A narrative review of high-level isolation unit operational and infrastructure features

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A narrative review of high-level isolation unit operational and infrastructure features

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ABSTRACT

High-level isolation units (HLIUs) are specially designed facilities for care and management of patients with suspected or confirmed high-consequence infectious diseases (HCIDs), equipped with unique infrastructure and operational features. While individual HLIUs have published on their experiences caring for patients with HCIDs and two previous HLIU consensus efforts have outlined key components of HLIUs, we aimed to summarise the existing literature that describes best practices, challenges and core features of these specialised facilities. A narrative review of the literature was conducted using keywords associated with HLIUs and HCIDs. A total of 100 articles were used throughout the manuscript from the literature search or from alternate methods like reference checks or snowballing. Articles were sorted into categories (eg, physical infrastructure, laboratory, internal transport); for each category, a synthesis of the relevant literature was conducted to describe best practices, experiences and operational features. The review and summary of HLIU experiences, best practices, challenges and components can serve as a resource for units continuing to improve readiness, or for hospitals in early stages of developing their HLIU teams and planning or constructing their units. The COVID-19 pandemic, a global outbreak of mpox, sporadic cases of viral haemorrhagic fevers in Europe and the USA, and recent outbreaks of Lassa fever, Sudan Ebolavirus, and Marburg emphasise the need for an extensive summary of HLIU practices to inform readiness and response.

INTRODUCTION

High-level isolation units (HLIUs), also known as biocontainment units, are designed for the management and provision of care of patients with high-consequence infectious diseases (HCIDs) (eg, viral haemorrhagic fevers (VHFs), Middle East respiratory syndrome, smallpox). HCIDs are generally classified as having high case fatality rates, limited or no treatment options, and pose a risk to contacts, healthcare workers (HCWs), and the general public. HLIUs have unique and advanced capabilities designed to provide high-quality care while minimising transmission risks through optimal infection prevention and control (IPC) functions. HLIUs have played critical roles in response to previous outbreaks of HCIDs or novel infectious diseases, including the 2014–2016 West Africa Ebola virus disease (EVD) outbreak, early weeks of the COVID-19 pandemic when SARS-CoV-2 emerged as a novel pathogen, and sporadic imported cases of other VHFs in the USA and Europe.

Although regional consensus efforts were conducted in the mid-2000s in Europe and the USA to outline key components and requirements of HLIUs, little has been done in the last decade to advance the field of high-level isolation globally. In the USA, The National Emerging Special Pathogens Training and Education Center (NETEC) partners with 13 federally designated US HLIUs (known as...
Regional Emerging Special Pathogen Treatment Centers (RESPTCs)) to enhance domestic capability to effectively manage special pathogens while also advancing HLIU-specific practices and operations.3 In 2018, NETEC hosted a workshop that brought together 22 HLIUs from the USA, Europe and Asia; the goal of the meeting was to share practices and increase networking and less about information dissemination.5 To our knowledge, no literature review exists summarising HLIU operational and infrastructural features. This paper aims to synthesise the literature and describe core HLIU features, components and practices.

**METHODS**

A narrative review of literature was conducted on PUBMED and EMBASE databases in April 2022 using various combinations of the following keywords: “high-level isolation unit”, “high-level isolation”, “biocontainment unit”, “high-consequence infectious disease”, “highly infectious disease” and “patient isolation.” Thereafter, searching techniques such as snowballing and reference check expanded the search strategy.

Criteria for inclusion were publication in English, publication in peer-reviewed journals, and a description of the capabilities, experiences or practices of HLIUs. Units considered to be an HLIU were identified based on the following definition by the European Network for Highly Infectious Diseases (EUNID), ‘a healthcare facility specifically designed to provide safe, secure, high-quality and appropriate care, with optimal infection containment and IPC procedures’ for suspected or confirmed HCID cases.1 Titles and abstracts were screened; full articles were reviewed if the abstract was deemed to potentially contain information related to the aim. Search results were eliminated in three stages: before screening (duplicate records), during screening of abstract and title, or during full-text review. Articles were uploaded to RefWorks, analysed and sorted based on content into one or more domains defined by NETEC in their Hospital Readiness Assessment (table 1).9 For each domain, a descriptive analysis and synthesis of results was conducted to describe practices and operational features.

**RESULTS AND DISCUSSION**

Sixty-five articles met the search criteria; snowballing and reference check resulted in 32 additional articles. Therefore, a total of 97 articles were sorted into the domains (mean=21.4 per domain, median=18.5, range: 8–34; table 2). Finally, three other articles were only used for the introduction.

