

CESSARi
Research on
cystic echinococcosis
in sub-Saharan Africa



Thomas Romig

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Stuttgart, Germany



Funding source:

DFG (German Research Agency)

Program 'German-African cooperation
projects in infectious diseases'

2009-2019

Total financial volume (9 years): 2.8 mio €



The consortium: countries and institutions (phase 1-3)



Germany:	University of Hohenheim (1-3) Ulm University Hospital & Medical Center (1-3)
Sudan:	Al-Neelain University, Khartoum (1-2) Ministry of Livestock, Central Laboratories (1-3) University of Gezira, Wad Medani (1-3)
Ethiopia:	Addis Ababa University, Addis Ababa (3)
Kenya:	African Medical and Research Foundation, Nairobi (1-2) Kenya Medical Research Institute, Nairobi (1-3) Meru University of Science and Technology (1-3)
Uganda:	Makerere University (1-2)
Zambia:	University of Zambia, Lusaka (2-3)
Namibia:	Ministry of the Environment, Windhoek (3)
South Africa:	University of the Witwatersrand, Johannesburg (1)



Research objectives



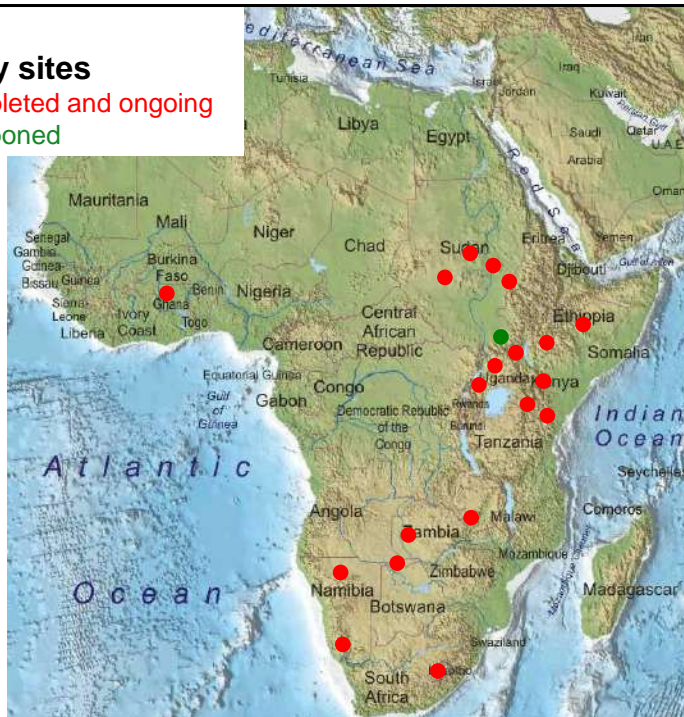
- 1) Correlations of *Echinococcus* genotypes with geographical distribution, host preference and infectivity to humans
- 2) Identification of wildlife-based cycles and their interaction with 'domestic' echinococcosis cycles
- 3) Clinical manifestation
- 4) Impact on public health and economy

Other aims

Training, networking and capacity building

Study sites

- completed and ongoing
- postponed





Activities depending on facilities present in each country:

Hospital records

Ultrasound screening surveys

Slaughterhouse surveys, fecal surveys of dogs

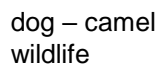
Wildlife surveys

Collection of isolates, molecular characterization

Estimate of public health and economic impact







Training and capacity building



Molecular biology in **Hohenheim**: 25 participants, 2-4 week courses

Abdominal ultrasound in **Pavia**: 20 participants

Abdominal ultrasound and percutaneous intervention in **Ankara**: 4 participants

Field ultrasound in **Nairobi**: 4 participants

Epidemiology in **Ulm**: 46 participants

Epidemiology in **Johannesburg**: 10 participants

Training and capacity building



41 academic theses completed or ongoing (BSc, MSc, PhD):

Sudan	14
Kenya	8
Germany	10
Uganda	6
Namibia	2
Zambia	1
South Africa	1
Ethiopia	1



Provided equipment

6 laboratories for basic molecular work (Sudan, Kenya, Uganda, Ghana)

4 sets of mobile ultrasound equipment (Sudan, Kenya, Uganda, Zambia)





Main difficulties / obstacles

War-related insecurity in South Sudan

Procedures to obtain research permits

International exchange of samples

Movement of equipment between institutions



Elmenteita, Kenya, April 2018



The international impact of HERACLES collaborative project



Adriano Casulli
On behalf of HERACLES consortium

- WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis;
- European Union Reference Laboratory for Parasites (EURLP),
Department of Infectious Diseases, Istituto Superiore di Sanità (Rome, Italy)




Human cystic Echinococcosis ReseArch
in CentraL and Eastern Societies

Research based, human focused

Timing: 1st October 2013 - 2018

Total costs: € 3.922.487,76



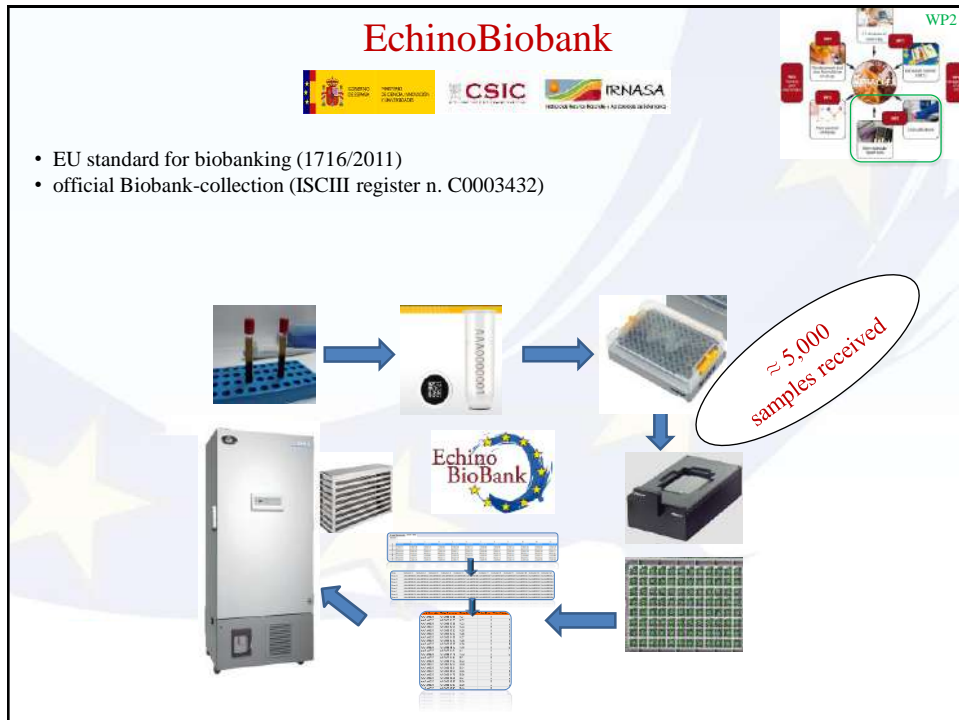

Beyond the Consortium: HERACLES extended network





CORE ACHIEVEMENTS

- Biggest research-based cross-sectional ultrasound-based population study ($\approx 25,000$)
- Creation of the European Register (ERCE) ($\approx 2,000$)
- Registered Echino-BioBank ($\approx 5,000$)
- Patent on anti-parasitic soluble drugs (Salts of benizimidazoles)
- First proteomic description of parasite exosomes in echinococcal cyst and...
- ...identification of biomarker candidates in exosome plasma by quantitative proteomic analysis












