

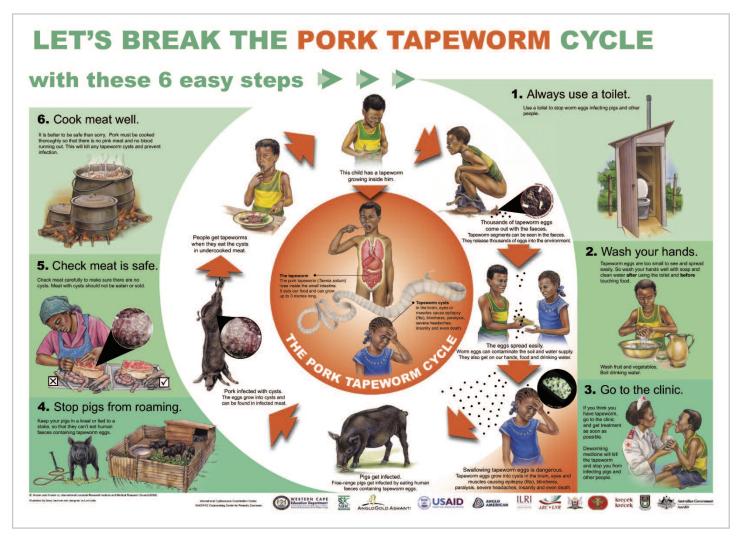


Protecting Livestock – Improving Human Lives

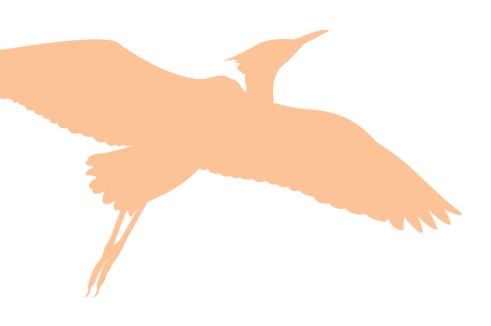
### It's time to eradicate the main cause of preventable epilepsy in the developing world through collaboration

Tangible steps for policy, decision-makers & health practitioners to break the cycle of cysticercosis – saving human lives and protecting precious resources and livelihoods

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# Breaking the cycle of cysticercosis

A new comprehensive study into the control of a parasite in pigs has reached compelling conclusions with key recommendations to combat this eradicable but neglected disease, which leads to around 5 million human infections and 50,000 human deaths each year. The most significant form of the disease is neurocysticercosis, which causes approximately 30% of epilepsy cases in humans in the developing world and impacts the economies of many poor countries. GALVmed's study results show that when used in combination, the pig vaccine Cysvax<sup>®</sup> and the dewormer treatment Paranthic™ 10%, eliminate the infectious cysts in pigs. However, an integrated human and animal health approach is needed to address lack of awareness of the disease, poor human hygiene and sanitation as well as poor animal husbandry practices.

#### How the disease is transmitted

Humans are the host for the pork tapeworm (*Taenia solium*), and affected people carry the tapeworm in their small intestine, often without symptoms. *T. solium* infects pigs and humans causing three forms of disease: Porcine Cysticercosis (pig meat), taeniasis (intestinal tract of humans) and neurocysticercosis (the human brain). At the taeniasis stage, the disease shows mild and non-specific symptoms (abdominal pain, nausea, diarrhoea or constipation may arise when the tapeworms become fully developed in the intestine).

The tapeworm eggs are periodically shed in the faeces and typically pigs ingest the eggs from the contaminated environment, food or water. The pigs subsequently become infected with the larval stages of the tapeworm and develop cysticerci (fluid-filled cavities, vesicles or blisters) in their musculature. The larval stage of the tapeworm may also develop in humans in subcutaneous sites (manifesting as skin nodules), musculature and the nervous tissue, especially the brain and ocular tissue. The disease whereby the musculature and nervous tissue is affected in humans and pigs is known as cysticercosis. When cysts develop in the brain, the condition is referred to as neurocysticercosis. Symptoms include severe headache, blindness, convulsions and epileptic seizures and can be fatal.

