

WHO activities towards harmonization of diagnosis and clinical management of *Echinococcus granulosus* infection/Cystic Echinococcosis

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4. Clínica Viedma, CenHEQuis (Centro de estudio, diagnóstico y tratamiento de la Hidatidosis/Equinococosis Quística - Center of Study, Diagnosis and Treatment of Hydatidosis/Cystic Echinococosis), Viedma, Río Negro, Argentina.
5. London School of Hygiene and Tropical Medicine, London, United Kingdom
6. World Health Organization, Department of the Control of Neglected Tropical Diseases, Geneva, Switzerland.

Background



Review

Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans[☆]

Enrico Brunetti^{a,*,1}, Peter Kern^b, Dominique Angèle Vuitton^c, Writing Panel for the WHO-IWGE²

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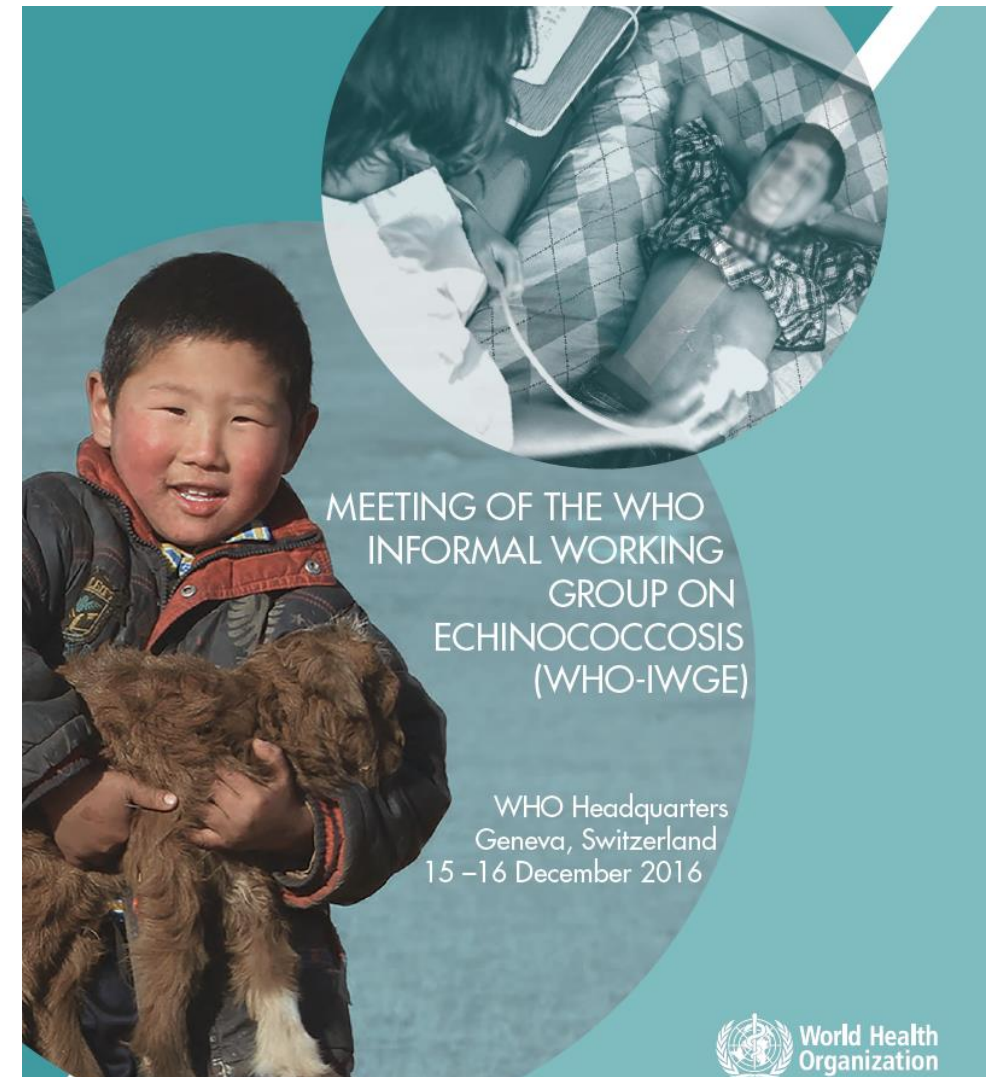
^b Comprehensive Infectious Diseases Centre, University Hospitals, Albert-Einstein-Allee 23, 89081 Ulm, Germany

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<https://doi.org/10.1016/j.actatropica.2009.11.001>

A series of meetings of the WHO Informal Working Group on Echinococcosis have taken place:

- Geneva, Switzerland, 15-16 December 2016
- Bern, Switzerland, 9-11 October 2019
- Lima, Peru, 29 November 2019



Guideline Development Group



Health Topics ▾

Countries ▾

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Call for public consultation – for experts to join the Guideline Development Group (GDG) on treatment of patients with cystic echinococcosis (CE)

