

NATIONAL CARP CONTROL PLAN

WHAT ARE THE CARP VIRUS
BIOCONTROL RISKS AND HOW
CAN THEY BE MANAGED?

Cyprinid herpesvirus 3 and its relevance to humans



This suite of documents contains those listed below.

NCCP TECHNICAL PAPERS

1. Carp biocontrol background
2. Epidemiology and release strategies
3. Carp biocontrol and water quality
4. Carp virus species specificity
5. Potential socio-economic impacts of carp biocontrol
6. NCCP implementation
7. NCCP engagement report
8. NCCP Murray and Murrumbidgee case study
9. NCCP Lachlan case study

NCCP RESEARCH (peer reviewed)

Will carp virus biocontrol be effective?

1. 2016-153: Preparing for Cyprinid herpesvirus 3: A carp biomass estimate for eastern Australia
2. 2018-120: Population dynamics and carp biomass estimates for Australia
3. 2017-148: Exploring genetic biocontrol options that could work synergistically with the carp virus
4. 2016-170: Development of hydrological, ecological and epidemiological modelling
5. 2017-135: Essential studies on Cyprinid herpesvirus 3 (CyHV-3) prior to release of the virus in Australian waters
6. 2020-104: Evaluating the role of direct fish-to-fish contact on horizontal transmission of koi herpesvirus
7. 2019-163 Understanding the genetics and genomics of carp strains and susceptibility to CyHV-3
8. 2017-094: Review of carp control via commercial exploitation

What are the carp virus biocontrol risks and how can they be managed?

9. 2017-055 and 2017-056: Water-quality risk assessment of carp biocontrol for Australian waterways
10. 2016-183: Cyprinid herpesvirus 3 and its relevance to humans
11. 2017-127: Defining best practice for viral susceptibility testing of non-target species to Cyprinid herpesvirus 3
12. 2019-176: Determination of the susceptibility of Silver Perch, Murray Cod and Rainbow Trout to infection with CyHV-3
13. 2016-152 and 2018-189: The socio-economic impact assessment and stakeholder engagement
Appendix 1: Getting the National Carp Control Plan right: Ensuring the plan addresses community and stakeholder needs, interests and concerns
Appendix 2: Findings of community attitude surveys
Appendix 3: Socio-economic impact assessment – commercial carp fishers
Appendix 4: Socio-economic impact assessment – tourism sector
Appendix 5: Stakeholder interviews
Appendix 6: Socio-economic impact assessment – native fish breeders and growers
Appendix 7: Socio-economic impact assessment – recreational fishing sector
Appendix 8: Socio-economic impact assessment – koi hobbyists and businesses
Appendix 9: Engaging with the NCCP: Summary of a stakeholder workshop
14. 2017-237: Risks, costs and water industry response
15. 2017-054: Social, economic and ecological risk assessment for use of Cyprinid herpesvirus 3 (CyHV-3) for carp biocontrol in Australia
Volume 1: Review of the literature, outbreak scenarios, exposure pathways and case studies
Volume 2: Assessment of risks to Matters of National Environmental Significance
Volume 3: Assessment of social risks
16. 2016-158: Development of strategies to optimise release and clean-up strategies
17. 2016-180: Assessment of options for utilisation of virus-infected carp
18. 2017-104: The likely medium- to long-term ecological outcomes of major carp population reductions
19. 2016-132: Expected benefits and costs associated with carp control in the Murray-Darling Basin

NCCP PLANNING INVESTIGATIONS

1. 2018-112: Carp questionnaire survey and community mapping tool
2. 2018-190: Biosecurity strategy for the koi (*Cyprinus carpio*) industry
3. 2017-222: Engineering options for the NCCP
4. NCCP Lachlan case study (in house) (refer to Technical Paper 9)
5. 2018-209: Various NCCP operations case studies for the Murray and Murrumbidgee river systems (refer to Technical Paper 8)



***Cyprinid herpesvirus 3* and its relevance to human health**

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Executive Summary

What the report is about

This report summarises the findings of a systematic literature review that sought to determine the impact on human health of the proposed release of the carp herpesvirus, Cyprinid herpesvirus 3. The literature review indicated that there is no published evidence of a direct zoonotic risk to human health from the virus. There was little published on how humans react emotively to mass mortality events of fish, however it could be reasonably assumed that the public may react adversely to mass mortality events. Rapid removal of the dead fish will mitigate adverse reactions.

Background

In Australia, carp (*Cyprinus carpio*) has been considered an invasive pest species following importation of the Boolarra strain of carp in the 1960s and floods in the 1970s causing the movement from isolated farm dams into the Murray-Darling Basin catchment. Since the mid-2000s, an integrated carp control program has been in development, including using Cyprinid herpesvirus 3 (CyHV-3), a species of Herpesvirales, as a biological control agent.

Recently CyHV-3 has been proposed as a potential biological control method for carp in Australia. While there is evidence evaluating the susceptibility of non-target species, concern remains around the ecological and environment impact of the release of the virus.

Aims/objectives

This report aims to review the published literature to provide a risk assessment of the potential impact on human health from the release of the virus into Australian inland water systems. The report also aims to consider the psychosocial effects of a mass fish die off after the release of the virus in the context of similar events that have previously occurred.

Methodology

A standard literature review was conducted for the purposes of developing background information to lead into the systematic literature review. A systematic review of the literature was conducted to review the relevance of Cyprinid herpesvirus 3 to human health. Standard search strategies were employed to search literary databases including to MEDLINE, PubMed and Google Scholar. Reference lists of included studies were examined for additional potentially useful literature.

The systematic literature search data extraction process involved two persons contemporaneously searching databases using a combination of pre-agreed MeSH subject headings and key words. Discrepancies in the retrieved articles were discussed and resolved by the persons conducting the data extraction. The abstracts of the retrieved studies were screened to identify which papers met the inclusion criteria. Information was extracted from the selected papers for inclusion in the discussion paper.

Results/key findings

Overall, there was no identified published literature in English to support any direct risk to human health from the carp herpesvirus CyHV-3. There is no published evidence to indicate that the virus has or will develop zoonotic capability. There was very little in the published literature on the impact to human health of mass mortality events associated with carp. The main reported impacted on humans due to mass mortality events of fish were in terms of loss of income where the fish in question were a cash crop.

Recommendations

While there is little published in English on how humans react emotively to mass mortality events of carp or other fish, it could be reasonably expected that there is likely to be a public reaction to mass mortality events of carp should the virus be released into Australian inland waterways. It is recommended that any plans for release of the virus also include strategies for management of collection and disposal of the dead fish, together with a communication plan for the general public.

Keywords

Cyprinid herpesvirus 3; human health.

Introduction

In Australia, carp (*Cyprinus carpio*) has been considered an invasive pest species following importation of the Boolarra strain of carp in the 1960s and floods in the 1970s causing the movement from isolated farm dams into the Murray-Darling Basin catchment [1, 2]. Since the mid-2000s, an integrated carp control program has been in development, including using *Cyprinid herpesvirus 3* (CyHV-3), a species of *Herpesvirales*, as a biological control agent [1, 2].

Herpesvirales

Herpesvirales are an order of viruses with linear, double-stranded DNA and an icosahedral capsid structure [3]. Infection with these viruses can cause both lytic and latent infection in a wide variety of hosts including mammals, birds, fish, reptiles, amphibians, and oysters [4, 5]. They tend to be highly species specific viruses and, due to the genetic difference between groups of the virus, are divided into 3 families:

Herpesviridae, *Malacoherpesviridae* and *Alloherpesviridae* [3-6].

Herpesviridae comprise more than 130 characterised viruses across 3 subfamilies that infect reptiles, birds, and mammals [5, 7]. Humans are host to 8 of the herpesviruses within this family [5, 8].

The *Malacoherpesviridae* family includes only 2 recognised herpesviruses that affect bivalve molluscs - the oyster herpesvirus OsHV-1 and the abalone herpesvirus AbHV-1 [9, 10].

The third family within *Herpesvirales*, *Alloherpesviridae*, is divided into 4 genera that infect fish and amphibians: *Batrachovirus*, *Cyprinivirus*, *Ictalurivirus*, and *Salmonivirus* [7]. A number of fish species are affected by these herpesviruses including catfish, carps, sturgeon, eel, and salmonid [7]. *Alloherpesviridae* can result in devastating disease and high mortality in fish populations, with symptoms including haemorrhaging, necrosis, dermatitis, hyperplasia, hypertrophy, and encephalitis [6]. Similar to other families of herpesviruses, *Alloherpesviridae* appear to cause disease only in one species of fish or in closely related members of the same genus [6]. This report will focus specifically on the *Alloherpesviridae* *Cyprinid herpesvirus 3*.

