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A systematic review on global zoonotic virus-associated mortality events in marine mammals

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ABSTRACT

Marine mammals play a critical role as sentinels for tracking the spread of zoonotic diseases, with viruses being the primary causative factor behind infectious disease induced mortality events. A systematic review was conducted to document marine mammal mortality events attributed to zoonotic viral infections in published literature across the globe. This rigorous search strategy yielded 2883 studies with 88 meeting inclusion criteria. The studies spanned from 1989 to 2023, with a peak in publications observed in 2020. Most of the included studies were retrospective, providing valuable insights into historical trends. The United States (U.S.) reported the highest number of mortality events followed by Spain, Italy, Brazil and the United Kingdom. Harbor seals were the most impacted species, particularly in regions like Anholt, Denmark and the New England Coast, U.S. Analysis revealed six main viruses responsible for mortality events, with *Morbillivirus* causing the highest proportion of deaths. Notably, the occurrence of these viral events varied geographically, with distinct patterns observed in different regions. Immunohistochemistry emerged as the most employed detection method. This study underscores the importance of global surveillance efforts in understanding and mitigating the impact of viral infections on marine mammal populations, thereby emphasizing the necessity of collaborative One Health approaches to address emerging threats at the human-animal-environment interface. Additionally, the potential transfer of zoonotic viruses to aquatic organisms used in food production, such as fish and shellfish, highlights the broader implications for food safety, food security and public health.

1. Introduction

Zoonoses (diseases that can spread from animals to humans) is one of the five distinct pillars of the One Health action framework [\[1\]](#page-7-0). The One Health concept aims to prevent and control zoonoses through collaboration and communication among stakeholders involved in animal, human and environmental health [[2](#page-7-0)]. It is estimated that about 60% of all emerging infectious diseases (EIDs) are zoonotic, with around 70% spreading from wild animals $[2–5]$ $[2–5]$. It is documented that EID events that originated from wildlife are significantly increasing temporally [[5](#page-7-0)]. Drivers of increasing EID events include climate change, urbanization, deforestation, unsustainable agricultural practices, trafficking and eating of wildlife animals [[6](#page-7-0)]. While the rise of zoonotic diseases in terrestrial settings is evident, attributable to heightened interactions between humans and animals, the extent of a comparable increase in such diseases in marine environments remains less apparent. According to a recent analysis, there has been a notable surge in infectious diseaserelated mass mortality events (ID-MME) among marine mammals over

the past three decades, with viruses being identified as the primary causative agents [\[7\]](#page-7-0).

Several viruses are known to cause zoonotic diseases in marine mammals. Calicivirus exemplifies a zoonotic virus that originates in the ocean and has crossed over from sea lions to swine, causing vesicular dermatitis and influenza-like illnesses in both marine mammals and swine. [8–[10](#page-7-0)]. *Parapoxvirus* is known to cause seal finger disease which results in nodular lesions (abnormal growth) in the skin around the neck and head in pinnipeds [[11\]](#page-7-0). Additionally, first responders during Unusual Mortality Events (UME) have contracted sealpox from marine mammals infected with parapoxviruses, resulting in symptoms like contagious pustular dermatitis or lesions [\[12](#page-7-0),[13\]](#page-7-0). Since 1988, morbilliviruses have been responsible for more than half of ID-MMEs in marine mammals, displaying symptoms such as skin lesions, pneumonia, brain infections, and pup abortions $[14,15]$ $[14,15]$ $[14,15]$ $[14,15]$. While distemper viruses are not typically transmissible to humans, evidence suggests that canine distemper virus (CDV) can adapt to human cell receptors, indicating a potential for zoonotic spillover [[16,17\]](#page-7-0). *Influenza A virus* (IAV) ranks as

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the second leading cause of viral ID-MMEs in marine mammals, with reports of harbor seal die-offs due to acute hemorrhagic pneumonia dating back to 1979 [\[7,18](#page-7-0)]. Several cases of conjunctivitis resulting from IAV spillover events from seals to humans were documented in 1981 [[19\]](#page-7-0). Therefore, a systematic review on marine mammal mortality events is essential to comprehensively understand the scope and impact of zoonotic viruses in marine ecosystems, thereby informing effective strategies for disease surveillance, prevention, and management.

