Operational guidelines for the elimination of human fascioliasis as a public health problem in the Americas
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Fascioliasis is a parasitic disease that affects people and a wide variety of mainly herbivorous animals. In Latin America and the Caribbean, it is caused by the trematode *Fasciola hepatica*. Fascioliasis is classified by the World Health Organization (WHO) as a neglected tropical disease.

The Pan American Health Organization, as part of the commitment to achieving the goals of the 2030 Agenda for Sustainable Development and those of the Sustainable Health Agenda for the Americas 2018–2030, launched an initiative to eliminate communicable diseases in the Region of the Americas. One of its objectives is to eliminate fascioliasis as a public health problem in the Region of the Americas by 2030, defined as a sustained prevalence less than or equal to 5%, by coprology, without high-intensity infections (400 eggs per gram of feces).

These operational guidelines have been developed to provide information and guidance to help endemic countries move toward achieving that goal. They were prepared with the support of country technical staff and expert professionals from the Region and from the WHO Collaborating Center on fascioliasis and its snail vectors, incorporating current practices and considering the challenges and particularities of areas with endemicity.

While fasciolosis in animals is a problem that generates economic losses in many countries of the Region, human fascioliasis is limited to environments with the ethnographic characteristics and socioeconomic determinants necessary for infection in humans. These operational guidelines focus on these areas, which are generally associated with small farmers and rural communities. They are based on the “One Health” approach, integrating the different sectors involved and working in synergy to make the interventions more effective and sustainable. To facilitate the understanding and description of these operational guidelines, they have been broken down into their different components.

In the human sector, guidelines for individual treatment with triclabendazole are described. Afterwards, the focus is on the treatment of endemic communities, describing the different modalities for preventive chemotherapy, the thresholds that trigger interventions, and the different considerations for implementing them.

To identify whether a program to eliminate fascioliasis as a public health problem is moving toward that goal and whether it has achieved its proposed objective, it is necessary to implement effective monitoring and evaluation actions, which are described in section 4.3.

While animal fasciolosis is a significant economic problem for many animal producers at any scale, the animal sector component of these operational guidelines focuses on public health programs. The indications included are aimed at small producers within a context of family livestock farming, which usually characterizes communities affected by fascioliasis. Considerations on the medications available to treat fasciolosis in animals are described. Treatment in animals should be done according to a treatment schedule based on local epidemiology and accompanied by comprehensive pasture and animal management measures. Relevant authorities, producer associations, and veterinary professionals should work together to develop and promote these schedules, and technical staff should support small producers to facilitate the implementation of measures appropriate to their conditions.

Many of the pathogens that cause neglected infectious diseases reproduce and transmit when there is inadequate water and sanitation. Access to drinking water, sanitation, and hygiene is essential to prevent, treat, and care for many of these diseases, including disease caused by *Fasciola*. People acquire *Fasciola* infection by ingesting metacercariae present in aquatic plants, food, and water. Therefore, the food safety sector plays a very important role in the prevention of fascioliasis.
The environment should also be considered for the control of fascioliasis, since the intermediate hosts are freshwater snails of the Lymnaeidae family. The control of snails through biological or chemical means is very limited, so efforts should focus on reducing the habitat of these snails.

No measure can be implemented and no action plan can be successful without the involvement and commitment of different actors. The health promotion and education sector plays an essential role in affected communities, and it is imperative that technical personnel (medical professionals, veterinarians, agronomists) stay up-to-date and are able to transfer the necessary and appropriate knowledge to small producers.

These operational guidelines have been developed based on existing WHO recommendations in the case of the human sector and evidence and best practices for the other sectors. However, there are recognized knowledge gaps. Attempts have been made to address these gaps through the suggestions or indications of regional experts and national program managers. Likewise, these guidelines should be reviewed and adapted as more knowledge and evidence emerge, in order to achieve the goals more efficiently and benefit the affected communities.

**Fascioliasis or fasciolosis?** Although there is no agreement among experts, there is a tendency to use the term fascioliasis when referring to the disease in humans, and fasciolosis when referring to the disease in animals. This document uses the terms this way. In addition, the term fascioliasis is used when the disease is considered generically.
1. Introduction

Trematodes of the species *Fasciola hepatica* and *F. gigantica* cause fascioliasis, a parasitic disease that affects people and a wide variety of animals, mainly herbivores. Human fascioliasis is classified by the World Health Organization (WHO) within the group of neglected tropical diseases, known in the Region of the Americas as neglected infectious diseases. This group of diseases, which is linked to poverty, also exacerbates health problems and social and economic inequities, and imposes a devastating human, social, and economic burden on more than 1 billion people in the world’s most vulnerable and marginalized populations. Human fascioliasis is included in the *Road map for neglected tropical diseases 2021-2030* (1, 2), as well as in the Pan American Health Organization (PAHO) initiative to eliminate communicable diseases (3).

1.1. Goals of the Pan American Health Organization

As part of the commitment to achieve the goals of the 2030 Agenda for Sustainable Development and the Sustainable Health Agenda for the Americas 2018–2030 (4), in 2019, PAHO launched a policy to apply an integrated and sustainable approach to communicable diseases in the Region of the Americas, known as the Initiative for the Elimination of Communicable Diseases (5). This policy states that the objective for fascioliasis is *to achieve the elimination of fascioliasis as a public health problem* in the Region of the Americas by 2030. In addition, it establishes these goals for 2030:

- Prevent mortality in at-risk school-age children, through screening and early treatment or preventive chemotherapy.
- Prevent serious morbidity (liver damage and severe anemia) in at-risk school-age children and adults, through screening and early treatment or preventive chemotherapy.

The elimination of human fascioliasis was defined as a public health problem during the development of these operational guidelines.

The objective of the Pan American Health Organization with regard to human fascioliasis is, by 2030, to eliminate human fascioliasis as a public health problem, defined as a sustained prevalence ≤5%, by coprology, without high-intensity infections (≥400 eggs per gram of feces). In this context, sustained means maintained over time.

The objective of eliminating high-intensity infections responds to the fact that *Fasciola* is a tissue parasite of the liver and bile ducts. It can cause significant acute and chronic morbidity, including weight loss, anemia, delayed growth and psychomotor development, and malnutrition in children and adults with high-intensity infections. The plan seeks to eliminate acute and chronic morbidity due to fascioliasis, for which the best indicator is the absence of high-intensity infections.
1.2. Development of the operational guidelines

These operational guidelines have been developed as an initiative of the PAHO Regional Program on Neglected Infectious Diseases, which has been working in coordination with the Pan American Center for Foot-and-Mouth Disease and Veterinary Public Health, to support and facilitate the implementation of efficient programs for the elimination of human fascioliasis in the Region of the Americas.

To develop these operational guidelines, work was carried out with professional officials from ministries of human health, animal health, and the environment in endemic countries in the Region, and with a group of regional and international experts. The methodology and participants involved are described in Annex 1.

The purpose of this document is to provide general operational guidelines for the elimination of human fascioliasis as a public health problem, with guidance that is plausible for the implementation of public health programs, based on tools that are currently available and striving to provide the necessary flexibility so that different countries can adapt them to their conditions. These operational guidelines are based on the available technical evidence; where information gaps exist, they are based on the suggestions and indications of regional and international experts and national program managers. In the future, as more evidence becomes available, the information included in these operational guidelines will be updated.

Box 1 presents different definitions related to infectious diseases to facilitate their identification and understanding.

**Box 1**

**Infectious diseases terminology**

PAHO has defined the terms **control**, **elimination**, **eradication**, and **extinction** in relation to neglected infectious diseases as follows (6):

- **Control**: reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level as a result of deliberate measures. To maintain this reduction, continuous intervention measures should be applied. Control may or may not be related to global targets set by WHO.

- **Elimination as a public health problem**: a term related to both infection and disease. Defined by the achievement of measurable global targets set by WHO in relation to a specific disease. Once these targets are reached, continued measures are required to maintain the achievement of the targets or make progress in interrupting transmission. The process of documenting the elimination of a health problem is called **validation**.

- **Elimination of transmission (also known as interruption of transmission)**: reduction to zero of the incidence of infection caused by a specific pathogenic agent in a defined geographical area, with minimal risk of reintroduction, as a result of deliberate efforts. To prevent recurrence of transmission, ongoing measures may be necessary. The process of documenting the elimination of transmission is called **verification**.

- **Eradication**: permanent reduction to zero of a specific pathogenic agent, as a result of deliberate measures, with no further risk of reintroduction. The process of documenting eradication is called **certification**.

- **Extinction**: refers to the eradication of the specific pathogenic agent so that it no longer exists in nature or in the laboratory. This may occur as a result of deliberate or unintentional measures.
2. Background

The *F. hepatica* parasite is present on all continents except Antarctica. *F. gigantica* is mainly found in tropical and subtropical areas of Asia and Africa.

The *Fasciola* transmission cycle is complex and involves many mammals as definitive hosts, mainly domestic ruminants, although it also affects wild ruminants, wild boars, rabbits, horses, donkeys, and pigs, among others. Humans can also act as definitive hosts (Figure 1). Fasciolosis is a disease of great veterinary relevance, which causes significant production losses, mainly in sheep and cattle. Transmission requires intermediate hosts, freshwater snails of the Lymnaeidae family, and the ingestion of aquatic or semiaquatic plants or water contaminated with the parasite’s metacercariae. It is associated with poor sanitation and inadequate food hygiene.

![Figure 1. Transmission cycle of Fasciola species](image)

The life cycle of *Fasciola* is about 14 to 23 weeks. The prepatent period (from the ingestion of the metacercariae to the elimination of eggs in feces) is about two months, but varies depending on the hosts and the level of infection. In humans it can last up to 3–4 months. It is estimated that adult parasites can live up to 11 years in sheep, 1 year in cattle, and 9–13 years in humans (7).

The parasite can infect people of all age groups, but children up to 15 years of age and young adults are the primary groups that experience acute and chronic consequences of the disease, including anemia, jaundice, and, eventually, damage to the bile ducts of the liver. In younger children, fascioliasis can cause anemia, stunted growth, wasting, cognitive impairment, and poor school performance. Those with high-intensity infections are more likely to suffer the serious consequences of human fascioliasis.

In 2012, experts estimated that there were 2 600 000 infected people, but this is almost certainly an underestimate (8). The main area of endemic fascioliasis in the Region of the Americas is the Andean highlands of the Plurinational State of Bolivia and Peru, where an estimated 250 000 people living in Indigenous communities are at risk of fascioliasis (3).
2.1. Epidemiology of fascioliasis in the Americas

Fascioliasis is an epidemiologically complex disease that occurs in different and varied contexts. The different epidemiological contexts reflect the variations and diversity of environments and conditions, including ethnographic and abiotic aspects such as demography, diet, habits, traditions and customs, species of domestic and wild animals, species of snails present, altitude, environmental conditions, seasonality, and rainfall.

Fascioliasis is a disease that is closely linked to environmental factors. Therefore, climate changes can affect its burden, geographical distribution, and spatiotemporal impact.

