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Review

Biocontainment Transport of Patients with High-Consequence Infectious Diseases: A Narrative Review and Integrated Operational Framework for Emergency Medical Systems

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Abstract

Background/Objectives: The transport of patients with high-consequence infectious diseases (HCIDs) links biosafety science and emergency medicine. The 2026 Bundibugyo virus disease epidemic and the multinational Andes virus outbreak associated with an expedition cruise ship have renewed attention on how such patients are moved safely between the community, hospitals and high-level isolation units. This narrative review synthesises the international literature on biocontainment transport and integrates it into an operational framework for emergency medical systems. **Methods:** A structured search of PubMed/MEDLINE and Scopus (to 10 October 2026), complemented by guidance from the World Health Organization, the European Centre for Disease Prevention and Control, the US Centers for Disease Control and Prevention and national authorities, was conducted, and the review was planned and written using the SANRA quality criteria. Evidence was organised across seven operational domains and combined with the operational experience of the Public Health Unit of the Italian Red Cross (CRI). **Results:** Of 2432 records identified, 1485 unique records were screened. The literature is dominated by aeromedical case reports, technical evaluations and expert consensus, with few comparative studies. Recurrent findings concern device integrity and air quality within transport isolators, the risk of self-contamination during doffing, heat strain and communication limits imposed by personal protective equipment, decontamination of vehicles and isolators, the maintenance of team readiness during periods of low activity, and the psychological burden on patients and staff. These findings are integrated into a framework comprising a four-link containment chain, a seven-phase operational workflow, a three-tier complexity classification and a role-based responsibility matrix. **Conclusions:** Biocontainment transport is better understood as an integrated emergency system than as a device-centred intervention. The proposed framework is a structured, consensus-based reference for planning, training and quality assurance; its components require prospective evaluation.

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1. Introduction

High-consequence infectious diseases (HCIDs) are acute infections that are transmissible from person to person, cause severe illness with high case-fatality rates, and require enhanced infection prevention and control measures and specialised clinical care [1,2].

The group includes filovirus diseases (Ebola and Marburg), Lassa fever, Crimean–Congo haemorrhagic fever, Andes virus infection and emerging respiratory pathogens with pandemic potential [2,3]. Effective countermeasures are available only for a minority of these pathogens: no licenced vaccine or specific antiviral treatment is available for Bundibugyo virus [4], and no specific treatment is available for Andes virus infection, whose management remains largely supportive [3,5]. For these reasons, containment remains the cornerstone of safe clinical care.

Two events in 2026 have brought HCID transport back to the centre of preparedness planning. In May 2026 the World Health Organization (WHO) declared the Bundibugyo virus disease epidemic in the Democratic Republic of the Congo and Uganda a Public Health Emergency of International Concern [6,7]; health care workers were among the earliest cases [8], and imported cases were reported in Europe [9]. In the same weeks, an outbreak of Andes virus—the only hantavirus with documented person-to-person transmission—was linked to the expedition cruise ship MV Hondius, with 13 cases among passengers and crew of 23 nationalities and a coordinated international response that required medical evacuation, repatriation, isolation and quarantine across several countries [10–12]. Both events required the safe movement of patients between the community, ports, airports, hospitals and high-level isolation units (HLIUs).

The containment of patients with dangerous infections has a long history. Flexible-film isolators were developed from gnotobiotic research and, in their negative-pressure version, used in hospitals for patients with dangerous infections in the 1970s [13–15]; dedicated containment care units originated alongside the biosafety level (BSL) 4 laboratories of the US Army Medical Research Institute of Infectious Diseases (whose medical containment suite became known as the "Slammer") in the late 1960s [16,17]; and containment aircraft transit isolators and aeromedical isolation teams were developed to move patients without interrupting the containment chain [18,19]. The 2014–2016 West African Ebola epidemic, and later the COVID-19 pandemic, prompted European and North American health systems to expand and formalise high-level containment transport (HLCT) [20–22].

Published reviews have focused mainly on aeromedical evacuation [20,21], whereas ground transport—the most frequent modality in daily practice—has received less attention [23,24]. Surveys have documented heterogeneous national arrangements, with only a minority of European isolation centres reporting both national and local guidelines for HCID patient transport [24]. Most of the available evidence consists of case reports, technical evaluations and expert consensus, and no single source addresses devices, procedures, team governance and human factors together.

In Italy, the Public Health Unit (Reparto di Sanità Pubblica, RSP) of the Italian Red Cross (CRI) has operated a biocontainment transport service since 2006 under an agreement with the Ministry of Health; between December 2020 and March 2022, during the COVID-19 pandemic, it transported 2326 patients by road: 1993 under biocontainment (590 in single-patient isolators and 1403 in a biocontainment minibus) [25] and 333 in vehicles with a physical barrier separating the driver from the patient compartment (service activity records), which do not meet biocontainment criteria and are not considered further in this review. The biocontainment activity covered 188,305 km [25]. This experience generated operational procedures that have been only partially described in the literature [23,25].

The aim of this narrative review is therefore twofold: (i) to synthesise the international literature and guidance on the biocontainment transport of HCID patients across its main operational domains, and (ii) to integrate this evidence with the operational experience of the RSP into a structured framework for emergency medical systems. The framework is presented as a consensus-based reference to support planning, training and quality assurance; it is not an empirical evaluation of transport outcomes.

2. Methods

The six criteria of the Scale for the Assessment of Narrative Review Articles (SANRA) [26] were used as a quality framework when planning and writing this narrative review. These criteria cover the justification of the article's importance, the statement of aims, the description of the literature search, referencing, scientific reasoning and the presentation of the evidence; the authors' self-assessment is provided in Supplementary Table S2. This self-assessment is not an independent appraisal of methodological quality and does not constitute a validation of the operational framework. A structured literature search was conducted in PubMed/MEDLINE and Scopus from database inception to 10 October 2026. Search strings combined terms for HCIDs and high-level containment (e.g., "biocontainment", "high-level isolation", "Ebola", "Marburg", "Lassa", "viral haemorrhagic fever", "hantavirus") with terms for patient transport and emergency medical services (e.g., "patient transport", "ambulance", "prehospital", "aeromedical", "transport isolator"). Six additional domain-specific searches addressed personal protective equipment (PPE), decontamination, the psychological impact on staff, governance, training and networks, isolation transport of COVID-19 patients, and person-to-person transmission of Andes virus. The complete search strings are reported in Supplementary Table S1. In Scopus, results were limited to English and Italian at the search stage; for PubMed records, the same language restriction was applied during screening.

