VitalTransformation

The impact of health technology made simple
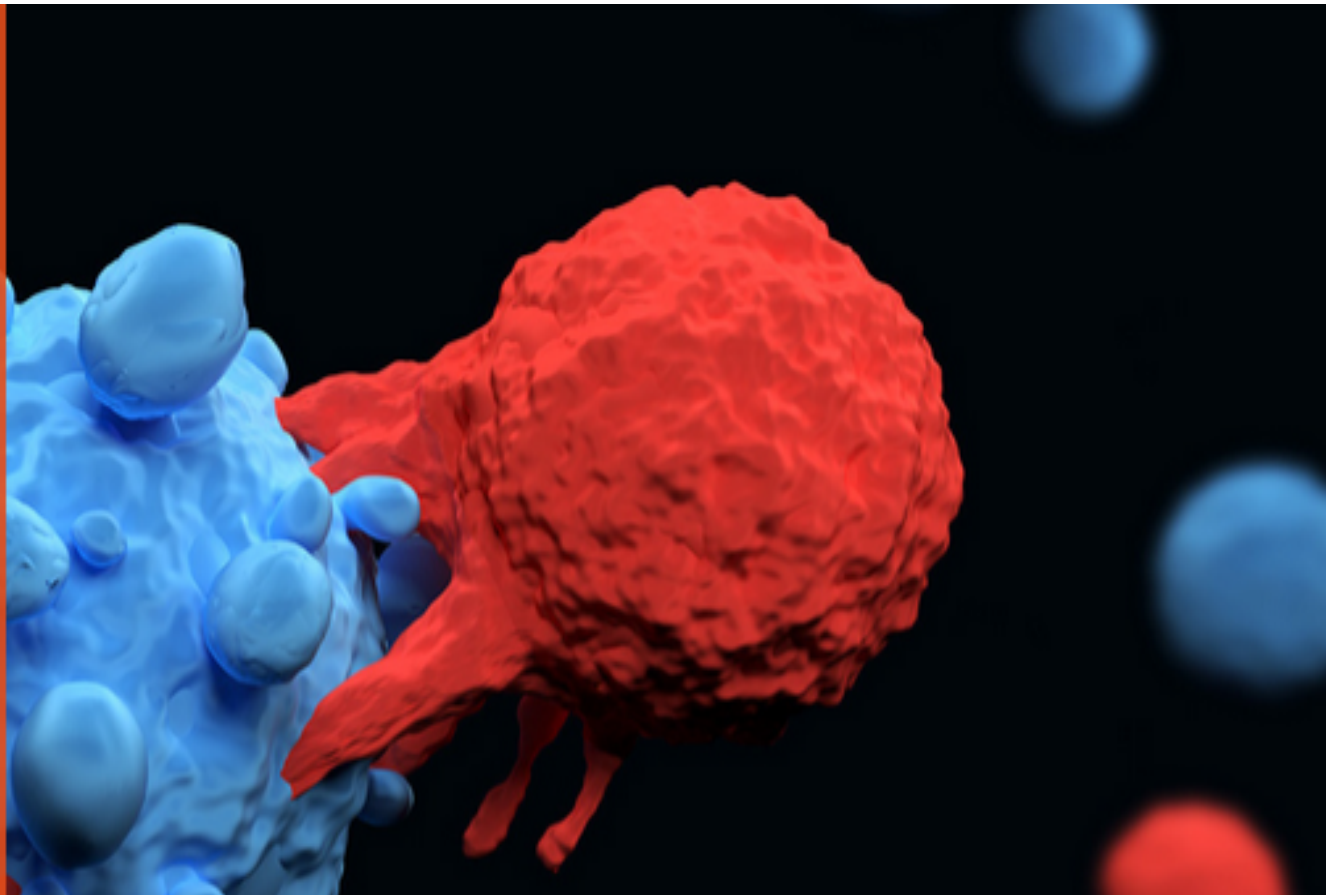
Zorginstituut Nederland

Webinar: RWE, CAR-T and Cancer – New Methods for Comparative Effectiveness

August 29th, 1-2pm CET

RWE, CAR-T, and Cancer
New Methods for Comparative Effectiveness

Anja Schiel, PhD
Lead Methodologist in
Regulatory and
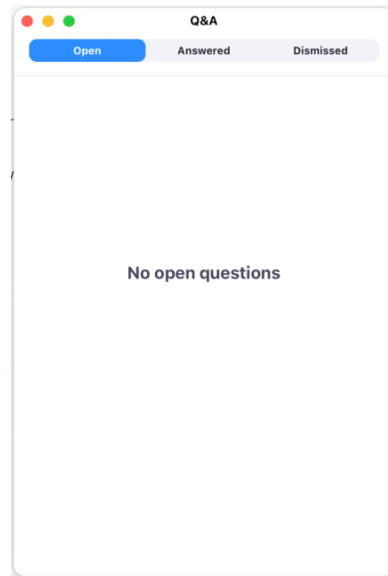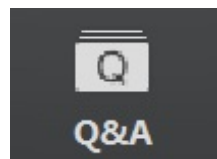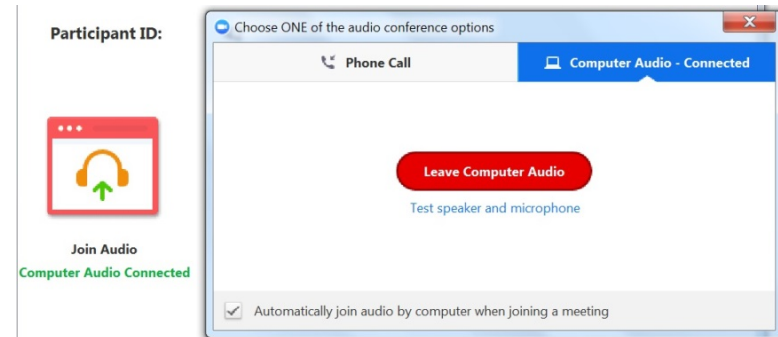Pharmacoeconomic Statistics
Norwegian Medicines Agency
(NoMA)

Amr Makady PharmD, PhD
Project Leader & Senior
Policy Advisor
Zorginstituut Nederland
(ZIN)

Duane Schulthess MBA
Managing Director
Vital Transformation

How is your connection? Ask a question?

