UK Health Security Agency

Hantavirus vaccine effectiveness following Andes virus exposure

A systematic evidence summary

Contents

Main messages

1. This systematic evidence summary (search up to 19 May 2026) identified and summarised evidence of the protective efficacy of vaccines for hantavirus in people or animals exposed to Andes virus.

2. Ten studies were included (1 to 10). All studies were conducted in animals (Syrian hamsters), no evidence in humans was identified.

3. All 10 studies reported on the effectiveness of hantavirus vaccines for exposure to Andes virus when used as pre-exposure prophylaxis (1 to 10). A range of vaccines were evaluated within these studies, including vesicular stomatitis virus (VSV) vaccines for different hantaviruses, deoxyribonucleic acid (DNA) vaccines for different hantaviruses, and messenger ribonucleic acid (mRNA) vaccines for Andes virus.

4. Available evidence suggested there may be a protective effect of various hantavirus vaccines when used as pre-exposure prophylaxis for Andes virus. This was suggested by some reductions in mortality, morbidity and viral load and increased antibody titres in hamsters given vaccines for hantavirus compared to control groups (unvaccinated hamsters, or hamsters given vaccines other than for hantavirus), however few studies tested for statistical significance and numbers were likely too small to show true effects.

5. Two studies also reported on the effectiveness of hantavirus vaccines for exposure to Andes virus when used as post-exposure prophylaxis (3, 6). Both studies evaluated the effectiveness of VSV vaccines expressing Andes virus proteins.

6. There was some evidence suggesting that hantavirus vaccines used as post-exposure prophylaxis for Andes virus may have resulted in reductions in mortality, but only for certain vaccines when given very close to the time of exposure. Only one study reported on changes in viral load (6), and evidence was too limited to draw any conclusions.

7. Critical appraisal was not performed, which restricts the interpretation of the findings, but important limitations have been highlighted. All studies were conducted in Syrian hamster models of infection which may not be generalisable to humans. Sample sizes were low, with small numbers of hamsters receiving the vaccines or control in each study (no more than 12 hamsters were included in any experimental group). Evidence for each type of vaccine was limited, with variations in comparators across different studies. Most studies did not undertake statistical comparison between vaccine and control groups. These limitations restrict the ability to draw definitive conclusions.

8. In summary, evidence for the protective efficacy of vaccines for hantavirus after exposure to Andes virus was only available from pre-clinical animal studies. While there was some evidence to suggest potential for effectiveness of hantavirus vaccines for pre-exposure

prophylaxis for Andes virus, sample sizes were small and may not show true effects. Post-exposure prophylaxis evidence was too limited to make any conclusions on effectiveness. Further evidence is required, particularly on effectiveness of hantavirus vaccines as pre- or post-exposure prophylaxis following exposure to Andes virus in humans.

Purpose

The purpose of this systematic evidence summary was to identify and summarise the available evidence of the effectiveness of vaccines developed for hantavirus when used as pre- or post-exposure prophylaxis in those exposed to Andes virus.

The review question was:

1. What is the protective efficacy of vaccines for hantavirus following exposure to Andes virus?

This systematic evidence summary was commissioned as part of the UKHSA response to the hantavirus outbreak in May 2026 to address an identified evidence gap on the cross-reactivity of vaccines for hantavirus for those exposed to Andes virus.

Methods

A systematic evidence summary was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant experimental (randomised, non-randomised, quasi-experimental), observational (cohort) and pre-clinical animal studies, published or available as preprint, up to 19 May 2026. Three databases were searched: Ovid Medline, Ovid Embase, Web of Science Preprint Citation Index.

Studies were included if they included humans or animals who had been exposed to Andes virus who were given any vaccine for hantavirus either before or after exposure to Andes virus. No other form of prophylaxis, such as transfer of antibodies from other vaccinated individuals or animals were included. Outcomes of interest in this review were any measure of prevention of infection, measures of disease severity (mortality, morbidity, or viral load [in animals only]), antibody titres, or T-cell assay outputs.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in Annexe A.

There was one clarification to the protocol:

- any hantavirus vaccine identified would be included, rather than just the examples listed in the protocol

Screening on title and abstract was undertaken in duplicate by 5 reviewers for 10% of records, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and excluded studies were checked by a second.

Data extraction was performed by one reviewer and checked by a second.

Evidence

In total, 1,125 studies were screened at title and abstract and 54 studies were screened at full text. Of these, 10 studies met the inclusion criteria. A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded on full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D.

Evidence has been presented separately for pre-exposure prophylaxis and post-exposure prophylaxis.

Pre-exposure prophylaxis

All 10 studies reported on the protective efficacy of vaccines when given before exposure to Andes virus. All studies were pre-clinical animal studies conducted in North America; 9 in the United States of America (USA) (1 to 8, 10), and one in Canada (9).

Humans

No studies were identified in humans.

Animals

Ten studies were identified that assessed the protective efficacy of hantavirus vaccines as pre-exposure prophylaxis for Andes virus strain Chile-9717869. All of these were in Syrian hamsters (1 to 10).

Identified studies are summarised below, with further details, including information about the exposure, vaccines and comparators used, provided in Annexe D.

Prevention of infection

No studies explicitly reported on prevention of infection. Four studies were identified that reported on clinical presentation following exposure to Andes virus and included information on hamsters that had no signs of severe disease; these have been summarised under Morbidity below (3, 5, 9, 10)

Mortality

All 10 studies reported on the effectiveness of vaccinations for hantaviruses on reducing mortality when given before exposure to Andes virus (1 to 10). As most study results were

presented in terms of number or percentage of animals surviving, all findings are reported here as survival.

The following vaccines were reported on:

- two studies reported on a vesicular stomatitis virus (VSV) vaccine for Andes virus (3, 7)
- one study reported on 2 different mRNA vaccines for Andes virus (5)
- one study reported on 2 different DNA vaccines for Andes virus (2)
- one study reported on 2 different VSV vaccines for Andes virus: one expressing Andes virus glycoproteins only, and one expressing a combination of Andes and Ebola virus glycoproteins (8)
- one study reported on 3 different VSV vaccines for Andes virus; one expressing Andes virus glycoproteins only, and 2 expressing different combinations of Andes and Ebola virus glycoproteins (6)
- one study reported on 2 different DNA vaccines for hantaviruses: one for Hantaan virus and one for Andes virus (10)
- one study reported on 2 different VSV vaccines for hantaviruses: one for Andes virus and one for Sin Nombre virus (9)
- one study reported on 2 different DNA vaccines for hantaviruses: one for Puumala virus, and one for Hantaan virus (1)
- one study reported on a DNA vaccine for Sin Nombre virus (4)

Brown and others conducted 2 separate studies, reported in one paper, which assessed the effectiveness of a single dose of a vaccine for Andes virus (VSV-G/ANDVGPC, dose: 10^5 plaque forming units [PFU]), compared to either an Ebola virus vaccine (VSV-G/ZEBOVGP, dose: 10^5 PFU) or a control vaccine of Dulbecco's Modified Eagle Medium (DMEM) (3). In their first study, 12 Syrian hamsters (sex: female, age: 5 to 6 weeks) were given the vaccine 28 days before challenge with Andes virus (dose: 100x lethal dose[LD]$_{50}$, equal to 154 focus forming units [FFU], by injection into the abdomen) and compared to 9 control hamsters vaccinated with Ebola virus vaccine. All hamsters given the Andes virus vaccine survived (12 out of 12), whereas in the group given the Ebola vaccine none survived (0%, 0 out of 9). Statistical comparison between groups was not performed.

In their second study, which evaluated the effectiveness of the same Andes virus vaccine, 57 Syrian hamsters (sex: female, age: 5 to 6 weeks old) were vaccinated in groups of 3 to 10 hamsters at 14, 7, or 3 days before challenge with Andes virus injected into the abdomen (dose: 100xLD$_{50}$, equal to 154 FFU), compared to either vaccination for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) or a control vaccine of DMEM. Results from this study are summarised in Table 1; statistical comparisons between the groups were not reported.

Table 1. Survival in hamsters exposed to Andes virus by timing of pre-exposure prophylaxis and vaccine type (from Brown and others (3))

Vaccine	Percentage survival Vaccination 14 days before challenge with Andes virus	Percentage survival Vaccination 7 days before challenge with Andes virus	Percentage survival Vaccination 3 days before challenge with Andes virus
VSV-G/ANDVGPC	100% (10 out of 10)	100% (10 out of 10)	100% (10 out of 10)
VSV-G/ZEBOVGP	0% (0 out of 6)	50% (3 out of 6)	83% (5 out of 6)
DMEM	0% (0 out of 3)	0% (0 out of 3)	0% (0 out of 3)

Prescott and others evaluated the effectiveness of a single dose of a vaccine for Andes virus (rVSV-G/ANDVGPC, dose: 10^5 PFU, compared to a sterile medium as control (7). Syrian hamsters (n=24, sex: female, age: 5 to 6 weeks) were challenged with Andes virus (dose: 200 FFU, via the nostril) at 6 or 12 months after vaccination. In those challenged 6 months after receiving the vaccine, 83.3% (5 out of 6) that received the Andes virus vaccine survived, compared to 16.7% (one out of 6) that received the control. In those challenged 12 months after receiving the vaccine, 83.3% (5 out of 6) that received the Andes virus vaccine survived, compared to 33.3% (2 out of 6) that received the control. Statistical comparisons between the groups were not performed.

Kuzmin and others evaluated the effectiveness of different Andes virus mRNA vaccines following challenge with Andes virus (5). Hamsters were vaccinated twice, with the second vaccine given 21 days after the first. Five groups of hamsters were given the following vaccines or control:

- 5µg LNP-encapsulated regular U-mRNA vaccine (contains Andes virus RNA)
- 25µg LNP-encapsulated U-mRNA vaccine (contains Andes virus RNA)
- 5µg N1-methylpseudouridine (modified) mRNA (contains Andes virus RNA)
- 25µg N1-methylpseudouridine (modified) mRNA (contains Andes virus RNA)
- control vaccine (LNP without any RNA)

Syrian hamsters (n=25 [5 groups of 5], sex: female, age: 10 weeks) were challenged with Andes virus (dose: 250 PFU) by injection into the muscle 21 days after receiving the second vaccine dose. Survival was measured for 28 days after challenge, with 100% survival in all groups except for hamsters vaccinated with 5µg modified mRNA (60% survival, 3 out of 5 survived), and those given the control vaccine (0% survival, 0 out of 5 survived). All hamsters that died were euthanised 10 days after challenge due to severe respiratory distress. Statistical comparisons between the groups were not performed.

Brocato and others conducted 2 studies, reported in the same paper, on the effectiveness of different dosing regimens of 2 Andes virus DNA vaccines; pWRG/AND-M(1.1) or pWRG/AND-M(opt2) (codon-optimised) compared to a control group that received no vaccination (2). In the first study, Syrian hamsters (7 to 8 in each group, but exact number not reported, sex: female, age: not reported) were vaccinated by injection with 4 doses of 200µg of either vaccine at 4-week intervals and then challenged with Andes virus (time between last vaccination and challenge not reported, dose: 200 PFU, injected into the muscle). The study did not report the numbers of hamsters that survived but did report that there were no statistically significant differences in survival between any of the groups 4 weeks after challenge, including the unvaccinated group (all $p>0.05$).

In the second study, Syrian hamsters (total number not reported, sex: female, age: not reported) were vaccinated with 3 doses (200µg) of either pWRG/AND-M(1.1), pWRG/AND-M(opt2) Andes virus vaccines, or phosphate buffered saline (control vaccine) at 4-week intervals (2). They were then challenged with Andes virus (time between last vaccination and challenge not reported, dose: 200 PFU). In hamsters vaccinated with pWRG/AND-M(1.1), 12.5% (one out of 8) survived 28 days after challenge. A comparison of survival between hamsters vaccinated with pWRG/AND-M(1.1) and the control group was not reported, but the study reported that there was a longer time to death compared to the control group ($p=0.01$). In hamsters vaccinated with pWRG/AND-M(opt2), 46.7% survived (7 out of 15) 28 days after challenge, which was significantly more than the control group ($p=0.001$). No hamsters survived in the control group.

Tsuda and others evaluated the effectiveness of a single dose of either a combined vaccine for both Andes and Ebola viruses (VSV-G/dual, dose: 10^5 PFU) or a single vaccine for Andes virus (VSV-G/ANDV, dose: 10^5 PFU) compared to a vaccine for Ebola virus (VSV-G/ZEBOV, dose: 10^5 PFU) (8). Syrian hamsters (n=12, sex: male, age: 5 to 6 weeks) were challenged by injection in the abdomen with Andes virus (dose: 100 x LD_{50}) 28 days after vaccination. All hamsters given the combined Andes and Ebola virus vaccine (3 out of 3) survived, 100% (6 out of 6) given the vaccine for Andes virus survived, but none (0 out of 3) given the vaccine for Ebola virus survived. All hamsters that died succumbed to their illness within 9 days of challenge. Statistical comparisons between groups were not performed.

Marceau and others evaluated the effectiveness of a single dose (10^5 PFU) of one of the following vaccines compared to each other (6):

- VSV-ANDV monovalent (vaccine for Andes virus only)
- VSV-ANDV-EBOV bivalent (vaccine for Andes and Ebola virus)
- VSV-EBOV-ANDV bivalent (vaccine for Andes and Ebola virus)
- VSV-EBOV monovalent (vaccine for Ebola virus)

Vaccines were given via the nostril or abdomen to groups of 6 hamsters at either 28 days or 3 days before challenge with Andes virus. Syrian hamsters (n=48, sex: female, age: 5 to 6 weeks) were challenged by injection in the abdomen with a lethal dose of Andes virus (200 FFU), and

survival was measured for up to 40 days following this challenge. Results are summarised in Table 2. Statistical comparisons between the groups were not reported.

