

The Science & Art of Clinical Medicine
Thomas Junghanss
Heidelberg University Hospital

Marcel

The gang

The disease

The local context

The research approach

WHO Guideline
development

More context

The dilemma

Rules
Developments over
time

Rules

Algorithms - thin & rigid
Models - thick & flexible

Algorithms escape the
context by ignoring it

Behind every thin rule is a
thick rule cleaning up
after it

Algorithms and models:
which for what?

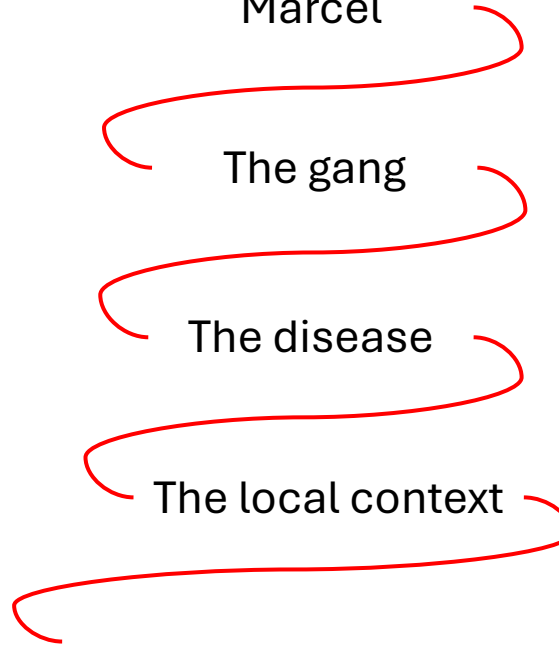
back to Marcel

Marcel

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The local context



The person
we are
celebrating

Peru 2010



The gang

Peru 2010



Hugo Garcia
Universidad Peruana Cayetano Heredia



Robert Gilman
John Hopkins Bloomberg School Public Health



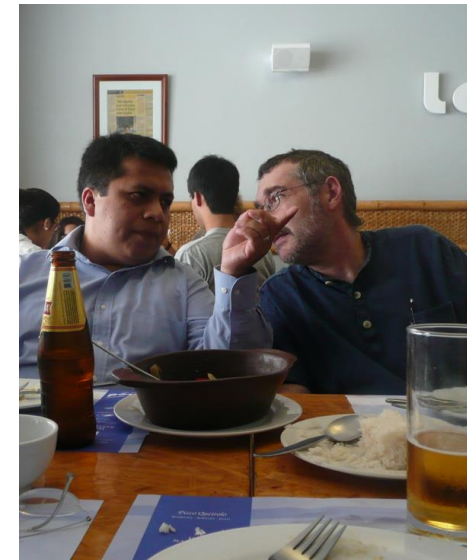
Ted Nash
NIH



Enrico Brunetti
Università di Pavia



Steffen Luntz
Heidelberg
University Hospital



Saul J. Santivañez
Instituto Peruano de
Parasitología Clínica y
Experimental



Marija Stojković
Heidelberg University
Hospital

**Infection
Transmission
Disease**

Cystic
echinococcosis
*Echinococcus
granulosus*

Zoonosis

*Neglected Tropical
Disease (NTD)*

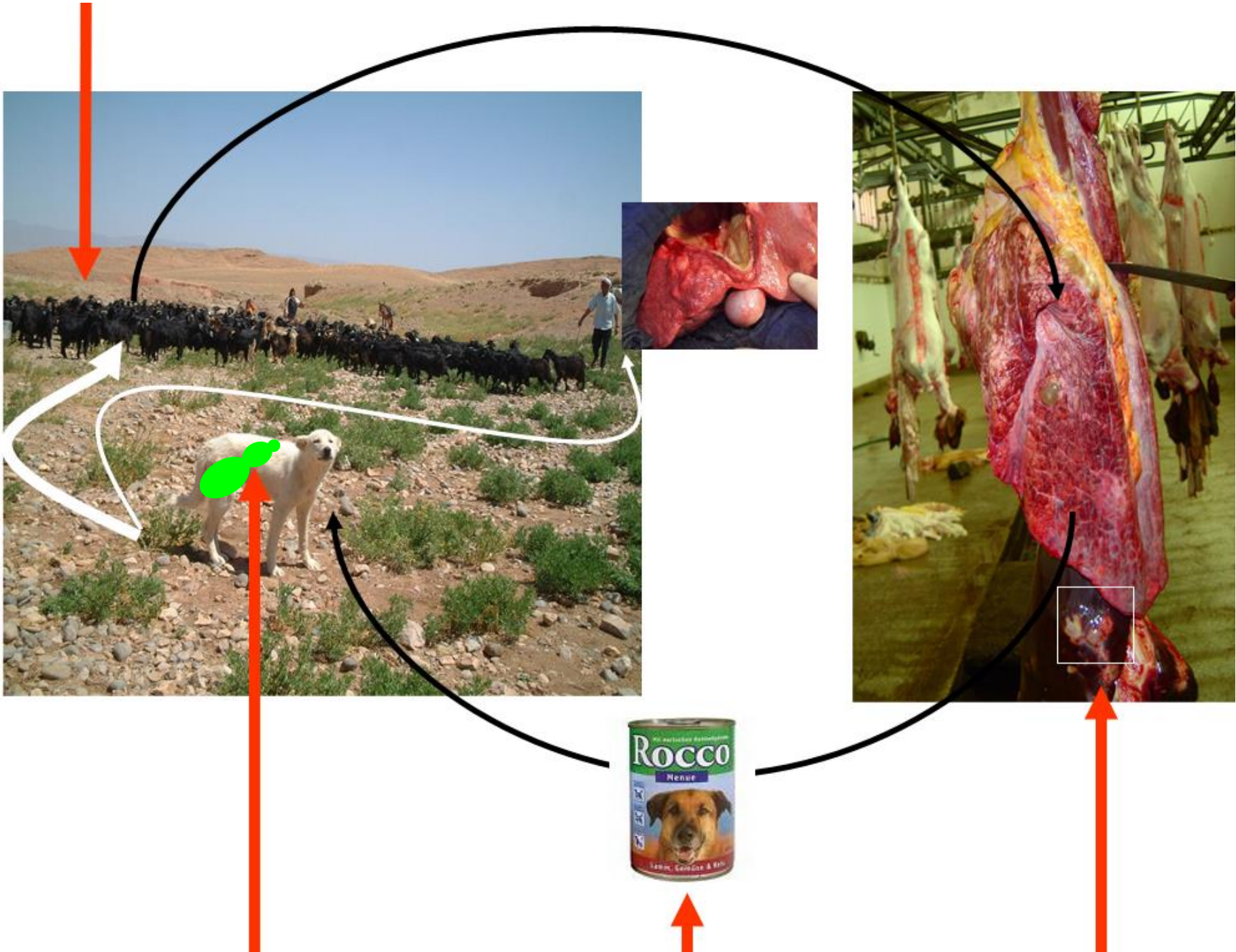
Rather: *global disease
of neglected patients
and populations*

