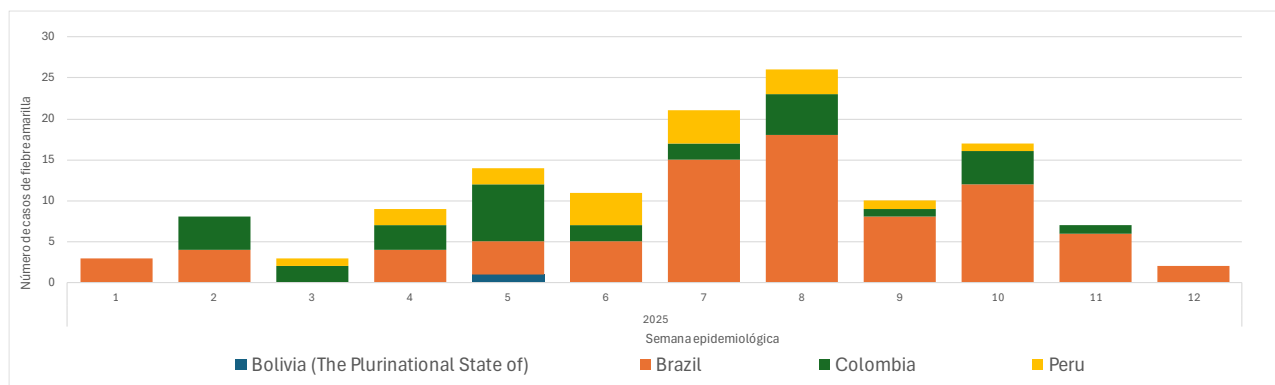


Given the increase in human cases of yellow fever in 2025 in countries of the Americas Region, the Pan American Health Organization / World Health Organization (PAHO / WHO) calls on Member States with areas at risk to continue their efforts to strengthen surveillance in endemic areas, vaccinate at-risk populations, and take the necessary actions to ensure that travelers going to areas where vaccination is recommended are properly informed and protected against yellow fever. In addition, PAHO/WHO highlights the need to strengthen clinical management, with emphasis on the detection and timely treatment of severe cases. PAHO/WHO also recommends the availability of reserve vaccine doses, in accordance with the availability of vaccines in each country, to guarantee a rapid response to possible outbreaks.

Summary of the Situation

Between epidemiological week (EW) 1 and EW 12 of 2025, 131 confirmed cases of yellow fever in humans have been reported in four countries of the Region, of which 53 have been fatal (1-4). These cases have been reported in the Plurinational State of Bolivia, with one fatal case; Brazil with 81 cases, including 31 fatal cases; Colombia with 31 cases, including 13 fatal cases; and Peru with 18 cases, including eight fatal cases (1-4).

Figure 1. Yellow fever cases by country and epidemiological week (EW) of onset of symptoms in the Americas Region*. EW 1 to EW 12 of 2025.