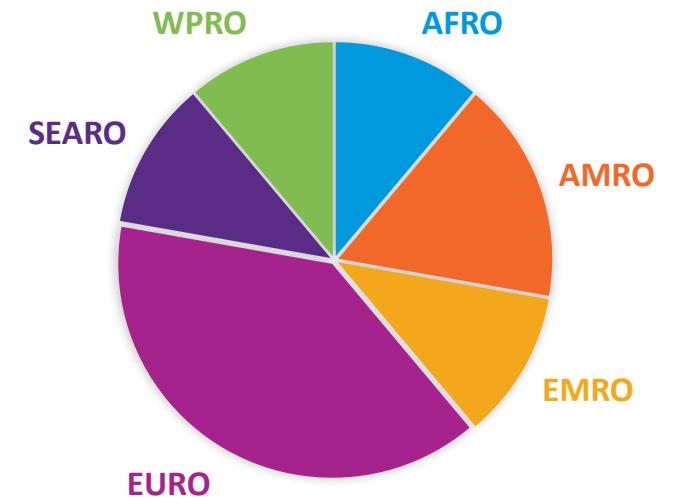
Deadline: 22 March 2022

7 March 2022 | Call for consultation

bit.ly/36JVNMY



17 Experts



Systematic Review Team

Paul Garner, Rebecca Kuehn (Liverpool School of Tropical Medicine, UK)

