

WP11: From HTA results to implementation

PSE/AP-HP Hospinnomics and AP-HP/URC-Eco & Team WP11

CHAVEZ PACHECO Xyomara
DARLINGTON Meryl
DUPONT Jean-Claude K.
DURAND-ZALESKI Isabelle
ROCHAIX Lise (WP leader)
SCARICA Raffaele

Meeting Warsaw January 2019

Outline

Introduction (LR)

I - Brief on research so far (RS/MD)

II - Timeline, deliverables and future planning (LR)

III - Collaborations (LR)

Two 'corner situations' ... into the Far West

1 - Decremental cost-effective interventions (DCEIs)

Ex1: Shift from Atorvastatin to Simvastatin:

- net cost saving of 131€/patient
- with a maximum loss of 0.03 QALY, Liew et al, 2012

Ex2: Pain management reductions and/or tapering (shift to lower doses)

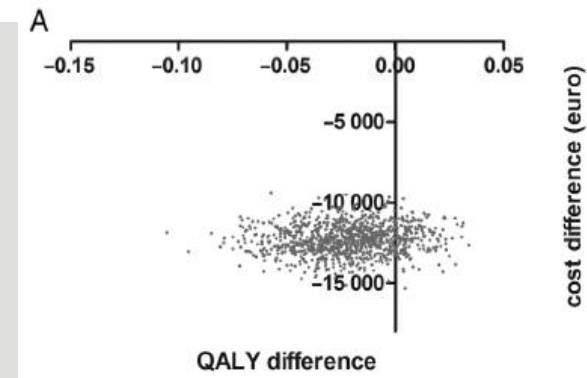
Ex3: Shift to NPIs (as substitutes to drug treatment) with lower efficacy

2 - Non pharmacological interventions (NPIs)

Complements (physical activity)

Substitutes (psychotherapy for mental health)

=> Growing interest, little evidence, virtually no guidance for implementation



Objective 1: Analysing the views and perspectives of HTA bodies, prescribers (health care professionals, hospitals) and the patient community in these two ‘corner situations’

Objective 2: Facilitating adoption and implementation of DCEIs or NPIs in a fair and transparent way

Task 1: Identify and categorize technologies offering prospects for efficiency gains outside incremental innovations captured in the NE quadrant (DCEIs and NPIs) => **Far West quadrant**

Task 2: Stakeholders' perspective: a political economy approach

Task 3: Toolbox and guidance on implementation

I - Brief on research so far:

Decremental Cost-Effective Interventions (DCEIs)

Method

Rafaella Scarica, URC-éco

Economic systematic review methodology

Review

How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: a five-step approach (part 1/3)

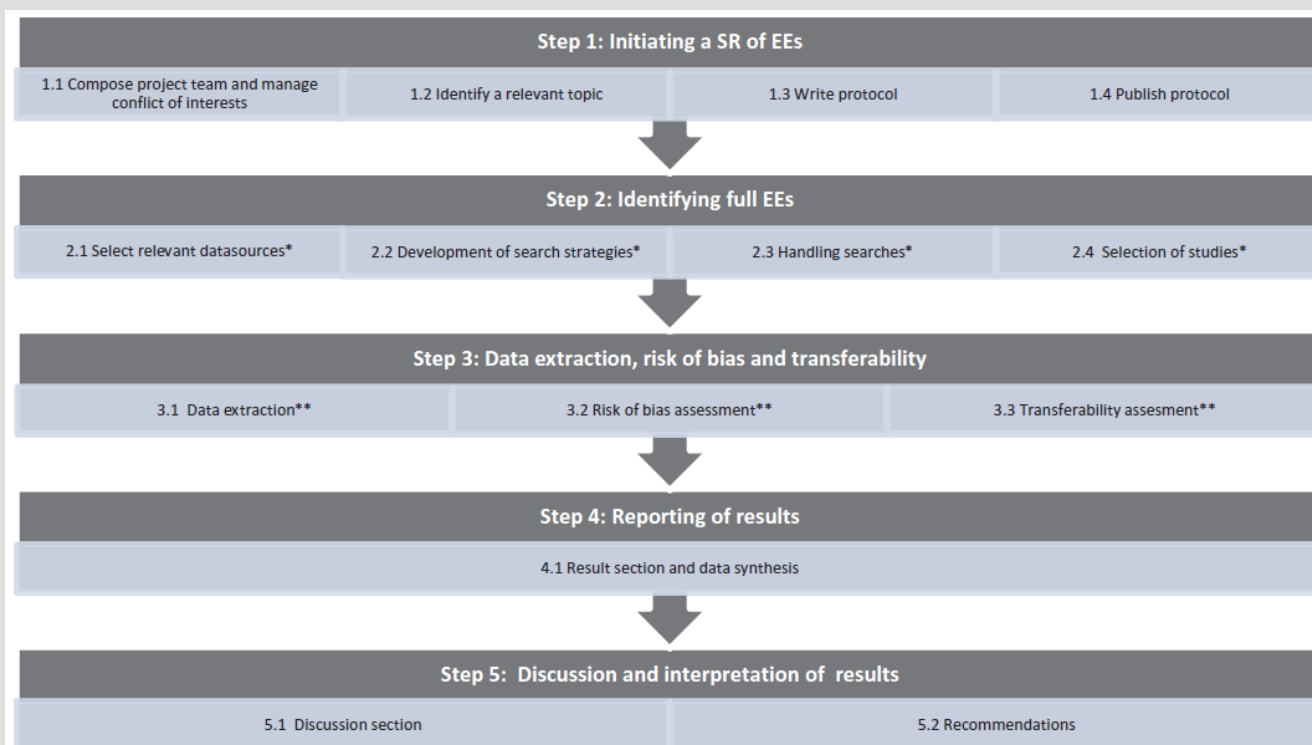
Ghislaine A.P.G. van Mastrigt ✉, Mickaël Hilgismann, Jacobus J.C. Arts, Pieter H. Broos, Jos Kleijnen, Silvia M.A.A. Evers & ...show all