Porcine cysticercosis is a zoonosis, meaning that it is a disease that can be transmitted from animals to people. Transmission between pigs and people is through consumption of infected raw or undercooked pork meat. The disease occurs where pigs range freely, sanitation is poor, home slaughter is performed and meat inspection is absent or inadequate, and is thus strongly associated with poverty and smallholder farming.



#### **Disease impact**

Taeniasis/cysticercosis infections are a serious public health risk and an agricultural problem in many low and middle income countries of Africa, Asia and Latin America. Worldwide there are believed to be around 5 million human cases and 50,000 human cysticercosis-associated deaths reported each year. Neurocysticercosis can cause severe headaches, blindness, convulsions, epileptic seizures and can be fatal. Neurocysticercosis is considered to be the most common parasitic infection of the human nervous system

and the most frequent preventable cause of epilepsy in the developing world. Millions of people fall ill and many die as a result of cysticercosis from eating unsafe food.

Whilst predominantly a disease, which has a major impact in low and middle-income countries, in the USA one in ten people who are hospitalised for neurocysticercosis die from the preventable disease.

## Cysticercosis



[Up to] 1 in 10 people hospitalized for neurocysticercosis in the United States dies from the preventable parasitic disease.

Image: Centers for Disease Control and Prevention

#### **Human Health**

In 2014, an FAO and WHO report<sup>1</sup> ranked *T. Solium* top of the list of 10 leading foodborne parasites "with the greatest global impact" yet it remains a neglected disease.

In 2015 a WHO Expert Group identified cysticercosis caused by *T. solium* as a leading cause of death from food-borne diseases, resulting in a total of 2.8 million Disability Adjusted Life Years (DALY)\* – a metric indicating the disease-related loss of one year of full health because of premature death or disability.<sup>2</sup>

According to the same WHO report, the total number of people suffering from neurocysticercosis, including symptomatic and asymptomatic cases, is estimated to be between 2.56 – 8.30 million people, based on the range of epilepsy prevalence data available. Various systematic reviews have confirmed long-held beliefs that approximately 30% of people living with epilepsy in countries endemic for cysticercosis show Neurocysticercosis (NCC) lesions in their brain. The DALYs estimate in this case excludes NCC-associated sequelae other than acquired epilepsy, of which it is the main cause in developing countries.

#### **Agriculture & Economic Losses**

DALYs do not reflect economic burden, e.g. cost of illness, losses in agricultural and food sectors and trade impacts.

Cysticercosis causes significant economic losses to pig farmers through carcass condemnation and lower selling prices.

In Zambia, 95% of farmers were unable to sell pigs where tapeworm cysts are visible on the pig's tongue and received a 45% loss in value for infected pigs. GALVmed conducted porcine cysticercosis field studies in Uganda, Tanzania, Zambia and Nepal. Across the four countries 86-100% of pig traders indicated that they reject and do not sell meat if cysts are present, leading to financial and nutritional losses.

Where farmers and traders are unaware of porcine cysticercosis, the consequences are more serious as infected meat is sold and consumed increasing the risk of neurocysticercosis, the leading cause of preventable epilepsy in humans.

\* Disability Adjusted Life Years (uncertainty Interval: 2.1 to 3.6 million)

2 The WHO Foodborne Disease Burden Epidemiology Reference Group

<sup>1</sup> http://www.fao.org/publications/card/en/c/ee07c6ae-b86c-4d5f-915c-94c93ded7d9e/ (last accessed 2nd Nov 2017)

#### A devastating disease defined as *eradicable* but which remains *neglected*

Although theoretically easy to control and declared "eradicable"<sup>3</sup>, cysticercosis remains neglected in most endemic countries. This is due to the lack of information and awareness about the extent of the problem, suitable diagnostics, management capacity, and appropriate prevention and control strategies.