• Human samples
• Animal samples
• Clinical data






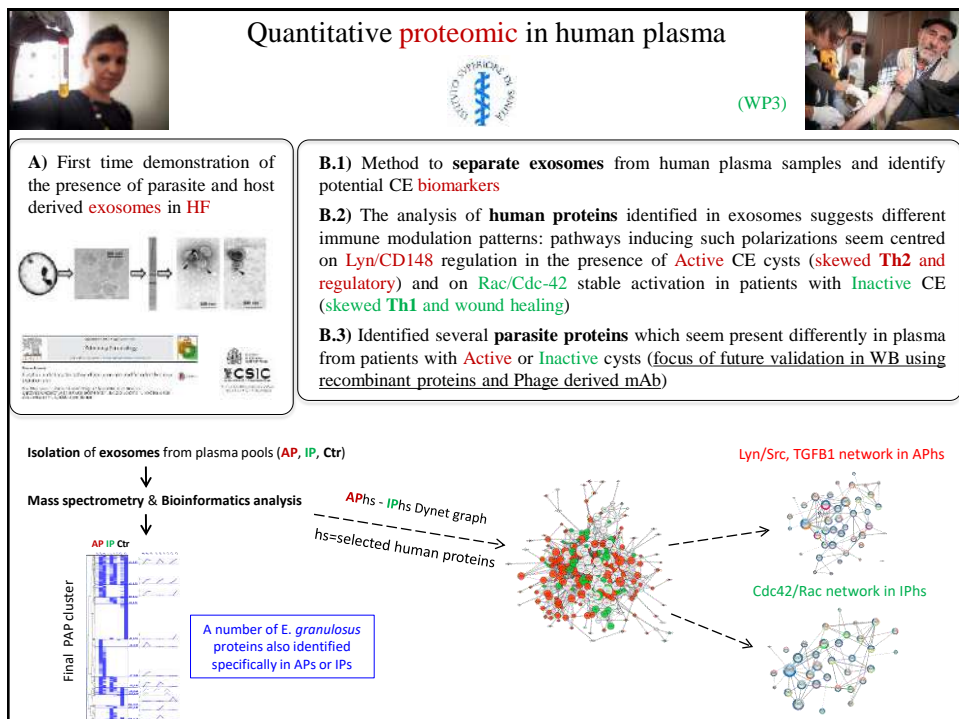
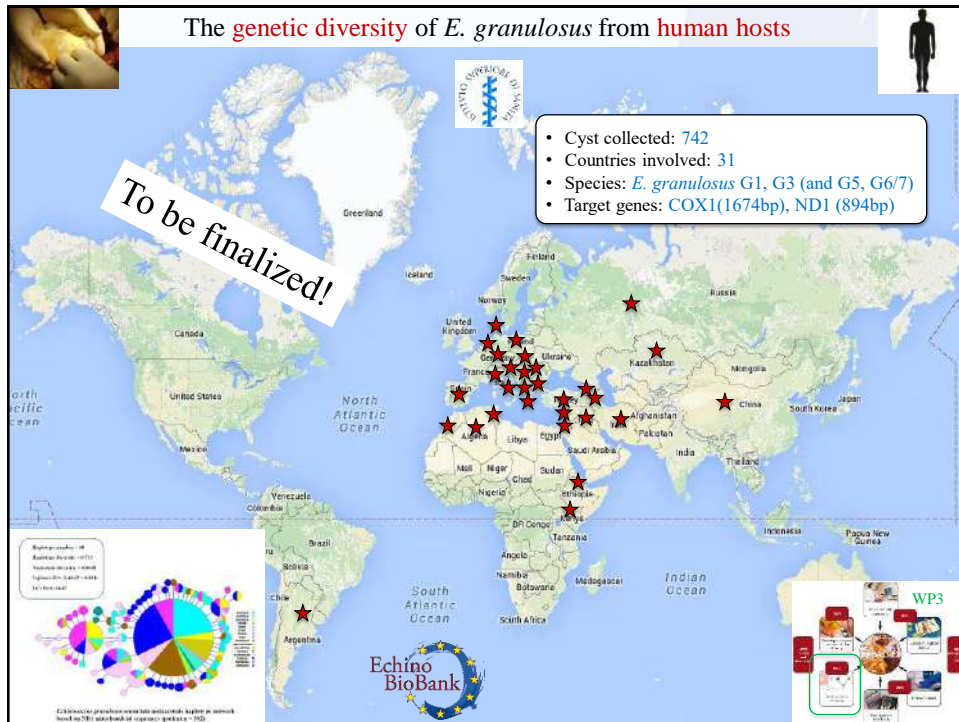
to foster systematic studies on CE

open resources



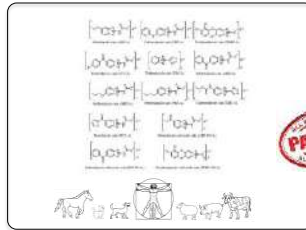


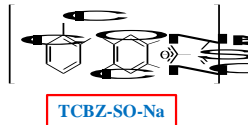
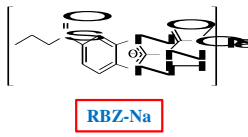


“SALTS of compounds having BENZIMIDALIC structure”

PLOS PATHOGENS
Progress in the pharmacological treatment of human cystic and alveolar echinococcosis: Compounds and therapeutic targets
Ben Salem Lounis¹, Anthony David², Anthony David², David Charnay³



- This invention consists of water-soluble BMZ salts as a **racemic mixture** as well as **enantiopure forms**.



Solubility at physiological pH (7.4):

- **RBZ-Na** = **14.49** mg/mL⁻¹
 (versus **0.06** mg mL⁻¹ unsalified form)
- **TCBZ-SO-Na** = **19.30** mg/mL⁻¹
 (versus **<0.005** mg mL⁻¹ unsalified form)



Efficacy of **RBZ-Na** and its **enantiomers**



- Animal model with secondary infection of *E. granulosus s.s.*
- **Aim:** Quantify parasite mass reduction, and damage to the parasite



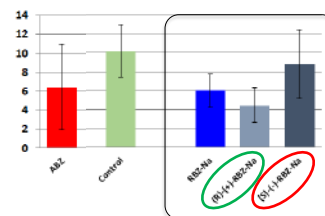
To be finalized!

Efficacy of the treatment


Compounds	Medium	Efficacy % ($\mu_c - \mu_i$) / $\mu_c \times 100$	
ABZ	DMSO	36.4*	
RBZ-Na	PBS	41,0*	Active
(R)-(+)-RBZ-Na	PBS	56,2*	Active
(S)-(-)-RBZ-Na	PBS	13,3	Inactive
Control	DMSO	-----	



- Statistical significance (P<0.05 ANOVA)

Weight of total cyst mass (in grams)



Results suggest a **therapeutic application of enantiopure forms of sulfoxides**


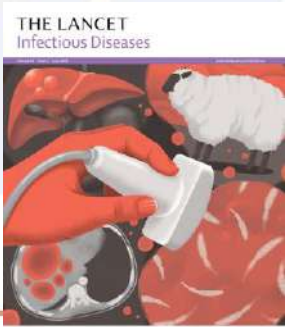
 **Prevalence of abdominal cystic echinococcosis in rural Bulgaria, Romania, and Turkey: a cross-sectional, ultrasound-based, population study from the HERACLES project**

Francesca Tamarozzi¹, Oksan Akhan², Carmen Michaela Cretu³, Kamenko Vitazov⁴, Devrim Altunç, Rossitza Chipeva, Turkmén Çiftçi, Cosma Marcello Constantiu, Massimo Febiani, Branimir Golemanov, Daria Janica, Patricia Albaladejo, Marlin Maitavere, Sora Ordon, Marius Potirnicu, Patricia Pezzetti, Alconeri Cosmin Popa, Loveliana Gabriela Popa, Mircea Ioan Popa, Valeriu Valea, Mar Tótes-Lucas, Enrico Brunetti, Adriano Fasella

- Biggest **cross-sectional study research-based** (ultrasound population surveys)
- Aiming to: estimate **%**, **cyst stage distribution**, **N of infected individuals**

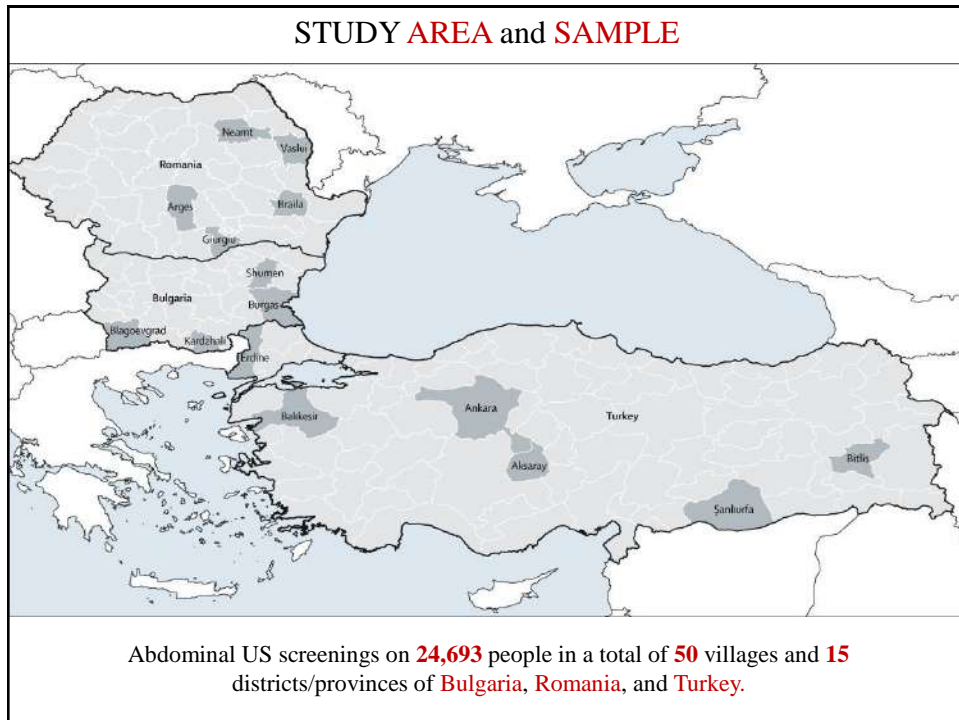
• First **original research** ever published by “THE LANCET Infectious Diseases” on echinococcosis

AREA, SAMPLE SELECTION and CASE DEFINITION

- Districts selected with **mid-range average annual hospital incidence** of CE;
- US by **convenience sampling**;
- **Consensus protocol & case definition/cyst staging** (WHO-IWGE);
- US lesions assessed by **2 sonographers** during screening;
- **Re-evaluation** by a core team.