How to prepare a systematic review of economic evaluations for clinical practice guidelines: database selection and search strategy development (part 2/3)

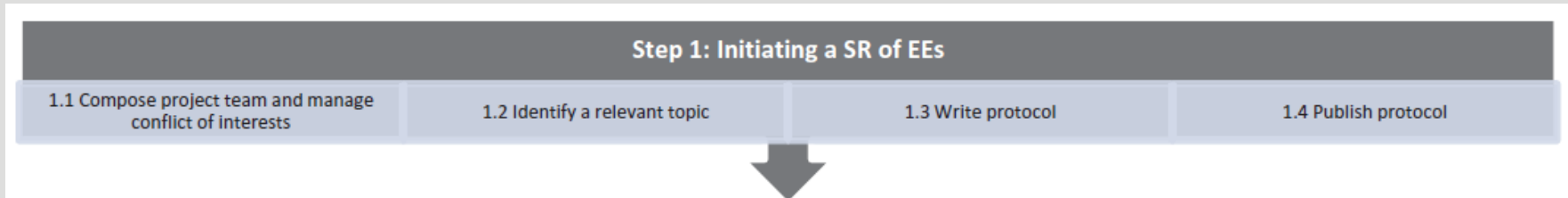
FW Thielen ✉, GAPG Van Mastrigt, LT Burgers, WM Bramer, HJM Majoie, SMAA Evers & ...show all

How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: data extraction, risk of bias, and transferability (part 3/3)

BFM Wijnen ✉, GAPG Van Mastrigt, WK Redekop, HJM Majoie, RJA De Kinderen & SMAA Evers



Economic systematic review initiating – Protocol



PROSPERO International prospective register of systematic reviews


**National Institute for
Health Research**

A systematic review of decrementally cost-effective health technologies.
Xyomara Chavez Pacheco, Meryl Darlington, Jean Claude K. Dupont, Isabelle Durand-Zaleski, Lise ROCHAIX, Raffaele SCARICA

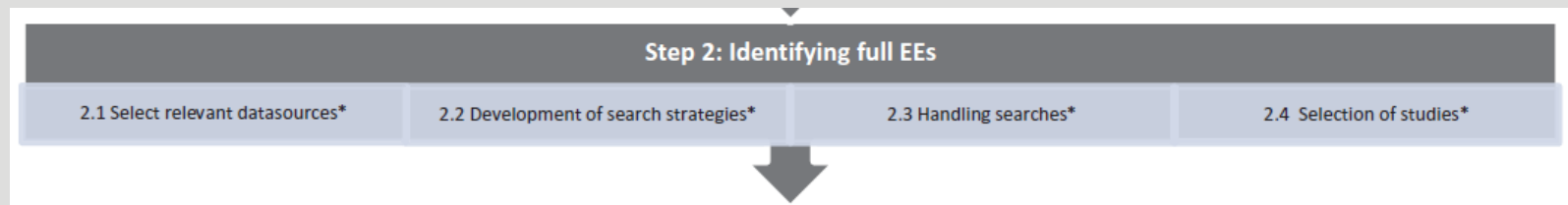
http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018095504

Review question

Which decrementally cost-effective health technologies (drugs, devices, interventions, services, diagnostic tests, and screening tests) could replace current standard care to allow for redistribution of resources leading to collective health gains?