Cyprinid herpesvirus 3

CyHV-3, initially referred to as koi herpesvirus, is a highly contagious virus in the *Alloherpesviridae* family that affects koi and common carp [6, 11, 12]. It is one of the four species in the *Cyprinivirus* genus and is generally detected by cell culture, real-time PCR, nested-PCR, TaqMan PCR, or by capturing viral particles with antibodies followed by loop-mediated isothermal amplification (LAMP) [13-15]. CyHV-3 has a similar morphology to other *Herpesvirales*, with virions diameter of 167-200nm according to the infected cell [16]. Whole genome sequencing has shown that CyHV-3 has the largest recorded genome among the herpesviruses at 295 kb [13, 16].

Outbreaks of CyHV-3 in carp populations were first reported in Germany in 1997 and from the USA and Israel in 1998 [11]. Over the following years, CyHV-3 spread rapidly to other countries, likely due to a combination of factors including global movement of fish due to farming and ornamental trade and inadequate testing and control to the prevent spread of the virus [11, 17]. By 2010, CyHV-3 had been identified in koi or common carp populations everywhere in the world except in Australia, northern Africa, and South America [14].

CyHV-3 has caused mass mortality in carp populations in a number of countries, with mortality rates up to 80-100% [2]. Horizontal transmission of the virus occurs rapidly and generally when water temperatures are between 18 and 28 degrees Celsius [2]. Direct transmission likely results from skin-to-skin contact between infected or carrier fish and non-infected fish, while fish droppings, plankton, sediments, aquatic invertebrates feeding by water filtration, and water are potential sources of indirect transmission [2]. The virus can remain asymptomatic in the carp body for long periods of time when temperature prevents virus replication, with new infection occurring following a change of water temperature to 18-28 degrees Celsius

[14]. CyHV-3 generally enters through the skin and then spreads through the bloodstream to the kidney and other organs [18]. While carp of all ages are susceptible to CyHV-3, juvenile fish (1-3 months, 2.5-6 grams) seem to be more affected than mature fish [14]. There is conflicting evidence about whether larvae (3 days post hatching) are susceptible to infection [2, 14].

Like with other *Herpesvirales*, infection can be latent or lytic [19]. Clinical signs are variable in individual fish and include lethargy, anorexia, folding of the dorsal fin, increased respiration, excess mucus production, uncoordinated swimming, hyperaemia, haemorrhaging on the skin, and necrosis of the gill and internal organs [2, 20]. The development of disease in carp is also variable, but clinical signs generally appear 2 to 3 days post infection and mortalities 6 to 8 days post infection [2, 18].

Due to the high mortality rate, CyHV-3 has been detrimental to the production of carp for food, resulted in financial and economic losses in the koi and common carp ornamental and farming industries. It is a recognised as an economically and sociologically important pathogen and is a disease notifiable to the World Organisation for Animal Health (OIE) and the European Union (EU) [14, 15, 21].

Recently CyHV-3 has been proposed as a potential biological control method for carp in Australia [22]. While there is evidence evaluating the susceptibility of non-target species [1], concern remains around the ecological and environment impact of the release of the virus [23]. This report aims to review the published literature to provide a risk assessment of the potential impact on human health from the release of the virus into Australian inland water systems. The report also aims to consider the psychosocial effects of a mass fish die off after the release of the virus in the context of similar events that have previously occurred.

Objectives

This project was undertaken at the National Centre for Epidemiology and Population Health (NCEPH) at the Australian National University for the Fisheries Research Development Corporation. This report provides an assessment based on the available published literature of the relevance to human health from the release of the *Cyprinid herpesvirus 3* into Australian inland water system. The relevance to human health includes: (1) risk of direct transmission and (2) impacts of mass mortality events.

Method

Background literature

A standard literature review was conducted for the purposes of developing background information to lead into the systematic literature review. A search of PubMed was conducted using the search terms: ("Cyprinid herpesvirus" OR "koi herpesvirus" OR "CyHV-3" OR "carp herpesvirus"). The search produced 264 publications of which the most relevant 50 were utilised for the background section of this report.

Zoonoses literature

An additional standard literature review was conducted to provide a summary analysis on zoonoses more generally. The initial search terms used in PubMed of ("zoonotic AND virus") produced over 4000 references, most of which were on the topic of influenza viruses. Narrowing the search terms to: ("fish" AND "virus" AND "zoonoses" AND "health") reduced the list to 13, of which most were related to swine influenza viruses despite the restricted search terms. A more targeted search to obtain information relating to the zoonotic potential of CyHV-3 was conducted using the reference lists of the publications retrieved in the background literature search.

Systematic review of the relevance of CyHV-3 to humans

Using SuperSearch, a systematic review was conducted using the terms: (cyhv-3 OR cyprinid herpesvirus 3) AND ((ecolog* OR environ* OR human*) AND impact*). This combination of terms sought to find any publications that would reference CyHV-3 virus and its impact on either ecology, the environment or humans (including human health).

When the search terms were limited to the 'title' AND 'abstract' fields only of the SuperSearch, a total of zero papers were retrieved. When the search terms were limited only to the abstract field, a total of 4 papers were retrieved. When further expanded to include 'any field', a total of 186 items were retrieved.

The resulting literature from the search was evaluated by two persons, using the same exclusion/inclusion criteria, to identify which papers were of relevance. Exclusion criteria included papers of a biochemical nature or on genetics research. Selected papers were all in restricted to English language with the exception of one paper in French. Papers published in other languages were not included. A total of 16 papers were deemed sufficiently relevant, with a further six being of potential relevance. The search also uncovered nine further papers related to the background of the virus that had not been identified during the initial background literature search.

In comparison with SuperSearch, using the same search terms in PubMed produced 2 papers and using SCOPUS resulted in 8 papers being identified. These searches were clearly more specific in output but resulted in fewer useful papers being identified. Both of the PubMed papers were captured by the SuperSearch, and seven of the SCOPUS papers has also previously been identified. The eighth paper was new to the search, and was considered relevant. This highlights the imperfections of search strategies and the need to be flexible when searching unusual topics that do not neatly fit into expected combinations of MeSH search terms.

The reference lists of retrieved publications were scanned to identify other potentially useful publications.

Only articles in English were considered for the review with the exception of one article in French.

Systematic review on mass mortality events and psychosocial impact on humans

A second SuperSearch was conducted using the terms: ("mass animal death*" OR "mass fish death*" OR "animal die-off" OR ("fish*die-off" OR "fish die off" OR "animal* die-off" OR "animal* die off") AND

(psychosocial* OR trauma* OR impact*). This sought to identify the publications on reactions from people to mass mortality events in animals. The inclusion of the term “fish kill*” did not change the search results.

When the search terms were limited to ‘Title’ AND ‘Abstract’, a total of 19 papers or media articles were retrieved. Every item was on the topic of mass fish deaths due to pollution or other events, and primarily in Asian countries. When expanded to only ‘Abstract’, a total of 101 items were identified. When the terms were included for ‘any field’, 1569 items were retrieved. A quick scan indicated that most were not relevant, and hence for this search the results were taken from using the search terms in the ‘Abstract’ field.

As per the first SuperSearch of the literature, two persons sifted the resultant items with exclusion and inclusion criteria. A total of 31 papers and media articles were deemed sufficiently relevant. As per previously, the reference lists of retrieved publications were scanned to identify other potentially useful publications.

Further information is provided at Appendix 1 on the databases used for the literature searches and the systematic review process.

Results and Discussion

Zoonotic risk of CyHV-3 to humans

Overall, there was no identified literature in English to support any direct risk to human health from the carp herpesvirus CyHV-3. While some viruses have achieved the ability to transmit from animals to humans, and in some cases the ability to then transmit human to human, there is no evidence to suggest that the carp herpesvirus has this capability or will develop this ability. While the order of Herpesvirales does include several important human pathogens, including herpes simplex viruses 1 and 2 as well as Kaposi's sarcoma-associated herpesvirus, the three distinct groups of viruses that form the three family levels of classification within the order are considered to be 'only tenuously related to each other' [24, 25]. As per the updated taxonomy of the herpesviruses [3], Herpesviridae retains the viruses of mammals, birds and reptile; Alloherpesviridae incorporates fish and frog viruses; and Malacoherpesviridae contains a bivalve virus. Such taxonomic separation noting the grouping of host species would indicate it unlikely for the CyHV-3 virus to develop the ability to transmit to and create disease in humans. Further supporting this are the studies from McColl [26, 27] indicate high species-specificity, even with fish.

Further it is important to note the temperature permissive range of CyHV-3, that being the temperature range at which the virus can survive. For CyHV-3, the permissive temperature range is 18 to 28° C [28, 29]. Temperatures outside this range do not support growth of the virus. As such the virus cannot infect mammals which have body temperatures higher than 28° C.

CyHV-3, like many pathogens, is capable of infecting only a limited range of host organisms, that being carp and koi, but excluding humans. As such the transmission risk to CyHV-3 would appear to be less than negligible with there being no identified published evidence of a transmission risk to humans.