If you are having problems with your connection, you can switch between phone and computer audio

The final 30 min of the webinar will be for audience Q&A, please use the question bar in the control panel

Disclosure

- This study was funded by a grant from the Dutch Government/Zorginstituut, the publication in the BMJ's Evidence Based Medicine is open access

BMJ Journals

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Are CAR-T therapies living up to their hype? A study using real-world data in two cohorts to determine how well they are actually working in practice compared with bone marrow transplants

Duane Schulthess[1], Daniel Gassull[1], Amr Makady[2], Anna Ludlow[1], Brian Rothman[3], Pieter ten Have[2], Yiyang Wu[4], Leeland Ekstrom[4], Monique Minnema[5], Madan Jagasia[3]

Author affiliations +

http://dx.doi.org/10.1136/bmjebm-2019-111226

Study Partners
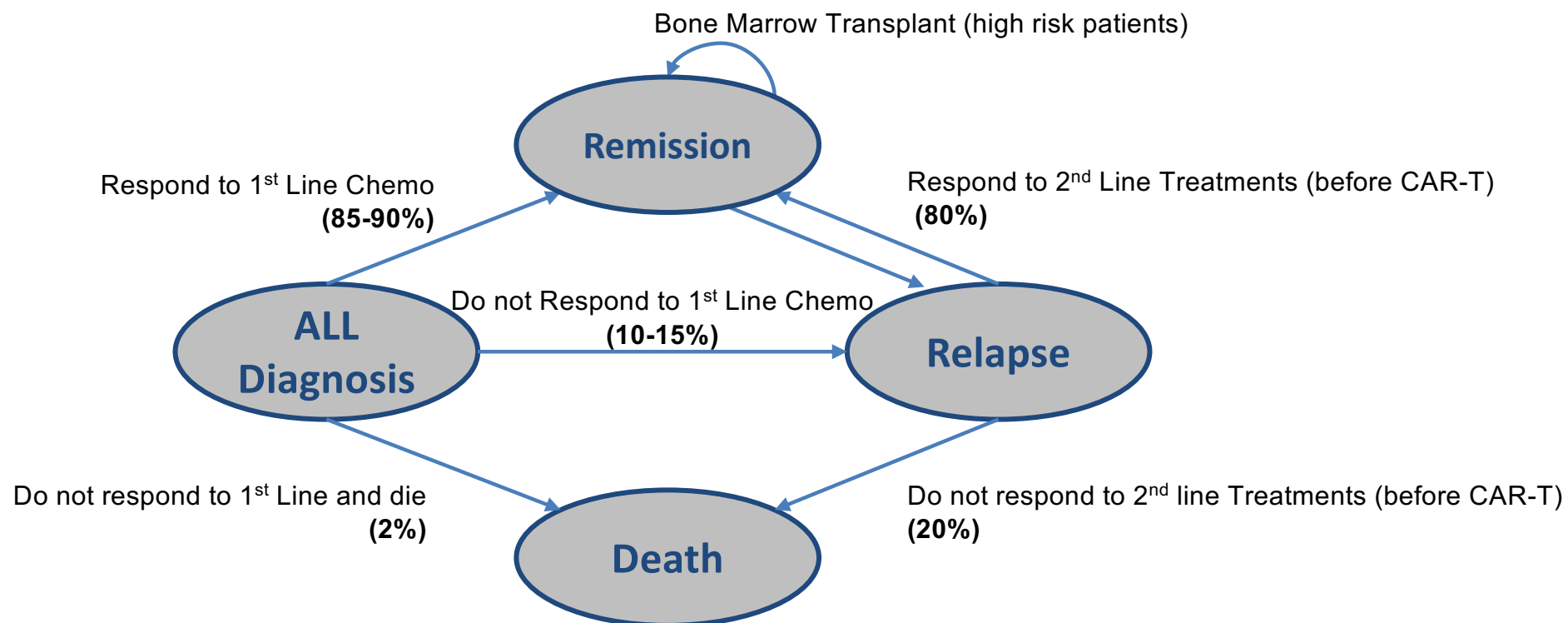
Why This Study? What Were We Trying to Figure Out?

- With the increasing use of new tools like FDA's breakthrough designation, there are demands for HTAs to make an accurate assessment of the long-term value and performance of therapies from smaller datasets and shorter outcomes.

