### Key considerations on implementation, monitoring, evaluation of echinococcosis control actions

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Principal Echinococcus species infecting humans						
Globally						
Species		Most important intermediate hosts	Definitive hosts			
E. granulosus	88	sheep	Domestic dog			
E. canadensis G6 G7	11	camels (goats S Am) pigs	Domestic dog			
E. multilocularis	<1*	Voles	Fox, wolves, domestic dog			

















	How frequently does dog dosing need to be to be? <ul> <li>Depends on what other control measures are able to be undertaken <u>effectively</u></li> </ul>					
	Location	Interval between dog dosing	Other control measures implemented effectively	Time to reach control		
	Uruguay	30 days	-	10 years		
	Rio Negro, Argentina	3 months	-	30 years		
	Rio Chico, Argentina	3 months	Sheep vaccination	8 years		
	Tierra del Fuego	6 months	Slaughter control Dog control	30 years		

#### • Frequently expressed difficulties with CE control:

- 1. Cannot prevent home slaughter
- 2. People will not dispose of offal safely
- 3. Cannot control stray/feral dogs
- 4. Cannot dose dogs reliably/frequently

None of these things are a problem if livestock are vaccinated and not infected

#### The EG95 Vaccine for Livestock

- There is only one type of vaccine
- It utilizes a recombinant antigen created in Australia and expressed in bacteria via a plasmid constructed in Australia
- Material was sent from Australia to New Zealand where the first animal trials were undertaken
- Subsequently many trials have been undertaken in New Zealand, Australia and numerous other countries
- Initially vaccine was produced both in Australia and in New Zealand
- The vaccine was licensed by AgResearch (NZ) and the University of Melbourne, equally, for commercial production in China
- For the past >10 years the vaccine has been available from Chongquing Auleon Biologicals (China), Tecnovax (Argentina) and the University of Melbourne
- All produce vaccine containing the same EG95 antigen

## Monitoring the effectiveness of a control program

- 1. Diagnosis of infection in dogs
- 2. Diagnosis of infection in livestock
- 3. Diagnosis of infection in children



#### 2. Diagnosis of infection in livestock

- Only possible at necropsy
- Only effective in animals ≥2 years of age
- Highly specific



### Cautionary note:

Care must be taken to monitor control programs using tests that have high <u>specificity</u>

Reason:

Because all false positives in a monitoring test will be interpreted as failures of the control program

#### Do NOT use serology for diagnosis of CE in animals

NONE of the tests that have published good results for specificity have been evaluated adequately... just because claims are published does not make them true (unfortunately).



















## Control programme Kyrgyzstan

P. R. Torgerson University of Zurich

# Is it Worth Controlling?

- Burden of Diseases
- Globally
- Locally



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# Burden of Cystic Echinococcosis Zürich Kyrgyzstan

- 1000-2000 surgical cases
- \$1000 or more per case treatment costs
- >>\$1,000,000 per year
- 3000 DALYs per year
- Including non treatment seeking, loss of employment etc
- \$2,000,000 per annum



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# Burden of Zoonoses

## Kyrgystan 2013





Brucellosis CE AE Rabies 2500 new cases / year 1200 new cases / year 200 new cases/year 1-10 cases/year

Tuberculosis HIV positive 6000 new cases/ year 700 new cases/ year



## Animal Disease Costs

- The hidden costs
- Reduction in meat production
- Reduction in lamb production
- 5-10%
- \$5.5 million per annum



## Economic costs Universität Zürich Can you afford not to control?

- \$2 million plus human illness
- \$5,5 million animal health
- 2%-4% human mortality in treated cases
  - 20-40 fatalities
- ? Mortality in untreated cases

## Cystic Echinococcosis Kyrgyzstan Sheep – pre control



The prevalence and abundance of hydatid cysts and abundance of protoscoleces stratified according to age for sheep !

Age (years)	Number sheep	Number infected	% Sheep infected (exact binomial confidence intervals)	
1	205	92	44.9 (37.9-52.0)	
2	264	140	53.0 (46.8–59.2) 58.9 (52.9–64.8) 82.5 (76.2–87.6)	
3	280	165		
4	188	155		
5	95	93	97.9 (92.6-99.7)	
≥6	49	49	100 (92.8-100)	
Mean across all age groups 1081		694	64.2 (61.3-67.1)	





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## Echinococcosis Kyrgyzstan Dogs-pre control