Environmental and ecological impacts and water-user concerns

Water-user concerns may relate to the risk of transmission but also the ecological and environment impact of the biomass of rotting fish as well as the visual impact resulting for a mass mortality event associated with carp. There was very little in the published literature or media on such events, although a few media items noted the importance of keeping beaches and waterways clean.

It is noted that there are possible concerns about impact of oxygen depletion due to MME of fish and rotting biomass. However, there was little in the literature on the impact of oxygen depletion in waterways as a result of a fish MME. It was instead reported for the the reverse; that is, low oxygen levels in waterways leading to mass deaths of fish MME. As such, it is not possible to provide comment on the direct impacts on human health from poor water quality nor from the impact of mass dead or decaying fish.

Psychosocial impact of mass mortality events

There is very little published in peer-reviewed journals on the topic of psychosocial impacts on humans of mass mortality events of animals. This is even true for those animals more readily anthropomorphised and more closely related to humans, such as whales and dolphins. The literature search retrieved a small number of papers on the subject, despite there being numerous events reported in the media and the published literature. Notably these papers were on the impact of death of a companion animal with which the human had an established relationship [30, 31].

While published studies have mapped the frequency, location and type of mass mortality events involving animals [32], there was little published on how people and populations respond or react to these events outside of concerns for animals of monetary value such as fish deaths affecting fisherman and herding animal deaths for shepherds [33, 34]. There was some concern reported in media articles regarding the possible increasing scale and frequency of the events, but this was more in the context of what this might signify in terms of global climate health [35-37].

The few media items on mass mortality events involving birds that were uncovered as part of the literature search reported people being distressed by the scenes of numerous injured and dying animals [38, 39]. The fact that the birds died in a visible urban environment likely added to the emotive reaction of the public. A lesser reaction could reasonably be expected for a similar event in a remote location out of the public eye.

The main reported reaction of humans to MME specifically involving fish is in terms of reaction to loss of income where the fish in question are a cash crop. MME involving fish were more likely to report on impact on the income of fisherman rather than any other impact. That is, any published aspects of ecology and environment were with regard to causality of the MME, rather than on what effect the MME might have on the environment due to biomass of dead fish.

It is reasonable to assume that children may experience distress when observing mass fish die-off events. However, no published literature was retrieved on this specific topic, with the most similar published material being on children's reactions to death of a companion animal.

Mass mortality events of carp and koi

The common carp, *Cyprinus carpio*, are an important food fish in some parts of the world. *C. carpio koi*, a subspecies of the common carp, are a popular ornamental fish. These fish have been extensively cultivated and transported and are now distributed throughout the world. Both fish are susceptible to CyHV-3.

Mass mortality events relating to CyHV-3 have been reported in numerous countries. The virus was first described in Israel and the USA in 1998 [40]. Since the first isolation of the virus, KHV has been found to have a nearly widespread distribution. It has been the causative agent for mortalities among common carp and koi in many countries in Europe as well as in South Africa, Asia, the USA and Canada [17, 28]. The extensive spread of the virus has been thought to be due to various factors including global trade in ornamental and aquarium fish, historic short-comings in diagnostic methods and lack of legislation to control and prevent incursion of the virus [17].

In terms of biomass and ecological impact of mass mortality events of carp, accounts from events from other countries are useful in understanding the context of what might occur in the Australian environment. Accounts from Canada report that within a relatively short period of time during the 2007 June-July spawning period for common carp, the mortality of carp may have exceeded 24,000 fish across nine affected lakes in south-central Ontario [17]. It is estimated that 90 tonnes of carp were disposed of at local landfills, equating to between 13,000 and 24,000 fish. These estimates did not include the carp that were disposed of on private land or those that decomposed in the lake. It was noted that while the fish died during this period of time, it was not known how long the fish had been infected. It was also noted that concurrent disease might have lowered the amount of virus needed to kill the fish, or that other concurrent bacterial infections might have been the primary cause of death after being debilitated by CyHV-3, indicating a synergistic action between the pathogens.

The events in Canada in 2007 and again in 2008 shared two important common features with other KHV-Associated wild carp mortality events. Firstly, CyHV-3 outbreaks in wild carp populations are temperature dependent with the range being 18-26° C. Secondly, only common carp have been affected, a finding supported by the research of McColl [1] who, having conducted infectivity tests with a variety of non-target fish species, concluded that that spill-over infections and species jump are highly unlikely with CyHV-3. found that. It is important to note that the presence of the virus in the waterways does not always lead to mass mortality events, with the critical predisposing factors being unclear [17]. However, the synergistic effects of other pathogens exacerbating the impact of the virus are a recognised factor in terms of magnitude of the die-off event.

In Japan, where koi are an important ornamental commodity and common carp are extensively farmed, the invasion by CyHV-3 of freshwater systems has caused large mass mortality events in wild carp populations. From April to July of 2004, it is estimated that more than 100,000 fish died in Lake Biwa, representing potentially 70% of the fish in the lake [28]. No further mass mortality events have been recorded from Lake Biwa, with the fish that survived the initial infection having developed antibodies and enhanced resistance to the virus [41].

Limitations

The major limitation of this project is that while the intent was to follow the systematic review process faithfully, little primary research existed on the topic to make conducting the review worthwhile and fruitful. This has been previously identified as an issue for systematic reviews [42]. In the situation of this project, while it was thought during the project proposal phase that there would be literature – either published articles or media – on the potential impacts of the carp herpesvirus to the environment, ecology or to human sensibilities, there in fact was very little. This was surprising given the world-wide reach of the virus and the fact that the virus is also present in countries where carp are native and have value as a cash crop. We can only report that there is a lack of high-quality evidence to support concerns about the potential for impact on humans of the carp herpesvirus and hence little direct relevance to human health.

The literature search was also limited to English and French only, due to the language capabilities of the authors. This is particularly relevant given that CyHV3 has significant impacts primarily in non-English speaking areas and countries including, for example, Japan, China and Indonesia.

Conclusion

The key findings of this series of literature searches include:

1. There is no published evidence of a risk that the virus has zoonotic potential.
2. Even in countries where carp are valued, there is little published in English on how humans react emotively to mass mortality events of carp or other fish. The reported human reactions were with regard to income loss for fisherman when fish had commercial value.
3. It could be reasonably expected that in certain locations – such as lakes and rivers that intersect urban environments – there is likely to be a public reaction to mass mortality events of carp. Rapid clean-up of the dead fish will mitigate adverse reactions from the public and in the media.
4. The virus does not have a 100% kill rate in naturally-occurring mass mortality events of carp, and those fish that survive the initial infection have immunity.
5. Higher kill rates are associated with carp spawning season and co-infections by other pathogens.
6. Further information could be obtained by searching literature in languages other than English.

Recommendations

While there was little in the published literature in English on the impact on human health of a mass die-off of carp should the virus be released into Australian inland waterways, it could be reasonably assumed that the public, particularly children, may react with distress to large numbers of dead and dying fish in visible or recreational waterways. It is recommended that any plans for release of the virus also include strategies for management of collection and disposal of the dead fish, together with a communication plan for the general public.

