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### **Emerging Risk of Hantavirus Outbreaks in South America and Probabilistic Spillover to Europe via Human Migration**

Dr. Fabiano de Abreu Agrela Rodrigues - Post-PhD in Neurosciences, specialist in Genomics  
Heraclitus Research and Analysis Center (CPAH), Department of Neurosciences and Genomics, Brazil & Portugal

Orcid: <https://orcid.org/0000-0002-5487-5852>

Corresponding author: [contato@cpah.com.br](mailto:contato@cpah.com.br)

MSc. Adriel Pereira da Silva Weber – MSc in Neuropsychology, Physicist, Specialist in People and Project Management

Heraclitus Research and Analysis Center (CPAH), Department of Physics, Brazil & Portugal

Orcid: <https://orcid.org/0009-0003-1157-8318>

Corresponding author: [contato@cpah.com.br](mailto:contato@cpah.com.br)

#### **Abstract**

Hantaviruses are diseases carried by rodents that can cause serious illness in humans, including hantavirus cardiopulmonary syndrome (HCPS) in the Americas and hemorrhagic fever with renal syndrome (HFRS) in parts of Europe and Asia. Brazil and Argentina are major hotspots for HCPS, with several different hantavirus genotypes in circulation and repeated local outbreaks. With growing migration and travel from South America to Europe, particularly to Spain and Portugal, there is increasing concern that hantavirus infections may be imported and go unrecognized in European countries where South American genotypes are not usually found. In this article, we present an expanded narrative review and a conceptual risk assessment that brings together epidemiological data from South America, reports from Europe, and a simplified probabilistic model that takes into account migration volumes, estimated incidence, and the likelihood of detecting cases. Our analysis indicates that, even with conservative assumptions, the expected number of imported hantavirus infections into the Iberian Peninsula over several years is not negligible. This is especially worrisome in the case of Andes virus, which has shown limited person-to-person

transmission. We examine both the biological and statistical aspects of transmission, differences in risk among migrant subgroups, and what this means for clinical practice and surveillance in Europe. We propose that hantavirus should be explicitly considered in the differential diagnosis of acute febrile illnesses with respiratory or renal involvement in European regions with substantial South American immigration, and we recommend targeted awareness efforts, improved diagnostic readiness, and the development of more detailed quantitative risk models.

**Keywords:** Hantavirus; hantavirus cardiopulmonary syndrome; South America; Brazil; Argentina; Europe; Portugal; Spain; migration; probabilistic risk assessment; emerging infections.

## 1. Introduction

Hantaviruses, members of the family *Hantaviridae*, are enveloped, negative-sense RNA viruses maintained in nature by persistent infections in rodent and more recently recognized, shrew and bat reservoirs (Jonsson et al., 2010). Human infection is typically acquired through inhalation of aerosols contaminated with virus-laden rodent urine, droppings, or saliva, although bites and direct contact are also possible. The clinical manifestations are geographically distinct: in Eurasia, hantaviruses classically cause hemorrhagic fever with renal syndrome (HFRS), while in the Americas they cause hantavirus cardiopulmonary syndrome (HCPS), characterized by severe pulmonary edema and shock, with case-fatality rates frequently exceeding 30% (Figueiredo et al., 2014; Martinez et al., 2020).

South America has become a critical region for hantavirus cardiopulmonary syndrome (HCPS). This is because Brazil and Argentina have several hantavirus genotypes and their

reservoirs in rodents. In addition, environmental changes, agricultural expansion, and climate fluctuations affect rodent populations and also the frequency with which people come into contact with them, which can trigger periodic HCPS epidemics. In our current global health scenario, these epidemics cannot be treated as exclusively local problems because they develop in a world of intense human mobility, very easily connecting endemic hantavirus areas in South America to those regions where these viruses are not normally present.

Europe is not unfamiliar with hantaviruses. Endemic HFRS caused by Puumala and Dobrava Belgrade viruses has long been documented in several European countries, including Finland, Sweden, Germany, and Slovenia (Vaheri et al., 2013; Heyman et al., 2011). However, clinical knowledge tends to focus on local hantavirus syndromes, and awareness of South American genotypes associated with HCPS is much more limited, especially in southern Europe. Meanwhile, both Spain and Portugal have become important destinations for South American immigrants, especially Brazilians, highlighting the epidemiological link between the two continents.