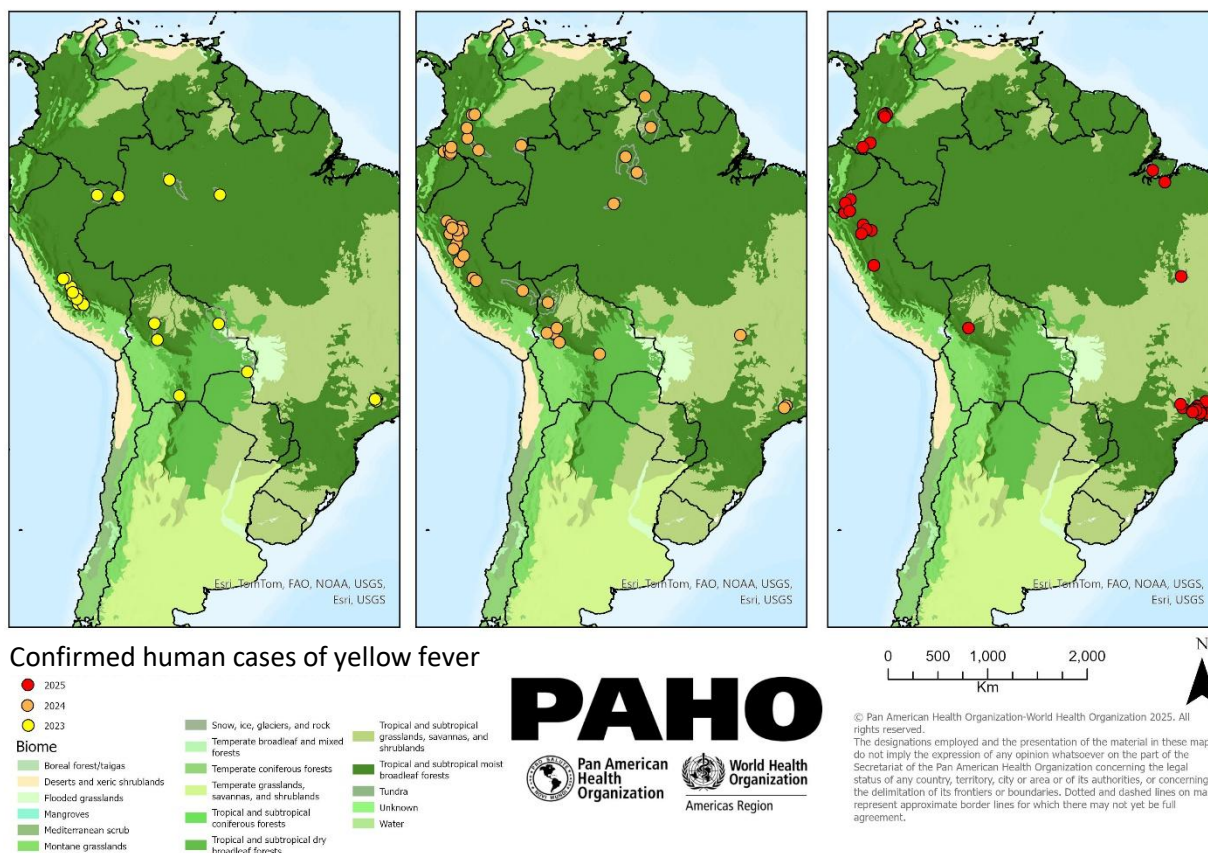


***Note:** Includes only cases for which onset of symptoms information is available by epidemiological week.

Source: Adapted from data provided by countries or published by Ministries of Health (1-4).

In 2024, yellow fever cases were mainly reported throughout the Amazon region of Bolivia, Brazil, Colombia, Guyana, and Peru. In 2025, however, cases have also been detected in the state of São Paulo in Brazil and the department of Tolima in Colombia, regions outside the Amazon region of both countries (**Figure 2**).

Figure 2. Confirmed human cases of yellow fever by year in the Americas Region, 2023 to 2025 (as of EW 12).



Source: Adapted from data provided by countries or published by Ministries of Health (1-4).

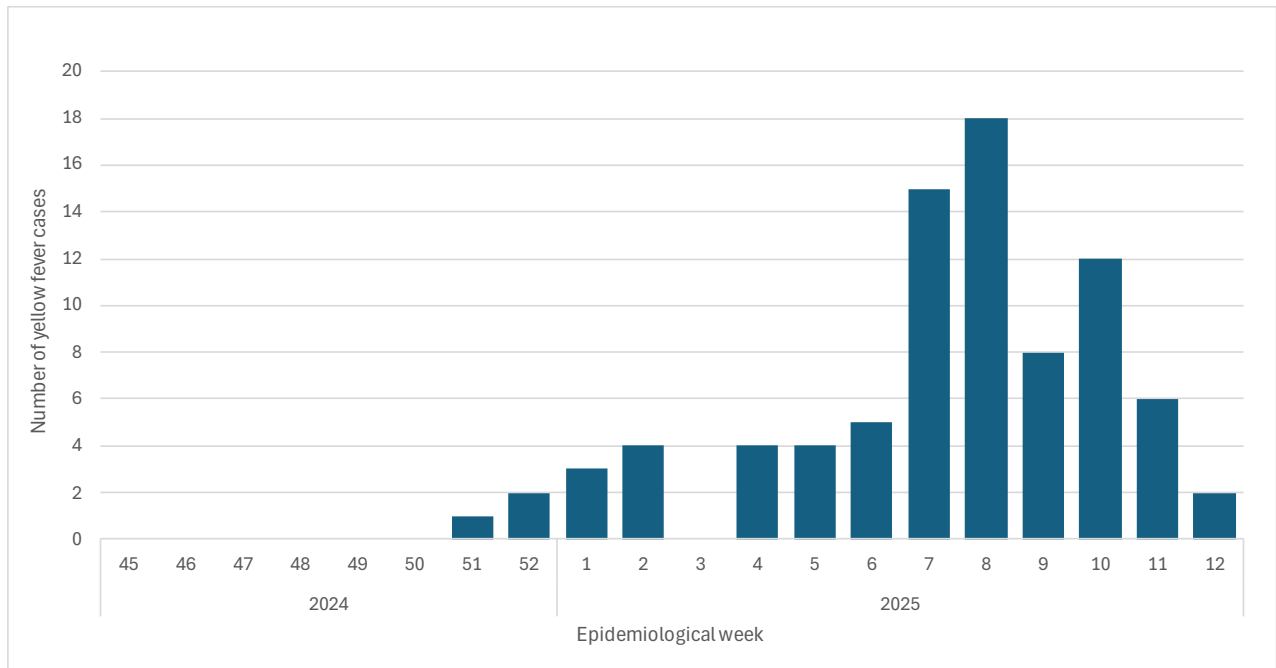
The epidemiological situation of yellow fever in the countries, in alphabetical order, that have reported confirmed cases in 2025 is presented below.

In **Bolivia**, a confirmed fatal case of yellow fever was reported in the municipality of Palos Blancos in the department of La Paz in EW 5 of 2025, in an individual with a history of travel to the municipality of Alto Beni in the province of Caranavi. The case is a 44-year-old male with a history of uncontrolled diabetes and no history of yellow fever vaccination. The date of onset of symptoms was 29 January 2025 and he died on 3 February 2025. The case was laboratory confirmed by positive IgM ELISA (1).