**Physical infrastructure**

HLIUs are equipped with enhanced physical infrastructure features that are designed to reduce the risk of pathogen transmission to HLIU staff, hospital and the community. Physical infrastructure components recommended for HLIUs include secure entry, sealable doors, high-efficiency particulate air (HEPA) filtration of exhausted air, anterooms, negative pressure, dedicated staff areas, onsite waste processing, easy-to-clean surfaces and the ability to surge, if necessary.1 3 These may not be equally available from unit-to-unit. Several HLIUs have described their decision-making processes for designing their units and physical infrastructure, most of which align with recommendations from HLIU consensus efforts.1 4 10 11 As of 2010, most European HLIUs were equipped with consensus efforts’ infrastructure recommendations, although use of HEPA filtration varied. 12 Importantly, costs to construct an HLIU and maintain the physical infrastructure can represent a significant barrier to establishing such units, which can range in the millions of dollars.1 10 12 13 Most HLIUs are in dedicated spaces within hospitals with separate air handling systems; however, a few HLIUs are within private buildings.6 12 HLIUs are generally either dedicated (eg, solely for HCID cases) or designated/flexible (used routinely for non-HCID cases when not activated).13 HLIU biosecurity measures, including secure entry and exit, controlled access, personnel verification and security presence when activated, are essential to managing the risk of HCID exposure to the rest of the hospital and public.13 14 Failures or defects in physical infrastructure can lead to catastrophic consequences; for example, air handling system failures can contaminate air flowing into adjacent non-HLIU rooms or units.15 Physical infrastructure should be reinforced and contingency plans in place for malfunctioning technical features, including processes for technical and mechanical support to handle issues before, during or after activation. Communication systems, which include phones, videos, intercoms, whiteboards and headsets, facilitate remote communications to minimise staff entering the unit; these systems also address potential communications challenges from personal protective equipment (PPE) use and allow for more HCWs on the care team without all having to enter the HLIU patient care room.10 12 16 Telehealth options are increasingly popular to augment units’ communication systems and care.17

The availability of technical infrastructure features significantly impacts the capacity of specialised HCID rooms. HLIU capabilities for HCIDs are relatively small, although HLIUs have reported greater capacity for respiratory diseases than VHF.6 12 However, most units have established surge plans to address large patient influxes.1 3 6 15 Approximately 80% of surveyed HLIUs from the USA, Europe and Asia in 2018 reported HCID surge plans, including plans for PPE, beds, equipment and waste handling.6

**Environmental infection & control**

Strict adherence to IPC measures in the HLIU is essential to prevent HCID transmission and is uniquely relevant to the health and safety of both HCWs and patients.18 Essential IPC components include usage of standard operating procedures (SOPs) that are familiar to staff detailing
### Table 1: Descriptions of HLIU organisational domains