US survey sessions, hosted in **community public structures**
(community hall, primary health-care centres, schools, mosques)





PUBLIC HEALTH EDUCATION CAMPAIGNS to 25,000 people and TRAINING to general practitioners and specialist physicians were provided during the US survey sessions.



Demographic characteristics of the study sample vs reference population

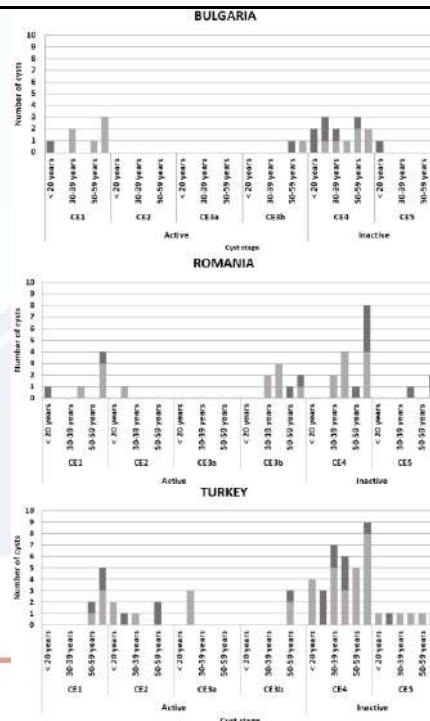
	Sample			Reference rural population, 2015		
	Women	Men	Total	Women	Men	Total
Bulgaria						
<20 years	927 (16.1%)	830 (29.0%)	1757 (20.4%)	165 258 (17.1%)	176 246 (18.4%)	341 504 (17.7%)
20-29 years	372 (6.5%)	190 (6.6%)	562 (6.5%)	92 267 (9.5%)	107 974 (11.3%)	200 241 (10.4%)
30-39 years	794 (13.8%)	301 (10.5%)	1095 (12.7%)	103 034 (10.6%)	122 412 (12.8%)	225 446 (11.7%)
40-49 years	1033 (18.0%)	334 (11.7%)	1367 (15.9%)	114 312 (11.8%)	133 987 (14.0%)	248 299 (12.9%)
50-59 years	1224 (21.3%)	484 (16.9%)	1708 (19.9%)	123 382 (12.7%)	137 727 (14.4%)	261 114 (13.6%)
≥60 years	1392 (24.2%)	721 (25.2%)	2113 (24.6%)	370 513 (38.2%)	279 485 (29.2%)	649 998 (33.7%)
Total	5742 (100%)	2860 (100%)	8602 (100%)	968 771 (100%)	957 831 (100%)	1 926 602 (100%)
Romania						
<20 years	993 (19.4%)	693 (29.7%)	1686 (22.6%)	1033 095 (22.6%)	1 094 626 (23.9%)	2 127 721 (23.3%)
20-29 years	398 (7.8%)	110 (4.7%)	508 (6.8%)	493 721 (10.8%)	584 333 (12.8%)	1 078 054 (11.8%)
30-39 years	656 (12.8%)	188 (8.1%)	844 (11.3%)	582 748 (12.8%)	645 339 (14.1%)	1 228 087 (13.4%)
40-49 years	844 (16.5%)	312 (13.4%)	1156 (15.5%)	599 120 (13.1%)	720 247 (15.8%)	1 319 367 (14.4%)
50-59 years	666 (13.0%)	315 (13.5%)	981 (13.1%)	490 349 (10.7%)	536 800 (11.7%)	1 027 149 (11.2%)
≥60 years	1569 (30.6%)	717 (30.7%)	2286 (30.6%)	1 366 271 (29.9%)	989 383 (21.6%)	2 355 654 (25.8%)
Total	5126 (100%)	2335 (100%)	7461 (100%)	4 565 304 (100%)	4 570 728 (100%)	9 136 032 (100%)
Turkey						
<20 years	1291 (26.9%)	1252 (33.8%)	2543 (29.5%)	3 038 126 (34.0%)	3 302 763 (35.7%)	6 340 889 (34.9%)
20-29 years	485 (10.1%)	322 (8.4%)	807 (9.4%)	1 178 004 (13.2%)	1 258 652 (14.0%)	2 436 656 (13.6%)
30-39 years	755 (15.7%)	534 (14.0%)	1289 (15.0%)	1 115 901 (12.5%)	1 168 183 (13.0%)	2 284 084 (12.8%)
40-49 years	758 (15.8%)	547 (14.3%)	1305 (15.1%)	1 036 607 (11.6%)	1 068 705 (11.9%)	2 105 312 (11.8%)
50-59 years	694 (14.5%)	514 (13.5%)	1208 (14.0%)	970 540 (10.9%)	946 874 (10.6%)	1 917 414 (10.7%)
≥60 years	816 (17.0%)	650 (17.0%)	1466 (17.0%)	1 584 716 (17.8%)	1 317 160 (14.7%)	2 901 876 (16.2%)
Total	4799 (100%)	3819 (100%)	8618 (100%)	8 923 894 (100%)	8 962 337 (100%)	17 886 231 (100%)

Table 1: Screened populations and reference rural populations, by sex and age group

Establishment of a prospective case retrieval system

Distribution of CE cyst stages by sex and age groups.

- Active cysts were found in people of all ages, including children, and in all investigated provinces.



Dark grey bars=males;
light grey bars=females.

Adjusted % of abdominal CE at national level

The crude % of CE infection was adjusted with direct standardisation by sex and age group by the 2015 country's rural population

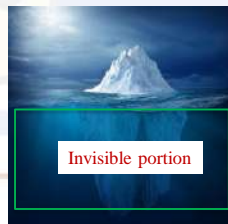


Cystic echinococcosis by imaging	
Bulgaria	
Abdominal cystic echinococcosis detected/ participants screened	31/8602
Crude prevalence	0.36% (0.26–0.50)
Standardised prevalence	
Reference Bulgarian rural population, 2015	0.41% (0.29–0.58)
Reference European population, 2013	0.39% (0.28–0.56)
Romania	
Abdominal cystic echinococcosis detected/ participants screened	35/7461
Crude prevalence	0.47% (0.28–0.79)
Standardised prevalence	
Reference Romanian rural population, 2015	0.41% (0.26–0.65)
Reference European population, 2013	0.42% (0.27–0.67)
Turkey	
Abdominal cystic echinococcosis detected/ participants screened	53/8618
Crude prevalence	0.61% (0.20–1.89)
Standardised prevalence	
Reference Turkish rural population, 2015	0.59% (0.19–1.85)
Reference European population, 2013	0.67% (0.21–2.13)

Conservative estimate of **number of individuals*** that may be affected with (abdominal) CE (in the rural population)

	BULGARIA	ROMANIA	TURKEY
	7,872 (5,520 - 11,220)	37,229 (23,405 - 59,166)	106,237 (33,829 - 330,751)
Active cysts	3,374 (1,398 - 8,129) [42,9%]	15,004 (8,432 - 26,683) [40,3%]	34,798 (17,505 - 69,109) [32,8%]
Inactive cysts	4,498 (2,395 - 8,439)	22,225 (11,180 - 44,132)	71,439 (15,941 - 316,737)

* estimated by multiplying the adjusted prevalence by the 2015 rural population;



TOP-DOWN dissemination (Bulgarian, Romanian, Turkish, English, Spanish, Italian)



TOP-DOWN dissemination

http://www.who.int/neglected_diseases/en/



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Diseases

Preventive chemotherapy and transmission control

Innovative and intensified disease management

Vector ecology and management

Neglected zoonotic diseases

Water, sanitation and hygiene

New approach needed to tackle parasitic liver disease in Europe and Turkey

31 August 2018 | Geneva — A cross-sectional study conducted in Bulgaria, Romania and Turkey has found that the true burden of cystic echinococcosis is poorly understood and that many cases remain asymptomatic, with no appropriate medical diagnosis and treatment. The study assessed the prevalence of the disease among rural populations in the three countries.