In **Brazil**, between EW 1 and EW 12 of 2025, 81 confirmed cases of yellow fever were reported, including 31 fatal cases (38.3% case fatality rate) (Figure 3). Cases were reported in the states of São Paulo (n= 34 cases, including 19 fatal cases), Pará (n= 41 cases, including seven fatal cases), Minas Gerais (n= 5 cases, including four fatal cases), and Tocantins (n= 1 fatal case). Males accounted for 87.7% of the cases (n= 71). The cases are between 2 and 75 years of age and initiated symptoms between 2 January and 17 March 2025. Only one of the cases had a history of yellow fever vaccination (2). The cases were probably exposed in the state of Pará, in the municipalities of Breves (n= 39), and Cametá (n= 1), while for one case the probable municipality of exposure is under investigation. For the São Paulo state, cases were reported in the municipalities of Águas de Lindoia (n= 1), Águas de São Pedro (n= 1), Amparo (n= 1),

Bragança Paulista (n= 1), Brotas (n= 2), Caçapava (n= 5), Campinas (n= 3), Joanópolis (n= 3), Nazaré Paulista (n=1), Pedra Bela (n= 2), Pedreira (n=1), Piracaia (n= 3), Socorro (n= 3), Tuiuti (n= 1), and Valinhos (n= 1), while for five cases the probable municipality of exposure is under investigation; in the state of Minas Gerais, cases were reported in the municipalities of Cambuí (n= 1), Extrema (n= 1), Monte Sião (n= 1), Pouso Alegre (n= 1), and Silvianópolis (n= 1); and in the state of Tocantins, cases were reported in the municipality of Monte do Carmo (n= 1) (2) **(Figure 4)**. All cases had a history of exposure in wild and/or wooded areas, due to occupational or recreational activities, and were laboratory confirmed (2).

Figure 3. Yellow fever cases by year and epidemiological week of onset of symptoms in Brazil, 2024 to EW 12 of 2025.

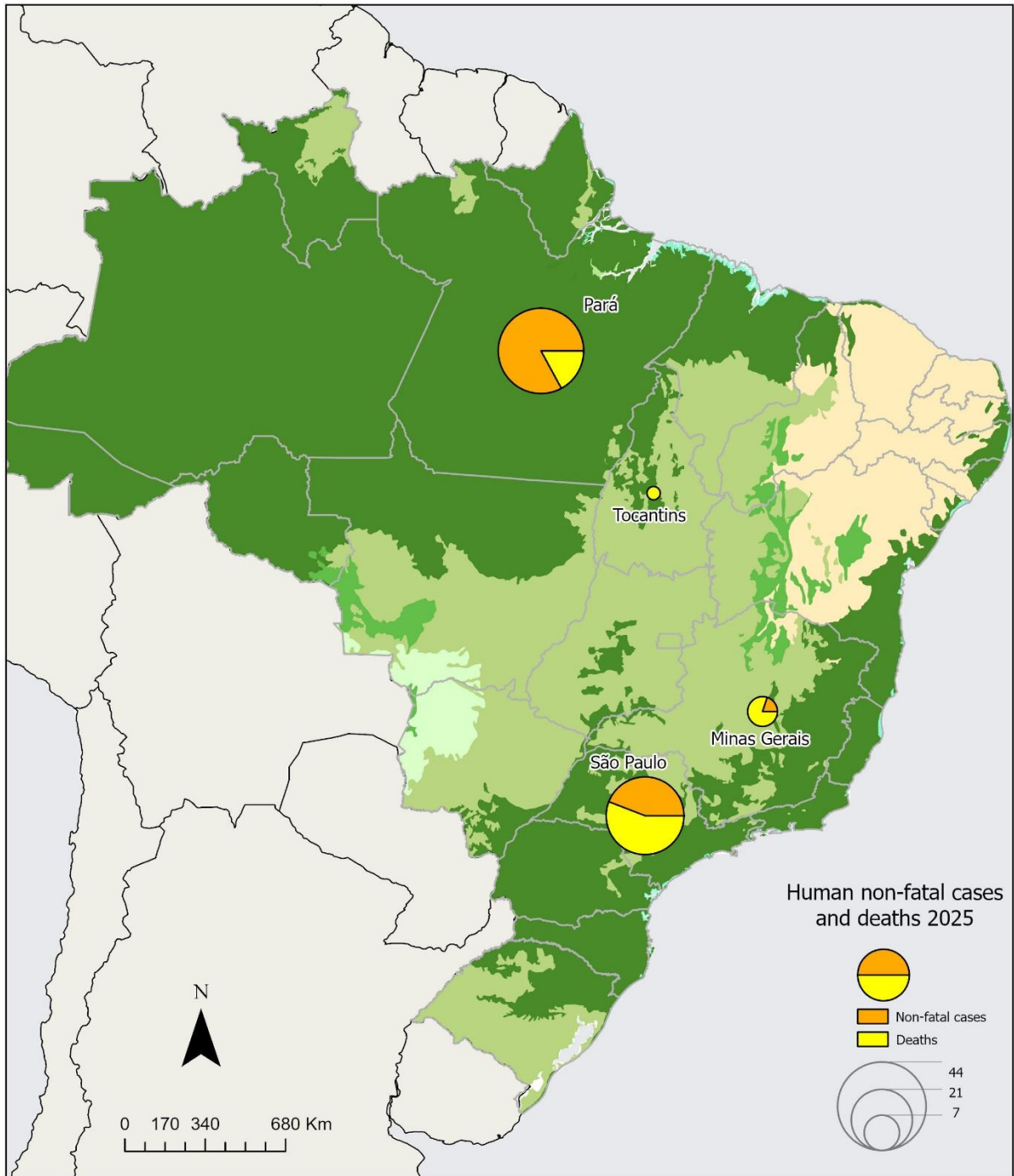


Source: Adapted from data provided by the Brazil International Health Regulations National Focal Point (IHR NFP) (2).