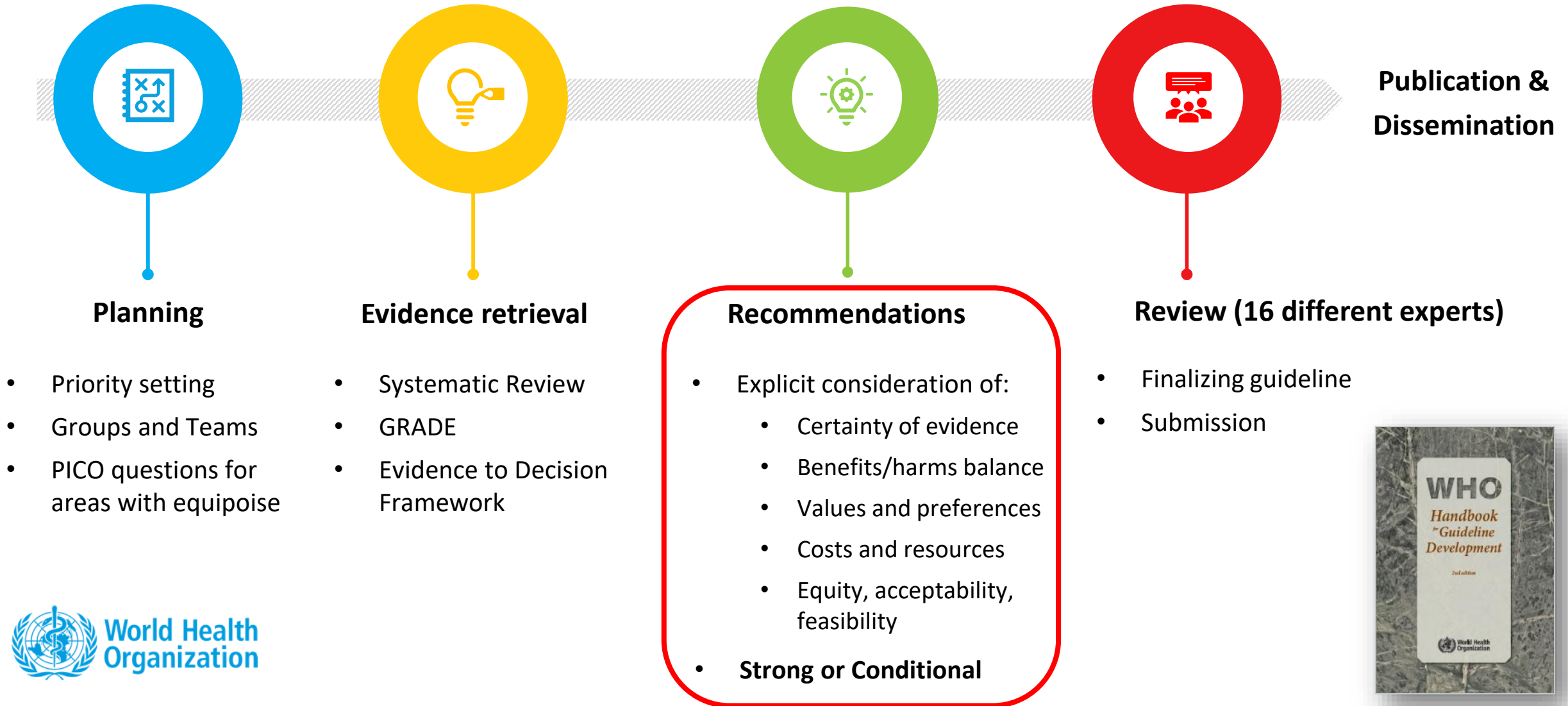
Methodologist

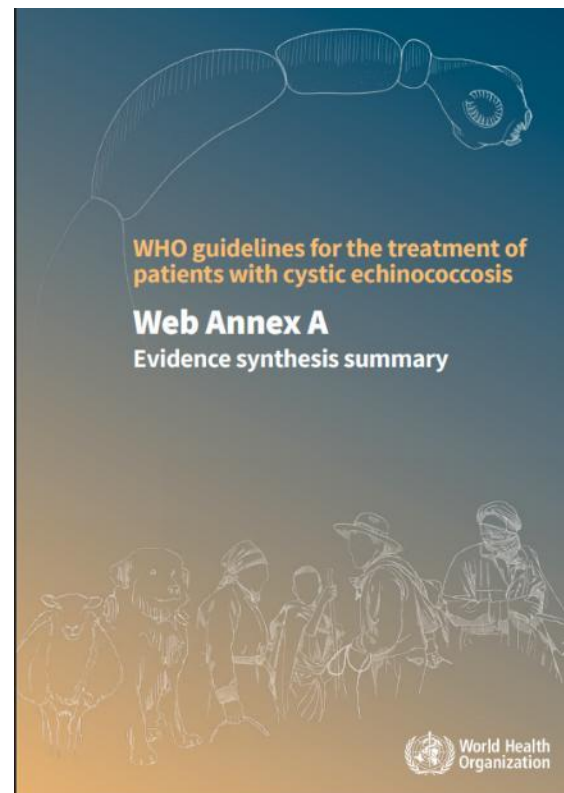
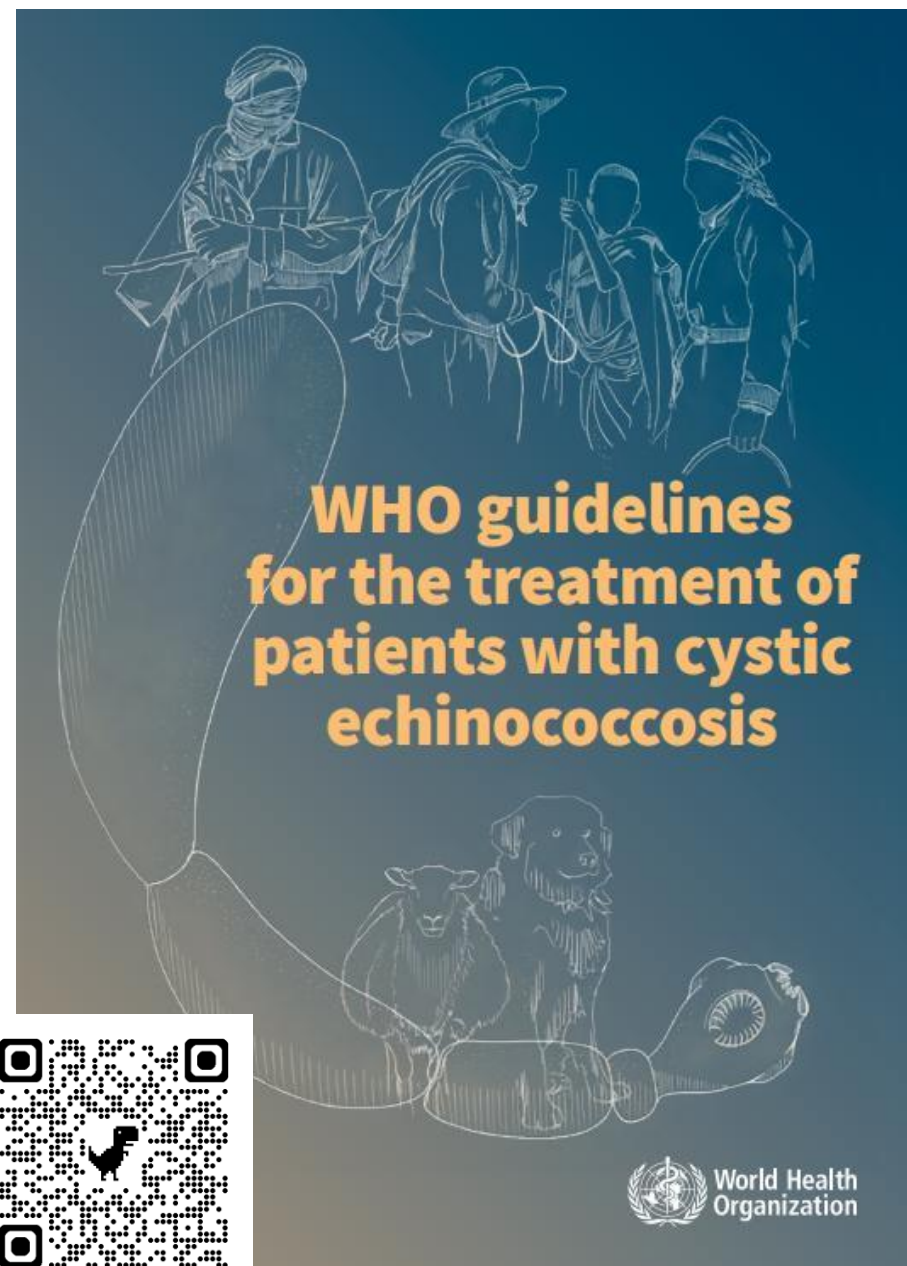
Priscilla Rupali (Christian Medical College, Vellore, India)

Chair

Timothy Pennel (University of Cape Town and Groote Schuur Hospital, South Africa) FOLLOWED BY Peter Chiodini (Hospital for Tropical Diseases and London School of Hygiene & Tropical Medicine, UK)