- VT has developed a methodology harnessing RWE extracted from hospital EHR systems where clinical trials have taken place which allows us to build an accurate pathway and historical control, even with limited patient populations
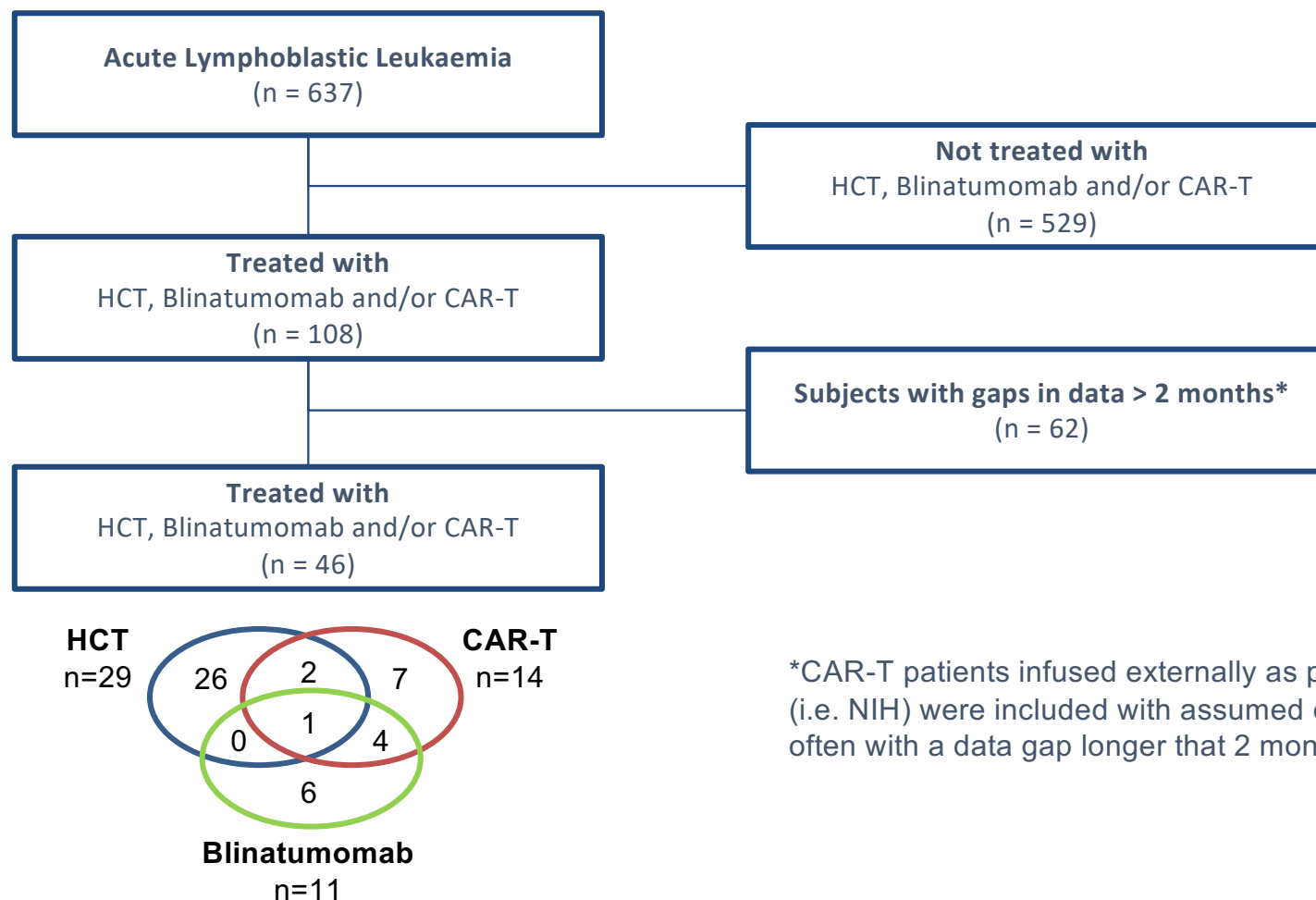
- This study was a proof of concept

Clinical States in Acute Lymphoblastic Leukaemia (ALL)

Bone Marrow Transplant (high risk patients)

Remission

Respond to 1st Line Chemo
(85-90%)

Respond to 2nd Line Treatments (before CAR-T)
(80%)

ALL Diagnosis

Do not Respond to 1st Line Chemo
(10-15%)

Relapse

Do not respond to 1st Line and die
(2%)

Do not respond to 2nd line Treatments (before CAR-T)
(20%)

Death

(1) Terwillinger T et al. Blood Cancer J. 2017 Jun; 7(6): e577.
(2) Treatment of Children With Acute Lymphocytic Leukemia (ALL) (https://www.cancer.org/cancer/leukemia-in-children/treating/children-with-all.html)

Dataset of Patients in this Study: Nashville Biosciences

Acute Lymphoblastic Leukaemia
(n = 637)

Not treated with
HCT, Blinatumomab and/or CAR-T
(n = 529)

Treated with
HCT, Blinatumomab and/or CAR-T
(n = 108)

Subjects with gaps in data > 2 months*
(n = 62)

Treated with
HCT, Blinatumomab and/or CAR-T
(n = 46)

HCT
n=29

CAR-T
n=14

Blinatumomab
n=11

26   2   7
0   1   4
6

*CAR-T patients infused externally as part of trials
(i.e. NIH) were included with assumed costs ,
often with a data gap longer that 2 months.