Table 2. Survival in hamsters exposed to Andes virus by timing of pre-exposure prophylaxis, vaccine type, and route of administration (from Marceau and others (6))

Vaccine *(route)*	Percentage survival Vaccination 28 days before challenge with Andes virus	Percentage survival Vaccination 3 days before challenge with Andes virus
VSV-ANDV ***(via nostril)***	100% (6 out of 6)	33.3% (2 out of 6)
VSV-ANDV ***(via abdomen)***	83.3% (5 out of 6)	100% (6 out of 6)
VSV-ANDV-EBOV ***(via nostril)***	100% (6 out of 6)	100% (6 out of 6)
VSV-ANDV-EBOV ***(via abdomen)***	100% (6 out of 6)	100% (6 out of 6)
VSV-EBOV-ANDV ***(via nostril)***	100% (6 out of 6)	100% (6 out of 6)
VSV-EBOV-ANDV ***(via abdomen)***	100% (6 out of 6)	100% (6 out of 6)
VSV-EBOV ***(via nostril)***	0% (0 out of 6)	0% (0 out of 6)
VSV-EBOV ***(via abdomen)***	0% (0 out of 6)	33.3% (2 out of 6)

Custer and others conducted 2 studies, reported in the same paper, that compared the effectiveness of vaccines for Hantaan virus (pWRG/HTN-M(x), DNA loading: ~0.75µg of plasmid DNA) and for Andes virus (pWRG/AND-M), to a control group vaccinated with plasmid pWRG7077 (10). In the first study, Syrian hamsters (n=39, sex: female, age: reported as ‘adult’) were vaccinated 3 times at 3-week intervals and challenged with Andes virus by an injection into the muscle (dose: 2,000 PFU [250 LD_{50}]) 21 days after the last vaccination. In hamsters vaccinated with the Hantaan virus vaccine, 37.5% survived (9 out of 24), whereas only 6.7% (one out of 15) of the control group survived. However, the difference in survival between these 2 groups was not statistically significant (p=0.057). For both the vaccinated and control groups, the mean time to death was 13 days from point of challenge. Hamsters that survived the initial challenge in this study were re-challenged with the same dose of Andes virus (time from last dose not reported), and all hamsters in both groups survived the second challenge (9 vaccinated; one control).

In the second study, 2 groups of Syrian hamsters (n=22, sex: female, age: reported as ‘adult’) were vaccinated 3 times at 3-week intervals with pWRG/AND-M or were unvaccinated (10). Both groups were then challenged with Andes virus by an injection into the muscle (time between last dose and challenge not reported, dose: 2,000 PFU [250 LD_{50}]). In hamsters vaccinated with the Andes virus vaccine 14.3% survived (2 out of 14), compared to 25.0% (2 out of 8) in the unvaccinated control group. Statistical comparison between the groups was not performed. For both groups, the mean time to death was between 12 and 13 days.

Warner and others evaluated the effectiveness of a single dose of a vaccine for Andes virus (rVSV-G/ANDVGPC, dose: 10^5 PFU) compared to a vaccine for Sin Nombre virus (rVSV-G/SNVGPC, dose: 10^5 PFU) or a vaccine for Lassa Virus as a control (rVSV-G/LASVGPC, dose: 10^5 PFU) (9). Syrian hamsters (n=18, sex: female, age: 5 to 6 weeks old) were challenged by injection into the abdomen with Andes virus (dose: 200 FFU) 28 days after vaccination. All hamsters vaccinated for Andes virus survived (6 out of 6), 83.3% (5 out of 6) of those vaccinated for Sin Nombre virus survived, but only 16.7% (one out of 6) in those vaccinated for Lassa virus survived. Survival was statistically significantly higher in those vaccinated for either Andes virus or Sin Nombre virus, compared to those vaccinated for Lassa virus (both $p<0.01$).

Brocato and others compared the effectiveness of vaccination in hamsters that were challenged with Andes virus through different routes to unvaccinated controls (1). In one study, Syrian hamsters (groups of 8 to 10 hamsters but total number not reported, sex: not reported, age: not reported) were vaccinated 3 times (at weekly intervals) with either a Puumala virus DNA vaccine (pWRG/PUU-M[s2], dose: 2µg) or a Hantaan virus DNA) vaccine (pWRG/HTN-M[x], dose: 2µg), or were not vaccinated. Hamsters were then challenged with Andes virus via the nostril at either 14 or 20 weeks after vaccination (challenge dose: 4,000 PFU). Survival was reported for up to 35 days following challenge. The number of hamsters that survived was not reported, but the study reported that significantly more hamsters that were vaccinated for Puumala virus survived than unvaccinated hamsters challenged at 14 weeks ($p=0.0428$) and those challenged at 20 weeks ($p<0.0001$). There were no significant differences in survival between hamsters vaccinated for Hantaan virus and unvaccinated hamsters at either 14 or 20 weeks after challenge (both $p>0.05$).

In a second study reported in the same paper, Syrian hamsters (groups of 9 to 10 hamsters, total number not reported, sex and age not reported) were vaccinated 3 times (at weekly intervals) with either a Puumala virus DNA vaccine (pWRG/PUU-M[s2], dose: 2µg) or a Hantaan virus DNA) vaccine (pWRG/HTN-M[x], dose: 2µg), or were not vaccinated. Hamsters were then challenged with Andes virus by an injection into the muscle 7 weeks after vaccination (dose: 2,000 PFU) (1). Survival was reported up to 35 days following challenge. The numbers of hamsters that survived was not reported, but the study did report that significantly more hamsters that were vaccinated with the vaccine for Puumala virus survived compared to unvaccinated hamsters ($p=0.0062$). There was no significant difference in survival between hamsters that were vaccinated with the vaccine for Hantaan virus and unvaccinated hamsters ($p>0.05$).

Hooper and others evaluated the effectiveness of a vaccine for Sin Nombre virus (pWRG/SN-M[opt], dose not reported) compared to no vaccination (4). Syrian hamsters (n=15, sex: female, age: 6 to 8 weeks) were either vaccinated 3 times at 3-week intervals, with the last dose given 5 weeks before challenge with Andes virus (dose: 200 PFU [25x LD_{50}], injection via muscle) or not vaccinated. In hamsters that were vaccinated with the Sin Nombre DNA vaccine 37.5% survived (3 out of 8), compared to 14.3% (one out of 7) in the unvaccinated group. There were no statistically significant differences in mortality between the vaccinated and the control hamsters (p=0.31).

Morbidity

Four studies reported on the effectiveness of vaccinations for hantaviruses on reducing morbidity when given before to exposure to Andes virus (3, 5, 9, 10). The effectiveness of the following vaccines was assessed:

- one study reported on a VSV vaccine for Andes virus (3)
- one study reported on 2 different mRNA vaccines for Andes virus (5)
- one study reported on a DNA vaccine for Andes virus (10)
- one study reported on 2 different VSV vaccines for hantaviruses: one for Andes virus and one for Sin Nombre virus (9)

Brown and others evaluated the effectiveness of a single dose of a vaccine for Andes virus (VSV-G/ANDVGPC, dose: 10^5) compared to a vaccine for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) (3). Syrian hamsters (n=33, sex: female, age: 5 to 6 weeks old) were challenged with Andes virus through an injection into the abdomen (dose: 100xLD_{50} [equal to 154 FFU]) 28 days after vaccination. No hamsters that were given the vaccine for Andes virus showed any sign of clinical infection, whereas all hamsters given the vaccine for Ebola virus showed symptoms including lethargy, hunched posture, and breathing abnormalities from the eighth day after challenge. All hamsters given the vaccine for Ebola virus had end-stage disease (severe respiratory distress) by the eleventh day after challenge. Statistical comparisons between groups were not performed.

Kuzmin and others evaluated the effectiveness of different Andes virus mRNA vaccines on reducing morbidity following challenge with Andes virus (5). Hamsters were vaccinated twice, with the second vaccine given 21 days after the first. Five groups of hamsters were given the following vaccines or control:

- 5µg LNP-encapsulated regular U-mRNA vaccine (contains Andes virus RNA)
- 25µg LNP-encapsulated U-mRNA vaccine (contains Andes virus RNA)
- 5µg N1-methylpseudouridine (modified) mRNA (contains Andes virus RNA)
- 25µg N1-methylpseudouridine (modified) mRNA (contains Andes virus RNA)
- control vaccine (LNP without any RNA)

Syrian hamsters (n=25 [5 groups of 5], sex: female, age: 10 weeks) were challenged with Andes virus (dose: 250 PFU) by injection into the muscle 21 days after receiving the second vaccine

dose. Two hamsters given the 5µg modified mRNA vaccine, and all given the control vaccine, abruptly began showing signs of severe disease (lack of movement or reactivity, hunched posture, breathing abnormalities, progressive respiratory distress) on the ninth day after challenge. Hamsters that developed severe disease were euthanised, and autopsies showed large amounts of liquid in the chest (pulmonary oedema). None of the other hamsters showed signs of disease, including changes in body weight or body temperature during follow up. Statistical comparisons between groups were not performed.

Custer and others compared a vaccine for Andes virus (pWRG/AND-M) to a control group that were not vaccinated (10). Syrian hamsters (n=22, sex: female, age: reported as 'adult') were either vaccinated 3 times at 3-week intervals with pWRG/AND-M or were not vaccinated, and then challenged with Andes virus via an injection into the muscle (time between last dose and challenge not reported, dose: 2,000 PFU [250 LD_{50}]). In the group that were given a vaccine for Andes virus, 85.7% (12 out of 14) developed hantavirus pulmonary syndrome. In the group that were unvaccinated, 75.0% (6 out of 8) developed hantavirus pulmonary syndrome. Statistical comparisons between groups were not performed.

Warner and others evaluated the effectiveness of a single dose of a vaccine for Andes virus (rVSV-G/ANDVGPC, dose: 10^5 PFU) compared to a vaccine for Sin Nombre virus (rVSV-G/SNVGPC, dose: 10^5 PFU:) and a vaccine for Lassa Virus as control (rVSV-G/LASVGPC: a VSV based Lassa virus vaccine) (9). Syrian hamsters (n=18, sex: female, age: 5 to 6 weeks old) were challenged by injection into the abdomen with Andes virus (dose: 200 FFU) 28 days after vaccination. Hamsters vaccinated for Andes virus or Sin Nombre virus were reported to have fewer signs of disease in lung, liver, and spleen tissue compared to those given a vaccine for Lassa virus, when hamsters were autopsied 7 days after challenge. Hamsters given Lassa virus vaccine showed moderate to severe pulmonary oedema, presence of blood and immune cells in the lungs, death of liver cells, and immune response to infection in the liver and spleen, which was not seen in hamsters vaccinated for Andes virus or Sin Nombre virus. Statistical comparisons between groups were not performed.

Viral load

Five studies reported on the effect of vaccinations for hantaviruses on viral load when given before exposure to Andes virus (3, 5, 6, 8, 9). The effectiveness of the following vaccines was assessed:

- one study reported on a VSV vaccine for Andes virus (3)
- one study reported on 2 different mRNA vaccines for Andes virus (5)
- one study reported on 3 different VSV vaccines for Andes virus; one expressing Andes virus glycoproteins only, and 2 expressing different combinations of Andes and Ebola virus glycoproteins (6)
- one study reported on 2 different VSV vaccines for Andes virus: one expressing Andes virus glycoproteins only, and one expressing a combination of Andes and Ebola virus glycoproteins (8)
- one study reported on a VSV vaccine for Andes virus (9)

Brown and others evaluated the effectiveness of a single dose of a vaccine for Andes virus (VSV-G/ANDVGPC, dose: 10^5 PFU) compared to vaccination with a vaccine for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) (3). Syrian hamsters (n=12, sex: female, age: 5 to 6 weeks old) were challenged with Andes virus through an injection into the abdomen (dose: 100xLD_{50} [equal to 154 FFU]) 28 days after vaccination. Three hamsters from each group were euthanised at 5 and 8 days after challenge, and Reverse Transcription Polymerase Chain Reaction (RT-PCR) was used to detect presence of viral RNA in lung, liver, and blood samples. In those given vaccine for Andes virus, no Andes virus RNA was detected in any samples collected at 5 or 8 days after challenge, whereas Andes virus RNA was detected at both timepoints in the group given the vaccine for Ebola virus. This difference was statistically significant ($p<0.05$ to $p<0.001$ across tissues and timepoints respectively).

Kuzmin and others evaluated the effectiveness of 4 different Andes virus mRNA vaccines and control following challenge with Andes virus (full details of interventions and groups reported above) (5). Liver tissues were collected from hamsters that died either from infection (2 out of 5 in the group given 5µg modified mRNA, 5 out of 5 in the group given the control vaccine), or from euthanasia at the end of the study. In hamsters that died from infection, high levels of Andes virus were detected. However, no virus was isolated in liver tissues of any hamsters that survived until the end of the study at 28 days after challenge with Andes virus. Statistical comparisons between groups were not clearly reported.

Marceau and others evaluated the effectiveness of a single dose (10^5 PFU) of one of the following vaccines: VSV-ANDV monovalent (vaccine for Andes virus), VSV-ANDV-EBOV bivalent (vaccine for Andes and Ebola virus), VSV-EBOV-ANDV bivalent (vaccine for Andes and Ebola virus), VSV-EBOV monovalent (control vaccine for Ebola virus) and a control group treated with DMEM (which was given one day post-exposure), when given via the nostril or abdomen to groups of 6 hamsters either 28 days or 3 days before challenge with Andes virus, compared with each other (6). Syrian hamsters (n=96, sex: female, age: 5 to 6 weeks) were challenged via injection into the abdomen with a lethal dose of Andes virus (200 FFU), and viral load was measured through RT-PCR on RNA extracts 8 days after challenge. Results of statistical comparisons between the groups, by route of challenge, are presented in detail in Table D.1, but in brief:

1. Vaccine given via the nostril 28 days before challenge: hamsters given VSV-ANDV, VSV-ANDV-EBOV or VSV-EBOV-ANDV had statistically significantly lower viral loads in both blood and lung tissue than hamsters in the control group vaccinated with DMEM or those that received VSV-EBOV (all $p<0.0001$). No statistically significant differences were seen between VSV-ANDV, VSV-ANDV-EBOV or VSV-EBOV-ANDV (all $p>0.05$).
2. Vaccine given by injection into abdomen 28 days before challenge: hamsters given VSV-ANDV, VSV-ANDV-EBOV, or VSV-EBOV-ANDV had statistically significantly lower viral loads in both blood and lung tissue (all $p<0.01$) than hamsters in the control group vaccinated with DMEM. No statistically significant differences were seen between vaccine groups (all $p>0.05$).

3. Vaccine given via the nostril 3 days before challenge: hamsters given VSV-ANDV, VSV-ANDV-EBOV or VSV-EBOV-ANDV had statistically significantly lower viral load in both blood and lung tissue than hamsters in the control group vaccinated with DMEM (all $p<0.05$). No statistically significant differences were seen between VSV-ANDV-EBOV or VSV-EBOV-ANDV (all $p>0.05$).
4. Vaccine given by injection into abdomen 3 days before challenge: hamsters given VSV-ANDV, VSV-ANDV-EBOV or VSV-EBOV-ANDV had statistically significantly lower viral load in both blood and lung tissue than hamsters in the control group vaccinated with DMEM or those that received VSV-EBOV (all $p<0.0001$).