Grey literature was retrieved from the websites of WHO, the European Centre for Disease Prevention and Control (ECDC), the US Centers for Disease Control and Prevention (CDC), the National Emerging Special Pathogens Training and Education Center (NETEC), the UK Health Security Agency and the Italian Ministry of Health, and reference lists of included articles were hand-searched. Records were eligible if they addressed the transport or prehospital management of patients with suspected or confirmed HCIDs, or the use of high-level containment transport devices, and were relevant to at least one domain of the framework: biosafety and devices; PPE; decontamination; operational workflow; complexity stratification and team composition; governance, training and networks; and human factors. Primary studies, reviews, case reports and series, technical evaluations and guidance documents were considered. Laboratory, molecular and veterinary studies without operational content, hospital infection control studies unrelated to these domains, and conference abstracts were excluded.

The searches identified 2432 records (PubMed, $n = 1004$; Scopus, $n = 1428$). After removal of 947 duplicates, 1485 unique records were screened on title and abstract; 1283 were excluded (1212 not relevant, 57 for language, 14 further duplicates or superseded versions), and 202 were assessed for their contribution to each domain (Supplementary Figure S1). When several sources reported overlapping evidence, the most recent, most comprehensive or highest-level source (systematic reviews and guidance documents over single reports) was retained. The remaining 102 assessed records were therefore not cited. In total, 100 sources identified through the database searches and 18 guidance documents, standards and other sources are cited in this review. Titles and abstracts were screened by one author (F.D.), supported by a preliminary AI-assisted classification that was verified record by record. The evidence was synthesised narratively by domain. Where published evidence was unavailable, operational content is explicitly identified as derived from the authors' field experience within the RSP biocontainment transport programme. A generative artificial intelligence tool, Claude (Opus 5.5; Anthropic), was used to support the development of the search strings, the deduplication of records, the preliminary classification of records for screening, the extraction of information from the included sources and the drafting and language editing of the text. The graphical abstract was generated with ChatGPT (GPT-5.6 Sol; OpenAI) on the basis of a content outline prepared by the authors.

All outputs were checked against the original sources and revised by the authors, who take full responsibility for the selection, synthesis and interpretation of the evidence.

3. Biosafety Framework and the Containment Chain

Biological agents are classified into four risk groups according to their infectivity, pathogenicity, transmissibility and the availability of prophylaxis or treatment, and laboratory work is matched to four corresponding containment levels [27–29]. HCID pathogens belong mainly to risk group 4 (e.g., Ebola, Marburg and Lassa viruses) and, for selected respiratory pathogens, to risk group 3 [27]. Laboratory risk-group classifications and the clinical or public-health designation of HCIDs serve different purposes and are not equivalent: the latter reflects person-to-person transmissibility, severity and the need for enhanced control measures in health care settings [1,2]. Decisions on clinical isolation, transport precautions and containment should therefore rest on a pathogen-specific risk assessment and on applicable guidance rather than on the laboratory risk group alone. In the framework proposed here, the risk group sets a minimum level of protection: patients infected with risk group 4 pathogens are always assigned to the high-complexity level (Section 8), but the final decision also takes into account the pathogen-specific risk assessment and applicable guidance. Translating these principles to patient care requires attention to the actual routes of transmission. Early analyses of viral haemorrhagic fevers identified parenteral inoculation of staff as the main danger and indicated that fomites and droplets must also be considered, whereas the role of small-particle aerosols remained debated [30]. Consensus recommendations of the European Network for Infectious Diseases (EUNID) built on this evidence to define infection control requirements for the clinical management of highly infectious diseases, including invasive procedures [2]. For Andes virus, viral RNA is consistently detectable in blood during the acute phase and infectious virus has been recovered from several body fluids, including saliva, gingival crevicular fluid, nasopharyngeal secretions and urine [31], which indicates plausible exposure pathways during close patient contact; however, the detection of viral material in biological specimens does not by itself establish a specific route of transmission. Current recommendations for Andes virus combine an airborne infection isolation room with gown, gloves, eye protection and an N95 or higher-level respirator, within a precautionary, layered, risk-based approach that reflects the uncertainty about the timing and route of infectiousness [3].

Compared with a fixed HLIU, the mobile environment adds vibration, acceleration, confined space, variable climate, prolonged task duration and limited access to the patient. Within the framework proposed here, safety during transport is conceptualised as a containment chain of four interdependent links: (1) PPE; (2) the physical containment envelope of the transport isolator or vehicle compartment; (3) negative pressure with high-efficiency particulate air (HEPA) filtration; and (4) structured decontamination. By analogy with the chain of survival, the failure of any single link can compromise the integrity of the whole system. The configuration of each link is not fixed but depends on the pathogen and its routes of transmission, on the transport platform and on the procedures anticipated during the mission [25]. In the RSP, single patients who are non-ambulatory, critically ill or at high risk of airborne transmission, or who need airway management and monitoring, are transported in a stretcher isolator mounted on the ambulance stretcher, in which the patient is enclosed in a plastic envelope kept under negative pressure by a blower and a HEPA filter, and the crew works outside it through glove ports while wearing full PPE, which provides a second level of protection [23,25]; groups of up to seven ambulatory, low-complexity patients are transported in a minibus in which the patients are seated inside a PVC envelope, also kept under negative pressure with HEPA filtration and separated from the crew [25]. Where no isolator is used, patient and crew share a sealed or lined vehicle