<table>
<thead>
<tr>
<th>Domains</th>
<th>Description of the domains</th>
<th>Capabilities within domains</th>
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</table>
| Physical infrastructure       | Facility’s identification and utilisation of physical spaces and infrastructure to provide high-level isolation care for patients suspected or confirmed to have special pathogens. Assess the capabilities enabled or impeded by the physical layout, infrastructure, air handling systems, communication systems, space utilisation and surge capacity of the identified isolation care spaces in emergency department, inpatient settings and other identified care areas.                                                                                                                                                                                                 | 1. Facility clinical care area capability  
2. Special pathogen isolation care area capability                                                                                      |
| Environmental infection control | Facility approach to supporting and maintaining appropriate operational infrastructure, infection prevention and control procedures. Assess integration of critical operating systems and personnel training to maintain operational infrastructure, cleaning and disinfection of spaces, equipment, and supplies, and utilisation of zones to reduce cross contamination when managing special pathogen events.                                                                                                                                                                           | 1. Critical operating systems capability  
2. Cleaning and disinfection capability  
3. Utilisation of zones capability                                                                                                                |
| Personnel management           | The facility’s capacity and capability to provide optimal staffing for patients with special pathogens. Assess staffing models and the infrastructure to support these personnel before, during and after activations for special pathogen events. This includes special pathogen response team member requirements, team composition, personnel cross-training and backfilling of roles during activation, and staff scheduling and planning during activations, and personnel monitoring in coordination with public health. | 1. Staffing capability  
2. Occupational health capability                                                                                                           |
| Training and exercise          | Facility’s capacity and capability to establish and maintain education, training and exercise programmes for special pathogen response teams. Assess the structure, consistency and maturity of the education, training and exercise programmes for facility personnel related to special pathogens. This includes pathogens included in the training programme materials, personnel training requirements, frequency and modalities of the training offerings, the maturity of exercises conducted and resultant feedback loops. | 1. Orientation and onboarding capability  
2. Special pathogen response team training and education capability  
3. Just-in-time Training capability  
4. Exercises capability                                                                                                                     |
| Emergency management           | Facility capacity and capability to integrate emergency response principles to special pathogen events. Assess physical and operational structures, functionality and maturity of emergency response plans for special pathogens, improvement processes and the frequency these plans are tested and revised; organisational knowledge and application of response plans, and use of a hospital incident command system or equivalent structure. | 1. Emergency management capability                                                                                                               |
| Personal protective equipment (PPE) | Facility’s capacity and capability to select, acquire, store and use PPE during a special pathogen event. Assess systems and mechanisms for the selection, acquisition, storage and utilisation of different PPE based on pathogen type and public health guidelines as well as PPE procedures and training related to PPE donning and doffing, conservation strategies, disposal and breach mitigation. | 1. Acquisition and inventory management capability  
2. PPE utilisation capability  
3. Donning and doffing space capability  
4. VHF: trained observer capability                                                                                                       |
| Intake and internal transport  | Facility capacity and capability to promptly identify and provide isolation care for patients suspected or confirmed to have special pathogens. Assess facility infrastructure, processes and training necessary to identify patients potentially infected with special pathogen, effectively isolate them for further evaluation, inform critical stakeholders and transport the individual to the appropriate location for the indicated level of care. | 1. Identify capability  
2. Isolate capability  
3. Inform capability  
4. Internal transport capability                                                                                                               |
| Treatment and care             | Facility’s capacity and capability to receive and care for different population groups suspected or confirmed to have a special pathogen. Assess the facility’s available levels of care by population type, duration of care provision, ability to provide laboratory testing, follow-up care, transport logistics and coordination for higher levels of care if indicated. | 1. Clinical care capability  
2. Adult care capability  
3. Labour and delivery care capability  
4. Neonatal care capability  
5. Paediatric care capability                                                                                                               |

Continued
appropriate usage of transmission-based PPE, hand hygiene, regular environmental disinfection and proper waste and sharps handling. Maintaining adequate IPC in the HLIU also assumes a functional operational infrastructure including adequate space, appropriate air handling systems, cleanable surfaces, necessary staffing, sufficient PPE and supplies, and frequent training.

Zone demarcation and unidirectional flow are additional environmental practices of IPC compliance in an HLIU. Zone demarcation involves designating ‘clean’ zones where staff, equipment and the environment are considered uncontaminated, a ‘dirty’ zone where patient care, cleaning or waste disposal occur and a ‘transition’ zone between the two areas. Unidirectional flow prevents pathogens from soiled materials or HCWs from encountering the clean zone. Adhering to established SOPs for each of the designated zones related to waste disposal process, patient transportation, supply passthrough and HCW movement is vital to maintaining the integrity of the zones.

**Personnel management**

Staffing can be a barrier to HLIU activation due to varying availability (eg, day/night, specific days). HLIU staff should be preidentified and trained well before working in the HLIU, which is commonly ensured by the HLIU leadership team. HLIU teams are interprofessional and consist of team members from several healthcare professions, including physicians, nurses, pharmacists, respiratory therapists, patient care/laboratory technicians, researchers and environmental services staff; this interprofessional approach naturally allows for a variety

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**Table 1** Continued

<table>
<thead>
<tr>
<th>Domains</th>
<th>Description of the domains</th>
<th>Capabilities within domains</th>
</tr>
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</table>
| Laboratory           | Facility’s capacity to collect, analyse, package, ship and store laboratory specimens for different types of special pathogens. Assess laboratory physical infrastructure, testing menu and availability of laboratory equipment/supplies, infection prevention and control processes, staffing capability and availability, and adherence to regulatory requirements necessary to provide laboratory services. | 1. Testing and biosafety capability  
2. Specimen collection, handling, storage and transport capability |
| Waste management     | Facility’s capacity and capability to manage biological waste generated during the care of patients suspected or confirmed to have special pathogens, inclusive of category A infectious substances. Assess waste management equipment capabilities, including identification and categorisation according to the different special pathogens, coordination with facilities and outside contractors, protocols and training for packaging, inactivating, storing and transporting all waste. | 1. Identification and management of special pathogen waste capability  
2. Storage of special pathogen waste capability  
3. Transport of special pathogen waste capability  
4. Onsite inactivation of category A infectious substance capability |
| Decedent management  | Facility capacity and capability to manage decedents. Assess protocols and training for personnel on safe containment and final disposition of human remains in coordination with critical internal and external stakeholders. | 1. Decedent management capability |
| Research             | Facility’s capacity and capability to establish and maintain rapid response research activities to manage special pathogen events. Assess the facility’s infrastructure and capacity to engage in different research activities related to special pathogens preparedness and response. This includes processes to acquire, administer and monitor investigational new drugs or other medical countermeasures as well as the availability and capacity of research personnel and special pathogen response team members to coordinate and support the implementation of research protocols for safe care delivery. | 1. Investigational therapeutics capability  
2. Research personnel capability |
| Prehospital          | Facility personnel’s awareness about local and regional transportation plans for individuals with special pathogens and the implantation of those plans with identified EMS agencies and other public health partners. Transportation planning and coordination process for patients suspected or confirmed to have special pathogens and the hospital’s interactions with EMS when transporting these patients. This includes the identification and preparation of EMS points of entry and internal transport routes, processes for communication prior to and during transport, and intrafacility expectations for EMS partners. | 1. Transportation planning capability  
2. EMS/hospital interface capability |