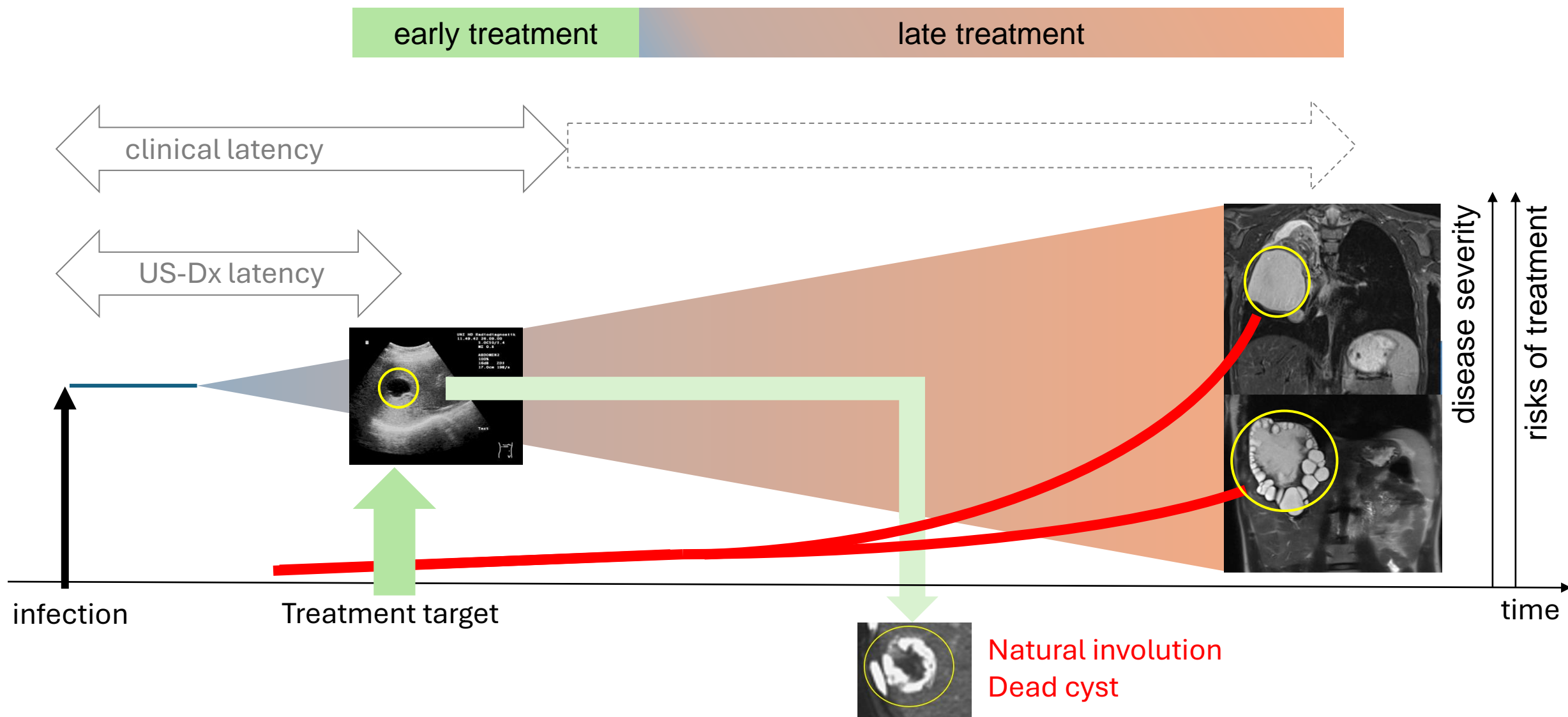


Infection
Transmission
Disease

Cystic
echinococcosis
*Echinococcus
granulosus*

PREVENTABLE!





The lucky patient

The parasite died before
the patient!

Around 30% of patients

**Regrettably, no way to
predict who is the
lucky one.**

Ultrasound machines
required to identify dead
cysts and let them alone
(watch & wait)

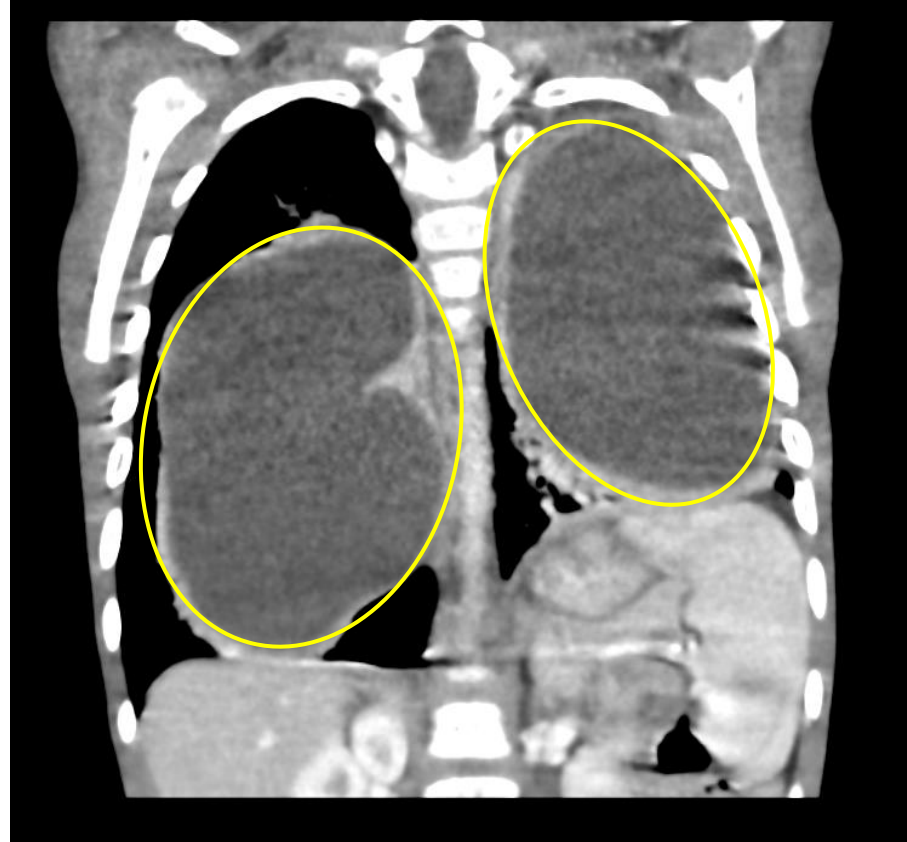


Image: Heidelberg University Hospital

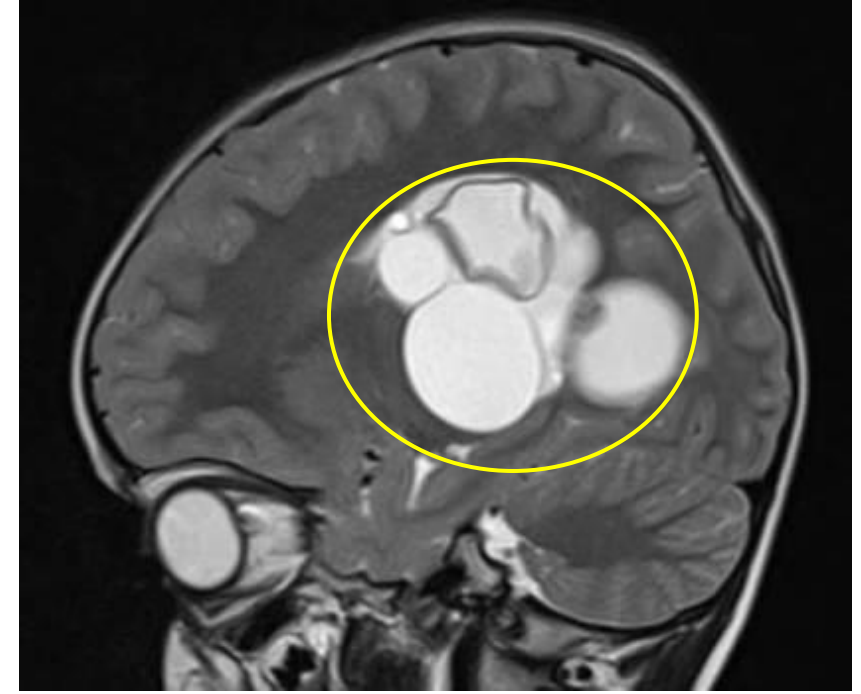
Advanced disease



Liver



Lung



Brain

Small active cysts

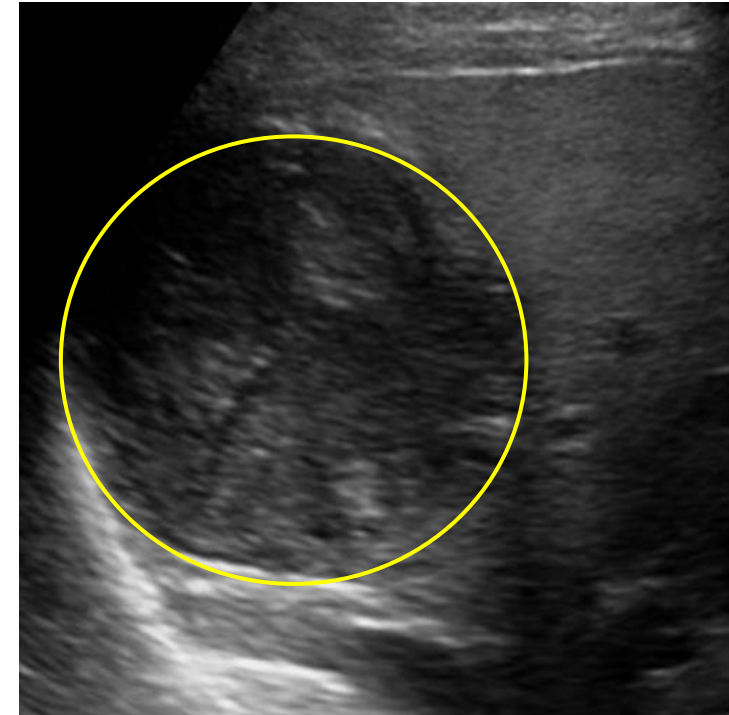
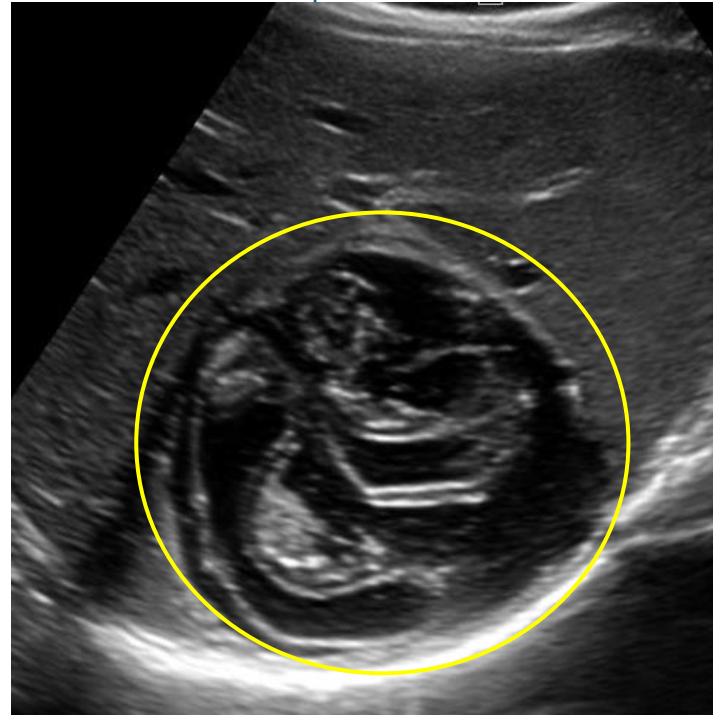
respond to