compartment, so that crew protection relies primarily on PPE and the whole compartment requires decontamination (Section 6). Each configuration also constrains clinical care: the space available, the power autonomy and compatibility of life-support devices with the sealed environment and even the choice of vascular access, which may be limited by the securing straps of the isolator, must be planned in advance [23,25]. Moreover, the presence of a containment component does not in itself guarantee protection, and each link requires verification of its effective operation before and during the mission. Envelope integrity is checked by visual inspection and by the measured negative pressure, which is a key indicator of correct operation but does not by itself prove the integrity of the whole isolator: containment also depends on airflow, on the position and size of any breach, on filtration, on dynamic conditions such as movement and loading, and on the presence of body fluids. While negative pressure is maintained, air tends to flow inward through small breaches, which limits the escape of contaminated air, whereas a fall in negative pressure suggests a major breach or a failure of the ventilation unit (Section 7). Pressure readings should therefore be interpreted together with the integrity checks specified by the manufacturer, and any breach should be identified and repaired, because negative pressure does not prevent the leakage of body fluids. PPE doffing is supervised through a buddy check or by a trained observer, an approach supported by the literature (Sections 5 and 9). Verification of decontamination is more difficult, because direct evidence that decontamination has been effective is rarely available in routine practice; it therefore relies mainly on the documented and observed completion of each step—agent, concentration and contact time—whereas biological indicators can be used to validate volumetric methods (Section 6). This conceptual model reflects the authors' operational consensus; the evidence relating to each link is reviewed in the following sections.

4. Transport Platforms and Device Architecture

The single-patient stretcher isolator is the primary physical barrier between the patient and the environment. Italian technical requirements [32] for the transport of patients infected with risk group 4 agents specify, among other features, assembly within minutes, a containment accessory for fluids, a negative pressure gradient greater than 6 Pa with respect to the external environment, absolute (HEPA) filtration compliant with EN 1822 [33], battery autonomy of at least 10 h and an airflow of 35–40 m^3/h, together with adequate O_2 and CO_2 concentrations for the vital functions of the patient. Air enters through a pre-filter at the foot of the isolator and is exhausted through the HEPA filter at the head end, so that small breaches of the envelope result in inward rather than outward airflow. Experimental studies of flexible-film negative-pressure isolators confirmed a high degree of containment and protection of staff when operated correctly [14,15]. The RSP uses a stretcher isolator of this type (Isoark N36, Beth-El Industries, Israel), whose care protocols during road transfer have been described previously [23].

The technical literature identifies several vulnerabilities of transport devices. During a ground transport exercise of approximately 414 km, carbon dioxide and humidity accumulated inside a stretcher isolator, reaching steady-state CO_2 concentrations of about 3000–4400 ppm; when failure of the blower unit was simulated, CO_2 exceeded 10,000 ppm within 8 min [34]. These data support systematic verification of the blower, filters and battery before departure, and three purposes of monitoring during transport should be distinguished. Monitoring of device performance verifies that containment is working: in the RSP, negative pressure is measured with an external digital manometer, and some isolators are equipped with an integrated air-quality monitoring system that displays the pressure difference, the hours of use of the filter and blower and alarm thresholds. Monitoring of the internal environment—temperature and relative humidity in all isolators

and, where available, CO_2 concentration—detects conditions that may harm the patient, such as heat or CO_2 accumulation. Clinical monitoring of the patient—pulse oximetry, electrocardiogram, non-invasive blood pressure, respiratory rate and end-tidal CO_2, with an integrated defibrillator—detects clinical deterioration, including deterioration caused by a device failure [23]. With the isolators used by the RSP, a spare blower unit is always carried; it is not used in parallel and is connected only if the primary unit fails and negative pressure can no longer be maintained. The replacement, which consists of reconnecting the air hose to the spare unit, is performed during transport by the biocontainment technician through a rapid but precise sequence that must be planned and rehearsed for the specific device. This solution is not universal and depends on the characteristics of the isolator: some models, for example, have a built-in redundant blower, and the manufacturer's instructions apply in each case. During the switch containment is temporarily reduced, so the crew relies on PPE, and the patient is closely monitored, also because CO_2 accumulates rapidly inside the envelope when ventilation stops [34]. Alarm thresholds and response procedures should be defined in advance according to the manufacturer's specifications and applicable protocols. In the aeromedical setting, a standard isolation unit lost leak tightness after a simulated explosive cabin decompression because the envelope ruptured from over-expansion [35]. In ground ambulances, an Ebola infection in a driver in Sierra Leone was attributed to body fluids leaking from the patient compartment into the cab [36]; an assessment of 14 vehicles found that the wall separating the two compartments often lacked a waterproof seal, that bulk body fluids were not removed before disinfection and that pressure from chlorine sprayers may have pushed fluids into the cab [36]. In the United States, the patient compartment of the ambulance was stripped of non-essential items and lined with a continuous envelope of plastic sheeting, and the cab was sealed from the patient compartment [37]. Conversely, a negative-pressure containment pod with filtration installed in the patient module of an ambulance reduced aerosol concentrations in the workspace [38].

Portable isolation units with the clinical team outside the envelope, widely used during the COVID-19 pandemic, enable long-distance transport but limit access to the patient. In a series of 13 long-distance aeromedical transports of COVID-19 patients in a portable isolation unit, the main limitations were restricted access, reduced manual dexterity through porthole gloves and line disconnections during loading; one patient experienced endotracheal tube displacement [39]. Reduced dexterity when working through containment systems has also been documented experimentally [40]. The 2025 national exercise of the US Portable Biocontainment Unit showed that paediatric transport requires specific planning, as children reported anxiety related to noise, vibration, movement and the appearance of staff in PPE, as well as communication difficulties [41].

Beyond single-patient isolators, the framework includes multi-patient systems: modified minibuses or coaches with an internal envelope and one or more HEPA-filtered negative-pressure units, used to move groups of ambulatory patients who do not require vital support, and portable isolation chambers for intra-hospital settings without fixed isolation rooms. Collective transport of critically ill patients has also been performed by air: a risk analysis based on failure modes, effects and criticality analysis allowed six flights carrying 36 critically ill COVID-19 patients without reported harm to patients or staff [42]. Finally, interoperability between devices—through connecting sleeves and transfer ports—allows a patient to be moved from a transport isolator to a fixed isolation room without interrupting the containment chain; where transfer ports are not available, the isolator is introduced into the receiving room before the patient is transferred.