EMS, Emergency Medical Services; HLIU, high-level isolation unit; VHF, viral haemorrhagic fever.
of clinical specialists including critical care and infectious diseases.\textsuperscript{1,3,12,18,25,26} HLIU staff compositions are relatively consistent globally, with some variation related to admission roles and patient management. Some units rely on specialised staff (eg, infectious diseases, critical care) to admit, manage and oversee clinical care during patient admission, while others primarily use hospitalists.\textsuperscript{12,25,27}

HLIU clinical teams are usually from the HLIU’s hospital.\textsuperscript{1,3,6,11,24,25,27} Some units contract non-medical staff through an external entity, although this is still not a particularly common practice as hospitals often have these resources onsite.\textsuperscript{24} While there are HLIUs (especially non-US units) that have non-volunteer members (ie, requirement as part of employment), HLIU programmes more frequently seek volunteers.\textsuperscript{1,3,6,11,24,25,27} During an activation, when staff members are deployed to the HLIU from other units in the hospital, those positions are usually backfilled with non-HLIU staff from the same unit or other staffing pools within the hospital to ensure functionality of other hospital units.\textsuperscript{10,11,27}

The care and well-being of unit staff is fundamental for a safe and effective HLIU response. Monitoring staff during and after activation for potential infection related to HLIU care (eg, temperature checks, symptom monitoring) allows for early identification of any potentially related symptoms.\textsuperscript{1,4,24,28} Medical professionals have reported anxiety and stress related to the care of HCIDs.\textsuperscript{29} Thus, it is vital to ensure staff have access to psychosocial care and support; although these are used in some units, a 2018 survey of 22 HLIUs found only 32% of units had psychosocial support for staff, demonstrating an area for growth for many units.\textsuperscript{6} One example of an effective psychosocial support mechanism are staff huddles or meetings, which have been used to promote emotional support and morale.\textsuperscript{11} Lastly, one article predicted that genetics could be used in the future to inform HLIU staff about risks from HCIDs, although it is unclear how and if this could be used for staff modelling.\textsuperscript{30}

### Table 2: Number of articles per domain

<table>
<thead>
<tr>
<th>Domain</th>
<th>No of articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decedent management</td>
<td>8</td>
</tr>
<tr>
<td>Emergency management</td>
<td>18</td>
</tr>
<tr>
<td>Environment/infection control</td>
<td>17</td>
</tr>
<tr>
<td>Intake and internal transport</td>
<td>16</td>
</tr>
<tr>
<td>Laboratory</td>
<td>16</td>
</tr>
<tr>
<td>Personal protective equipment</td>
<td>26</td>
</tr>
<tr>
<td>Personnel management</td>
<td>34</td>
</tr>
<tr>
<td>Physical infrastructure</td>
<td>32</td>
</tr>
<tr>
<td>Research</td>
<td>12</td>
</tr>
<tr>
<td>Training and exercises</td>
<td>21</td>
</tr>
<tr>
<td>Treatment and care</td>
<td>38</td>
</tr>
<tr>
<td>Waste management</td>
<td>19</td>
</tr>
</tbody>
</table>

### Training and exercise

Consistent training and exercise can lead to increased staff confidence, translating into improved safety and effective care. A highly trained and educated staff is a fundamental HLIU element and a core recommendation from consensus efforts.\textsuperscript{13}

Planning and training are essential steps in HLIU preparedness; testing a plan during an exercise provides an opportunity to use, evaluate and identify gaps in SOPs, while an after-action review can function as a checklist for necessary improvements.\textsuperscript{31} Along with HLIU skills and SOPs, incorporation of Hospital Incident Command System (ICS), unit activation, transport and research processes have been highlighted as areas to exercise.\textsuperscript{32}