Sources & Structure of Data

NashBio & Vanderbilt University Medical Centre

For these 637 patients, we obtained data for…

ICD codes records   > 500 k data-points

HCPCS codes   > 750 k data-points

Medicines   > 2.5 M drugs

Patient records notes   (for CAR-T infusions)

Dates of Birth and Death

… over a period of 10 years

+

Literature and Public Sources

ICD 9 & ICD10

CMS procedures data   HCPCS costs

Medicare B & D & CMS   Meds costs

Additional costs on HCT and CAR-T were added using public information sources (e.g. product labels) and following consultations with Vanderbilt and Dutch Medical Practitioners

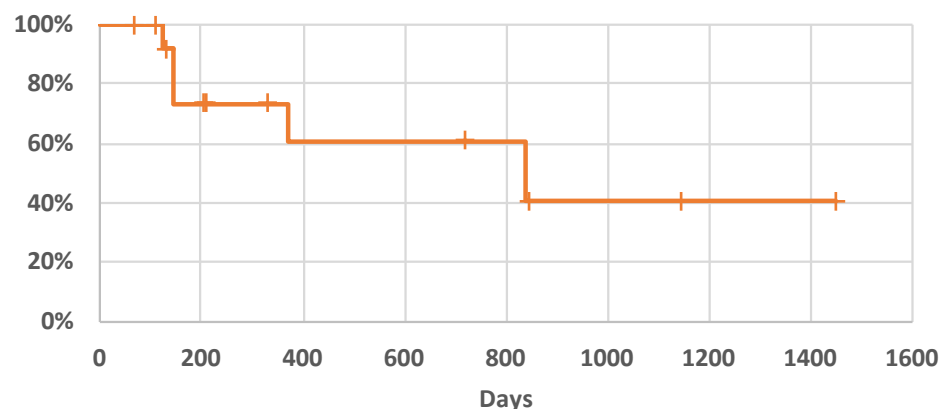# How We Determined Treatments and Relapses
Number of hospital procedures and medications prescribed at activity peaks

© Vital Transformation 2018
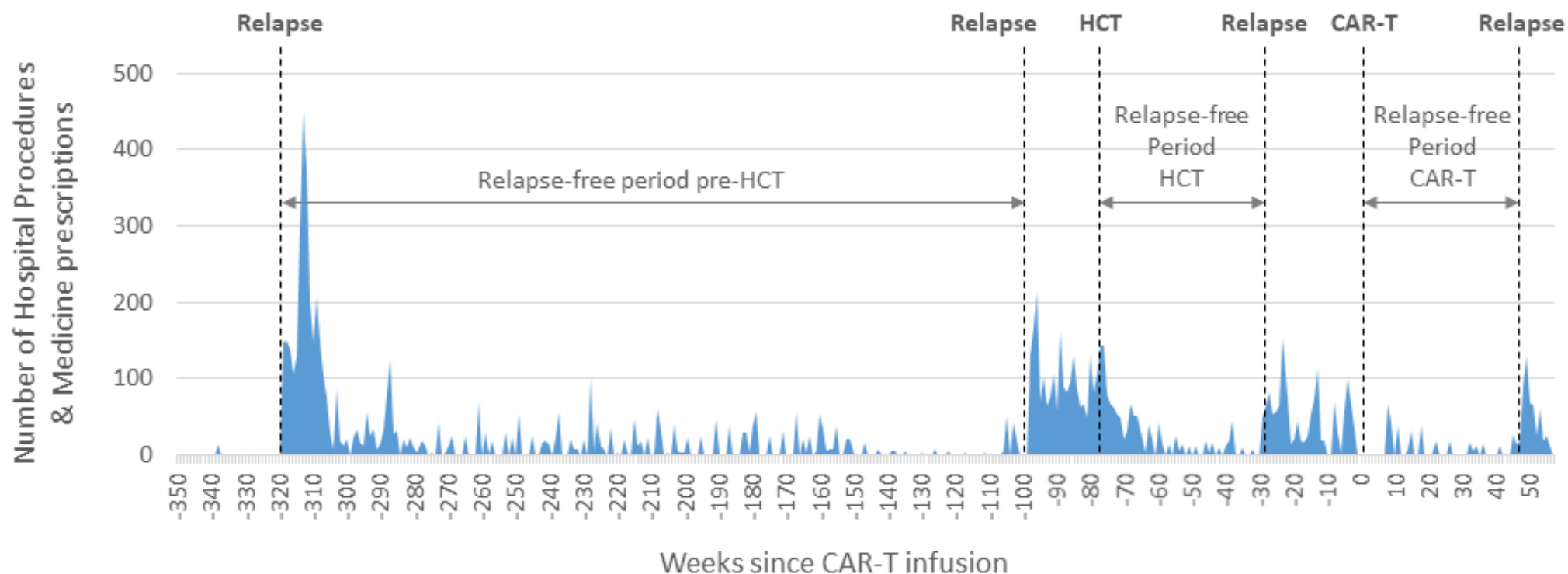
Kaplan-Meier curves on Relapse-Free Survival