#### A problem projected to increase

Over the next 25 years, pork demand is projected to increase by 40% in the developing world. To meet this demand, pig populations are growing. Uganda's pig population has doubled in the last 10 years, and a similar trend is observed in other developing countries. This growth is not being matched by an increase in meat inspection, awareness raising of cysticercosis amongst pig farmers, pig traders, policy makers and consumers, nor much-needed education programmes in animal husbandry and the importance of hygiene, sanitation and food safety.

#### Working with partners to develop tools for porcine cysticercosis control

In July 2016, the innovative vaccine technology (TSOL18) developed by Professor Marshall Lightowlers at the University of Melbourne became the first licensed vaccine (Cysvax<sup>®</sup>) for porcine cysticercosis. This followed publication in *The New England Journal of Medicine*<sup>4</sup> of the results from a trial undertaken to eliminate *T. solium* transmission from the Tumbes region of northern Peru. The findings recognised the contribution of the TSOL18 vaccine to be critical in achieving the highest level of disease control. The licencing of the Cysvax<sup>®</sup> vaccine represents a major step towards the integrated control of this prevalent human disease. The University of Melbourne, Indian Immunologicals Limited (IIL) and GALVmed have collaborated in a public-private partnership for six years to make the vaccine available to those in low and middle income countries where porcine cysticercosis has a tremendous effect on human health and the economy.

GALVmed also supports the licensing and distribution of dewormer treatment oxfendazole (Paranthic<sup>™</sup> 10%) developed by Moroccan-based manufacturing partner, MCI Sante Animale. The registration of Paranthic<sup>™</sup> 10% for use in pigs was another significant step in the development of tools for porcine cysticercosis control. Administered alongside Cysvax<sup>®</sup>, Paranthic<sup>™</sup> 10% is used to control the cystic stage of the parasite in pigs, which breaks the life cycle of the tapeworm that is transmitted to humans. GALVmed is working with MCI to extend the registration of Paranthic<sup>™</sup> 10% to additional countries in Africa.

#### About the studies

GALVmed gained national and ethical approvals to undertake field trials to evaluate the effectiveness of the combined use of the pig vaccine Cysvax®, (that can prevent new infections), and Paranthic™ 10%, the oral dewormer (the pharmacological treatment to expel the parasitic worms), determining if the treatment can eliminate infections in pigs in some of the most affected regions of the world including: Uganda, Tanzania, Zambia and Nepal. This was combined with increasing awareness about the disease and the risk factors.

By identifying risk factors for disease and targets for preventive healthcare and improved disease control, it is hoped that the results from these studies will inform policy decisions and evidence-based practice.

- 3 International task force for disease eradication (Carter Centre).
- 4 Elimination of Taenia solium Transmission in Northern Peru (Garcia et al.) http://www.nejm.org/doi/full/10.1056/NEJMoa1515520?query=featured\_home

#### **Study results**

Study results suggest that when used in combination, the tools – Cysvax® vaccine and dewormer treatment Paranthic™ 10%, can eliminate cysticercosis in pigs. Results available for Nepal and Uganda, showed no cysts in pigs after four, three monthly mass treatments of Cysvax® and Paranthic™ 10%. These studies achieved high compliance with and acceptance amongst the smallholder farmers.