Fascioliasis has an irregular geographic distribution, and its prevalence can vary considerably in relatively small areas. This variability is due in part to the irregular distribution of susceptible snail hosts and their habitats. The disease tends to be focalized and it is important to identify these foci. In the Americas, fascioliasis is caused by *F. hepatica*. Regarding intermediate host snails, *F. hepatica* is mainly transmitted by snails of the genus *Galba*, which is primarily associated with the species *G. truncatula* (Latin America), *G. cousini* (Latin America), and *G. cubensis* or *G. viator* (Latin America and the Caribbean). The species *Pseudosuccinea columella* is also a significant host in Latin America and Cuba (7, 9).

The distribution of the disease in people bears little relationship to that of the disease in animals: high prevalence in people is not necessarily related to high prevalence in animals (7). Therefore, to identify areas where the disease is a public health problem, human disease data are needed, as animal data do not necessarily indicate that a public health problem exists.

2.1.1. Current situation

To provide context for these operational guidelines, in April 2022, a literature review on human fascioliasis in Latin America and the Caribbean since 2010 was conducted (unpublished). The summary is presented below. The review was carried out through the broadest possible search in PubMed and SciELO for each country or territory in the Region. A total of 1317 articles were found, but only 50 were identified as relevant to fascioliasis in humans.

Although many data prior to 2010 show very high prevalences (greater than 30%), those reported since 2010 are much lower. This may be due, among other factors, to: (a) publications not identified through the methodology used; (b) more recent data that have not been published; (c) lack of surveillance, especially in areas that present the necessary factors for fascioliasis to be a problem in people; and (d) control programs in some countries that include mass drug administration in endemic communities and certain improvements in living conditions, resulting in a true decrease in morbidity and prevalence in the populations served.

Prevalence data should be interpreted with caution since, in many cases in the studies reviewed, different techniques were used to determine prevalence; details about sampling or diagnostic methods were not included; or tests developed by the researchers themselves were used (with no validation data or unreviewed validation).

The various epidemiological situations associated with fascioliasis are the ones described by Mas-Coma and collaborators in 1999 (10):

- **Sporadic fascioliasis**: includes isolated autochthonous cases or imported cases.
- **Endemic fascioliasis**: there are three types of endemic situations that can be differentiated based on the prevalence obtained using coprological methods:
- **Hypoendemic fascioliasis**: coprological prevalence under 1% and average infection intensity less than 50 eggs per gram.

- **Mesoendemic fascioliasis**: coprological prevalence between 1% and 10%, and average infection intensity between 50 and 300 eggs per gram.

- **Hyperendemic fascioliasis**: coprological prevalence over 10% and average infection intensity over 300 eggs per gram.

- **Epidemic fascioliasis**: can occur in areas where the disease is endemic in people or where it is endemic in animals but not in people.

Sporadic fascioliasis has been described in countries such as Brazil, Chile, Colombia, Cuba, Ecuador, Uruguay, and the Bolivarian Republic of Venezuela. No reports of epidemic fascioliasis in Latin America and the Caribbean since 2010 were found.

According to the bibliographic review, countries in which areas with endemicity have been reported since 2010 are:

- **Argentina**: A bibliographic review conducted by Mera y Sierra and collaborators (11), published in 2011, identified 58 reports for a total of 619 cases in humans, in 13 provinces. The first case was identified in 1924. Most cases were identified in high altitude areas, especially in Catamarca, Mendoza, and San Luis, and the authors noted that the distribution in humans did not coincide with the distribution in animals. According to a publication from 2013, in the region of El Juncal, La Toma, in the province of San Luis, a prevalence of 2.3% was detected using microscopy (12).

- **Plurinational State of Bolivia**: During the 1990s and earlier, some of the highest prevalences of fascioliasis in the world were found in the Bolivian highlands, bordering Lake Titicaca. In an article published by Esteban and collaborators in 1999 (13), in a sample in 24 locations using the Kato-Katz method, a prevalence of fascioliasis of 14.8% was found, with a range from 0% to 68.2%.

In 2008, a pilot project to control fascioliasis was carried out in Huacullani, using 10 mg/kg of triclabendazole in a mass drug administration campaign (14). The project demonstrated that triclabendazole was safe and effective. Based on this, the Ministry of Health of the Plurinational State of Bolivia decided to launch a mass drug administration program in networks 4, 5, 6, and 9 of the department of La Paz. These triclabendazole programs were implemented annually from 2008 to 2021, with the exception of 2011, 2015, 2018, and 2020.

Since 2010, only three publications were identified that mentioned the prevalence in humans. The studies by Valero and collaborators (15) and Villegas and collaborators (14) in the Huacullani region, published in 2012, mention a prevalence of 21.56% using MM3-COPRO ELISA, but the sampling had been carried out in 2008. In 2019, Mollinedo and collaborators (16) published data from the sampling carried out in 2017. The prevalence using only Kato-Katz was 1.05% in Batallas, 0.2% in Puerto Pérez, 0.7% in Huacullani-Tiahuanaco, 0.7% in Laja, 0.6% in Pucarani, and 0% in Viacha.

- **Haiti**: Animal fasciolosis is documented in Haiti. However, no cases of human fascioliasis were reported until 2012. The only article identified through the literature review mentions a prevalence of 6.5% using Western blot (17). Since there are no coprological data, it is difficult to say if there are areas with endemicity or if the disease is sporadic.

- **Mexico**: According to the introduction in the article by Zumaquero-Ríos and collaborators (18), human fascioliasis in Mexico was considered sporadic, with only 50 cases reported before the middle of the twentieth century. Human cases were reported in the states of Mexico, Veracruz, Tabasco, Chiapas, Hidalgo, Morelos, Oaxaca, San Luis Potosi, Sinaloa, and Puebla. Puebla was the state where the most cases had been reported. However, there is a lack of current data. The only recent article found is the one mentioned, by Zumaquero-Ríos, which reports a prevalence of 1.6% in Atlixco (Puebla) using the Kato-Katz method.
- **Peru:** An article published by Marcos and collaborators in 2007 indicates fascioliasis as an emerging disease in Peru given that the review of data from 1963 to 2005 detected 1701 cases. Analysis of these data showed an increase in cases over time. Potential reasons provided for this increase are improved detection, but also an increase in cases. By 2010, human *Fasciola* infection had already been reported in 18 departments, and animal fasciolosis in 21 departments, of Peru’s 24 departments. The data found on human fascioliasis in the different departments are:

  - **Apurímac:** In the district of Santa María de Chicmo, Andahuaylas province, a prevalence of 5.3% was detected (methodology not specified). Although the publications are from 2019 and 2021, the sampling was done from 2016 to 2017.
  
  - **Cajamarca:**
    - **Cajamarca Province:** Local prevalences of up to 47.7% and an average of 24.4% were found using Kato-Katz and a formalin-ether concentration, and of 5.24% using Kato-Katz. However, the sampling was prior to December 2007. In Barios del Inca, a prevalence of 6.30% was found using Lumbreras rapid sedimentation during sampling in 2014.
    - **In Condebamba,** a prevalence of 5.1% was found using Lumbreras rapid sedimentation during sampling in 2014.
  
  - **Cusco:**
    - **Anta Province:** Several publications show a prevalence of 5.2% to 7.4% using Kato-Katz or Lumbreras rapid sedimentation.
    - **Paucartambo Province:** Several publications show a prevalence of up to 10.3% using Kato-Katz or Lumbreras rapid sedimentation.
    - **Junín:** According to a publication from 2012, based on sampling in 2009, a prevalence of 5.1% was detected using Lumbreras rapid sedimentation.
    - **Madre de Dios:** In the Yomibato community of Manu National Park, 2.3% positives were found using microscopy in a sample from 2012, but no positives were found in 2014.

2.2. Diagnosis of fascioliasis

2.2.1. Diagnosis in humans

The diagnosis of *Fasciola* is complex and there is no standard technique. The use of several techniques with different principles could achieve greater diagnostic resolution, although their use would be limited in large-scale monitoring due to logistical complexities and costs. A summary of the different types of tests is included in this section, but details of the different diagnostic methods and their assessment can be found in several review articles.

Microscopic techniques that detect parasite eggs in feces have low sensitivity, which is generally even lower in cases of low infection intensity. The prepatent period (the period between infection and egg shedding) is 3–4 months. Sensitivity can be increased by taking more readings per sample or by taking repeated readings. For example, El-Morshedy and collaborators demonstrated that the sensitivity of the Kato test can be increased by making three readings of the same sample (with one slide, they observed a sensitivity of 66–79%, while with three slides it was 96–99%). However, they did not detect differences when doing this for three consecutive days. Sedimentation-based microscopy tests appear to be more sensitive than flotation techniques. Rapid sedimentation modified by Lumbreras has proved to be more effective than others. In the case of Maco Flores and collaborators, this test proved to be more sensitive than spontaneous sedimentation and formalin-ether
concentration. Quantification of the number of eggs in feces is important, as it reflects the intensity of the infection. The most widely used quantitative test in humans is the Kato-Katz method and infection intensities are described as low, moderate, and high (Table 1) (43).

<table>
<thead>
<tr>
<th>Infection intensity based on eggs per gram (epg) of feces</th>
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<tbody>
<tr>
<td>LOW 1–99 epg</td>
</tr>
<tr>
<td>MODERATE 100–399 epg</td>
</tr>
<tr>
<td>HIGH ≥400 epg</td>
</tr>
</tbody>
</table>

Some microscopy techniques that require special devices (such as FLOTAC or Flukefinder®) are generally more sensitive, but also more expensive and difficult to use in large surveys (37).

Numerous serological tests have the advantage that they can detect infection 2–3 weeks after infection, which is much earlier than the detection of eggs. However, different serological tests have variable characteristics and different performance. Many commercial tests claim very high sensitivity and specificity. However, few validations have been conducted in the field. Some ELISA (enzyme linked immunosorbent assay) kit manufacturers still rely on crude antigens produced by parasites, which affects specificity, batch-to-batch reliability, and production scale-up. Antibody detection tests do not differentiate past from current infections, but an immunoglobulin M (IgM) ELISA (Fas2-ELISA) has been developed that can potentially differentiate acute and chronic infection. Maco Flores and collaborators (42) demonstrated that this Fas2-ELISA is highly sensitive and superior to the Western blot and Arc 2 (immunoelectrophoresis). A systematic review on serological tests for fascioliasis in humans conducted by Muñoz Zambrano and collaborators (38) in 2020 concluded that in general, the specificity is slightly higher than the sensitivity. However, the quality of the evidence could not demonstrate their usefulness during the acute phase of the disease.

The use of serology to determine prevalence to trigger treatment on a population scale (see section 4.2) has already been discussed. However, the following should be considered:

- As described, the existing serological tests are very varied, have different performance, and are not always available. They also do not detect the intensity of infection. Before considering the use of a serological test, it is important to check if it has been independently and blindly validated, and that the controls used for the validation (especially to verify specificity) were adequate.

- Depending on the technique, people can remain positive for several months and perhaps years after treatment, which would not necessarily indicate a prevalence of current infection, since it would also reflect past exposure (35, 40).

- Serological tests can detect early infections. This could be confirmed using microscopy about 2–3 months later in people who have had positive serology, to confirm that it is indeed a recent infection.