Tsuda and others evaluated the effect of a single dose of a combined vaccine for both Andes virus and Ebola (VSV-G/dual, dose: 10^5 PFU) or a single vaccine for Andes virus (VSV-G/ANDV, dose: 10^5 PFU) compared to a vaccine for Ebola virus (VSV-G/ZEBOV, dose: 10^5 PFU) (8). Three hamsters from each group were euthanised at day 6 or 9 after challenge with Andes virus (challenged 28 days after vaccination, dose: 100xLD_{50}, route: injection through the abdomen). In hamsters given the dual vaccine for Andes and Ebola virus, 88.9% (8 out of 9) hamsters had no detectable Andes virus RNA in blood, lung, liver, or spleen tissue, with the remaining hamster having very low levels detected on day 9 (less than 10^1 FFU or 200ng RNA). In hamsters given vaccine for Andes virus, there were no detectable Andes virus RNA in blood, lung, liver, or spleen tissue at either time point. In hamsters given vaccine for Ebola virus, there was detectable Andes virus RNA in all samples at both time points. Statistical comparisons between the groups were not performed.

Warner and others evaluated the effectiveness of a single dose (10^5 PFU) of a vaccine for Andes virus (rVSV-G/ANDVGPC) compared to a vaccine for Lassa Virus (rVSV-G/LASVGPC) (9). Syrian hamsters (n=18, sex: female, age: 5 to 6 weeks old) were challenged via abdomen with Andes virus (dose: 200 FFU) 28 days after vaccination. Serum and tissue samples were taken from 3 hamsters in each group at 8 days after challenge. In hamsters given the vaccine for Andes virus, there was no detectable Andes virus RNA. Statistical comparisons between groups were not performed.

Antibody titres

Five studies reported on the effect of vaccinations for hantaviruses on antibody titres when given before exposure to Andes virus (3 to 5, 7, 8). The effectiveness of the following vaccines was assessed:

- two studies reported on a VSV vaccine for Andes virus (3, 7)
- one study reported on 2 different mRNA vaccines for Andes virus (5)
- one study reported on 2 different VSV vaccines for Andes virus: one expressing Andes virus glycoproteins only, and one expressing a combination of Andes and Ebola virus glycoproteins (8)
- one study reported on a DNA vaccine for Sin Nombre virus (4)

Brown and others conducted 2 studies, reported in the same paper, which assessed the effectiveness of a single dose of a vaccine for Andes virus (VSV-G/ANDVGPC, dose: 10^5 PFU) on antibody titres (3). In their first study, vaccination with Andes virus was compared to vaccination for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) in 33 Syrian hamsters (sex: female, age: 5 to 6 weeks). Vaccines were given 28 days before challenge with Andes virus in an injection into the abdomen (dose: 100xLD_{50}, equal to 154 FFU).

N-specific antibodies were tested in serum samples collected immediately before, and 45 days after challenge with Andes virus using a cross-reactive N-specific enzyme-linked immunosorbent assay (ELISA). Before challenge, all hamsters were negative for N-specific antibodies. Following challenge, only hamsters vaccinated with Andes virus survived and so could be tested. Of the 12 surviving hamsters, the study reported borderline levels (80 antibody dilutions) of N-specific antibodies in 2 hamsters, very low (40 antibody dilutions) in one hamster, and undetectable levels (less than 40 antibody dilutions) in 9 hamsters.

Further testing of serum samples for neutralising antibodies was done using a Plaque Reduction Neutralization Test $(PRNT)_{80}$ assay. Before challenge, there were detectable neutralising antibodies in the group given Andes virus vaccine, but not in those vaccinated with the vaccine for Ebola virus. In survivors after challenge, the titres of neutralising antibodies had decreased.

In their second study, which evaluated the effect of the same vaccines on antibody titres, 57 Syrian hamsters (sex: female, age: 5 to 6 weeks old) were vaccinated in groups of 3 to 10 hamsters at 14, 7, or 3 days before challenge with Andes virus via the abdomen (dose: 100xLD_{50}, equal to 154 FFU), compared against either vaccination for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) or control vaccination with DMEM (3). Serum samples were collected immediately before challenge and then 45 days after, using cross reactive N-specific ELISA. Forty-five days after challenge, hamsters that were given a vaccine for Andes virus 14 days before the challenge had high levels of Andes virus specific antibodies, whereas those vaccinated at 7 or 3 days before challenge did not. At 45 days after challenge, all surviving hamsters had similar antibody titres.

Prescott and others evaluated the effect of a single dose of a vaccine for Andes virus (rVSV-G/ANDVGPC, dose: 10^5 PFU) on antibody titres, compared to a sterile medium as control (7). Syrian hamsters (n=24, sex: female, age: 5 to 6 weeks) were challenged with Andes virus (dose: 200 FFU, via the nostril) 6 or 12 months after vaccination. Serum antibodies were collected 42 days after challenge and tested using ELISA. In hamsters challenged 6 months after vaccination, the 5 survivors in the group that received the Andes virus vaccine had ELISA titres of 800 (n=1), 1,600 (n=2), and over 3,200 (n=2), whereas the one survivor from the control group had an ELISA titre of 1,600. In hamsters challenged at 12 months after vaccination, the 5 survivors in the group that received the Andes virus vaccine had ELISA titres of 800 (n=1), 1,600 (n=1), and over 3,200 (n=3), and the 2 survivors in the control group had ELISA titres of over 3,200.

Kuzmin and others evaluated the effectiveness of 4 different Andes virus mRNA vaccines and control (LNP without any RNA) following challenge with Andes virus (full details of interventions and groups reported above) (5). Before challenge, all but 2 vaccinated hamsters had detectable $PRNT_{50}$ neutralising antibody titres, ranging from 1:49 to 1:946 after booster vaccination. The authors reported that the infectious challenge further boosted titres that were already detectable before challenge. Twenty-eight days after challenge, no or low-levels of N-specific antibodies were detected in vaccinated hamsters, in contrast to previous survivors of Andes virus infection (number not reported).

Tsuda and others evaluated the effect of a single dose of either a combined vaccine for both Andes virus and Ebola (VSV-G/dual, dose: 10^5 PFU) or a single vaccine for Andes virus (VSV-G/ANDV, dose: 10^5 PFU) compared to a vaccine for Ebola virus (VSV-G/ZEBOV, dose: 10^5 PFU) (8). Immunoglobulin G end-point dilution titres were used to test serum samples collected one day before and 43 days after challenge with Andes virus. In hamsters given any of the VSV vaccines, no antibody responses were detected in surviving hamsters.

Hooper and others evaluated the effectiveness of a vaccine for Sin Nombre virus (pWRG/SN-M[opt], dose unclear) compared to no vaccination (4). Syrian hamsters (n=15, sex: female, age: 6 to 8 weeks) were either vaccinated 3 times at 3-week intervals, with the last dose given 5 weeks before challenge with Andes virus (dose: 200 PFU [25xLD_{50}, route: injection through muscle) or were not vaccinated. The authors reported that the blood serum from hamsters given a vaccine for Sin Nombre virus, had little cross-neutralisation activity against Andes virus (measured using PRNT titre, specific data was not reported in the paper).

T-cell assay outputs

No studies were identified that reported on T-cell assay outputs.

Post-exposure prophylaxis

Two studies were identified that assessed the protective efficacy of vaccines when given after exposure to Andes virus (3, 6). Both were animal studies conducted in the USA.

Humans

No studies were identified in humans.

Animals

Two studies were identified that assessed the protective efficacy of hantavirus vaccines in Syrian hamsters (3, 6). All studies assessed the effectiveness of vaccines when given after challenge with Andes virus strain Chile-9717869. The 2 identified studies reported on the following vaccines:

- one study reported on a VSV vaccine for Andes virus (3)

- one study reported on 3 different VSV vaccines for Andes virus; one expressing Andes virus glycoproteins only, and 2 expressing different combinations of Andes and Ebola virus glycoproteins (6)

Identified studies are summarised below, with further details provided in Table D.2.

Prevention of infection

No studies were identified that reported on prevention of infection.

Mortality

Both studies identified reported on mortality. However, as study results were presented in terms of number or percentage of animals that survived, the findings are reported here as survival.

Brown and others reported on the effectiveness of a single dose of a vaccine for Andes virus (VSV-G/ANDVGPC, dose: 10^5 PFU) compared to vaccination for Ebola virus (VSV-G/ZEBOVGP, dose: 10^5 PFU) or control vaccination with DMEM (3). Syrian hamsters (n=57, sex: female, age: not reported) were challenged with Andes virus (dose: 100xLD_{50} [equal to 154 FFU], injected via the abdomen) and vaccinated at either one, 3 or 5 days after challenge. Results from this study are summarised in Table 3. Statistical comparisons between the groups were not reported.

Table 3. Survival in hamsters exposed to Andes virus by timing of post-exposure prophylaxis and vaccine type (from Brown and others (3))

Vaccine	Percentage survival Vaccination one day after challenge with Andes virus	Percentage survival Vaccination 3 days after challenge with Andes virus	Percentage survival Vaccination 5 days after challenge with Andes virus
VSV-G/ANDVGPC	90% (9 out of 10)	0% (0 out of 10)	0% (0 out of 10)
VSV-G/ZEBOVGP	100% (6 out of 6)	66.7% (4 out of 6)	0% (0 out of 6)
DMEM	0% (0 out of 3)	0% (0 out of 3)	0% (0 out of 3)

Marceau and others evaluated the effectiveness of a single dose of one of the following vaccines: VSV-ANDV monovalent (vaccine for Andes virus), VSV-ANDV-EBOV bivalent (vaccine for Andes and Ebola virus), VSV-EBOV-ANDV bivalent (vaccine for Andes and Ebola virus) or VSV-EBOV monovalent (vaccine for Ebola virus), when given via the nostril or abdomen (dose 10^5 PFU) to groups of 6 hamsters at either one, 3 or 5 days after challenge with Andes virus, compared to each other or a control group (vaccinated with DMEM given at day one post-exposure) (6). Syrian hamsters (n=156, sex: female, age: 5 to 6 weeks) were challenged by injection into the abdomen with a lethal dose of Andes virus (200 FFU), and

survival was measured for up to 40 days following this challenge. Results are summarised in Table 4; statistical comparisons between the groups were not reported.

Table 4. Survival in hamsters exposed to Andes virus by timing of post-exposure prophylaxis (from Marceau and others (6))

Vaccine *(route)*	Percentage survival Vaccination one day after challenge with Andes virus	Percentage survival Vaccination after 3 days after challenge with Andes virus	Percentage survival Vaccination after 5 days after challenge with Andes virus
VSV-ANDV ***(via nostril)***	0% (0 out of 6)	0% (0 out of 6)	0% (0 out of 6)
VSV-ANDV ***(via abdomen)***	33.3% (2 out of 6)	0% (0 out of 6)	17.0% (1 out of 6)
VSV-ANDV-EBOV ***(intranasal)***	50.0% (3 out of 6)	0% (0 out of 6)	0% (0 out of 6)
VSV-ANDV-EBOV ***(via abdomen)***	100% (6 out of 6)	17.0% (1 out of 6)	0% (0 out of 6)
VSV-EBOV-ANDV ***(via nostril)***	100% (6 out of 6)	0% (0 out of 6)	0% (0 out of 6)
VSV-EBOV-ANDV ***(via abdomen)***	100% (6 out of 6)	83.3% (5 out of 6)	0% (0 out of 6)
VSV-EBOV ***(via nostril)***	83.3% (5 out of 6)	0% (0 out of 6)	0% (0 out of 6)
VSV-EBOV ***(via abdomen)***	100% (6 out of 6)	66.7% (4 out of 6)	100% (6 out of 6)
DMEM ***(via nostril)***	0% (0 out of 6)	Not given	Not given
DMEM ***(via abdomen)***	0% (0 out of 6)	Not given	Not given

Morbidity

No studies were identified that reported on morbidity.

Viral load

One study evaluated the effect of post-exposure vaccination on viral load (6).

Marceau and others evaluated the effectiveness of a single dose (10^5 PFU) of one of the following vaccines on viral load: VSV-ANDV monovalent (vaccine for Andes virus), VSV-EBOV monovalent (control vaccine for Ebola virus), VSV-ANDV-EBOV bivalent (vaccine for Andes and

Ebola virus), or VSV-EBOV-ANDV bivalent (vaccine for Andes and Ebola virus), when given via the nostril or abdomen to groups of 3 hamsters one day after challenge with Andes virus, compared with each other and a DMEM-treated control group (6). Syrian hamsters were challenged by injection through the abdomen with a lethal dose of Andes virus (200 FFU), and viral load was measured through RT-PCR on RNA extracts 8 days after challenge. Detailed statistical comparisons between the groups, by route of challenge, are presented in Table D.1, but in brief:

1. Vaccine given via the nostril one day after challenge: only hamsters given VSV-EBOV-ANDV showed statistically significant lower viral loads in blood or lung tissue compared to control group vaccinated with DMEM ($p<0.05$). VSV-EBOV-ANDV and VSV-EBOV had statistically significant lower blood viral loads than both VSV-ANDV and VSV-ANDV-EBOV (all $p<0.05$). No other statistically significant differences were seen between the other vaccines (all $p>0.05$).
2. Vaccine given by injection into abdomen one day after challenge: hamsters given VSV-EBOV-ANDV showed statistically significant lower viral load in lung tissue compared to control group vaccinated with DMEM ($p<0.05$). VSV-ANDV and VSV-ANDV-EBOV did not differ statistically significantly from the compared to control group vaccinated with DMEM in lung tissue (all $p>0.05$). No other statistically significant differences were seen between the other vaccines (all $p>0.05$). There were no statistically significant differences between any groups for viral loads in blood (all $p>0.05$)

Antibody titres

No studies were identified that reported on antibody titres.

T-cell assay outputs

No studies were identified that reported on T-cell assay outputs.

Health inequalities

No studies were identified in humans, therefore no evidence on any of the populations for whom outcomes may differ (full list in Annexe A) was available.

Limitations

This systematic evidence summary used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

Critical appraisal was not performed due to the rapid completion of this work. This restricts the interpretation of the findings, although important limitations of the evidence have been highlighted in this report.