5. Personal Protective Equipment

PPE is the link of the containment chain that depends most directly on human performance. A Cochrane review of PPE for highly infectious diseases found low- to very-low-certainty evidence that covering more of the body improves protection, usually at the cost of more difficult donning and doffing and lower comfort; double gloving, following structured doffing guidance, spoken instructions during doffing and glove disinfection before removal may reduce contamination [43]. A series of rapid reviews, with certainty of evidence assessed using GRADE, informed the WHO infection prevention and control guideline for Ebola and Marburg disease [1,44]. Heat stress imposed by PPE in hot environments is itself a safety risk [45], and a literature review of physiological strain in HCID care identified heat strain and dehydration as an occupational health concern that can impair performance [46]. These data support the principle, adopted in the framework, that PPE selection must balance biological protection, chemical resistance to the selected decontaminant and ergonomic compatibility with the wearer's role [47,48].

Doffing is the most critical phase. In a simulation study, all health care workers wearing Ebola-level PPE made at least one protocol deviation during doffing, and some deviations were committed by the doffing assistants or trained observers themselves [49]. Using surrogate viruses, a structured doffing protocol supervised by a trained monitor protected against self-contamination with enveloped virus, while contamination with a non-enveloped surrogate persisted on inner gloves when alcohol-based hand rub was used for glove hygiene [50]. In a randomised trial, an intervention package combined with teamwork training significantly reduced self-contamination and improved teamwork scores [51]. Consensus documents have translated these findings into unified PPE ensembles and core principles applicable across protocols [47,48].

Several aspects are specific to transport. Prolonged transports require a prospective plan for PPE changes, because comfort decreases and the risk of inadvertent self-contamination increases over time [45,46]. Powered air-purifying respirators reduce speech intelligibility, mainly because of fan noise: in a pilot study only 67% of spoken words were correctly identified, and one model scored below the 70% benchmark used for respirator certification [52]. PPE impairs communication among staff, between staff and patients and between patients and their families, and closed-loop communication has been adopted to mitigate these barriers [53]; in the framework, laryngophones or in-ear radio systems are positioned so as not to interfere with the doffing sequence. In a randomised manikin trial, the quality of cardiopulmonary resuscitation was not affected by chemical–biological–radiological–nuclear PPE, whereas tourniquet application, decompression of tension pneumothorax and peripheral venous and intraosseous access took significantly longer [54]; reduced dexterity is a recognised limitation of both PPE and isolator glove ports [39,40]. For outer gloves, the framework distinguishes between operators who handle isolator zippers, for whom cut-resistant neoprene gloves are preferred, and clinicians who need tactile sensitivity, who use nitrile gloves; because the acceptable quality level of gloves is self-declared by manufacturers in Europe, it should be considered in procurement. Driver PPE must remain compatible with safe vehicle operation: sealed boots impair pedal control and fogging of eye protection reduces visual acuity, so individual fitting trials are recommended. For Andes virus, recommendations on respiratory protection changed during the 2026 outbreak—from medical masks to FFP2 or N95 respirators for passengers and crew—exposing the absence of clear guidance for outbreaks with person-to-person transmission [3,55].

6. Decontamination

In the framework, decontamination is a multi-stage process performed at defined time points—on departure from the point of origin, on arrival at the destination and on return to base—and subdivided into technical decontamination (chemical inactivation at a safe distance), remediation and physical cleaning. Disinfectant selection must consider both virucidal efficacy and compatibility with materials. Sodium hypochlorite is effective but corrosive; in a contact-kill assay against Ebola virus on aircraft-relevant materials, an aircraft cleaning product performed similarly to hypochlorite without its corrosive properties [56]. Standard operating procedures for disinfecting aircraft after a suspected highly infectious disease case have been defined [57], and an aerosol-based protocol has recently been proposed to reconcile antimicrobial efficacy with material compatibility in areas that are inaccessible to manual disinfection [58]. Laboratory evidence on hygiene and virucidal interventions has also been summarised for the two pathogens of the 2026 events, Bundibugyo virus and Andes virus [59].

Volumetric methods complement surface disinfection. Hydrogen peroxide vapour was used for the terminal decontamination of the isolators and rooms of a UK HLIU after an Ebola case and allowed the unit to return to service more quickly than formaldehyde [60]. For a portable isolation unit, fumigation with hydrogen peroxide achieved complete inactivation of biological indicators but only limited inactivation of a viral surrogate suspended in organic liquids, which led to a combined protocol of fumigation, surface wiping and a second fumigation [61]. These findings, together with the observation that high-pressure spraying of chlorine in an ambulance whose bulk fluids had not been removed may have spread contamination [36], support the sequence used in the framework, in which gross contamination is removed at low pressure before volumetric and surface decontamination. In Europe, protocols for the disinfection of ambulances and equipment were available in about 70% of isolation centres in 2009 [24]. The framework includes the preferred organisational model of a decontamination unit with unidirectional personnel flow, negative pressure, doffing stations and waste collection, and the minimum requirement of an improvised station with contained waste collection under field conditions.

Finally, the framework proposes monitoring of decontaminant consumption per transport as an exploratory process indicator: a sudden reduction in consumption at constant activity should prompt a procedural review by the coordinator, because it may signal the omission of decontamination steps. In practice, each mission starts with a standard supply of decontaminant and an additional reserve, so that the amount used can be estimated on return. Consumption may, however, also vary for reasons unrelated to compliance, such as the type of vehicle and device, the duration and nature of the mission, the procedures performed and the degree of soiling. The indicator should therefore be interpreted together with standardised documentation of these factors and, where feasible, compared with direct audits of critical decontamination steps. This indicator derives from the authors' operational experience and has not been formally validated as a measure of adherence.