- Serology can be useful, especially when there are difficulties obtaining stool samples, either due to logistics or the idiosyncrasies of the communities to be evaluated. In these cases, serology could be used as a screening test to evaluate whether human fascioliasis is or has been present in the area. Positive cases can then be confirmed using microscopy or coproantigens, thus verifying whether the infection is current. This requires follow-up of positive patients, which has its logistical challenges, and still requires coprological samples, although from a much smaller number of people.
MM3-COPRO is a method for detecting parasitic coproantigens that was initially used in veterinary medicine and is now commercially produced (Bio-X Diagnostics, Belgium). It has recently been improved to optimize its performance and is known as eMM3-COPRO. Coproantigen detects Fasciola antigens 6–8 weeks after infection and is negative a couple of weeks after clearing the infection. A field evaluation of the MM3-COPRO ELISA showed that it was sensitive and specific using human samples [13] and that this test could be very useful for samples, but not for determining the level of infection.

Different molecular tests with high sensitivity and specificity in feces have been described [44–47]. However, inconsistencies have been reported. They do not detect infections during the prepatent period (as they are based on the detection of parasite eggs) and they are expensive techniques.

### 2.2.2. Diagnosis in animals

The diagnosis of fasciolosis in animals is based on clinical symptoms accompanied by seasonality, historical presence of the disease, and presence of intermediate host snails. Confirmation can be by microscopy, serology, or post-mortem inspection of livers. The diagnosis of fasciolosis in animals has been reviewed by Álvarez Rojas and collaborators, among others [48]. Diagnostic methods in animals include:

- **Microscopy:**
  - In veterinary medicine, the identification of eggs in feces is preferred, using sedimentation techniques or a combination of flotation (zinc sulfate) and sedimentation. These techniques are routinely used but are not always reliable. They detect infection after eight weeks.
  - There are also devices such as FLOTAC and Flukefinder® which, as mentioned above, are more sensitive, but also more expensive.
- Detection of antibodies against the parasite:
  - This is mainly used to evaluate prevalence at herd level based on the detection of anti-\textit{Fasciola} antibodies. A wide variety of antigens have been used to detect such antibodies, including excretory or secretory products, tegument, crude extracts of adult parasites, and recombinant proteins. Antibody detection tests are not related to parasite load.
  - Antibodies can be detected two weeks after infection, but persist after treatment, and do not differentiate current infection from past infection.
  - There is a risk of cross-reactions with antibodies produced by other parasites (depending on the type of antigen used, with parasites from genera such as \textit{Echinococcus, Taenia, Dicrocoelium}, etc.).
  - Some of these tests have been adapted to monitor antibodies in milk tanks on dairy farms.

- Detection of parasite antigens:
  - Antigens in serum samples can be detected one week after infection. There are reports that they are related to the level of infection, but they only detect parasites that are migrating through the liver.
  - The coproantigen MM3-COPRO was initially used in veterinary medicine. It has recently been improved to optimize its performance, and is known as eMM3-COPRO. It has been described as sensitive and specific and was recently field-validated in sheep (49). Coproantigen detects \textit{Fasciola} antigens 4–8 weeks after infection and is negative a couple of weeks after clearing the infection. There is a relationship between positivity and parasite load. Individual samples can be used, and also pooled samples. The test can be used for sheep and goats, but not for horses. Some countries have commercial tests.
3. Elimination of human fascioliasis as a public health problem through the “One Health” approach

To achieve the elimination of human fascioliasis as a public health problem — that is, to achieve a sustained prevalence of less than or equal to 5%, by coprology, without high-intensity infections (400 eggs or more per gram) — effective and sustainable measures are needed. This is why it is necessary to follow the “One Health” approach (see the definition in Box 2), integrating the different components and working in synergy with other relevant areas.

In 2021, PAHO Member States committed to “One Health: a comprehensive approach for addressing health threats at the human-animal-environment interface,” in order to promote coordination and collaboration between the different governance frameworks of human, animal, plant, and environmental health programs (50).

To facilitate the joint and efficient work of the different sectors, it is essential to have good, effective coordination. It is beneficial to have a multisector One Health committee for the elimination of human fascioliasis to facilitate this work. This committee should:

- Facilitate the joint, harmonious, and efficient work of the different sectors.
- Define the objectives and corroborate the action plan at the national level and facilitate its transfer to the subnational level through the different sectors.
- Specify the functions and responsibilities of the sectors involved.
- Carry out joint activities, such as raising community awareness.

It is important for the committee to meet periodically and have an active and dynamic role.
“One Health” is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems.

It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent.

The approach mobilizes multiple sectors, disciplines, and communities at different levels of society, to work together to promote well-being and address threats to health and ecosystems, while addressing the collective need for clean water, energy, and air, and safe and nutritious food, taking action on climate change and contributing to sustainable development.


In addition to fascioliasis, there are other neglected zoonotic diseases that can infect both humans and domestic and wild animals. Two examples are cystic echinococcosis or hydatid disease and taeniasis/cysticercosis complex. These parasitic diseases also have great relevance from the point of view of public health, in addition to their implications for and direct impact on livestock production and the commercialization of products of animal origin. In some countries in the Region of the Americas, they continue to asymmetrically affect lower-income sectors such as small producers, livestock sector workers, and other at-risk subpopulations. For a more rational and efficient use of the resources allocated to fighting against these diseases, it is recommended that countries work on the development of comprehensive plans that include joint actions for the elimination of these (or other) zoonoses, to be implemented by the public health and animal health authorities, as well as other national actors.

As stated earlier, to be more efficient, it is very important for the different sectors to work together. However, to facilitate the understanding and description of different sectors’ activities, this document breaks down these operational guidelines into their different components, which are: the human sector, the animal sector, sanitation, environment, food safety, and promotion of health and education (Figure 2). These components are described in detail in the following sections. Coordination has already been described in this section.
3.1. Types of interventions to eliminate fascioliasis as a public health problem

For human fascioliasis, the One Health approach is the best strategy to reduce the risk of infection and reinfection (51). One Health interventions should be adapted to the epidemiological and transmission characteristics of the endemic area.

Although there is a great diversity of actions and interventions that can be implemented, the essential package of interventions is preventive chemotherapy. In addition, it is necessary to implement a series of measures that are complementary to preventive chemotherapy (43):

- **Rapid impact interventions**: veterinary public health measures, including treatment of domestic animals, monitoring of intermediate hosts to determine active transmission foci, direct actions to control intermediate hosts, and fencing of grazing areas and bodies of fresh water suspected of being infected.

- **Longer-term measures**: promotion of information, education, and communication, control or management of intermediate host snails, and drainage of grazing lands.

3.2. Operational plan: steps for implementing an action plan for the elimination of human fascioliasis as a public health problem.

When implementing a plan to eliminate fascioliasis as a public health problem with the integration of different sectors, it is important to follow certain steps. These have to be adapted to the current situation and each country’s objectives and resources. In general, the steps to follow, and the sections in which they are detailed, are as follows (represented in Figure 3):

1. **Identification of human fascioliasis as a public health problem**:
   a) There may be recent evidence that human fascioliasis is a public health problem. If this is the case, a baseline (prevalence and infection intensity survey) would have to be established, as described in section 4.3.
   b) If there is unconfirmed suspicion that fascioliasis is a public health problem, for example, because the data are more than five years old or there are only sporadic cases, a rapid assessment is suggested (described in section 4.3).

2. **Advocacy for the political engagement of stakeholders**. Once human fascioliasis is recognized as a public health problem, it is necessary to obtain the political commitment to achieve elimination. For this, the following is necessary:
   a) Political commitment, which provides an adequate national and subnational legal framework.
   b) Intrasectoral and intersectoral commitment, which should be achieved through a multisectoral One Health committee, as described above.

3. **Agreement on a technical plan**. The national technical plan should incorporate and adapt the measures suggested in these operational guidelines [sections 4–9] to local conditions, identifying general priorities and priorities for different areas. The national technical plan should be adapted, if necessary, and transferred to the different subnational levels.

4. **Delimitation of the work area**. Definition of the areas for implementation of the activities [section 4.2.1].
5. **Implementation of elimination activities.** The activities that have been identified and agreed upon in point 3 above should be implemented. Progress and impact will be evaluated, as described in section 4.3. If necessary, adjustments will have to be made to the national technical plan.

![Diagram of implementation process](image)

**Figure 3.** Steps for implementing an action plan for the elimination of human fascioliasis as a public health problem.
4. Interventions in humans

Interventions for humans include individual treatment and population-level treatment.

4.1. Individual treatment

Symptoms of human fascioliasis in the acute phase may include fever; gastrointestinal problems, such as nausea, vomiting, and diarrhea; hepatomegaly; liver function abnormalities; skin rash; difficulty breathing; and abdominal pain or tenderness, in addition to high eosinophilia. The chronic phase (after the parasite settles in the bile ducts) is characterized by inflammation and hyperplasia and thickening of the bile ducts and the gallbladder, giving rise to lithiasis or biliary obstruction. Symptoms of this phase may include biliary colic, nausea, intolerance to fatty foods, right upper quadrant pain, epigastric pain, obstructive jaundice, and pruritus, which are a result of blockage in the biliary tract and inflammation in the gallbladder. Inflammation of the liver and pancreas may also occur.

4.1.1. Treatment

Triclabendazole, which has been used in veterinary medicine since 1983 and in humans since 1989, is the drug of choice for treating fascioliasis. It is active against adult parasites in the bile ducts and young parasites that migrate through the liver. The following cure percentages have been reported: 79.4–83% with a single dose of 10 mg/kg and 92.2–93.9% with two doses of 10 mg/kg every 12 hours [52]. Egg reduction rates were in the range 74–90.3% after one treatment and 84.2–99.9% after two treatments [14].

WHO recommends a single 10 mg/kg oral dose of triclabendazole. In case of therapeutic failure (when the medication does not produce the desired effect) or if the medical professional in charge of the patient considers it necessary, two doses of 10 mg/kg can be given every 12–24 hours for a total dose of 20 mg/kg [43]. Triclabendazole should be given with high-fat foods, as this increases its serum concentration.
For individual treatment, the WHO recommendation is to use a single dose of 10 mg/kg of triclabendazole. However, if countries have local evidence of the need to use two 10 mg/kg doses 12–24 hours apart, countries can choose this option.

There are discordant results regarding the effectiveness of nitazoxanide ([18, 53–55]) for the treatment of fascioliasis.

To evaluate the effectiveness of treatment in individual cases, it is suggested to use microscopy 10–15 days after the treatment, and repeat it after 30 days. If the patient remains positive, this can be confirmed by ultrasound after 30–35 days. However, in some circumstances it may be difficult to follow this scheme due to distances and the lack of availability of nearby laboratories. In such cases, doctors will need to decide the best option based on the situation and available resources. One action to remedy these limitations is the technical strengthening of intermediate laboratories in endemic areas, providing personnel, equipment, and materials to increase the availability of this service in the most remote areas.

It is not recommended to use serological tests to evaluate the effectiveness of treatment, as antibody levels remain high and tests continue to be positive following treatment.

4.1.2. Therapeutic failure and resistance to triclabendazole

Although resistance to triclabendazole in humans appears to be rare and sporadic ([56]), cases of therapeutic failure that could be related to drug resistance have been reported in the Region ([55, 57, 58]). It should be considered that therapeutic failure may be due to other reasons such as the quality of the medication, the dose used, and the patient’s immune status, and not only drug resistance. In endemic areas, reinfection of the patient should also be ruled out.