Main focal areas for HLIU staff training include PPE donning and doffing, using checklists and a trained observer, IPC and skills training in PPE, waste management, and specimen collection and processing. Other areas incorporated into training are team building and communication. Training can be offered hands-on or virtually, although hands-on application of skills and SOPs is core to competency development. Regardless of the focus area of training, strict competency verification is essential.\textsuperscript{25} Having a predetermined cadence of training (eg, quarterly) was highlighted for maintaining familiarity with the skills for safe care in an HLIU.\textsuperscript{1,3,26,33}

Challenges to HLIU training and exercise include staffing, resource availability, competing priorities and funding.\textsuperscript{33} Continued training, education and exercises are time-intensive and resource-intensive, but essential to maintaining readiness.\textsuperscript{34} To provide safe and effective care in HLIUs, these challenges must be addressed to provide regular training, education and exercise.

### Emergency management

Incident management and risk communication often challenge the healthcare sector, amplified more so with the need to align messaging with public health and stakeholders. This alignment and coordination are important for HLIU activation, regardless of whether the activation occurs due to aeromedical transport with time for preplanning, or because of a local case presentation. Critical sectors within the emergency management domain, including the ICS for HLIU settings, have seen significant benefits and will continue to evolve in parallel with the maturation of HLIU facilities and networks.\textsuperscript{35}

Consensus efforts such as EUNID and organisations such as NETEC provide an apparatus for national or regional collaboration and consistency.\textsuperscript{36} During HLIU activation, the hospital works alongside emergency management offices to provide consistent updates while augmenting facilitation of response with local and federal partners.\textsuperscript{10}

To date, several surveys have evaluated deficiencies, standards and staff competencies related to the Centers for Disease Control and Prevention Identify, Isolate and Inform algorithm for a patient with EVD or another HCID, with emphasis on the value of standardised
processes across the healthcare sector. The paradigm created by New York Health and Hospitals, ‘Ready or not, patients will present’, highlights the importance of HCID readiness for all healthcare entry points.  

**Personal protective equipment**

PPE is worn to minimise the wearer’s exposure to hazards. PPE for HLIU care often consists of multiple, intentionally redundant elements to minimise the likelihood of patient-to-HCW transmission. HLIU PPE recommendations should reflect known pathogen characteristics that influence transmission risk. In a study that examined rates of HCW self-contamination by enveloped and non-enveloped surrogate viruses during simulated patient care, the non-enveloped virus more frequently contaminated HCWs inner PPE layers and skin, suggesting that careful doffing of multiple glove layers combined with strong glove sanitising agents may be indicated, especially for select viruses. A US HLIU survey found most units used tiers of PPE dependent on patient acuity and the likelihood that an HCW will come into close contact with a site of high microbial burden. Importantly, knowledge gaps in the pathophysiology and transmission dynamics of many pathogens hinder the development of PPE guidance. Elucidating these and other characteristics of HCIDs concerning PPE should be research priorities.

Key risks related to PPE in HLIUs include impairment of occupational well-being, performance and contamination of PPE, or the environment during donning, doffing and care. A previous investigation demonstrated raised core body temperature in HCWs performing care in an HLIU, a subset of whom reported symptoms of heat exhaustion. Another investigation demonstrated that HCWs experience an increase in physical load while doffing PPE. Restricting the number of hours HCWs are permitted to wear PPE and including balancing aids are strategies that have been employed to mitigate the physical effects of PPE on HCWs. The impact of PPE on HCW clinical performance is less clear. While cognition and dexterity were not diminished in participants of a single-centre trial evaluating the effect of PPE on performance of standardised non-clinical tasks, a multicentre survey of surgeons during the COVID-19 pandemic revealed perceptions among respondents that PPE impeded visibility and other non-technical skills. Inadvertent contamination despite PPE use has been demonstrated and evidence supports the importance of supervision and communication with a trained observer when donning and doffing PPE. Characterising the risks of PPE through actual experiences is critical to developing safe devices and practices and is an area for further study.

Decontamination of PPE using a germicide (e.g., diluted bleach) by spray or wipe, or use of a decontamination shower, is another consideration for reducing risks during the doffing process. However, wet decontamination requires appropriate infrastructure to address runoff and drainage in HLIU environments; moreover, use of spray decontamination, while employed in the field, has raised concerns about the potential for aerosolising particles on the contaminated PPE.