7. Operational Workflow

Reviews of aeromedical HLCT have organised best practices into pre-flight, in-flight and post-flight phases [20,21], and similar structures are described for ground transport by emergency medical services (EMS), whose experience in the United States emphasised ambulance preparation, PPE selection and environmental decontamination [37]. National and regional systems have formalised these elements in concepts of operations [62], dedicated transport teams [63], combined land–air evacuation pathways [64], military aeromedical capabilities [65–67] and guidance from public health agencies [68–70]. In Italy, it has been recommended that HCID transports be performed by specialised teams linked to

HLIUs rather than by routine EMS ambulances, using vehicles with controlled ventilation, negative pressure, HEPA filtration, intercom systems and separation of the driver from the patient, and combining domestic aeromedical flights with special ambulances over long distances; PPE alone is not sufficient without extensive training and dedicated areas for ambulance decontamination [71]. Since 2005 the Italian Air Force has maintained a rapid-response aeromedical isolation team at Pratica di Mare, using aircraft transit isolators and staffed by teams of at least three physicians (team leader, infectious disease specialist and anaesthesiologist) and six nurses, in formal collaboration with the Spallanzani Institute [66]; its first operational flight, in 2006, transported a patient with multidrug-resistant tuberculosis [65,67]. Comparisons of guidelines in Western countries [72] and European surveys [22,24] show considerable variability in equipment, staffing and procedures.

The framework structures each mission into seven sequential phases: pre-alert/alert, materials preparation, initial briefing, transport, decontamination, materials restoration and debriefing. During pre-alert, the coordinator collects structured information on the patient (weight, mobility, confirmed or suspected diagnosis, current vital support, monitoring needs and clinical complexity) and on logistics (origin and destination, access routes, vertical mobility constraints and manoeuvring space for the isolator). Materials preparation includes isolator assembly and a pre-transport checklist covering the integrity of the envelope and zipper, the closure of access ports and cable glands, the integrity of glove ports, the installation and locking of the HEPA filter, the battery charge and the negative-pressure function. In the RSP protocol, negative pressure is measured at three points (head, centre and feet) with a differential manometer and compared with the device reference value: a progressive decline over successive transports suggests filter saturation, whereas an abrupt decline suggests an acute structural or mechanical failure. The air-quality data described above [34] support including ventilation and blower function in this check.

The initial briefing consolidates information among team members and external agencies. Transport execution comprises patient preparation, loading, monitoring during transport and handover at destination, with specific adaptations for mechanical ventilation and multiple infusions. An operational debriefing involving all team members is held at the end of each mission or transport to review clinical, logistical and communication aspects and to identify improvements [25]; it is distinct from psychological support (Section 10).

Large-scale operations add a coordination dimension. During the first COVID-19 wave, a regional medical evacuation operation in Lombardy transferred 121 intensive care patients, mostly by air, to other Italian regions and to Germany, with outcomes comparable to those of patients who remained in regional intensive care units and one life-threatening event during transport [73]. Aeromedical evacuation to the Spallanzani Institute in Rome was used for patients with COVID-19 and complex coinfections [74]. A global tabletop exercise on long-range air transport of patients with viral haemorrhagic fever found that many countries rely on the same organisations for this capability, which may become a bottleneck when several countries request evacuation simultaneously [75]. A review of EMS in the United States identified non-standardised licencing, inconsistent medical direction and difficulties in implementing PPE as vulnerabilities to HCIDs [76].

8. Complexity Stratification and Team Composition

During the COVID-19 pandemic, the heterogeneity of patients—from ambulatory, mildly symptomatic individuals to mechanically ventilated patients—required a scalable approach to device selection and staffing. The framework uses a classification algorithm based on parameters that can be assessed quickly by the coordinator: risk group of the pathogen, the patient's ability to walk, the need for monitoring, for non-invasive or invasive respiratory support and for infusion pumps, and the type and expected duration of the

transfer (intra-hospital, extra-hospital or aeromedical). Three complexity levels are defined (Table 1). The classification measures the overall complexity of the mission—clinical needs, devices to be managed inside the containment system, biological risk and logistics—rather than the clinical severity of the patient alone [23,25]. The parameters are combined hierarchically rather than summed: the level is determined by the most demanding criterion present; patients infected with risk group 4 pathogens are therefore assigned to the high-complexity level irrespective of their clinical status, because of the biosafety requirements of the mission; and, when information is incomplete or uncertain, the worst plausible scenario is assumed and the higher level is assigned [25]. Clinical instability or an expected deterioration during transport lead to the next level. Transport duration—short (within the same hospital), medium (less than one hour) or long (more than one hour)—does not change the level by itself but determines patient preparation, such as sedation, urinary catheterisation, preventive airway management or the application of defibrillator pads [23]; the use of the optimal rather than the minimum team for long transports is an operational criterion proposed by the authors and has not been specifically validated. The minimum configurations in Table 1 reflect the space available in a biocontainment ambulance and, for medium- and high-complexity transports, ensure one person for each essential function—driving, isolator management and clinical care; the optimal configuration adds a second clinician (an anaesthesiologist or intensive care physician together with a nurse) when the patient requires mechanical ventilation or multiple infusions or is haemodynamically unstable, when procedures inside the envelope may be needed, or when the transport is long. The integration of an early warning score such as the National Early Warning Score 2 (NEWS2) has been proposed to make the assessment of clinical risk more objective [25]. This classification was derived from a retrospective analysis of RSP transports and refined through structured post-mission briefings [25]; it is a proposed operational framework and has not been prospectively validated against clinical outcomes.

Table 1. Transport complexity classification, clinical characteristics, recommended device and team composition (proposed operational framework adapted from [25], not yet prospectively validated).

Complexity	Clinical Characteristics	Device	Team Composition
Low	Patient able to walk independently; no life support; no monitoring	Stretcher isolator or biocontainment minibus	Minimum 2 (driver, operator); optimal 3 (dedicated driver, 2 operators); minibus: 2 operators, one of whom drives
Medium	Sub-intensive care: continuous monitoring, non-invasive respiratory support (HFNC or NIV) or infusion pumps; not intubated	Stretcher isolator on ambulance	Minimum 3 (driver, operator, nurse); optimal 4 (driver, operator, nurse, physician)
High	Critically ill patient: endotracheal tube or SGA with mechanical ventilation, multiple life-support measures, continuous or invasive monitoring; any patient infected with a risk group 4 pathogen	Stretcher isolator on dedicated biocontainment ambulance	Minimum 3 (driver, operator, physician); optimal 4 (driver, operator, anaesthesiologist or intensive care physician, nurse)

HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; SGA, supraglottic airway.