4.2. Treatment of populations

4.2.1. Identification of at-risk populations

Before starting a public health program, it is important to identify at-risk populations in order to delimit the work area. Populations should be identified based on the following criteria, which must all be present:

- Endemicity of fascioliasis in humans, defined using coprological tests.
- AND the presence of key risk factors for the transmission cycle (e.g., the presence of intermediate host snails; see section 8).
- AND the existence of socioeconomic factors that promote infection in humans (e.g., consumption of watercress or wild aquatic plants).
4.2.2. Preventive chemotherapy and modality according to the prevalence threshold

WHO recommends preventive chemotherapy (PC) \(^{(43, 52)}\), which is described as the periodic use of antiparasitic drugs on a massive scale, regardless of individual infection status, as a public health tool. PC aims to not only treat people with parasites, but also prevent morbidity and reduce transmission. PC can be implemented using different modalities \(^{(59–62)}\):

- **Mass drug administration.** Anthelmintic drugs are administered to the entire population of a geographic area (for example, department, province, district, municipality, or community), except people or age groups in which it is contraindicated, at regular intervals, regardless of each person’s infection status. Success depends, among other things, on the level of coverage, frequency of administration, and effectiveness of the drug. It requires a significant degree of community participation and commitment.

- **Targeted preventive chemotherapy.** Anthelmintic drugs are administered at regular intervals to certain at-risk groups in the population, based on age, sex, or other social characteristics such as occupation (e.g., school-age children), regardless of their infection status.

- **Selective preventive chemotherapy.** After a regular screening exercise in a population group in an endemic area, all individuals found to be infected (or suspected of being infected) receive anthelmintic drugs.

PC can be implemented under the following conditions: house-to-house distribution (mobile teams), distribution stations (fixed teams), distribution at specific locations, and distribution at community gathering places \(^{(62)}\).

The selection of the PC modality for the elimination of human fascioliasis as a public health problem depends, among other factors, on the fascioliasis prevalence level, the presence of risk factors (the intermediate host snails and socioeconomic aspects), countries’ experiences when implementing PC, and existing resources.

The **suggested threshold to trigger PC** is a prevalence greater than 5%, based on coprological tests, in communities where socioeconomic risk factors are also present and intermediate host snails have been identified:

- If the initial prevalence is equal to or less than 5%, individual treatment is suggested.
- If the prevalence by coprology is greater than 5% or there are high-intensity infections (more than 400 eggs per gram of feces), PC as mass drug administration or targeted chemotherapy is suggested \(^{(43)}\).
- If the prevalence is less than or equal to 5% after at least five years of PC, it is suggested to do another round of PC, in this case targeted chemotherapy or selective chemotherapy.
4.2.3. Drug of choice

The drug of choice for PC is a single dose of 10 mg/kg of triclabendazole (43, 52).

4.2.4. Eligible population

The entire population aged 5–65 years in an endemic area is eligible to receive triclabendazole, taking into account that:

- Although the WHO recommendation is for ages 5 and above (52), in the Plurinational State of Bolivia it has been used in approximately 6000 children aged 4–5 years (since they start school at age 4) without serious adverse effects. Thus, the inclusion of children starting at 4 years of age can also be considered, emphasizing effective pharmacovigilance.
The pharmaceutical manufacturer of triclabendazole recommends it up to 65 years of age, since there are no data on older people. However, experience in the Plurinational State of Bolivia suggests that it can be used in people over 65 years of age, as long as they are in good health.

Severely ill people, people suffering from acute gastrointestinal symptoms (vomiting, diarrhea, abdominal pain), pregnant or breastfeeding women, people with liver dysfunction, or people who have already received treatment for fascioliasis should be excluded from PC with triclabendazole. Children under 4 years of age and pregnant and breastfeeding women should not receive PC, but can be treated individually under medical supervision (43, 52).

4.2.5. Frequency of preventive chemotherapy

PC can be implemented every 12–24 months depending on the modality and prevalence (43).

When starting a mass drug administration program, an annual frequency is suggested until the results of the impact survey suggest that it should be done every two years or until fascioliasis is considered to have been eliminated as a public health problem. More details can be found in section 4.3 on monitoring and evaluation and in Figure 4.

In the case of selective PC, it is suggested to actively search for cases at regular intervals (annually, every two years, or according to the interval deemed necessary in each area) as long as positive cases are found. If it is deemed appropriate, for example, due to an increase in the number of cases, the frequency could be increased. For more details, see section 4.2.8.

4.2.6. Coordination with other preventive chemotherapy programs

Experiences from other PC programs such as soil-transmitted helminth control programs can be extremely useful. If the country has experience with other programs, it is recommended to promote synergies in terms of personnel, logistics, and health promotion and education. However, there is no evidence to support simultaneous treatment for soil-transmitted helminths and fascioliasis, which is why the two campaigns should be implemented separately, at different times.

4.2.7. Adverse reactions

Adverse reactions to triclabendazole are usually mild. The most common are abdominal pain, epigastric pain, and sweating, and the least common are nausea, vomiting, dizziness, cough, fever, urticaria, and pruritus (52). However, it is important to monitor adverse reactions in each PC campaign, regardless of the modality.

PAHO has published a manual on safety when administering medicines (63) to provide practical tools, including training modules and work guides, for national neglected infectious diseases programs to use during planning, preparation, and monitoring.

The adverse reaction notification process should follow each country’s pharmacovigilance regulations.
4.2.8. Specific considerations for selective preventive chemotherapy

This PC modality is used when, after a regular screening exercise in a population group residing in an area where the disease is endemic, all infected people (or those presumed infected, since they live in at-risk communities, as described in section 4.2.1) are given anthelmintic medications. In the case of fascioliasis, the following is suggested:

- Conduct an active search for people who are considered at-risk due to their relationship with the risk factors (homes near areas with intermediate host snails, consumption of watercress or other aquatic plants, etc.) to obtain the necessary samples and detect positive people.

- Implement selective chemotherapy, treating at least the positive person and the entire family with triclabendazole. Any other person who is suspected of being positive due to shared risk factors should also be treated. Depending on the risk factors, treatment of the entire community may be considered.

- It is important to strengthen the technical capacities of intermediate laboratories in endemic areas (with personnel, equipment, and material) so that they can implement coprological tests and carry out sampling with the necessary frequency.

4.3. Monitoring and evaluation

To identify whether a program to eliminate fascioliasis as a public health problem is on track to achieve its goal or has reached the proposed goal, which is the elimination of human fascioliasis as a public health problem, it is necessary to conduct a good monitoring and evaluation plan.

The monitoring and evaluation plan should include (in the following order):

1. **Rapid assessment.** In case of suspicion of endemicity, this is used to indicate whether a population survey is necessary.

2. **Baseline survey.** The prevalence and infection intensity reported in this survey will enable definition of the need for treatment and selection of the modality.

3. **Analysis and monitoring of coverage.** This is used to determine whether at least 75% of the target population was treated and to evaluate the implementation of PC.

4. **Surveillance of sentinel sites.** This is used to monitor the program’s progress. The results will allow authorities to see where they should strengthen actions.

5. **Impact assessment survey.** The results of this survey will allow the country to determine whether it should make changes to the frequency and modality of PC.

More details about the different components are provided below.

4.3.1. Rapid assessment

In communities where endemic fascioliasis is suspected, a rapid assessment can determine the need for a baseline population survey.

Rapid assessments can be done in schools (in the population of children ages 5–14, as this sample generally shows a higher prevalence and infection intensity) or in the entire community, as appropriate. It is suggested to take at least 50 samples and, if any positive samples are found, then undertake a baseline population survey.
4.3.2. Baseline survey

This should be a prevalence survey in the at-risk population, using a random probabilistic sample that is representative of the population. The at-risk population is defined in section 4.2.1. This survey helps to delimit the intervention area and define both the need and modality for PC, as described in section 4.2.2.

**Target population:** mainly school-age boys and girls (ages 5–14), since this group generally has the highest prevalence and infection intensity. When there is evidence that fascioliasis occurs in adults, the survey should also be implemented in that group.

4.3.3. Monitoring of preventive chemotherapy coverage

After starting a round of PC, it is important to monitor coverage to see how the program is performing. This involves reviewing whether the population that should receive PC (the target population) actually received the treatment.

To calculate program coverage, the following formula should be used:

\[
\left( \frac{\text{Number of individuals who took preventive chemotherapy}}{\text{Number of individuals in the target population}} \right) \times 100
\]

The number of individuals in the target population is not always easy to estimate; it is preferable to use the most recent population data available.

It is recommended to analyze the coverage after each round of deworming, and implement rapid monitoring of coverage in the first two weeks after PC to identify and treat populations that have not accessed PC, in order to achieve optimal coverage (75% or higher). It is also recommended to perform data quality evaluations each time problems are identified through analysis of administrative coverage, or at least once during the first two years of program activities. For more details on the procedures and steps to design and implement PC registries, it is suggested to consult the related documents published by PAHO [61, 64].

To achieve the expected impact, both in reducing the prevalence and intensity of infections, preventive chemotherapy should cover at least 75% of the target population.

The value of 75% is indicative, as there is not enough evidence to determine a definitive value; therefore, this figure should be reevaluated as more evidence becomes available. While this is the minimum value, national programs can increase it if necessary.

4.3.4. Surveillance of sentinel sites

To monitor the progress of a public health program, ideally the sentinel site surveillance should be conducted every year; otherwise, every two years.

Surveillance of sentinel sites serves to monitor the parasitological indicators of prevalence and infection intensity in population surveys. It is used to see how the program is going. Since it measures frequencies of infection in high-risk sites at regular periods rather than the
true prevalence in the population, the data cannot be extrapolated to the entire population. The results will allow authorities to identify areas where they should strengthen actions, make decisions to improve the implementation of PC, strengthen interventions to improve access to and the quality of water, sanitation, and hygiene, and correlate their data with deworming coverage, among other actions.

When taking samples (three slides of the same sample for Kato-Katz), the following should be taken into account (43, 62):

- **Number of samples**: 50–100 boys and girls (ages 5–14) per school.
- The schools should be in at-risk communities, according to the criteria described in section 4.2.1.
- **Target population smaller than 2 million**: one or two schools per 200,000 people.
- **Target population larger than 2 million**: one school per 500,000 people.
- Schools in areas with higher prevalences should be chosen for regular monitoring, but randomly selected schools should also be included to avoid bias. It is recommended to select 50% of the schools randomly and the other 50% by convenience. For example, schools that have very good deworming coverage as well as those with low coverage should be selected in order to determine whether their coverages are reflected in the recorded prevalence and infection intensity results.
  
  It is recommended that 50% of the schools selected for surveillance stay the same over the years, while the other 50% rotate and change using random selection. This will prevent the bias that occurs when taking samples from the same sentinel schools.
- **Note**: This survey is suggested in children aged 5–14, since they usually show a higher prevalence and infection intensity. However, if a higher prevalence has been detected in adults, or primarily in adults, surveillance should be carried out in villages or communities rather than schools.

The survey should be conducted at least nine months after the last intervention to allow time to evaluate any new infections after treatment, since the prepatent period (the period in which the eggs are not yet detected) is 3–4 months.

### 4.3.5. Impact assessment

To assess the impact of a program and for the final evaluation, it is necessary to carry out prevalence surveys in the population. These surveys should use the same methodology as the baseline survey, with a statistical design and random probabilistic sampling that is representative of the population, in order to determine the true prevalence.