Inhabiting diverse environments, capable of extensive travel and long life-spans, marine mammals could serve as sentinel species for identifying potential "hot spots" of zoonotic viral diseases, offering

valuable insights into various habitats [\[20\]](#page-7-0). Marine mammal fatalities or strandings can serve as indicators that alert researchers to the potential presence of diseases in wild animals that are otherwise challenging to access [\[21](#page-7-0)]. Marine mammals are classified as "stranded" when discovered either deceased on the shore or afloat in the water, or when found alive on the beach but unable to return to the water [\[22](#page-7-0)]. Several infectious disease agents, including phocine distemper virus (PDV) responsible for an outbreak that resulted in over 18,000 harbor seal deaths in Europe in 1988 [\[23](#page-7-0)], phocine herpesvirus (PhHV1) isolated from harbor seals in 1985 [\[24](#page-7-0)], and *Brucella* bacteria in various species [[25,26](#page-7-0)], were initially identified in stranded marine mammals.

Fig. 1. PRISMA review process flow chart generated by Covidence.

Recognizing areas experiencing a rise in ID-MMEs and/or mortality "hot spots" are essential for applying the Generalizable One Health Framework (GOHF) [\[27](#page-7-0)]. This framework offers a structured five-step approach to prevent and control zoonotic viruses, thereby mitigating the risk of outbreaks. Over the years, several viruses have been implicated in marine mammal mortalities, primarily morbilliviruses and Influenza A [\[7,](#page-7-0)[28](#page-8-0)]. To identify additional viruses accountable for the majority of ID-MMEs and their implications for specific marine mammal species, a critical step involves thoroughly examining existing literature from diverse sources. This process aids in prioritizing a list of zoonotic diseases among marine mammals that pose significant concerns to various global populations.

Zoonotic viruses found in marine mammals, such as morbilliviruses and influenza viruses, can potentially be transferred to other aquatic organisms used in food production and aquaculture through shared marine environments and direct contact. These viruses can contaminate water bodies, which are then inhabited by fish and shellfish farmed for human consumption [[29\]](#page-8-0). The transmission can occur through the shedding of viral particles by infected marine mammals, which can then be ingested or come into contact with aquaculture species, leading to outbreaks within these populations [[30\]](#page-8-0). Utilizing marine mammals as sentinel species to monitor regions with increased zoonotic viral outbreaks is essential for safeguarding food production [[20,](#page-7-0)[31\]](#page-8-0). A recent study showed that metagenomic sequences of fecal and serum samples from marine mammals aligned with sequences of viral families known to cause mortality events in fish and bivalves [\[32](#page-8-0)]. Marine mammals, due to their position in the marine food web and their interactions with various marine environments, can provide early warning of the presence of pathogens and their transmission pathways [[20\]](#page-7-0). This proactive approach allows for the timely implementation of biosecurity measures and surveillance protocols in aquaculture industries, thereby reducing the risk of zoonotic virus transmission to food production systems and ultimately protecting public health.

In addition to pinpointing zoonotic viruses posing the highest risk to

diverse marine mammal populations, it is crucial to acknowledge commonly utilized laboratory techniques. This recognition is essential for developing effective One Health plans, protocols, and procedures for zoonotic viral disease detection and mitigation [\[27](#page-7-0)]. Previous reviews on marine mammal viruses either focused on disease manifestations, disease drivers, one particular virus of concern or marine mammal species, are out dated, or were not written systematically according to the Preferred Reporting Items for Systematic reviews and MetaAnalysis (PRISMA) [\[7,11,](#page-7-0)[28,33](#page-8-0)–45]. To analyze viruses responsible for zoonotic mortality events in marine mammals and their detection methods, we conducted a systematic literature review, scrutinizing the scope and details of relevant information available in existing literature up to 2023. Therefore, the aims of this review were to (i) compile instances of virus mortality events in marine mammals worldwide, pinpointing regions of heightened occurrence and areas with underreported events, (ii) determine the predominant viruses responsible for these mortality events up to 2024, (iii) assess the prevalent viral detection techniques utilized during such incidents, and (iv) ascertain the marine mammal species most impacted by these virus-induced mortality events.

