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An Updated Review of Literature for Aeromedical Evacuation High-Level Containment Transport during the COVID-19 Pandemic

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Introduction

The treatment and handling of patients with highly hazardous communicable diseases (HHCDs) takes a great deal of coordination and attention to detail, which is amplified during an Air Medical Evacuation (AE). The combination of these two tasks can drastically increase the risk of infection to healthcare and transport workers, as well as potentially endanger the departure and receiving communities. While there are myriad reasons in which an AE high-level containment transport (AE-HLCT) would be required to take place (e.g., military or governmental request, distance to a facility with high-level isolation capabilities, challenges to ground transport), it must always be done with the utmost attention to detail and the best available policies and procedures.

In 2019, our team published a commentary calling for guidelines and greater global cooperation surrounding the policies and procedures associated with AE-HLCT.[1] We believed then as we do now that the best way to ensure the safety of all personnel and communities involved in transporting patients with HHCDs is through open communication regarding the success and failures of these events, working toward the development of standards and consensus guidelines with safety for all (patient, workers, and community) at the forefront. Later that same year, we also published a review of the peer-reviewed literature associated with AE-HLCT[2] which showed a dearth of research within the field and limited case-study publications. The intention was to combine the publicly available information into a single source for utilization by the AE community to establish best practices, and for scholars to expand upon to push the field of AE-HLCT forward.

Since that publication, the COVID-19 pandemic has resulted in numerous AE of patients with COVID-19, including mass evacuation of passengers of the Diamond Princess cruise ship, some of whom tested positive before transport.[3] Although COVID-19 is no longer considered a HHCD, there is no doubt that early in the pandemic, when few cases were confirmed in the US and information was evolving quickly, it was initially treated as an HHCD, particularly around early ground transports and AE.[4] As a result of these transports, we felt it was important to re-examine the new literature associated with AE of HHCDs to determine what new innovations may have developed as a result of the COVID-19 pandemic and the increased number of AE-HLCTs that were conducted.

Methods

A literature review[5] was performed utilizing PubMed/MEDLINE and Google Scholar with a date range of February 2019 through October 2021. The search took place November 2021. This date range was selected so as not to capture papers from our previous literature search,[2] but to focus on the innovations that have taken place since and new best-practices that have been published. The search terms utilized were: 1) "aeromedical isolation," 2) "aeromedical evacuation" OR "transportation of patients" OR "air ambulance" OR "HEMS" OR "Helicopter" AND "ebola" OR "lassa" OR "viral hemorrhagic" OR "highly infectious" OR "highly hazardous" OR "high-consequence infectious disease" OR "contagious" OR "communicable" OR "Middle East respiratory syndrome (MERS)" OR "SARS" OR "smallpox" OR "VHF" OR "Crimean-Congo Hemorrhagic Fever," 3) "aeromedical evacuation" AND "transportation of patients" AND "SARS-CoV-2" OR "COVID-19" OR "2019-nCoV" OR "Wuhan virus" 4) "mobile" OR "transport" AND "isolation" OR "containment" AND "patient" AND "ebola" OR "lassa" OR "viral hemorrhagic" OR "highly infectious" OR "highly hazardous" OR "high-consequence infectious disease" OR "contagious" OR "communicable" OR "Middle East respiratory syndrome (MERS)" OR "SARS" OR "smallpox" OR "VHF" OR "Crimean-Congo Hemorrhagic Fever". Authors selected articles published in 2019 or later years and screened abstracts for the following criteria: peer-reviewed literature, written in English, and described air medical evacuation high-level containment transport of persons with COVID-19 or HHCDs (Figure 1).

Results and Discussion

Our methodology identified 19 publications meeting the inclusion criteria (Figure 1, Table 1). As with our previous paper[2], we broke down the synthesis into the 'preflight', 'in-flight', and 'postflight' environments. This was done to allow for an easier comparison between the two papers and for practitioners to utilize both papers in a similar fashion.