All included studies were conducted in Syrian hamster animal models; no studies were identified in humans. Animal studies may not accurately reflect the effectiveness of vaccines in humans. However, studies report that Syrian hamsters develop disease after Andes virus challenge that is similar to severe disease in humans (11).

Studies that performed statistical comparisons were limited. The lack of statistical comparisons means that conclusions cannot reasonably be drawn about potential differences in treatment and whether one vaccine may be better than another. This is further confounded by the variety of vaccines and comparators evaluated within studies included.

Sample sizes in all studies included were small, with studies conducting experiments in small groups of hamsters (up to 12 per group), limiting the number that received the vaccine or comparator and virus exposure in each study. This restricts the reliability of findings and the sample sizes may be too small to demonstrate true differences between groups, even when statistical significance has been reported.

The evidence in this review was limited to vaccines only (active vaccination). No other form of prophylaxis, such as transfer of antibodies from other vaccinated individuals were included as part of this review. In-vitro studies were not included in this review.

Evidence gaps

No studies were identified in humans.

There was no evidence identified on prevention of infection or T-cell assay outputs when vaccination for hantaviruses was used as pre-exposure prophylaxis following exposure to Andes virus.

Evidence on post-exposure prophylaxis was limited to 2 studies. No evidence was identified on prevention of infection, morbidity, neutralising antibodies or T-cell assay outputs when vaccination was used as post-exposure prophylaxis following exposure to Andes virus.

Conclusion

The effectiveness of vaccines for hantavirus when used as pre-exposure prophylaxis for exposure to Andes virus was evaluated by 10 pre-clinical animal studies, but no evidence was available in humans. Evidence from animal studies (all in Syrian hamsters) suggests most vaccines tested may have a protective effect, with some reductions in mortality, morbidity, and

viral load and increased antibody titres in hamsters given vaccines for hantavirus compared to control groups (unvaccinated hamsters, or hamsters given vaccines other than for hantavirus). However very few studies tested for statistically significant differences between groups, and the numbers of hamsters included in the studies were likely too low to show a significant difference if it did exist. A number of different vaccines, regimens and comparators were used by the studies, and it was not possible to determine from the available evidence whether one vaccine may be more effective than another.

Evidence for post-exposure prophylaxis was more limited. Two studies were identified, both conducted in hamsters. There was some evidence suggesting that there may be reductions in mortality, but only for certain vaccines when given very close to the time of exposure. The evidence on viral load was too limited to draw any firm conclusions.

In summary, while there is some evidence to suggest potential for effectiveness of hantavirus vaccines for pre-exposure prophylaxis for Andes virus, further evidence is required, particularly from studies in humans.

Acknowledgments

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Disclaimer

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- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal independent peer review but not an external peer review
- are only valid as of the date stated on the review

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10. Custer DM and others. 'Active and passive vaccination against hantavirus pulmonary syndrome with Andes virus M genome segment-based DNA vaccine' Journal of Virology 2003: volume 77, issue 18, pages 9,894 to 9,905
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Annexe A. Protocol

Review question

The review question is:

1. What is the protective efficacy of vaccines for hantavirus following exposure to Andes virus?

A search for primary evidence to answer this review question will be conducted up to 19 May 2026.

Eligibility criteria

Table A.1. Inclusion and exclusion criteria

	Included	Excluded

Population	• people exposed to Andes virus
	  ○ children (0 to 17 years)
	  ○ adults (18 years and over)
	  If available:
	  ○ immunocompromised adults
	  ○ pregnant women
	• animals exposed to Andes virus	

Context	The review is interested in evidence from use in humans in real life contexts, but as vaccines for hantavirus are still in development, pre-clinical studies in animals will also be included to inform the question	
Settings	Any	
Intervention or exposure	Hantavirus vaccines (monotherapy): • Hantavax • Bivalent HFRS vaccine • ANDV DNA vaccine • MVA-Hanta vaccine • HTNV/PUUV DNA vaccine • mRNA hantavirus vaccine • INO-008	
Comparator	Not required	

	Included	Excluded
	Any comparator will be included where reported	
Outcomes	Any measure of prevention of infection Disease severity: • mortality • morbidity • Iin animals only: viral load Antibody titres including any neutralising/pseudovirus neutralising titres T cell assay outputs Outcomes will be reported separately for pre- and post-exposure prophylaxis	
Language	English	Any other language
Date of publication	Up to 19 May 2026	
Study design	Experimental studies including: • randomised-controlled trials • non-randomised controlled trials • quasi-experimental studies Observational studies, including: • cohort studies Animal studies	Reviews (all types) Modelling studies Qualitative studies Cross-over designs Cross-sectional studies Case-control studies Descriptive studies including case series, case reports Mixed methods In vitro studies
Publication type	Peer-reviewed published research Preprints	Conference abstracts Editorials Letters News articles Grey literature Clinical trial records

Identification of studies

The following databases will be searched for studies published up to 19 May 2026: Ovid Medline, Ovid Embase, Web of Science Preprint Citation Index. The search strategy is presented in Search strategy below.

Screening

Title and abstract screening will be undertaken in duplicate by at least 2 reviewers for at least 10% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include country, study period or timeframe, study design, intervention (including dose, administration and timing), participants, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second. Data that is only available in graphs or figures and not in text will not be extracted.

Risk of bias assessment

Risk of bias of included studies will not be formally assessed in this systematic evidence summary due to time constraints, but important limitations of the evidence will be highlighted.

Synthesis

Where studies are similar enough to combine and present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of participants in each study, effect size and variance and a summary of the risk of bias across studies reporting each outcome will be summarised and presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health inequalities

The following health equity considerations have been raised as relevant to this topic, and where they relate to outcomes in this review, will be taken into account in the interpretation of the evidence, when information is available:

Geographic equity

Remote or rural populations may have higher exposure but have limited access to advanced care and diagnostics and vaccines (particularly post-exposure) could reduce reliance on intensive care. However, these same populations may face barriers to rapid vaccine deployment, cold chain or timely administration.

Access to interventions due to socioeconomic factors

People affected by poverty often have less access to interventions due to affordability, accessibility and health literacy. Similarly, efficacy studies should also consider acceptability of interventions due to cultural or religious beliefs across populations and the impact on effectiveness when implemented.

Age and sex

Children, pregnant women and those with co-morbidities (already included in the study population)

Likelihood of exposure

Variation by exposure and differences in risk context for example, occupation, housing, climate. For example, there are likely to be gender differentials in both occupational exposure and vaccine uptake. This may include male-dominated farm workforces such as agriculture, farming, forestry, construction, cleaning, waste management and pest control, and conversely a female-dominated health and care workforce in many contexts. This may lead to selection bias in study populations, while mobile workforces may lead to information bias in outcomes.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 20 May 2026)

1. exp Orthohantavirus/ (3,939)
2. Orthohantavir*.tw,kf. (429)
3. Hantaan virus/ (588)
4. Hantavirus Infections/ (1,528)
5. hantaan virus*.tw,kf. (825)
6. hantaanvir*.tw,kf. (4)
7. hantavir*.tw,kf. (4,151)
8. hanta vir*.tw,kf. (49)
9. Andes vir*.tw,kf. (254)
10. ANDV.tw,kf. (207)
11. ANDV?CHI-9717869.tw,kf. (0)
12. ANDV?ARG.tw,kf. (0)
13. ANDV?CHI-7913.tw,kf. (0)
14. ANDV?Epilink?96.tw,kf. (0)
15. ANDV?Epuyen?18?19.tw,kf. (0)
16. korean h?emorrhagic fever*.tw,kf. (102)
17. Hemorrhagic Fever with Renal Syndrome/ (2,955)
18. h?emorrhagic nephroso-nephritis virus*.tw,kf. (3)
19. (h?emorrhagic fever adj2 renal syndrome*).tw,kf. (2,401)
20. hfrs.tw,kf. (2,057)
21. Hantavirus Pulmonary Syndrome/ (673)
22. Hantavirus Pulmonary Syndrome.tw,kf. (804)
23. Puumala virus/ (495)
24. Puumala vir*.tw,kf. (628)
25. Seoul virus/ (166)
26. Seoul vir*.tw,kf. (310)
27. Sin Nombre virus/ (168)
28. sin nombre vir*.tw,kf. (347)
29. muerto canyon vir*.tw,kf. (8)
30. four corners vir*.tw,kf. (9)
31. Dobrava.tw,kf. (307)
32. castelo dos sonhos.tw,kf. (9)
33. CASV.tw,kf. (18)
34. Lechiguanas.tw,kf. (17)
35. LECV.tw,kf. (3)
36. Oran.tw,kf. (368)
37. ORNV.tw,kf. (32)
38. Laguna negra.tw,kf. (40)
39. LANV.tw,kf. (8)
40. Rio mamore.tw,kf. (28)

41. Araucaria.tw,kf. (427)
42. ARAUV.tw,kf. (2)
43. Araraquara.tw,kf. (230)
44. ARQV.tw,kf. (2)
45. Bermejo.tw,kf. (61)
46. BMJV.tw,kf. (0)
47. Juquitiba.tw,kf. (40)
48. JUQV.tw,kf. (9)
49. Bolivia vir*.tw,kf. (3)
50. BMIV.tw,kf. (14)
51. Anajatuba.tw,kf. (12)
52. Tunari.tw,kf. (9)
53. Andes central plata.tw,kf. (1)
54. Seewis.tw,kf. (30)
55. Saaremaa.tw,kf. (72)
56. or/1-55 [Hanta virus terms] (8,591)
57. exp Vaccines/ (308,564)
58. exp Immunization/ (232,140)
59. vaccin*.tw,kf. (497861)
60. immuni#ation*.tw,kf. (137,925)
61. immuni#e*.tw,kf. (65,662)
62. hantavax.tw,kf. (9)
63. Bivalent HFRS.tw,kf. (1)
64. ANDV DNA vaccin*.tw,kf. (5)
65. MVA Hanta vaccin*.tw,kf. (0)
66. HTNV PUUV DNA vaccin*.tw,kf. (2)
67. mRNA hantavirus vaccin*.tw,kf. (0)
68. INM008.tw,kf. (0)
69. ADI 65533.tw,kf. (0)
70. ADI 65534.tw,kf. (2)
71. INM007.tw,kf. (0)
72. Zapnometinib.tw,kf. (12)
73. or/57-72 (690619)
74. (immune adj (system* or response or protect*)).tw,kf. (398,862)
75. exp Immunity/ (450,981)
76. immunity.tw,kf. (315,719)
77. antibod*.tw,kf. (1,058,450)
78. anti-bod*.tw,kf. (617)
79. antigen*.tw,kf. (763,576)
80. Antibodies/ or Antibodies, Viral/ (206,573)
81. exp Antibodies, Neutralizing/ (23,543)
82. exp Antigens/ (1,237,694)
83. or/74-82 (2,838,389)
84. Cross Reactions/ (39,718)

85. cross react*.tw,kf. (68,382)
86. cross protect*.tw,kf. (5,536)
87. cross recog*.tw,kf. (500)
88. heterologous reactiv*.tw,kf. (20)
89. (cross adj (neutrali#e* or neutrali#ation or neutrali#ing)).tw,kf. (2,513)
90. (activ* adj (neutrali#e* or neutrali#ation or neutrali#ing)).tw,kf. (237)
91. cross bind*.tw,kf. (181)
92. cross antigenicit*.tw,kf. (112)
93. (conserv* adj3 epitope*).tw,kf. (3,917)
94. broad reactivity.tw,kf. (335)
95. pan reactivity.tw,kf. (19)
96. ((Shar* or similar* or alternat* or related) adj7 epitope*).tw,kf. (7,735)
97. ((Shar* or similar* or alternat* or related) adj7 antigen*).tw,kf. (37,154)
98. ((Shar* or similar* or alternat* or related) adj7 disease*).tw,kf. (314,385)
99. ((Shar* or similar* or alternat* or related) adj7 pathogen*).tw,kf. (53,369)
100. ((Shar* or similar* or alternat* or related) adj7 virus*).tw,kf. (48,899)
101. ((Shar* or similar* or alternat* or related) adj7 strain*).tw,kf. (63,159)
102. ((Pathogen* or strain* or disease* or virus) adj5 "not targeted").tw,kf. (60)
103. or/84-102 (587,833)
104. 56 and 73 (587)
105. 56 and 83 and 103 (410)
106. 104 or 105 (931)
107. limit 106 to (comment or editorial or letter or news or newspaper article) (21)
108. 106 not 107 (910)

Embase (1974 to 19 May 2026)

1. Orthohantavir*.tw,kf. (456)
2. exp Hantavirus/ (5490)
3. exp Hantavirus infection/ (3,305)
4. hantaan virus*.tw,kf. (947)
5. hantaanvir*.tw,kf. (7)
6. hantavir*.tw,kf. (4805)
7. hanta vir*.tw,kf. (97)
8. Andes vir*.tw,kf. (288)
9. ANDV.tw,kf. (236)
10. ANDV?CHI-9717869.tw,kf. (0)
11. ANDV?ARG.tw,kf. (0)
12. ANDV?CHI-7913.tw,kf. (0)
13. ANDV?Epilink?96.tw,kf. (0)
14. ANDV?Epuyen?18?19.tw,kf. (0)
15. korean h?emorrhagic fever*.tw,kf. (111)
16. exp hemorrhagic fever with renal syndrome/ (1,577)
17. h?emorrhagic nephroso-nephritis virus*.tw,kf. (0)

18. (h?emorrhagic fever adj2 renal syndrome*).tw,kf. (2,732)
19. hfrs.tw,kf. (2542)
20. Hantavirus pulmonary syndrome/ (1,016)
21. Hantavirus Pulmonary Syndrome.tw,kf. (893)
22. Puumala virus/ (1,041)
23. Puumala vir*.tw,kf. (721)
24. Seoul virus/ (347)
25. Seoul vir*.tw,kf. (345)
26. Sin Nombre virus/ (300)
27. sin nombre vir*.tw,kf. (371)
28. muerto canyon vir*.tw,kf. (9)
29. four corners vir*.tw,kf. (9)
30. Dobrava.tw,kf. (363)
31. castelo dos sonhos.tw,kf. (10)
32. CASV.tw,kf. (17)
33. Lechiguanas.tw,kf. (19)
34. LECV.tw,kf. (5)
35. Oran.tw,kf. (687)
36. ORNV.tw,kf. (29)
37. Laguna negra.tw,kf. (48)
38. LANV.tw,kf. (9)
39. Rio mamore.tw,kf. (35)
40. Araucaria.tw,kf. (480)
41. ARAUV.tw,kf. (2)
42. Araraquara.tw,kf. (309)
43. ARQV.tw,kf. (2)
44. Bermejo.tw,kf. (142)
45. BMJV.tw,kf. (1)
46. Juquitiba.tw,kf. (46)
47. JUQV.tw,kf. (10)
48. Bolivia vir*.tw,kf. (3)
49. BMIV.tw,kf. (17)
50. Anajatuba.tw,kf. (13)
51. Tunari.tw,kf. (11)
52. Andes central plata.tw,kf. (1)
53. Seewis.tw,kf. (34)
54. Saaremaa.tw,kf. (86)
55. or/1-54 (10,273)
56. exp vaccine/ (510,910)
57. exp immunization/ (458,216)
58. vaccin*.tw,kf. (602,014)
59. immuni#ation*.tw,kf. (165,501)
60. immuni#e*.tw,kf. (77,661)
61. hantavax.tw,kf. (30)