It is recommended to conduct impact surveys every five years in the areas where PC has been implemented. However, if the country has an intermittent program and sentinel surveillance shows that the parasitological indicators have not changed, the impact survey could be delayed since it is expensive and complex.

Impact surveys should be conducted at least nine months after the last intervention to allow time for reinfection, as described for sentinel site surveillance.

**Target population**: mainly school-age boys and girls (ages 5–14), since this group generally has the highest prevalence and infection intensity. When there is evidence of fascioliasis in adults, the survey should also be implemented in that group.
4.3.6. Post-treatment surveillance

When an annual preventive chemotherapy program is implemented and the impact survey identifies a prevalence of less than 5% without high-intensity infections, it is suggested to perform another round of PC after two years. If, at the next evaluation (at least nine months after PC), prevalence remains below 5%, with no high-intensity infections, then fascioliasis can be considered eliminated as a public health problem and treatment should be done case by case (Figure 4). At that time, post-elimination surveillance would begin.

If, at any time, prevalence is greater than 5% or there are high-intensity infections, then the annual program should be restarted until a new impact survey is carried out after five years.

4.3.7. Notification

In endemic countries, it is important that fascioliasis is included in national public health and veterinary public health plans (in areas where human fascioliasis is endemic) and that the necessary technical and financial resources are allocated.

In many Latin American and Caribbean countries, fascioliasis in people is not notifiable within the country (Annex 2). However, it is suggested that notification of confirmed cases be mandatory for countries with areas that are endemic for human fascioliasis.

Regarding the notification of human fascioliasis, in countries with endemic areas, monthly notification is suggested; and in countries with sporadic cases, notification is suggested within one month of a case detection.
5. Interventions in animals

While fasciolosis in animals is a problem in many countries and regions, it is only a problem in humans where there are ethnographic characteristics and socioeconomic determinants conducive to infection in humans.

Fasciolosis is an important economic problem for many producers at any scale. However, this section focuses on the management of fasciolosis from the perspective of a public health program, aimed at small producers engaged in family farming in rural communities, since they are the ones at risk of human fascioliasis. In this context, from a public health perspective, the objective is to reduce infection prevalence and intensity in order to reduce transmission, while keeping in mind the economic importance of animals for family producers.

5.1. Drugs available for the treatment of fasciolosis in veterinary medicine

There are currently no vaccines against fasciolosis. In veterinary medicine, seven main fasciolosis drugs are used, belonging to four main chemical groups: albendazole and triclabendazole (benzimidazoles); nitroxynil (halogenated phenol); closantel, oxyclozanide, and rafonxanide (salicylanilides); and clorsulon (sulfonamide), as shown in Table 2 (65).

The effectiveness of these drugs depends on the stage of the parasite. For example, albendazole, oxyclozanide, and clorsulon show high effectiveness against adult parasites, but have no action against larval forms. Only triclabendazole has activity against larval, juvenile, and adult forms.

Not all medicines are available in all countries (Annex 2) or registered for use in the different species. It is important to follow the manufacturers’ recommendations, especially regarding dosage and the withdrawal period.

5.1.1. Considerations on the use of drugs in veterinary medicine

- **Animal species:** Most drugs can be used in sheep and cattle, although their effectiveness may vary depending on the species, dose, and route used. Some are used off-label when there are no other options:
  - For dairy cows, products requiring short milk withdrawal periods are preferred. Some products are approved for use during lactation, such as albendazole, oxyclozanide, and clorsulon (depending on the registration in different countries). However, if possible, treatment should be administered during the “dry cow” period.
  - Triclabendazole at 12 mg/kg and closantel at 10 mg/kg have been used for horses (66, 67), and triclabendazole at 18 mg/kg and closantel at 20 mg/kg have been used for donkeys (68), although off-label.
For llamas and alpacas, albendazole is used at 10 mg/kg (with caution in young animals if high doses are used), clorsulon at 7 mg/kg (69), and closantel.

The effectiveness of albendazole, triclabendazole (15 mg/kg), and clorsulon has been demonstrated in goats (70, 71). The use of closantel has also been mentioned, although it is not registered for goats and would initially require higher doses than for sheep, since it is eliminated more quickly. Some products use different dosages and have different withdrawal periods for goats and sheep.

**Withdrawal period:** Also known as withdrawal time, this is the required waiting time from when a drug is administered to an animal until this animal or its products are suitable for human consumption. If it is not respected, drug residues may appear in products, such as meat, milk or its derivatives, such as cheese, from animals that have been medicated. It is important to respect the manufacturers’ recommendations and take these periods into account when choosing a medication. It should be noted that some medications such as triclabendazole have a withdrawal period in meat of more than 50 days and in milk of 40–90 days, depending on the different formulations.

### Table 2: Medications effective against *Fasciola hepatica* used in veterinary medicine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stage when effective against <em>Fasciola</em></th>
<th>Route</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albendazole (benzimidazole)</td>
<td><strong>Adults.</strong> From 12 weeks in sheep and from 12–16 weeks in cattle</td>
<td>Oral, intraruminal</td>
<td>- Higher doses than for nematodes (4.75–7.5 mg/kg for sheep and 10 mg/kg for cattle).&lt;br&gt;- Milk withdrawal period: 60 hours. One of the products of choice for dairy cows.&lt;br&gt;- Used in alpacas and llamas, with caution when using high doses in young animals.&lt;br&gt;- Use in goats is mentioned.</td>
</tr>
<tr>
<td>Triclabendazole (benzimidazole)</td>
<td><strong>All.</strong> From 2 days in sheep and from 2 weeks in cattle</td>
<td>Oral, topical</td>
<td>- More ineffective topically than orally for young stages.&lt;br&gt;- Withdrawal period for meat &gt;50 days, in milk 40–90 days.&lt;br&gt;- Use in goats is mentioned. Also off-label use in horses and donkeys.</td>
</tr>
<tr>
<td>Nitroxynil (halogenated phenol)</td>
<td>After 8–10 weeks</td>
<td>Injectable</td>
<td></td>
</tr>
<tr>
<td>Closantel (salicylanilide)</td>
<td>After 7–8 weeks</td>
<td>Oral, injectable, topical</td>
<td>- Can be used in alpacas.&lt;br&gt;- Use in goats is mentioned. Also off-label use in horses and donkeys.</td>
</tr>
<tr>
<td>Oxyclozanide (salicylanilide)</td>
<td><strong>Adults.</strong> From 12 weeks in sheep. Less effective in cattle</td>
<td>Oral</td>
<td>- Withdrawal period for meat, 14 days; in milk, 72 hours.&lt;br&gt;- One of the products of choice for dairy cows.</td>
</tr>
<tr>
<td>Rafoxanide (salicylanilide)</td>
<td>Late juveniles (6–8 weeks) in sheep, not very effective in cattle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clorsulon (sulfonamide)</td>
<td><strong>Adults.</strong> From 12 weeks, or late juveniles (6–8 weeks) with higher doses</td>
<td>Oral, injectable</td>
<td>- Ineffective subcutaneously at 2 mg/kg, but effective at 4–16 mg/kg.&lt;br&gt;- Use in goats is mentioned.</td>
</tr>
</tbody>
</table>

**Note:** Drugs from the same chemical group are shown in the same color in this box.
- **Product combinations:**
  - Combinations to extend effectiveness against *Fasciola*: Some combinations of products are effective against more parasite stages than when used alone. For example, the combination of nitroxynil and clorsulon in cattle is effective against parasites more than 2 weeks old (72, 73). However, the combination of products is recommended only when necessary to avoid promotion of multidrug resistance.
  - Combinations to broaden the spectrum of activity: Commercial combinations to simultaneously treat other parasites exist, for example closantel and ivermectin, or levamisole and triclabendazole. The time to apply the treatment will depend on each active ingredient and the seasonality of each target parasite. It is recommended to always choose a narrow-spectrum product rather than a combination for *Fasciola* control, unless there is a need to include other parasites. Unnecessary use of combinations accelerates the development of resistance. **Product combinations should be used only when necessary.**

- **Resistance:** Reports of resistance to triclabendazole (Box 3) and other drugs used for the control of fasciolosis are increasing, causing great concern (74). It is the responsibility of all stakeholders to help minimize increases in resistance:
  - Repeated treatment with the same active substance for prolonged periods could lead to the selection of resistance genes. Therefore, the use of drugs with different mechanisms of action, administered in rotation or in combined formulations, should be considered.

**BOX 3  Use of triclabendazole for animal treatment**

- The use of triclabendazole in animals should be avoided if possible and other options should be promoted (especially for mass treatments).
- One-time treatments have minimal risk and quality products should always be used, and used appropriately.

- Resistance to triclabendazole is documented, although the prevalence of resistance is unknown. This resistance is extremely important, as triclabendazole is the medication of choice for treatment in humans. It was first described in sheep in Australia, although it presumably arose independently in other regions.
- It is good practice to monitor treatment efficacy with a fecal egg count reduction test (or using a coproantigen, if available). This will almost certainly not be feasible for small producers. However, it may be possible for extension agents or other organizations, associations, or authorities to do this on a regular basis to ensure effectiveness and monitor resistance in the area. It is always important not to confuse reinfections with treatment failure or resistance.
- The responsible and prudent use of antiparasitics is recommended to help manage resistance. To achieve this, joint efforts are required from all stakeholders regarding product authorization, production, control, importation, exportation, distribution, and use. This includes the competent authorities, the pharmaceutical industry, distributors and sellers, veterinarians, and producers. For more details on practical methods to control parasites and reduce selection due to resistance, as well as the responsibilities
of the various stakeholders, it is recommended to read the World Organisation for Animal Health report on the responsible and prudent use of antiparasitics to help control resistance in grazing livestock species [Figure 5].


- **Pharmacovigilance:** It is recommended to always use registered products of adequate quality, whether well-known brands or generic products:

  Regarding pharmacovigilance, it is very important for the competent authority responsible for veterinary drug registration to establish and implement an efficient regulatory framework for the registration of antiparasitics, and for the monitoring of safe and effective use of these products when they become available on the market.

  - Pharmacovigilance should be included in national regulations and its implementation should be effective. Pharmacovigilance and dialogue between authorities and pharmaceutical companies should be promoted.
  
  - It is important to emphasize the importance of the problem with regulatory authorities and industry unions, so that they fulfill their respective roles in the use of quality products and implement other measures to reduce parasite resistance.
  
  - It would be beneficial to have an American network of regulatory agencies that would cooperate and exchange information about antiparasitic products and resistance.

- **Information for producers and veterinarians:** In some countries, information brochures have been developed for producers, explaining the fasciolosis medications available in the country, the doses that should be used for the species they are approved for, and the withdrawal periods. An example is the table produced in the United Kingdom for the different commercial products available for cattle [75]. This type of information, developed by associations of producers, associations of veterinary professionals, extension agencies, competent authorities, or combinations of these groups, is very useful for informing veterinary professionals and local producers and is a recommended practice.
5.2. Strategies for the treatment of animal fasciolosis

Treatment can be curative or strategic and preventive. Strategic and preventive treatment is preferable, and therefore is the focus of this section.