As expected, many of the early transports of patients with COVID-19 used established protocols for HHCD, which were built from the most recent transports of patients with Ebola virus disease (EVD). Early in the pandemic when SARS-CoV-2 was a novel pathogen and the world knew very little about it, following the established AE protocols for patients with HHCD was proper; however, as the pandemic expanded and more information on SARS-CoV-2 was established (e.g., its transmission route, severity of disease), protocols were naturally adjusted. In this paper, we focus on new innovations implemented and described in the literature that were not previously discussed in our other work.[1,2]

a. Preflight

a. Types of Diseases and Transports

Articles published since 2019 primarily focused on COVID-19: three articles (all published pre-pandemic) exclusively focused on EVD transport,[6-8] three discussed AE of both COVID-19 and other HHCDs,[9-11] and thirteen focused solely on COVID-19 transport.[12-24] This represents an increased focus on respiratory pathogens since our previous review. This is understandable, as EVD and other viral hemorrhagic fevers –which are transmitted primarily via contact or droplets – had been the previous driver of AE-HLCT; however, even in the early days of the COVID-19 pandemic before studies confirmed it to be true, there was concern that the virus was potentially airborne.[25,26]

As a novel disease, published guidelines and recommendations on the safe AE transport of patients with suspected or confirmed COVID-19 were lacking, leading many organizations to refer to approaches and experience from AE-HLCT (e.g., EVD).[9,24] In the authors' awareness, the first air transport of persons with known SARS-CoV-2 infection occurred on Feb 17, 2020, when evacuees from the cruise ship Diamond Princess were flown from Japan to the US.[3] The reader should keep in mind that at the time, experts had limited understanding of COVID-19's mechanisms of transmission, propensity for asymptomatic transmission, infection fatality rate, and sequelae of infection. While engineering and administrative controls and personal protective equipment (PPE) were able to mitigate risk to flight medical team members, more limited measures were available to reduce risk to other passengers, and the ability to provide more than basic first aid care was severely restricted.[3] As the COVID-19 pandemic expanded, the rapid surge in the need for AE transports of patients with COVID-19 resulted in programs around the world conducting AE and attempting to implement strict infection prevention and control (IPC) measures.

Although not reflected in the literature, the increased operations tempo of AE-HLCT at the beginning of the COVID-19 pandemic likely resulted in many organizations conducting AE-HLCT that had never done such a transport and likely did not have significant pre-planning for such operations. This is further exacerbated by the complexities of moving more than one patient when many of the examples they had to draw from were for single AE-HLCT. Standardized and available procedures from previous AE-HLCT experience would likely have been very beneficial to those who found themselves needing to conduct an AE-HLCT for the first time; however, there was – and remains – a lack of publicly available AE-HLCT guidelines or recommendations.[1]

As noted, the COVID-19 pandemic created the challenge of moving multiple patients in a single transport; prior to the COVID-19 pandemic, most articles describing AE-HLCT focused on single patient transports,[2] with a few exceptions of multi-patient/containerized models for transport such as the Transport Isolation System or Containerized Biocontainment Care System.[27,28] As AE needs during the early months of the COVID-19 pandemic quickly surpassed the availability of single units, several articles describe the collective evacuation of multiple patients, including groups with high-risk exposures[13] or AE-HLCT of multiple critically ill patients to neighboring countries or regions to alleviate shortages (e.g., ventilators, intensive care beds, healthcare worker shortages) in regions with hospitals stretched beyond capacity.[19,22]

b. Decision-making Process

Early in the COVID-19 pandemic, when knowledge and information on SARS-CoV-2 transmission or severity was lacking, AE programs had to make decisions on how to safely provide care while protecting their teams. This included the decision on whether to provide transportation for patients with suspected or confirmed COVID-19 at all, how to protect their crews given supply chain shortages of critical PPE components, and what IPC measures needed to be put in place for any transport, regardless of a patient's COVID-19 status, given the potential that any patient could have an asymptomatic infection.

Three articles published decision-making frameworks for AE of patients with COVID-19.[10,14,16] Bredmose et al. detailed a decision support tool for development of guidelines for helicopter transport, while Hilbert-Carius et al. included decision trees used by several organizations to evaluate the safe transfer of a COVID-19 mission. Martin posited five overarching questions for programs to consider in justifying transport decisions and then prove they have the highly skilled personnel and appropriate equipment to be considered competent for such high-risk transports. Questions included suitability of the aircraft for special transport, critical care capabilities in-flight, patient isolation capabilities, communication strategies, and willingness of employees to undertake such missions; if answers caused doubts or concerns, the clear decision is the program could not safely undertake COVID-19 transports.[10] These were important frameworks for these organizations to share with their peers confronting similar questions at that time, and such frameworks have an important role in the future of AE-HLCT.