This article has three main goals. First, we review the current hantavirus epidemiology in South America, with a focus on Brazil and Argentina as likely sources of future case surges. Second, we describe the European situation, considering both the circulation of locally acquired hantaviruses and the migration routes that link South America to Europe. Third, we present and examine a simplified probabilistic framework to estimate the risk of imported infections and to show how underdiagnosis and low clinical suspicion can significantly increase the real impact on European health systems, even when the absolute probability of importation appears low.

## **2. Hantaviruses and hantavirus disease: biological and clinical overview**

### **2.1 Viral diversity and reservoirs**

Hantaviruses are genetically diverse and exhibit strong host specificity. Distinct viral genotypes are associated with specific rodent species, which in turn define the ecological niches and geographic distribution of human disease (Jonsson et al., 2010). In South America, multiple genotypes such as Andes virus, Araraquara virus, Juquitiba virus, and others have been described, predominantly associated with *Oligoryzomys* and other sigmodontine rodents (Figueiredo et al., 2014; Martinez et al., 2020).

A key characteristic of hantaviruses is that they remain stable in the environment. Although they are enveloped viruses and can be inactivated by heat and ultraviolet light, under favorable conditions they can stay infectious for hours to days in dried rodent urine, droppings, or nesting material (Vaheri et al., 2013). This matters directly for how they spread: activities that stir up contaminated dust, like sweeping enclosed spaces, handling stored grain, or working in agricultural settings, can release infectious particles into the air, which people then inhale.

## **2.2 Transmission routes and rare human-to-human spread**

The main way hantaviruses spread is from rodents to humans. How much a person is exposed depends on how many infected rodents are around, how much virus they shed, how well the environment preserves the virus, and what people are doing in that setting. From a more “physical” point of view, you can think of the risk of infection by inhalation as depending on the amount of virus in the air (viral particles per unit of air) and how much air a person breathes over time. In high-risk situations, such as cleaning cabins with heavy rodent infestations, the total inhaled dose (particle concentration × air volume inhaled × duration of exposure) can become high enough to overwhelm the body’s defenses.

Human-to-human transmission is historically considered negligible for most hantaviruses. However, Andes virus, which circulates in Argentina and Chile, has demonstrated limited person-to-person transmission in close contacts, including household

members and healthcare workers (Martinez et al., 2020). This feature significantly distinguishes Andes virus from most other hantaviruses and has implications for imported cases: while large sustained transmission chains are unlikely, specific clusters in confined environments cannot be ruled out.

### **2.3 Clinical manifestations and severity**

HCPS typically presents after an incubation period of 1 to 4 weeks, starting with a prodrome of fever, myalgia, and headache, often indistinguishable from other acute febrile illnesses. This is followed by a cardiopulmonary phase characterized by cough, hypoxia, rapidly progressive non-cardiogenic pulmonary edema, and shock (Figueiredo et al., 2014). Case-fatality rates in South America have been reported between 30% and 40%, though estimates vary by region, genotype, and access to intensive care. Survivors often experience prolonged convalescence but generally recover without chronic sequelae.

In contrast, European HFRS presents with fever, abdominal pain, and acute kidney injury, with lower case-fatality rates for *Puumala virus* (typically <1%) and higher for *Dobrava-Belgrade virus* (up to 12%) (Vaheri et al., 2013; Papa et al., 2020; European Centre for Disease Prevention and Control, 2023). For European clinicians, this difference in clinical phenotype is important: an imported HCPS case from South America might initially be confused with severe viral pneumonia or even COVID-19, delaying appropriate diagnosis and supportive care.

### **3. South American epidemiology: Brazil and Argentina as hotspots**

Brazil and Argentina provide paradigmatic examples of HCPS-endemic areas. In Brazil, hundreds of confirmed HCPS cases have been reported since the 1990s, with concentrations in southern and southeastern states and in regions of agricultural frontier (Figueiredo et al., 2014). Cases often emerge in clusters following ecological events that

favor rodent proliferation, such as increased rainfall linked to El Niño–Southern Oscillation phenomena. Land-use changes, deforestation, and crop expansion bring humans into closer contact with rodent habitats, increasing the frequency of high-risk exposures.