	Arecoline purgation Sensitivity for intestinal stages	PCR True prevalence		e		
		Sensitivity for eggs in faeces	Specificity	Total	Restrained dogs: hunting type, non-hunting type	Free-roaming dogs: hunting type, non-hunting type
Echinococcus granulosus	38% (27–50%)	78% (57–87%)	93% (88–96%)	19% (15–25%)		
Echinococcus multilocularis	21% (11–34%)	50% (29–72%)	100% (97–100%)	18% (12–30%)	11% (6–29%)	26% (17-44%)
					30% (14–56%), 9.4% (5–19%)	44% (25–69%), 24% (16–42%)

## Control of Echinococcosis<sup>universität Zürich</sup> Tools available

- Treatment of dogs praziquantel
- Control of dogs
- Control of animal slaughter
- Vaccination of sheep
- Education

## Control of Echinococcosis<sup>Universität Zürich</sup> Dogs



## Control of Echinococcosis<sup>Universität Zürich</sup> Integrated Control

- Treat dogs
- Vaccinate sheep
- Control of slaughter
- Control old sheep
- Education

- Praziquantel
- 100% effective against Echinococcus spp
- Dogs become reinfected after treatment
- Repeat treatments
- Frequency depends on how quickly they become reinfected
- Recommend x 4 per year
- Coincide with slaughter of animals
  - Autumn

## Control of Echinococcosis<sup>Universität Zürich</sup> Dogs

- 700,000 1 million dogs in Kyrgyzstan
- 4 million pills per year!
- Treat at least 70% of dogs
- Recommend licensing dogs
  - "Dog tax"
  - In some countries this pays for the programme
- Cull stray or unwanted dogs

## Control of Echinococcosis<sup>Universität Zürich</sup> Control of Animal Slaughter

- All sheep should be slaughtered in a proscribed place
- Veterinary supervision of slaughter
- Condemn and destroy infected offal
- Particular care of old sheep!

## Control of Echinococcosis<sup>Universität Zürich</sup> Control of Animal Slaughter

- Problems
- Lack of slaughter facilities
- Costs
- Culture





## Control of Echinococcosis<sup>Iniversität Zürich</sup> Vaccination of Sheep

- EG95 vaccine
- 99% protection in sheep
- Available in China
- No cysts in sheep
- No Echinococcus in dogs
- No hydatid disease in humans

## Control of Echinococcosis<sup>Universität Zürich</sup> Vaccination of Sheep

- EG95 vaccine
- Needs to be licensed in Central Asian Countries
  - Eurasian union
- May also benefit the health of the sheep
  - "Sub clinical" disease
  - Improves productivity
- May be combined with other vaccination programmes
  - Brucellosis
  - Clostridial diseases

## Control of Echinococcosis<sup>universität Zürich</sup> Education







- Needs a sustained and prolonged control effort
- Decades not years
- Commitment from Government
- Legislation to enforce
- In Kyrgyz Republic
- \$2 million- \$3 million
- Prevents \$8 million- \$10 million losses

- In Kyrgyz Republic
- \$2 million- \$3 million per annum investment
- Prevents \$8 million \$10 million losses
- Reduce from 800-1000 cases per year to 100 or less
- <\$20 per DALY averted</p>
- Highly cost effective

- In Kyrgyz Republic
- We have the tools
- It should be cost effective
- Programmes are underway
## Control of Echinococcosis

- Registration of dogs
  - Dog passport
  - Ear tattoos
- Dogs treated x 4 per year
  - Village and district vets are provided with praziquantel
  - Supervise treatment
  - Passport signed
- Destruction of stray dogs
- Surveillance of dogs
- Surveillance in livestock / abbatoirs
- Education programme
- Human surveillance
  - Notifiable disease



## Dog Treatments Kyrgyzstan

	Dehelmintization of dogs a	nd cats 2017					
Name of rayon	Наименование регионов	План за 2017 год/Plan for 2017			Фактически обработанных за 2017 год/Have been treated 2017		
		собаки/dogs	кошки/cats	всего/total	собаки/dogs	кошки/cats	всего/total
		Batke	n oblast				
Batken	Баткенский	14,000		14,000	14,321	0	14,321
Kadamzhai	Кадамжайский	25,000		25,000	27,687	0	27,687
Leilek	Лейлекский	22,000		22,000	19,356	31	19,387
TOTAL	Итого по области:	61,000	0	61,000	61,364	31	61,395
•		Osh	oblast	•	•		
Alai	Алайский	19,964		19,964	16,442	0	16,442
Aravan	Араванский	25,000		25,000	23,987	0	23,987
Chon-Alai	Чон-Алайский	4,652		4,652	4,565	20	4,585
Kara-Kuldzha	Кара-Кульджинский	30,000		30,000	27,936	249	28,185
Kara-Suu	Кара-Суйский	72,000		72,000	52,231	11,592	63,823
Nookat	Ноокатский	18,000	20,000	38,000	18,169	4,993	23,162
Uzgen	Узгенский	78,400		78,400	76,485	0	76,485
TOTAL	Итого по области:	248,016	20,000	268,016	219,815	16,854	236,669

## Human Surveillance Universität Zürich

Table 1. The total numbers of cases and the annual incidence of CE and AE per 100,000 reported by district in Osh Oblast in 2013 (CIs, 95% confidence intervals).