2. Methods

2.1. Literature search strategy and selection

This review was performed according to the PRISMA guidelines [\[35](#page-8-0)] using the Covidence systematic review software [\[46](#page-8-0)]. We searched PubMed, Web of Science, and Scopus in July 2022 and updated this once in September 2023 to capture current references. These queries were performed without any time restrictions and only published articles limited to the language English were accepted. The search terms used were input as: ("marine mammal") OR ("whale")) OR ("dolphin")) OR ("porpoise")) OR ("pinniped")) OR ("cetacean")) OR ("seal")) OR ("sea lion")) OR ("walrus")) OR ("sirenian")) OR ("manatee")) OR ("dugong")) OR ("fissiped")) OR ("polar bear")) OR ("sea otter")) AND

Striped dolphin Bottlenose dolphin Common dolphin Grey seal Mediterranean Striped dolphin sea otter Guiana dolphin Indo-Pacific Bottlenose dolphin
Cuvier's beaked whale Harbor porpoise Baikal seals sea lion Harp seal White-heaked dolphin Risso's dolphin Siberian seals Fin whale Caspian seals Long-finned pilot whale Atlantic spotted dolphin Undetermined dolphin species Sperm whale Pygmy sperm whale Fraser's dolphin False killer whale Spinner dolphin South American sea lion Indo-Pacific humpbacked dolphins Melon-headed whale neotropical otters Stejneger's beaked whale Mediterranean monk seal Blainville's beaked whale Southern right whale Short-finned pilot whale Clymene dolphin California sea lion True's beaked whale Rough-toothed dolphin Humpback whale Dwarf sperm whale Pygmy killer whale

Fig. 2. Total virus-caused marine mammal mortalities separated by species common name.

("zoonotic")) OR ("epizootic")) AND ("virus")) AND ("mortality"). The criteria for article inclusion in this review was that the study included a virus mortality event that involved a marine mammal. Titles and abstracts were initially screened by two authors (KV and HW) in Covidence for inclusion criteria and the articles that were deemed eligible were exported into End Note v20.5 to retrieve the full text format. Conflicts between the authors during the initial screening process were tracked using Covidence and resolved by excluding articles that (i) no marine virus mortality event occurred, (ii) no viral testing was conducted, iii) no marine mammal death, and (iv) the article was a review article. All eligible full text articles were imported back into Covidence for full text review and data extraction.

2.2. Data extraction and synthesis

A data extraction template was created in Covidence to extract all relevant data. The following information was extracted from the eligible publications: Covidence identification number, study identification, title, publication year, journal name, retrospective study (yes or no), location of mortality event (s) (country and region), longitude, latitude, date the mortality event occurred, marine mammal taxonomic group (cetacean, pinniped, fissiped, and/or sirenian), marine mammal common name, marine mammal scientific name (genus and specie), total mortality count, virus genus, virus species or strain, detection method(s) and source of virus transmission (unknown, avian, aerosol, cross-species

transmission or endemic). Cetaceans include whales, dolphins and porpoises; pinnipeds include seals, sea lions, and walruses; fissipeds include polar bears and sea otters; sirenians include dugongs and manatees. A study was considered retrospective if it was published within 5 years after the marine mammal mortality event. If longitude and latitude were not clearly stated in the methods section of the journal articles, then it was extrapolated using Google Maps [\[47](#page-8-0)] from the region listed. Summary statistics and figures were computed using R v4.3.2 [\[48](#page-8-0)]. Figures and maps were produced using the packages, ggplot2 [[49\]](#page-8-0) and tidyverse [\[50](#page-8-0)] for R and Tulane Universities' ArcGIS online Portal ([https://tulane.maps.arcgis.com/apps/mapviewer/index.html\)](https://tulane.maps.arcgis.com/apps/mapviewer/index.html).

3. Results

3.1. Selected studies

The search strategy is summarized in [Fig.](#page-1-0) 1. The database search retrieved 2883 studies with 1692 from Scopus, 602 from Web of Science and 589 from PubMed. After exclusion of 734 duplicates, 2149 studies were screened with 1993 studies deemed irrelevant. A total of 156 studies were assessed for eligibility and 68 studies were excluded. A total of 88 studies [51–[138](#page-8-0)] were included in the systematic review and details of the included studies are shown in supplementary_material_2.xlsx file. Those studies were published from 1989 to 2023, with the most virus-caused marine mammal mortality publications occurring in 2020