References

1. McColl, K.A., *Final report: Phase 3 of the carp herpesvirus project (CyHV-3)*, 2016, PetSmart Toolkit publication. Invasive Animals Cooperative Research Centre: Canberra, Australia.
2. Boutier, M., et al., *Cyprinid Herpesvirus 3: An Archetype of Fish Alloherpesviruses*. Adv Virus Res, 2015. **93**: p. 161-256.
3. Davison, A., et al., *The Order Herpesvirales*. Arch Virol, 2009. **154**(1): p. 171-177.
4. Osterrieder, K., ed. *Cell Biology of Herpes Viruses*. Advances in Anatomy, Embryology and Cell Biology 2017, Springer International Publishing: Cham, Switzerland. 223.
5. Brown, J.C. and Newcomb, W.W., *Herpesvirus capsid assembly: insights from structural analysis*. Current Opinion in Virology, 2011. **1**(2): p. 142-149.
6. Hanson, L., Dishon, A., and Kotler, M., *Herpesviruses that infect fish*. Viruses, 2011. **3**(11): p. 2160-91.
7. Hanson, L., et al., *Chapter 9 - Alloherpesviruses of Fish*, in *Aquaculture Virology*, F.S.B. Kibenge and M. Godoy, Editors. 2016, Academic Press. p. 153-172.
8. Whitley, R.J., *Chapter 68: Herpesviruses*, in *Medical Microbiology*, S. Baron, Editor 1996, University of Texas Medical Branch at Galveston: Galveston (TX).
9. Savin, K.W., et al., *A neurotropic herpesvirus infecting the gastropod, abalone, shares ancestry with oyster herpesvirus and a herpesvirus associated with the amphioxus genome*. Virology Journal, 2010. **7**(1): p. 308.
10. Waltzek, T.B., et al., *Phylogenetic relationships in the family Alloherpesviridae*. Dis Aquat Organ, 2009. **84**(3): p. 179-94.
11. El-Matbouli, M., Rucker, U., and Soliman, H., *Detection of Cyprinid herpesvirus-3 (CyHV-3) DNA in infected fish tissues by nested polymerase chain reaction*. Dis Aquat Organ, 2007. **78**(1): p. 23-8.
12. Avarre, J.C., et al., *Investigation of Cyprinid herpesvirus-3 genetic diversity by a multi-locus variable number of tandem repeats analysis*. J Virol Methods, 2011. **173**(2): p. 320-7.
13. Davison, A.J., et al., *Comparative genomics of carp herpesviruses*. J Virol, 2013. **87**(5): p. 2908-22.
14. Michel, B., et al., *Cyprinid herpesvirus 3*. Emerg Infect Dis, 2010. **16**(12): p. 1835-43.
15. Gotesman, M., et al., *CyHV-3: the third cyprinid herpesvirus*. Dis Aquat Organ, 2013. **105**(2): p. 163-74.
16. Rakus, K., et al., *Cyprinid herpesvirus 3: an interesting virus for applied and fundamental research*. Vet Res, 2013. **44**: p. 85.
17. Garver, K.A., et al., *Mass mortality associated with koi herpesvirus in wild common carp in Canada*. J Wildl Dis, 2010. **46**(4): p. 1242-51.
18. McDermott, C. and Palmeiro, B., *Selected emerging infectious diseases of ornamental fish*. Vet Clin North Am Exot Anim Pract, 2013. **16**(2): p. 261-82.
19. Eide, K.E., et al., *Investigation of koi herpesvirus latency in koi*. J Virol, 2011. **85**(10): p. 4954-62.
20. Cheng, L., et al., *Koi herpesvirus epizootic in cultured carp and koi, Cyprinus carpio L., in Taiwan*. J Fish Dis, 2011. **34**(7): p. 547-54.
21. Engelsma, M.Y., et al., *Detection of novel strains of cyprinid herpesvirus closely related to koi herpesvirus*. Dis Aquat Organ, 2013. **107**(2): p. 113-20.
22. Saunders, G., et al., *Modern approaches for the biological control of vertebrate pests: An Australian perspective*. Biological Control, 2010. **52**(3): p. 288-295.
23. Lighten, J. and van Oosterhout, C., *Biocontrol of common carp in Australia poses risks to biosecurity*. Nature Ecology & Evolution, 2017. **1**(0087).
24. Davison, A.J., *Channel catfish virus: a new type of herpesvirus*. Virology, 1992. **186**(1): p. 9-14.
25. Davison, A.J., *Evolution of the herpesviruses*. Vet Microbiol, 2002. **86**(1-2): p. 69-88.
26. McColl, K.A., Cooke, B.D., and Sunarto, A., *Viral biocontrol of invasive vertebrates: Lessons from the past applied to cyprinid herpesvirus-3 and carp (Cyprinus carpio) control in Australia*. Biological Control, 2014. **72**: p. 109-117.
27. McColl, K.A., Sunarto, A., and Holmes, E.C., *Cyprinid herpesvirus 3 and its evolutionary future as a biological control agent for carp in Australia*. Virol J, 2016. **13**(1): p. 206.
28. Uchii, K., et al., *Distribution of the introduced cyprinid herpesvirus 3 in a wild population of common carp, Cyprinus carpio L.* J Fish Dis, 2009. **32**(10): p. 857-64.

29. Gilad, O., et al., *Molecular comparison of isolates of an emerging fish pathogen, koi herpesvirus, and the effect of water temperature on mortality of experimentally infected koi*. J Gen Virol, 2003. **84**(Pt 10): p. 2661-7.
30. Amiot, C.E. and Bastian, B., *Solidarity with Animals: Assessing a Relevant Dimension of Social Identification with Animals*. PLoS One, 2017. **12**(1): p. e0168184.
31. Eckerd, L.M., Barnett, J.E., and Jett-Dias, L., *Grief following pet and human loss: Closeness is key*. Death Stud, 2016. **40**(5): p. 275-82.
32. Fey, S.B., et al., *Recent shifts in the occurrence, cause, and magnitude of animal mass mortality events*. Proc Natl Acad Sci U S A, 2015. **112**(4): p. 1083-8.
33. Chua, G. *AVA support for farmers hit by mass fish deaths*. in *The Straits Times* 2014 14 February, Singapore Press Holdings Limited: Singapore.
34. *Vietnam: Aid in rice, cash, proposed for fishermen hit by mass fish deaths*. in *Asia News Monitor* 2016 20 May, Thai News Service Group: Bangkok.
35. Gorman, J. *Animals die in large numbers, and researchers scratch their heads*. in *New York Times (Online)* 2016 18 Jan, New York Times Company: New York.
36. Kaplan, S. *In pitiful animal die-offs across the globe — from antelopes to bees to seabirds — climate change may be culprit*. in *Washington Post - Blogs* 2016 WP Company LLC d/b/a The Washington Post: Washington DC.
37. Nerenberg, A. *Those mass deaths sign of the times; we've been warned*. in *The Gazette* 2011 14 June, Informart: Montreal.
38. *Aflockalypse reaches Italy as turtle doves fall from the sky [Eire Region]*. in *Daily Mail* 2011 8 January, Solo Syndication: London.
39. Lang, O. *The mystery of mass bird deaths*. BBC News 2011; Available from: <http://www.bbc.com/news/world-us-canada-12135380>.
40. Hedrick, R.P., et al., *A Herpesvirus Associated with Mass Mortality of Juvenile and Adult Koi, a Strain of Common Carp*. Journal of Aquatic Animal Health, 2000. **12**(1): p. 44-57.
41. Ronen, A., et al., *Efficient vaccine against the virus causing a lethal disease in cultured Cyprinus carpio*. Vaccine, 2003. **21**(32): p. 4677-84.
42. Averis, A. and Pearson, A., *Filling the gaps: identifying nursing research priorities through the analysis of completed systematic reviews*. JBI Reports, 2003. **1**(3): p. 49-126.
43. Anlezark, A., Dawe, S., and Hayman, S., *An aid to systematic reviews of research in vocational education and training in Australia*, 2005, National Centre for Vocational Education Research and the Australian National Training Authority: Adelaide SA.

Appendix 1

This appendix provides further information on the databases used in the literature searches and systematic review processes.

Systematic review

The aim of a systematic review is to develop a concise summary of the best available evidence that addresses a clearly defined question in a particular area of interest [43]. A systematic review uses explicit and rigorous methods to identify, critically appraise and synthesise relevant research around a specific research question. As the process is criterion-based and follows a series of standardised and transparent steps, the review process can be replicated by another researcher working separately and independently. A systematic review is undertaken by a team of at least two persons, or more as needed depending upon the scope of the research question and the anticipated volume of research articles that may be uncovered. The outcome of the process is collective and reduces potential bias, therefore adding rigour to the research findings.

SuperSearch (Proquest)

SuperSearch is a name given by the ANU Library to the Summon® Service from the vendor Proquest. Searching SuperSearch provides results from Scopus, MedLine (Medline from Ovid), Web of Science, amongst others from the databases that ANU Library subscribes to and therefore has fulltext access. It is a web-scale discovery tool that searches the contents of multiple library catalogues and databases simultaneously. "Web-scale" refers to the attempt to match the kind of broad and deep search familiar to Google and other web search tools. SuperSearch uses an index of keywords to formulate search results from the ANU subscription content in the first instance. The Summon Index contains over 2 billion items. Content is indexed at the record level (full-text, metadata, or both) from information provided directly by publishers and content providers.

However, SuperSearch does not offer the more sophisticated search options that may be found when accessing the native interface for the individual databases and therefore some results may be missed. To overcome this, supplemental searching of the databases directly is recommended.

Scopus

Scopus is the largest abstract and citation database of peer-reviewed research literature with more than 20,500 titles from more than 5,000 international publishers. It includes all MEDLINE content as well as 30million+ more records. The scope is beyond just biomedical content and includes some conference papers.

Scopus enables the capacity to limit or exclude the displayed search results to specified keywords selected in the limits of the search, as well as the capacity to sort by cited references.

Proquest

ProQuest contains cross disciplinary and allied health content, including Sociological Abstracts which indexes and provides abstracts for international literature in sociology and related disciplines in the social and behavioural sciences. Included are journal articles, books, book chapters, dissertations, and conference papers, as well as citations to book reviews from 1952 to the present. ProQuest also contains newspaper content.

PubMed

PubMed comprises more than 23 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites.

PubMed searches that are limited to MeSH controlled vocabulary or the MEDLINE subset will only produce MEDLINE citations in the results. Using a broader keyword search results in a more extensive although less controlled set of literature.

Factiva

Factiva is a global news database of nearly 33,000 premium sources, including licensed publications and influential websites. News and business information is provided in 22 languages from 118 countries. Source documents include newspapers, magazines, newswires, media programs, websites, company reports and images from Reuters and Knight Ridder.