"This multicentre study provides, for the first time, the evidence of the number of people who are infected with echinococcosis that shows the real burden of this neglected parasitic infectious disease in the EU's European Region," said Dr Adriano Casulli, Director of WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis (in humans and animals). "It is important to introduce new health policies to prioritize its control in endemic rural areas."

Active abdominal cysts were found in participants from all three countries and across all age groups. Participants in whom cystic echinococcosis was diagnosed or suspected were referred to hospitals in the respective country for clinical management.

1 / 10

Human cystic Echinococcosis ReseArch in Central and Eastern Societies®

Related links

- Prevalence of abdominal cystic echinococcosis in rural Bulgaria, Romania, and Turkey: a cross-sectional, ultrasound-based, population study from the HERACLES project
- Tanizotoi F, Aikhan O, Cretu OM, Vitolina K, Ajmo D, Chipvas R, et al. Lancet Infect Dis, 2018; 18:769–78. doi: 10.1016/S1473-3099(18)30221-4.
- HERACLES project
- Human cystic Echinococcosis Research in Central and Eastern Societies
- Echinococcosis website

from SCIENCE to POLICY:

- “With the aim of improving surveillance of CE, we encourage international agencies (eg, **EFSA**, **ECDC**, and **WHO**) to lobby the **European Commission** to champion **new health policies** for the notification of human and animal CE”.



Funding is much appreciated but...
...real value lies in colleagues, friends and all the people contributing!

The state of the European Register of Cystic Echinococcosis 5 years after its inception



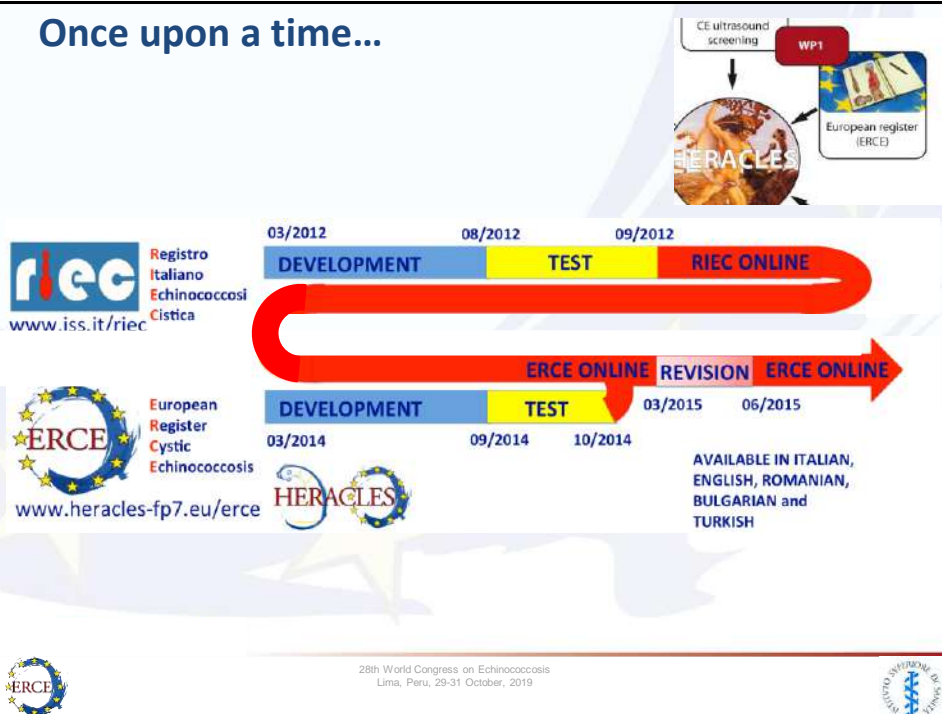
Francesca Tamarozzi DVM MD MSc PhD Microbiologist, Dipl SIUMB
Researcher

WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis
Foodborne and Neglected Parasitic Diseases Unit
Department of Infectious Diseases
ISTITUTO SUPERIORE di SANITÀ, Rome, ITALY
E-mail: francesca.tamarozzi@iss.it



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Lima, Peru, 29-31 October, 2019

Once upon a time...



UNDERREPORTING/ MISREPORTING

- Heterogeneous notification (incl. within Europe)
- Missing data of patients managed as outpatients
- Problems with data duplication
- No distinction between CE and AE
- No collection of clinical data



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Objectives

Questions

Data collected

- | | | |
|------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|--------------------------------------------|
| • To indicate the burden of CE in Europe | ▶ How many CE patients are seen in ERCE network centres? | ▶ ERCE code |
| • To bring the importance of CE to the attention of health authorities | ▶ Where do they come from? | ▶ Demographic info |
| • To encourage the planning and implementation of public health policies toward its management and control | ▶ How are they managed? (appropriateness and cost) | ▶ History |
| • To support biological, epidemiological and clinical research on CE | ▶ What is the natural and post-treatment evolution of cysts | ▶ Follow-up
▶ Cysts uniquely identified |

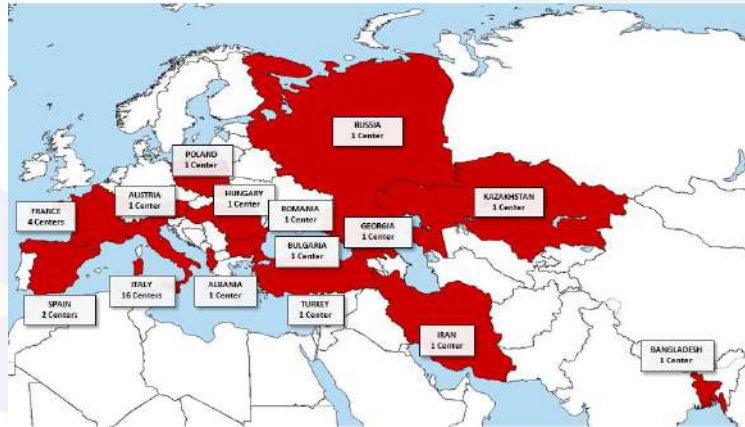


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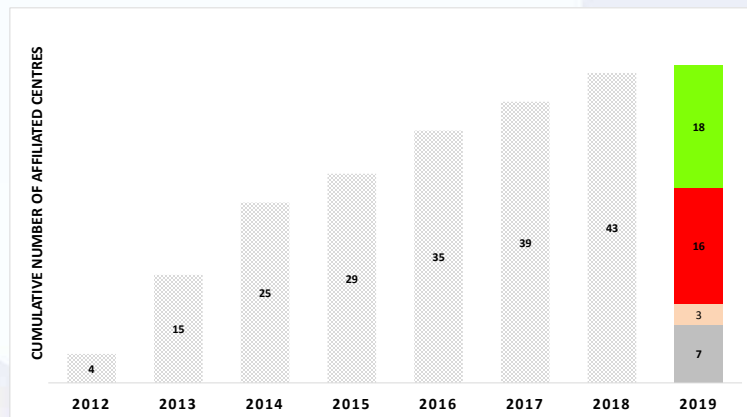


On March 31st 2019

44 affiliated centres (1 more from Afghanistan in the meantime)
 34 having registered at least 1 patient (map)
 15 Countries (7 extra-european)