5.2.1. Curative treatment

Curative treatment is essential when there are clinical symptoms. In acute cases, medications that are effective against immature stages should be used.

5.2.2. Strategic and preventive treatment

Eradication or elimination of the parasite is not a practical or feasible option. Control measures aim to reduce the number of parasites in hosts and pastures using the minimum number of treatments per year, in order to reduce the risk of developing resistance, prevalence, disease, and economic losses.

There is no universal strategy for the treatment of fasciolosis. The treatment strategy should be based on local epidemiology to determine the time of year when the maximum effect can be obtained with the minimum number of treatments (Box 4). The timing of treatment depends on the region's climate characteristics (temperatures, rainfall, etc.) and local transmission patterns. The transmission of fasciolosis can be ongoing throughout the year, monoseasonal, or biseasonal.

In addition, the following should be considered: type of animal management in the area, available medications, species that need treatment, and socioeconomic conditions of the producers, in this case mainly small producers dedicated to family farming.

It is essential that each area of interest produce its own treatment schedule for fasciolosis based on local epidemiology, species present in the area, available medications, and producers' socioeconomic conditions.

Relevant authorities, producer associations, and veterinary professionals should work together to develop and promote these schedules.

In addition to sheep and cattle, other species such as goats, pigs, donkeys, and camelids play an epidemiological role. Not all species have the same relevance from the point of view of Fasciola transmission. Sheep and cattle play a primary role (76), followed by pigs and donkeys (77, 78). Horses are less relevant in terms of transmission, while camelids hardly participate in transmission due to their peculiar defecation habits (79). Regardless of their role in the parasite's transmission, it is important to consider all the species for the prevention of clinical cases in animals, since animals play a very important role in family farming and some species such as alpacas are very susceptible to fasciolosis. The epidemiological role may also vary, depending on grazing characteristics; for example, whether or not goats are browsing. When browsing, goats have less exposure to parasites in general, but if they cannot browse and they graze with sheep, they will have the same parasites.

Sheep are at risk of acute fasciolosis, so a medication effective against the immature stages may be necessary around eight weeks after the peak snail season. Acute fasciolosis is less common in cattle than in sheep, so they require fewer curative treatments. Treatment in cattle can be targeted at eliminating mature parasites to control chronic disease and reduce pasture contamination (80).
Each affected locality (especially where fascioliasis prevalence has been described above 5% in people) should develop – in coordination with the Ministry of Agriculture (or equivalent) at the national and subnational levels, veterinary professionals, and producers in the area – a strategic plan to control fasciolosis (treatment schedule), considering the epidemiology and transmission factors in the area:

- Climate conditions and temperatures.
- Delimitation of temporary and permanent biotypes.
- Presence, distribution, and ecology of host snails and their infection status.
- Local risk factors such as the presence of irrigation and management strategies.
- Species of animals to treat (either due to their role in the transmission of Fasciola or to prevent disease cases).
- Available medications and their characteristics.
- Responsible and prudent use of antiparasitics.
- Management of pastures, including community pastures.
- Incentives for producers.

The schedule should be part of a **comprehensive management** of the problem, promoting other interventions described in these operational guidelines.

Management and treatment schedules have proved to be extremely useful, as they provide guidelines for veterinarians, extension agents, and local producers. They have been developed for commercial producers in specific areas of different countries, such as Australia (72, 73).

### 5.3. **Pasture management and other management measures**

Fasciolosis control should include pasture management and other management strategies that help reduce and prevent transmission. It is useful to map grazing areas and livestock movements over time to identify the high-risk areas (areas with the presence of host snails or ecosystems favorable for their establishment), since this helps to better understand the local fasciolosis epidemiology and the control options.

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5.3.1. Management of pastures and water sources

The different management options for pastures (Box 5) and water sources include:

- **Fencing and protection of high-risk areas:** to prevent animals from entering contaminated pastures, specifically those with lentic waters (closed bodies of water). These include muddy areas around streams and canals and temporary or permanent ponds during critical seasons. During drought years, both snails and livestock concentrate in these areas, so the risk of infection can be very high. This measure not only prevents animals from becoming infected, but also prevents animals from contaminating water sources:
  - Fencing of high-risk areas is especially indicated for the most susceptible animals: sheep, llamas, alpacas, goats, and calves.
  - If an alternative water supply for animal drinking and washing is not available, natural lotic water sources (in which the movement of water is predominantly in one direction, such as rivers and streams), preferably those with little human use, should be used.

- **Drainage of wet areas:** See the section on environmental management.

- **Prevention or repair of leaks from pipes and drinking troughs:** since water leaks can create an ideal habitat for snails.

- **Construction of drinking troughs:** If drinking troughs are built, they should be clean, firm, and without vegetation around them. They should be maintained and periodically checked to ensure that they are not colonized with intermediate hosts. For example, in Cuba, if they are built in cement at ground level, they are quickly colonized by *G. cubensis*.

- **Avoid co-grazing:** especially the most susceptible species. For example, co-grazing of sheep with cattle should be avoided if possible, as sheep are more susceptible. Caution should also be taken with pasture rotations between different species. In practice, this can be difficult for producers in family farming systems.

- **Rotational grazing and low-risk grazing:** Pastures can be rotated to avoid the highest risk areas at key times and strategic grazing schemes can be developed that reduce the infectivity of an area. The feasibility of this measure depends on the pastures that are available.

- **Hay and silage:** Despite the inconsistency of the data [81], it is recommended to use good hay or silage, since in some cases this has helped to reduce metacercariae and since fresh pasture is more likely to be a source of infection.

**BOX 5** Pasture and animal management measures in family farming

- In the context of small producers and family farming, implementation of the aforementioned management measures may be impractical, too costly, or simply unfeasible.

- Even when the measures that can be taken are imperfect, reducing the risk of infection is always useful. It is important that veterinary professionals and outreach personnel work with family farmers to identify the most serious problems, reduce risk areas, and implement management measures appropriate to the local situation and considering existing limitations.

- In communities where communal grazing is practiced, these measures should be discussed with the entire community.
5.3.2. Movement of animals

Animals can help spread fasciolosis (due to dispersion of both the parasites and the intermediate hosts) if they infect water sources and pastures when they move to other areas. This can be minimized with proper animal treatment, quarantines, and pasture management. It has been described that animals such as horses and mules could play a mechanical role, for example, by transporting snails in mud stuck to their hooves (77; 82).

5.4. Policies of the Ministry of Agriculture (or its equivalent)

In many Latin American and Caribbean countries, fascioliasis in animals is not notifiable within the country (Annex 2).

It is important for the Ministry of Agriculture (or its equivalent) to support the different subnational levels (states, provinces, districts), especially where fascioliasis is a problem in humans, in the implementation of fasciolosis control measures, especially for small family farmers.

The responsible authorities should:

- Provide an appropriate legislative framework to:
  - Register and authorize adequate, quality anti-fasciolosis products.
  - Conduct efficient pharmacovigilance.
  - Support the implementation of fasciolosis control in the field.
  - Regulate slaughter of animals, whether in commercial slaughterhouses or at local slaughterers, if the latter are permitted.

- Provide technical support:
  - Develop and promote animal fasciolosis control strategies appropriate to the region and type of producers (small family producer in areas with high risk of fascioliasis in people), producing appropriate treatment schedules (as described in section 5.2) and promoting comprehensive management measures.

- Demonstrate the benefits of fasciolosis control, especially the economic benefits.

- Provide resources, if possible (such as medicines, logistics, etc.), to family farmers in fascioliasis areas. These resources can be integrated into other existing programs, such as vaccination campaigns for other diseases.
People acquire fascioliasis by ingesting metacercariae present in food and water. Sources of infection may vary depending on local conditions. A good description of the different sources of infection is found in the review by Mas-Coma and collaborators (83). The different sources of infection include:

- Wild or cultivated aquatic plants.
- Terrestrial plants that need frequent irrigation.
- Contaminated water.
- Terrestrial plants and vegetables that have been immersed in contaminated water for washing.
- Contaminated plant-based foods or vegetables.
- Raw liver infected with juvenile parasites.
- Drinks or juices prepared with contaminated water.
- Meals prepared with contaminated water.
- Utensils washed using contaminated water.

### 6.1. Food safety and control measures for plants and vegetables

Control measures are diverse, depending on the source of infection. The following control measures are generally applicable to plants and vegetables:

- Avoid consumption of aquatic plants, wild or cultivated in risk areas.
- When growing vegetables, use water free of human and animal fecal contamination.
- Properly handle plants and vegetables after picking or harvesting them so that they do not become contaminated (for example, do not use contaminated water to wash plants and vegetables).
- If possible, cook vegetables at 60 °C. The use of chemicals is not recommended, as many help release the metacercariae, but do not kill them. Refrigeration and freezing are not efficient control methods (83).
- Avoid the use of raw plants and vegetables in food preparation.
6.2. Food safety and control measures for water

People can be infected by drinking or using water with metacercariae that have been detached from plants. This includes drinking water, water used to prepare juices or meals, and water used to wash kitchen utensils.

To prevent infection through water, the following is recommended:

- Use safe water. More information on access to safe water, sanitation, and hygiene (WASH) services can be found in section 7.
- Avoid using water collected from sources located in areas with snail hosts.
- Boil suspicious (unsafe) water that will be used for drinks, juices, meals, or washing kitchen utensils.

Also consider filtering any suspicious water. Filters should prevent the passage of *F. hepatica* metacercariae (which have an approximate diameter of 180–206 μm). Chlorinating water is not sufficient.

6.3. Food safety and control measures for animal products

Livers infected with fasciolosis should be discarded as they are not suitable for human consumption: the young parasite stages could infect people if the livers are consumed raw or undercooked.

This measure should be implemented in both commercial slaughterhouses and at local slaughters. In commercial slaughterhouses with veterinary supervision, this should be a routine procedure for infected livers. This is more complicated in the case of local slaughters (whether in backyards or by local butchers), since there is no veterinary supervision. In the event that this type of slaughter is authorized in the country, the education of local slaughterers and butchers is important.

From a family and educational point of view, the message to be transmitted is to always cook the livers and ensure that they reach a temperature of at least 60 °C. In practical terms, livers should be cooked until they change color.

6.4. Implementation of food safety measures

As described in the previous sections, food safety measures involve many stakeholders and it is important for each stakeholder to play their role correctly.

For example, the respective authorities should facilitate the use of safe water, carry out inspections during the slaughter or butchering of animals, and facilitate the dissemination of health promotion and education messages, whether for schools, housewives, or the entire community. For more details on health promotion and education, see section 9.

To prevent human fascioliasis through food safety, it is important to understand the cultural idiosyncrasies and behaviors of affected communities, identifying the sources of infection, key prevention messages, and the best way to transmit these messages.

The objective should be to give practical guidance, adapted to the community.
7. Sanitation

Many of the pathogens that cause neglected infectious diseases reproduce and transmit when there is inadequate water and sanitation. Access to WASH services is essential to prevent, treat, and care for many of these diseases, including fascioliasis. WASH intervention activities are useful not only to help eliminate fascioliasis as a public health problem, but also to control or eliminate other neglected infectious diseases.