Fig. 3. World map of total virus-caused marine mammal deaths (in log) by marine mammal type. The green dot sizes in the figure legend correspond to the total log marine mammal deaths from 0 to 4.22608. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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 $[65,66,75,79,80,82–85]$ $[65,66,75,79,80,82–85]$ $[65,66,75,79,80,82–85]$ $[65,66,75,79,80,82–85]$ $[65,66,75,79,80,82–85]$ $[65,66,75,79,80,82–85]$ (Fig. S1). There was a noticeable gap in publications between 2001 and 2006 and 2006–2009. Only 41% of the 88 studies were considered as retrospective studies [[54,55,58,60](#page-8-0), [66,68,](#page-8-0)70–[74,76,78](#page-8-0)–80,[82,84,85,91](#page-8-0)–95[,97](#page-8-0),[98,100,102](#page-9-0)–104,[108,110,](#page-9-0) 114–[116,119,124,125,127](#page-9-0),[129,138\]](#page-9-0), while 59% were non-retro spective $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ $[51–53,56,59,61,62,64,65,67,69,75,77,81,83,86–90,96,99,$ [101,105](#page-9-0)–107[,109,111](#page-9-0)–113[,117,118](#page-9-0),120–[123,128,130](#page-9-0)–137].

3.2. Occurrence of marine mammal mortality events caused by viruses

A total of 30 countries reported virus-caused mortality events with a total of 124,094 marine mammal deaths. These countries included Australia, Azerbaijan, Belgium, Brazil, Bulgaria, Canada, Denmark, Ecuador, France, Germany, Greece, Ireland, Israel, Italy, Japan, Kazakhstan, Mauritius, Netherlands, Peru, Poland, Portugal, Romania, Russia, Spain, Sweden, Taiwan, Thailand, Ukraine, United Kingdom (U. K.), and United States (U.S.) (Fig. S2). Within the 88 studies, the U.S. reported the most marine mammal mortalities (24%) [[51,57,61](#page-8-0),[66,68,76,78,82](#page-8-0),[84,](#page-8-0)[101,103,114,115](#page-9-0),[117,120,122](#page-9-0),124–[127](#page-9-0) ,[129](#page-9-0)], followed by Spain (20%) [[52,62,63,70](#page-8-0),[71,74,79,83](#page-8-0),93–[95](#page-8-0), [102,108,125](#page-9-0),[128,130\]](#page-9-0), Italy (15%) [[73,80,86,87,97](#page-8-0),[99,105](#page-9-0),110–[112](#page-9-0), [131,132,135](#page-9-0)], Brazil (8%) [[60,72,75,81](#page-8-0),[90,96\]](#page-8-0), UK (6%) [\[55,65](#page-8-0), [67,77,91\]](#page-8-0), Australia (5%) [\[100,106,113,138\]](#page-9-0), Netherlands (5%) [[64,85,91](#page-8-0),[107](#page-9-0)], Denmark (3%) [[53,69,91](#page-8-0)], Germany (3%) [\[56,85](#page-8-0),[115](#page-9-0)], Ireland (3%) [\[125,134\]](#page-9-0), Russia (3%) [[54,59,](#page-8-0)[123](#page-9-0)], Canada (2%) [[67](#page-8-0)[,129\]](#page-9-0), and Portugal (2%) [[92,](#page-8-0)[102](#page-9-0)]. The other 12 countries not listed above were reported in 1% of the publications. The top 10 countries with the most virus-caused marine mammal mortalities were, Denmark, U.S., Spain, Portugal, Italy, Germany, U.K., France, Brazil, and Australia (Table S1). Denmark and the U.S. had the highest mortalities at 68390 (55%) and 47,996 (38%), respectively, with harbor seals (*Phoca vitulina*) being the most impacted from both countries (89.7%) (Table S1). Anholt and the New England Coast were specific locations where the most marine mammal viral mortalities occurred in Denmark and the U.S., respectively.