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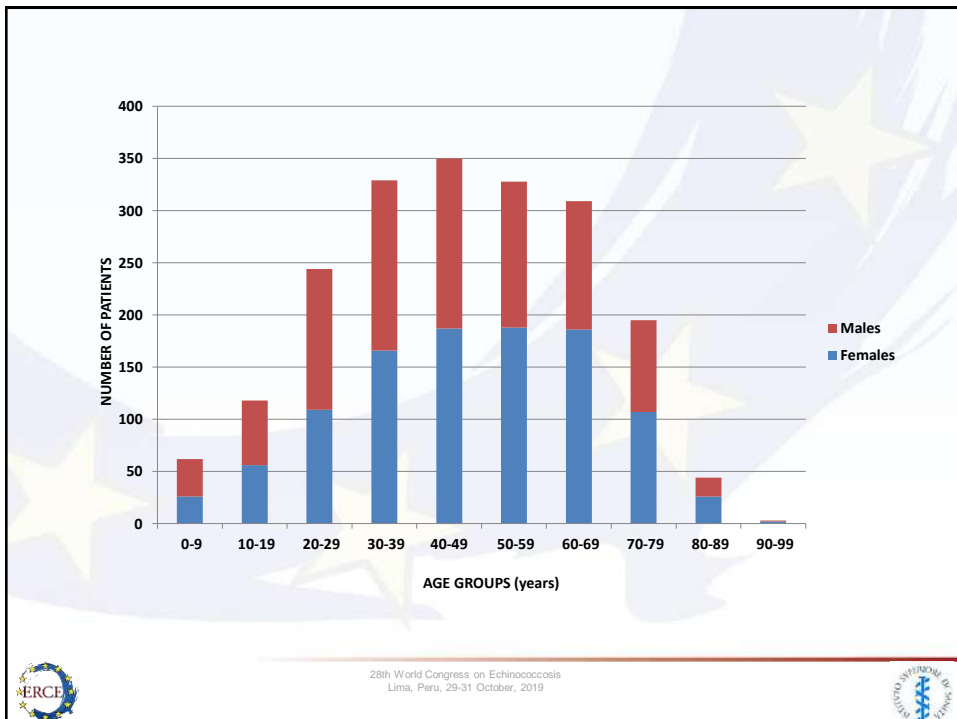
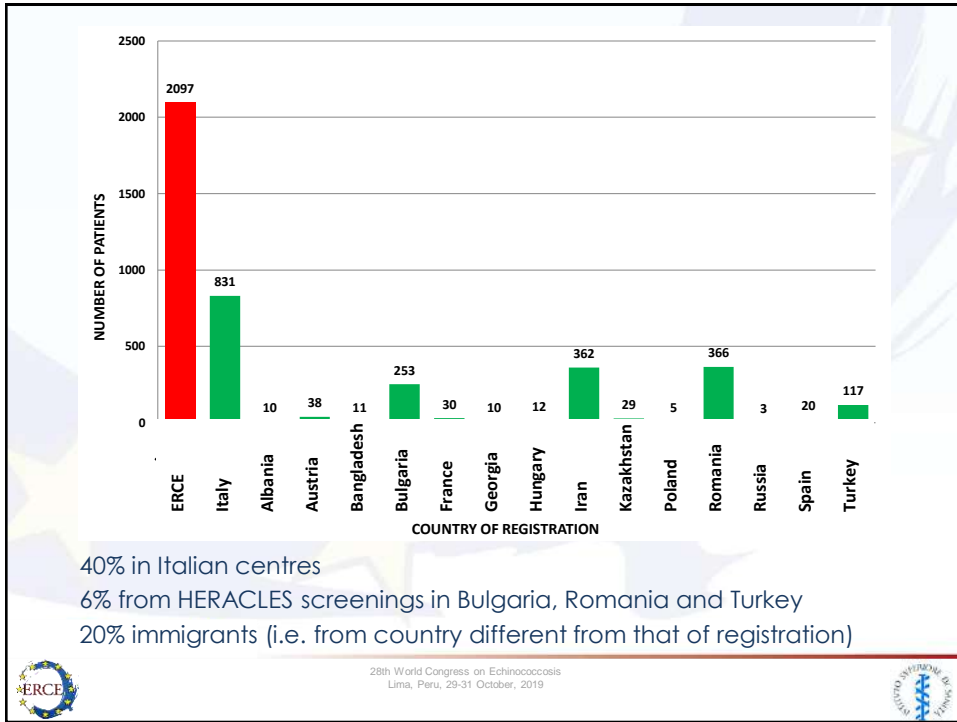


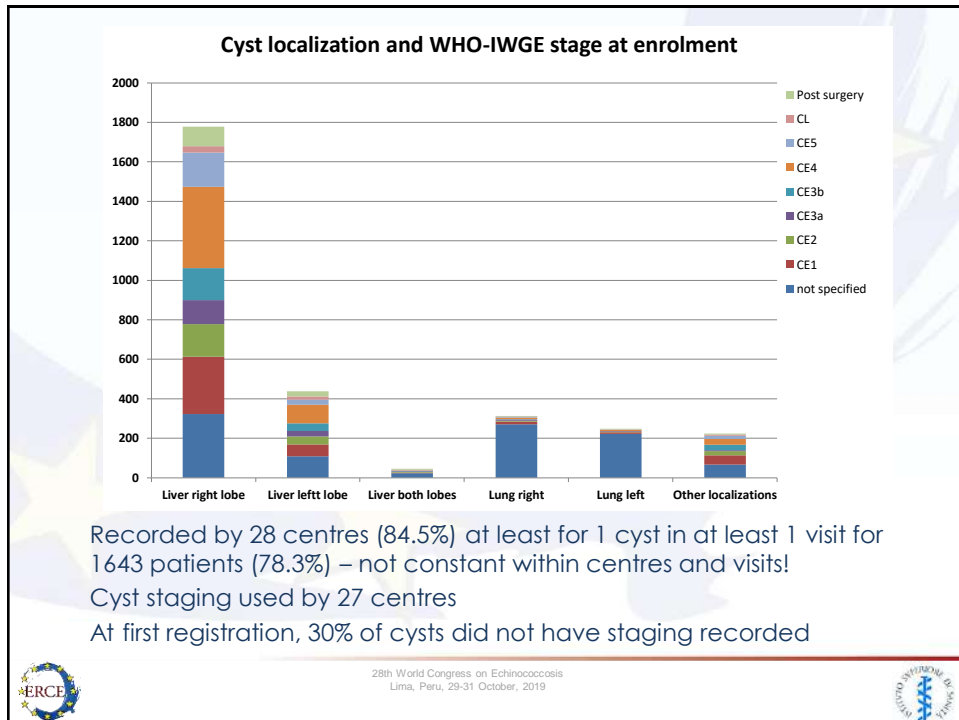
- never entered data
- affiliated but data entered by a national coordinating centre
- at least 1 patients recorded but no activity <18 months
- activity in <18 months



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STAGE	N *	ABZ**	Surgery with no specification of prophylaxis with ABZ	Surgery with specified associated prophylaxis with ABZ	Percutaneous treatment with no specification of prophylaxis with ABZ	Percutaneous treatment with specified associated prophylaxis with ABZ	Watch and Wait
CE1	159	66	35	19	12	25	2
CE2	100	41	22	21	0	15§	1
CE3a	94	41	5	6	2	11	29
CE3b	210	83	4	60	0	4	59
CE4-CE5	210	17*	2	14	0	0	177

17 centres (51.5%) recorded at least 1 follow-up visit for at least 1 patient
435 patients have at least 1 follow-up visit recorded (1.6%-84.2% pt/centre)

* ANALYSIS BY "CYST STAGE – LOCATION – MANAGEMENT OBSERVATION"
(N= 523 patients, 726 cysts, 920 OBSERVATIONS)
§ n=11 treated by modified percutaneous treatment ° n=4 treatment for other cysts

CAVEAT: no info about symptoms/complications or patient-specific conditions
1 Extra-European centre systematically no stage and all surgery (most w/o ABZ)

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Conclusions

New centres constantly joining
→ interest

Somehow complementarity
with hospital-derived data

Suitable starting platform for
prospective data collection to
overcome extreme difficulty of
clinical trials

Voluntary adhesion and filling

Difficult to compare with official
records

Variable, suboptimal (...) data
completeness and quality
(partly deriving from lack of
knowledge of staging and
stage-specific approach?)




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"AWARNESS AIM"

- Only number of patients with CE and basic demographic data
- High number of centres, wide geographical distribution
- Little time and effort

"CLINICAL AIM"

- Individuation of clinical questions and variables to address them
- Small number of highly committed centres
- Project-like commitment

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Patrizia ROSSI, Francesca TAMAROZZI, Fabio GALATI, Okan AKHAN, Carmen M CRETU, Kamena VUTOVA, Mar SILES-LUCAS, Enrico BRUNETTI, Adriano CASULLI, on behalf of the ERCE network*


*In alphabetical order: Andrea ANGHEBEN, Nikolay BAGMET, Moncef BELHASSEN, Solange BRESSON-HADNI, Fabrizio BRUSCHI, Guido CALLERI, Barbara CASTIGLIONI, Cathy CHEMLA, Leonardo CHIANURA, Balazs DEZSENYI, Maria Teresa GIORDANI, Valbona GJONI, Levan GOGICHAISHVILI, Delia GOLETTI, Majid HARANDI, Gulziya ISMAILOVA, Fazal KARIM, Emma LAPINI, Felix LÖTSCH, Scilla MASTRANDREA, Guido MENOZZI,, Andrè PAUGAM, Alfonso RECORDARE, Malgorzata SULIMA, Antonella TEGGI, Carlo TORTI, Giustina VITALE, Martine WALLON, Lorenzo ZAMMARCHI

Funding from the European Commission Seventh Framework Programme (FP7/2007-2013) under the project HERACLES, grant agreement n°[602051] and PERITAS project under the framework of EU-LAC Health (<http://eulachealth.eu/>) and Ministries of Health of participating countries



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The South American Initiative for the surveillance, control and prevention of Cystic Echinococcosis/Hidatidosis

Background

1999 – PAHO convenes a Working Group on “perspectives and possibilities for control and eradication of hydatid disease” in San Carlos de Bariloche, Argentina (International Congress of AIH/WAE). Among its main recommendations it’s included the elaboration of a Regional Project for control and elimination.

2001 – The Southern Cone Subregional Project for Control and Surveillance of Hydatidosis: Argentina, Brazil, Chile and Uruguay is part of the mandate that PAHO/WHO received from the Member States in the RIMSA XII, held in Sao Paulo, Brazil, in 2001.