Argentina has also documented regular HCPS cases and, critically, has provided the most robust evidence of person-to-person transmission of Andes virus. Investigations of clusters in Patagonia have documented transmission chains involving household contacts and healthcare workers, especially in settings with close, unprotected contact with respiratory secretions from severely ill patients (Martinez et al., 2020). While these events remain relatively rare, they highlight the potential for limited secondary spread following introduction into a susceptible population.

Estimating the true incidence of hantavirus infection in Brazil and Argentina is challenging. Surveillance is often focused on severe HCPS cases, while milder or atypical infections may go unrecognized. Furthermore, laboratory capacity for hantavirus diagnosis, PCR and serology, is unevenly distributed, especially in rural areas. Published incidence estimates vary, but values on the order of 1–5 clinically apparent cases per 100,000 persons per year in high-risk regions are likely conservative, considering probable underreporting (Figueiredo et al., 2014; Martinez et al., 2020).

When we look at the whole situation, it's clear that new waves of hantavirus can happen, and even bigger outbreaks in South America are possible. Strange weather, fast changes in how land is used because of the economy, and the social problems that were already there can all mix together and create the right conditions for the disease to spread more often and more strongly from rodents and mice to people.

#### **4. European context: endemic hantaviruses and migration from South America**

Europe has a long history of hantavirus circulation, but the epidemiological pattern is heterogeneous. Northern and central European countries report endemic HFRS associated principally with *Puumala virus*, transmitted by the bank vole (*Myodes glareolus*), and *Dobrava-Belgrade virus*, carried by *Apodemus* species (Heyman et al., 2011; Vaheri et al., 2013). Incidence is strongly influenced by rodent population cycles; years of high vole density correspond to peaks of human cases.

In Southern Europe, including Iberia, hantavirus infections have historically been less common, but serological evidence and sporadic human cases suggest low-level circulation (Papa et al., 2020). Underdiagnosis is likely, given the overlap of symptoms with other endemic diseases and the limited routine testing for hantaviruses outside highly endemic areas.

In parallel, European demography has been reshaped by migration. Over the past two decades, Spain and Portugal have become important destinations for South American migrants, with Brazilians featuring prominently among non-EU nationals. Official statistics from European agencies and national institutes document tens to hundreds of thousands of new residence permits or registrations for South American citizens in Iberian countries annually, alongside substantial tourist and short-term travel. These migration flows create a continuous “bridge” connecting hantavirus-endemic regions in South America with European health systems that may have limited experience with HCPS.

What really turns imported hantavirus infections into a concern is the simple fact that people are constantly on the move. Unlike vector-borne diseases, which depend on certain insects to keep spreading in a place, hantaviruses can only stick around if there are suitable rodent hosts in the area. In Europe, at least for now, the bigger issue isn't that South American hantaviruses will suddenly become established and endemic, but that infected

travelers may show up from time to time and, in some cases, especially with Andes virus, spark small clusters of infections.

## 5. A simplified probabilistic- statistical model for importation risk

### 5.1 Conceptual framework

To move beyond qualitative statements, we consider a simple probabilistic model that estimates the expected number of imported hantavirus cases to a European country over a given time period. At its core, the model connects three components:

1. **Source risk in South America:** the incidence of HCPS in the population that contributes to migrants and travelers.
2. **Mobility:** the volume of people moving from South America to the European destination.
3. **Detection:** the probability that an imported infection is clinically recognized and diagnosed.

Let:

- $N$  = number of arrivals from South America to the European country per year (including immigrants and travelers).
- $I$  = annual incidence of clinically apparent hantavirus infection per person in the relevant South American population.
- $p_{travel}$  = probability that an infected individual travels while infectious or symptomatic (or shortly before symptom onset).
- $p_{detect}$  = probability that an imported case is detected and correctly diagnosed in Europe.

The expected number of *detected* imported cases per year,  $E$ , is approximated by:

$$E \approx N \times I \times p_{travel} \times p_{detect}$$

The expected number of *total* imported infections (including undiagnosed cases) would be:

$$E_{total} \approx N \times I \times p_{travel}.$$

This is a deliberately simple formulation, but it enables transparent exploration of parameter ranges and uncertainty.