Appendix 2

List of articles reviewed

1. Carp were introduced into our waters more than 100 years...[Derived Headline]. Stock Journal. 2017 27 April 2017.
2. Amiot CE, Bastian B. Solidarity with Animals: Assessing a Relevant Dimension of Social Identification with Animals. PLoS One. 2017;12(1):e0168184.
3. Anlezark A, Dawe S, Hayman S. An aid to systematic reviews of research in vocational education and training in Australia. 2005.
4. Averis A, Pearson A. Filling the gaps: identifying nursing research priorities through the analysis of completed systematic reviews. JBI Reports. 2003;1(3):49-126.
5. Brown OK, Symons DK. "My pet has passed": Relations of adult attachment styles and current feelings of grief and trauma after the event. Death studies. 2016;40(4):247-55.
6. Davison AJ. Channel catfish virus: a new type of herpesvirus. Virology. 1992;186(1):9-14.
7. Davison AJ. Evolution of the herpesviruses. Veterinary microbiology. 2002;86(1-2):69-88.
8. Eckerd LM, Barnett JE, Jett-Dias L. Grief following pet and human loss: Closeness is key. Death studies. 2016;40(5):275-82.
9. Fey SB, Siepielski AM, Nussle S, Cervantes-Yoshida K, Hwan JL, Huber ER, et al. Recent shifts in the occurrence, cause, and magnitude of animal mass mortality events. Proceedings of the National Academy of Sciences of the United States of America. 2015;112(4):1083-8.
10. Gilad O, Yun S, Adkison MA, Way K, Willits NH, Bercovier H, et al. Molecular comparison of isolates of an emerging fish pathogen, koi herpesvirus, and the effect of water temperature on mortality of experimentally infected koi. The Journal of general virology. 2003;84(Pt 10):2661-7.
11. Hedrick RP, Gilad O, Yun S, Spangenberg JV, Marty GD, Nordhausen RW, et al. A Herpesvirus Associated with Mass Mortality of Juvenile and Adult Koi, a Strain of Common Carp. Journal of Aquatic Animal Health. 2000;12(1):44-57.
12. Rakus KL, Irnazarow I, Adamek M, Palmeira L, Kawana Y, Hirono I, et al. Gene expression analysis of common carp (*Cyprinus carpio* L.) lines during Cyprinid herpesvirus 3 infection yields insights into differential immune responses. Developmental and comparative immunology. 2012;37(1):65-76.
13. Ronen A, Perelberg A, Abramowitz J, Hutoran M, Tinman S, Bejerano I, et al. Efficient vaccine against the virus causing a lethal disease in cultured *Cyprinus carpio*. Vaccine. 2003;21(32):4677-84.
14. WA: Tens of thousands of fish found dead in WA river. AAP General News Wire. 2005 21 March.
15. Maldives mass fish deaths attributed to bacterial infection. BBC Monitoring South Asia. 2008 21 May.
16. Lake aeration plan to cut fish deaths. The Northern Times. 2010 15 October.
17. Oceans on brink of catastrophe. The Independent. 2011 21 June.
18. Are mass deaths something fishy or just nature? The Northern Territory News. 2011 28 January.
19. Those mass deaths sign of the times; we've been warned. The Gazette. 2011 14 June.
20. Aflockalypse reaches Italy as turtle doves fall from the sky [Eire Region]. Daily Mail. 2011 8 January.
21. Waterways likely to return to their pre-flood glory in weeks. Sunshine Coast Daily. 2013 4 February.
22. Mass fish deaths off Caspian Sea Kazakhstan's coast - environmentalists. Interfax: Kazakhstan General Newswire. 2014 19 May.
23. Keep our precious beaches clean. Geelong Advertiser. 2015 13 Nov.
24. The Environmental Protection Authority believes recent barway work at the...[Derived Headline]. The Examiner. 2015 7 July.
25. Notice of availability of the draft environmental impact statement for the long-term plan to protect adult salmon in the Lower Kalmath River. Federal Information & News Dispatch, Inc. 2016.
26. Vietnamese activists, bloggers decry lack of government transparency over mass fish kill. Federal

Information & News Dispatch, Inc. 2016.

27. Roundup: Vietnam facing continuous environmental incidents. Xinhua News Agency - CEIS. 2016 19 June.
28. Vietnam: Sea pollution-affected fishermen in Thua Thien-Hue get support. Asia News Monitor. 2016 11 Aug.
29. Vietnam: Central marine environment not yet need clean-up technology. Asia News Monitor. 2016 1 September.
30. Vietnam: Aid in rice, cash, proposed for fishermen hit by mass fish deaths. Asia News Monitor. 2016 20 May.
31. The Murray cod's mortal enemy has met its nemesis. Environmental scientist...[Derived Headline]. The Land. 2016 10/27/
2016 Oct 27.
32. Coordinator to drive carp plan. The Burdekin Advocate. 2016 10/28/
2016 Oct 28.
33. The \$15 million Murray Darling Basin-wide carp cull initiative is...[Derived Headline]. The Land. 2016 11/03/
2016 Nov 03.
34. The source of our waterways. The Advertiser. 2016 12/31/
2016 Dec 31.
35. Environment; Save the Sound launches unified water study of Long Island Sound. Chemicals & Chemistry. 2017 2 June.
36. The corporation in charge of plans to release a herpes...[Derived Headline]. The Dungog Chronicle. 2017 18 Jan 2017.
37. Australian scientists reject claims carp eradication plan will be catastrophe. Xinhua News Agency-CEIS. 2017 23 Feb 2017.
38. Immunology - Immunoproteins; Study Findings on Immunoproteins Are Outlined in Reports from Australian Animal Health Laboratory (Transcriptomic analysis of common carp anterior kidney during Cyprinid herpesvirus 3 infection: Immunoglobulin repertoire and homologue ...). Science Letter. 2017 3 Mar 2017.
39. Australia: Controlling feral fish with Carp Love 200C campaign. MENA Report. 2017 26 Aug 2016.
40. Herpesvirus; Findings from University of Sydney Update Understanding of Herpesvirus (Cyprinid herpesvirus 3 and its evolutionary future as a biological control agent for carp in Australia). Life Science Weekly. 2017:3801.
41. Researchers warn of serious risks from Australia carp control plans [press release]. European Union News2017.
42. Plan to eradicate invasive carp from Australia's rivers could harm native species: expert. Xinhua News Agency - CEIS. 2017 07/02/
2017 Jul 02.
43. YANGTZE RIVER FISHERIES RESEARCH INSTITUTE, CHINESE ACADEMY OF FISHERY SCIENCES; Patent Issued for Cyprinid Herpesvirus II-Sensitive Brain Tissue Cell Line of Carassius Auratus Gibelio and Establishing Method and Use (USPTO 9598671). Journal of Engineering. 2017:3920.
44. Letters to the editor. The Murray Valley Standard. 2017 05/04/
2017 May 04.
45. Adamek M, Rakus KL, Brogden G, Matras M, Chyb J, Hirono I, et al. Interaction between type I interferon and Cyprinid herpesvirus 3 in two genetic lines of common carp *Cyprinus carpio*. Diseases of aquatic organisms. 2014;111(2):107-18.
46. Adamek M, Syakuri H, Harris S, Rakus KL, Brogden G, Matras M, et al. Cyprinid herpesvirus 3 infection disrupts the skin barrier of common carp (*Cyprinus carpio* L.). Veterinary microbiology. 2013;162(2-4):456-70.
47. Adler T. The expiration of respiration. Science News. 1996 10 Feb.
48. Arvin A, Campadelli-Fiume G, Mocarski E, Moore PS, Roizman B, Whitley RJ, et al., editors.

Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis. Cambridge: Cambridge University Press; 2007.