Guideline Development Overview

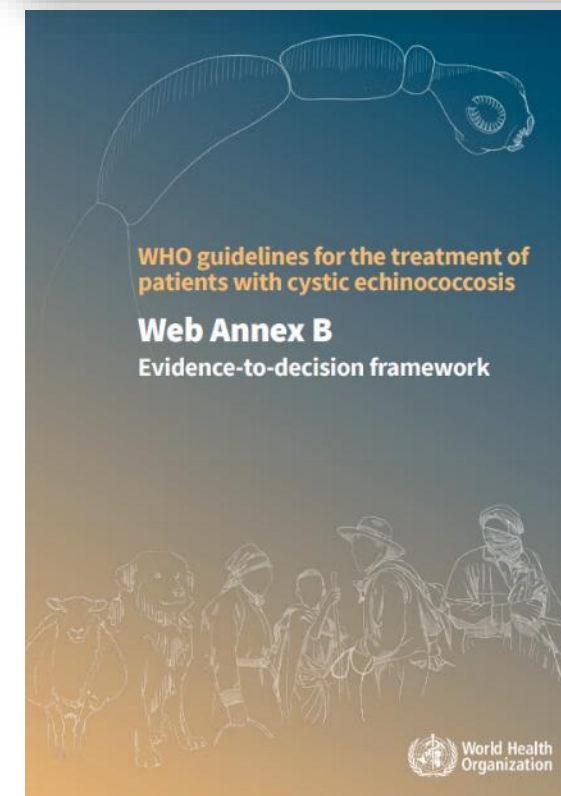




16 June 2025

Treatment of uncomplicated hepatic cystic echinococcosis (hydatid disease) (Review)

Kuehn R, Uchiumi LJ, Tamarozzi F



Writing Team

Meritxell Donadeu (WHO Consultant, Australia); Bernadette Abela and Katie Corridan (WHO/NTD); Priscilla Rupali, Hanna Alexander and Jisha Sara John (Christian Medical College, Vellore, India); Rebecca Kuehn and Paul Garner (Liverpool School of Tropical Medicine, UK).

Scope of the Guideline -1

- Enable clinicians in their **respective healthcare environments** to manage CE patients **appropriately** and at the **highest standards of care** possible
- Reduce and avoid over- and mistreatment of patients
- Providing recommendations on the indications of the four main management modalities:
 - (1) anti-parasitic drug treatment,
 - (2) percutaneous methods,
 - (3) surgery,
 - (4) “watch & wait”
- depending on the stage and localization of the cysts
- For UNCOMPLICATED LIVER CE and small uncomplicated lung CE
- Where areas of equipoise exist

1.3 Objectives and scope of these guidelines

The purpose of these guidelines is to provide guidance on the choice of treatment so that patients (adults and children) with CE cysts can be offered and receive appropriate and equitable treatment. The aim is to ensure that patients receive the most appropriate and affordable management in the context of infrastructure and expertise sufficient to ensure its safety, and without unnecessary invasive procedures or treatment, to avoid iatrogenic complications by using invasive interventions.

For complicated CE liver cysts, surgery is usually the treatment of choice, based on best medical practice as conveyed by the WHO-IWGE (9). These guidelines are focused on the different choices for uncomplicated liver cysts. Pulmonary CE is usually managed by surgical intervention, but these guidelines evaluate the option of using ALB alone to treat small pulmonary cysts.

For uncomplicated inactive cysts, there are no recommendations in these guidelines since current best medical practice is follow-up with imaging (ultrasonography, CT or MRI), also known as the “watch and wait” approach (9, 14). Surgery should be avoided as far as possible unless the inactive cyst is causing complications (e.g. cyst causing portal hypertension).

Table 2. Health care system tiers for managing different treatment options for CE, according to available expertise and resources

Tier	Health care worker technical expertise required	Surgical infrastructure required	Radiological capacity required	Laboratory required	Intervention(s) possible
Tier 1	Medical doctor	Not available	Referral access to ultrasonography	Access to facilities for complete blood cell count, liver function tests.	Albendazole
Tier 2	General surgeon Anaesthesiologist Nursing care	Operating theatre Inpatient facility with monitoring	Ultrasound on site	Laboratory tests as needed for anaesthesia	Tier 1 and Surgery (non-radical only)
Tier 3 (includes expertise and facilities available in tier 2)	Surgeon with laparoscopic skills and surgeon, radiologist or physician with a relevant speciality trained in PAIR and S-CAT	General surgery and laparoscopic surgery facilities Inpatient facility with monitoring and access to ICU	CT scan Fluoroscopy	Laboratory tests as needed for anaesthesia	Tier 2 and Surgery (radical and non-radical) Laparoscopic Surgery PAIR Standard catheterization
Tier 4 (includes expertise and facilities available in tier 3)	General and laparoscopic surgeons Interventional Radiologists Thoracic Surgeon	Interventional Radiology Facilities and Procedure Room	MRI and MRCP	Routine clinical pathology, biochemistry and microbiology	Tier 3 and Modified Catheterization Technique Thoracic (lung) surgery