Drug treatment

**How to find the patients
with small active cysts?**

Screening

6 months
albendazole



+/- 12 months

**Minimally Invasive:
Percutaneous methods**

Only certain cyst stages

**Availability of method
low**

PAIR

WHO/CDS/CSR/APH/2001.6

WHO

2001



Historical photo of the
pioneers Filice & **Brunetti**

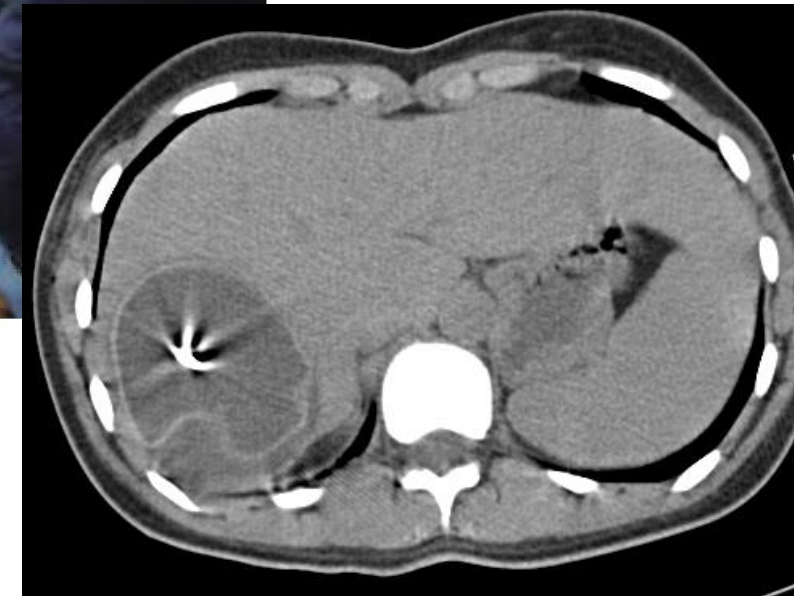
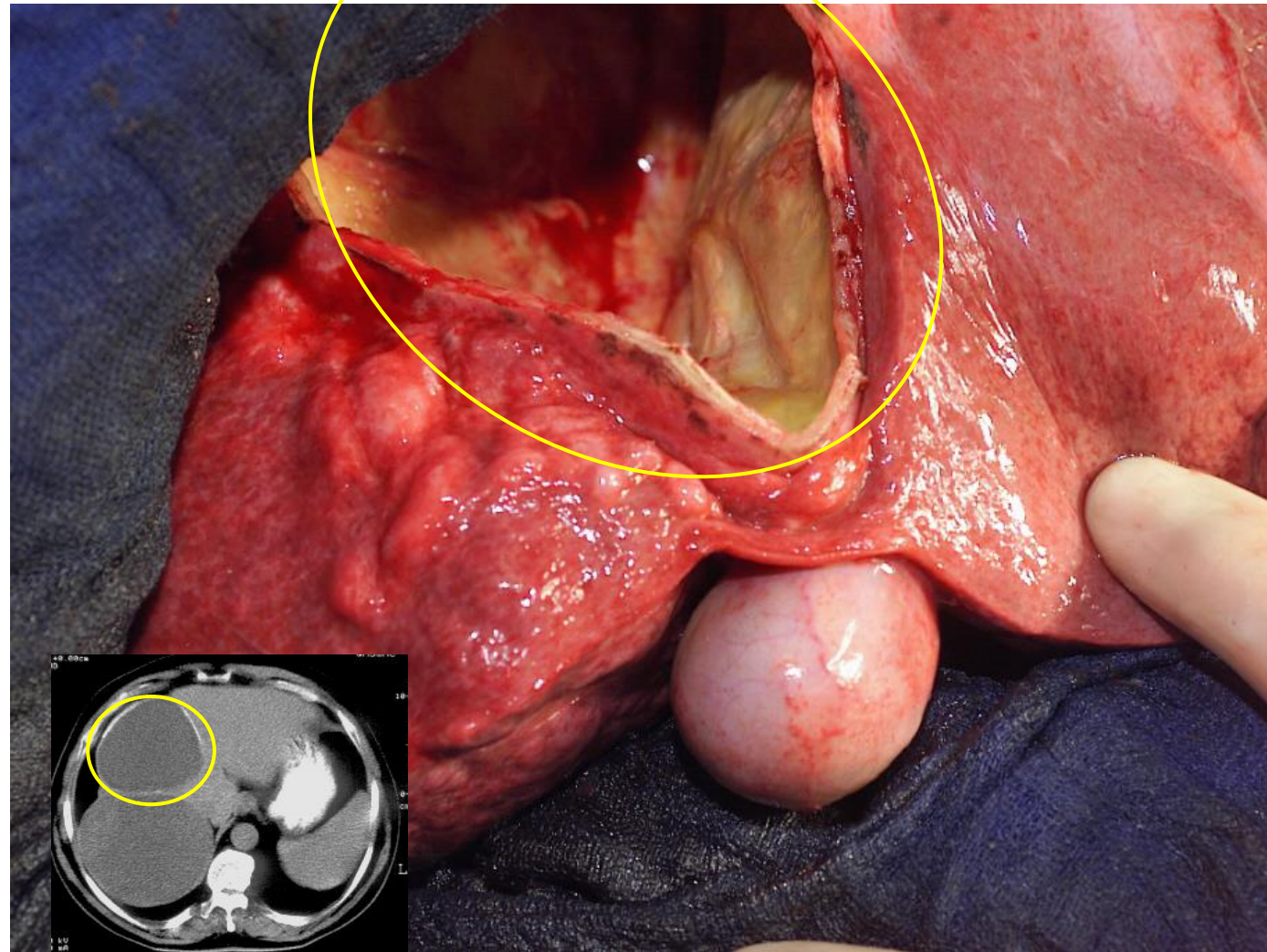


Image: Heidelberg University Hospital

Advanced disease:

Surgery

Demanding

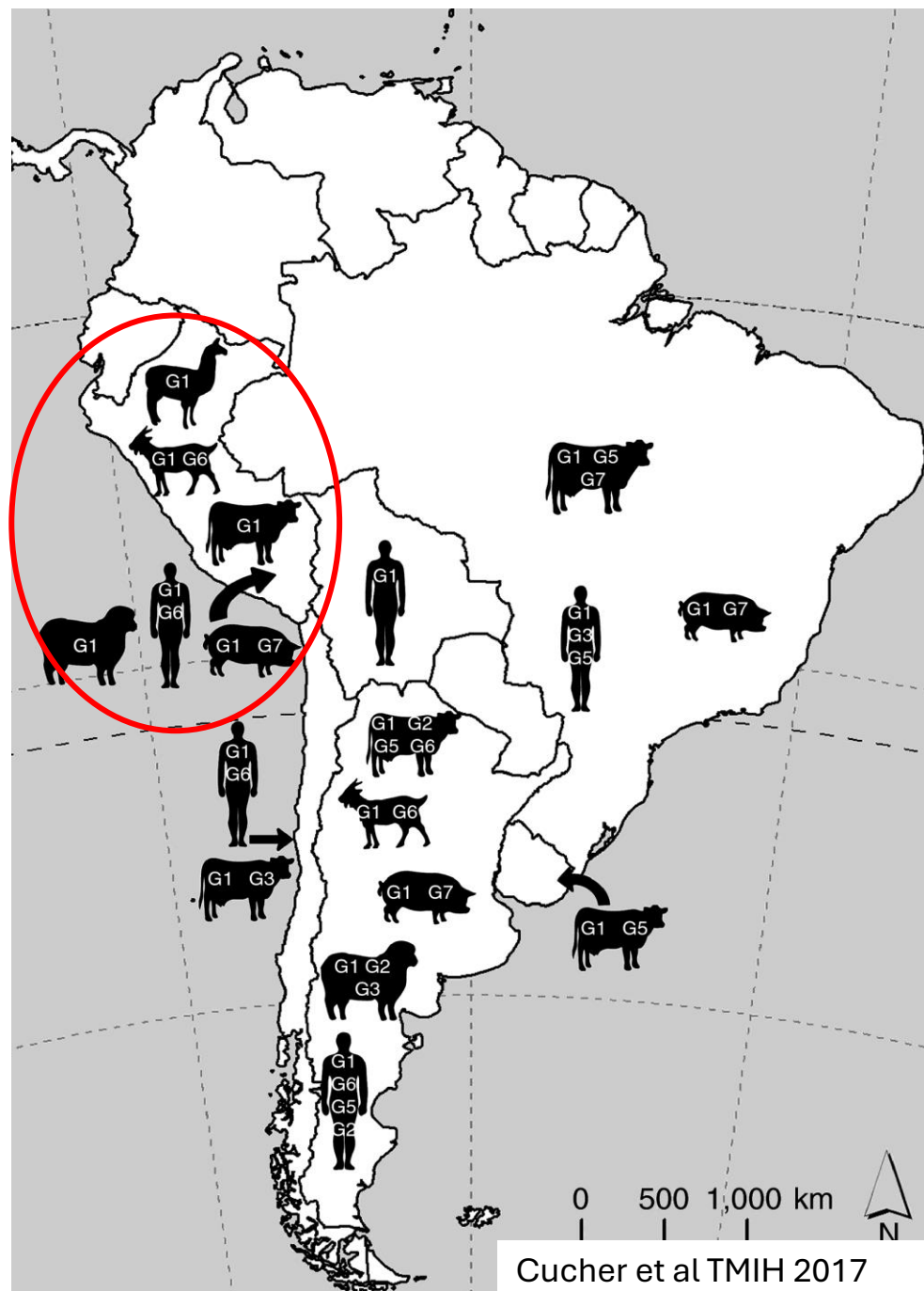


The local context

Latin America

Peru

In sheep, lama,
goat, cattle
raising regions of
the Andes



The local context

Peru



The local
context

Peru





The research approach

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The research
approach

Clinical Trial

Planning grant



CLINICAL TRIAL PLANNING GRANT
Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Notice of Award