Albrecht et al. published a table (as of April 5, 2020) with transport concepts for patients with COVID-19 in several European countries, including for helicopter emergency medical services (HEMS) and fixed-wing aircraft.[9] Due to the many unknowns, most European countries early in the pandemic preferred ground-based transportation of confirmed cases. Only air rescue providers in Germany, Netherlands, Switzerland, Norway, and Italy were intentionally operating transports of patients with COVID-19 in helicopters and only Switzerland was conducting fixed-wing transports in Europe at that time[9] (in the US, the Department of Defense's Transport Isolation System was first used on April 8, 2020 for COVID-19 patient movement on a fixed wing aircraft[21]).

In a May 2020 survey to HEMS providers, 85% of HEMS organizations would transport patients with suspected or confirmed COVID-19; of the 15% that would not, 70% felt they did not have the ability to adequately protect their pilots from infection, 50% listed increased downtime due to decontamination as an issue, and 20% noted they did not have adequate supply of PPE to safely provide care.[12] Similarly, another survey conducted between May to August 2020 of the American College of Emergency Physicians Air Medical Section found that 89% of respondents would transport patients infected with COVID-19.[20] HEMS AE-HLCT is an important component of AE-HLCT that is underexplored in the literature, as much of the previous focus of AE-HLCT has been for long-distance transports from countries where a HHCD exposure or infection occurs to a higher-resource isolation unit outside of the region. However, HEMS AE-HLCT deserves greater consideration; although it may add additional complexities, the benefits bridging the gap between ground transport and fixed-wing transport are clear. Air transport via HEMS is considered the preferred mode of transport for patients with time-critical conditions, due to the ability to provide medical interventions en route and better post-transfer survival rates.[16] Particularly during the pandemic, HEMS AE-HLCT allowed for more localized, shorter distance transports.

Prior to the pandemic, AE-HLCT was focused on patients with high-risk exposures to or confirmed infection with a HHCD and had dedicated transport groups for that level of care. The pandemic changed this paradigm; any patient, regardless of reason for AE, had the potential to be pre-symptomatic or asymptomatic with COVID-19. This emphasized the need for preventative protection of all crew involved in AEs during the pandemic and the importance of having a risk averse approach at that time.[10] Indeed, even HEMS programs in the US that did not plan to take COVID-19 positive patients protected crew with PPE in case of an asymptomatic patient.[12] Several manuscripts emphasized the importance of this prevention to ensure service continuity,[10,12,14] since unprotected exposure to a patient with COVID-19 early in the pandemic could lead to weeks of quarantine that could impact staffing and create shortages of personnel to sustain operations. Martin advocated for a risk averse approach to standard healthcare guidelines when AE-specific guidelines were lacking, citing the more confined, challenging, and high-risk environments of AE environments compared to conventional hospital settings.[10]

c. Rotary-Wing and Fixed-Wing Aircraft

Several COVID-19-related articles describe COVID-19 transports in rotary-wing aircraft[9,12,14,20,24]; this is a contrast to most of the articles reviewed in the first literature review[2] where fixed-wing aircraft were more commonly utilized for AE-HLCT. This difference is likely due to the widespread community transmission of COVID-19 in Europe and North America and the need for shorter distance transports, compared to the more contained nature of previous HHCD outbreaks in those areas and the focus of AE-HLCT from the region of HHCD exposure or infection to specialized HHCD units in the US or Europe. Rotary-wing aircraft have particularly limited cabin space and air circulation, posing specific challenges with reducing transmission to crew members.[12,20] However, they also were readily and effectively utilized to redistribute cases regionally where demand for ICU beds exceeded capacity.[24] Articles that described collective evacuation[13,17,19,22] and those that discussed containerized systems[7,8,15,21] focused on fixed-wing aircraft. Long-distance flights for COVID-19 transports (overseas flights or between European countries) were also more likely to use fixed-wing aircraft.[16]

d. Layout/Space Assessment

Airflow in aircrafts vary by airframes.[7] In a C-130, cabin air is vented out through the cockpit – a problematic direction from an infectious disease standpoint – although there are ventilation systems and updates that can alter this.[7] Several studies tested airflow in both fixed wing and rotary wing aircrafts.[15,29] De Wit et al. conducted a study on stationary aircraft to determine the safest positioning of clinicians and suspected or confirmed patients with COVID-19 during the flight and the risk of exposure to aircrew in the cockpit.[15] Physical barriers between the cockpit and cabin in both types of aircraft were found to provide a degree of protection from nonclinical crew, but such barriers could become an issue during an emergency landing or other in-flight emergency.[15] However, in mid-2020, just 35% of respondents from the American College of Emergency Physicians Air Medical Section reported that the airframe permitted complete separation of cockpit from the patient care compartment.[20] Spoelder et al. considered a separation sheet between the cockpit and the cabin in helicopter transports but elected not to include as it would interfere with the direction of the small constant movement of air from the cockpit to the cabin and out through cabin air exhaust ducts.[24] Clearly, if one decides to erect a barrier within an aircraft it must be done with consideration of emergency evacuation routes, fire protocols, among other considerations, to determine its appropriateness for the aircraft and the AE-HLCT.