## 5.2 Parameter ranges and numerical illustration

### Migration volume ( $N$ ).

For illustration, consider Spain and Portugal combined. Public data over recent years show on the order of 200,000 to 400,000 annual arrivals from South America when summing new residence permits, regularizations, and substantial tourist flow. We adopt  $N = 300,000$  as a central value for an Iberian “receiving region.”

### Incidence ( $I$ ).

In high-risk regions of Brazil and Argentina, published HCPS incidence estimates range around 1 to 5 cases per 100,000 persons per year, acknowledging underreporting (Figueiredo et al., 2014; Martinez et al., 2020). To capture this, we consider  $I$  in the interval:  $I \in [1 \times 10^{-5}, 5 \times 10^{-5}]$ .

### Travel during infectious period ( $p_{travel}$ ).

HCPS has a relatively short symptomatic period; most patients become severely ill and unlikely to travel once advanced respiratory symptoms develop. However, travel can occur during the incubation period or early prodrome, before severe disease. As a plausible range, we consider:  $p_{travel} \in [0.01, 0.05]$ , meaning that between 1% and 5% of infected individuals would travel during the critical window.

### Detection ( $p_{detect}$ ).

Detection depends on clinical suspicion, availability of tests, and laboratory capacity. In non-endemic European settings, particularly where HCPS is unfamiliar, many cases could

be misclassified as other causes of severe pneumonia. We thus consider a wide range:  $p_{detect} \in [0.1, 0.5]$ .

Using mid-range values, for example  $I = 3 \times 10^{-5}$ ,  $p_{travel} = 0.03$ ,  $p_{detect} = 0.3$ , we obtain:  $E \approx 300,000 \times 3 \times 10^{-5} \times 0.03 \times 0.3 \approx 0.081$  detected cases/year. This corresponds to roughly one detected imported case every 10 to 15 years in Iberia, under these assumptions.

However, considering the same parameters without the detection filter:  $E_{total} \approx 0.27$  infections/year, suggesting that roughly one imported infection every few years could occur, with only a fraction being recognized.

### 5.3 Sensitivity and outbreak scenarios

The model is highly sensitive to changes in  $I$  and  $N$ . During a recognized outbreak in South America, incidence in affected regions could temporarily increase by an order of magnitude. If, for example,  $I$  rises to  $3 \times 10^{-4}$  (30 per 100,000) in a specific region supplying a significant fraction of migrants, and if travel volumes ( $N$ ) remain stable, the expected number of imported infections could approach several per year.

Sudden surges in migration—such as those driven by political or economic crises—can also push  $N$  upward. If both  $N$  and  $I$  rise at the same time (for example, when a crisis overlaps with an outbreak), then even cautious estimates of  $p_{travel}$  and  $p_{detect}$  can lead to an expected number of imported cases on the order of a few per year for a single European country.

Although these numbers appear small, two considerations are important. First, from a probabilistic perspective, even low annual expectations accumulate over time; a 0.5 expected cases per year implies that one or more imported cases are quite likely over a decade. Second, each missed or misdiagnosed case carries a high risk of severe outcome, and, in the case of Andes virus, the possibility, however limited, of secondary transmission.

## 6. Physical and statistical aspects of exposure and transmission

The risk of hantavirus infection is the product of multiple layers of probability: environmental contamination, particle aerosolization, inhalation, and successful viral replication in the host. On a micro-scale, one can model the dose of inhaled viral particles as:  $D = C \times V \times t$ , where  $C$  is the concentration of viral particles in air (particles per unit volume),  $V$  is the inhalation rate (volume per unit time), and  $t$  is duration of exposure. Laboratory and field studies suggest that the probability of infection increases with dose, often following an exponential or sigmoidal dose response relationship. Thus, short exposures to highly contaminated air or longer exposures to moderately contaminated environments can lead to infection.

When we look at the whole population, the chance of an outbreak depends on which groups are most exposed. Because people live and work in different ways, the risk is not shared equally. Small groups, like farm workers, people living in poorly built homes in rural areas, or people who often clean places full of rodents, can end up with many more infections than others. When we think about cases reaching Europe, these high-risk groups matter even more, especially if they are also more likely to move to other countries.

In Europe, there is still some luck involved, even though cases coming from other countries are still rare. In theory, one person with Andes virus, especially someone living in a crowded home or in shared housing for migrant workers, could pass the virus to a few others through close contact. This is not very likely, but it is possible, and the effects could be serious, because many doctors have little experience with hantavirus cardiopulmonary syndrome. It is one of those situations where the chance is small, but the damage could be big, so it is better to act early and invest in prevention.