Country	Nepal	Tanzania	Uganda	Zambia
Baseline prevalence of porcine cysticercosis in the study area	33%	13%	16%	38%
Number of households (HH) enrolled*	184	890	454	271
Breed of pigs	Nearly all indigenous	Mostly crossbred	Mostly crossbred	Nearly all indigenous
Number of interventions completed (planned)	4 (4)	2 (3)	4 (6)	4 (6)
Number of pigs treated at each intervention**	213 - 253	1,359 - 1,087	1,599 - 2,310	237 (total)
Coverage achieved at each intervention	89 to 95%	83% to 86%	89 to 95%	79 to 97%
Number of adverse reactions	0	0	0	0
Cysts found in pigs after 4 interventions	0	Not done yet	0	Not done yet

\* Majority of farmers had fewer than five pigs

\*\*Vaccine and dewormer interventions at three and four month intervals

#### Landscaping studies

Landscaping studies were undertaken in India, Nepal and four target countries in Africa: South Africa, Tanzania, Uganda and Zambia.

A comprehensive literature review was undertaken in India as well as a detailed primary study covering 7 states: Assam, Bihar, Jharkhand, Meghalaya, Mizoram, Nagaland and Uttar Pradesh. The primary survey involved over 670 pig farmers, nearly 190 small-scale pig traders and 150 policy implementers such as local government officials from both human and animal health sectors. In Africa, over 1,900 pig farmers and more than 50 pig traders were surveyed in the highest pig production areas in Tanzania, Uganda and Zambia. Nearly 90 policy makers from multiple organisations across the four African countries were interviewed for knowledge, attitudes and practices (KAP) to assess the status of the disease and to identify gaps and opportunities and existing frameworks for prevention and control. Common themes emerged in these countries with high prevalence of cysticercosis in pigs and humans caused by *T. solium*, emphasising the necessity of a combined human and animal health approach to tackle the disease.

## Major risk factors in transmission of the disease, challenges and actions needed for effective control of *T. solium*

For effective control of cysticercosis, the following need to be addressed:

Challenges	Supporting Statistics***	Action Needed
Lack of awareness Pig farmers in areas where cysticercosis is endemic are largely unaware of the risks to humans of <i>T. solium</i> infection which results from the sale and consumption of infected pork. This is a major risk factor in transmission of the disease.	In Nepal, between 61% and 95% of pig farmers in the different study areas were unaware that consumption of infected meat could cause disease in people and it was observed that areas with lower awareness had a higher prevalence of porcine cysticercosis. In Tanzania and Uganda 81.5% of pig farmers were unaware of tapeworm infection in humans. In Uganda 99% of pig farmers did not know that consumption of infected meat could cause disease in people.	Education Strengthen education/ sensitisation, make training widely available, and build capacity. Raise awareness of the disease and how to break the cycle.
Policy makers' lack awareness and understanding of cysticercosis contributes to it remaining a <i>neglected</i> disease.	In Nepal where incidence of neurocysticercosis ranges from 12% - 47% in epileptic patients, Taeniasis/cysticercosis is at the top of the list of the six most prioritised zoonotic diseases, but there is no programme in place to address it. The India literature review indicated a critical gap in country-level evidence.	Policy sensitisation The available evidence and statistics on the prevalence and burden caused by cysticercosis in human health and economic terms should be shared with policy makers. The need for a collaborative human and animal, one-health approach to the control of cysticercosis should also be shared with policy makers. Legislate for notification of disease. Improved surveillance.
Poor sanitation and hygiene Many households do not have latrines. Even where latrines exist, they are not always used and open defecation continues to be practised. Pigs are free roaming for all or part of the day and often have access to latrines or sites of open defecation. These are major risk factors in	<ul> <li>95% of households (HH) in Tanzania had latrines which were always used but 45% of latrines were accessible to pigs.</li> <li>70% in Uganda had latrines, 39% of which were always used and 34% were accessible to pigs.</li> <li>In Zambia 92% of HH had latrines, which were always used with only 11% of HH saying latrines were open to pigs (100% of which were allowed to roam freely for some</li> </ul>	Food safety, improved sanitation and hygiene are all crucial to preventing the transmission of <i>T. solium.</i>
transmission of the disease.	or part of the day).	Continues overleaf >>>

\*\*\*Sample sizes: Nepal 184 Households (HH); Tanzania 890HH; Uganda 454HH; Zambia 271HH