62. Bivalent HFRS.tw,kf. (2)
63. ANDV DNA vaccin*.tw,kf. (7)
64. MVA Hanta vaccin*.tw,kf. (0)
65. HTNV PUUV DNA vaccin*.tw,kf. (5)
66. mRNA hantavirus vaccin*.tw,kf. (0)
67. INM008.tw,kf. (0)
68. ADI 65533.tw,kf. (0)
69. ADI 65534.tw,kf. (2)
70. INM007.tw,kf. (0)
71. Zapnometinib.tw,kf. (13)
72. or/56-71 (877842)
73. exp immunity/ (2,162,046)
74. immunity.tw,kf. (399,361)
75. (immune adj (system* or response or protect*)).tw,kf. (545,956)
76. antibod*.tw,kf. (1,437,967)
77. anti-bod*.tw,kf. (1,966)
78. antibody/ or exp virus antibody/ (313,030)
79. exp neutralizing antibody/ (64,151)
80. exp antigen/ (2,298,805)
81. antigen*.tw,kf. (961,290)
82. or/73-81 (4,828,989)
83. cross reaction/ (51,908)
84. cross react*.tw,kf. (81,395)
85. cross protect*.tw,kf. (6,120)
86. cross recog*.tw,kf. (632)
87. heterologous reactiv*.tw,kf. (17)
88. heterologous immunity/ (1428)
89. (cross adj (neutrali#e* or neutrali#ation or neutrali#ing)).tw,kf. (2,763)
90. (activ* adj (neutrali#e* or neutrali#ation or neutrali#ing)).tw,kf. (301)
91. cross bind*.tw,kf. (233)
92. cross antigenicit*.tw,kf. (119)
93. (epitope* adj3 conserv*).tw,kf. (4,553)
94. broad reactivity.tw,kf. (381)
95. pan reactivity.tw,kf. (88)
96. ((Shar* or similar* or alternat* or related) adj7 epitope*).tw,kf. (9,690)
97. ((Shar* or similar* or alternat* or related) adj7 antigen*).tw,kf. (44,796)
98. ((Shar* or similar* or alternat* or related) adj7 disease*).tw,kf. (459,356)
99. ((Shar* or similar* or alternat* or related) adj7 pathogen*).tw,kf. (65,567)
100. ((Shar* or similar* or alternat* or related) adj7 virus*).tw,kf. (56,112)
101. ((Shar* or similar* or alternat* or related) adj7 strain*).tw,kf. (69,084)
102. ((Pathogen* or strain* or disease* or virus) adj5 "not targeted").tw,kf. (77)
103. or/83-102 (776,201)
104. 55 and 72 (912)
105. 55 and 82 and 103 (504)

106. 104 or 105 (1,324)
107 limit 106 to ("clinical trial (clinicaltrials.gov)" or conference abstract or conference paper or "conference review" or editorial or letter) (150)
108. 106 not 107 (1,174)

Web of Science Preprint Citation Index (1990 to current)

Date of search: 21 May 2026

Search 1:

TS=(Orthohantavir*) OR TS=("hantaan virus*") OR TS=(hantaanvir*) OR TS=(hantavir*) OR TS=("hanta vir*") OR TS=("Andes vir*") OR TS=(ANDV) OR TS=(ANDV$CHI-9717869) OR TS=(ANDV$ARG) OR TS=(ANDV$CHI-7913) OR TS=(ANDV$Epilink 96) OR TS=(ANDV$Epuyen 18 19) OR TS=("korean h$emorrhagic fever*") OR TS=("h$emorrhagic nephroso-nephritis virus*") OR TS=(("h$emorrhagic fever" NEAR/1 "renal syndrome*")) OR TS=(hfrs) OR TS=("Hantavirus Pulmonary Syndrome") OR TS=("Puumala vir*") OR TS=("Seoul vir*") OR TS=("sin nombre vir*") OR TS=("muerto canyon vir*") OR TS=("four corners vir*") OR TS=(Dobrava) OR TS=("castelo dos sonhos") OR TS=(CASV) OR TS=(Lechiguanas) OR TS=(LECV) OR TS=(Oran) OR TS=(ORNV) OR TS=("Laguna negra") OR TS=(LANV) OR TS=("Rio mamore") OR TS=(Araucaria) OR TS=(ARAUV) OR TS=(Araraquara) OR TS=(ARQV) OR TS=(Bermejo) OR TS=(BMJV) OR TS=(Juquitiba) OR TS=(JUQV) OR TS=("Bolivia vir*") OR TS=(BMIV) OR TS=(Anajatuba) OR TS=(Tunari) OR TS=("Andes central plata") OR TS=(Seewis) OR TS=(Saaremaa)

AND

TS=(vaccin*) OR TS=(immuni?ation*) OR TS=(immuni?e*) OR TS=(hantavax) OR TS=("Bivalent HFRS") OR TS=("ANDV DNA vaccin*") OR TS=("MVA Hanta vaccin*") OR TS=("HTNV PUUV DNA vaccin*") OR TS=("mRNA hantavirus vaccin*") OR TS=(INM008) OR TS=("ADI 65533") OR TS=("ADI 65534") OR TS=(INM007) OR TS=(Zapnometinib)

Search 2:

TS=(Orthohantavir*) OR TS=("hantaan virus*") OR TS=(hantaanvir*) OR TS=(hantavir*) OR TS=("hanta vir*") OR TS=("Andes vir*") OR TS=(ANDV) OR TS=(ANDV$CHI-9717869) OR TS=(ANDV$ARG) OR TS=(ANDV$CHI-7913) OR TS=(ANDV$Epilink 96) OR TS=(ANDV$Epuyen 18 19) OR TS=("korean h$emorrhagic fever virus*") OR TS=("h$emorrhagic nephroso-nephritis virus*") OR TS=(("h$emorrhagic fever" NEAR/1 "renal syndrome*")) OR TS=(hfrs) OR TS=("Hantavirus Pulmonary Syndrome") OR TS=("Puumala vir*") OR TS=("Seoul vir*") OR TS=("sin nombre vir*") OR TS=("muerto canyon vir*") OR TS=("four corners vir*") OR TS=(Dobrava) OR TS=("castelo dos sonhos") OR TS=(CASV) OR TS=(Lechiguanas) OR TS=(LECV) OR TS=(Oran) OR TS=(ORNV) OR TS=("Laguna negra") OR TS=(LANV) OR TS=("Rio mamore") OR TS=(Araucaria) OR TS=(ARAUV) OR TS=(Araraquara) OR TS=(ARQV) OR TS=(Bermejo) OR TS=(BMJV) OR TS=(Juquitiba) OR

TS=(JUQV) OR TS=("Bolivia vir*") OR TS=(BMIV) OR TS=(Anajatuba) OR TS=(Tunari) OR TS=("Andes central plata") OR TS=(Seewis) OR TS=(Saaremaa)

AND

TS=(immunity) OR (TS=((immune NEAR/0 (system* OR response OR protect*)))) OR TS=(antibod*) OR TS=(anti-bod*) OR TS=(antigen*)

AND

TS=("cross react*") OR TS=("cross protect*") OR TS=("cross recog*") OR TS=("heterologous reactiv*") OR (TS=((cross NEAR/0 (neutrali?e* OR neutrali?ation OR neutrali?ing)))) OR (TS=((activ* NEAR/0 (neutrali?e* OR neutrali?ation OR neutrali?ing)))) OR TS=("cross bind*") OR TS=("cross antigenicit*") OR TS=((epitope* NEAR/2 conserv*)) OR TS=("broad reactivity") OR TS=("pan reactivity") OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 epitope*))) OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 antigen*))) OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 disease*))) OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 pathogen*))) OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 virus*))) OR (TS=(((Shar* OR similar* OR alternat* OR related) NEAR/6 strain*))) OR (TS=(((Pathogen* OR strain* OR disease* OR virus) NEAR/4 "not targeted")))

Search 1 or search 2: 18 results

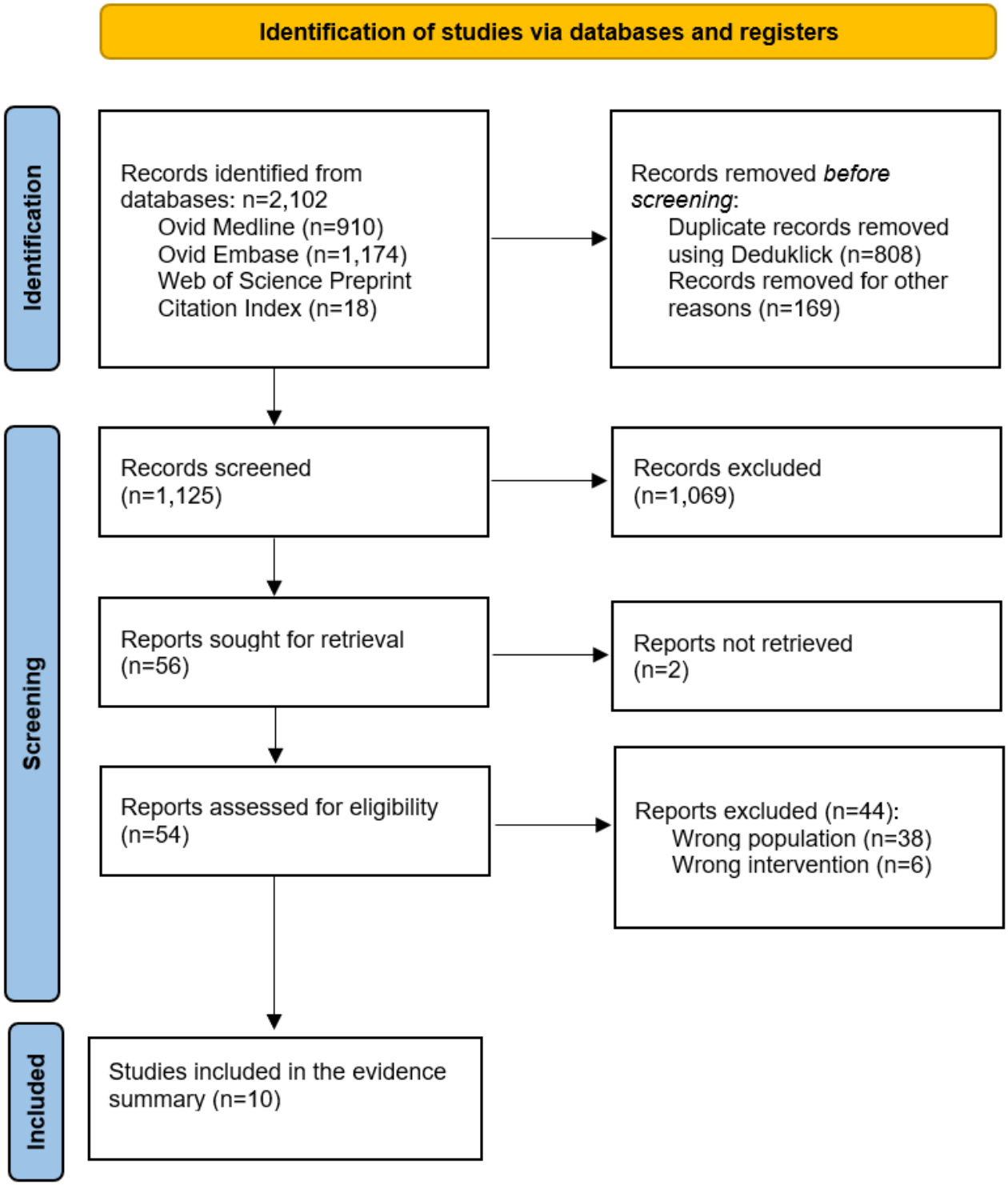
Deviations

There were no deviations from the protocol, but one clarification was made:

- any hantavirus vaccine identified would be included, rather than just the examples listed in the protocol

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this evidence summary, ultimately including 10 studies.

From identification of studies via databases and registers, n=2,102 records identified from databases:

- Ovid Medline (n=910)
- Ovid Embase (n=1,174)
- Web of Science Preprint Citation Index (n=18)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=808)
- records removed for other reasons (n=169)

n=1,125 records screened, of which n=1,069 were excluded, leaving n=56 papers sought for retrieval, of which n=2 were not retrieved.

Of the n=54 papers assessed for eligibility, n=44 reports were excluded:

- wrong population (n=38)
- wrong intervention (n=6)

n=10 papers included in the evidence summary.