## **7. Implications for Europe: clinical and public health perspectives**

From a clinical standpoint, the most immediate concern is that cases may simply be missed. Emergency physicians, pulmonologists, and intensivists in Spain and Portugal are used to seeing pneumonia caused by familiar pathogens like bacteria, influenza, or SARS-CoV-2. HCPS can look very similar, especially in the early stages, and may end up being classified as viral pneumonia or ARDS of unknown origin. Remembering that a patient who has recently spent time in rural or peri-urban areas of Brazil or Argentina might have a hantavirus infection is key to ordering the right diagnostic tests.

The public health implications reach far beyond any one patient. Even a small number of imported cases can expose weaknesses in surveillance, laboratory capacity, and day-to-day infection control practices. For Andes virus in particular, consistent use of respiratory protection in hospitals matters, especially during procedures that can generate aerosols. Building up laboratory networks so they can perform PCR and antibody testing for hantaviruses, including South American strains, would make it easier to confirm or rule out suspected cases without long delays.

Targeted strategies may include:

- Incorporating concise questions about recent travel to South America and exposure to rural or rodent-prone environments into triage protocols for severe acute respiratory illness.
- Providing focused training or alerts to clinicians in regions with high South American migrant populations, especially in metropolitan areas of Spain and Portugal.
- Ensuring that reference laboratories are prepared to test for hantaviruses and can rapidly support local hospitals.
- Integrating hantavirus into national or regional surveillance frameworks for emerging infections, at least as a notifiable pathogen when suspected in travelers.

These measures can be implemented with relatively low cost compared to the potential harm of missed severe cases.

## 8. Limitations and future directions

The simplified model we present here is not meant to fully quantify the risk. Instead, it offers an order-of-magnitude view that underlines our main point: the risk exists and has been largely overlooked. That said, several limitations need to be acknowledged:

1. **Data gaps in South America.** Incidence estimates are uncertain and probably fall short of the true number of infections. A substantial proportion of infections may be asymptomatic or only mildly symptomatic.
2. **Heterogeneous migration patterns.** We have treated migrants and travelers as a single, homogeneous group, whereas in reality their risk is stratified by factors such as occupation, region of origin, socioeconomic status, and travel patterns.
3. **Variable detection probability.** The probability of diagnosis in Europe depends on local awareness, test availability, and clinical suspicion, all of which vary widely between institutions and over time.
4. **Environmental establishment not modeled.** We have not incorporated into the model the (currently considered low) possibility that South American hantaviruses could establish sustained transmission cycles in European rodent populations.

In the future, research should try to fix these gaps by using better data and more detailed models. For example, we could combine what we know about how people travel, such as airline routes and busy travel seasons, with detailed maps showing where hantaviruses are most common in South America. This would help us estimate the risk of infected people arriving in Europe more accurately. Studies that look for hantavirus antibodies in South American migrants in Europe could show how many have been exposed

before and how often people get infected without feeling sick. At the same time, checking the genetic material of hantaviruses found in Europe would help us notice when South American strains arrive and see how they spread over time.

## **9. Conclusions**

Hantaviruses remain a significant public health concern in South America, with Brazil and Argentina acting as major centers of HCPS activity. In a world with intense population movement, these localized threats do not remain confined to the regions where they start. For European countries with large South American communities, especially Spain and Portugal, there is a real risk of occasional imported hantavirus cases, including severe HCPS caused by Andes virus and other genotypes, even if the likelihood in any single year is relatively low.

Our simple risk estimates indicate that, over a span of several years, some imported infections are likely to occur, and many of them may be missed if doctors are not thinking about hantavirus and if lab support is limited. Given the high fatality rate of HCPS and the fact that certain genotypes can spread from person to person, even if only under specific conditions, this calls for action in advance rather than after the fact. Key steps include raising awareness among clinicians, improving access to reliable diagnostic tests, and making sure hantavirus is part of routine surveillance for severe acute respiratory infections in European areas with large South American communities.

Rather than generating alarm, acknowledging this risk allows European health systems to act early, ensuring that when cases do occur, they are detected, correctly diagnosed and managed with appropriate clinical and infection-control measures.

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