Harbor seals (*Phoca vitulina*) (92.2%) were reported to have the most mortalities caused by viruses, followed by striped dolphins (*Stenella coeruleoalba*) (1.7%), bottlenose dolphins (*Tursiops truncatus*) (1.1%), common dolphins (*Delphinus delphis*) (1%), grey seals (*Halichoerus grypus*) (0.9%), Mediterranean striped dolphins (*Stenella coeruleoalba*) (0.73%), sea otters (*Enhydra lutris*) (0.46%), Guiana dolphins (*Sotalia guianensis*) (0.28%), Indio-Pacific bottlenose dolphins (*Tursiops aduncus*) (0.21%), and Cuvier's beaked whales (*Ziphius cavirostris*) (0.21%) ([Fig.](#page-2-0) 2). Most of the seal deaths concentrated around the North American and Northern Europe regions, while dolphin and whale deaths concentrated around Southern U.S., Southern Brazil, and Southern European countries ([Fig.](#page-3-0) 3). Pinnipeds (seals, sea lions, and walrus') suffered the most mortalities at 92.3%, with seals being the most affected group at 91.5% (Figure's S3 $\&$ S4). The highest mortalities occurred in 1988 for pinnipeds, followed by 2004 for cetaceans (whale, dolphin and porpoise), and 2002 for fissipeds (sea otters) (Fig. 4). The highest mortalities from the different marine mammal taxonomic groups were

Fig. 4. Total virus-(in log) caused marine mammal mortalities (in log) separated by mortality event start date and taxonomic group.

Fig. 5. Total number (in log) of marine mammal mortalities caused by different virus genus and/or species separated by marine mammal type.

Harbor seals (114,435 mortalities) for pinnipeds, stripped dolphins (*Stenella coeruleoalba*) (2065 mortalities) for cetaceans, and sea otters (*Enhydra lutris*) (572 mortalities) for fissipeds.

3.3. Viral etiology agents and their detection methods

From all the 88 included studies, a total of six viruses caused marine mammal mortality events. These viruses included *Morbillivirus, Influenza A, Herpesvirus, Adenovirus,* and *Parvovirus. Morbilliviruses* caused the most marine mammal mortalities at 62%, followed by *Influenza A* at 35%*, Herpesvirus* at 3%*, Anellovirus* at 0.05%*,* and *Parvovirus* at 0.003%, *Morbillivirus/Adenovirus* (co-infection) 0.003%, respectively (Fig. S4).

Parvovirus caused higher mortalities in seals, *Morbillivirus/Adenovirus* (co-infection) in otters, *Morbillivirus* in seals and dolphins, *Influenza A* in seals, *Herpesvirus* in seals, and *Anellovirus* in seals (Fig. 5). *Morbillivirus* (88.6%) caused the most mortalities in Denmark, *Influenza A* (99.9%) in the USA, *Herpesvirus* (49.9%) in the USA, *Morbillivirus/Adenvovirus* (51.3%) (co-infection) in the USA, *Anellovirus* (100%) in the USA, and *Parvovirus* (100%) in the Netherlands (Table S2). Most of the deaths caused by *Morbillivirus* occurred around the Northeastern and southern U.S., Southern Brazil, Northern and Southern European countries (Fig. S6). Different strains and subfamilies caused mortalities from their respective viral genus or species. Canine distemper virus (CDV) was the most abundant species from *Anellovirus,* followed by phocineherpesvirus-1 (PhHV-1) for *Herpesvirus,* H7N7 for *Influenza A*, cetacean morbillivirus (CeMV) for *Morbillivirus,* CDV and cetacean adenvirus-2 (CAdV-2) of *Morbillivirus/Adenovirus* co-infection, and seal annellovirus-3 (SeAV3) for *Parvovirus* [\(Fig.](#page-6-0) 6). Note that most of the *Morbillivirus* strains or subfamilies were unknown or not reported in the selected studies. 100% of the *Influenza A* viruses came from avian sources with H7N7 causing the most mortalities in Harbor seals (*Phoca vitulina*) on the New England Coast (USA) in 1979. 50.1% of *Morbillivirus* mortalities came from unknown sources, while 32.8% were crossspecies transmission, 16.8% were endemic and 0.32% were aerosol. For *Herpesvirus,* 89.1% were from unknown sources, 10.8% were crossspecies transmission and 0.179% were endemic. All other viruses were 100% from unknown sources.

For identification of the etiology agents, immunohistochemistry (IHC) (27%) was the most employed detection method followed by histology (15%), pathology (14%), immunoperoxidase staining (14%), and sequencing (13%), respectively (Fig. S5). Studies that used histological methods but did not include an antibody-based immune-stain were designated under "histology." PCR was mostly used to detect *Anellovirus* and *Herpesvirus*, while reverse-transcriptase PCR (RT-PCR) was used to detect *Morbillivirus.* Histology was mostly used to detect *Morbillivirus/Adenovirus*, while sequencing was mostly used to detect *Influenza A.* For *Parvovirus* histology was the most used method (Table S3).

