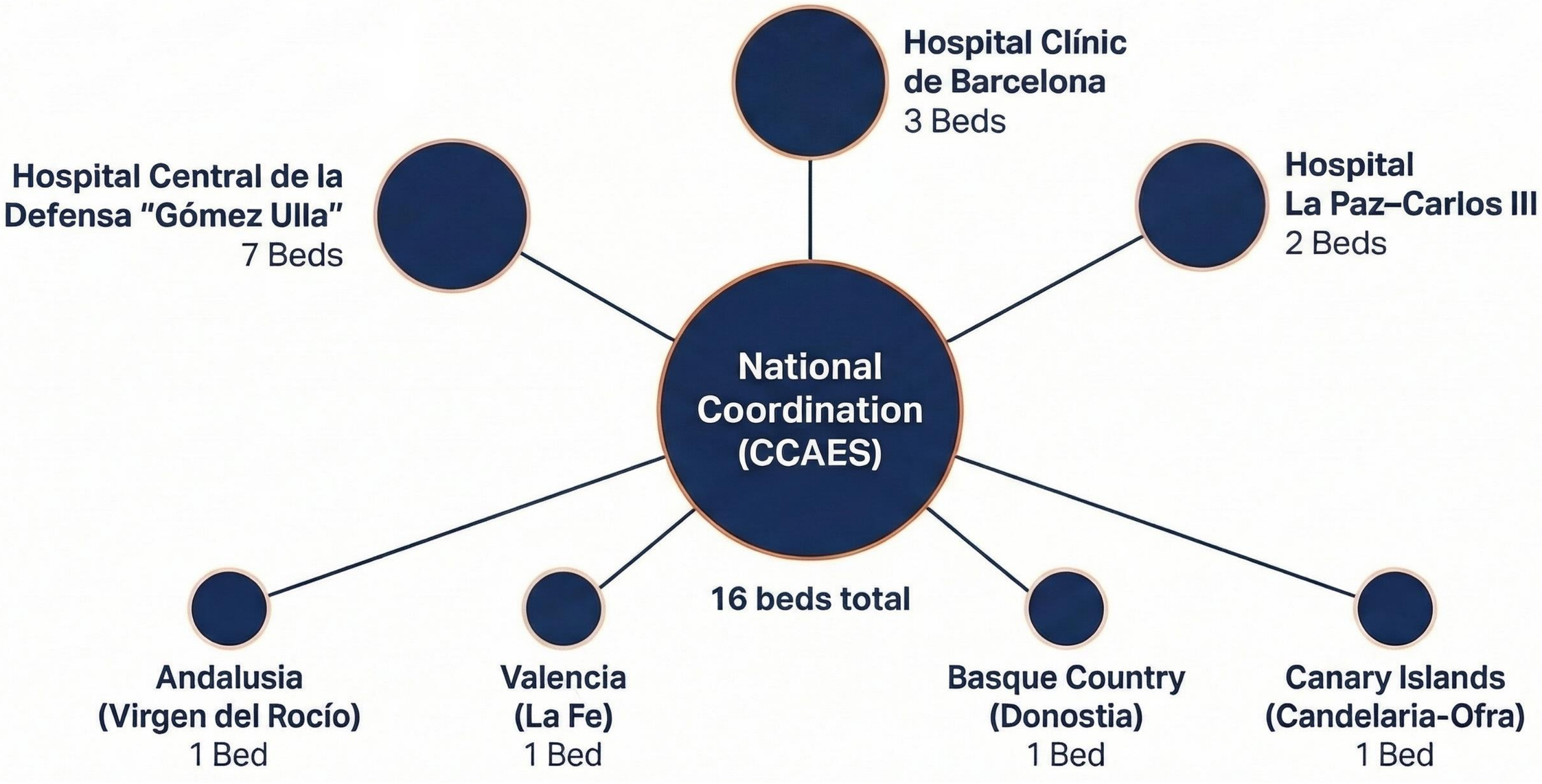
≥ 47 Total HLIUs

≥ 191 Specialized High-Containment Beds

Country	HLIUs	High-Containment Beds
Germany	7	55
Italy	2	33
Spain	7	16
UK	4	12
France	5	

CCAES, Ministerio de Sanidad. *Estructura y funcionamiento de la Red de Hospitales para la Atención a Enfermedades Infecciosas de Alto Riesgo en España (Red UATAN).* 2025. *Mapping of existing facilities for high-consequence infectious diseases and assessment of high-level isolation units (WP10 – Deliverable 10.1).* SHARP Joint Action (EU Health Programme 2014–2020); 2024.

Spain's Fortress Against Biothreats: The UATAN Network



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The International Framework: EUNID, EuroNHID, and NETEC

Collaborative Value: These frameworks enable critical cross-border knowledge sharing and standardize global health security.

EUNID: Established crucial consensus definitions and architectural design frameworks for European high-level isolation units.

EuroNHID: Assessed European isolation capabilities and harmonized transnational infection control and biosafety standards.

NETEC: Developed comprehensive readiness assessment domains spanning infrastructure, training, and personnel management.

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Key Take-Home Messages

Vulnerability in Routine Care:

Standard hospitals amplify nosocomial **transmission before highly infectious pathogens are suspected.**

Strategic Infrastructure:

Specialized High-Level Isolation Units **protect healthcare workers and stabilize regional health systems.**

The Modern Paradigm:

Effective protocols **balance strict biosafety containment with advanced, dignified intensive clinical care.**

Collaboration is Essential:

Outbreak preparedness requires rigorous staff training, **national coordination**, and continuous **international cooperation**.

MUCHAS GRACIAS

MERCI BEAUCOUP

GRAZIE MILLE

ÇOK TEŞEKKÜR EDERİM