Issue Date: 09/01/2010



Grant Number: 1R34AI091427-01

Principal Investigator(s):

Thomas Junghanss

Project Title: Phase II clinical trial of stage specific treatment of cystic echinococcosis

Batrum, Claus
Dean's Office
INF 672
Heidelberg, 69120
GERMANY

Award e-mailed to: martina.manns@med.uni-heidelberg.de

Budget Period: 09/01/2010 – 08/31/2011

Project Period: 09/01/2010 – 08/31/2011

The gang

Peru 2010



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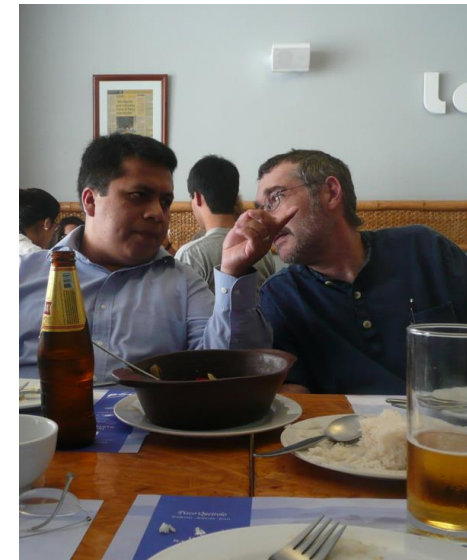
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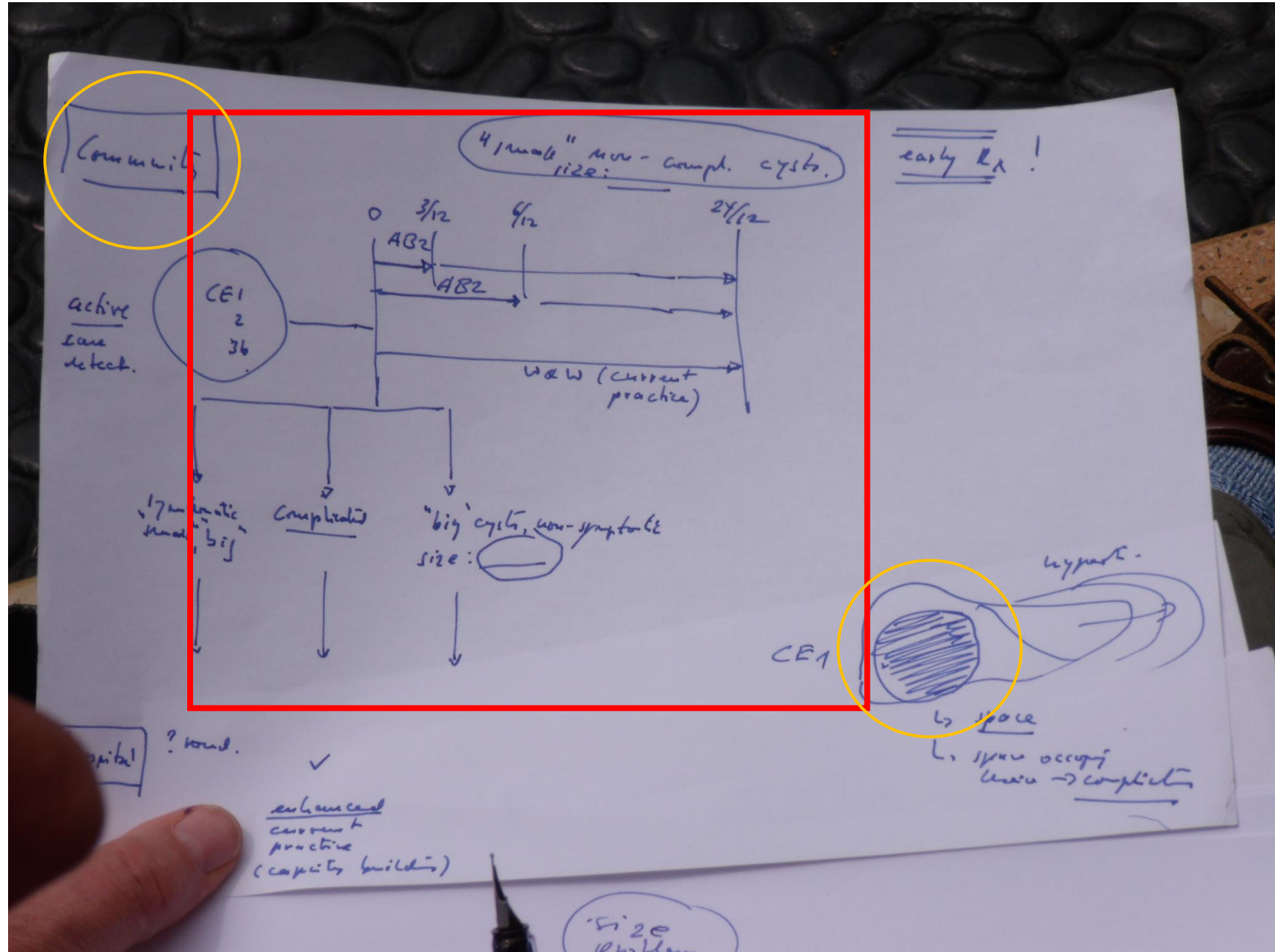


Marija Stojković
Heidelberg University
Hospital

The research approach

RCT

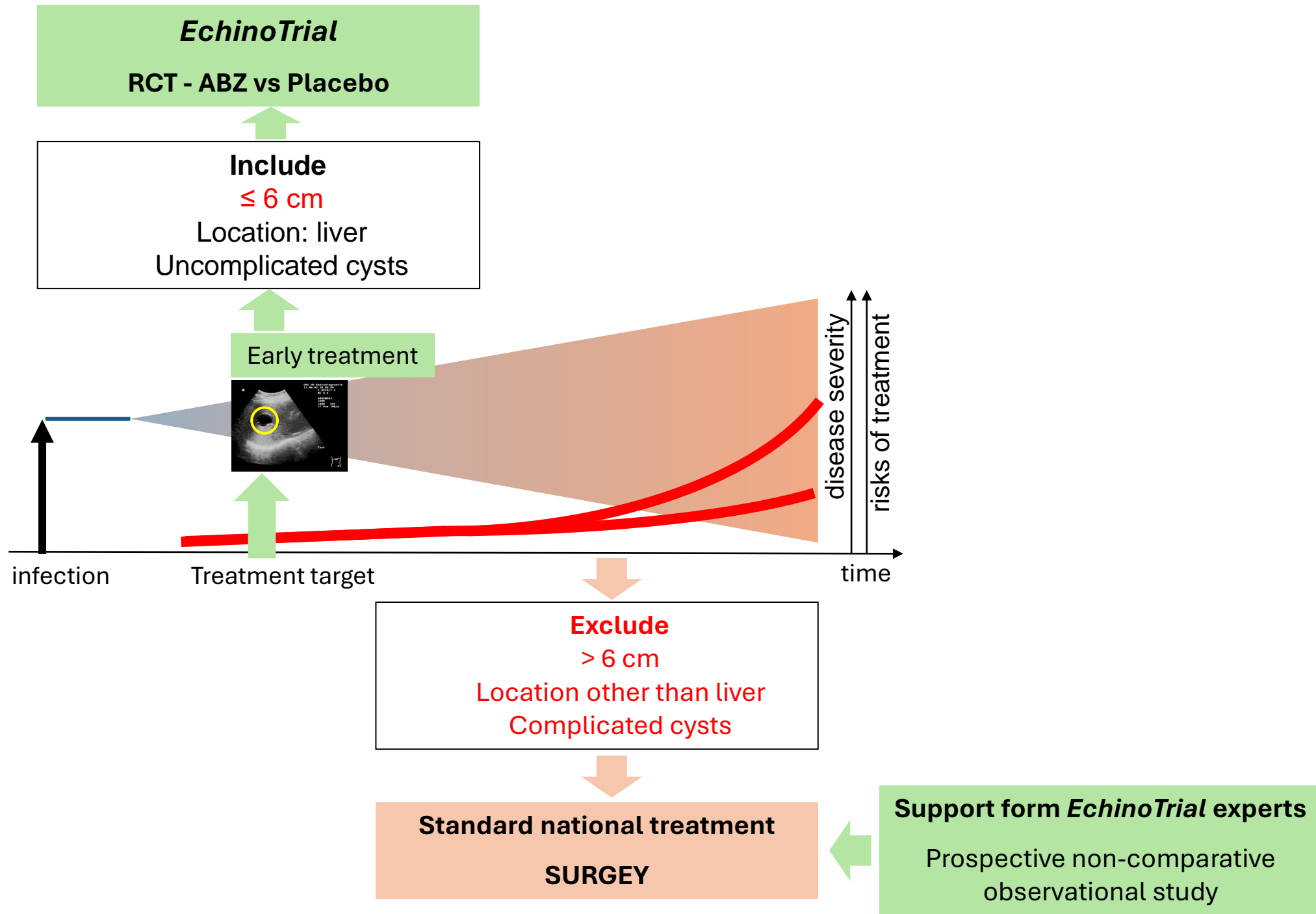
We faced the resistance of the community, patients and organs to the format of algorithms