During 2025 (EW 1 to EW 12), 442 events involving dead non-human primates (epizootics) were reported in Brazil. Of this total, 47 (10.6%) were confirmed for yellow fever by laboratory criteria (n= 37) and by epidemiological link (n= 10), 40 in the state of São Paulo and seven in the state of Minas Gerais (2) **(Figures 5)**.

All of the human cases of yellow fever recorded in São Paulo and Minas Gerais came from areas where, according to the Ecological Corridors Model, cases were expected to occur in the 2024/2025 period or from areas previously affected by both human cases and yellow fever epizootics (5) **(Figure 5)**. This distribution is reflected in the Ecological Corridors Model, illustrated in Figure 4 of the Epidemiological Alert: Yellow Fever in the Americas Region, 3 February 2025 (6).

Figure 4. Yellow fever human cases by state. Brazil, EW 1 to EW 12 of 2025.

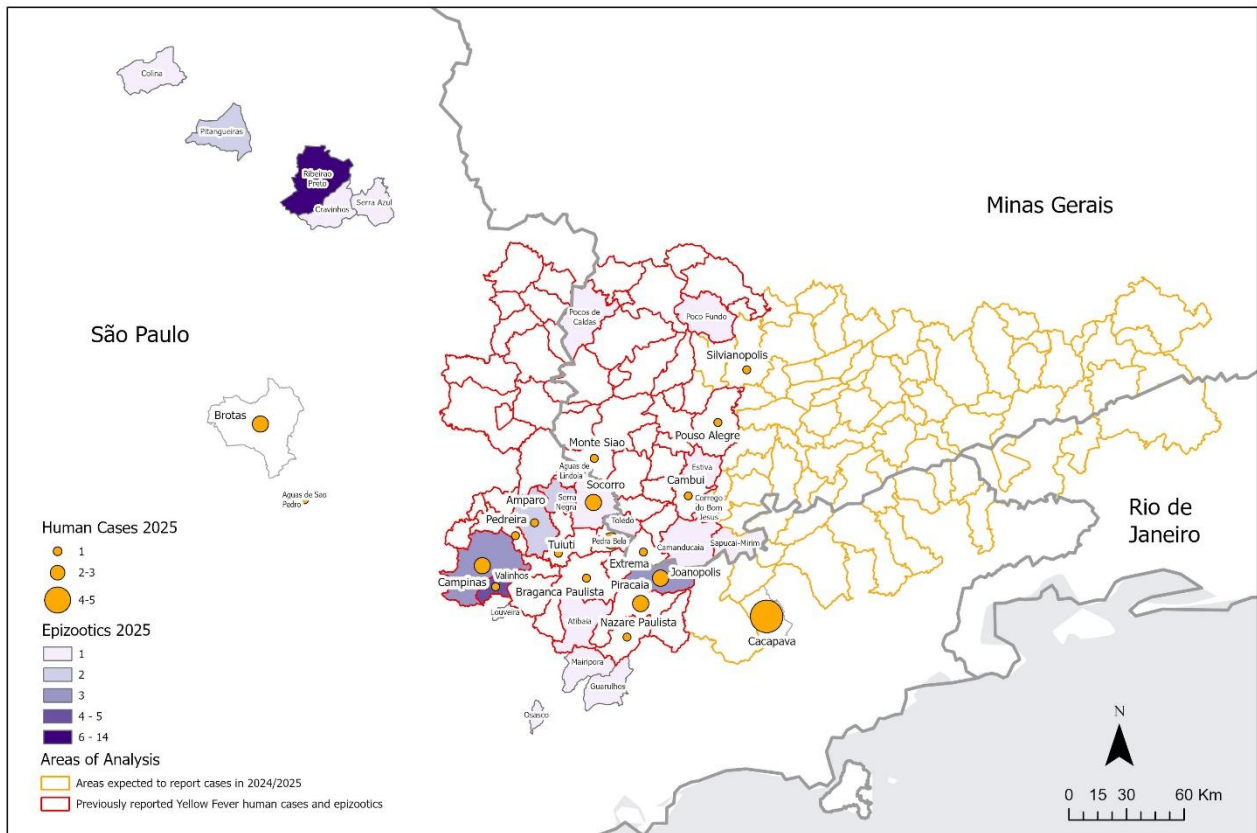


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 Map production:
 PAHO Health Emergencies Department (PHE)
 Health Emergency Information and Risk Assessment Unit (HIM)



Source: Adapted from data provided by the Brazil International Health Regulations National Focal Point (IHR NFP) (2).

Figure 5. Yellow fever cases in humans and confirmed yellow fever epizootics. States of Sao Paulo and Minas Gerais, Brazil, EW 1 to EW 12 of 2025.