District	CE	Incidence (CIs)	AE	Incidence
Aravan	0	0 (0-3.6)	0	0 (0-3.6)
Uzgen	34	17(11.5-23.7)	0	0(0-1.8)
Kara-Kulija	9	10(4.7 - 19.5)	3	3.4(0.7-10.0)
Nookat	36	17(11.4 - 22.1)	2	0.9(0.1-3.1)
Kara-Suu	65	20 (15.3-25.2)	5	1.6(0.5 - 3.5)
Alay	11	15(7.6-27.3)	42	58 (42-79)
Chon-Alay	0	0(0-15.8)	8	34 (14-66)
Total	155	16 (13.2–18.1)	60	6.0 (4.5-7.7)



## Animal Surveillance

- Dogs
  - Coproscopy data
- Sheep
  - Abattoir data







№ Ылацлын аталышы		Күнү	Иттин салмагы	Колдонулган дары	
2	AXMOKOK Yuur	10/09-1	30	15 E I	
2	XILLER	-4-	40	Azurone Burn	
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## Control of Echinococcosis

- Registration of dogs
  - Many dogs remain unregistered
  - Dog population uncertain
- Dogs treated x 4 per year
  - If dogs are registered, treatment regime is not adhered to
  - Veterinary services problem
  - Vets give out tablets rather than treating the dogs
- Destruction of stray dogs
  - No auditing if this takes place
- Surveillance of dogs
  - 10-20% of dogs remain taeniid egg positive despite "treatment"
  - Poor data collection
- Surveillance in livestock / abattoir
  - Poor data collection, few abattoirs
- Education programme
- Human surveillance
  - Very efficient system

## Control of Echinococcosis

- Registration of dogs
  - Improved system required
- Dogs treated x 4 per year
  - Vet teams to treat entire district or villages at set times
- Destruction of stray dogs
  - Rabies outbreaks results in complete clearance of dogs from district
  - It is possible
- Surveillance in livestock / abattoir
  - More abattoir facilities
  - Ban home slaughter
- Dog surveillance
  - Simple coproscopy taeniid egg prevalence
- Introduce vaccination of sheep



#### **OIE PVS EVALUATION FOLLOW-UP**

#### **REPORT OF THE**

#### VETERINARY SERVICES OF

#### **KYRGYZ REPUBLIC**

#### February 1<sup>st</sup> – 12<sup>th</sup>, 2016

• systematic tattoo and passport for all dogs, useless for current phase of diseases control;

• deworming of dogs 4 times a year with the intention to cover the parasitic cycle is unrealistic;



## **Control of Alveolar Echinococcosis**



Wildlife cycle



### Transmission AE -Kyrgyzstan



#### Foxes 65%

#### **Альвеококкоз**





















## Male patient 19 yrs old

- Presents to local hospital
- Initial complaints: pain in the right kidney area
- Imaging reveled extensive AE involvement of both liver lobes, no jaundice, no liver failure
- Considered inoperable
- Referred for living donor liver transplantation in India

### Male patient 19 yrs old



BM 01.07.2018

AE in Kirgistan









### Female patient 24 yrs old

### Present to First City Hospital, Bishkek in 2014. Initial complains: fatigue, weight loss and anemia

### Female patient 24 yrs old



- On long term albendazole since 2014
- Normal liver values, clinical asymptomatic,
- Fully recovered



Picture taken with permission from the patient



## Control of Alveolar Echinococcosis

- Treat dogs
- Fox treatment baits
- Has had some effect in Europe
- Difficult
- Dogs continuously reinfected from wild life

# Echinococcosis Control Kyrgyzstan

- Major weakness in veterinary sector
- Poor motivation
- Poorly trained
- Surveillance and treatment of dogs is poorly executed
- No abattoirs
- Medical surveillance is competent



The 28<sup>th</sup> World Congress of Echinococcosis

重庆演龙生物制品有限公司 Chongqing Auleon Biologicals Co., Ltd.