## Major risk factors in transmission of the disease, challenges and actions needed for effective control of *T. solium*

For effective control of cysticercosis, the following need to be addressed:

Challenges	Supporting Statistics***	Action Needed
Lack of meat inspection	In Nepal, more than 90% of farmers consumed pork and had experience of home slaughter without proper meat inspection.	There is a great need for implementation of meat inspection legislation at regional and national levels immediately.
Poor husbandry practices	<ul> <li>95% of households (HH) in Tanzania had latrines which were always used but 45% of latrines were accessible to pigs.</li> <li>70% in Uganda had latrines, 39% of which were always used and 34% were accessible to pigs.</li> <li>In Zambia 92% of HH had latrines, which were always used with only 11% of HH saying latrines were open to pigs (100% of which were allowed to roam freely for some or part of the day).</li> </ul>	Good pig husbandry practices such as using pig sites, maintaining hygiene and deworming need to be encouraged particularly in rural areas where animal husbandry practices allow pigs to come into contact with human faeces.
Lack of awareness of and access to the vaccine and dewormer	In Nepal, between 61% and 95% of pig farmers in the different study areas were unaware that consumption of nfected meat could cause disease in people and it was observed that areas with lower awareness had a higher prevalence of porcine cysticercosis. In Tanzania and Uganda 81.5% of pig farmers were unaware of tapeworm infection in humans. In Uganda 99% of pig farmers did not know that consumption of infected meat could cause disease in people.	Work to secure sustainable supply and adoption of PC tools (the vaccine and dewormer) for pig farmers. This should be accompanied by education and other awareness initiatives.
Lack of an integrated approach	In Nepal where incidence of neurocysticercosis ranges from 12% – 47% in epileptic patients, Taeniasis/cysticercosis is at the top of the list of the 6 most prioritised zoonotic diseases, but there is no programme in place to address it. The India literature review indicated a critical gap in country-level evidence.	Human treatment should go hand in hand with that of pigs. At the global level, a One Health approach should be fostered to ensure collaboration across ministries, academia, industry, and other stakeholders. Due to competing needs and limited resources, donor support will be invaluable.

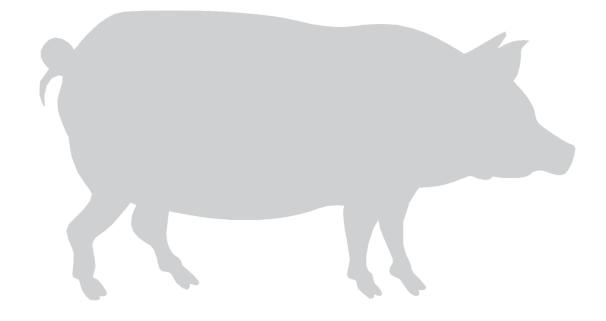
\*\*\*Sample sizes: Nepal 184 Households (HH); Tanzania 890HH; Uganda 454HH; Zambia 271HH

### **Recommendations**

A combined human and animal health approach is required to tackle cysticercosis. Integrating the use of porcine cysticercosis control tools Cysvax® and Paranthic™ 10% with sensitisation programmes for pig farmers, traders and consumers on the disease; WASH (Water, Sanitation and Hygiene) programmes and training in food safety and animal husbandry is required to break the cycle of cysticercosis.

Selection of the specific strategy depends on cost-effectiveness analyses based on solid field data, currently unavailable, though urgently needed as well as on health priorities and resources of the country.

A One Health approach involving human, veterinary, environmental and social sectors is essential for *T. solium* to be controlled and eventually eliminated. The success of any intervention is largely dependent on the level of societal and political acceptance, commitment and engagement.



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#### **Useful links/documents**

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GALVmed welcomes all questions and suggestions regarding porcine cysticercosis. Please contact: **info@galvmed.org** 



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