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 Map production:
 PAHO Health Emergencies Department (PHE)
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Source: Adapted from data provided by the Brazil International Health Regulations National Focal Point (IHR NFP) (2) and Secretaria de Vigilância em Saúde e Ambiente - Nota Informativa N° 35/2024-CGARB/DEDT/SVSA/MS. Brasília: Saude; 2025. Available from: <https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/estudos-e-notas-informativas/2024/nota-informativa-no-35-2024.pdf> (5).

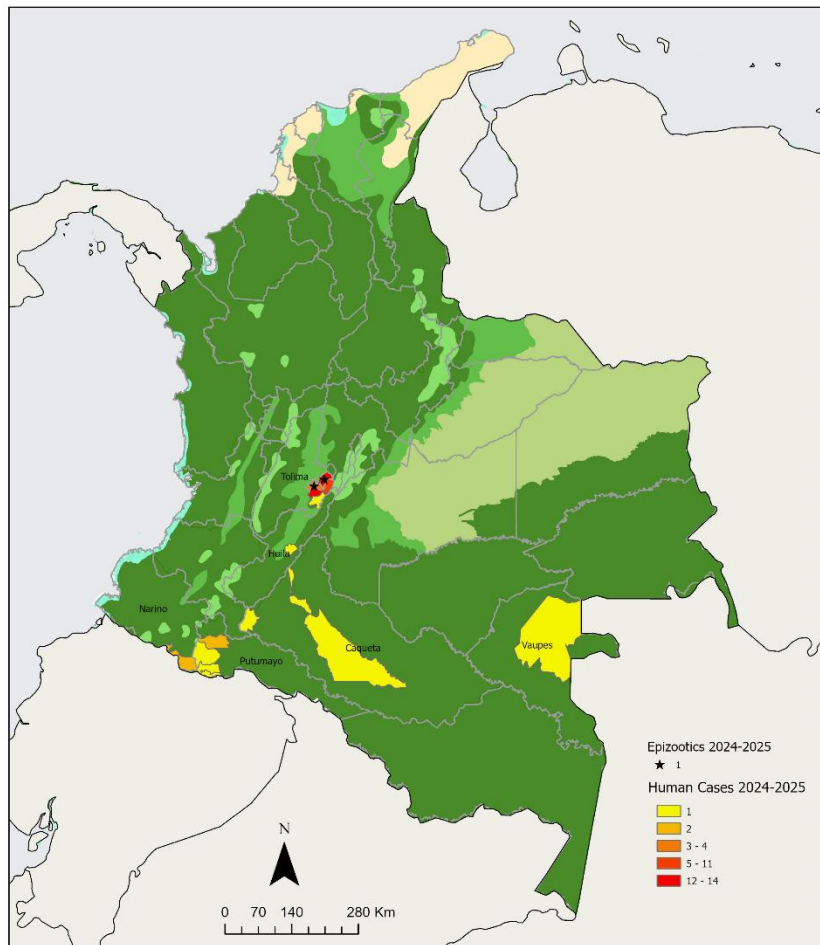
In **Colombia**, a total of 31 confirmed cases of yellow fever, including 13 deaths, have been reported in the period between EW 1 and EW 11 of 2025 (3). The cases correspond to persons residing in the departments of Caquetá (n= 1 fatal case), Putumayo (n= 1 case), and Tolima (n= 29 cases, including 12 deaths) (**Figure 6**). The cases correspond to persons aged between 13 and 83 years, who initiated symptoms between 6 January and 12 March 2025. All cases had a history of exposure in areas at risk for yellow fever, in the context of work activities that included agriculture, and had no documented history of vaccination against yellow fever (3).

The outbreak recorded in the department of Tolima that started at the end of 2024 and continues during 2025, occurs in the rural area adjacent to the southwestern area of the Bosque de Galilea Regional Natural Park in four municipalities that are identified as high risk (3): Cunday (n= 14 cases, including four deaths), Dolores (n= 1 fatal case), Prado (n= 15 cases, including five deaths), Purificación (n= 4 cases, including three deaths), and Villarica (n= 10 cases, including,

five deaths). Of the total number of confirmed cases, 76% were male (n= 32 cases), with ages ranging from 11 to 89 years. The date of onset of symptoms of the cases ranges from 8 September 2024 to 12 March 2025. In this outbreak, 18 deaths have been recorded for a preliminary case fatality rate of 42.8% (3).

During 2025 (EW 1 to EW 11), two events involving dead non-human primates (epizootics) were reported in Colombia. Of this total, two were confirmed for yellow fever by laboratory criteria, all in the department of Tolima (**Figure 6**) (3).

Figure 6. Yellow fever cases in humans and confirmed epizootics by department. Colombia, 2024 as of EW 11 of 2025.



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 Map production:
 PAHO Health Emergencies Department (PHE)
 Health Emergency Information and Risk Assessment Unit (HEIRU)



Source: Adapted from data provided by the Colombia International Health Regulations National Focal Point (IHR NFP) (3).