Scope of the Guideline -2

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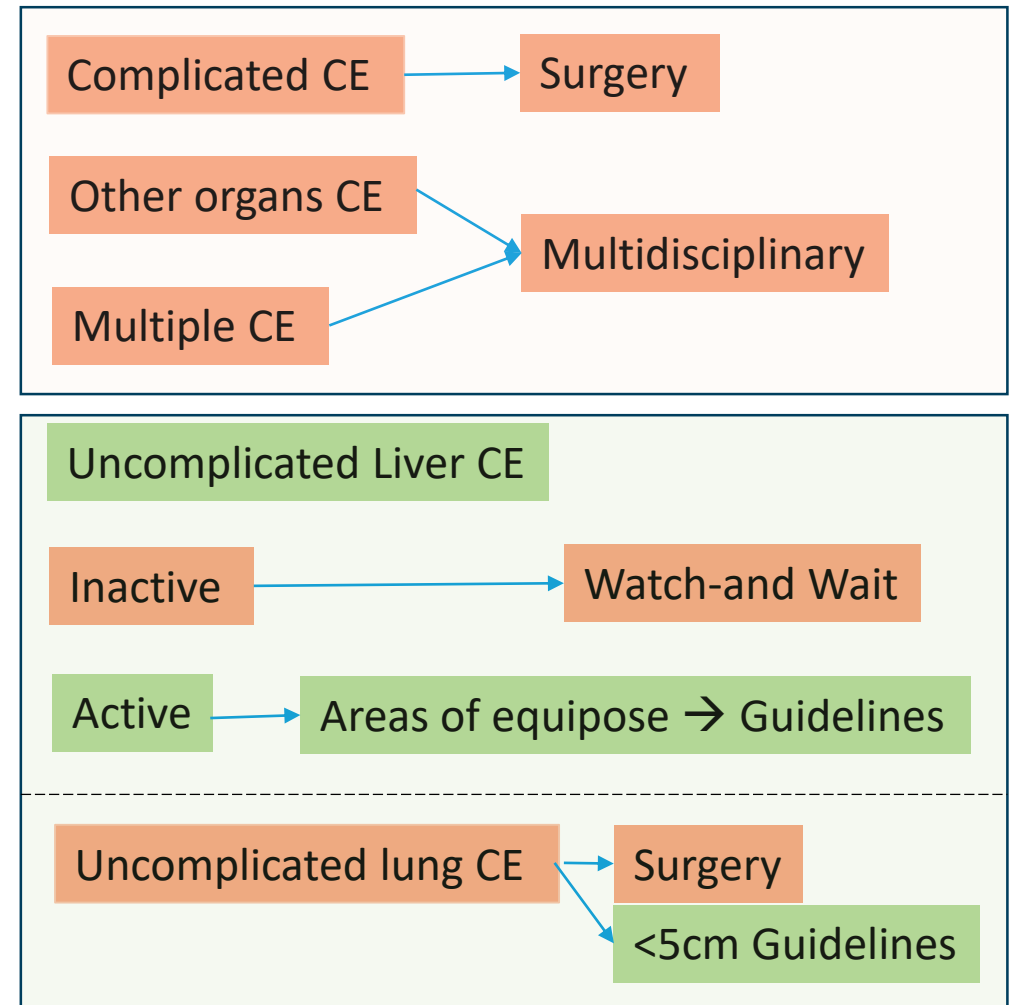
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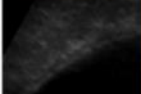
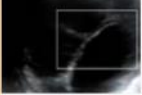

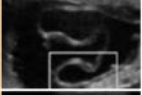
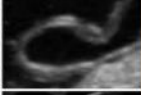
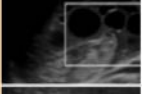
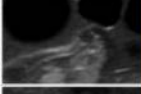
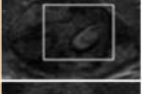
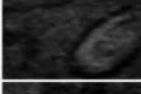
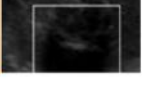

Scope of the Guideline - 3 cont.

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Scope of the Guideline - 4

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 - (4) “watch & wait”
- **depending on the stage and localization of the cysts**
- For UNCOMPLICATED LIVER CE and small uncomplicated lung CE
- Where **areas of equipoise** exist

	Ultrasound image	Particulars of pathognomonic sign	Stage	Viability*
Cystic echinococcal cysts			CE1	Viable
			CE2	Viable
			CE3a	Viable or non-viable
			CE3b	Viable
			CE4	Low viability or non-viable
			CE5	Non-viable

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Active cysts, likely to contain viable protoscolices:	
CE1. Active, unilocular, liquid content	Well-defined univesicular cyst, with round or oval shape, anechoic content, posterior acoustic enhancement, with or without low intensity floating echoes upon decubitus change (moving “hydatid sand”) and with visible pathognomonic “double wall sign” consisting in the inner hyperechoic laminated layer and outer hypoechoic adventitial layer.
CE2. Active, multivesicular, liquid content	Well-defined multivesicular cyst, with round or oval shape, posterior acoustic enhancement, one or more daughter cysts filling in part or completely the fluid-filled cyst; the pathognomonic “honeycomb” appearance is provided by the thin, regular, continuous and avascular clearly distinguishable adjacent walls of juxtaposed daughter cysts (giving a septated appearance), without solid content.
CE3a. Transitional unilocular, liquid content with detached parasitic layers	Well-defined univesicular cyst with round or oval shape, posterior acoustic enhancement, and with partial or complete detachment of the laminated layer, visible as a hyperechoic thin and regular layer floating in the anechoic cyst content, giving a pathognomonic appearance, referred to as the “water lily sign”. The whole layer must be identified as a continuous hyperechoic structure, in different views. Low-intensity floating echoes upon decubitus change (moving “hydatid sand”) may be present.
CE3b. Active multivesicular cyst, with partially solid content with daughter cysts	Well-defined multivesicular cyst with round or oval shape, posterior acoustic enhancement, and heterogeneous structure, encompassing avascular solid components and hypoechoic folded structures deriving from degenerating layers and one or more round daughter cysts with anechoic content, giving the pathognomonic “Swiss cheese” appearance.
Inactive stages:	
CE4. Solid content	Well-defined round or oval mass with or without posterior acoustic enhancement and with heterogeneous avascular solid content formed by the degenerated cyst layers, and hypoechoic folded structures deriving from degenerating layers in the mass and giving the pathognomonic “ball of wool” or “cerebroid” appearance. Unlikely to contain viable protoscolices.
CE5. Solid content with eggshell calcified wall	Well-defined round or oval mass with posterior acoustic shadow deriving from a complete or nearly complete egg-shell calcified wall, and heterogeneous avascular solid content (when acoustic shadow allows visualization) formed by the degenerated cyst layers and hypoechoic folded structures deriving from degenerating layers in the mass and giving the pathognomonic “ball of wool” or “canalicular” appearance. Non-viable.