Inadequate supply chains during a pandemic can necessitate decontamination, continency and crisis PPE standards, which in turn require (1) rapid assessment of PPE alternatives, (2) introduction of new PPE elements and unconventional use of familiar PPE elements, such as reusing materials designed for single use and (3) additional infrastructure to reprocess PPE designed for single use. Emerging data suggest that ultraviolet germicidal irradiation, dry heat or moist heat (with or without the use of microwave steam bags) inactivation and hydrogen peroxide effectively decontaminate N95 respirators without compromising the integrity of respirator materials.

Alternatives to traditional PPE include patient isolator tents, such as the ALIMA Cube and the Trexler isolator. These isolation systems have built-in, fully protected slots where medical professionals can insert their arms to administer patient care activities, without direct contact to a patient’s skin or fluids, but also the environment within the tent. These systems decrease PPE needs and costs, increase working time in a shift and limit contamination of the surrounding environment; however, patient tolerability, particularly for children, is a concern, as is potential limits on employment of certain critical care interventions.

**Intake and internal transport**

The decision to admit a patient into an HLIU is influenced by several factors, including the suspected or confirmed pathogen, the preparedness of the HLIU team and facility, patient acuity, financial and regulatory considerations, and the requestor (e.g., local, regional or national authorities; organisations responding to an HCID emergency with an exposed or infected employee). Although no consensus list of HCIDs warranting HLIU-level care exists, recommendations for diseases that might be considered for HLIU admission include VHF, novel infectious diseases and smallpox. A 2018 survey of select HLIUs found consensus among respondents that VHF and smallpox would be managed in an HLIU, but HLIU uses varied for other diseases. Unsurprisingly, multiple simultaneous patient admissions require altered HLIU patient intake procedures and considerations for escalated staffing, waste management and PPE use; exercises and drills are effective in testing and revising these procedures.

Although it is possible for an HLIU to activate for a suspected or confirmed case that presented to the facility’s emergency department, it is more likely that cases will be transported from outside of the facility. Regardless of location of initial presentation, the internal transport route to the unit entrance should be controlled, direct, secured and away from heavily trafficked areas. Security can assist in closing off traffic and keeping patients, staff,
and hospital visitors away from the route. An internal transport team should receive the patient, composed of trained HLIU staff wearing PPE and equipped with spill kits and other decontamination supplies; on intake of the patient into the HLIU, this team should decontaminate the entire pathway from hospital entry point to the HLIU. Portable isolation units (eg, EpiShuttle, Isopod) can be used to minimise exposure risks to transport teams; however, they can hinder direct patient access, are expensive and many are not reusable.

**Research and innovation are needed to develop portable isolation units that allow for direct patient care and are cost-effective.**

**Treatment & care**

The ability to provide HCID treatment and care within an HLIU includes a well-trained staff with the needed expertise. Ideally, HLIUs would manage a variety of specialised patients (adult, paediatric, intensive care patients, obstetrical patients and newborns); however, not all units have the staff expertise or resources. Most previously surveyed HLIUs reported they could provide care to adults and the staff expertise or resources. Most previously surveyed HLIUs reported they could provide care to adults and children, while a smaller number have adult-only beds, and fewer possess only paediatric beds. HLIUs should have clinical equipment in-unit for basic management needs (eg, for vital signs). For more complex equipment like ventilators, many units rely on other hospital wards, although some store this equipment within the HLIU. Access to expertise in maintaining vascular access, managing ventilators and renal replacement therapy is critical for patients with HCIDs. For specialised procedures, units may have predetermined or trained teams on standby. Several case reports outline HLIU-specific clinical care experiences, primarily with EVD or other VHFs.

Advanced planning to include integration of specialised medical consultants, including nurses with expertise in infectious diseases, critical care, adult, paediatrics, neonatal care and obstetrics, is important to provide the best care for all patients. For paediatric patients, HLIUs should have predetermined procedures and policies to handle or limit parental involvement. Although some HLIUs have provided care to pregnant individuals with a confirmed or suspected HCID, these specific experiences are not described at length in the literature.

Many medications and treatments for special pathogens are investigational new drugs (INDs) used only via clinical trial protocol(s) and emergency or compassionate use authorisations; thus, supportive care is of utmost importance. Incorporating planning and exercises involving INDs into the HCID care plan will increase HLIU readiness to provide specialised care.

More in-depth best practices for clinical care treatment by organ system for those with HCIDs have been evaluated by some HLIUs in the USA and Europe. It is important to continue building and improving best practices and policies for care of patients with an HCID. Providing the ability and resources for global collaboration and research offers the best opportunity to understand and advance the current knowledge and best practices of HCID treatment and care.