2. *In-Flight*

a. *PPE*

Most articles that utilized PPE for COVID-19 included filtering facepiece respirators (e.g., N95, FFP2/3), goggles or face shields, gloves, and a protective gown.[9,11,12,16,20] In rotary-wing aircraft, most programs required pilots to wear a N95 respirator[12,20]; however, some US HEMS organizations that did not plan to transport patients with COVID-19 early in the pandemic referred to difficulties in protecting pilots and issues with pilots wearing a N95 respirator (e.g., possibly causing goggles to fog, reduction in ability to communicate) as the primary reasons for that decision.[12] The significant strains in PPE supply chain at the time were discussed in several reviewed articles.[11,12,16] Peddle et al. recognized the need to ensure adequate supply of PPE (0-120 days) and created a PPE utilization flow chart for all medical and crew members and each transport phase (e.g., patient arrival, assessment, transport, destination arrival, decontamination), for both fixed wing and rotary wing aircraft.[11]

b. Type of Isolation Units

Eleven articles discussed various types of systems, including single patient isolation units (PIUs) and larger containerized/multi-patient systems that provide a portable isolation facility large enough for both the patient (or multiple patients) and medical staff wearing PPE (e.g., the Transport Isolation System [TIS, Containerized Biocontainment Care System [CBCS]).[6-9,12,14,16,17,19,21-23] The previous literature review many of these sytems.[2]

Containerized/multi-patient systems were primarily discussed in articles pre-pandemic, apart from the Transport Isolation System that can be utilized on either the C-17 or C-130 aircraft.[8,21] The first operational flight performed using the Transport Isolation System, rapidly developed for EVD by the US Air Force in 2014, was conducted in April 2020 to medically evacuate three government contractors that tested positive with COVID-19 from Afghanistan to Ramstein Air Base in Germany.[21] Between April and July 2020, the Transport Isolation System was utilized 18 times for AE of patients with COVID-19. Bleeg et al. describe another containerized system developed and conceived by Denmark for EVD transport.[6] The system is used on a C-130 aircraft and has separate modules for patient care and medical crew respite. Medical teams are donned in P4 insultation suits while in the module with the patient. The system, which has a tricolored concept of red, yellow, and green zones, has a capacity of 1-2 patients with EVD, but can accommodate twelve routine patients or three critically ill patients.[6]

Since the publication of our last article, the EpiShuttle[30] (EpiGuard AS, Oslo, Norway), a reusable PIU, was developed; four of the articles discussed its use as the PIU for a COVID-19 transport.[9,14,16,23] Additionally, Switzerland's Rega also developed a similar unit, referred to as the Rega PIU.[9] Both have been tested and approved for rotary and fixed wing aircrafts[9,23] and the use of these PIUs were reported on both types of aircraft. During a described transport, the EpiShuttle was fixed on a stretcher module for security during transport and standard air ambulance equipment, including advanced monitoring, ventilator, suction and infusion pumps, portable ultrasound, and an array of medications were available onboard.[23]

There are costs and benefits to consider with both containerized/multi-patient systems and PIUs. Albrecht et al. argued that containerized/multi-patient systems do not offer an additional benefit for the disease.[9] The use of full PPE during transport of COVID-19 cases, particularly when AEs last several hours, can be exhausting and physically stressful for medical teams, which can lead to medical errors.[9,16,24] For long-lasting missions, PIUs offer benefit to allow medical teams to deliver care during the transport without the use of PPE and were increasingly used by teams as the COVID-19 pandemic progressed.[16] However, while medical providers do wear full PPE while caring for patients in containerized/multi-patient systems, each system allows for medical crew to doff out of PPE during transport to allow for rest periods.[7,8,21] These larger systems served important roles during COVID-19 patient movement.[21]