RCT
Drug vs. Placebo

Inclusion criteria

Exclusion criteria



Early treatment requires screening

Prevalence

**5 % age group 11-20 years
highest proportion of small active cysts**

Screening

10,000 consenting individuals

Sample size target

250 patients

To be considered and taken care of

Patients with advanced, symptomatic and complicated CE cysts

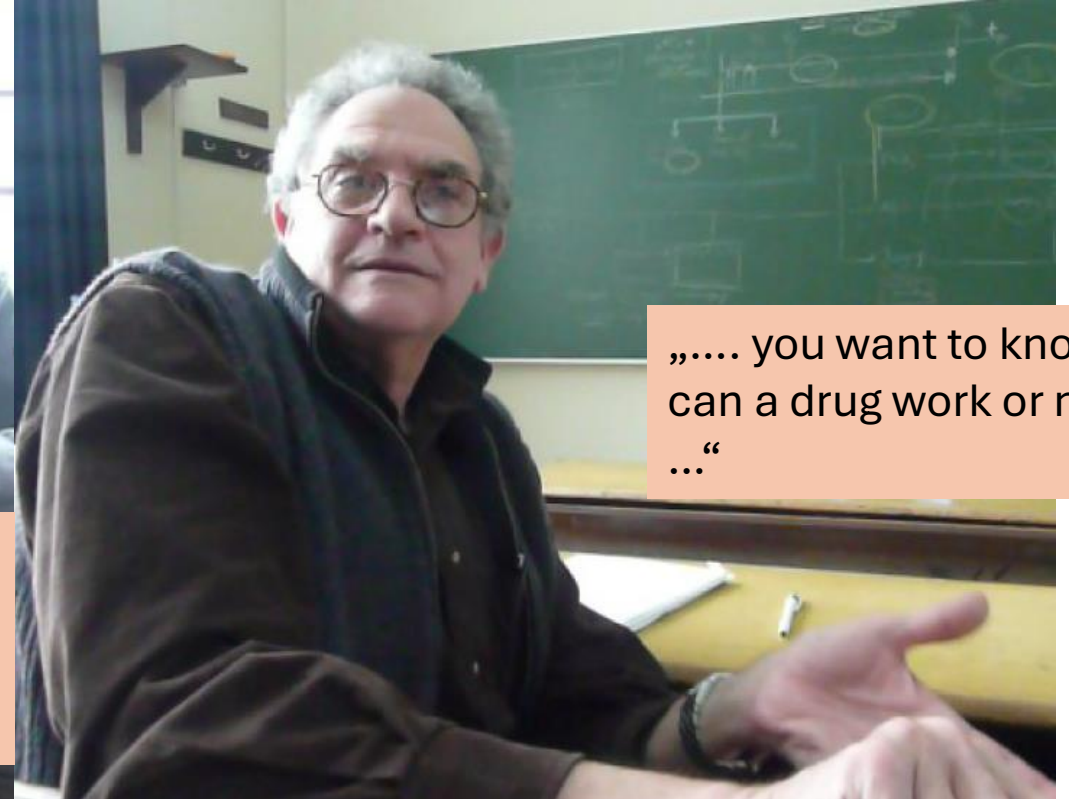
Patients with liver pathology other than CE

„....if you want to shape
it ... how it is done later
on ... in real life ...“



„...what is going to work
in that situation that
you have a good study
...”

***What happens with
the RCT results
when the trial is over***

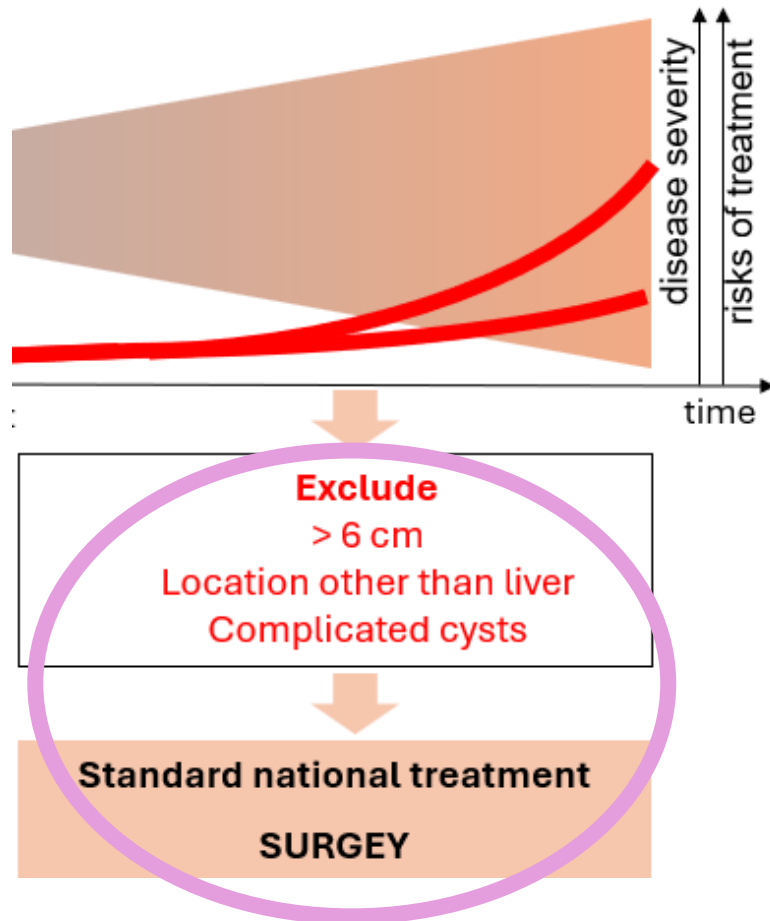


„.... you want to know
can a drug work or not
...“

***The RCT algorithm escapes
the context by ignoring it***

APPLICATION FOR FEDERAL ASSISTANCE SF 424 (R&R)		3. DATE RECEIVED BY STATE	State Application Identifier
1. TYPE OF SUBMISSION*		4.a. Federal Identifier	
<input type="radio"/> Pre-application <input checked="" type="radio"/> Application <input type="radio"/> Changed/Corrected Application		b. Agency Routing Number	
2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number	
5. APPLICANT INFORMATION		UEI*: R2CESKBNTS36	
Legal Name*: UNIVERSIDAD PERUANA CAYETANO HEREDIA Department: Division: Street1*: UNIVERSIDAD PERUANA CAYETANO HEREDIA Street2: APDO 4314 City*: LIMA County: State*: Province: Country*: PER: PERU ZIP / Postal Code*: 15102			