1.1.2 Diagnosis

The diagnosis of CE is based on imaging techniques, primarily ultrasound or magnetic resonance imaging (MRI), while computed tomography (CT) is less reliable (6), complemented by serology when imaging is not conclusive. Contrast-enhancement imaging allows excluding CE diagnosis in a case where the cyst takes contrast. No antigen detection tests are commercially available. Antibody detecting serological tests complement imaging findings, yet their limitations warrant careful consideration. In cases of sero-negativity, confirming a presumptive diagnosis might involve demonstrating the presence of protoscolices and/or hooks by microscopic examination of the cyst fluid, histology, polymerase chain reaction (PCR) of cyst material (7) or observation of changes in the cyst ultrasound appearances on treatment, such as detachment of parasite layers in an unilocular cyst (suspected CE1) after percutaneous puncture or administration of ALB. Currently, there are no WHO guidelines for the diagnostic of CE, and this has been identified as a key research priority (section 6).

6. Research priorities

Research priorities

- 1 Prospective comparative trials to update recommendations.
- 2 Health services research on provision of access to services in endemic areas.
- 3 Survey on patient preferences for the treatment and management of CE.
- 4 For all PICO questions the duration of the ALB regimen needs to be assessed in RCT. In addition, for those where a procedure is recommended, the potential role of combination with praziquantel also needs to be addressed with a proper RCT.
- 5 Include additional questions to these guidelines such as the management of treatment failures after PAIR.
- 6 Develop WHO CE diagnostic guidelines.
- 7 Improved diagnostic tools for specific use cases.