Containerized/multi-patient systems require larger airframes, which might be a limiting factor, especially in a global pandemic when there's high demand for AE transports and most transports were conducted by private air ambulance providers without access to large aircraft.[23] As such, particularly in Europe, there was a shift to PIU solutions[9,23] (in the US, only 4% of US HEMS respondents reported use of an isolation pod/containment device when transporting known COVID-19 cases[20]). PIUs can also better facilitate easier transfers between aircraft and ground ambulances and vice versa, particularly versions like the EpiShuttle which are becoming increasingly smaller and readily fit into various transportation vehicles.[9,16] Moreover, the use of a PIU enables both air and ground teams to be protected without the need for N95 respirators and other PPE, which can be reserved during times of shortages for frontline healthcare teams. It should be noted, however, that PIUs themselves are costly: while soft shell models like the IsoPod are around USD5000, hard shelled models like the EpiShuttle cost around USD40,000[31]; that price is not inclusive of consumable filters and disinfection procedures. They are, however, reusable. Given high costs of PIUs and the limited number of larger containment systems designed for multi-patient AE-HLCT, further research and efforts are needed to find solutions for HHCD transport in lower resource settings.[23]

c. Collective Evacuation

Collective evacuations are a unique consideration that were not reviewed in our previous manuscript.[2] In the first few weeks of the pandemic, collective evacuation flights were conducted to return nationals to their home countries from Wuhan, China, although these flights did not include known infected patients. Later flights responding in other countries with early outbreaks of COVID-19 may have moved known cases, including the Diamond Princess evacuation. Collective evacuation flights also allowed for regional redistribution of patients, avoiding saturation of ICU beds from a system perspective by transferring intensive care patients to neighboring countries or regions with greater bed capacity. The documented experiences of organizations that conducted collective evacuation of confirmed and/or suspected cases of COVID-19[13,17,19,22] add to the body of literature – which, prior to COVID-19 was severely lacking – on considerations and challenges of multiple patient AE-HLCT transport, from 4-6 critically ill patients at a time to potentially hundreds of exposed or positive cases on a single transport.

Articles that discussed collective evacuation described the aircraft being configured around zones to contain infectious patients to a single area and minimize exposure risks to those outside of that zone: a clean/cold zone for medical crew rest, a warm zone for equipment storage and medical team preparation, and a dirty/hot zone for patients, in which all crew wore PPE. Martinez et al. noted that non-medical aircrew required for flight were contained in the cargo bay, given PPE and just-in-time training, and supervised by the medical director or biosecurity team to ensure adherence to infection prevention and control measures.[19]

d. Procedures / Capabilities In-Flight

Several articles included transport experience and considerations for clinical care provided inflight.[9,12,16-20,22,24] These included transports in both HEMS and fixed wing aircraft, use of PIUs, and collective evaluation of intensive care patients. Albrecht et al. conducted a study showing achievability of emergency airway management inside the Rega PIU that compared airway management in a PIU with airway management under standard protective measures during an AE; although subjectively more challenging compared to standard measures, there was no difference in success rates.[9] As of early April 2020, 46 intubated patients were transported using the Rega PIU.[9]

Several studies showed moderate- to high-risk aerosol generating procedures were conducted during HEMS transport of known or suspected patients with COVID-19 without the use of a PIU[12,16,20]; this reinforces the importance of adherence to safe PPE behaviors and other measures. Lemay et al. noted that proning, an effective measure for COVID-19 patients with acute respiratory distress syndrome, is impossible in many settings and recommended patients with this condition should therefore be transferred early before facing refractory hypoxemia.[18]

Experiences of French and German Armed Forces providing intensive care to patients with COVID-19 during collective evacuations in fixed-wing aircraft indicated significant resources and interventions were needed to prepare critically ill, mechanically ventilated patients for AE and to stabilize during flight (e.g., deepening anesthesia, treating circulatory instability).[19,22] As such, recommendations from these experiences include a maximum of 2 patients per AE team. During HEMS transports of 67 ventilated critical care patients with COVID-19 in the Netherlands, 13 adverse events occurred: equipment related events (3 times), crew resource management events (5 times), and unplanned disconnection of tubes (5 times).[24] None of the events resulted in long-term harm to patients.

e. Other Contingency Procedures

Cabin decompression at altitude was again cited as a concern, similar to the previous review.[2] Lemay et al. noted that if cabin decompression occurs, passengers have to put on oxygen masks, which would involve the medical team removing their respiratory protection; to prevent this situation, EVAQ (Quebec Aeromedical Evacuation Services) opted to fly at a lower altitude, which increased flight durations.[18] Previous concerns with soft-shelled PIUs included leaking internal air during rapid decompression. The Swiss Rega PIU included a built-in air bag that allows for additional air volume expansion to combat potential leakage.[9] The hard-shelled EpiShuttle has been tested for rapid decompression and flotation in case of an emergency landing in water.[23] Contingency preparations and procedures for HHCDs are always important, but never more critical than when providing HHCD care in the air.