**Relapse-free Survival
CAR-T
3 survival probability 46% (95% CI 08 – 79%)**

**Relapse-free Survival
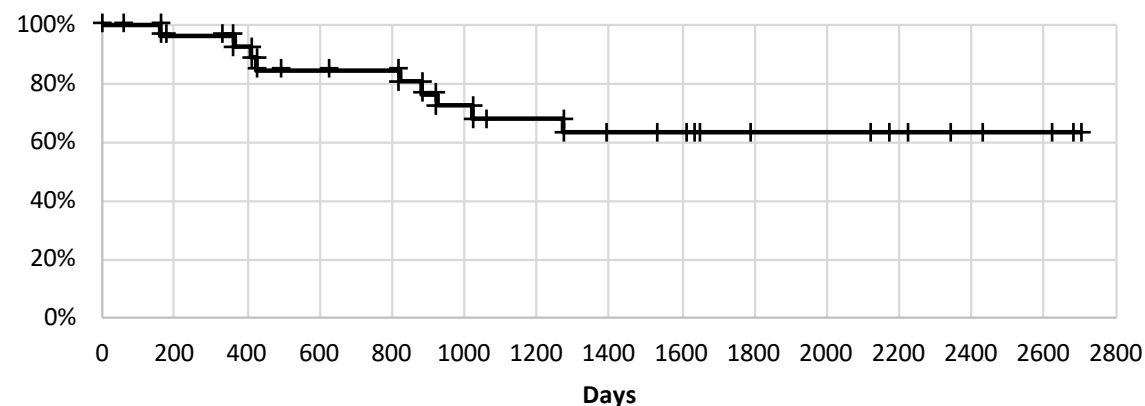HCT
3 year survival probability 68% (95% CI 46 – 83%)**

Days

Days

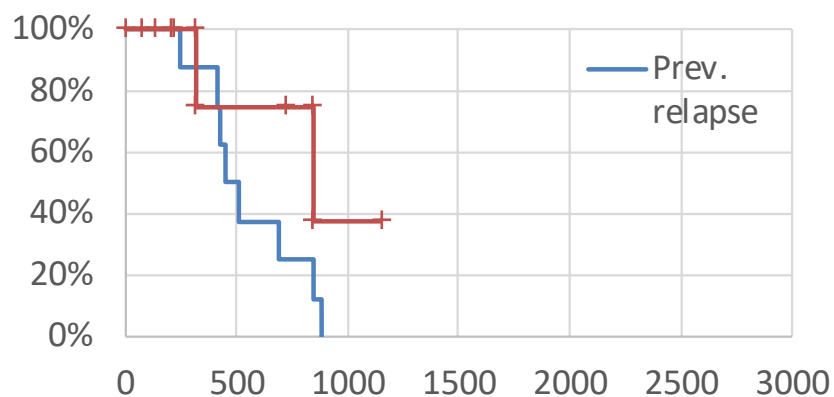| # subjects	14	10	6	6	5	2	1	1	0

29	26	24	21	20	17	15	13	12	8	8	6	4	3	0

Data censoring (slash) represents the end of available data, not death, as only 25% of our patient records included a death code.

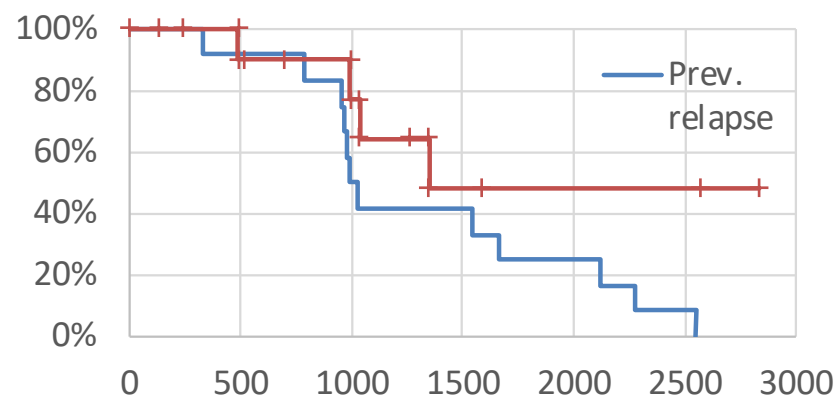# Comparison CAR-T & HCT vs Respective Previous Relapses
Disease burden CAR-T compared to HCT cohort (*p*=0.0001)

Relapse-free Survival
CAR-T Subjects

Relapse-free Survival
HCT Subjects

# subjects							
CAR-T	8	4	1	0	0	0	0
Prev. relapse	8	5	0	0	0	0	0

# Subjects							
Chem + HCT	12	9	6	3	2	2	0
Prev. relapse	12	11	6	5	3	1	0

Total Costs, Adjusted 3% Net Present Value (NPV)

	NPV 3%	Annual Costs				
		Infusion	Year 1	Year 2	Year 3*	Year 4*
CAR-T Treatment Cost Only	**-$118,250**	$56,217	$48,091	$14,529	$4,389.43	$1,326.11
HCT	**-$303,065**	$152,437	$84,152	$34,657	$24,812	$25,487
CAR-T Including $475k for Therapy	**-$579,415**	$531,217	$48,091	$14,529	$4,389.43	$1,326.11
		* CAR-T cost extrapolated from previous two years.				

Given the Success Of Our Proof of Concept, We Are Launching A New RWE Project in Diffuse Large B-cell Lymphoma

- Build a historical control for DLBCL treatments pre-CAR-T

- Derive an accurate understanding of the treatment pathways of CAR-T therapies Kymriah® and Yescarta® in clinical practice for the treatment of DLBCL in Europe and the US

- Analyse the pathway, performance and economic costs of hospital exempted CAR-T therapies developed EU academic institutions

- Quantify the time required from the point of T-cell extraction to infusion for all CAR-T products

- Develop a firm understanding of similarities and differences in the DLBCL treatment pathways between the USA and Europe

Zorginstituut Nederland

Effectiveness and Cost-effectiveness of Gene Therapies: Challenges & opportunities

Amr Makady PharmD, PhD

EBMT Registry Meeting

15.04.2019, Leiden

Innovation & New Treatment modalities

REVIEW ARTICLE

Journal for ImmunoTherapy of Cancer

A New Class of

Matth

GENOME EDITING IS A
cell with single base-p
and the engineering o
create a new class of medicine
diseases. Genome editing has
rection of variants that cause
antigen receptor (CAR) T-cell
I describe the development of
ficacy, specificity, delivery, an
graphic, available at NEJM.org