PICOs

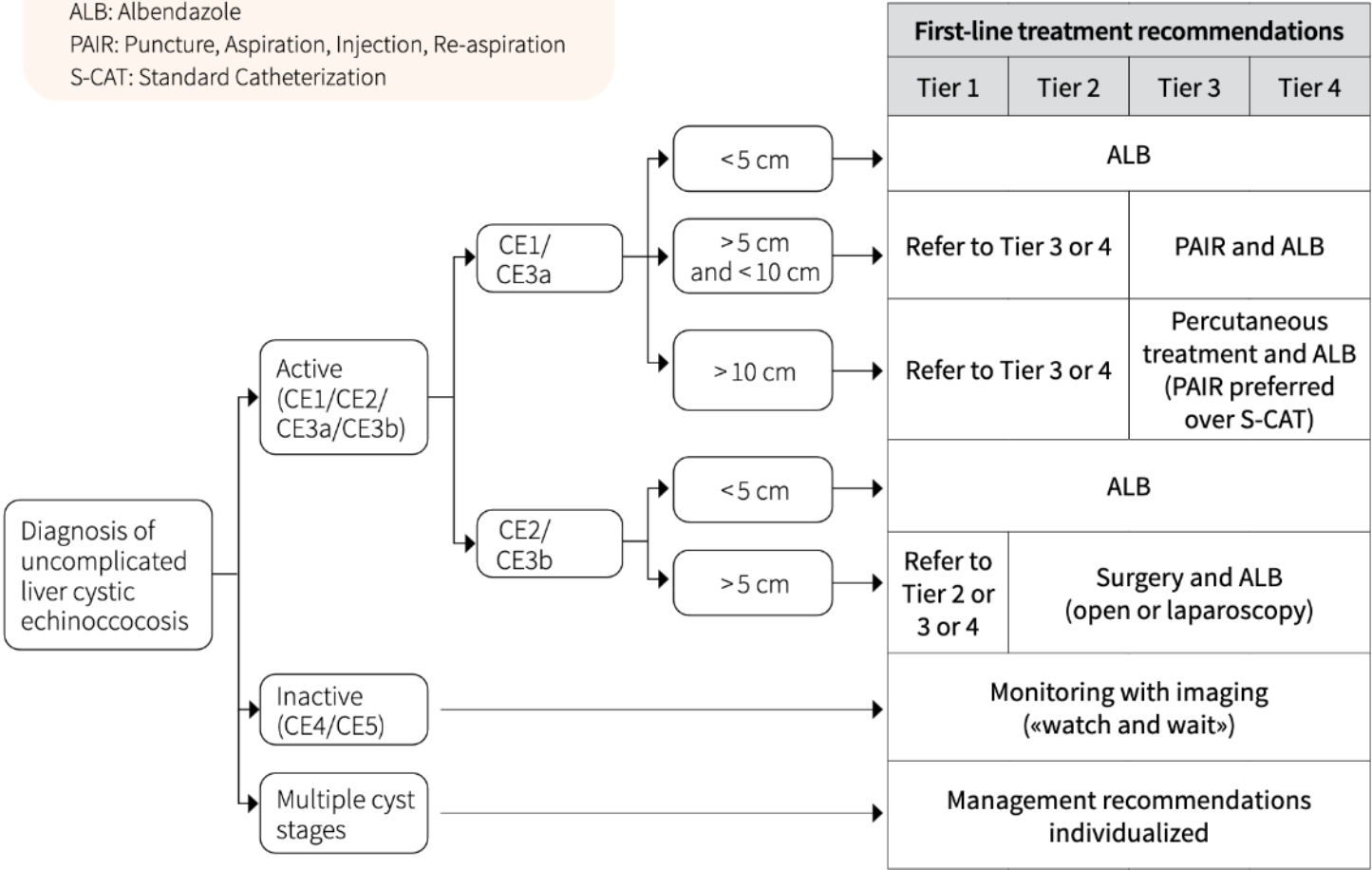


Research (PICO) questions

- | | |
|-----|--|
| P1 | For treating uncomplicated hepatic cyst types CE1 or CE3a < 5 cm, is PAIR combined with ALB as effective and safe as ALB alone? |
| P2 | For treating uncomplicated hepatic cyst types CE1 or CE3a 5–10 cm, is PAIR combined with ALB as effective and safe as ALB alone? |
| P3 | For treating uncomplicated hepatic cyst types CE1 or CE3a 5–10 cm, is surgery combined with ALB as effective and safe as PAIR combined with ALB? |
| P4 | For treating uncomplicated hepatic cyst types CE1 or CE3a > 10 cm, is standard catheterization combined with ALB as effective and safe as PAIR combined with ALB? |
| P5 | For treating uncomplicated hepatic cyst types CE1 or CE3a > 10 cm, is standard catheterization combined with ALB as effective and safe compared to surgery combined with ALB? |
| P6 | For treating uncomplicated hepatic cyst types CE2 or CE3b ≤ 5 cm, is surgery combined with ALB as effective and safe as ALB alone? |
| P7 | For treating uncomplicated hepatic cyst types CE2 or CE3b 5–10 cm, is surgery combined with ALB as effective and safe as ALB alone? |
| P8 | For treating uncomplicated hepatic cyst types CE2 or CE3b of any size, is laparoscopic surgery combined with ALB as effective and safe as open surgery combined with ALB? |
| P9 | For treating uncomplicated hepatic cyst types CE2 or CE3b of any size, is modified catheterization technique (Mo-CAT) combined with ALB as effective and safe as surgery combined with ALB? |
| P10 | Is praziquantel combined with ALB as effective and safe as ALB alone for treating active cysts (cyst types CE1, CE2 or CE3a, CE3b) when given pre- and post- percutaneous or surgical interventions? |
| P11 | For treating uncomplicated lung CE cysts of ≤ 5 cm, is ALB as effective and safe as surgery combined with ALB? |

Recommendations

Key:
ALB: Albendazole
PAIR: Puncture, Aspiration, Injection, Re-aspiration
S-CAT: Standard Catheterization



Use of praziquantel combined with ALB post-percutaneous/surgical procedures for hepatic cyst types CE1, CE2, CE3a, CE3b

Recommendation 6:
In CE patients undergoing percutaneous or surgical interventions, when spillage is suspected or has occurred, the combination praziquantel and ALB is suggested.
Conditional recommendation based on expert consensus.

Background	ALB is most often used in the treatment of CE, alone or in addition to invasive interventions. Recently, attention has been given to the addition of praziquantel pre- and post-intervention, combined with ALB.
Summary of the evidence	<p>This recommendation is based on PICO question 10.</p> <p>No trials were identified. The GDG formulated the recommendation based on pharmacological data, expert consensus, risk benefit assessment and clinician experience.</p> <p>Praziquantel has been reported to have a protoscolicidal effect but is not parasiticidal for the cysts (14). Pharmacological data indicate that the combination of praziquantel and ALB enhances efficacy by increasing ALB sulfoxide levels, the pharmacologically active metabolite, resulting in markedly increased protoscolicidal activity, enhancing the efficacy of treatment and reducing the risk of recurrence or complications associated with spillage. Biological plausibility has been reported by Cobo et al. (29).</p>
Certainty of the evidence	There is no evidence available to support the use of praziquantel combined with ALB when performing invasive interventions. The recommendation was formulated by the GDG using expert consensus within the evidence-to-decision framework.
Additional factors considered	<ul style="list-style-type: none">Benefits and harms The GDG acknowledges potential benefits, such as enhanced therapeutic activity, broader applicability and risk mitigation, associated with the praziquantel and ALB combination. The concerns raised include limited experience, cost issues and uncertainties regarding specific outcomes. There is a lack of data regarding undesirable effects.Health equity, acceptability, resource implications, and feasibility The high cost of praziquantel in some countries could potentially create access barriers, highlighting a concern for health equity, acceptability and feasibility. Efforts should be made to make praziquantel more affordable and accessible, especially in low- and middle-income regions where CE is endemic.
Implementation considerations	<ol style="list-style-type: none">In case of suspected or ascertained cyst fluid spillage, ALB should be given at a dose of 10–15 mg/kg/day in two divided doses (up to 400 mg twice a day) for a minimum of 3 months, usually, 6–12 months after the intervention, as considered appropriate by the clinician.Praziquantel should be given at a dose of 40–50 mg/kg/day divided into two daily doses for 2 weeks after the intervention. Because praziquantel does not have an effect on the cyst (as compared to ALB), 2 weeks are suggested. However, the period can be increased to a maximum of 4 weeks if considered appropriate by the clinician.ALB and praziquantel can be given simultaneously during a fat-rich meal to increase their bioavailability.Some clinicians use praziquantel in combination with ALB for 2 weeks prior to procedure (29). More evidence is needed to make this practice a recommendation.