Contingency procedures should be well incorporated as injects into exercises during training. Future articles should discuss and explore procedures for aircraft related emergency situations, such as fire or a water landing. For example, in a water landing if personnel are in PPE that includes a suit or boot covers, then it would be important to remove these prior to entering the water to avoid the very real possibility of drowning.

3. Postflight

a. Decontamination

Few articles discussed decontamination following AE of HHCDs or COVID-19. Garibaldi et al. describe disinfection of the aircraft, with a focus on Lufthansa Technik studies, similar to what was described in our previous literature review.[2,7] Berry et al. described decontamination methods of HEMS transports in the US in early 2020.[12] The most common method of decontamination was manual surface wiping (95% of surveyed services), followed by germicidal spray (67%).[12] Rarer and less labor-intensive methods of decontamination, including UV germicidal irradiation (UVGI), could provide for shorter average downtimes between reservicing of the aircraft; however, few services reported using or having access to UVGI.[12] With what we now know regarding SARS-CoV-2, a great deal of surface decontamination is likely not required, as fomite transmission is not a key transmission pathway.[32,33] However, for future microorganisms that are hardier in the environment or pose a greater fomite transmission risk, these questions of decontamination need to be resolved and done so in a way as not to degrade aircraft material like seals.

No international guidelines exist for protection of aircraft in a collective evacuation situation, and while CDC and ECDC have recommendations for EVD, they were not adaptable to an airborne disease.[17] Koch et al. describe manual cleaning and disinfection of all surfaces in the dirty area followed by application of an aircraft-approved disinfectant by a fogging machine; all 68 environmental samples in the clean zone that they collected during a flight were negative.[17] They did not, however, describe the specifics of the disinfectant or considerations for decision-making to protect the aircraft.

Albrecht et al. and Schwabe et al. both discussed the benefit of a PIU model of transport in allowing for quicker reservicing of the aircraft for additional transports, a critical consideration during times of the pandemic surge and ability to redistribute patients needing a higher level of care more rapidly.[9,23] Following transports, reusable PIUs (e.g., EpiShuttle) can be closed, the outside disinfected, and then transported to another location for a more thorough cleaning and disinfection.[9,23] Schwabe et al. did note that following AEs with the EpiShuttle, the aircraft was disinfected with peroxide wipes and a nebulizer.[23]

Conclusions

Although COVID-19 is not considered a HHCD and does not warrant the specialized practices inherent to high-level containment, its emergence as a novel disease with limited global knowledge led to protocols and practices used for HHCDs being applied to transport of patients confirmed or suspected to be infected with it. Unlike previous HHCD outbreaks or epidemics, a single organization did not have the capacity to transport all suspected or confirmed cases of the disease, and there appears to have been far more AE-HLCT than with any other previously confirmed or suspect HHCD. As such, agencies and organizations responsible for transporting patients with the novel disease – most of which had not previously conducted a HHCD transport – had to rapidly implement plans to safely transport patients and protect AE staff. Although those processes were updated and adapted as more information was learned about COVID-19, the early days of the pandemic led to significant innovations and lessons learned in AE-HLCT.

As an emerging infectious disease, there was a lack of published guidelines on safely transporting patients with COVID-19; as such, many organizations adapted their EVD-related protocols for COVID-19 transports. However, as available guidelines and recommendations on AE-HLCT were, and continue to be, lacking, and as the need for COVID-19 transports quickly surpassed the capacity of experienced and designated HHCD organizations, a higher operational tempo for AE-HLCT meant that many groups with likely limited operational planning or exercising for AE-HLCT conducted COVID-19, with minimal existing guidance or available practices to adapt.

Moreover, AE-HLCT prior to the COVID-19 pandemic was heavily focused on single-patient transports; COVID-19, however, has led to experiences of evacuation of multiple patients to a level that can conceivably be required with an emerging infectious disease event. While these experiences have generated lessons learned and advanced our knowledge of and practices for multiple patient transports, increased attention and greater exercising, research, and considerations for operationalization of multiple patient transports is warranted. This includes both transports of multiple critically ill patients and transports of tens to hundreds of exposed, suspected, or confirmed patients on, for example, repatriation flights, as well as many simultaneous patient transports being conducted and coordinated by different agencies.