4. Discussion

Despite the observed rise in virus-associated mortality events among marine mammals, this systematic review indicates that only 30 countries documented such incidents. Notably, Mexico, Central American nations, Chile, China, India, several Southeast Asian countries, all countries in Africa and the Middle Eastern countries did not report any instances of marine mammal mortalities, despite their oceanic proximity. Most of the seal, whale and dolphin mortality events were reported in Europe and North America. It could be that these countries have excessive marine mammal stranding networks [\[140\]](#page-9-0), while other parts of the world lack such networks. The lack of reporting could lead to underreporting of ID-MMEs. It is important to point out that this review exclusively considered publications from peer-reviewed journals, potentially resulting in an underestimation of virus-caused marine

Fig. 6. Proportion of virus strains and/or subfamilies to their corresponding virus genus or species (x-axis). BWMV: beaked whale morbillivirus; CDV: canine distemper virus; CAdv-2: Canine adenovirus type 2; CeMV: cetacean morbillivirus; H3N8: influenza A virus subtype H3N8; H5N1: influenza A virus subtype H5N1; H5N8: influenza A virus subtype H5N8; H7N7: influenza A virus subtype H7N7; PDV: phocine distemper virus; PhHV-1: phocine herpesvirus-1; SealAV: novel seal anellovirus; SeAV3: seal annellovirus 3; ZcAv: novel California sea lion anellovirus.

mammal mortalities. A considerable number of events could be reported in other databases or reports (i.e. federal or state morbidity and mortality reports) rather than in published literature [[140](#page-9-0)]. Other factors may contribute to the underreporting of marine mammal deaths by several countries, such as, constrained resources [\[36](#page-8-0)], absence of robust data management systems [\[140\]](#page-9-0), insufficient awareness regarding the significance of ID-MMEs [\[141\]](#page-9-0), regulatory gaps [[142](#page-9-0)], and limited international collaborations [\[140\]](#page-9-0).

Seals, in particular harbor seals, exhibited the highest occurrence of mortalities among all 88 published literatures, with fatalities attributed to all viruses except *Adenovirus*. Harbor seals have one of the widest pinniped distribution in coastal areas across the world [[143](#page-9-0)], and are documented to haul-out (temporarily leave the water) up to 12 h a day [[144](#page-9-0)], which may increase their chances of coming into contact with infected terrestrial animals or contaminated urban stormwater run-off. Phylogenetic analysis of the seal parvovirus (SeAV3) [\[107\]](#page-9-0), detected in the brain of a harbor seal from Pieterburan Netherlands, showed the closest similarity with Chipmunk parvovirus [[107](#page-9-0)] suggesting terrestrial zoonotic viral transfer. Additional support for terrestrial zoonotic transmission was observed in the phylogenetic analysis of seal anellovirus (SealAV), revealing resemblances to sea lion anellovirus and three feline anelloviruses [[114](#page-9-0)]. The phocid herpesvirus-1 (PhHV-1, subfamily *Alphaherpesvirinae*) detected in harbor seals from Washington, USA [[66\]](#page-8-0) was first isolated in 1985 in the Netherlands and is associated with mortalities in neonates from rehabilitation facilities in the northeastern Pacific [\[145\]](#page-9-0), further displaying how far these zoonotic viruses can spread from one continent to another.

The most mortalities in harbor seals were caused by *Morbillivirus* [[53,61,67](#page-8-0),[69,78,91](#page-8-0)[,110,133](#page-9-0),[134](#page-9-0)] and *Influenza A* [\[51](#page-8-0),[57](#page-8-0)]. Canine distemper virus (CDV), phocine distemper virus (PDV) and cetacean distemper virus (CeMV) were the *Morbillivirus* strains causing harbor seal mortalities. PDV was the etiologic agent causing the largest mortality of harbor seals in 1988 from Danish island of Anholt [\[146\]](#page-9-0). Several hypotheses as to why this large mortality event occurred include: (i) high temperatures caused a large population of seals to congregate on land facilitating rapid transmission of pathogens $[147]$ $[147]$ $[147]$, (ii) cross-species