RESEARCH ARTICLE   **Open Access**

Evaluating in vivo efficacy – toxicity profile of TEG001 in humanized mice xenografts against primary human AML disease and healthy hematopoietic cells

Inez Johanna[1†], Trudy Straetemans[1†], Sabine Heijhuurs[1], Tineke Aarts-Riemens[1], Håkan Norell[2], Laura Bongiovanni[3], Alain de Bruin[3], Zsolt Sebestyen[1†] and Jürgen Kuball[1*†]

Abstract

Background: v9δ2T cells, which express Vγ9 and Vδ2 chains of the T cell receptor (TCR), mediate cancer immune

Challenges to Conventional HTA

- Phase I/II data in combination with claims of curation.

1. Short-term evidence is not (usually) enough to substantiate the claim
2. Data on hard end-points is (usually) not yet available
3. A go/no-go decision <u>has</u> to be made
4. Current (cost-)effectiveness methodology and policy frameworks do not facilitate better decision making

Can pay-for-performance schemes based on RWE offer a solution?

Horizonscanning, HTA & Industry: the story of the acacia tree and giraffes

Can we <u>act</u> on our Horizonscanning activities?

In the Lord of the Rings, even trees can move!

From Reactive to Proactive HTA

Conventional Process (Reactive):

- Manufacturer prepares dossier with evidence on: effectiveness, cost-effectiveness and budget impact

- Evidence hinges on sponsored phase I/II/III trials

- ZIN reviews dossiers prepared and issues advice to MoH (e.g. renegotiation of price; sluismiddelen)

Advantages:

- We have the opporunity to critique evidence but are not obliged to acquire/develop it

Disadvantages:

- We are dependent on external parties for evidence on effectiveness, cost-effectiveness and budget impact
- Sponsored data is not without its biases (!)

Can RWE inform proactive HTA?

Proactive HTA:

- Independent analyses of all available clinical evidence
- Insights into factors most affecting estimates of clincial effectiveness and cost-effectiveness

- <u>BUT:</u> limited knowledge on how to do so

Real-World Evidence?

"All health data generated outside the context of RCT's"

CAR-T Therapies: Reimbursement advice

Acute lymphoblastic leukemia (ALL) (up to 25 years old)

Kymriah®

- Therapeutic <u>added</u> value
- Budget Impact limited
- No pharmacoeconomic analysis due to limited budget impact

Diffuse large B-cell lymphoma (DLBCL)

Yescarta®

- Therapeutic <u>added</u> value
- Unreliable ICER thus no price reduction %age possible
- Do not include in package until price is negotiated
- Follow-up on long term via EBMT

Kymriah®

- <u>No added</u> therapeutic value

And they lived happily ever after?

Within our remit to:

- Follow-up on clinical effectiveness and cost-effectiveness
- Re-evaluate products' performance in real-life

- Question: how do we best do this?

Important to remember context!
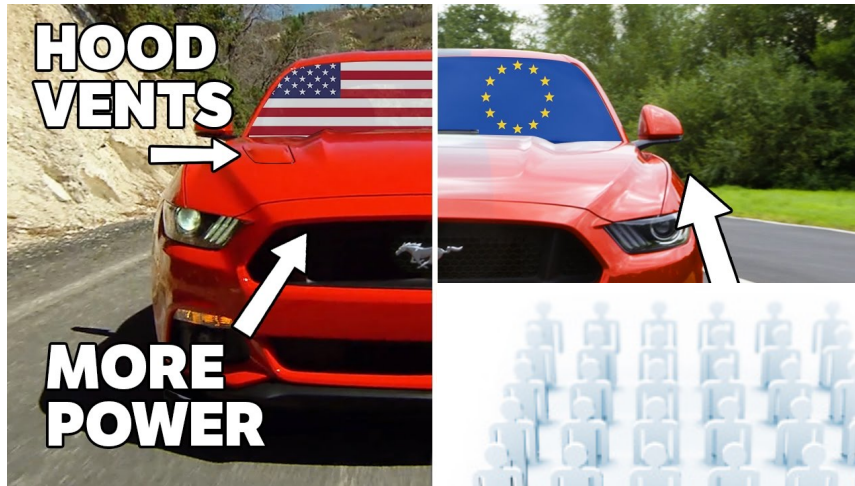
If You or Your Institution/Organisation Would Like To Contribute To Our DLBCL Study:

Contact us at:

info@vitaltransformation.com

The question usually asked:
Why is what is good enough for approval not good enough for reimbursement?

The question now is:
Why is what *was* good enough for approval
not *relevant* for reimbursement?