Annexe C. Excluded full texts

Wrong population (38 studies)

Aram M and others. 'A Multi-Valent Hantavirus Vaccine Based on Recombinant Modified Vaccinia Ankara Reduces Viral Load in a Mouse Infection Model' Vaccines 2025: volume 13, issue 3, page 4

Boudreau EF and others. 'A Phase 1 clinical trial of Hantaan virus and Puumala virus M-segment DNA vaccines for hemorrhagic fever with renal syndrome' Vaccine 2012: volume 30, issue 11, pages 1,951 to 1,958

Brocato RL and others. 'Preclinical evaluation of a fully human, quadrivalent-hantavirus polyclonal antibody derived from a non-human source' mBio 2024: volume 15, issue 10, e0160024

Bucht G and others. 'Modifying the cellular transport of DNA-based vaccines alters the immune response to hantavirus nucleocapsid protein' Vaccine 2001: volume 19, issue 28, pages 3,820 to 3,829

Chen Y and others. 'History of incomplete vaccination may associate with occurrence of hemorrhagic fever with renal syndrome with relieved clinical symptoms' Journal of Medical Virology 2016: volume 88, issue 7, pages 1,168 to 1,172

Cho HW and others. 'Antibody responses in humans to an inactivated hantavirus vaccine (Hantavax)' Vaccine 1999: volume 17, issue 20, pages 2,569 to 2,575

Choi Y and others. 'Inactivated Hantaan virus vaccine derived from suspension culture of Vero cells' Vaccine 2003: volume 21, issue 17, pages 1,867 to 1,873

Dargeviciute A and others. 'Yeast-expressed Puumala hantavirus nucleocapsid protein induces protection in a bank vole model' Vaccine 2002: volume 20, issue 29, pages 3,523 to 3,531

Duehr J and others. 'Neutralizing Monoclonal Antibodies against the Gn and the Gc of the Andes Virus Glycoprotein Spike Complex Protect from Virus Challenge in a Preclinical Hamster Model' mBio 2020: volume 11, issue 2, page 24

Elgh F and others. 'Development of humoral cross-reactivity to the nucleocapsid protein of heterologous hantaviruses in nephropathia epidemica' FEMS Immunology and Medical Microbiology 1998: volume 22, issue 4, pages 309 to 315

Guan MD and others. 'Safety and immunogenicity of bivalent inactivated vaccine against haemorrhagic fever with renal syndrome in a phase II trial on healthy Chinese volunteers' International Journal of Biotechnology 2007: volume 9, pages 261 to 266

Hao H and others. 'Genetic immunization with Hantavirus vaccine combining expression of G2 glycoprotein and fused interleukin-2' Genetic Vaccines and Therapy 2008: volume 6, page 15

Hooper JW and others. 'DNA vaccination with the Hantaan virus M gene protects Hamsters against three of four HFRS hantaviruses and elicits a high-titer neutralizing antibody response in Rhesus monkeys' Journal of Virology 2001: volume 75, issue 18, pages 8,469 to 8,477

Hooper JW and others. 'Hantaan/Andes virus DNA vaccine elicits a broadly cross-reactive neutralizing antibody response in nonhuman primates' Virology 2006: volume 347, issue 1, pages 208 to 216

Hooper JW and others. 'A Phase 1 clinical trial of Hantaan virus and Puumala virus M-segment DNA vaccines for haemorrhagic fever with renal syndrome delivered by intramuscular electroporation' Clinical Microbiology and Infection 2014: volume 20, pages 110 to 117

Hooper JW and others. 'Phase 1 clinical trial of Hantaan and Puumala virus DNA vaccines delivered by needle-free injection' npj Vaccines 2024: volume 9, issue 1, page 221

Jiang DB and others. 'Construction and evaluation of DNA vaccine encoding Hantavirus glycoprotein N-terminal fused with lysosome-associated membrane protein' Vaccine 2015: volume 33, issue 29, pages 3,367 to 3,376

Jiang DB and others. 'Recombinant DNA vaccine of Hantavirus Gn and LAMP1 induced long-term immune protection in mice' Antiviral Research 2017: volume 138, pages 32 to 39

Khan A and others. 'A Systems Vaccinology Approach Reveals the Mechanisms of Immunogenic Responses to Hantavax Vaccination in Humans' Scientific Reports 2019: volume 9, issue 1, pages 4,760

Klingstrom J and others. 'Vaccination of C57/BL6 mice with Dobrava hantavirus nucleocapsid protein in Freund's adjuvant induced partial protection against challenge' Vaccine 2004: volume 22, issue 29, pages 4,029 to 4,034

Lee BH and others. 'A pseudotype vesicular stomatitis virus containing Hantaan virus envelope glycoproteins G1 and G2 as an alternative to hantavirus vaccine in mice' Vaccine 2006: volume 24, issue 15, pages 2,928 to 2,934

Li J and others. 'HSP70 gene fused with Hantavirus S segment DNA significantly enhances the DNA vaccine potency against hantaviral nucleocapsid protein in vivo' Vaccine 2007: volume 25, issue 2, pages 239 to 252

Li K and others. 'Induction of Hantaan virus-specific immune responses in C57BL/6 mice by immunization with a modified recombinant adenovirus containing the chimeric gene, GcS0.7' International Journal of Molecular Medicine 2013: volume 32, issue 3, pages 709 to 716

Li Z and others. 'The assessment of Hantaan virus-specific antibody responses after the immunization program for hemorrhagic fever with renal syndrome in northwest China' Human vaccines & Immunotherapeutics 2017: volume 13, issue 4, pages 802 to 807

Liu X and others. 'Changes of HFRS Incidence Caused by Vaccine Intervention in Yichun City, China, 2005-2013' Medical Science Monitor 2016: volume 22, pages 295 to 301

Liu YY and others. 'Pathogenicity of novel hantavirus isolate and antigenicity and immunogenicity of novel strain-based inactivated vaccine' Vaccine 2023: volume 41, issue 49, pages 7,482 to 7,490

Lu Q and others. 'Immune responses to inactivated vaccine in people naturally infected with hantaviruses' Journal of Medical Virology 1996: volume 49, issue 4, pages 333 to 335

Ma Y and others. 'Protective $CD8^+$ T-cell response against Hantaan virus infection induced by immunization with designed linear multi-epitope peptides in HLA-A2.1/K^b transgenic mice' Virology Journal 2020: volume 17, issue 1, page 146

Maes P and others. 'Truncated recombinant Dobrava hantavirus nucleocapsid proteins induce strong, long-lasting immune responses in mice' Intervirology 2006: volume 49, issue 5, pages 253 to 260

Seon SH and others. 'An Unmodified rVSV-Hantaan Virus GP Vaccine Candidate Elicits Durable Neutralizing Antibodies in Mice' SSRN. 2026: volume 11

Sohn YM and others. 'Primary humoral immune responses to formalin inactivated hemorrhagic fever with renal syndrome vaccine (Hantavax): consideration of active immunization in South Korea' Yonsei Medical Journal 2001: volume 42, issue 3, pages 278 to 284

Song JY and others. 'Long-term immunogenicity and safety of inactivated Hantaan virus vaccine (Hantavax TM) in healthy adults' Vaccine 2016: volume 34, issue 10, pages 1,289 to 1,295

Song JY and others. 'Immunogenicity and safety of a modified three-dose priming and booster schedule for the Hantaan virus vaccine (Hantavax): A multi-center phase III clinical trial in healthy adults' Vaccine 2020: volume 38, issue 50, pages 8,016 to 8,023

Yi Y and others. 'Effectiveness of inactivated hantavirus vaccine on the disease severity of hemorrhagic fever with renal syndrome' Kidney Research and Clinical Practice 2018: volume 37, issue 4, pages 366 to 372

Zhang H and others. 'Single dose recombinant VSV based vaccine elicits robust and durable neutralizing antibody against Hantaan virus' npj Vaccines 2024: volume 9, issue 1, page 28

Zhang J and others. 'A comprehensive investigation of Glycoprotein-based nucleic acid vaccines for Hantaan Virus' npj Vaccines 2024: volume 9, issue 1, page 196

Zhao C and others. 'Immunogenicity of a multi-epitope DNA vaccine against hantavirus' Human vaccines & Immunotherapeutics 2012: volume 8, issue 2, pages 208 to 215

Zheng Y and others. 'Persistence of immune responses to vaccine against haemorrhagic fever with renal syndrome in healthy adults aged 16-60 years: results from an open-label2-year follow-up study' Infectious Diseases 2018: volume 50, issue 1, pages 21 to 26

Wrong intervention (6 studies)

Garrido JL and others. Two recombinant human monoclonal antibodies that protect against lethal Andes hantavirus infection in vivo' Science Translational Medicine 2018: volume 10, issue 468, page 21

Haese N and others. 'Antiviral Biologic Produced in DNA Vaccine/Goose Platform Protects Hamsters Against Hantavirus Pulmonary Syndrome When Administered Post-exposure' PLOS Neglected Tropical Diseases [electronic resource] 2015: volume 9, issue 6, e0003803

Hammerbeck CD and others. 'Depletion of Alveolar Macrophages Does Not Prevent Hantavirus Disease Pathogenesis in Golden Syrian Hamsters' Journal of Virology 2016: volume 90, issue 14, pages 6,200 to 6,215

Hooper JW and others. 'A lethal disease model for hantavirus pulmonary syndrome' Virology 2001: volume 289, issue 1, pages 6 to 14

Hooper JW and others. 'Immune serum produced by DNA vaccination protects hamsters against lethal respiratory challenge with Andes virus' Journal of Virology 2008: volume 82, issue 3, pages 1,332 to 1,338

Ramos KE and others. 'Hantavirus Gn^{H} Nanoparticle Immunogen Elicits a Cross-Neutralizing Antibody Response in Mice' ACS Infectious Diseases 2025: volume 11, issue 11, pages 3,061 to 3,070

Annexe D. Data extraction tables

Table D.1. Summary of studies reporting protective efficacy following administration of hantavirus vaccines as pre-exposure prophylaxis for Andes virus

Note: Only outcomes for which evidence was identified in at least one study are included in the table. No evidence was identified for the outcomes of prevention of infection or T-cell assay outputs.

Abbreviations: DMEM: Dulbecco's Modified Eagle Medium; DNA: Deoxyribonucleic Acid; ELISA: Enzyme-Linked Immunosorbent Assay; FFU: Focus-Forming Units; GMT: Geometric Mean Titre; GP: Glycoprotein; GPC: Glycoprotein precursor; Gn/Gc: Glycoprotein n and Glycoprotein c; LD_{50}: 50% of lethal dose; LNP: Lipid Nanoparticle; mRNA: Messenger Ribonucleic Acid; µg: microgram; NP: Nucleoprotein; PBS: Phosphate-Buffered Saline; PFU: Plaque-Forming Units; PRNT: Plaque Reduction Neutralisation Test; $PRNT_{50}$: 50% Plaque Reduction Neutralisation Test; $PRNT_{80}$: 80% Plaque Reduction Neutralisation Test; RNA: Ribonucleic Acid; SNV: Sin Nombre virus; USA: United States of America; VSV: Vesicular Stomatitis Virus; ZEBOV: Zaire ebolavirus.

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
Brocato and others, 2013 (1) USA Study 1 (Two studies reported in same paper)	Syrian hamsters (n not reported; experimental group challenged via nostril: 8 to 10 per group) Sex: not reported Age: not reported	Andes virus strain Chile-9717869 Challenge via nostril: dose of 4,000 PFU (challenge performed either 14 or 20 weeks after vaccination)	Puumula virus DNA vaccine (pWRG/PUU-M[s2]) Hantaan DNA vaccine (pWRG/HTN-M[x]) 3 times at weekly intervals Dose: 2µg plasmid DNA per shot	Control (unvaccinated)	Survival reported up to 35 days after challenge: Puumula virus DNA vaccine: Survival rate was statistically significantly higher compared to control hamsters (14 weeks: p=0.0428, 20 weeks: p<0.0001) Hantaan virus DNA vaccine: Survival rate did not statistically significantly differ compared to control hamsters (both p>0.05), however there was evidence of partial protection (non-significant increase in survival rate)	Not reported	Not reported	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
Brocato and others, 2013 (1) USA Study 2 (Two studies reported in same paper)	Syrian hamsters (n not reported; experimental group challenged via injection into muscle: 9 to 10 per group) Sex: not reported Age: not reported	Andes virus strain Chile-9717869 Challenge via injection into muscle: dose of 2,000 PFU (challenge performed 7 weeks after vaccination)	Puumula virus DNA vaccine (pWRG/PUU-M[s2]) Hantaan DNA vaccine (pWRG/HTN-M[x]) 3 times at weekly intervals Dose: 2µg plasmid DNA per shot	Control (unvaccinated)	Survival reported up to 35 days after challenge: Puumula virus DNA vaccine: Survival rate was statistically significantly higher compared to control hamsters (p=0.0062) Hantaan virus DNA vaccine: Survival rate did not statistically significantly differ compared to control hamsters, however there was evidence of partial protection (non-significant increase in survival rate, p value not reported)	Not reported	Not reported	Not reported
Brocato and others, 2021 (2) USA Study 1 (Two studies reported in same paper)	Syrian hamsters (n not reported) Sex: female Age: not reported	Andes virus strain Chile-9717869 Challenge via injection into muscle: dose of 200 PFU	pWRG/AND-M(1.1) Andes virus DNA vaccine pWRG/AND-M(opt2) codon-optimised Andes virus DNA vaccine Given via an injection under	Control (unvaccinated) Each other	Survival did not differ significantly between the vaccinated or unvaccinated hamsters (p>0.05, exact numbers of surviving hamsters not reported)	Not reported	Not reported	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			the skin or via injection into muscle, 4 doses at 4-week intervals (week 0, 4, 8, 12) before challenge. Dose: 200µg					
Brocato and others, 2021 (2) USA Study 2 (Two studies reported in same paper)	Syrian hamsters (n not reported) Sex: female Age: not reported	Andes virus strain Chile-9717869 Challenge via injection into muscle: dose of 200 PFU	pWRG/AND-M(1.1) Andes virus DNA vaccine. pWRG/AND-M(opt2) codon-optimised Andes virus DNA vaccine Given via an injection under the skin or via injection into muscle, 3 doses at 4-week intervals (week 0, 4, and 8) before challenge. Dose: 200µg	Control (vaccinated with 0.2 mL PBS via thigh) Each other	One out of 8 (12.5%) hamsters vaccinated with the non-optimised vaccine survived, but there was a statistically significant delay in death compared to the control hamsters (p=0.0137). Mortality rate is not compared with the control group for this vaccine. 7 out of 15 (46.7%) hamsters vaccinated with the optimised vaccine survived until the end of the study (28 days after challenge). This was statistically significantly higher compared to the control hamsters (p=0.0014).	Not reported	Not reported	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
					There were no survivors in the control group (n not reported)			
Brown and others, 2011 (3) USA Study 1 (Two studies reported in same paper)	Syrian hamsters (n=33) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge via injection into abdomen: 100 x LD_{50} (equal to 154 FFU)	VSV-G/ANDVGPC (expressing Andes virus glycoprotein), given 28 days before challenge via the abdomen	Control (vaccinated with 10^5 PFU expressing Zaire ebolavirus (strain Mayinga-76) glycoprotein [VSV-G/ZEBOVGP] via the abdomen)	VSV-G/ANDVGPC vaccine: 12 out of 12 survived (100%) by day 11 Control vaccine: 0 of 9 survived (0%) by day 11	Control: showed clinical signs of Andes virus infection beginning at 8 days after challenge (lethargy, hunched posture, and breathing abnormalities), progressing to end-stage disease (severe respiratory distress) in all hamsters by day 11 Vaccinated: those receiving the ANDVGPC vaccine did not show any clinical signs of infection at any point after challenge	Groups of 3 control and 3 study hamsters were euthanised at both day 5 and day 8 after challenge (12 hamsters total; 6 per group). RT-PCR was used to detect viral RNA. Control: Significant levels of Andes virus RNA were detected at day 5, increasing by approximately one-half log units by day 8. At both days 5 and 8, lung tissue showed the highest viral RNA load, followed by liver. Blood samples had lower levels of viral RNA than lung and liver tissue. Vaccinated: No Andes virus RNA was detected in any tissues collected at either day 5 or day 8 in the 6 hamsters	To test Andes virus N-specific antibodies, a cross-reactive N-specific ELISA was used. Serum samples were collected immediately before challenge (28 days after vaccination) and 45 days after Andes virus challenge in surviving hamsters. **Before challenge:** Both the control (n=15) and the vaccinated hamsters (n=17) were negative for N-specific antibodies. **After challenge:** There were no surviving control hamsters, so this was not tested. Of the surviving 12 vaccinated hamsters, there were borderline levels (80 antibody