Since the first global WASH strategy to combat neglected infectious diseases was published in 2015, collaboration between both sectors has strengthened. The new WHO road map for neglected tropical diseases 2021–2030 (2) recognizes the need to take intersectoral measures. More specifically, the cross-cutting goal related to WASH is to achieve universal access “to at least basic water supply, sanitation, and hygiene services in areas where neglected tropical diseases are endemic: to achieve targets 6.1 and 6.2 of Sustainable Development Goal 6.” The road map calls for cooperation between the WASH and neglected tropical diseases sectors beyond their usual boundaries, including working jointly with the veterinary public health sector as part of the One Health approach. Complementing this road map, WHO has published the global strategy on water, sanitation, and hygiene to combat neglected diseases, which includes details on the role of WASH in the prevention and care of neglected infectious diseases (84) (Figure 6).

WHO has also produced a practical guide for collaboration between the WASH sector and the health sector. This guide provides tools to support such collaboration, based on the creation of partnerships, mobilization of resources, and design, implementation, and evaluation of interventions (85, 86).

Sanitation measures that address fascioliasis have two main objectives:

- Prevent the contamination of water sources and plants by infected people (prevention of contamination by animals is included in section 8).
- Promote the use of safe water.
7.1. Sanitation

Sanitation is important not only for the elimination of fascioliasis as a public health problem, but also for many other infectious agents. Improved sanitation should always be an objective, although it requires investment and time.

To interrupt or minimize the parasite transmission cycle, it is essential to prevent people from contaminating water sources. It is important to have adequate latrines or bathrooms that are used by all family members. This may be difficult in grazing or crop areas far from the households. Open defecation should be avoided, especially near areas where water and snails are found, so as not to perpetuate the transmission cycle.

Sewage should not be used for irrigation nor should it be dumped into natural water sources such as streams.

7.2. Safe water

As described in the section on food safety, people can be infected with fascioliasis by drinking water with metacercariae, or when eating and washing food or cleaning kitchen utensils.

Access to and use of safe water should be facilitated and promoted, especially for drinking, food washing and preparation, handwashing, and cleaning kitchen utensils.

The construction of flowing artesian wells, which promote the spread of snail habitats, should not be promoted.

It is recommended to work from the beginning with national and local authorities and institutions to develop an action plan and interventions that improve the coverage of health infrastructure and the availability of safe water.
8. Environment

To control the *F. hepatica* transmission cycle, there are two important issues related to the environment: controlling intermediate host snails, and preventing contamination of water sources by animal feces. Prevention of contamination of water sources by human feces was discussed in the section on sanitation (section 7).

8.1. Snail control

In the *F. hepatica* transmission cycle, freshwater snails of the Lymnaeidae family act as intermediate hosts. Not all snails in the Lymnaeidae family transmit *F. hepatica*. One of the main hosts is the species *G. truncatula*, which is mud-colored and 3–5 mm in size, with a pointed spiral tip (Figure 7). However, there are many other species in the Americas, such as *G. cubensis/viator*, *G. cousini*, and *P. columella*, that can act as intermediate hosts (7).

Snails of the genus *Galba* thrive in humid areas and prefer moderate temperatures, between 5 °C and 25 °C. Their preferred habitats are shallow water, waterlogged areas, mudflats, dikes, ditches, banks of ponds or slow-moving streams, spring puddles, and reeds. Additionally, livestock wells and drinking troughs can provide suitable habitats. Heavy rains can wash away snails to establish new colonies. They can also be carried by birds and other animals.

Usually, snails hibernate during the winter and emerge in the spring when the temperature reaches 10 °C. A very dry period makes them inactive and they survive deep in the mud until it rains again. Very cold weather during winter reduces the snail population, and prolonged below-freezing temperatures kill most snails. However, both climate change and changes in the anthropogenic habitat influence the dispersal of lymnaeid snails, contributing both to the expansion of areas with endemicity and to the appearance of new transmission foci (87, 88).

Elimination of snails of the Lymnaeidae family is extremely difficult, as snails of the genus *Galba* are hermaphrodites and several, including *P. columella* and many of the *Galba* species, self-fertilize. Thus, a single specimen (both from the remnant of an existing population or the arrival of a new colonizing specimen) can establish and have descendants in an area, which will soon see an increase in its population density of vector snails. However, the control of host snail populations is an essential component to achieving sustainability in the control of fasciolosis transmission.

There are three main ways to control snails: through biological control, chemical control, and habitat management. However, they have limitations, are not very effective, or are difficult to implement, as described later (7).

- **Biological control:** Snails have natural predators, such as certain species of ducks, starlings, and thrushes. It has been suggested that domestic ducks and geese could help control snails, but they can also help their spread. Other measures that have been suggested for biological control for snails of the genus *Galba* include the larvae of certain ground beetles, the larvae of marsh flies, and snails of the genus *Zonitoides* (e.g., *Zonitoides nitidus*), a type of carnivorous snail that feeds on other snails. Biological control of *G. cubensis* using competing snails, such as the planorbid *Helisoma duryi* and the thiariid *Tarebia granifera*, has been studied in Cuba with good results (89). Firefly larvae...
Lampyris noctiluca) are also known for their malacophagy. However, none of these methods are used frequently or extensively, since they can produce a natural imbalance and require ecological studies that support their implementation and evaluation.

- **Chemical control:** Molluscicides such as niclosamide were used in the past to kill snails. However, chemicals also affect other organisms and the ecology of the area and can have detrimental effects on wildlife. When molluscicides are applied to waterways, the effects are transmitted downstream. Success with these measures has been limited. Currently, in many countries, there are no products authorized to kill snails.

- **Control through management of the snail habitat:**
  - Drainage: draining wet, waterlogged areas can help make fields less conducive to snails. This option is becoming less popular or may not even be allowed in certain habitats within conservation programs. It is also an expensive option in the short term.
  - Fencing: another option is fencing, especially of wet, swampy, and muddy areas, often with many reeds [ideal for snails], to prevent access by livestock to infected fields at critical times of the year. In some cases, this option may not be viable for small producers.
  - Reduction of favorable habitats: drastic transformations of the ecosystem, particularly when associated with human activity, can lead to the creation of new habitats or more favorable environmental conditions, which can favor the establishment of host snails in new areas or can make them more abundant, leading to an increased risk of transmission [90, 91]. When feasible, the separation of livestock areas from agricultural areas should be encouraged, the creation of artificial bodies of freshwater should be avoided, and the presence of host snails should be monitored in bodies of water such as artificial lagoons, dams, and irrigation canals.

Communities, small producers, and family farmers can take steps to **reduce the habitat suitable for snails.** Apart from draining risk areas if feasible, the following can be done: clean irrigation ditches and canals, prevent water leaks and mudflats, and keep drinking troughs and surrounding areas clean. Options should be evaluated at the local level.

### 8.2. Other important aspects of mollusk control

#### 8.2.1. Identification of host snails in the field

This is an essential part of establishing risk areas, understanding the ecology of transmission, and planning control strategies. The differentiation of species from a morphological point of view can be very complex in the Lymnaeidae family, particularly among the cryptic species of the genus Galba in the Americas [9]. However, the creation of dichotomous keys adapted to the different species characteristic of different areas could help to discern important host snails such as P. columella and G. cousini from the other host species, using few resources. As an example, there is a dichotomous key for Cuba [92]. A microsatellite-based multiplex polymerase chain reaction (PCR) has been developed and validated with field samples to confirm G. cousini and to differentiate G. truncatula, G. schirazensis, and G. cubensis/viator without the need for gene sequencing. This simplifies and economizes the diagnosis in terms of time, resources, and data analysis [93].
8.2.2. Identification of active transmission foci based on the detection of infected snail hosts in the field

Conventional parasitological methods such as the dissection of snails in the prepatent stage or the emission of cercariae can only be performed by specialized personnel, are laborious, and tend to have low sensitivity (94). An ELISA test, which is more sensitive than conventional parasitological methods, was developed in Cuba to detect F. hepatica in infected snails (95). It has been used to monitor risk areas to detect active transmission foci. PCR-based detection of F. hepatica DNA in snails has higher sensitivity than all the methods previously mentioned (94). Several methods have been developed and applied to samples of snails obtained in the field from different host species in the Americas (96–99).

The host snail is a key link in parasite transmission and in the effectiveness and sustainability of short- and long-term control strategies. Therefore, the following should be encouraged: initiatives to promote and strengthen medical malacology in the Region; basic and applied studies that include snail biology, genetics, and ecology, and interactions with the parasite and environmental factors; development of practical and innovative ways to monitor and control snails; resources to support malacological studies and initiatives; training of parasitological, veterinary, and epidemiological professionals in basic aspects of medical malacology related to limneid mollusks; and raising awareness among health and community actors about the role of snail hosts in transmission and the need to get involved in their control.

8.3. Preventing contamination of water sources by animals

To interrupt or minimize the parasite transmission cycle, it is essential to prevent the contamination of water sources by animals. To achieve this, the following can be done:

- Fencing water sources to prevent animals from contaminating water sources and their surroundings. However, in many cases, streams are the water sources for animals, so it is necessary to provide an alternative water supply (drinking troughs and drinking water), which is not always possible.
- Preventing the accumulation of animal excreta where water sources could become contaminated.
Community participation and social mobilization are essential for the success of a program to eliminate fascioliasis as a public health problem. It is important to include the communities, their leaders, and women, when analyzing the problem, planning solutions, implementing actions, monitoring, and evaluating (Box 6).

Health training, promotion, and education are fundamental when attempting to engage different sectors and achieve sustainable behavior change. Health training and education should reach and involve the different parties involved:

**BOX 6**

**How to improve the effectiveness of key messages to stimulate a change in behavior**

- **Identify** specific key messages for the different target groups.
- **Adapt** key messages to the audience.
- **Communication experts** should be available to advise on how to transmit the messages. For example, they should advise teachers on how to transmit messages to children, or with adult education specialists on how to achieve better socialization and acceptance by the community.

- **Communities affected by fascioliasis:** Messages to communities should use simple language and local language and names. Some considerations (Box 7) are:
  - Work should be done with teachers from schools in the affected areas, and messages should be included in the school curriculum.
  - Booklets or posters adapted to local situations can be used.
  - Radio messages, popular theater, and modern technologies can be considered, as long as they are applicable in the specific contexts of the affected communities.
  - Key messages should include the transmission cycle, food safety measures applicable in the community (see food safety details in section 6), sanitation and safe water measures, and other control measures described in these operational guidelines that can be implemented in the community.
BOX 7 Some practical messages to disseminate in the community

- Use safe water for drinking or preparing juices, washing and preparing food, washing hands, and washing kitchen utensils. When in doubt, boil water before using it.
- Avoid eating aquatic plants, whether domestic or wild. If consumed, wash them with safe water and cook them well.
- Avoid putting herbs with short stems and other wild plants in the mouth, if they were obtained in risk areas (streams, creeks, irrigation canals, etc.).
- Liver from local animals should be cooked well.
- Always use latrines or bathrooms. If they are not available, never defecate near streams or water sources.

Family producers and farmers (Box 8):

- It is important that small producers who have animals understand the advantages of prevention, strategic treatment in animals, and management measures that help prevent and control the transmission cycle.
- It is important to demonstrate the benefits to producers, especially the economic benefits.
- Outreach workers and agricultural technicians play a fundamental role in advising producers regarding the treatment schedule (products, species, doses, times) and management measures that help control fasciolosis.
- As part of management measures, producers should receive help in identifying areas at risk and should be supported in the actions they take to reduce risk.
- It is important for farmers to understand how to prevent the contamination of crops; for example, by not using water contaminated by humans or animals or by using safe water to wash their products.
- Livestock associations, producer associations, cooperatives, and other local organizations can play a critical role in disseminating information.