**Laboratory testing**

Rare, laboratory-acquired illnesses via unintentional exposures to an HCID have been described. Laboratories in or associated with HLIUs should maintain an enhanced Biosafety Level 3 (BSL3)+ status (i.e., laboratories over and above the minimum requirements for Biosafety Level 3 [BSL3] laboratories) with specifically trained staff to ensure proper management, handling and testing of HCID specimen while minimising risk to staff or other outside entities.

An important component of HLIUs is the ability to perform point-of-care testing for standard diagnostic and monitoring blood tests within the unit, including complete blood count, electrolytes, creatinine, glucose, liver function tests, blood coagulation monitoring, rapid malaria testing, troponin level, blood gas testing and blood culture capability. Blood group testing and cross match are also useful but can be a challenge within an HLIU. Point-of-care samples do not require centrifugation, reducing the risk of aerosolisation. All procedures are performed carefully to minimise the creation of splashes/aerosols and use of sharps. A survey of global HLIUs found that clinical laboratory diagnostic testing was performed within the HLIU (63%), within the patient care room (21%), or outside of the HLIU (16%).

Much like HLIU patient care rooms, laboratories should ideally be equipped with spaces for PPE management and dedicated sealed entrances/exits to ensure maximum protection against any HCID. The laboratory should consist of an anteroom and at least one separate laboratory room. Access to the laboratory is restricted to prevent continuous traffic flow and prevent airflow disturbances that might interfere with cabinet airflow. Biological safety cabinets with a HEPA supply and exhaust filter are required for patient testing. Testing, certification and repairs to biological safety cabinets should be conducted in line with normal BSL3+ practices. Specifically, biological safety cabinets should be tested and certified at the time of installation or when moved, the HEPA filter is replaced, and maintenance occurs at least once a year.

HLIUs should have established protocols and necessary physical space for the safe handling, storage and transport of HCID specimens. HLIUs have reported preparing patient specimens for receipt by the laboratory using varied combinations of surface decontamination, airlocks, light boxes and dunk tanks. For transportation, a specified transport route and a clear chain of custody should be established at each point between the HLIU and the laboratory.

**Waste management**

Waste produced in the HLIU will depend on the pathogen’s classification; in the USA, category A waste is...

Lukowski J, et al. BMJ Glob Health 2023;8:e012037. doi:10.1136/bmjgh-2023-012037
defined as any infectious substance that is ‘capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals when exposure to it occurs’. Handling of category A waste is extremely high-risk; well-defined plans, comprehensive training, and exercising of protocols is critical to minimising exposure risks while handling waste.

HCID care can generate large volumes of medical waste due to high staff-to-patient ratios, PPE usage, and the disposal of supplies and equipment that cannot be decontaminated or reused. An autoclave or incinerator is recommended to deactivate solid waste before transport; autoclaving minimises risk and allows it to be disposed of as regular medical waste. However, not all HLIUs have the capabilities to sterilise waste onsite, often due to costs and logistical concerns: autoclaves were available in 68% of surveyed HLIUs in 2018. The absence of in-unit waste processing capability can be costly, with transportation costs potentially ranging in the hundreds of thousands of dollars.

Of note, at least one HLIU equipped with an autoclave deemed in-hospital autoclave capacity insufficient due to the excessive amounts of waste generated while managing EVD and chose to outsource waste destruction to an external facility. Biological and chemical indicators can be used with each autoclave cycle to ensure sterilisation before transporting the waste off the unit. However, autoclave validation at some HLIUs has revealed that the factory default setting may be ineffective for certain types of medical waste, highlighting the crucial need for adequate waste packaging. Thus, a well-executed training plan, exercises and drills can ensure that waste management processes are executed efficiently and effectively.

Liquid waste management was one of only two HLIU operations for which the EUNID effort was unable to reach consensus, further verified by a 2009 survey of European units. During the 2014 EVD epidemic, two HLIUs in the USA opted to use a hospital grade disinfectant over the recommended contact time prior to flushing in a toilet, while other units used a solidifying agent and disposed as solid waste. HLIUs, governing organisations and the wastewater industry have differed in their approaches and recommendations for HCID liquid waste disposal; these differences and a lack of evidence-based practices encourages increased investigation and evidence generation in this space.

Decedent management

Experiences with decedent management in HLIUs are not well described in published literature, although consensus findings for the management of highly infectious decedents have been recently described. Caring for a deceased patient in an HLIU requires additional considerations and processes to ensure safe, respectful and systematic management. In the case of EVD, the risk to a HCW is highest following the patient’s death. Methodic development and intentional training of SOPs with dedicated staff is needed to address the high-risk nature of the task. IPC principles are important to integrate into these processes. To maintain readiness, SOPs must integrate regulatory requirements into the processes that include the continuity of decedent management from the facility to mortuary/crematory/final resting place.