Uncomplicated lung CE cysts
≤ 5 cm

Recommendation 7:
In patients with uncomplicated active lung CE cysts < 5 cm, surgery is suggested. ALB should not be given before surgery. When spillage is suspected or has occurred, ALB after surgery is suggested. Lung surgery requires tier 4 settings.
Conditional recommendation based on expert consensus.

Target Product Profiles (TPP) for diagnostics for *E. granulosus*/Cystic echinococcosis in animals and humans for PUBLIC HEALTH PURPOSES

COMING
SOON!

6. Research priorities

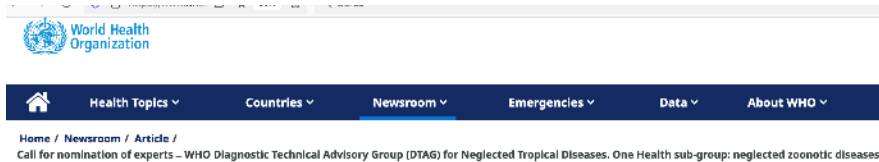
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TPP structure

The role of the subgroups is:

1. Understand the current diagnostics landscape and set diagnostic priorities
2. To prepare new or review existing TPPs for **teniasis/cysticercosis, cystic echinococcosis, FBT and rabies**
3. To describe the programmatic use case to scientists and product developers



Call for nomination of experts – WHO Diagnostic Technical Advisory Group (DTAG) for Neglected Tropical Diseases. One Health sub-group: neglected zoonotic diseases

Deadline: 5 April 2024

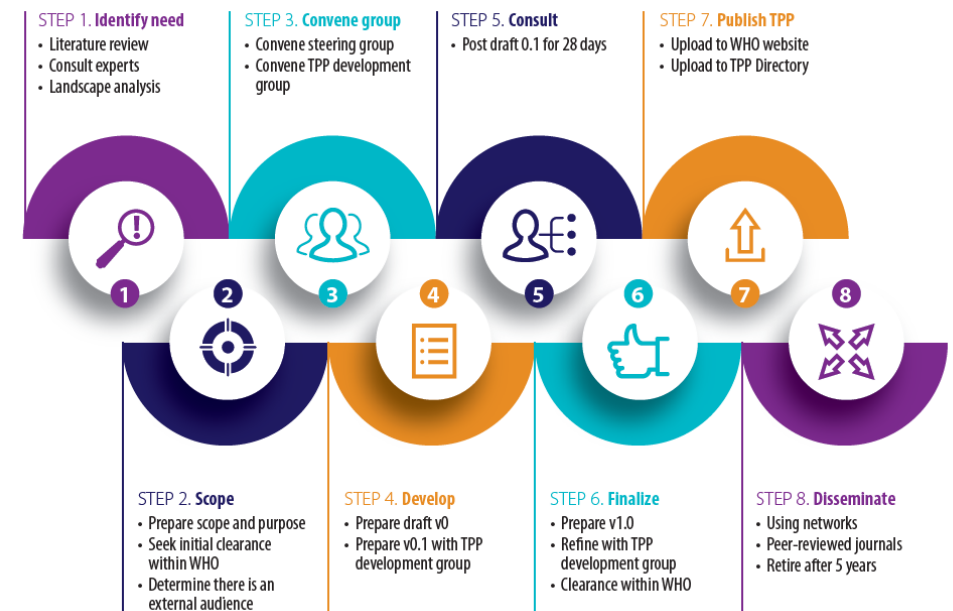
DTAG One Health subgroup - Members

Core group (12 members)

AFRO: P. Gichuki, R. Miambo
AMRO: R. Wallace, V. Periago, A. Strailey
EMRO: M. Fasihi Harandi
EURO: C. Freuling, F. Tamarozzi
SEARO: G. Singh
WPRO: M. Lighthowers, MB. Qian, SH. Kim

Subject matter expert

Taeniasis/cysticercosis: A. Fleury, S. Gabriel, R. Jambou, V. Khieu, B. Ngowi
Echinococcosis: G. Minbaeva, L. Uchiyumi, T. Manciuili
FBT: S. Mas Coma, B. Sripa, ST. Hong, M. Adriko, MD Bargues, V. Khieu
Rabies: A. Latz



1- Product use summary	2- Design		3- Performance		4- Product configuration	5- Product cost and channels
1.1- Use case	2.1- Portability	2.8- Biomarker	3.1- Species differentiation		4.1- Shipping conditions	5.1- Target pricing per test
	2.2- Instrument power/requirement	2.9- Type of analysis	Analytical Se / Limit of detection			5.2- Capital cost
1.2- Target population	2.3- Water requirement	2.10- Detection	3.2- Diagnostic/ Clinical sensitivity	3.8- Ease of use	4.2- Storage conditions	5.3- Product lead times
1.3- Lowest infrastructure level	2.4- Maintenance and calibration	2.11- Quality control	3.3- Diagnostic/ Clinical specificity	3.9- Ease of results interpretation	4.3- Service and support	5.4- Target launch countries
	2.5- Sample type/collection	2.12- Supplies needed	3.4- Time to results	3.10- Operating temperature		5.5- Product registration
1.4- Lowest user level	2.6- Sample preparation – transfer to device	2.13- Safety	3.5- Result stability	3.11- Equivalence of matrices*	4.4- Labelling and instructions for use	5.6- Procurement
1.5- Training requirements	2.7- Sample volume		3.6- Throughput	3.12 Reproducibility and robustness		5.7- Test pack size
			3.7- Target shelf life/ stability			