BOX 8 Some practical messages for family farmers and producers

- Stay up to date with the animal treatment schedule (medications, doses, species, and times), as recommended by technical staff.
- Identify risk areas within your environments.
- Implement the management measures recommended by technical staff, for example:
  - Avoid grazing the most susceptible species in high-risk areas.
  - If possible, prevent animals from defecating near streams or stagnant waters.
  - Provide drinking troughs.
  - Prevent water leaks around drinking troughs and pipes.
  - Drain swampy areas suitable for snails.
  - Clean irrigation ditches and canals.
  - Do not use sewage for irrigation.
Professional training:

- Health personnel should strengthen their knowledge about clinical symptoms, differential diagnosis, and treatment. Health personnel (including community agents) should be informed about possible local sources of infection.

- Local veterinary professionals, agronomists, extension agents, and agricultural technicians should have the necessary updated information to be able to advise small producers appropriately. For example, they should be up to date on the appropriate treatment schedule for the area.

- Professionals should also be trained in how best to transfer this knowledge to local populations; for example, using local names and considering the characteristics and limitations of the community.

9.1. Regional exchange

In the Americas, some countries have produced promotional materials for fascioliasis control. Countries are encouraged to exchange materials and ideas and to share what they learn.

Examples of materials:


Annex 1. Methodology used to prepare these operational guidelines, and participants in the different meetings

The methodology used to prepare these operational guidelines, in chronological order, was as follows:

1. In April 2022, a bibliographic review on fascioliasis in Latin America and the Caribbean was carried out, focusing on its distribution and epidemiology since 2010. A summary of this review is in section 2.1 of this document.

2. In September 2022, two virtual meetings were held with the national and provincial managers of the fascioliasis programs and epidemiological professionals from the Plurinational State of Bolivia and Peru, to review the data collected during the bibliographical review, obtain additional information, and better understand their situation and needs. The list of participants is in sections 9.2 and 9.3 below.

3. In February 2023, an online questionnaire on the status of fascioliasis control programs in the Americas was conducted. This questionnaire was sent for completion to the national managers of fascioliasis programs, both in the health and animal health sectors, to the 10 countries that report human cases of the disease (Argentina, Plurinational State of Bolivia, Brazil, Chile, Cuba, Ecuador, Mexico, Peru, Uruguay, and Bolivarian Republic of Venezuela). There were 15 responses. A graphic summary of some of the key results is included in Annex 2.

4. In May 2023, a virtual meeting was organized with experts from the Region and the WHO Collaborating Center on Fascioliasis to define the theoretical framework and principles for these operational guidelines. The list of participants is in point c below. The meeting followed a guided discussion format, which incorporated the information obtained in the previous steps.

5. At the end of June 2023, a virtual meeting was held with experts from the Plurinational State of Bolivia and Peru to obtain feedback on the guidance suggested by the experts. This meeting was held over two days in sessions of two hours per day. The list of participants is in section 9.4 below.

6. The draft operational guidelines were prepared, based on the guidance proposed by the experts and feedback from countries.

7. During July and August 2023, the draft guidelines were shared with experts for review. Their comments were incorporated and this final version was produced.

Participants in the meeting with the Plurinational State of Bolivia, September 2022

Delegates from the Ministry of Health, the Departmental Service (La Paz Headquarters), the National Service of Agricultural Health and Food Safety, and the Vice Ministry of Rural Development and Lands: Fernando Abad Lanza Amuzquibar, Alvaro Argandoña, Freddy Armijo, Marcelo Melean Callisaya Quispe, Erasmo Cordero López, Kelly Natalia Laura Cuellar, Maya Espinoza, Lilian Flores Sermiños, Daniel Gareca Vaca, Liliana Justianiano, Ramiro Omar Mamani, Alcides Medina Pacheco, Miguel Ángel Quispe Gonza, Grover Paredes, Marín Ruiz Daza.

PAHO delegates: Meritxell Donadeu, Percy Halkyer, Ana Luciáñez, Baldomero Molina Flores, Marco Antonio Natal Vigilato, Maria Nazario, Rubén Santiago Nicholls, Alfonso Tenorio.
Participants in the meeting with Peru, September 2022


PAHO delegates: Meritxell Donadeu, Ana Luciáñez, Baldomero Molina Flores, Marco Antonio Natal Vigilato, María Nazario, Rubén Santiago Nicholls, Hans Salas, María Ester Salazar.

Participants in the expert meeting, May 2023

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guest experts</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annia Alba Menéndez</td>
<td>Department of Parasitology, Research, Diagnostic and Reference Center. Pedro Kouri Institute of Tropical Medicine</td>
<td>Cuba</td>
</tr>
<tr>
<td>René Angles Riveros</td>
<td>Faculty of Medicine, Universidad Mayor de San Andrés, La Paz</td>
<td>Plurinational State of Bolivia</td>
</tr>
<tr>
<td>Rolando Ayaqui Flores</td>
<td>Faculty of Medicine, National University of San Agustín, Arequipa</td>
<td>Peru</td>
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<tr>
<td>María Dolores Bargues</td>
<td>Department of Parasitology, Faculty of Pharmacy, University of Valencia</td>
<td>Spain</td>
</tr>
<tr>
<td>Miguel M. Cabada</td>
<td>Institute of Tropical Medicine, Universidad Peruana Cayetano, Heredia, and Infectious Diseases Division, University of Texas</td>
<td>Peru and United States of America</td>
</tr>
<tr>
<td>Omar dos Santos Carvalho</td>
<td>Rene Rachou Institute, Oswaldo Cruz Foundation</td>
<td>Brazil</td>
</tr>
<tr>
<td>Santiago Mas Coma</td>
<td>WHO Collaborating Center on Fascioliasis and its Snail Vectors</td>
<td>Spain</td>
</tr>
<tr>
<td>Marcelo Molento</td>
<td>Department of Veterinary Medicine, Federal University of Paraná</td>
<td>Brazil</td>
</tr>
<tr>
<td>Iván Darío Vélez Bernal</td>
<td>Program for the Study and Control of Tropical Diseases, University of Antioquia</td>
<td>Colombia</td>
</tr>
<tr>
<td><strong>PAHO/WHO organizers</strong></td>
<td></td>
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<tr>
<td>Albis Gabrielli</td>
<td>WHO</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Ana Luciáñez</td>
<td>PAHO</td>
<td>United States of America</td>
</tr>
<tr>
<td>Baldomero Molina Flores</td>
<td>PANAFTOSA</td>
<td>Brazil</td>
</tr>
<tr>
<td>Santiago Nicholls</td>
<td>PAHO</td>
<td>United States of America</td>
</tr>
<tr>
<td>Meritxell Donadeu</td>
<td>PAHO Consultant</td>
<td>Australia</td>
</tr>
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</table>

Participants in the meeting with representatives from the Plurinational State of Bolivia and Peru, June 2023

Participants from the Plurinational State of Bolivia: Delegates from the Ministry of Health; Departmental Service (La Paz Headquarters); National Service of Agricultural Health and Food Safety; and Vice Ministry of Rural Development and Lands: Dina Condori, Erasmo Cordero, Carla Espinoza, Miguel Angel Estrada, Daniel Gareca, Alfredo Laime, Fernando Lanza, Blas Mamani, Pedro Medina, Óscar Mendoza, Grover Paredes, Elizardo Peralta, Lily Susana.

Participants from Peru: Delegates from the Peruvian Ministry of Health (national level) and from departments with endemicity; and delegates from the Ministry of Health’s Health Strategy on Zoonoses, and the Directorate of Animal Health: Isidro Antitupa Janampa, Román Bances Santa María, Rubén Bascope Quispe, José Luis Bustamante Navarro, Eric Callapiña Enriquez, Cesar Augusto Canales Santillán, Olimpia Chuqista Alcarraz, Dante de la Vega Cavero, Luis Arturo Estares Porras, Ulbaldo Flores Barrueta, Ángel Gómez Marín, Yonny Gonzales Almonacid, Hector Guevara Pineda, Luis Miguel Huaman Ticona, Naum Huicho Yanasupu, Marco Marino Mercado Apaza, Rodolfo Miranda Obando, William Quispe Paredes, Jesús Rodríguez Chávez, Raymundo Rojas Neyra, Robinson Rojas Rivera, Brizeida Valdez Castillo, Nury Vargas Mayuri, Nathaly Velarde Warthon.

PAHO delegates: Patricia Chávez, Meritxell Donadeu, Percy Halkyer, Ana Luciáñez, Baldomero Molina Flores, Rubén Santiago Nicholls, Maria Esther Salazar, Maria Jesús Sánchez.
Annex 2. Results of the questionnaire on fascioliasis control in the Americas

The following are the results for some of the key survey questions.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Argentina</th>
<th>Plurinational State of Bolivia</th>
<th>Brazil</th>
<th>Chile</th>
<th>Cuba</th>
<th>Ecuador</th>
<th>Mexico</th>
<th>Peru</th>
<th>Bolivarian Republic of Venezuela</th>
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<tbody>
<tr>
<td>Albendazole</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Triclabendazole</td>
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<td>X</td>
<td>X</td>
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<td>X</td>
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<td>Nitroxynil</td>
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<td>X</td>
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<td>Closantel</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Oxyclozanide</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Rafoxanide</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Clorsulon</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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1. Veterinary medications available in different countries for fasciolosis control

<table>
<thead>
<tr>
<th>Mandatory declaration</th>
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<th>Brazil</th>
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<th>Chile</th>
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<th>Ecuador</th>
<th>Mexico</th>
<th>Peru</th>
<th>Bolivarian Republic of Venezuela</th>
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</thead>
<tbody>
<tr>
<td>Yes, in humans</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, in animals</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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</table>

2. Is fascioliasis a notifiable disease in your country?
Fascioliasis is a parasitic disease that affects people and a wide variety of animals, essentially herbivores. In Latin America and the Caribbean, it is caused by the trematode *Fasciola hepatica*. Fascioliasis is classified by the World Health Organization (WHO) as a neglected tropical disease. The Pan American Health Organization, as part of its commitment to achieving the goals of the 2030 Agenda for Sustainable Development and the Sustainable Health Agenda for the Americas 2018–2030, launched an initiative to eliminate communicable diseases in the Region of the Americas. Its objectives include the elimination of fascioliasis as a public health problem in the Region of the Americas by 2030. These operational guidelines have been developed to provide information and guidance to help endemic countries move toward achieving that goal. They were prepared with the support of country technical staff and expert professionals from the Region and from the WHO Collaborating Center on fascioliasis and its snail vectors, incorporating current practices and considering the challenges and particularities of areas with endemicity. While fasciolosis in animals is a problem that generates economic losses in many countries of the Region, human fascioliasis is limited to environments with the ethnographic characteristics and socioeconomic determinants necessary for infection in humans. These operational guidelines focus on these areas, which are generally associated with small farmers and rural communities. They are part of the “One Health” approach, integrating the different sectors involved and working in synergy to make the interventions more effective and sustainable.