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							receiving the VSVG/ANDVGPC vaccine. These results indicate complete protection against Andes virus replication in vaccinated hamsters Viral RNA levels were significantly lower in vaccinated hamsters compared to unvaccinated hamsters across tissues and timepoints ($p < 0.05$ to $p < 0.001$)	dilutions) of N-specific antibodies in 2, very low levels (40 antibody dilutions) in 1, and undetectable levels (<40 antibody dilutions) in 9 hamsters. **PRNT80 Neutralising Antibody Test:** **Before challenge:** The control hamsters showed no detectable Andes virus Gn/Gc neutralising antibodies (n=15). All of the vaccinated hamsters showed relatively high levels of neutralising antibodies (320 antibody dilutions in 7 hamsters, 640 antibody dilutions in 4 and 1280 antibody dilutions in 6). **After challenge:** There were no surviving control hamsters, so this was not tested. Of

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
								the surviving vaccinated hamsters (n=12), the titres of neutralising antibodies dropped 45 days after challenge (1,280 antibody dilutions in one hamster, 640 antibody dilutions in one, 320 antibody dilutions in 3, 160 antibody dilutions in 5, 80 antibody dilutions in one and 40 antibody dilutions in one).
Brown and others, 2011 (3) USA Study 2 (two studies reported in the same paper)	Syrian hamsters (n=57) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge via injection into abdomen: 100 x LD_{50} (equal to 154 FFU)	VSV-G/ANDVGPC (expressing Andes virus glycoprotein), given 14, 7, or 3 days before challenge via the abdomen	Control (vaccinated with 10^5 PFU expressing Zaire ebolavirus (strain Mayinga-76) glycoprotein [VSV-G/ZEBOVGP] via the abdomen) Control (DMEM via the abdomen)	**Vaccinated 14 days before challenge:** • VSV-G/ANDVGPC vaccine: 10 out of 10 survived (100%) • VSV-G/ZEBOVGP vaccine: 0 out of 6 survived (0%) • DMEM vaccine: 0 out of 3 survived (0%) **Vaccinated 7 days before challenge:** • VSV-G/ANDVGPC	Not reported	Not reported	Serum samples were collected immediately before challenge and 45 days after challenge from all surviving hamsters. Antibody responses: Hamsters immunised at 14 days before challenge had high levels of Andes virus N-specific antibodies, whereas those vaccinated at 3 or 7 days before challenge did not.

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
					vaccine: 10 out of 10 survived (100%) • VSV-G/ZEBOVGP vaccine: 3 out of 6 survived (50%) • DMEM vaccine: 0 out of 3 survived (0%) **Vaccinated 3 days before challenge:** • VSV-G/ANDVGPC vaccine: 10 out of 10 survived (100%) • VSV-G/ZEBOVGP vaccine: 5 out of 6 survived (83%) • DMEM vaccine: 0 out of 3 survived (0%)			Before challenge, serum showed high levels of neutralising antibodies at 28 days after vaccination and moderate levels at 14 days but no neutralising antibodies were detected at 7 or 3 days. At 45 days after challenge, all surviving hamsters showed similar antibody titres.
Custer and others, 2003 (10) USA Study 1 (two studies reported in the same paper)	Syrian hamsters (n=39) Sex: Female Age: 6 to 8 weeks	Andes virus strain Chile-9717869 Challenge by injection into abdomen: 2,000 FFU	HTNV M DNA vaccine plasmid (pWRG/HTN-M(x) [a vaccine that contains Hantaan virus DNA]) Administered 3 times at 3-week intervals (n=24)	Control (vaccinated with negative control plasmid [pWRG7077]), ~0.75µg delivered via gene gun	HTNV M DNA vaccine: 9 out of 24 survived (37.5%) Control vaccine: 1 out of 15 survived (6.7%) Protection against lethal ANDV	Not reported	Not reported	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			delivered via gene gun, DNA loading: ~0.75µg of plasmid DNA		challenge was not statistically significant (but suggestive) (p=0.057) Mean day of death: Vaccinated: 13 Control: 13 Hamsters that survived the first challenge were rechallenged with the same dose (time since last dose not reported), all hamsters survived re-challenge			
Custer and others, 2003 (10) USA Study 2 (2 studies reported in the same paper)	Syrian hamsters (n=22) Sex: Female Age: 6 to 8 weeks	Andes virus strain Chile-9717869 Challenge by injection into abdomen: 2,000 FFU	ANDV M genome segment-based DNA vaccine (pWRG/AND-M [a vaccine that contains Andes virus DNA]) Given 3 times at 3-week intervals with pWRG/AND-M (n=14) delivered via gene gun	Control (unvaccinated)	ANDV M genome segment-based DNA vaccine: 2 out of 14 survived (14.3%) Control: 2 out of 8 survived (25%) No statistical test reported Mean day of death: ANDV M genome segment-based DNA vaccine: 12 and 13 Control: 12 and 13	ANDV M genome segment-based DNA vaccine: 12 out of 14 (85.7%) developed HPS before death Control: 6 of 8 (75%) developed HPS before death	Not reported	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
Hooper and others, 2013 (4) USA	Syrian hamsters (n=15) Sex: female Age: 6 to 8 weeks	Andes virus strain Chile-9717869 Challenge via injection into muscle: dose 200 PFU	SNV DNA vaccine (pWRG/SN-M[opt]) (contains DNA from Sin Nombre virus) Given 3 times at 3-week intervals, last dose 5 weeks before challenge using a gene gun (dose unclear)	Control (unvaccinated)	SNV DNA vaccine: 3 out of 8 survived (37.5%) Control: 1 out of 7 survived (14.3%) There were no statistically significant differences in mortality between the control and the SNV DNA vaccinated hamsters (p=0.31)	Not reported	Not reported	ANDV PRNT: Serum from vaccinated hamsters had little cross-neutralisation activity (SNV DNA vaccine and Andes virus challenge): data not presented in paper
Kuzmin and others, 2024 (5) USA	Syrian hamsters (n=25) Sex: female Age: 10 weeks	Andes virus strain Chile-9717869 Challenge via injection into muscle: dose 250 PFU	Andes virus mRNA vaccines: LNP-encapsulated vaccines, either U-mRNA vaccine (contains Andes virus mRNA) or N1-methylpseudouridine- modified mRNA vaccine (contains a slightly altered form of Andes virus mRNA) Doses: 5µg or 25µg prime-boost regimen	Control (vaccinated with empty lipid nanoparticles without mRNA vaccine), same dosing and administration regimen	Survival was assessed up to 28 days after challenge. LNP-encapsulated regular uridine (U)-mRNA vaccine: 5 out of 5 survived (100%) 25µg LNP-encapsulated U-mRNA vaccine: 5 out of 5 survived (100%) 5µg N1-methylpseudouridine (modified) mRNA: 3 out of 5 survived (60%)	All 5 control hamsters and 2 hamsters vaccinated with 5µg modified-mRNA vaccine abruptly showed signs of severe disease 9 days after challenge. The observed clinical signs were lack of movement/reactivity, hunched posture, rapid shallow breathing, and progressive respiratory distress.	Liver tissues were collected at death (either following euthanisation due to severe disease or euthanisation at the end of the experiment). High titres of Andes virus were detected in all hamsters euthanised following severe disease. No virus was isolated from the liver tissues of hamsters that survived to the end of the experiment.	Neutralising antibody titres were detectable after vaccination and before challenge and increased after the booster dose (day 21). After boosting, all but 2 vaccinated hamsters showed detectable $PRNT_{50}$, ranging from 1:49 to 1:946, indicating that serum could be diluted 49- to 946-fold and still achieve 50% virus neutralisation. The challenge further increased neutralising antibody

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			given via injection into muscle, vaccinated on day 0, booster dose given on day 21) Dose groups: 5µg U-mRNA vaccine: 5 hamsters 25µg U-mRNA vaccine: 5 hamsters 5µg modified mRNA vaccine: 5 hamsters 25µg modified mRNA vaccine: 5 hamsters		25µg N1-methylpseudouridine (modified) mRNA: 5 out of 5 survived (100%) Control group (0 out of 5 survived (0%)	Findings observed after death: pulmonary oedema All other hamsters survived until the end of the experiment and showed no signs of disease, including changes in body weight or body temperature.		titres relative to before challenge levels. To assess sterilising immunity, sera were collected 28 days after challenge. No of low-levels of N-specific antibodies were detected in vaccinated hamsters, in contrast to previous survivors of ANDV infection (n not reported).
Marceau and others, 2024 (6) USA	Syrian hamsters (n=333) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge via injection into abdomen: dose 200 FFU	VSV-ANDV vaccine, (monovalent, vaccine for Andes virus only) VSV-ANDV-EBOV bivalent vaccine (bivalent, vaccine for Andes and Ebola virus) VSV-EBOV-ANDV vaccine	Control (vaccinated with DMEM) Control (vaccinated with monovalent vaccine for Ebola virus [VSV-EBOV vaccine]) Same dose and administration	Survival was assessed up to 40 days after challenge. **Given 28 days before challenge**: • VSV-EBOV control via nostril: 0 out of 6 survived (0%; deaths occurred between days 6 and 11 after challenge).	Not reported	Viral load measured in lung and blood samples of 3 hamsters per group 8 days after challenge with Andes virus. **Given 28 days before challenge (via nostril):** • VSV-ANDV: Viral loads in both blood and lung tissue were significantly lower	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			(bivalent, vaccine for Andes and Ebola virus) Given 28 or 3 days before challenge, dose of 0.1mL when given through the nostril, 0.4mL when given via the abdomen (10^5 PFU)	regimen as intervention	• VSV-EBOV control injection via abdomen: 0 out of 6 survived (0%, deaths occurred between days 6 and 11 after challenge) • VSV-ANDV via nostril: 6 out of 6 survived (100%) • VSV-ANDV injection via abdomen 5 out of 6 survived (83.3%) • VSV-ANDV-EBOV via nostril: 6 out of 6 survived (100%) • VSV-ANDV-EBOV injection via abdomen: 6 out of 6 survived (100%) • VSV-EBOV-ANDV via nostril: 6 out of 6 survived (100%) • VSV-EBOV-ANDV injection via abdomen: 6 out of 6 survived (100%)		than in the DMEM control group and the VSV-EBOV control group (all p<0.0001). No significant differences were observed compared with the other vaccine groups (p>0.05) • VSV-ANDV-EBOV: Viral loads in blood and lung tissue were significantly lower than in the DMEM control group and the VSV-EBOV control group (all p<0.0001). No significant differences were observed compared with the other vaccine groups (all p>0.05) • VSV-EBOV-ANDV: Viral loads in blood and lung tissue were significantly lower than in the DMEM control group and the VSV-EBOV	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
					There is no data for control hamsters as they received treatment only on day 1 after challenge. **Given 3 days before challenge**: • VSV-ANDV via nostril: 2 out of 6 survived (33%) • VSV-ANDV injection via abdomen: 6 out of 6 survived (100%) • VSV-ANDV-EBOV via nostril: 6 out of 6 survived (100%) • VSV-ANDV-EBOV injection via abdomen: 6 out of 6 survived (100%) • VSV-EBOV-ANDV via nostril: 6 out of 6 survived (100%) • VSV-EBOV-ANDV injection via abdomen: 6 out of 6 survived (100%) • VSV-EBOV via nostril: 0 out of 6 survived (0%)		control group (all p<0.0001). No significant differences were observed compared with the other vaccine groups. (p>0.05) • VSV-EBOV: No statistically significant difference in viral load in blood and lung tissue compared to the DMEM control group (p>0.05) **Given 28 days before challenge (via abdomen):** • VSV-ANDV: Lung and blood viral load was significantly lower than in the DMEM control group (p<0.0001 and p<0.01, respectively). No statistical differences with other vaccines were reported (p>0.05)	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
					• VSV-EBOV injection via abdomen: 2 out of 6 survived (33.3%) There is no data for control hamsters as they received treatment only on day 1 after challenge.		• VSV-ANDV-EBOV: Lung and blood viral load was significantly lower than in the DMEM control group ($p<0.0001$ and $p<0.01$, respectively). No statistical differences with other vaccines were reported ($p>0.05$) • VSV-EBOV-ANDV: Lung and blood viral load was significantly lower than in the DMEM control group ($p<0.0001$ and $p<0.01$, respectively). No statistical differences with other vaccines reported ($p>0.05$). • VSV-EBOV: Lung viral load was significantly lower than in the DMEM control group ($p<0.001$), while no significant difference was observed in blood	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							viral load. No statistical differences with other vaccines reported (all p>0.05) **Given 3 days before challenge (via nostril):** • VSV-ANDV: Viral loads in lung tissue and blood were significantly lower than in the DMEM control group (p<0.0001 and p<0.01, respectively). No statistical differences with other vaccines reported (p>0.05) • VSV-ANDV-EBOV: Viral loads in lung tissue were significantly lower than in the DMEM control group (p<0.001), VSV-EBOV control group (p<0.05), and VSV-ANDV (p<0.01). Blood viral loads were	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							also significantly lower than in the DMEM control group (p<0.001), VSV-EBOV control (p<0.05), and VSV-ANDV (p<0.05) • VSV-EBOV-ANDV: Viral loads in lung tissue were significantly lower than in the DMEM control group (p<0.001), VSV-EBOV control (p<0.05), and VSV-ANDV (p<0.01). Blood viral loads were also significantly lower than in the DMEM control group (p<0.001), VSV-EBOV control (p<0.05), and VSV-ANDV (p<0.05). • VSV-EBOV: Viral loads in blood and lung tissue were not significantly different from the intranasal DMEM control group	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							(p>0.05). However, viral loads were significantly higher than in the VSV-ANDV-EBOV and VSV-EBOV-ANDV groups (all p<0.05) **Given 3 days before challenge (via abdomen):** • VSV-ANDV: Viral loads in both blood and lung tissue were significantly lower than in the DMEM control group (both p<0.0001) and the VSV-EBOV control group (p<0.0001). No statistical differences with other vaccines reported (p>0.05) • VSV-ANDV-EBOV: Viral loads in both blood and lung tissue were significantly lower than in the DMEM control group (both p<0.0001)	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							and the VSV-EBOV control group (p<0.0001). No statistical differences with other vaccines reported (p>0.05) • VSV-EBOV-ANDV: Viral loads in both blood and lung tissue were significantly lower than in the DMEM control group (both p<0.0001) and the VSV-EBOV control group (p<0.0001). No statistical differences with other vaccines reported (p>0.05). • VSV-EBOV: Lung viral load was significantly lower than in the DMEM control group (p<0.001). However, lung viral loads were significantly higher than in all other vaccine groups (all p<0.0001). In blood, no	