The COVID-19 pandemic led to several innovations, including decision support frameworks[10,14,16] and advancements in portable isolation units. The EpiShuttle and Rega PIU, both developed prior to the COVID-19 pandemic, were utilized by diverse groups in Europe, Canada, and Saudi Arabia.[9,14,16,23] Their use during COVID-19 provided data on decontamination methods, reusability and turnaround time required, and ability to provide patient care, all which helps to better understand the benefits and drawbacks of hard-sided PIUs for AE-HCLTs. However, questions on hard-sided PIUs still remain, including impact on skin integrity and potential development of pressure ulcers in patients if used for extended durations. More research and exercising of these devices are needed to understand their role in AE-HCLTs and continue to advance these units. In addition, HEMS AE-HLCT were utilized much more frequently than described in the literature in our first review. Although limitations with HEMS AE-HLCT exist, their use was effective during regional redistribution of patients with COVID-19 for time-critical transports and highlighted their use as a critical conduit in AE-HLCT between ground and fixed wing aircraft.

Despite the literature on AE-HCLT essentially doubling since our previous literature review in 2019, gaps still exist that remain to be addressed. Optimal decontamination methods for use on aircraft require further investigation, particularly for circumstances when a quick turnaround of the aircraft is needed. UV irradiation, a rarer method of disinfection for aircraft that was reported to be employed by some HEMS organizations during the COVID-19 pandemic and led to shorter-than-average downtime,[12] should be explored for its effectiveness and feasibility for AE-HLCT. In addition, little advancement for emergency procedures was published in the literature, and future articles should discuss and provide guidance on procedures for emergency situations during AE-HLCT. Moreover, there appears to be a lack of information-sharing and coordination between organizations conducting AE-HLCT, further amplified during the COVID-19 pandemic; however, this could be a result of the peer-reviewed nature of our study. Finally, the pandemic has brought a number of new considerations for AE-HLCT in thinking about challenges of transport of an airborne HHCD; greater collaboration, research, and guidelines are needed for airborne-specific as well as disease-agnostic practices for AE-HLCT.

This review is not without limitations. First, only articles that were available or translated into English were included in this review, thereby potentially limiting representation from other global regions. Second, this was not a systematic literature review but rather an update to a previous literature review; as with the last review,[2] the review was limited to published literature and therefore does not include procedures and policies that air transport teams might have published in lay articles. As such, while the search was comprehensive, it was not exhaustive. Lastly, some AE-HLCT lessons learned and experiences from the first years of COVID-19 are likely still to be published or were published following this review's time frame (e.g., an article published in 2022 detailing US Air Force transports using the Transport Isolation System as well as the Negatively Pressurized Conex [NPC], which completely replaced the Transport Isolation System[34]). Despite these limitations, this review provides a notable contribution to the literature by providing an update on AE-HLCT that otherwise would have not been synthesized.

In conclusion, the lessons gleaned from the early days of the COVID-19 pandemic have undoubtedly advanced the field of AE-HLCT, and many groups that had previously only exercised their AE-HLCT procedures and plans have now put those processes into practice. Learnings from the COVID-19 pandemic could have enduring changes to the AE-HLCT field, and we may be better prepared for the HHCD event. However, challenges and gaps remain to be addressed in the field, particularly in preparation for emerging respiratory pathogens.

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2. [*Blinded for peer review]*

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Figure 1. PRISMA Chart for aeromedical evacuation high-level containment transport (AE-HLCT) literature review