In **Peru**, between EW 1 and EW 10 of 2025, 18 cases of yellow fever have been confirmed, including eight deaths. Cases were confirmed in the departments of Huanuco, Chaglla district (n= 1 fatal case); department of San Martin, Chazuta district (n= 1 fatal case), Morales district (n= 1 case), Pinto Recodo district (n= 2 cases including one fatal case) and Saposoa district (n=

1 case), and the department of Amazonas, Cenepa district (n= 1 case), Imaza district (n= 7 cases including two fatal cases), Nieva district (n= 1 fatal case) and Rio Santiago district (n= 3 cases including two fatal cases) (4). The 18 confirmed cases were males between 18 and 83 years of age, with onset of symptoms between 15 January and 12 March 2025 (4). All cases had a history of exposure in wild and/or wooded areas, due to agricultural work activities, and 72% had no history of vaccination against yellow fever (4).

Recommendations for health authorities

In the Americas Region, the risk of yellow fever outbreaks is high. Although immunization remains one of the most effective public health interventions to prevent this disease, most of the cases reported during 2024 did not have a history of yellow fever vaccination.

PAHO/WHO encourages Member States with areas at risk to continue surveillance and vaccination efforts in endemic areas.

It is essential that countries achieve vaccination coverage of at least 95% in populations in at-risk areas, in a homogeneous manner, and that health authorities ensure that they have a strategic reserve inventory that allows them to maintain routine vaccination and, at the same time, respond effectively to possible outbreaks (7).

Epidemiological surveillance

It is recommended that Member States with risk areas for yellow fever implement the following strategies to strengthen surveillance (8):

- Issue epidemiological alerts to municipalities and health services, with emphasis on case definitions. Case notification should be immediate, even if it is a suspected case and regardless of yellow fever vaccination status.
- Conduct an active search for cases with symptoms compatible with the definition of a suspected case and/or with acute febrile icteric syndrome in the areas where cases have occurred, as well as in the surrounding municipalities and places visited by the cases during the 3 to 6 days prior to the onset of the disease.
- Conduct retrospective investigations of death certificates to identify possible cases compatible with the case definition.
- Intensify surveillance actions for epizootics, given that the death of non-human primates can serve as an early warning to identify yellow fever circulation, which would indicate the need to reinforce vaccination actions, especially in areas where human cases and epizootics have not yet been detected. In areas with confirmed transmission, efforts to identify vectors and locally involved primates can provide valuable information to support risk communication, health education and targeted vaccination activities.
- If possible, geo-reference the points of occurrence of death of non-human primates and the probable place of exposure of human cases to establish the "ecological corridors" of yellow fever in order to identify the areas of greatest risk to anticipate preventive measures and optimize vaccination actions.
- Collaborate with the agricultural sector and involve companies that employ workers in activities involving exposure to forest areas to implement health communication

measures. It is recommended to act with the support of community surveillance in the areas considered to be at greatest risk.

Laboratory diagnosis

The diagnosis of yellow fever is made mainly by virological methods (detection of virus or genetic material in serum or tissue) or, in some cases, by serological tests for the detection of antibodies (9).

Virological diagnosis

- **Molecular detection:** During the first 5 days from the onset of symptoms (viraemic phase) it is possible to detect viral RNA from serum by molecular techniques, such as conventional or real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR). Sometimes, viral RNA can be detected for up to 10 days (or more) from the onset of symptoms. For this reason, it is recommended that both PCR and IgM ELISA be performed on samples collected between days 5-10. A positive result (in the presence of adequate controls) confirms the diagnosis regardless of the day the sample was taken (9).
- **Post-mortem diagnosis:** Histopathological study with immunohistochemistry on liver sections is the "gold standard" method for the diagnosis of yellow fever in fatal cases. In addition, molecular methods from fresh or paraffin-preserved tissue samples can also be used for confirmation of cases. Detection can be performed under BSL2 (biosafety level 2) containment conditions (9).

Serological diagnosis

Serology (detection of specific antibodies) is useful to make the diagnosis of yellow fever during the post-viremic phase of the disease (i.e., from day 5 from the onset of symptoms) (9).

A positive IgM result by ELISA (mainly IgM capture, MAC-ELISA) or any other immunoassay (indirect immunofluorescence) on a sample taken on or after day 5 of onset of symptoms is presumptive of recent yellow fever virus infection. Currently, there are no validated commercial kits for IgM detection by ELISA. Therefore, "home-made" (*in-house*) procedures using purified complete antigen can be standardized (9).

Confirmation of a yellow fever case by IgM ELISA will depend on the epidemiological situation and the result of the differential laboratory diagnosis. Thus, in areas with circulation of other flaviviruses (mainly dengue and Zika), the probability of cross-reactivity is higher.

Other serological techniques include detection of IgG by ELISA and of neutralizing antibodies by plaque reduction neutralization technique (PRNT). IgG ELISA is useful with paired samples (taken at least one week apart), while PRNT (90%) can be useful with paired samples, or with a single post-viremic sample as long as the assay includes multiple flaviviruses (9).

A seroconversion (negative result in the first sample and positive in the second), a more than 4-fold increase in antibody titers in paired samples, or detectable yellow fever antibody titers in a post-viremic sample (PRNT 90%) is presumptive of yellow fever infection. Confirmation of a yellow fever case by these techniques will depend on the epidemiological situation and the differential laboratory result, since in areas of co-circulation with other flaviviruses, the possibility of cross-reactivity is greater (9).

Also, in areas where active vaccination campaigns are carried out, the detection of post-vaccination antibodies may occur, so the diagnosis must be carefully interpreted (9).