transmission from infected seal populations [\[148\]](#page-9-0), (iii) toxic algal blooms [\[147\]](#page-9-0), and (iv) marine pollution [[149](#page-9-0)]. This outbreak still remains the largest within our included publications with origins of possible cetacean and/or canine [[134](#page-9-0)]. *Influenza A* H7N7 strain caused the highest harbor seal death in 1979 followed by H3N8 in 2011, both originating from avian origin in New England, USA [\[51](#page-8-0),[57\]](#page-8-0). The H7N7 strain has been implicated in high poultry mortality events causing significant economic losses [\[139,150,151\]](#page-9-0). The frequent outbreaks of Influenza in the Pacific Northeast necessitate consistent surveillance of wild bird populations, as strains have the potential to transmit to humans and seriously impact food production. This was evidenced during the 1979 outbreak when individuals handling infected seals contracted conjunctivitis [[19\]](#page-7-0).

The most employed method of viral detection to identify the etiology agents was IHC which allows for visualization of protein expression from tissue samples using specific antibodies to target certain viral antigens; prior knowledge of the targeted protein antigen is needed to develop antibodies to develop such assays. This method is qualitative, can be time consuming and maybe subjective in result interpretation [[152](#page-9-0)]. Other methods, such as sequencing or quantitative PCR (qPCR) may be needed to quantify or confirm qualitative viral results produced by IHC tissue testing. Sequencing can be used to identify newly emerging viral pathogens within marine mammal populations that may go undetected using IHC or PCR based methods, because prior knowledge of the viral target amplification genetic region or antigen is needed to develop such assays. Metagenomic sequencing, in particular, can be utilized as a tool to detect novel viruses in marine mammals and humans, and it can also be employed across various food industries to enhance food safety and security [153–[155\]](#page-9-0). In addition, nearly half of the studies included in this review were classified as retrospective studies. Enhancing the monitoring of viral outbreaks leading to mortality events in marine mammals, with the potential to spill over to other organisms, necessitates the development of more rapid detection methods. This is crucial for achieving a more comprehensive One Health surveillance of zoonotic viral diseases.

5. Conclusions

Collecting data on marine mammal mortality events is crucial for identifying trends and potential viral hotspots, especially within the framework of One Health surveillance and food safety. This approach recognizes the interconnectedness of human, animal, and environmental health, emphasizing the importance of monitoring and addressing health issues at their interface. Marine mammals serve as sentinel species, providing early warnings of environmental changes and potential health threats that could affect humans and other animals in the same ecosystems. Surveillance of marine mammal mortality events not only protects these vulnerable species but also provides insights into zoonotic diseases that may pose risks to human populations while protecting food production and aquaculture. While IHC has been the most employed method for viral detection in marine mammals, its limitations necessitate the adoption of more precise and robust molecular diagnostic tools. IHC, though valuable for visualizing protein expression, is qualitative, time-consuming, and may be subjective in result interpretation. Molecular diagnostic approaches such as qPCR and sequencing offer significant advantages. qPCR provides quantitative data, allowing for a more precise measurement of viral loads, and can confirm the presence of specific viral pathogens with high sensitivity and specificity. Sequencing enables the identification of novel and emerging viral pathogens that might be missed by IHC or even qPCR, which rely on prior knowledge of the viral genome or antigens. Integrating molecular diagnostics into routine surveillance can enhance the detection of viral outbreaks in marine mammal populations and other marine organisms, providing a more comprehensive understanding of viral diversity and evolution. This is particularly important given the zoonotic potential of many marine mammal viruses. Molecular diagnostics can facilitate a more rapid and accurate identification of viral pathogens, enabling timely interventions to prevent the spread of infections within marine ecosystems and to other species, including humans. Establishing global marine mortality response networks is crucial to effectively mitigate the spread of viruses. Advancing diagnostic approaches by incorporating molecular techniques will significantly improve our ability to monitor and respond to these events, strengthening One Health surveillance efforts and better protecting marine mammal populations, human health, food safety, food security and overall ecosystem stability.

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CRediT authorship contribution statement

Katie Vigil: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Huiyun Wu:** Writing – review & editing, Visualization, Formal analysis, Data curation. **Tiong Gim Aw:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Data availability

All relevant data are within the manuscript and its Supporting Information files.

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Appendix A. Supplementary data

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