High-complexity transports are supported by a growing clinical literature. Invasive organ support has been provided within isolator tents in a UK HLIU without additional risk to staff [77]. For hantavirus cardiopulmonary syndrome, for which no cure exists, extracorporeal membrane oxygenation (ECMO) has improved survival and early recognition is essential during critical care transport [5]; prone positioning has been used during transfer

as a bridge to ECMO [78], and imported Andes virus infection in Europe required prolonged ECMO together with infection control measures for persistent viral shedding [79]. For aeromedical evacuation, patients should be stabilised before departure, and procedures that may be needed in flight—such as intubation and the placement of intravenous lines and urinary catheters—should preferably be performed in the departure hospital, also because of hypoxia and gas expansion at altitude [66]. Reports of tube displacement and line disconnection in portable isolation units [39] and the use of formal risk analysis for collective transport [42] indicate that high-complexity transports require dedicated critical care staff and pre-planned procedures for airway and vascular access management inside the envelope.

The type of transfer further modulates complexity. Intra-hospital transfers focus on maintaining clean pathways. Extra-hospital transfers introduce requirements that increase with distance—from transfers within the area of the originating facility to inter-provincial or inter-regional transfers—concerning reserve PPE, en-route decontamination capacity and planned stops. Aeromedical transfers add requirements related to cabin pressure, gas expansion within devices [35] and aviation certification.

9. Governance, Networks and Competency Maintenance

The framework assigns accountability for each operational domain through a responsibility matrix rather than a purely hierarchical structure (Table 2). Five functional roles are identified: biocontainment technician (device logistics and decontamination), team leader (operational coordination and quality supervision within the vehicle), coordinator (overall transport management and resource planning, external to direct intervention), physician (clinical decision-making) and nurse (clinical patient management in support of, or in the absence of, the physician). The clinical component is activated according to the complexity level. Responsibilities are distinguished by function: the biocontainment technician, who may also act as team leader, is responsible for the physical movement of the patient and of the isolator and for containment; the physician (or, in the absence of a physician, the nurse) for clinical care; and the team leader for coordination within the vehicle, while the coordinator manages communication with the sending and receiving facilities and any change in destination [25]. Because the relevant clinical information is usually shared between the sending facility, the transport team and the receiving facility before the transfer, during the pre-alert phase, and then updated as the mission proceeds, handover at destination is the final step of a continuous exchange: clinical responsibility passes to the receiving team once the physician or nurse has handed over the updated information. If the patient deteriorates during transport, the decision on the clinical intervention—what is needed and how urgently—rests with the responsible health professional (the physician or, in the absence of a physician, the nurse, within the limits of their competence and applicable regulations), whereas the biocontainment technician is responsible for the containment measures needed to deliver it safely and the team leader coordinates the response. Protecting the safety of the crew and ensuring the safe transport of the patient are equally essential. For this reason, planning deliberately overestimates clinical risk: when deterioration is anticipated or invasive procedures may become necessary, they are performed before departure—airway management, vascular access and application of defibrillator pads—and the equipment that might be needed is placed inside the isolator in advance, because manoeuvres performed through the envelope are difficult and carry a higher risk of complications for both patient and crew [23]. If an urgent intervention nonetheless becomes necessary during transport, it is not withheld for reasons of containment. Because all crew members wear the PPE required for the pathogen even when the patient is transported in an isolator, the isolator can be opened if the patient's condition requires it: the clinical decision remains with the

responsible health professional, while the interruption of containment is carried out in coordination with the biocontainment technician. Once the isolator is opened, the crew is exposed but still protected by PPE, which becomes the remaining barrier; the clinical need is therefore weighed against the loss of one level of protection, and on return the vehicle, equipment and personnel require enhanced decontamination.

Table 2. Responsibility matrix for biocontainment transport team roles across operational domains.

Role	Pre-Transport Health Assessment	Logistical Assessment	Patient Transfer	Decontamination	Clinical Management During Transport	Technical Isolator Management
Biocontainment technician	CC	E	E	E		E
Team leader	CC	C	C	CC	C	CC
Coordinator	CC	E	V	V		
Physician	E	CC	CC	CC	E	CC
Nurse	CC/E *	CC	CC	CC	CC/E *	CC

E, executes; V, verifies; C, coordinates; CC, collaborates; empty cell, not involved. * The nurse executes the pre-transport clinical assessment and clinical management in the absence of a physician, within the limits of their competence. During patient transfer, the biocontainment technician executes the physical movement of the patient and of the isolator, while the physician and the nurse remain responsible for clinical management. When one person covers more than one role (e.g., a biocontainment technician acting as team leader), the responsibilities of both roles apply. Communication with the sending and receiving facilities and the coordination of handover rest with the coordinator.

Comparable governance tools have been described in fixed facilities: the incident command system has been adapted to the activation of hospital biocontainment units [80], and HLIU frameworks developed by European consensus define organisational and infection control requirements [2,81]. At the system level, the US National Special Pathogen System of Care stratifies facilities by capability [82], the German STAKOB network links public health competence centres and treatment centres [83], and global analyses have mapped HLIU capabilities and gaps [84,85]. In Italy, the Spallanzani Institute has described its response model for viral haemorrhagic fevers [86], and new biocontainment capacity has been developed at the regional level [87]. Transport services need to be integrated into these networks, with shared protocols for handover and for compatible devices [62,63].

Competency maintenance is a continuing governance responsibility, particularly for teams with low operational frequency, in whom procedural drift—the progressive, unconscious omission of critical steps—may occur. A 12-year analysis in an HCID hospital found a bimodal pattern of occupational exposure, with the highest exposure density among staff with less than two years of experience and a renewed increase among staff with more than ten years, which the authors linked to complacency and burnout [88]. Among US critical care air transport clinicians, those without recent operational experience were no more likely to pass revalidation than first-time students [89]. Readiness checklists used during periods of inactivity identified staffing and waste management as the greatest threats to activation [90], and staffing and just-in-time training remain common challenges across HLIUs [91]. Interventions supported by the literature include simulation-based mastery learning for PPE [92], safety officers who monitor staff safety during care and transport [93], supervision of PPE practices with real-time feedback [94], buddy systems with frequent training [95] and the explicit adoption of high-reliability principles [96]. Scheduled full-scale exercises with complete PPE and representative isolators are therefore the primary

mitigation strategy in the framework, complemented by exploratory process indicators such as decontaminant consumption (Section 6).