Interpretation of serology results and differential diagnosis

The cross-reactivity of serological techniques observed mainly in secondary flavivirus infections should be considered in areas where co-circulation of yellow fever virus with other flaviviruses (dengue, St. Louis encephalitis, Zika, and others of the Japanese encephalitis complex) is documented and there is a probability that the population has been previously infected. Also, it should be taken into account that in individuals previously vaccinated against yellow fever, vaccine-induced IgM can be detected for several months or even years (9).

Therefore, it is recommended that the detection of antibodies to other flaviviruses be carried out in parallel and that the results be carefully interpreted taking into account the vaccination history, as well as the epidemiological information available (9).

In general, the plaque reduction neutralization technique (PRNT) offers higher specificity than IgM and IgG detection. However, cross-reactivity has also been documented for neutralization assays, so it is also recommended to perform this technique using antigens for several flaviviruses (9).

On the other hand, the differential diagnosis of yellow fever should include other febrile and febrile-icteric syndromes such as dengue, leptospirosis, malaria, viral hepatitis, among others, depending on the epidemiological profile of the affected country or area.

A case of yellow fever will be confirmed by serological techniques only if the differential laboratory diagnosis, taking into account the epidemiological profile of the country, is negative for other flaviviruses.

Post-vaccination immune response

Vaccination induces a relatively low viremia that decreases after 4 to 7 days. Simultaneously, an IgM-type response develops which cannot be differentiated from the IgM response induced by natural infection. Approximately 10 days after vaccination, the person is considered to be protected against a natural infection. Thus, the vaccinal IgM response will be detectable around day 5 onwards with a peak usually occurring two weeks after vaccination. Thereafter, the levels of these antibodies tend to decline. In a significant proportion of vaccinated persons the IgM response can be detected for up to one month after vaccination, and in some cases (mainly travelers), even for up to 3-4 years. On the other hand, neutralizing antibodies induced by vaccination can be detected for several decades. All in all, the interpretation of serological results in vaccinated persons is complex, particularly those who have been recently vaccinated, so the results should be carefully evaluated (9).

Guidance for laboratory diagnosis in the Americas Region is published in the PAHO document on **Laboratory Diagnosis of Yellow Fever Virus Infection** dated 9 September 2018 (9).

Clinical management

Yellow fever is a severe viral hemorrhagic disease, with an abrupt onset and a lethality of 30-60% in its severe forms (10). It is a dynamic, systemic disease that presents in three clinical phases: a)

infection phase characterized by elevated body temperature, b) remission phase, with the presence of albuminuria, and c) toxemic phase, in which hemorrhagic manifestations and signs of acute liver failure appear, such as jaundice and hepatic encephalopathy (11).

There is currently no specific treatment for yellow fever. Therefore, early detection of suspected or confirmed cases, monitoring of vital signs, life support measures, and management of acute liver failure continue to be the recommended strategies for management (11). Three levels of care should be considered for patient care:

- Basic health units (primary care): management of mild cases or patients without a confirmed diagnosis of the disease, generally those whose symptoms started two or three days before (group A).
- Medium complexity hospitals: patients in the remission phase of the disease, who may be those with a suspicion or diagnosis of yellow fever and whose symptoms began three or four days earlier (group B).
- Intensive care units (ICU): management of severe cases, with hepatic and renal complications (group C).

The following is an outline for the stratified care of yellow fever patients, based on the early identification of warning signs and severity, as well as clinical and laboratory findings, with the objective of ensuring timely, adequate and supportive management according to the level of care required.

Table 1. Schema for stratified care of patients with yellow fever.

Group	Clinical Condition	Recommended actions
<p>Group A (Primary Care - Infection Phase)</p>	<p>Fever, abdominal pain, nausea, possible mild bleeding, mild to moderate dehydration.</p>	<ul style="list-style-type: none"> • Oral and intravenous hydration according to water losses. • Initial volumetric expansion of 20 ml/kg if necessary. • Consciousness level monitoring. • Pain and fever management with dipyrene (max. 8 g/day) or paracetamol (max. 2 g/day). • Avoid NSAIDs. • Monitor AST > 5 LSN, platelets < 50,000/mm³ and proteinuria, with close follow-up to detect progression to severe forms. • Re-evaluation in 24 hours to determine evolution and possible reclassification to Group B. • Evaluate whether primary care services have the infrastructure to carry out continuous monitoring of the patient, and if there is no capacity in primary care, the patient should be sent directly to hospitalization for monitoring.
<p>Group B (Hospitalization - Referral Phase)</p>	<p>Severe dehydration, persistent vomiting, diarrhea, altered urinary excretion, hemodynamic instability.</p>	<ul style="list-style-type: none"> • Immediate hospitalization with monitoring of cardiac, renal, hepatic and metabolic parameters. • Second volumetric expansion if necessary. • Initiate vasoactive drugs without delay if hypovolemic shock is present. Monitor level of consciousness, abdominal pain and onset of severe bleeding. • Monitoring AST > 2,000 U/L, serum creatinine > 2.0 mg/dl and RNI > 1.5, with specialized medical support. • Evaluate need for transfer to ICU (Group C).
<p>Group C (Intensive Care Unit - Toxemic Phase)</p>	<p>Acute liver failure (jaundice, alterations in liver function tests), acute renal failure, hepatic encephalopathy, severe bleeding.</p>	<ul style="list-style-type: none"> • Referral to ICU for specialized management. • Continuous monitoring and advanced supportive care. • Use of vasoactive drugs to maintain hemodynamic stability. • Ventilatory support if necessary. • Dialysis in cases of acute renal failure. • Application of specific protocols according to local availability.