Healthcare Technology Assessment (HTA)

- *is the* *systematic evaluation* *of the* *properties, effects**, and/or* *impacts* *of health technology.*

Purpose- *to address the direct, indirect, intended, and unintended benefits and consequences of the adoption of healthcare technology .*
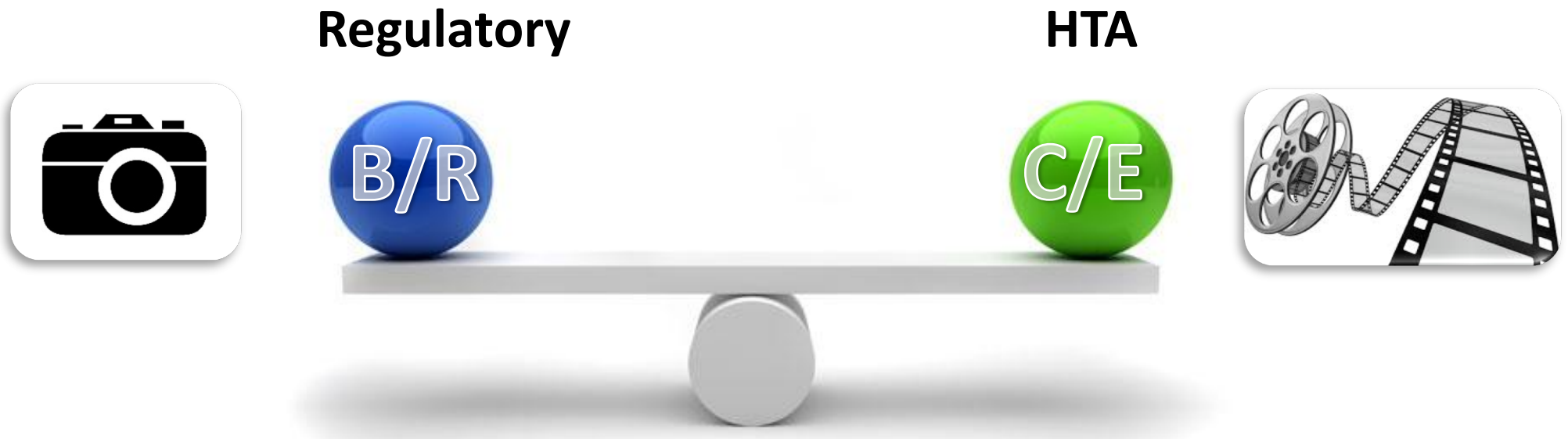
-Hailey, Babidge, Cameron, & Davignon 2010

Models to 'predict' the future

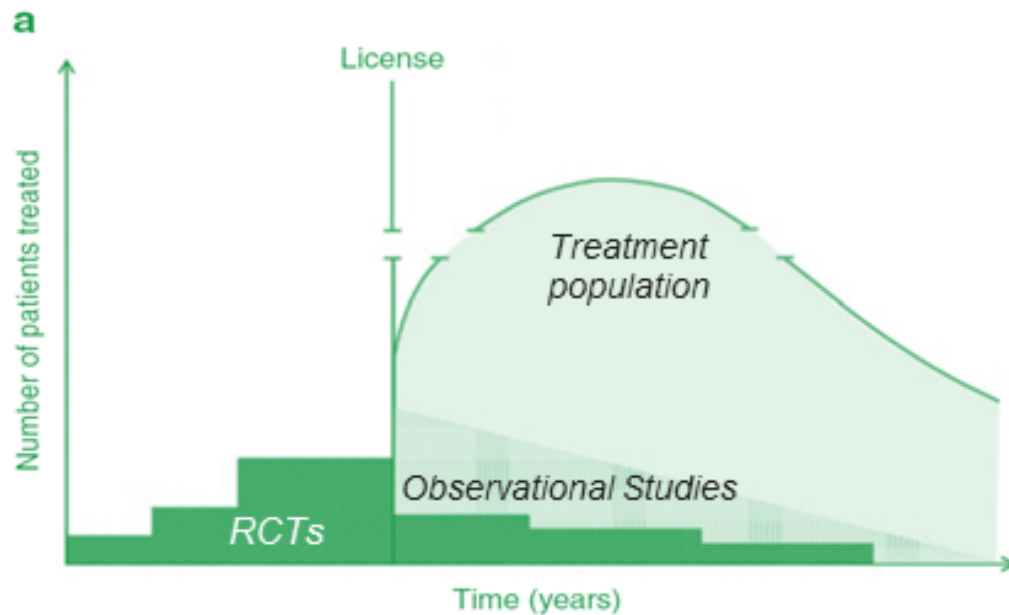- All models are wrong; some models are useful

  George E. P. Box; Norman R. Draper (1987)