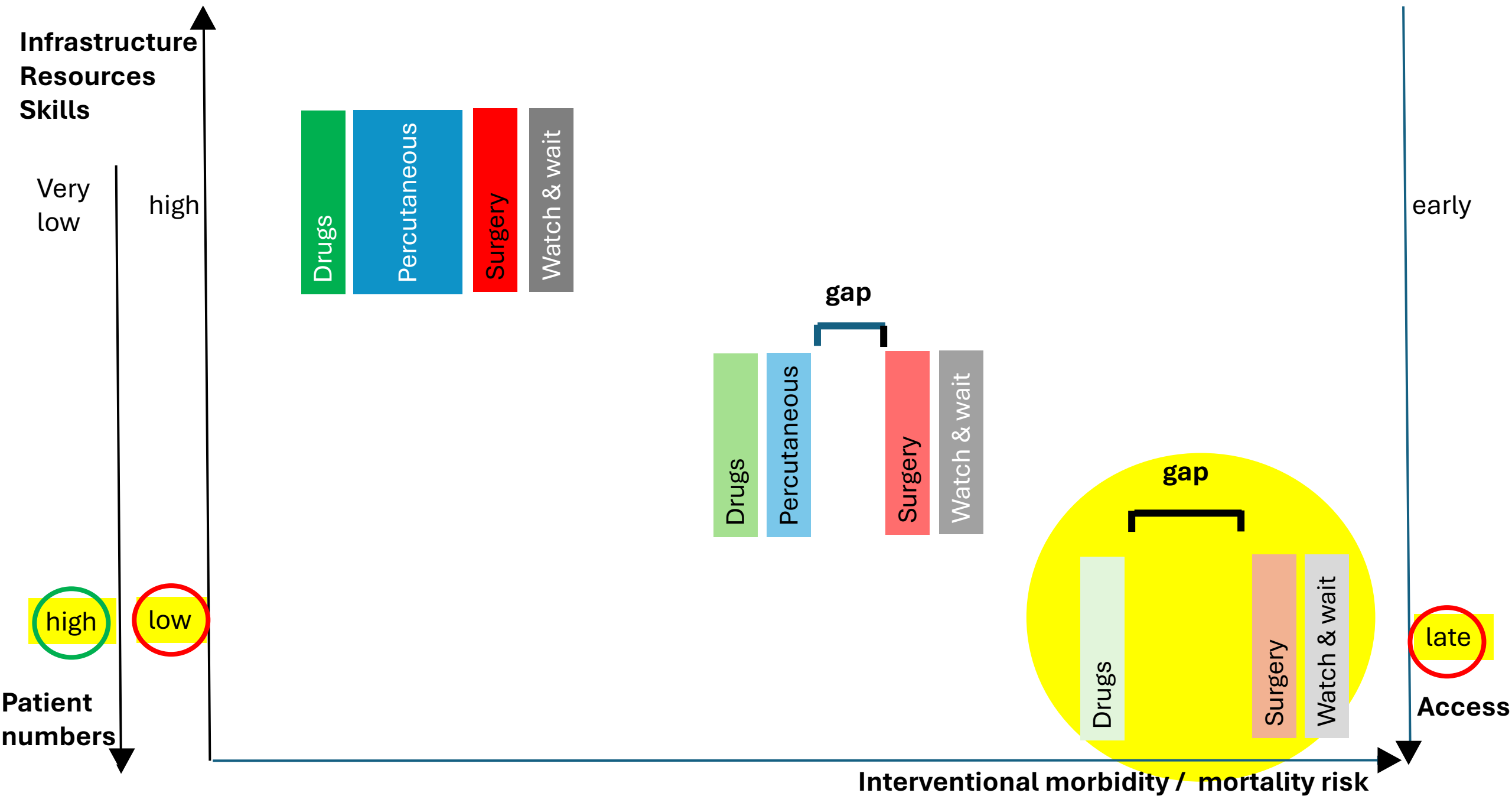
Reasonable scientific merits and percentile range. So, in principle fundable. However, never made it to receive the grant.



Reviewer comments:

**“Discussion of management of all other forms of CE is not relevant to this proposal” –
No objections against “standard national treatment – exclusively surgery”**

**No objections against screening.
No questioning if the Wilson & Jungner classic screening criteria are fulfilled.**



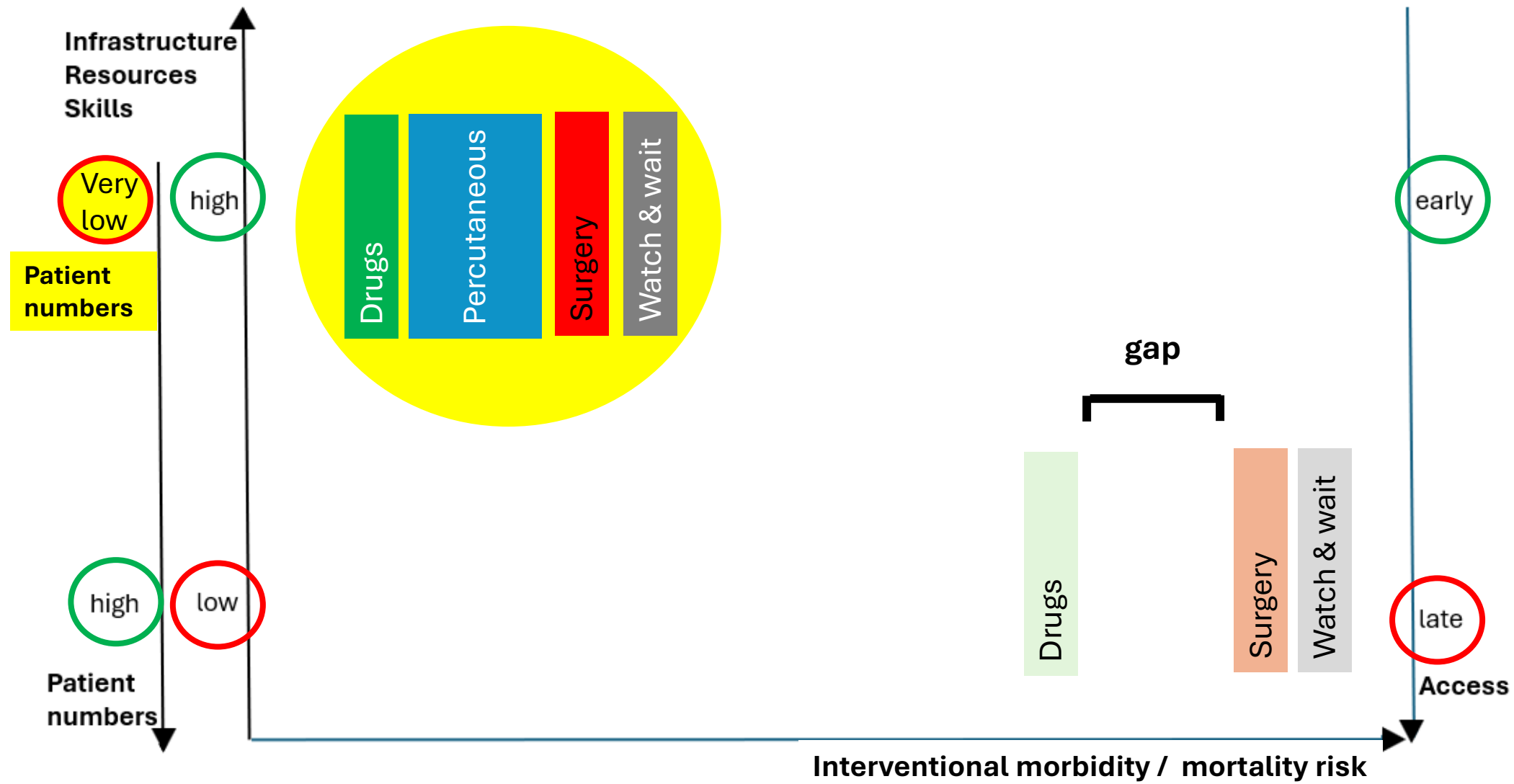
Research
priority:
RCTs

e.g.
Switzerland,
Germany

The dilemma

Peru

“Large RCT on individual cyst stages comparing

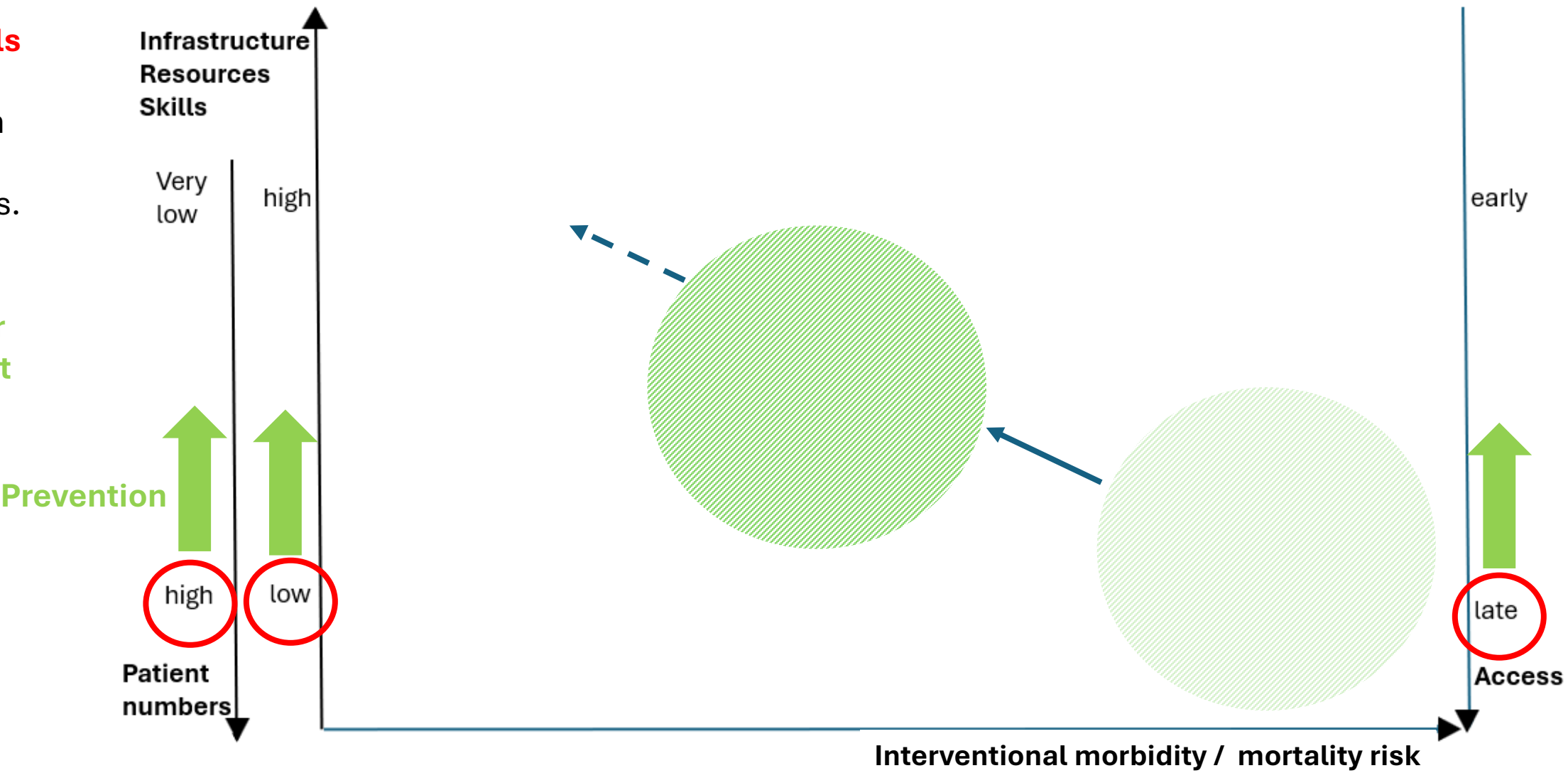


MODEL **integrating prevention, development of infrastructure, resources & skills into the research approach**

Pragmatic clinical trials

an option -
with limits in
resource-
poor settings.