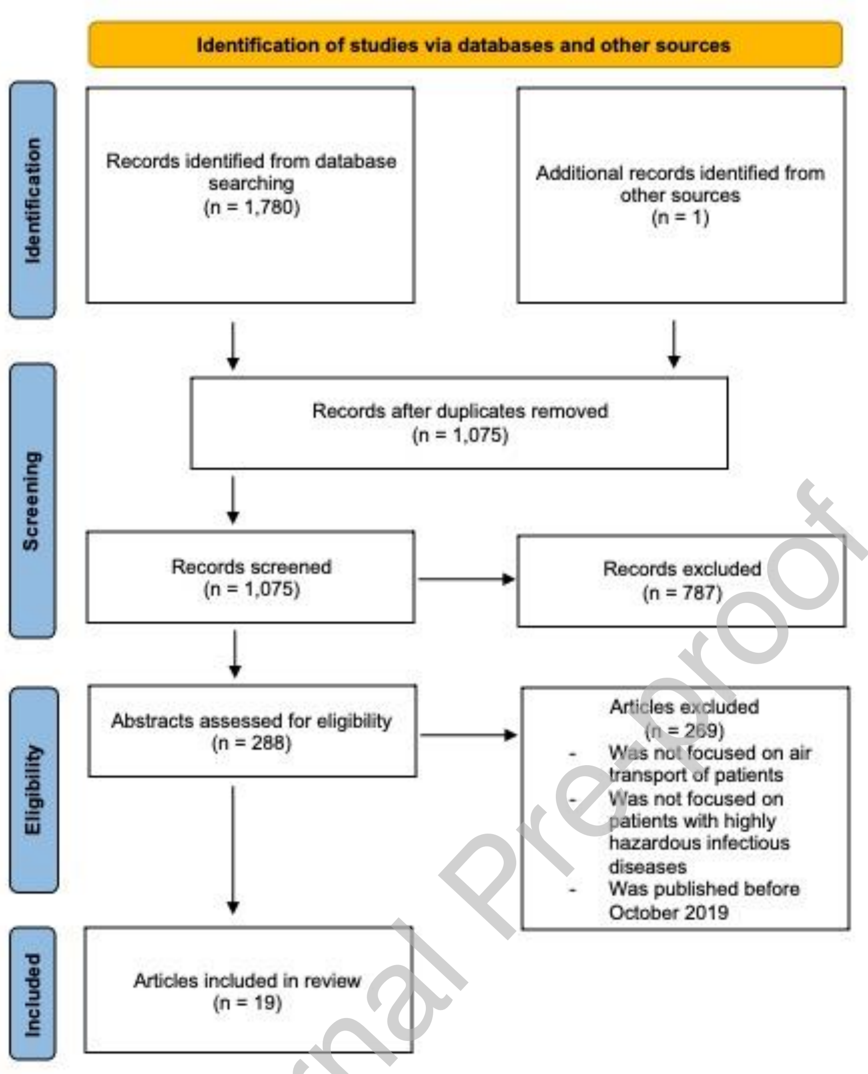

Table 1. Summary of aeromedical evacuation high-level containment transport (AE-HLCT) with "X" indicating the subject was included in the article.

	Pre-Flight										In-Flight							Post-Flight			
First Author Year Country (Military or Civilian)	Disease Type, COVID-19	Disease Type, Other	Decision to Air Medical Transport	Training/Drills	Regulations and legal limitation	Communication Plan	Rotary-Wing Aircraft	Fixed-Wing Aircraft	Layout/Space Assessment	Other Preparations	Personnel	Personal Protective Equipment	Type of Isolation Units	Procedures/Capabilities inflight	Liquid and Solid Waste Handling	Death inflight	Other Contingency Procedures	Decontamination	Equipment Reuse	Waste Disposal	Personnel Monitoring
Albrecht 2020 Switzerland/Europe (Civilian)	X	X		X			X	X		X	X	X	X	X		X					
Berry 2021 United States (Civilian)	X		X	X			X	X	X	X	X	X	X	X				X			
Bleeg 2019 Denmark (Military)		X	X			X		X	X	X	X	X	X								
Borges 2020 Brazil (Military)	X		X	X				X	X	X	X	X									X
Bredmose 2020 Norway/Scotland/ Finland/Germany/ Australia (Civilian)	X		X	X		X	X		X	X	X	X	X	X			X	X			X
de Wit 2021 Denmark (Civilian)	X						X	X	X	X		X									

Garibaldi 2019 United States (Civilian/Military)		X	X		X	X		X	X	X		X	X				X	X			
Hilbert-Carius 2020 Europe (Civilian)	X		X	X			X	X		X		X	X	X				X			
King 2019 United States (Military)		X		X				X	X		X		X								
Koch 2021 France (Military)	X		X					X	X	X	X	X	X				X	X			X
Lemay 2020 Canada (Civilian)	X					X		X	X	X		X		X			X				
Martin 2020 United States (Civilian)	X	X	X	X	X	X		X	X	X	X	X		X			X	X			
Martinez 2021 France (Military)	X		X	X				X	X	X	X	X	X	X			X				X
Meng 2021 United States (Civilian)	X			X			X		X	X		X		X							X
Peddle 2020 Canada (Civilian)	X	X		X			X	X		X	X	X									
Reynolds 2021 United States (Military)	X			X				X			X		X								

Sammito 2021 France/Germany (Military)	X		X					X		X	X		X	X							
Schwabe 2020 Germany (Civilian)	X		X	X		X		X	X	X	X		X	X			X	X			
Spoelder 2021 Netherlands (Civilian)	X			X	X	X	X		X	X	X	X		X			X				X

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