Source: Adapted from Pan American Health Organization. Clinical Management of Yellow Fever in the Region of the Americas. Experiences and Recommendations for Health Services. Washington, D.C.: PAHO; 2023. Available from: <https://iris.paho.org/handle/10665.2/57318> (11).

Complete management recommendations are available in the document Clinical Management of Yellow Fever in the Region of the Americas. Experiences and Recommendations for Health Services, which is available from: <https://iris.paho.org/handle/10665.2/57318> (11).

Vaccination

The yellow fever vaccine is safe, affordable, and a single dose is sufficient to confer lifelong immunity and protection, without the need for booster doses (12).

PAHO/WHO reiterates the following recommendations to national authorities (13):

Routine vaccination:

- **Universal childhood vaccination** in endemic countries at 12 months of age, administered simultaneously with measles, mumps, and rubella (MMR) vaccine or according to the national immunization schedule of each country. Most of these countries administer simultaneously at 12 months of age with the first dose of MMR vaccine.
- Ensure vaccination of all travelers to endemic areas at least **10 days before travel**. Recommendations for international travelers on yellow fever vaccination are available in the International Travel and Health document, which is available from: <https://www.who.int/publications/i/item/9789241580472> (14).
- **To have a reserve inventory in the country** to maintain routine vaccination and to respond in a timely manner in case of outbreaks.

Preventive or update campaigns:

- Update the **risk assessment**, taking into account changes in ecological factors, migrations, vaccination coverage, socioeconomic activities, as well as the risk of urbanization, to guide vaccination and control measures in at-risk areas.
- In countries with yellow fever vaccination for expanded age groups, it is recommended to perform **cohort analysis of susceptible** populations to identify the target population and, based on this, estimate the campaign target and the necessary supplies.
- Prioritize vaccination in at-risk areas, reaching at **least 95% coverage** in residents of these areas (urban, rural and jungle), through different strategies to address unvaccinated populations, age groups with suboptimal coverage, professional and occupational risk groups, such as workers in activities involving exposure to jungle/forest areas.
- In countries with yellow fever vaccination for extended age groups, it is suggested to apply the cohort estimation method to identify the susceptible population at higher risk, such as workers in activities involving exposure in jungle/forest areas.
- Given that the global supply of yellow fever vaccines has been limited in recent years, it is important to plan the campaign in advance to ensure vaccine availability. A useful tool for this process is campaign micro-planning to determine the most effective tactics for target population, optimize resources, and establish the vaccination schedule, preferably during inter-epidemic periods.

Vaccination during outbreak response:

- Vaccination in response to outbreaks should consider a careful assessment of the target population based on exposure risk and vaccination history.
- Vaccine stocks should be permanently checked to reduce the possibility of stock-outs in case of outbreaks.
- In case of limited dose availability, the use of "split" doses of yellow fever vaccine (0.1 ml) subcutaneously is recommended, as recommended by the WHO Strategic Advisory Group of Experts (SAGE) and the PAHO Strategic Advisory Group (SAG formerly TAG) (15, 16). Children under two years of age, pregnant women, and persons living with HIV who are eligible for vaccination should receive a standard dose of 0.5 ml. A "split" dose does not meet the requirements of the International Health Regulations as proof of vaccination for international travel.
- Training of health personnel is necessary for the use, registration and subsequent follow-up of users who receive the fractionated dose as part of the outbreak response.
- It is important to carry out adequate risk communication aimed at health care workers and the general population regarding the term "fractional dose" in order to avoid resistance to vaccination and misinformation.

Precautions and contraindications:

- Age 6 to 9 months, ≥ 60 years, pregnancy and lactation are precautions for vaccination. A risk-benefit analysis is recommended for persons with vaccination precautions.
- The vaccine is contraindicated in:
 - a. Children under 6 months of age; and it is not recommended in children 6 to 8 months of age, except in outbreak situations.
 - b. Persons with a history of severe hypersensitivity reactions to egg.
 - c. Persons with immunodeficiency such as symptomatic HIV or with CD4+ count < 200 cells/ml.

Surveillance of events suspected to be attributable to vaccination or immunization (ESAVI):

- Surveillance of events suspected to be attributable to vaccination or immunization (ESAVI) should be strengthened during the implementation of yellow fever vaccination campaigns, including all the actors involved: National Regulatory Authorities, National Pharmacovigilance Centers and those in charge of epidemiological surveillance
- It is essential to train vaccination teams in the precautions and contraindications of yellow fever vaccines and to define a standardized flow for selecting persons to be vaccinated, in order to minimize immunization errors and the risk of HAVI, e.g. vaccination of immunocompromised persons.
- It is necessary to ensure the conditions for sample collection and processing and interpretation in the process of investigation of severe cases that may correspond to cases of neurotropic or viscerotropic disease. Case investigation should help to meet the Brighton Collaboration criteria for certainty and should be carried out according to the PAHO ESAVI surveillance manual (17).

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Useful links

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