10. Human Factors: Patient and Operator Dimensions

For conscious patients, the transport isolator imposes physical confinement, a muffled acoustic environment and reduced physical contact with caregivers. Patients treated for Ebola in a biocontainment unit described feelings of lack of control, social and emotional isolation and loneliness, to which staff PPE contributed [97]. Children in the US Portable Biocontainment Unit reported anxiety related to noise, vibration and the appearance of staff in PPE, and communication difficulties were common [41]. During aeromedical evacuation in an aircraft transit isolator, the predicted incidence of motion sickness was about 2% for a 6 h flight, supporting individual rather than routine prophylaxis [98]. Confinement within the isolator is itself recognised as a psychological stressor during aeromedical evacuation [66]. Telemedicine platforms have been developed to support communication with isolated patients [99]. In the framework, a clear pre-transport explanation of the device and of each phase is the primary non-pharmacological intervention; synchronised team behaviour and calm, professional communication reassure the patient, and light procedural sedation may be considered by the physician when these measures are insufficient.

For staff, systematic reviews and meta-analyses consistently show a psychological burden among health care workers involved in epidemic and pandemic responses. Compared with lower-risk colleagues, staff in direct contact with affected patients had higher odds of acute or post-traumatic stress and psychological distress [100]; frequent symptoms included concern about transmitting infection to family members, perceived stress, sleep difficulties and burnout [101]. Workers in a US biocontainment unit reported isolation, changes in home life and episodes of discrimination, and many used behavioural health counselling [102]. Psychological stress was also reported among health care professionals caring for Ebola patients in Europe [103]; the experience of Red Cross nurses deployed to an Ebola treatment centre highlighted the need for preparation and support before, during and after deployment [104]; psychological stress was also described among EMS providers, whose perceived danger decreased with adequate education and transparent communication from their organisation [105]. During the 2026 Bundibugyo virus disease response, a minimum package of mental health and psychosocial support has been proposed, spanning preparation before deployment, protection and support during the response, confidential follow-up afterwards and continuous learning, and including psychological first aid, peer support, supportive supervision and referral pathways; robust comparative evidence of effectiveness, however, remains scarce [106].

Evidence on interventions remains limited. A Cochrane mixed-methods review of interventions to support the resilience and mental health of frontline workers found limited evidence on the effectiveness of such interventions [107], and a systematic review of early interventions identified psychological first aid, eye movement desensitisation and reprocessing, and trauma risk management as the approaches with the most consistent support [108]. The framework distinguishes operational review from psychological support. The operational debriefing held after each mission reviews performance and procedures and is not a psychological intervention (Section 7). Individual psychological support is offered on a voluntary and confidential basis to any team member who requests it and is provided by psychologists of the CRI psychosocial service, who can refer staff for clinical assessment when indicated. In addition, group discussion sessions open to all personnel involved in transports are held periodically, on a voluntary basis, moderated by a psychologist. None of these activities is intended as a structured psychological intervention for the prevention of post-traumatic stress disorder. Coordinators and team leaders share responsibility for

recognising early signs of stress. These elements are derived from field experience and require formal evaluation with validated instruments.

11. The Integrated Operational Framework

Table 3 summarises the framework by domain, together with the main supporting evidence and the level of evidence on which each component rests. The framework combines four elements: the four-link containment chain; the seven-phase operational workflow with its pre-transport checklist; the three-tier complexity classification that links patient characteristics to devices and team composition; and the responsibility matrix that defines accountability across domains. Human factors and competency maintenance are treated as structural components rather than ancillary considerations. Most components rest on regulatory requirements, technical evaluations and expert consensus; only a few are supported by comparative studies.

Table 3. Integrated operational framework: components, supporting evidence and level of evidence.

Domain	Framework Component	Main Supporting Evidence	Level of Evidence
Biosafety and containment chain	Four-link containment chain (PPE, envelope, negative pressure with HEPA filtration, decontamination)	Risk group classification [27,28]; transmission routes [30,31]; EUNID consensus [2]	Regulatory standards; expert consensus
Devices	Isolator requirements; pre-transport verification of negative pressure, filter, blower and battery; interoperability	National requirements [32]; isolator containment [15]; air quality [34]; decompression [35]; ambulance compartment [36,38]; portable units [39,41]	Regulatory standards; technical evaluations; case reports
PPE	Role-specific PPE; supervised doffing; planned PPE changes; communication aids	Cochrane review [43]; WHO evidence synthesis [44]; doffing studies [49–51]; heat strain [45,46]; communication [52,53]	Systematic reviews (low certainty); simulation studies
Decontamination	Three time points; sequence of gross removal, volumetric and surface decontamination; exploratory consumption indicator	Disinfectant efficacy [56,59]; aircraft [57,58]; hydrogen peroxide vapour [60,61]	Laboratory and technical studies; indicator based on expert consensus
Operational workflow	Seven phases; structured pre-alert; checklist; debriefing	Aeromedical reviews [20,21]; EMS experience [37]; concepts of operations [62,63]	Reviews of case reports; expert consensus
Complexity and team	Three-tier classification linking patient status to device and team	Critical care in isolators [77]; HCPS transport [5,78,79]; risk analysis [42]	Case reports; expert consensus (not validated)
Governance and competency	Responsibility matrix; coordinator role; exercises; readiness monitoring	Incident command [80]; networks [82,83]; experience and revalidation [88,89]; readiness [90]; training [51,92]	Observational studies; expert consensus
Human factors	Pre-transport communication; operational debriefing; voluntary psychological support and periodic group sessions; referral pathways	Patient experience [41,97]; staff burden [100–102]; interventions [107,108]	Systematic reviews; qualitative studies; expert consensus

EUNID, European Network for Infectious Diseases; HCPS, hantavirus cardiopulmonary syndrome; HEPA, high-efficiency particulate air; PPE, personal protective equipment.

12. Discussion

This review shows that the literature on biocontainment transport is fragmented and largely descriptive. Aeromedical evacuation is better documented than ground transport, and evidence on devices, PPE and decontamination comes mainly from technical evaluations and simulation studies, while governance and human factors are addressed mostly by qualitative studies and expert consensus. The contribution of the proposed framework lies not in new devices or techniques but in the explicit integration of these domains, which may help emergency medical systems to plan, train and audit HCID transport. Its novelty is therefore modest, and its value should be judged by its usefulness as a structured reference rather than as evidence of effectiveness.