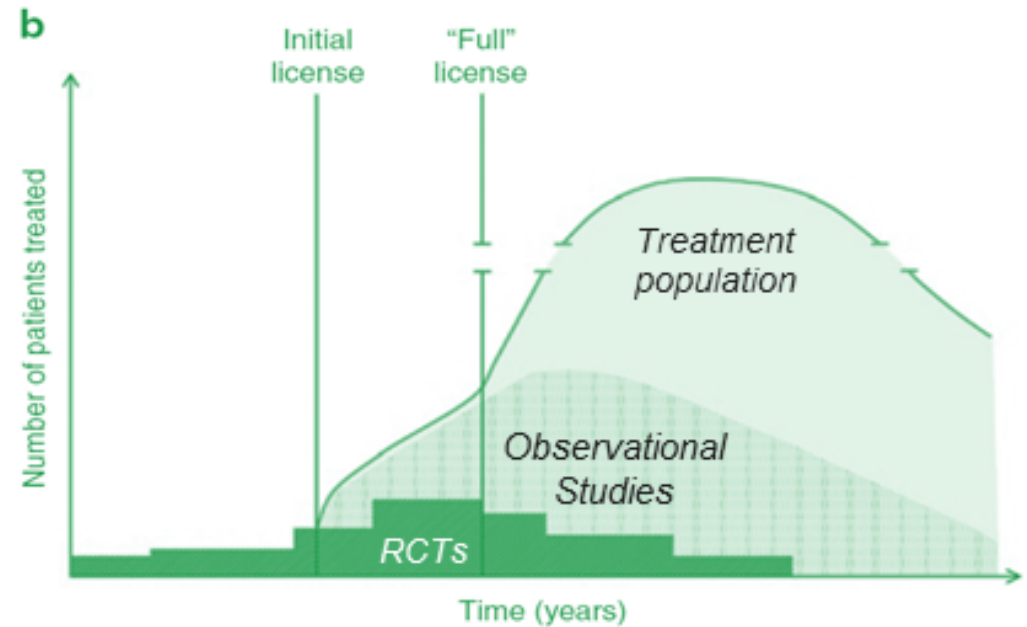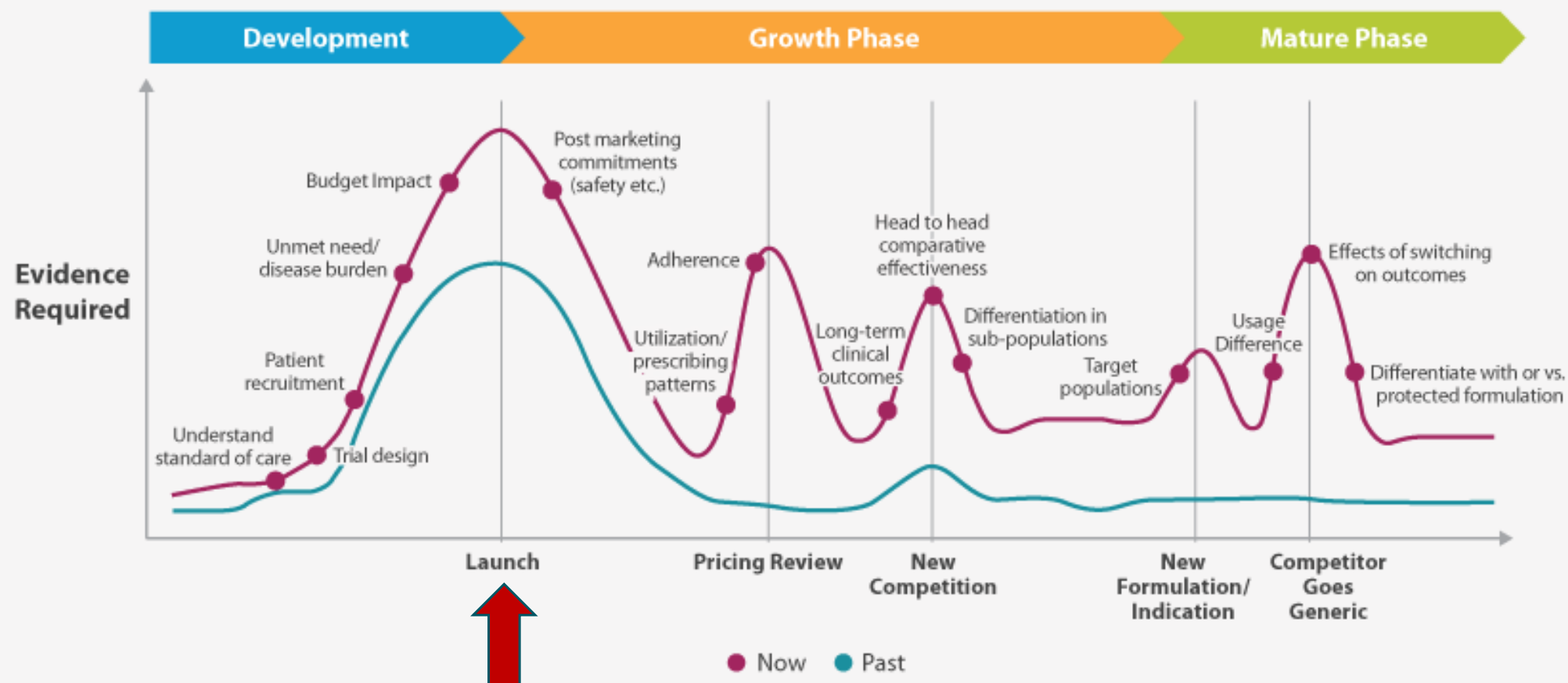- Health economic models predict the future based on available data from different sources

Regulatory   **HTA**

What are we really interested in?

Context is relative!

N. Allen et al. / Health Policy 113 (2013) 305–312

■	MC
■	MI
■	MA
■	SC
■	SA
■	PC
■	PI
■	PA
■	FC
■	EX
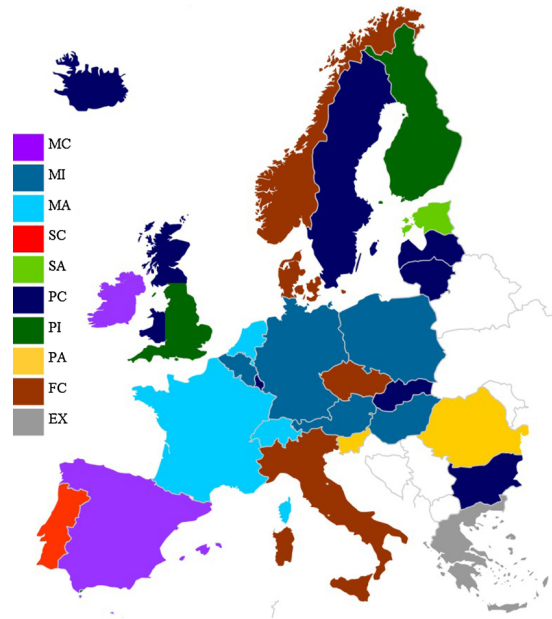
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