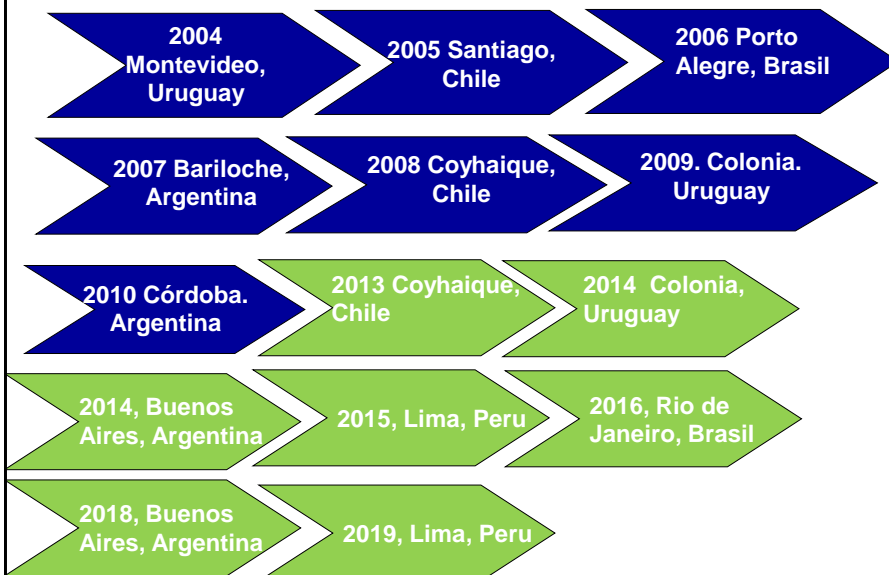
Background

2013 – Coyhaique, Chile, the Subregional Project is transformed ➤ into a South American Initiative for the control and Surveillance of EQ, incorporating new countries and neotropical echinococcosis.

Actuality including ARGENTINA, BRASIL, CHILE, PARAGUAY, ➤ PERU AND URUGUAY



Annual Meetings of the Initiative



ACTIVITIES: Projects TCC

“Prevention and control of Hydatid disease in Peru”. Uruguay - Perú. 2007.


“Strengthening of international cooperation and technical exchange” Perú – Uruguay 2010”.

“Integrated Plan for prevention and control of cystic echinococcosis in the border area Brazil – Uruguay” .

“Elimination of the Hydatid Disease in Tierra del Fuego” Argentina - Chile. 2007/2008.

“Plan for prevention and control of Hydatid disease in Tupiza, Bolivia” Bolivia - Uruguay.

ACTIVITIES . Surveillance (anual epi report)



PANAFTOSA
Salud Pública Veterinaria

Informe Equinocosis - N° 1 - Septiembre de 2015
EQUINOCOCOSIS


Informe Epidemiológico en la Región de América del Sur - 2009-2014

Informe producido por los representantes de la "Iniciativa para el control de la Equinocosis quística: Argentina, Brasil, Chile, Perú y Uruguay".

SUMARIO EJECUTIVO

OBJETIVO DEL INFORME

El presente es el primer informe epidemiológico de la situación de la EQ en los países miembros de la Iniciativa para el control de la EQ en América del Sur (la "Iniciativa"). Por ser el primer informe, el documento recoge datos históricos para la base que permita comparaciones e presenta va desde Enero del 2009



PANAFTOSA
Salud Pública Veterinaria

Informe Equinocosis - N° 3 - Marzo 2019
EQUINOCOCOSIS

Informe Epidemiológico en la Región de América del Sur -2016-2017

SUMARIO EJECUTIVO


La Iniciativa Sudamericana para el Control y Vigilancia de la Equinocosis Quística/Hidatidosis expresa la importancia de los esfuerzos que los países están prestando a esta enfermedad zoonótica, a través del grupo de profesionales y académicos de Argentina, Brasil, Chile, Paraguay, Perú y Uruguay, bajo la secretaría técnica del Centro Panamericano de Fiebre Alta y Salud Pública Veterinaria de la Organización Panamericana de Salud/ Organización Mundial de Salud (PANAFTOSA-OPS/OMS), y tiene como principal objetivo la preparación de estrategias y

INTRODUCCIÓN


La Equinocosis quística (EQ) es causada por el Echinococcus granulosus (EG), helmineto cestodo adaptado a los animales carnívoros y herbívoros. El ciclo de transmisión del parásito se encuentra en la figura 1.

Brevemente, el EG requiere dos hospederos mamíferos para completar su ciclo de vida: un hospedero definitivo (carnívoro, especialmente el perro) donde se desarrolla la fase adulta y un hospedero intermediario (ovinos, caprinos, cerdos, bovinos, guanacos, etc.), donde se desarrolla la fase larvaria (quistes hidatídicos).

El ciclo se cierra cuando los carnívoros se alimentan de las vísceras de lo hospedero intermediario. Esto ocurre típicamente a través del

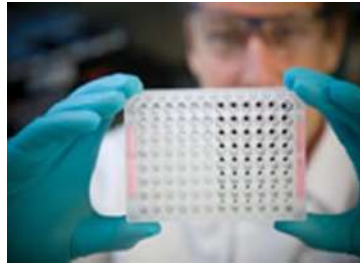


can
Organization



ACTIVITIES: Laboratory

- **Laboratory working group**
 - Strengthening laboratory capacities
 - Training in INSP Chile (Peru; Argentina)
 - Ensure and maintain quality
 - Protocols evaluation/comparison
 - Communication and network
 - Collaboration



ACTIVITIES: Evaluation program (Uruguay)

- **Held during September 2016**
- **International Experts; Government representatives; PAHO/PANAFTOSA**
- **Major conclusion: Successful program – Uruguay's National Zoonosis Commission – Most Advanced**
- **CE/H is controlled in some specific areas**
- **For elimination some recommendations:**
 - Assurance of the financial and human resources
 - Maintenance of the dosage lines
 - Intensification of US surveillance (kids 6-14)
 - Intensification of surveillance in dogs
 - Intensification of surveillance in the sheep
 - Information management robust database
 - Maintenance of the excellent component of education and health communication



ACTIVITIES: Training (Course)

- On line course on epidemiology and control of CE Duration 1 year (First 2014, Second 2016).
- More than 30 conferences of experts on different topics.
- Participation of 7 Universities of 4 countries: Argentina, Brazil, Peru and Uruguay.



PREVENCIÓN Y CONTROL DE LA
HIDATIDOSIS
EN EL NIVEL LOCAL

INICIATIVA SUDAMERICANA PARA EL CONTROL Y VIGILANCIA DE LA
EQUINOCOCOSIS QUÍSTICA/HIDATIDOSIS



ACTIVITIES: Training (Guideline)



Special report

Cystic echinococcosis in South America:
a call for action

Carlos F. Pavletic,¹ Edmundo Larrieu,² Eduardo A. Guamera,³ Natalia Casas,⁴ Pilar Irabedra,⁵ Ciro Ferreira,⁵ Julio Sayes,⁵ Cesar M. Gavidia,⁶ Eduardo Caldas,⁷ Michael Laurence Zini Lise,⁷ Melody Maxwell,⁸ Marcos Arezo,⁹ Ana María Navarro,¹⁰ Marco A. N. Vigilato,¹¹ Ottorino Cosivi,¹¹ Marcos Espinal,¹¹ and Victor J. Del Rio Vilas¹¹

Suggested citation

Pavletic CF, Larrieu E, Guamera EA, Casas N, Irabedra P, Ferreira C, et al. South America: a call for action. Rev Panam Salud Publica. 2017;41:e42.

ABSTRACT

Cystic echinococcosis (CE) or *hidatidosis*, a parasitic zoonosis caused *Taeniidae*, species *Echinococcus granulosus*, is endemic in Argentina and southern Brazil. This report presents CE figures for these five countries proposes indicators to measure national control programs.

Nearly 5 000 new CE cases were diagnosed annually in the five countries. The average case fatality rate was 2.9%, which suggests that CE led to app

Map of South America showing the prevalence of Cystic echinococcosis (CE) by country. The map is color-coded by prevalence ranges: 0-0.05, 0.05-0.10, 0.10-0.15, 0.15-0.20, 0.20-0.25, 0.25-0.30, 0.30-0.35, 0.35-0.40, 0.40-0.45, 0.45-0.50, 0.50-0.55, 0.55-0.60, 0.60-0.65, 0.65-0.70, 0.70-0.75, 0.75-0.80, 0.80-0.85, 0.85-0.90, 0.90-0.95, 0.95-1.00. The map also shows the distribution of CE cases by country: Argentina, Brazil, Chile, Colombia, Ecuador, Peru, Uruguay, Venezuela, and Suriname.