**Broad
stakeholder
involvement**



Rules
Developments over
time

Rules
Algorithms - thin & rigid
Models - thick & flexible

Algorithms escape the
context by ignoring it

Behind every thin rule is a
thick rule cleaning up
after it

Algorithms and models:
which for what?

RULES
Developments
over time

*Tools of
measurement
and calculation*

Models or
paradigms

laws

Greco-Roman
roots

The proliferation of algorithms intersected with the flourishing economy of the Industrial Revolution.

Standardization of 'everything' enforced the 'frozen' context, the precondition for algorithms. Partial success

advanced the dream of 'Modernity' to reach perfection.

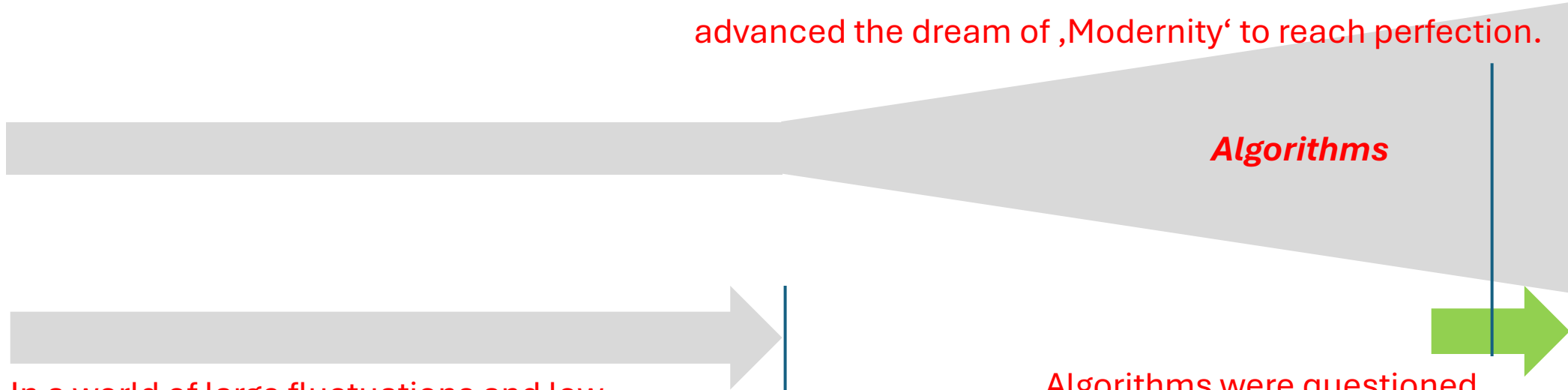
Algorithms

In a world of large fluctuations and low predictability, exceptions were the rule

Algorithms were questioned
and models re-surfaced

18th century

21st century



RULES

ALGORITHMS

thin
rigid

Implicitly assume a predictable stable context:

All possibilities can be foreseen,

The future extrapolated from the past,

The process can be broken down to clearly defined components,

Standardization and uniformity,

Averages can be trusted.

MODELS

thick
flexible

Full of examples, caveats, observations, exceptions

Anticipates:

Variability (patients, organs, health care settings)

Unpredictability of events during interventions

A few thoughts about RULES

Implicit rules

Explicit rules

Rules are part
of our lives

Everywhere,
always

Supporting and
constraining

and

we take them
(too often?)
for granted



TJ

Queuing, an **Implicit rule**

OTTOLENGHI



Explicit rule

Tomato soup

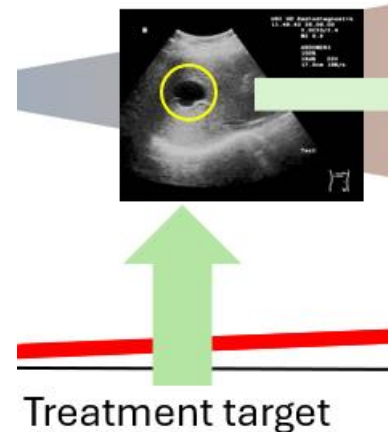
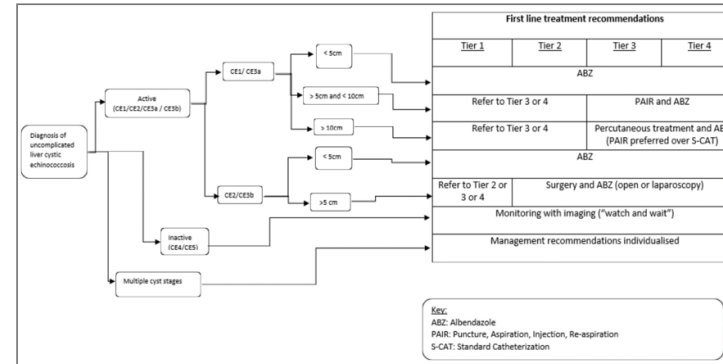
60g	unsalted butter
3 tbsp	olive oil
2	onions, peeled and finely chopped (360g)
2	large garlic cloves, peeled and crushed
400g	sweet red cherry tomatoes (ie, Datterini or similar)
4 tbsp	tomato paste

- 1 Preheat the oven to 160C.
- 2 Put the butter, oil, the onions and a teaspoon of salt in a large saute pan on a medium heat and cook, stirring often, for 18-20 minutes, until soft and deeply golden brown (you don't want the onions to burn or become crisp, so lower the heat as necessary).

RULES

Neglected diseases (NTDs) and other fields of clinical medicine not ready or not suited for exclusively algorithmic approaches.

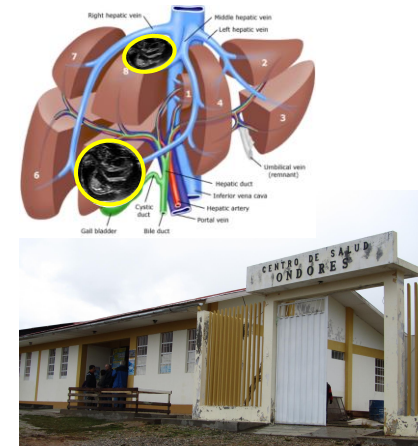
ALGORITHMS



Algorithms escape the context and lacking evidence by ignoring it.

MODELS

Under conditions of uncertainty and lacking evidence, models are a flexible way to treat patients.



Ambiguity in a model is a feature, not a bug – is a good companion

RULES

Now we can answer the question:

What happens when an algorithm fails what we so often observe in clinical medicine?

Premature implementation of algorithms supports unjustified confidence, pretends routine.

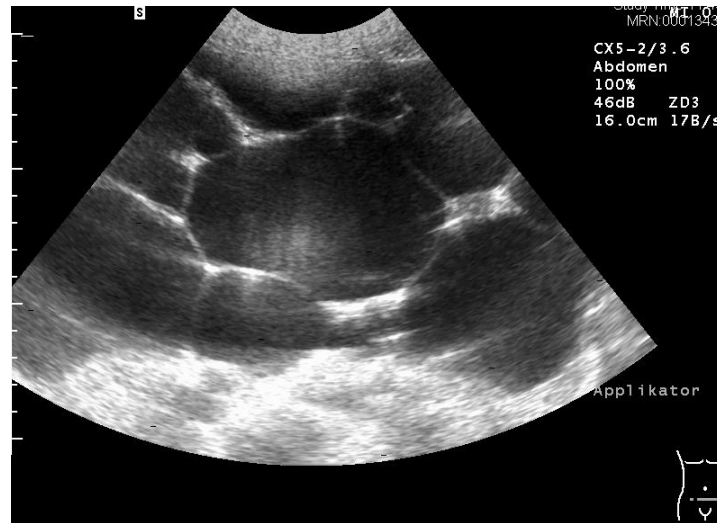
Careful consideration if a thin, a thick rule or a combination promises the best fit for a problem.

ALGORITHMS

The patient becomes an emergency

Entering what is called 'revision(s)'

More complex than the initial condition.



Behind every thin rule is a thick rule cleaning up after it.

MODELS

thick

flexible

Analogies to well established procedures

Models / **Manuals** provide

expert-based biologically and clinically plausible advice

generate testable hypotheses of real-life scenarios

Foster learning

RULES

What does it mean for complex problems (diseases)?