The 2026 events illustrate why each domain matters. A systematic review of health care-associated Andes virus exposures found that infections among health care personnel occurred when transmission-based precautions were delayed or breached, with none or inadequate PPE in the reports describing such infections [109]; household and nosocomial transmission had already been documented in Chile [110]. During the 2026 outbreak, a health care worker not directly involved in patient care had a transient low-positive PCR result without seroconversion, which the authors interpreted as possible asymptomatic infection with low-level viraemia after indirect exposure; this interpretation remains uncertain [111]. In Spain, the response relied on the network of high-level isolation and treatment units built after the 2014 Ebola epidemic [112]; in Italy, regional public health services implemented rapid surveillance of high-risk contacts [113]; and reports from the multinational response described challenges for prehospital care, health care facilities and public health systems [114]. A rapid assessment by the European Society of Clinical Microbiology and Infectious Diseases recommended standard and contact precautions for health care workers caring for suspected cases, noting that airborne precautions with N95 or FFP2 respirators would have been reasonable, and highlighted that, in maritime settings, the land-based location of advanced critical care leaves a narrow window within which a critically ill patient can be transferred safely [115]. Earlier reports of nosocomial Crimean–Congo haemorrhagic fever after aeromedical evacuation [116] and of Lassa fever without transmission to health care workers under standard precautions [117] show that the risk depends strongly on clinical procedures and on the consistent application of precautions. Overall, respiratory protection, including N95 or FFP2 respirators, may be justified for Andes virus as a precautionary measure in specific circumstances, such as close contact and aerosol-generating procedures; such recommendations should, however, be distinguished from the claim that airborne transmission has been definitively established, which the available evidence does not currently support.

During the COVID-19 programme of the RSP, personnel involved in biocontainment transport were included in an occupational health surveillance programme. Within this framework, no documented occupational infections attributable to biocontainment transport, and no confirmed patient-to-staff transmission events during transport, were identified. This observation is reported only as operational context and should not be interpreted as an estimate of risk: surveillance was not designed as a study, the number of exposed staff and the sensitivity of surveillance for asymptomatic infection were not formally assessed, the period largely coincided with the vaccination of health care workers against SARS-CoV-2, and SARS-CoV-2 is a risk group 3 pathogen, so the observation cannot be extrapolated to risk group 4 agents. Structured symptom-monitoring tools for staff, such as those developed for biocontainment units [118], could support a prospective assessment.

The framework may be transferable to other settings, including systems with limited resources, where the classification algorithm and responsibility matrix could help to allocate scarce biocontainment assets, and, potentially, to other high-risk transport scenarios,

such as chemical or radiological emergencies. These scenarios, however, involve hazards, contamination mechanisms, protective equipment and decontamination procedures that differ substantially from those of infectious diseases; at most, the organisational elements of the framework—the containment-chain logic, the phased workflow and clear team governance—might be applicable, and only after specific adaptations. Its transferability has not been tested.

This review has limitations. As a narrative review, it is exposed to selection bias despite the structured search, and the synthesis is qualitative; screening was performed by a single author, supported by an AI-assisted preliminary classification, rather than by two independent reviewers. Only two databases and two languages were searched, and part of the relevant experience is reported in grey literature or not published. Many sources are case reports, simulation studies or expert opinion, so the certainty of the evidence is generally low. The operational components derive from a single service, the RSP, and some elements—particularly the coordinator role—may require adaptation to other institutional settings. The psychological content has not been assessed with validated instruments. Finally, the framework has not been prospectively validated.

Future work should include a prospective study of the RSP transport dataset, with ethical approval and appropriate statistical analysis, to describe activity, complexity and adverse events; validation of the complexity classification against clinical outcomes; evaluation of decontamination adherence and of the decontaminant-consumption indicator; and assessment of the psychological impact on transport staff with validated instruments, such as the Impact of Event Scale-Revised or the Maslach Burnout Inventory.

13. Conclusions

The transport of HCID patients is a critical and still poorly evidenced interface between biosafety and emergency medicine. The available literature supports attention to device integrity and air quality, safe doffing and the physiological limits of PPE, validated decontamination, the maintenance of team readiness and the psychological needs of patients and staff. The integrated framework proposed here—containment chain, operational workflow, complexity classification and responsibility matrix—organises these elements into a structured reference for emergency medical systems. Because it rests mainly on technical evidence and expert consensus, its components should be evaluated prospectively.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ecm3040036/s1, Table S1: Search strategies; Figure S1: Flow of record identification, screening and selection; Table S2: Self-assessment by the authors according to the Scale for the Assessment of Narrative Review Articles (SANRA). Reference [26] is cited in the Supplementary Materials.

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Abbreviations

The following abbreviations are used in this manuscript:

BSL	Biosafety level
CDC	Centers for Disease Control and Prevention
CRI	Italian Red Cross (Croce Rossa Italiana)
ECDC	European Centre for Disease Prevention and Control
ECMO	Extracorporeal membrane oxygenation
EMS	Emergency medical services
EUNID	European Network for Infectious Diseases
FFP2	Filtering face piece class 2
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HCID	High-consequence infectious disease
HCPS	Hantavirus cardiopulmonary syndrome
HEPA	High-efficiency particulate air
HFNC	High-flow nasal cannula
HLCT	High-level containment transport
HLIU	High-level isolation unit
NETEC	National Emerging Special Pathogens Training and Education Center
NEWS2	National Early Warning Score 2
NIV	Non-invasive ventilation
PCR	Polymerase chain reaction
PPE	Personal protective equipment
RSP	Public Health Unit of the Italian Red Cross (Reparto di Sanità Pubblica)
SANRA	Scale for the Assessment of Narrative Review Articles
SGA	Supraglottic airway
STAKOB	Permanent Working Group of Competence and Treatment Centres for High-Consequence Infectious Diseases (Ständiger Arbeitskreis der Kompetenz- und Behandlungszentren)
WHO	World Health Organization

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