THE LAST PAPER

First inter-laboratory comparison exercise in Latin America
for the diagnosis of *Echinococcus granulosus* sensu lato in
dog faeces

Journal:	Revista Panamericana de Salud Pública/Pan American Journal of Public Health
Manuscript ID:	2018-01075.R1
Manuscript Type:	Original Research
DeCS Keywords	<p>At the bottom of this page, you will be required to confirm that the words you provide here conform to the DeCS standards outlined at DeCS (http://decs.bvs.br target=_new>http://decs.bvs.br)</p> <p>echinococcosis, dogs, Polymerase Chain Reaction, enzyme immune assay, South America</p>
Language:	English
Subject List:	Diagnostic techniques/Técnicas de diagnóstico, Veterinary health/Salud veterinaria, Disease surveillance/Vigilancia epidemiológica

SCHOLARONE[™]
Manuscripts

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ACTION PLAN. THE LAST EFFORT

**PLAN DE ACCION PARA FORTALECER LA
VIGILANCIA Y EL CONTROL DE LA HIDATIDOSIS /
EQUINOCOCCOSIS QUISTICA**

2019/2023

**ORGANIZACIÓN PANAMERICANA DE LA SALUD
CENTRO PANAMERICANO DE FIEBRE AFTOSA**

ACTION PLAN. THE LAST EFFORT

**PLAN DE ACCION PARA FORTALECER LA
VIGILANCIA Y EL CONTROL DE LA HIDATIDOSIS /
EQUINOCOCCOSIS QUISTICA**

- Grupo de puntos focales oficiales de los países, responsables por las decisiones referentes al Programa Regional
- Secretaria de Panaftosa
- Grupo consultivo y propositivo (Universidades, expertos)

OBJETIVO	INDICADOR	META 2022
EJECUTAR EL MANEJO DE CASOS DE EQ	Número de países que han ejecutado tamizajes con pruebas sensibles serológicas o ultrasonográficas para EQ Número de países que monitorean y caracterizan el tratamiento de personas sometidas a tamizajes de EQ	7 7
FORTALECER LA PREVENCIÓN DE EQ MEDIANTE EL CONCEPTO DE UNA SALUD	Número de países con endemidad que tienen capacidad y procesos establecidos para controlar o eliminar la EQ mediante un enfoque de salud pública veterinaria y “Una salud”	7
FORTALECER LA COORDINACIÓN TRANSFRONTERIZA PARA LA VIGILANCIA Y CONTROL DE EQ	Número de países con endemidad que colaboran para fortalecer la vigilancia transfronteriza de fuentes animales de EQ	7
ELABORAR Y EJECUTAR MEDIDAS PARA ALCANZAR EL CONTROL Y ELIMINACIÓN DE EQ	Número de países con EQ que han alcanzado las metas de eliminación y han implantado medidas para prevenir el resurgimiento o la reintroducción	3

Reforzar los sistemas de vigilancia epidemiológica

Caracterizar epidemiológicamente las ares endémicas de cada país. Definición de escenarios. Estimación de las poblaciones en riesgo por las autoridades nacionales de cada país

Definir flujos de información desde los niveles locales hasta su consolidación regional

Analizar la información. Producir informes epidemiológicos anuales consolidados desde PANAFTOSA/OPS/OMS

Desarrollar sistemas automatizados de información para la notificación de los países a PANAFTOSA/OPS/OMS

Desarrollar redes de laboratorio regional y de los países en base a los Laboratorios Nacionales Oficiales

Evaluar técnicas disponibles. Ensayos Inter laboratorios coordinados por

PANAFTOSA/OPS/OMS incluyendo laboratorios nacionales y de laboratorios de la red nacional

Armonizar técnicas seroepidemiológica en el diagnóstico de la hidatidosis humana y animal para facilitar la comparación y análisis de resultados

Evaluar el impacto y factibilidad de nuevas estrategias de control

Evaluar programas nacionales y regionales de hidatidosis

Mejorar las capacidades de diagnóstico precoz y tratamiento

Adecuar los programas de educación sanitaria

Propender a la cooperación técnica internacional.

Intercambios y capacitación de profesionales

Thank you! Gracias! Merci!



Development of **New Diagnostic and Treatment Options** for Helminthic **Neglected Diseases**

NDTND



Adriano Casulli

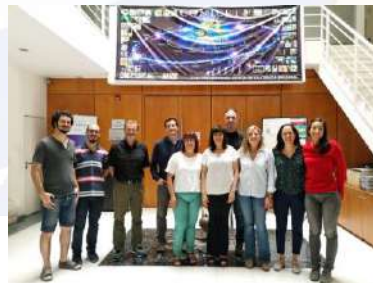


- WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis;
 - European Union Reference Laboratory for Parasites (EURLP),
- Department of Infectious Diseases, Istituto Superiore di Sanità (Rome, Italy)

4 countries involved:



- Facultad de Ciencias, Udelar, **URUGUAY**: Estela Castillo, Uriel Koziol
- Facultades de Medicina, UNLP y UBA, **ARGENTINA**: Betina Córscico, **Mara Rosenzvit (coordinator)**
- University of Würzburg, **GERMANY**: Klaus Brehm
- Istituto Superiore di Sanità, **ITALY**: Adriano Casulli
- San Matteo Hospital Foundation, **ITALY**: Enrico Brunetti

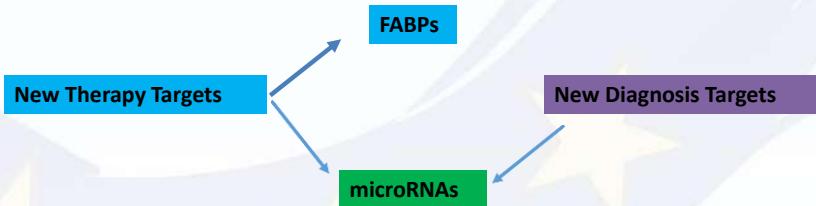


Starting date: November, 2017
Ending date: November, 2020

Goals

- **Goal 1:** Evaluate **Fatty acid-binding proteins (FABPs)** as **drug targets** for tapeworm diseases
- **Goal 2:** Evaluate **miRNAs** as **therapeutic targets** for tapeworm diseases
- **Goal 3:** Evaluate **miRNAs** and other small RNAs as **biomarkers** of CE and AE

IN PROGRESS



NDTND project **aims** at developing **new compounds** that bind and inhibit essential and unique molecules of these parasites, and to find **new detection tools** to improve the status of both treatment and early diagnosis of helminthic NTDs (CE and AE).

Ultrasound screenings for cystic echinococcosis:

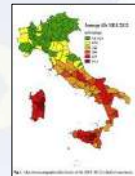
ITALY



Provinces in **Sardinia** region: **Nuoro** and **Oristano**
562 people screened by ultrasound




Province in **Calabria** region: **Catanzaro**
2,712 people screened by ultrasound



Ultrasound screenings for cystic echinococcosis:


ALBANIA




MAIN OBJECTIVES:

1. To generate data on the **prevalence of CE** in target rural areas of estimated mid-endemicity in **Albania**;
2. To estimate the **number of people affected by CE** in rural **Albania**.

Expected field work:
3 areas of mid-prevalence in the country, with a total of **4,500** people screened by ultrasound.




IN PROGRESS

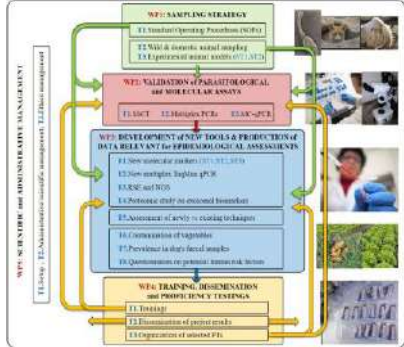


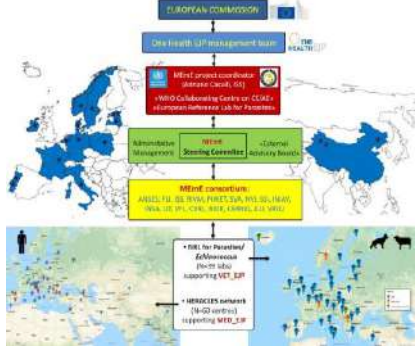
Multi-centre study on *Echinococcus multilocularis* and *Echinococcus granulosus* s.l. in Europe: development and harmonization of diagnostic methods in the food chain (MEmE)

MEmE:

Composition: 17 partners from Europe and Asia
Timing: January 2020 - June 2022
Funding: 2.496.126 € for European partners







Project funded by the European Commission under One Health European Joint Programme (Horizon 2020)

PERITAS

“MOLECULAR EPIDEMIOLOGICAL STUDIES on PATHWAYS of TRANSMISSION and LONG LASTING CAPACITY BUILDING to PREVENT CYSTIC ECHINOCOCCOSIS INFECTION”