49. Avarre JC, Madeira JP, Santika A, Zainun Z, Baud M, Cabon J, et al. Investigation of Cyprinid herpesvirus-3 genetic diversity by a multi-locus variable number of tandem repeats analysis. *Journal of virological methods*. 2011;173(2):320-7.
50. Avarre JC, Santika A, Bentenni A, Zainun Z, Madeira JP, Maskur M, et al. Spatio-temporal analysis of cyprinid herpesvirus 3 genetic diversity at a local scale. *Journal of fish diseases*. 2012;35(10):767-74.
51. Barr E. Disease to assist carp cull. *The Express*. 2017 30 May 2017.
52. Baumer A, Fabian M, Wilkens MR, Steinhagen D, Runge M. Epidemiology of cyprinid herpesvirus-3 infection in latently infected carp from aquaculture. *Diseases of aquatic organisms*. 2013;105(2):101-8.
53. Becker JA, Tweedie A, Rimmer A, Landos M, Lintermans M, Whittington RJ. Incursions of Cyprinid herpesvirus 2 in goldfish populations in Australia despite quarantine practices. *Aquaculture*. 2014;432:53-9.
54. Bergmann SM, Monro ES, Kempter J. Can water disinfection prevent the transmission of infectious koi herpesvirus to naive carp? - a case report. *Journal of fish diseases*. 2017;40(7):885-93.
55. Bergmann SM, Sadowski J, Kielpinski M, Bartłomiejczyk M, Fichtner D, Riebe R, et al. Susceptibility of koi x crucian carp and koi x goldfish hybrids to koi herpesvirus (KHV) and the development of KHV disease (KHVD). *Journal of fish diseases*. 2010;33(3):267-72.
56. Boutier M, Ronsmans M, Rakus K, Jazowiecka-Rakus J, Vancsok C, Morvan L, et al. Cyprinid Herpesvirus 3: An Archetype of Fish Alloherpesviruses. *Advances in virus research*. 2015;93:161-256.
57. Brown JC, Newcomb WW. Herpesvirus capsid assembly: insights from structural analysis. *Current Opinion in Virology*. 2011;1(2):142-9.
58. Brown OK, Symons DK. "My pet has passed": Relations of adult attachment styles and current feelings of grief and trauma after the event. *Death studies*. 2016;40(4):247-55.
59. Cahu C. Les grands défis de l'aquaculture en France et dans le monde. *Responsabilité & Environnement*. 2013;70(24-30):95.
60. Casey G. Carp dumping causing a smell. *The Times*. 2017 03/16/2017 Mar 16.
61. Chapman S. Should we release the deadly carp virus into our rivers and water supplies? *The Murray Valley Standard*. 2016 16 Aug.
62. Cheng L, Chen CY, Tsai MA, Wang PC, Hsu JP, Chern RS, et al. Koi herpesvirus epizootic in cultured carp and koi, *Cyprinus carpio* L., in Taiwan. *Journal of fish diseases*. 2011;34(7):547-54.
63. Chesson T. Clearer waters ahead for River Murray. *The Advertiser*. 2017 04/04/2017 Apr 04.
64. Chua G. AVA support for farmers hit by mass fish deaths. *The Straits Times*. 2014 14 February.
65. Connery G. Carp are the target of the ACT government's catch-and-destroy mission...[Derived Headline]. *The Canberra Times*. 2017 04/06/2017 Apr 06.
66. Cornwell ER, Anderson GB, Wooster GA, Getchell RG, Groocock GH, Casey JW, et al. Low prevalence of Cyprinid Herpesvirus 3 Found in common carp (*Cyprinus carpio carpio*) collected from nine locations in the Great Lakes. *Journal of wildlife diseases*. 2012;48(4):1092-6.
67. Danek T, Kalous L, Vesel T, Krasova E, Reschova S, Rylkova K, et al. Massive mortality of Prussian carp *Carassius gibelio* in the upper Elbe basin associated with herpesviral hematopoietic necrosis (CyHV-2). *Diseases of aquatic organisms*. 2012;102(2):87-95.
68. Davidovich M, Dishon A, Ilouze M, Kotler M. Susceptibility of cyprinid cultured cells to cyprinid herpesvirus 3. *Archives of virology*. 2007;152(8):1541-6.
69. Davis B-J. Public to get a say prior to herpes release. *Newcastle Herald*. 2017 01/17/2017 Jan 17.
70. Davis B-J. Carp cooking the bomb. *Maitland Mercury*. 2017 01/30/2017 Jan 30.

71. Davis B-J. MP backs herpes, but not timeline. Maitland Mercury. 2017 06/05/2017 Jun 05.
72. Davis B-J. COPY Holy carp, it tastes good. The Dungog Chronicle. 2017 02/01/2017 Feb 01.
73. Davison A, Eberle R, Ehlers B, Hayward G, McGeoch D, Minson A, et al. The Order *Herpesvirales*. Archives of virology. 2009;154(1):171-7.
74. Davison AJ, Kurobe T, Gatherer D, Cunningham C, Korf I, Fukuda H, et al. Comparative genomics of carp herpesviruses. Journal of virology. 2013;87(5):2908-22.
75. Dishon A, Davidovich M, Ilouze M, Kotler M. Persistence of cyprinid herpesvirus 3 in infected cultured carp cells. Journal of virology. 2007;81(9):4828-36.
76. Druce A. Cash in carp cull clean-up? The Land. 2016 08/25/2016 Aug 25.
77. Eide KE, Miller-Morgan T, Heidel JR, Kent ML, Bildfell RJ, Lapatra S, et al. Investigation of koi herpesvirus latency in koi. Journal of virology. 2011;85(10):4954-62.
78. El-Matbouli M, Rucker U, Soliman H. Detection of Cyprinid herpesvirus-3 (CyHV-3) DNA in infected fish tissues by nested polymerase chain reaction. Diseases of aquatic organisms. 2007;78(1):23-8.
79. El-Matbouli M, Saleh M, Soliman H. Detection of cyprinid herpesvirus type 3 in goldfish cohabiting with CyHV-3-infected koi carp (*Cyprinus carpio koi*). The Veterinary record. 2007;161(23):792-3.
80. El-Matbouli M, Soliman H. Transmission of Cyprinid herpesvirus-3 (CyHV-3) from goldfish to naive common carp by cohabitation. Research in veterinary science. 2011;90(3):536-9.
81. Engelsma MY, Way K, Dodge MJ, Voorbergen-Laarman M, Panzarin V, Abbadi M, et al. Detection of novel strains of cyprinid herpesvirus closely related to koi herpesvirus. Diseases of aquatic organisms. 2013;107(2):113-20.
82. Fabian M, Baumer A, Adamek M, Steinhagen D. Transmission of Cyprinid herpesvirus 3 by wild fish species--results from infection experiments. Journal of fish diseases. 2016;39(5):625-8.
83. Fabian M, Baumer A, Steinhagen D. Do wild fish species contribute to the transmission of koi herpesvirus to carp in hatchery ponds? Journal of fish diseases. 2013;36(5):505-14.
84. Fichi G, Cardeti G, Cocumelli C, Vendramin N, Toffan A, Eleni C, et al. Detection of Cyprinid herpesvirus 2 in association with an *Aeromonas sobria* infection of *Carassius carassius* (L.), in Italy. Journal of fish diseases. 2013;36(10):823-30.
85. Foley M. land print Carp explosion risks Basin Plan benefits. The Land. 2017 03/16/2017 Mar 16.
86. Fuchs W, Fichtner D, Bergmann SM, Mettenleiter TC. Generation and characterization of koi herpesvirus recombinants lacking viral enzymes of nucleotide metabolism. Archives of virology. 2011;156(6):1059-63.
87. Fuchs W, Granzow H, Dauber M, Fichtner D, Mettenleiter TC. Identification of structural proteins of koi herpesvirus. Archives of virology. 2014;159(12):3257-68.
88. Garver KA, Al-Hussiney L, Hawley LM, Schroeder T, Edes S, LePage V, et al. Mass mortality associated with koi herpesvirus in wild common carp in Canada. Journal of wildlife diseases. 2010;46(4):1242-51.
89. Gilad O. Characterization and control of the koi herpesvirus (KHV), a newly recognized pathogen of koi (*Cyprinus carpio koi*) and common carp (*Cyprinus carpio carpio*). Ann Arbor: University of California, Davis; 2003.
90. Gorman J. Animals die in large numbers, and researchers scratch their heads. New York Times (Online). 2016 18 Jan.
91. Gorman J. The mystery of dying murrelets: [Science Desk]. New York Times. 2016 19 January.
92. Gotesman M, Kattlun J, Bergmann SM, El-Matbouli M. CyHV-3: the third cyprinid herpesvirus. Diseases of aquatic organisms. 2013;105(2):163-74.
93. Gotesman M, Soliman H, Besch R, El-Matbouli M. In vitro inhibition of Cyprinid herpesvirus-3 replication by RNAi. Journal of virological methods. 2014;206:63-6.
94. Han JE, Kim JH, Renault T, Choresca C, Jr., Shin SP, Jun JW, et al. Identifying the viral genes