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
							significant difference was observed compared to the DMEM control group ($p>0.05$), but viral loads were significantly higher than in all other vaccine groups (all $p<0.001$)	
Prescott and others, 2014 (7). USA	Syrian hamsters (n=24) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge given via nostril: dose 200 FFU	rVSV-G/ANDVGPC (a VSV vaccine expressing Andes virus glycoprotein) Given 6 and 12 months before challenge, dose of 10^5 PFU given via injection into the abdomen	Control (vaccination with sterile medium), injection via the abdomen	**After 6 months**: • rVSV-G/ANDVGPC vaccine: 5 out of 6 survived (83.3%) • Control vaccine: 1 out of 6 survived (16.7%) **After 12 months**: • rVSV-G/ANDVGPC vaccine: 5 out of 6 survived (83.3%) • Control vaccine: 2 out of 6 survived (33.3%)	Not reported	Not reported	Serum antibodies were collected 42 days after challenge using ELISA test. **After 6 months:** Of 6 vaccinated hamsters, one did not survive; one had an ELISA titre of 800, 2 had a titre of 1,600, and 2 had a titre of equal to or more than 3,200. Of 6 control hamsters, 5 did not survive; one had an ELISA titre of 1,600. **After 12 months**: Of 6 vaccinated hamsters, one did not survive; one had an ELISA titre of 800,

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
								one had a titre of 1,600, and 3 had a titre of equal to or more than 3,200. Of 6 control hamsters that received the control, 4 did not survive; 2 had an ELISA titre of equal to or more than 3,200
Tsuda and others, 2011 (8) USA	Syrian hamsters (n=12) Sex: male Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge via injection into abdomen: 100xLD_{50}	VSV-G/Dual (bivalent recombinant vesicular stomatitis virus vaccine expressing both Andes virus and Zaire Ebola virus glycoproteins) VSV-G/ANDV (monovalent recombinant vesicular stomatitis virus vaccine expressing Andes virus glycoprotein) Given 28 days after vaccination,	Control (vaccinated with 10^5 PFU monovalent [VSV-G/ZEBOV] expressing Ebola virus glycoproteins), injection via the abdomen	VSV-G/Dual: 6 out of 6 survived (100%) VSV-G/ANDV: 3 out of 3 survived (100%) VSV-G/ZEBOV: 0 out of 3 survived (0%; all succumbed within 9 days of challenge)	Not reported	Groups of 3 hamsters were euthanised at day 6 or 9 after infection. VSV-G/Dual: except one hamster on day 9 after challenge (extremely low viral RNA levels detected in spleen on day 9: less than 10^1 FFU equivalent/200 ng RNA), all other hamsters showed no detectable ANDV viral RNA in blood, lung, liver, spleen VSV-G/ANDV: No detectable ANDV viral RNA in blood, lung, liver, spleen	Protective efficacy (Immunoglobulin G end-point dilution titres, serum samples collected one day before and 43 days after challenge): VSV-G/Dual: • Anti-ANDV NP (before): less than 100 • Anti-ANDV NP (after): less than 100 VSV-G/ANDV: • Anti-ANDV NP (before): less than 100 • Anti-ANDV NP (after): less than 100

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			dose of 10^5 PFU injected via the abdomen				VSV-G/ZEBOV: No detectable Andes virus RNA in all samples at both time points	VSV-G/ZEBOV: • Anti-ANDV NP (before): less than 100 • Anti-ANDV NP (after): Not able to be determined due to before hamster loss. The authors suggested that all 3 VSV vaccine vectors confer complete and largely sterile protection after a single immunisation against lethal Andes virus challenge
Warner and others, 2019 (9) Canada	Syrian hamsters (n=18) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenge via injection into abdomen: dose 200 FFU	rVSV-G/ANDVGPC (a VSV vaccine expressing Andes virus glycoprotein) rVSV-G/SNVGPC (a VSV vaccine expressing Sin Nombre virus glycoproteins), Given 28 days before challenge, at dose of 10^5	Control (vaccinated with LASV DNA vaccine [rVSV-G/LASVGPC], a VSV-based Lassa virus vaccine, injection via the abdomen, dose 10^5 PFU	rVSV-G/ANDVGPC: 6 out of 6 survived (100%) and statistically significant compared to rVSV-G/LASVGPC vaccine where one out of 6 survived [16.7%], $p<0.01$) rVSV-G/SNVGPC: 5 out of 6 survived (83.3%), statistically significant compared to rVSV-G/LASVGPC	rVSV-G/ANDVGPC: Significantly reduced pathology in tissues compared to the control vaccine (rVSV-G/LASVGPC), which showed moderate to severe pulmonary oedema, haemorrhaging and infiltration of mononuclear cells in the lungs, hepatocellular necrosis, and infiltration of lymphocytes into the	rVSV-G/ANDVGPC vaccine (n=3): No detectable ANDV RNA at 8 days after challenge	Not reported

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, findings are reported as survival)	Morbidity	Viral load	Antibody titres
			PFU injected via abdomen		(1 out of 6 survived [16.7%], p<0.01)	liver and spleen. Staining of lungs, liver and spleen was performed 7 days following Andes virus challenge rVSV-G/SNVGPC: There was little to no histological change in tissue samples, similar to rVSV-G/ANDVGPC		

Table D.2. Summary of studies reporting prevention of infection or outcomes of disease severity following administration of hantavirus vaccines as post-exposure prophylaxis for Andes virus

Note: Only outcomes for which evidence was identified are included in the table. No evidence was identified for the outcomes of prevention of infection, morbidity, antibody titres or T-cell assay outputs

Abbreviations: DMEM: Dulbecco's Modified Eagle Medium; FFU: Focus-Forming Units; LD_{50}: 50% of lethal dose; USA: United States of America; VSV-G/ZEBOVGP: Vesicular Stomatitis Virus expressing Zaire Ebola virus glycoproteins; VSV-ANDV: Vesicular Stomatitis Virus-Based Andes virus; VSV-ANDV-EBOV: Bivalent Vesicular Stomatitis Virus Vaccine expressing Andes virus and Ebola virus glycoproteins; VSV-EBOV: Vesicular Stomatitis Virus-Based Ebola Virus Vaccine; VSV-EBOV-ANDV: Bivalent Vesicular Stomatitis Virus Vaccine expressing Ebola virus and Andes virus glycoproteins

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, the findings are reported as survival)	Viral load
Brown and others, 2011 (3) USA	Syrian hamsters (n=57) Sex: female Age: 5 to 6 weeks	Andes virus strain Chile-9717869 Challenged via injection to abdomen: 100 x LD_{50} (equal to 154 FFU)	Single dose of 10^5 PFU of VSV-G/ANDVGPC (expressing Andes virus glycoprotein) Given 1, 3, or 5 days after challenge Injected via abdomen	Control (single dose of 10^5 PFU VSV-G/ZEBOVGP [expressing Zaire ebolavirus strain Mayinga-76 glycoprotein]) or Control (single dose of DMEM) Given 1, 3, or 5 days after challenge Injected via abdomen	**One day after challenge**: • VSV-G/ANDVGPC: 9 out of 10 (90%) • VSV-G/ZEBOVGP: 6 out of 6 (100%) • DMEM control: 0 out of 3 (0%) **3 days after challenge:** • VSV-G/ANDVGPC: 0 out of 10 survived (0%) • VSV-G/ZEBOVGP: 4 out of 6 survived (67%) • DMEM control: 0 out of 3 survived: (0%) **5 days after challenge:** • VSV-G/ANDVGPC: 0 out of 10 survived (0%) • VSV-G/ZEBOVGP: 0 out of 6 survived (0%) • DMEM control: 0 out of 3 survived (0%) In hamsters given any vaccine 5 days after challenge, all deaths were between days 9 and 11 after challenge.	Not reported
Marceau and others, 2024	Syrian hamsters (n=333)	Andes virus strain Chile-9717869	VSV-ANDV vaccine	Control (vaccinated with DMEM)	Survival assessed up to 40 days after challenge, control hamsters received	Viral load measured in lung and blood samples of 3 hamsters per

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, the findings are reported as survival)	Viral load
(6) USA	Sex: female Age: 5 to 6 weeks	Challenged via injection to abdomen, dose: 200 FFU	(monovalent, vaccine for Andes virus only) VSV-ANDV-EBOV vaccine (bivalent, vaccine for Andes and Ebola virus) VSV-EBOV-ANDV vaccine (bivalent, vaccine for Andes and Ebola virus) Given 1, 3 or 5 days after challenge, Injected via abdomen or given via nostril	or: Control (vaccinated with monovalent vaccine for Ebola virus [VSV-EBOV vaccine]) or: Each other Control vaccines given 1, 3 or 5 days after challenge Injected via abdomen or given via nostril	treatment on day one after challenge only. **Given one day after challenge**: • VSV-ANDV (via nostril): 0 out of 6 survived (0%) • VSV-ANDV (via abdomen): 2 out of 6 survived (33.3%) • VSV-ANDV-EBOV (via nostril): 3 out of 6 survived (50.0%) • VSV-ANDV-EBOV (via abdomen): 6 out of 6 survived (100%) • VSV-EBOV-ANDV (via nostril): 6 out of 6 survived (100%) • VSV-EBOV-ANDV (via abdomen): 6 out of 6 survived (100%) • VSV-EBOV control (via nostril): 5 out of 6 survived (83.3%) • VSV-EBOV control (via abdomen): 6 out of 6 survived (100%) • DMEM control (via nostril): 0 out of 6 survived (0%) • DMEM control (via abdomen): 0 out of 6 survived (0%) **Given 3 days after challenge**: • VSV-ANDV (via nostril): 0 out of 6 survived (0%) • VSV-ANDV (via abdomen): 0 out of 6 survived (0%) • VSV-ANDV-EBOV (via nostril): 0 out of 6 survived (0%) • VSV-ANDV-EBOV (via abdomen): 1 out of 6 survived (16.7%)	group at 8 days after Andes virus challenge. **Given one day after challenge (via nostril):** • VSV-ANDV: No statistically significant difference in viral load in blood or lungs compared to DMEM control group. Statistically significantly higher viral load in blood compared to VSV-EBOV control ($p<0.05$) and VSV-EBOV-ANDV ($p<0.05$). Statistically significantly higher viral load in blood compared to both VSV-EBOV control ($p<0.01$) and VSV-ANDV-EBOV ($p<0.05$) • VSV-ANDV-EBOV: No statistically significant difference in viral load in blood or lungs compared to DMEM control group. In blood only, statistically significantly higher viral load compared to VSV-EBOV control ($p<0.05$) • VSV-EBOV-ANDV: Statistically significantly lower viral load in lung and blood tissue compared to DMEM control ($p<0.05$). Statistically significantly lower viral load in lung tissue compared to VSV-ANDV-EBOV ($p<0.05$), and statistically significantly lower viral load in blood compared to VSV-ANDV (<0.05) • VSV-EBOV (control): Statistically significantly lower viral load in lung and blood tissue compared to DMEM control ($p<0.05$).

Author, year, country	Population	Exposure	Intervention	Comparator	Mortality (as study results were presented in terms of surviving animals, the findings are reported as survival)	Viral load
					• VSV-EBOV-ANDV (via nostril): 0 out of 6 survived (0%) • VSV-EBOV-ANDV (via abdomen): 5 out of 6 survived (83.3%) • VSV-EBOV control (via nostril): 0 out of 6 survived (0%) • VSV-EBOV control (via abdomen): 4 out of 6 survived (66.7%) **Given 5 days after challenge**: • VSV-ANDV (via nostril): 0 out of 6 survived (0%) • VSV-ANDV (via abdomen): 0 out of 6 survived (16.7%) • VSV-ANDV-EBOV (via nostril): 0 out of 6 survived (0%) • VSV-ANDV-EBOV (via abdomen): 0 out of 6 survived (0%) • VSV-EBOV-ANDV (via nostril): 0 out of 6 survived (0%) • VSV-EBOV-ANDV (via abdomen): 0 out of 6 survived (0%) • VSV-EBOV control (via nostril): 0 out of 6 survived (0%) • VSV-EBOV control (via abdomen): 6 out of 6 survived (100%)	Statistically significantly lower viral load in lung tissue compared to VSV-ANDV ($p<0.05$), and statistically significantly lower viral load in blood compared to VSV-ANDV ($p<0.001$) and VSV-ANDV-EBOV ($p<0.05$) **Given one day after challenge (via abdomen):** • VSV-ANDV: No statistically significant difference in viral load in blood or lungs compared to DMEM control group • VSV-ANDV-EBOV: No statistically significant difference in viral load in blood or lungs compared to DMEM control group • VSV-EBOV-ANDV: Statistically significantly lower viral load in lung tissue compared to DMEM control ($p<0.05$). No statistically significant difference in viral load in blood compared to DMEM control. • VSV-EBOV (control): Statistically significantly lower viral load in lung tissue compared to DMEM control ($p<0.05$). No statistically significant difference in viral load in blood compared to DMEM control.

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UK Health Security Agency (UKHSA) prevents, prepares for and responds to infectious diseases and environmental, radiological and chemical hazards, to keep all our communities safe, save lives and protect livelihoods. We provide scientific and operational leadership, working with local, national and international partners to protect the public's health.

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