Adriano Casulli

HERACLES - European Reference Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis;
 • European Union Reference Laboratory for Parasites (EURLP),
 Department of Infectious Diseases, Istituto Superiore di Sanità (Rome, Italy)

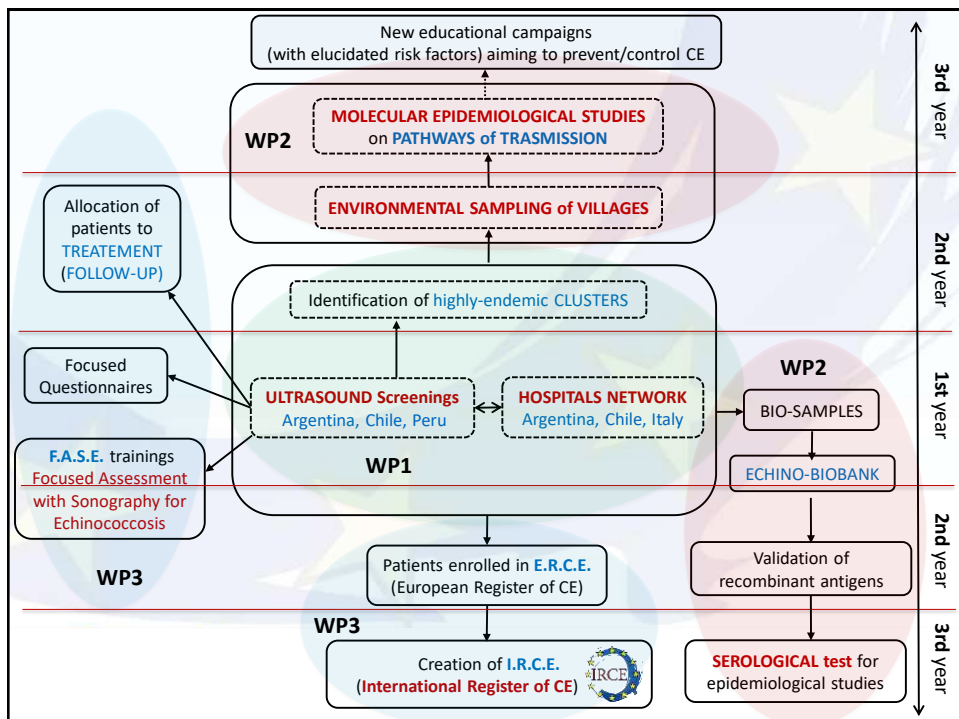
PARTNERS

- **ITALY** - Istituto Superiore di Sanita' - Adriano Casulli (coordinator)
- **SPAIN** - Agencia Estatal Consejo Superior de Investigaciones Científicas - Mar Siles-Lucas
- **SPAIN** - Instituto de Salud Carlos III - Maria Jesus Perteguer Prieto
- **CHILE** - Universidad Austral de Chile - Gerardo Acosta
- **ARGENTINA** - National University of Rio Negro - Edmundo Larrieu (Leonardo Uchiumi)
- **PERU** - Universidad Peruana Cayetano Heredia - Saul Santivanez

5 countries; 6 Institutes; 3y duration; Total project cost: 1.083.580 €.

PERITAS

was Alexander the Great's favorite dog, who accompanied him during his military exploits.



What is PERITAS:

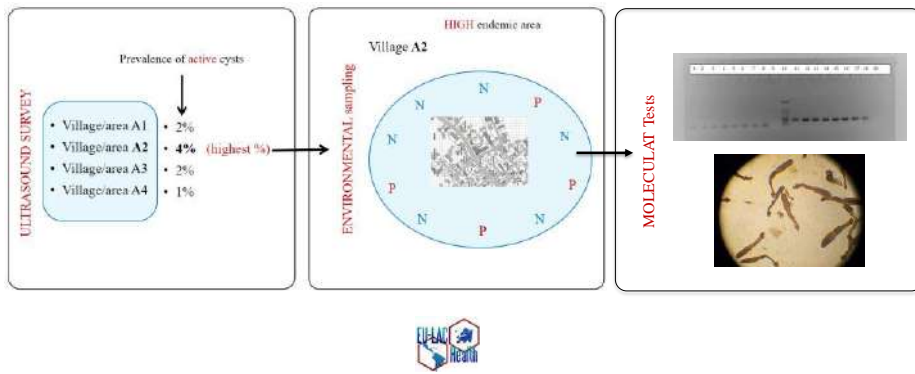
- **STAGE_1: CROSS-SECTIONAL**

Ultrasound-based population surveys for endemic CE cluster identification.

- **STAGE_2: CASE-CONTROL**

Village-based study for environmental sampling.

STAGE_3: Double blind MOLECULAR TESTS



STEP 1: ULTRASOUND POPULATION SCREENINGS

CROSS-SECTIONAL study (2019)

- To individuate villages/areas with high prevalence of abdominal active CE.
- Administration of risk factors questionnaire targeting hand-to-mouth habits.

- ✓ **Chile** → 2,435 screened in **Coquimbo**
- ✓ **Argentina** → 581 screened in **Rio Negro**
- ✓ **Peru** → 790 screened in **Junin**



STEP 2: ENVIRONMENTAL SAMPLING of MATRICES

CASE-CONTROL study (2019-2020)

- To individuate and compare matrices contaminated by *E. granulosus s.l.* eggs in **cases and controls households** and in **common areas**

VILLAGE**HOUSEHOLDS**

(5 CE positives and 15 negatives)
Judgmental sampling

COMMON AREAS

(3 sites per village)
(Town square; Main Park; Outdoor market)

• **MATRICES:**

Family shoes; Own dog faeces; Own dog fur;
Self-grown vegetables; Soil

• **MATRICES:**

Soil; Dispersed dog faecal samples; Market
sold vegetables; Flies

STEP 3: MICROSCOPY and MOLECULAR ANALYSIS

DOUBLE-BLIND TESTS (2020-21)

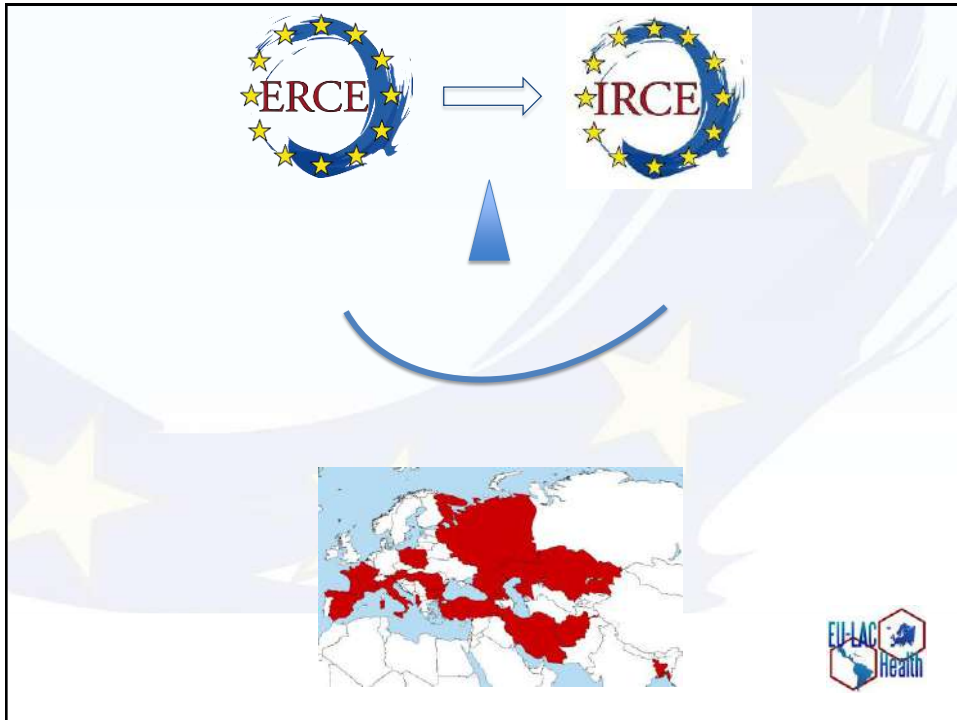
MATRICES:

- Soil
- Shoes soles
- Dog's feces
- Dog's fur
- Lettuce
- Flies

**PROCEDURES:**

1. Protocols
2. Training
3. Recovery tests
4. Analysis
 - Sample enrichment;
 - Eggs isolation;
 - DNA extraction;
 - PCR amplification.





Main RESEARCH QUESTIONS to be answered:

- There is any correlation between environmental contamination and human infections?
- Which are the main matrices contaminated by *E. granulosus s.l.* eggs?
- Which are the at-risk behaviours/habits associated with odds of CE infection?