- encoding envelope glycoproteins for differentiation of Cyprinid herpesvirus 3 isolates. *Viruses*. 2013;5(2):568-76.
95. Hansen M. Big questions asked of Carp-a-geddon. *Daily Liberal and Macquarie Advocate*. 2016 16 Aug 2016.
 96. Hanson L, Dishon A, Kotler M. Herpesviruses that infect fish. *Viruses*. 2011;3(11):2160-91.
 97. Hanson L, Doszpoly A, van Beurden SJ, Viadanna P, Waltzek TB. Chapter 9 - Alloherpesviruses of Fish. In: Kibenge FSB, Godoy M, editors. *Aquaculture Virology*: Academic Press; 2016. p. 153-72.
 98. Harris C. What is blackwater? *The Daily Advertiser*. 2016 11/05/ 2016 Nov 05.
 99. Holmes EC. Virology: Pathogenic passengers. *Nature*. 2011;478(7369):319-20.
 100. Honjo MN, Minamoto T, Kawabata Z. Reservoirs of Cyprinid herpesvirus 3 (CyHV-3) DNA in sediments of natural lakes and ponds. *Veterinary microbiology*. 2012;155(2-4):183-90.
 101. Hori Y, Tam B, Gough WA, Ho-Foong E, Karagatzides JD, Liberda EN, et al. Use of traditional environmental knowledge to assess the impact of climate change on subsistence fishing in the James Bay Region of Northern Ontario, Canada. *Rural and Remote Health*. 2012;12(2):1878.
 102. Ilouze M, Davidovich M, Diamant A, Kotler M, Dishon A. The outbreak of carp disease caused by CyHV-3 as a model for new emerging viral diseases in aquaculture: a review. *Ecological Research*. 2011;26(5):885-92.
 103. Ilouze M, Dishon A, Kotler M. Coordinated and sequential transcription of the cyprinid herpesvirus-3 annotated genes. *Virus research*. 2012;169(1):98-106.
 104. Ilouze M, Dishon A, Kotler M. Down-regulation of the cyprinid herpesvirus-3 annotated genes in cultured cells maintained at restrictive high temperature. *Virus research*. 2012;169(1):289-95.
 105. Ito T, Kurita J, Yuasa K. Differences in the susceptibility of Japanese indigenous and domesticated Eurasian common carp (*Cyprinus carpio*), identified by mitochondrial DNA typing, to cyprinid herpesvirus 3 (CyHV-3). *Veterinary microbiology*. 2014;171(1-2):31-40.
 106. Jeney Z, Jeney G. Recent achievements in studies on diseases of common carp (*Cyprinus carpio* L.). *Aquaculture*. 1995;129(1):397-420.
 107. Kawabata Zi. Environmental change, pathogens, and human linkages. Part 1: ecological case studies. *Ecological Research*. 2011;26(5):863.
 108. Kawabata Zi, Minamoto T, Honjo MN, Uchii K, Yamanaka H, Suzuki AA, et al. Environment-KHV-carp-human linkage as a model for environmental diseases. *Ecological Research*. 2011;26(6):1011-6.
 109. Kempter J, Sadowski J, Schutze H, Fischer U, Dauber M, Fichtner D, et al. Koi herpes virus: do acipenserid restitution programs pose a threat to carp farms in the disease-free zones? *Acta Ichthyologica et Piscatoria*. 2009;39(2):119-26.
 110. Kim HJ, Kwon SR. Evidence for two koi herpesvirus (KHV) genotypes in South Korea. *Diseases of aquatic organisms*. 2013;104(3):197-202.
 111. Kotsios N. Carp rise in a perfect spawn. *The Weekly Times*. 2017 02/01/ 2017 Feb 01.
 112. Kotsios N. All-clear sought for fish. *The Weekly Times*. 2017 05/31/ 2017 May 31.
 113. Le Lievre K. Virus concern for koi owners. *The Canberra Times*. 2017 1 Jan 2017.
 114. Lighten J, van Oosterhout C. Biocontrol of common carp in Australia poses risks to biosecurity. *Nature Ecology & Evolution*. 2017;1(0087).
 115. Ma YP, Liu ZX, Hao L, Ma JY, Liang ZL, Li YG, et al. Analysing codon usage bias of cyprinid herpesvirus 3 and adaptation of this virus to the hosts. *Journal of fish diseases*. 2015;38(7):665-73.
 116. McColl KA. Final report: Phase 3 of the carp herpesvirus project (CyHV-3). Canberra: PetSmart Toolkit publication. Invasive Animals Cooperative Research Centre; 2016.
 117. McColl KA, Cooke BD, Sunarto A. Viral biocontrol of invasive vertebrates: Lessons from the past applied to cyprinid herpesvirus-3 and carp (*Cyprinus carpio*) control in Australia. *Biological Control*. 2014;72:109-17.
 118. McColl KA, Sunarto A, Holmes EC. Cyprinid herpesvirus 3 and its evolutionary future as a biological control agent for carp in Australia. *Virol J*. 2016;13(1):206.

119. McDermott C, Palmeiro B. Selected emerging infectious diseases of ornamental fish. *The veterinary clinics of North America Exotic animal practice*. 2013;16(2):261-82.
120. Michel B, Fournier G, Loeffrig F, Costes B, Vanderplasschen A. Cyprinid herpesvirus 3. *Emerging infectious diseases*. 2010;16(12):1835-43.
121. Mikkelsen S. Vet in call to help save river. *The Noosa Journal*. 2010 19 November.
122. Miller J. Political Happy Hour: Political Happy Hour. *Boston Globe (Online)*. 2017 03/13/2017 Mar 13.
123. Minamoto T, Honjo MN, Yamanaka H, Tanaka N, Itayama T, Kawabata Z. Detection of cyprinid herpesvirus-3 DNA in lake plankton. *Research in veterinary science*. 2011;90(3):530-2.
124. Minamoto T, Honjo MN, Yamanaka H, Uchii K, Kawabata Z. Nationwide Cyprinid herpesvirus 3 contamination in natural rivers of Japan. *Research in veterinary science*. 2012;93(1):508-14.
125. Minamoto T, Pu X, Xie J, Dong Y, Wu D, Kong H, et al. Monitoring fish pathogenic viruses in natural lakes in Yunnan, China. *Limnology*. 2015;16(1):69-77.
126. Muench S. Dead fish found in dumpster day after die-off. *Arizona Republic*. 2007 6 Jun.
127. Naik G. U.S. News: Bird die-offs? Not that rare. *Wall Street Journal*. 2011 8 Jan.
128. Negenborn J, van der Marel MC, Ganter M, Steinhagen D. Cyprinid herpesvirus-3 (CyHV-3) disturbs osmotic balance in carp (*Cyprinus carpio* L.)--A potential cause of mortality. *Veterinary microbiology*. 2015;177(3-4):280-8.
129. Nolan D, Stephens F, Crockford M, Jones JB, Snow M. Detection and characterization of viruses of the genus *Megalocytivirus* in ornamental fish imported into an Australian border quarantine premises: an emerging risk to national biosecurity. *Journal of fish diseases*. 2015;38(2):187-95.
130. Oidtmann B, Peeler E, Lyngstad T, Brun E, Bang Jensen B, Stärk KDC. Risk-based methods for fish and terrestrial animal disease surveillance. *Preventive Veterinary Medicine*. 2013;112(1):13-26.
131. Osterrieder K, editor. *Cell Biology of Herpes Viruses*. Cham, Switzerland: Springer International Publishing; 2017.
132. Peeler EJ, Oidtmann BC, Midtlyng PJ, Miossec L, Gozlan RE. Non-native aquatic animals introductions have driven disease emergence in Europe. *Biological Invasions*. 2011;13(6):1291-303.
133. Peeler EJ, Taylor NG. The application of epidemiology in aquatic animal health -opportunities and challenges. *Veterinary research*. 2011;42(1):94.
134. Peif S. Lack of oxygen killing thousands of small fish in Windsor Lake. *McClatchy - Tribune Business News*. 2010 9 September.
135. Piackova V, Flajshans M, Pokorova D, Reschova S, Gela D, Cizek A, et al. Sensitivity of common carp, *Cyprinus carpio* L., strains and crossbreeds reared in the Czech Republic to infection by cyprinid herpesvirus 3 (CyHV-3; KHV). *Journal of fish diseases*. 2013;36(1):75-80.
136. Piazzon MC, Wentzel AS, Tijhaar EJ, Rakus KL, Vanderplasschen A, Wiegertjes GF, et al. Cyprinid Herpesvirus 3 II10 Inhibits Inflammatory Activities of Carp Macrophages and Promotes Proliferation of Igm+ B Cells and Memory T Cells in a Manner Similar to Carp II10. *Journal of immunology (Baltimore, Md : 1950)*. 2015;195(8):3694-704.
137. Rakus K, Ouyang P, Boutier M, Ronsmans M, Reschner A, Vancsok C, et al. Cyprinid herpesvirus 3: an interesting virus for applied and fundamental research. *Veterinary research*. 2013;44:85.
138. Rakus KL, Irnazarow I, Adamek M, Palmeira L, Kawana Y, Hirono I, et al. Gene expression analysis of common carp (*Cyprinus carpio* L.) lines during Cyprinid herpesvirus 3 infection yields insights into differential immune responses. *Developmental and comparative immunology*. 2012;37(1):65-76.
139. Rathore G, Kumar G, Raja Swaminathan T, Swain P. Koi herpes virus: a review and risk assessment of Indian aquaculture. *Indian journal of virology: an official organ of Indian Virological Society*. 2012;23(2):124-33.
140. Reed AN, Izume S, Dolan BP, LaPatra S, Kent M, Dong J, et al. Identification of B cells as a major site for cyprinid herpesvirus 3 latency. *Journal of virology*. 2014;88(16):9297-309.
141. Ronsmans M, Boutier M, Rakus K, Farnir F, Desmecht D, Ectors F, et al. Sensitivity and permissivity of *Cyprinus carpio* to cyprinid herpesvirus 3 during the early stages of its development: importance of the epidermal mucus as an innate immune barrier. *Veterinary research*. 2014;45:100.
142. Saunders G, Cooke B, McColl K, Shine R, Peacock T. Modern approaches for the biological