#### Large-scale Vaccination of EG95 Vaccine Significantly Interfered with the Dog-sheep/goat Transmission Chain of Hydatidosis

Ran, Zhiguang PhD/Prof Chongqing Auleon Biologicals Co., Ltd, China Oct 30, 2019; Lima, Peru





	因病	致行	Ĩ,	因病	绝户	家庭作	青况
		120			家庭成员名		
身份	姓名	性别	职业	出生年份	死亡年份*	死亡时年龄	死因
母亲	阿地	女	牧民	1944		-	4
父亲	久才	男	牧民	1943	1987	42	肝包虫
大儿子	素昂	男	IL	1970	1995	25	肝包虫
二儿子	索保	男	工人	1975	- 0	-	-
三儿子	依穷	男	牧民	1979	1995	16	肝包虫
四儿子	达桑	男	牧民	1982	2004	22	泡型肝包虫
大女儿	康吉	女	牧民	1971	1998	27	肝包虫
二女儿	琼吉	女	牧民	1986	2010	24	泡型肝包虫
外孙	久美尖措	男	牧民	1992	2011	19	泡型肝包虫
大女婿	次成	男	牧民	1970	2000	30	脑包虫可能
姑姑	班吉	女	牧民	1948	1973	25	肝包虫

. C

#### ss of Echinococcosis

#### e echinococcosis stroyed a family in nghai province, China

- household member 11
- 5 died with cystic **Echinococcosis**
- 3 died from alveolar **Echinococcosis**
- 1 died from suspicious coenurus cerebralis

**庆澳龙生物制品有限公司** ongqing Auleon Biologicals Co., Ltd.













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AOLONG	

#### The 28<sup>th</sup> World Congress of Echinococcosis

#### The vaccine has been widely used highly endemic area of China

Unit: million doses

Year	Gansu	Inner Mongolia	Ningxia	Qinghai	Sichuan	Tibet	Xinjiang	Subtotal
2019	1.985	9.097	0.8	10.5	3.759	9.133	5	40.274
2018	2.505	10.56	/	11.00	5.93	8.93	6.002	44.927
2017	0.001	11.514	1.4	10.9	10.553	7.195	6.202	47.765
2016	1.6625	11	0.6	7.008	8.404	3.221	9.021	40.9165
Subtotal	6.1535	42.171	2	39.408	28.646	28.479	26.225	173.8825

Due to government pricing in China, the vaccine is very cheap: 2CNY (equivalent to US \$0.28) per dose. 重庆决定生物制品有限公司 Chongqing Auleon Biologicals Co., Ltd.





		Tł	ne 28 <sup>th</sup> World Congress of Echinococcosis	
Province	Year	Ab Pos rate (sampling)		
	2016	89.20%	Llich anti ECOE antihadu nasitiya vata	
Sichuan	2017	85.60%	High anti EG95 antibody positive rate	
	2018	87.30%		
	2016	70.00%		
	2017	78.69%		
	2018	83.12%		
	2016	/		
Tibet	2017	84.37%		
	2018	85.38%	Antibody positive	
	2016	73.41%		
Gansu	2017	75.97%	rate was between	
	2018	86.51%	60.9% to 89.2%.	
	<b>2016</b>	<b>60.90%</b>	00.3/0 10 89.2/0.	
Xinjiang	2017	63.57%		
	2018 73.25%			
	<b>2016</b>	82.07%		
Ningxia	2017	85.00%		
	2018	86.74%	<b>重庆澳龙生物制品有限</b> 公司 Chongging Auleon Biologicals Co., Ltd	



#### Significantly decreased prevalence after 3-year large-scale immunization

OLONG

Drovinco	Prevalence in sh	eep/goat herds	Prevalence in dogs		
Province	2014/2015	2017/2018	2014/2015	2017/2018	
Sichuan	5.34%	4.03%	25.00%	13.80%	
Tibet	44.72%	20.16%	4.09%	1.82%	
Qinghai	41.76%	7.83%	29.63%	5.16%	
Gansu	5.76%	4.42%	5.16%	2.57%	
Xinjiang	9.80%	4.51%	9.84%	4.05%	
Ningxia	6.24%	1.23%	12.88% (coproELISA)	2.04% (coproELISA)	
Inner Mongolia	1.12%	0.83%	3.12%	1.04%	

Slaughter examination & necropsy of sheep/goat: from 5.34%- 44.72% to 1.23%-20.16%; Arecoline purgation of dogs: from 3.12%-29.63% to 1.04%-13.8%.

> 重庆澳龙生物制品有限公司 Chongqing Auleon Biologicals Co., Ltd.







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## Thanks for your attention

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