For diseases with low certainty of evidence

For highly variable (polyphonic) contexts?



TJ

ALGORITHMS

in parts suitable algorithms are embedded:

MODELS

Preference for models in which

Not (yet) standardized components are clearly highlighted

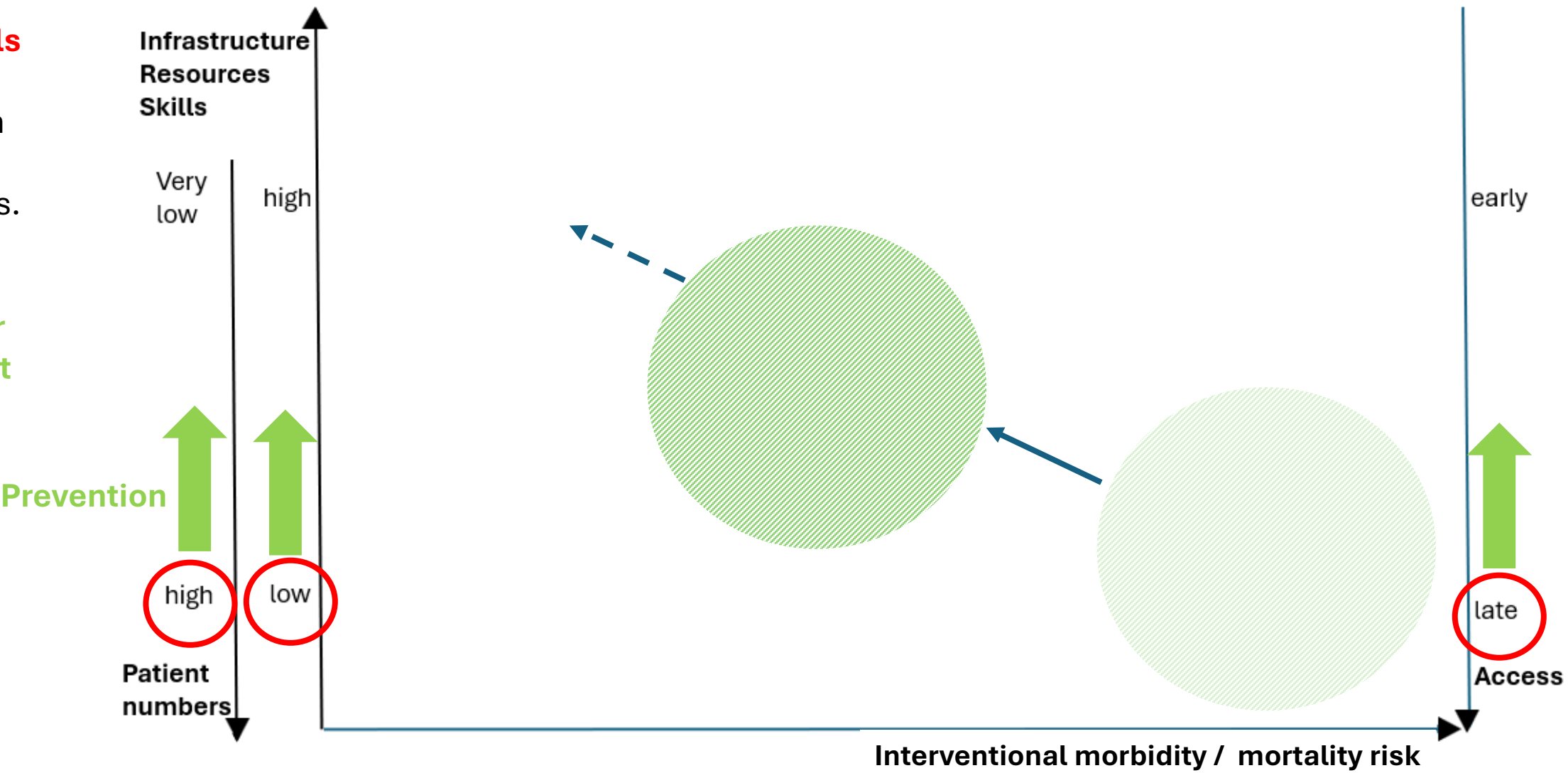
Guidance by examples, observations, exceptions drawing from general (biologically and clinically plausible) principles.

MODEL **integrating prevention, development of infrastructure, resources & skills into the research approach**

Pragmatic clinical trials

an option -
with limits in
resource-
poor settings.

**Broad
stakeholder
involvement**





We walked
through shared experience
through changing times and perceptions

Maybe ‘Science and Art of Clinical Medicine’, can best described as

changing landscapes – models - captured with maps of various
scales and layers – contexts, where

thin and thick rules need to be selected and applied wisely, and

ambiguity is a good companion.

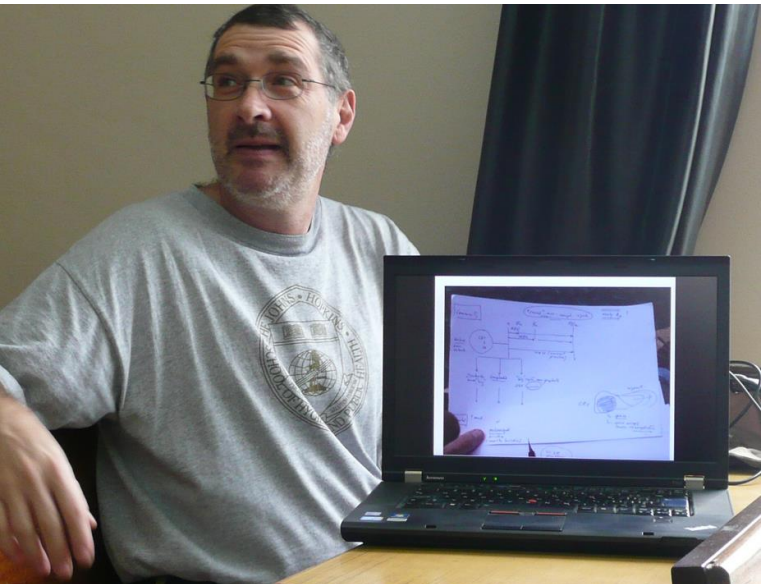
The journey extends far beyond the neighbouring fields of science.

Clinical science, the art of practicing medicine, fine arts,
architecture ... have more in common than we currently realize and
put into action.

*Regrettably, I could only cover a glimpse of what is called ‘Western tradition’. It would be an enormous - though very much
needed - task to expand across other traditions.*



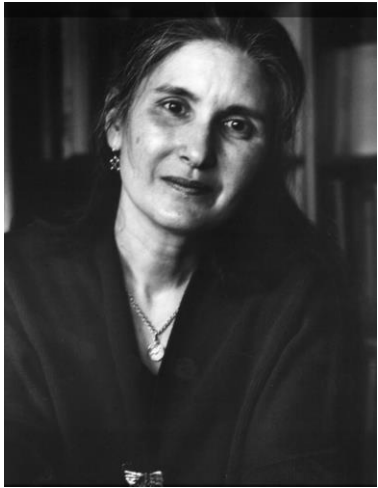
back to Marcel



„....if you want to shape
it ... how it is done later
on ... in real life ...“

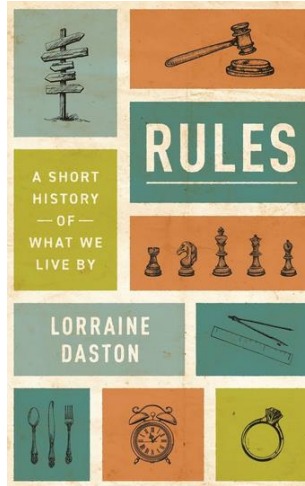


References



Lorraine Daston
1951 -

<https://www.faz.net/aktuell/feuilleton/debatten/zum-70-geburtstag-der-wissenschaftshistorikerin-lorraine-daston-17378994.html>

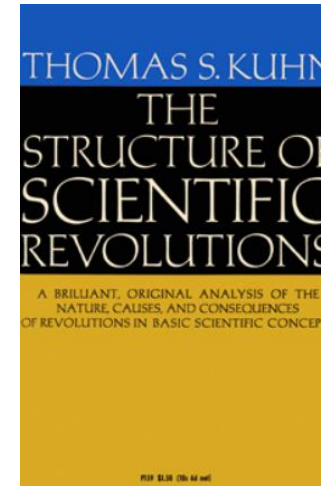


Princeton
University Press
2022

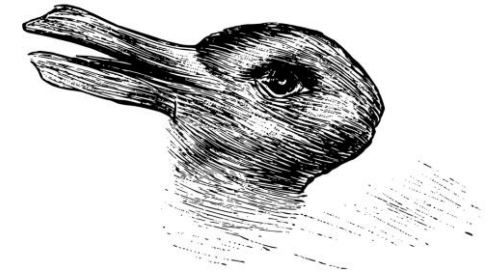
“The book is an invitation to further enquiry and debate about rules at their most diverse”



Thomas S Kuhn
1922-1996



University of
Chicago Press
1962



First published in the
humoristic Munic Weekly
,Flying Pages‘ 1892

Acknowledgements

Marija Stojković (Fotos Peru), Steffen Luntz (Fotos Peru)