- control of vertebrate pests: An Australian perspective. *Biological Control*. 2010;52(3):288-95.
143. Savin KW, Cocks BG, Wong F, Sawbridge T, Cogan N, Savage D, et al. A neurotropic herpesvirus infecting the gastropod, abalone, shares ancestry with oyster herpesvirus and a herpesvirus associated with the amphioxus genome. *Virology Journal*. 2010;7(1):308.
 144. Shamsi S, Turner A, Wassens S. Description and genetic characterization of a new *Contracaecum* larval type (Nematoda: Anisakidae) from Australia. *Journal of helminthology*. 2017:1-7.
 145. Shepherd T. Carp diem in plan to kill off toxic pest. *The Advertiser*. 2017 3 Jun 2017.
 146. Shepherd T, Gailberger J. Fishy business over carp cull. *The Advertiser*. 2016 10/27/2016 Oct 27.
 147. Shepherd T, Gailberger J. It's Carpagedd on for fish pest. *The Advertiser*. 2016 10/27/2016 Oct 27.
 148. Sibthorpe C. Plea to help keep fishing spots tidier. *The Canberra Times*. 2017 02/24/2017 Feb 24.
 149. Sunarto A, Liongue C, McColl KA, Adams MM, Bulach D, Crane MS, et al. Koi herpesvirus encodes and expresses a functional interleukin-10. *Journal of virology*. 2012;86(21):11512-20.
 150. Sunarto A, McColl KA. Expression of immune-related genes of common carp during cyprinid herpesvirus 3 infection. *Diseases of aquatic organisms*. 2015;113(2):127-35.
 151. Sunarto A, McColl KA, Crane MS, Sumiati T, Hyatt AD, Barnes AC, et al. Isolation and characterization of koi herpesvirus (KHV) from Indonesia: identification of a new genetic lineage. *Journal of fish diseases*. 2011;34(2):87-101.
 152. Syakuri H, Adamek M, Brogden G, Rakus KL, Matras M, Irnazarow I, et al. Intestinal barrier of carp (*Cyprinus carpio* L.) during a cyprinid herpesvirus 3-infection: molecular identification and regulation of the mRNA expression of claudin encoding genes. *Fish & shellfish immunology*. 2013;34(1):305-14.
 153. Takahara T, Honjo MN, Uchii K, Minamoto T, Doi H, Ito T, et al. Effects of daily temperature fluctuation on the survival of carp infected with Cyprinid herpesvirus 3. *Aquaculture*. 2014;433:208-13.
 154. Taylor NG, Dixon PF, Jeffery KR, Peeler EJ, Denham KL, Way K. Koi herpesvirus: distribution and prospects for control in England and Wales. *Journal of fish diseases*. 2010;33(3):221-30.
 155. Taylor NGH, Norman RA, Way K, Peeler EJ. Modelling the koi herpesvirus (KHV) epidemic highlights the importance of active surveillance within a national control policy. *Journal of Applied Ecology*. 2011;48(2):348-55.
 156. Thrush MA, Peeler EJ. A model to approximate lake temperature from gridded daily air temperature records and its application in risk assessment for the establishment of fish diseases in the UK. *Transboundary and emerging diseases*. 2013;60(5):460-71.
 157. Uchii K, Matsui K, Iida T, Kawabata Z. Distribution of the introduced cyprinid herpesvirus 3 in a wild population of common carp, *Cyprinus carpio* L. *Journal of fish diseases*. 2009;32(10):857-64.
 158. Uchii K, Minamoto T, Honjo MN, Kawabata Z. Seasonal reactivation enables Cyprinid herpesvirus 3 to persist in a wild host population. *FEMS microbiology ecology*. 2014;87(2):536-42.
 159. van der Veer G, Nentwig W. Environmental and economic impact assessment of alien and invasive fish species in Europe using the generic impact scoring system. *Ecology of Freshwater Fish*. 2015;24(4):646-56.
 160. Waltzek TB. *Phylogenetics and improved diagnostics for the cypriniviruses*. Ann Arbor: University of California, Davis; 2010.
 161. Waltzek TB, Kelley GO, Alfaro ME, Kurobe T, Davison AJ, Hedrick RP. Phylogenetic relationships in the family Alloherpesviridae. *Diseases of aquatic organisms*. 2009;84(3):179-94.
 162. Waltzek TB, Kelley GO, Stone DM, Way K, Hanson L, Fukuda H, et al. Koi herpesvirus represents a third cyprinid herpesvirus (CyHV-3) in the family Herpesviridae. *The Journal of general virology*. 2005;86(Pt 6):1659-67.
 163. Whitley RJ. Chapter 68: Herpesviruses. In: Baron S, editor. *Medical Microbiology*. 4th edition ed. Galveston (TX): University of Texas Medical Branch at Galveston; 1996.
 164. Whittington RJ, Chong R. Global trade in ornamental fish from an Australian perspective: The case for revised import risk analysis and management strategies. *Preventive Veterinary Medicine*. 2007;81(1):92-116.

165. Williams M. Lake Elsinore continues to dwindle: Its health is good despite lower levels caused by drought, water officials say. Orange County Register. 2015 5 April.
166. Willis B. Carp explosion a river crisis. The Advertiser. 2017 03/28/2017 Mar 28.
167. Wipatayotin A. Cabinet orders identification of river polluters. Bangkok Post. 2007 28 March.
168. Yoshida N, Sasaki RK, Kasai H, Yoshimizu M. Inactivation of koi-herpesvirus in water using bacteria isolated from carp intestines and carp habitats. Journal of fish diseases. 2013;36(12):997-1005.
169. Yuasa K, Kurita J, Kawana M, Kiryu I, Oseko N, Sano M. Development of mRNA-specific RT-PCR for the detection of koi herpesvirus (KHV) replication stage. Diseases of aquatic organisms. 2012;100(1):11-8.
170. Zhang Q, Gui J-F. Virus genomes and virus-host interactions in aquaculture animals. Science China Life Sciences. 2015;58(2):156-69.
171. Zhao Y, Wang T, Yu Z, Wang H, Liu B, Wu C, et al. Inhibiting cyprinid herpesvirus-3 replication with CRISPR/Cas9. Biotechnology letters. 2016;38(4):573-8.
172. Zheng S, Wang Q, Bergmann SM, Li Y, Zeng W, Wang Y, et al. Investigation of latent infections caused by cyprinid herpesvirus 3 in koi (*Cyprinus carpio*) in southern China. Journal of veterinary diagnostic investigation: official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc. 2017;29(3):366-9.

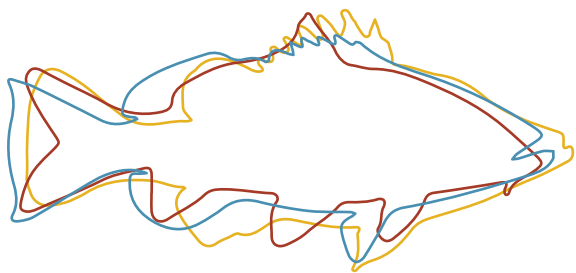
FRDC FINAL REPORT CHECKLIST

Project Title:	Cyprinid herpesvirus 3 and its relevance to human health.		
Principal Investigators:	Dr Katrina ROPER and Ms Laura FORD		
Project Number:	2016-183		
Description:	The report summarises the findings of a systematic literature review that sought to determine the impact on human health of the proposed release of the carp herpesvirus, Cyprinid herpesvirus 3. The literature review indicated that there is no published evidence of a direct zoonotic risk to human health from the virus. There was little published on how humans react emotively to mass mortality events of fish, however it could be reasonably assumed that the public may react adversely to mass mortality events. Rapid removal of the dead fish will mitigate adverse reactions.		
Published Date:		Year:	2018
ISBN:	ISBN 978-0-646-98525-1	ISSN:	N/A
Key Words:	Cyprinid herpesvirus; human health.		

Please use this checklist to self-assess your report before submitting to FRDC. Checklist should accompany the report.

	Is it included (Y/N)	Comments
Foreword (optional)	N	
Acknowledgments	Y	
Abbreviations	N	
Executive Summary	Y	
– What the report is about	Y	
– Background – why project was undertaken	Y	
– Aims/objectives – what you wanted to achieve at the beginning	Y	
– Methodology – outline how you did the project	Y	
– Results/key findings – this should outline what you found or key results	Y	
– Implications for relevant stakeholders	N	
– Recommendations	Y	
Introduction	Y	
Objectives	Y	
Methodology	Y	
Results	Y	
Discussion	Y	
Conclusion	Y	
Implications	N	
Recommendations	Y	
Further development	N	

Extension and Adoption	N	
Project coverage	N	
Glossary	N	
Project materials developed	N	
Appendices	Y	



NATIONAL CARP CONTROL PLAN

The National Carp Control Plan is managed by the
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