Partnerships and planning with internal and external agencies, including mortuaries, crematoriums and funeral directors, are critical to build trust, coordinate, develop memorandums of understanding, and training exercises in advance of a real-world event. This is critical for the HLIU staff and external partners who may adapt standard practices to the HCID; for example, avoiding an autopsy, embalmment or the viewing of a body by families. These modifications have the potential to impact the family members and loved ones along with certain cultural considerations of the decedent which should be accounted for.

Research

Research infrastructures for special pathogens involve resources, complex research facilities and institutions, and other services fundamental for successful and timely implementation of biomedical research. These infrastructures can belong to individual organisations and/or be comprised of networks of institutions collaborating and working together towards a common goal of protecting communities against biological threats.

Despite the existence of expertise and federal funding sources, published literature regarding coordinated research infrastructure for emergent pathogens in the USA revolves around NETEC’s Special Pathogens Research Network (SPRN). SPRN provides an organisational structure to leverage the expertise and improve the readiness to conduct clinical research of current US HLIUs during an HCID event. SPRN has previously coordinated clinical research focused on investigational therapeutics for EVD and played a leading role during the Adaptive COVID-19 Treatment Trial (ACTT). The SPRN and its central Institutional Review Board infrastructure were critical to the rapid onboarding of participating sites and enrolment of subjects at multiple RESPTCs into the ACTT: 26% of patients across ACTT trials were enrolled from a RESPTC SPRN site, with an average study approval time of 2 days.

In 2002, the European Strategic Forum for Research Infrastructures was created to develop a unified strategy for scientific research in Europe and to overcome the fragmentation of research efforts at national and regional levels, leading to a roadmap for the development of European research infrastructures. As a result, in 2009, the European Research Infrastructure Consortium (ERIC) was created to provide legal status for these infrastructures. Two resulting facilities include the European Clinical Research Infrastructure Network (ERIC), created to facilitate the implementation of international clinical trials in Europe; and the European Research...
Infrastructure on Highly Pathogenic Agents, created to coordinate research and development of methods to combat HCIDs. Literature supports fostering research networks and infrastructures that will focus on readiness and training, guidelines and policy creation, resource creation and distribution, and global collaboration to face future HCID challenges. Given the preference to treat HCID cases in HLIs, HLIs should continue to expand their research capabilities and network to leverage their position to rapidly implement research protocols when activated.

Conclusions
This article explores the experience, practices and operational features of global HLIs across various domains; we believe this is the first review to summarise HLIs operations. The elucidation and synthesis of HLIs experiences, best practices, challenges and components can serve as a resource for units continuing to improve readiness, or for hospitals in early stages of developing their HLIs teams and planning or constructing their units. Recent and ongoing outbreaks of VHFs emphasise the need for an extensive summary of HLIs practices to inform readiness and response.

The multinational nature of this review aims to encourage collaboration, engagement and coordination among global HLIs. Although HLIs and solutions are highly dependent on local legislation, physical spacing, resource availability and regional and national HCID experiences, there is opportunity for HLIs to learn from each other and advance operational priorities. New HCID threats encourage HLIs to continually adapt and refine readiness activities, sharing of knowledge, experiences and practices among this unique global community can further advance HLIs practices as well as those for broader HCID preparedness and response.

There are limitations to this review. Definitions and nomenclature for HLIs vary; our findings were based on previous US and European consensus effort definitions. This likely led to the clear geographical gaps in locations of HLIs that have published on their experiences or practices; indeed, articles were exclusively from Asia, Europe and North America. Additionally, there is an inherent bias in the exclusion of non-English and non-peer-reviewed materials; as such, important discussions on experiences and high-level isolation capabilities in other languages or in the grey literature were not included and it prevented the review from being truly global in nature. Although we did not identify (and therefore include in this analysis) peer-reviewed articles from sub-Saharan Africa, the Middle East and North Africa, South America and East Asia, there are likely efforts to enhance and advance isolation capabilities for HCIDs in each of these regions that would be incredibly valuable to increasing global understanding of and readiness for HCID care and management. More research and review of experiences and capabilities outside of peer-reviewed literature, with a focus on regions not included in this review, are needed. HCID events in the last decade have reinforced the critical role of HLIs in national and global health security. HLIs expertise includes other benefits, such as common platforms for exchanging training, protocols, research, lab, processes, workflows and a national and growing international network of peers. Integration of evidence, HLIs best practices and research-based sharing can serve as the standard for HCID response, enhancing global preparedness beyond just HCIDs and improving national, regional and global health security.

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