We will identify health technologies with a cost and small quality reduction profile that could potentially replace current standard care to allow for redistribution of resources. Implementation of these decrementally cost-effective technologies could lead to collective health gains.

Economic systematic review – Identifying Full EEs



Inclusion criteria

- The intervention is being applied to human subjects.
- All studies comparing at least two health technologies.
- Studies should demonstrate decrementally cost-effective interventions.
- The interventions will be evaluated in a country defined as an upper-middle-income or high-income economy by the World Bank's 2018 country classification income level.

Exclusion criteria

- Publications reporting on methodological issues, discussion articles, partial economic evaluations, comment letters and editorials are excluded.



Economic systematic review methodology – Quality assessment

*International Journal of Technology Assessment in Health Care, 21:2 (2005), 240–245.
Copyright © 2005 Cambridge University Press. Printed in the U.S.A.*

Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria

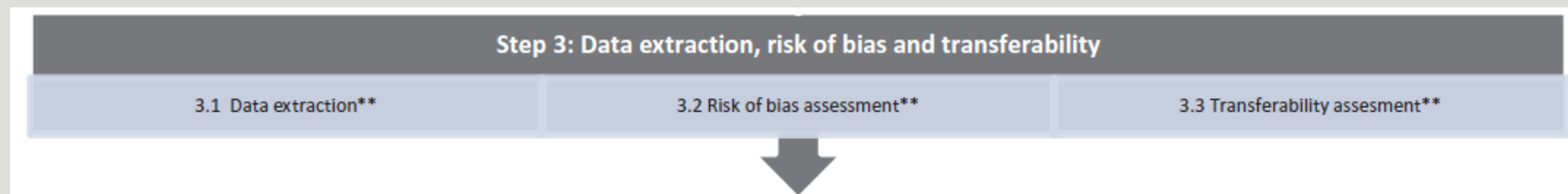
Silvia Evers, Mariëlle Goossens
Maastricht University, Institute for Rehabilitation Research

Henrica de Vet, Maurits van Tulder
VU University Medical Centre

André Ament
Maastricht University

CHEC-extended items (Evers et al. 2005; Odnoletkova et al. 2014)	
1	Is the study population clearly described?
2	Are competing alternatives clearly described?
3	Is a well-defined research question posed in answerable form?
4	Is the economic study design appropriate to the stated objective?
5	Are the structural assumptions and the validation methods of the model properly reported?
6	Is the chosen time horizon appropriate in order to include relevant costs and consequences?
7	Is the actual perspective chosen appropriate?
8	Are all important and relevant costs for each alternative identified?
9	Are all costs measured appropriately in physical units?
10	Are costs valued appropriately?
11	Are all important and relevant outcomes for each alternative identified?
12	Are all outcomes measured appropriately?
13	Are outcomes valued appropriately?
14	Is an appropriate incremental analysis of costs and outcomes of alternatives performed?
15	Are all future costs and outcomes discounted appropriately?
16	Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?
17	Do the conclusions follow from the data reported?
18	Does the study discuss the generalizability of the results to other settings and patient/client groups?
19	Does the article/report indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?
20	Are ethical and distributional issues discussed appropriately?

Economic systematic review methodology – data extraction, risk of bias and transferability



How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: data extraction, risk of bias, and transferability (part 3/3)

BFM Wijnen ✉, GAPG Van Mastrigt, WK Redekop, HJM Majoie, RJA De Kinderen & SMAA Evers

EXPERT REVIEW
OF PHARMACOECONOMICS & OUTCOMES RESEARCH

Expert Review of Pharmacoeconomics & Outcomes Research

ISSN: 1473-7167 (Print) 1744-8379 (Online) Journal homepage: <http://www.tandfonline.com/loi/ierp20>

Risk of bias in model-based economic evaluations: the ECOBIAS checklist

Charles Christian Adarkwah, Paul F. van Gils, Mickaël Hiligsmann & Silvia M.A.A. Evers

	Original Papers
Eur J Health Econom 2005 · 6:334–346 DOI 10.1007/s10198-005-0322-1 Published online: 26 October 2005 © Springer Medizin Verlag 2005	Stephanie Boulenger¹ · John Nixon² · Michael Drummond² · Philippe Ulmann¹ Stephen Rice² · Gerard de Pouvourville¹ ¹ Collège des Économistes de la Santé, Paris, France ² Centre for Reviews and Dissemination, University of York, York, UK
	Can economic evaluations be made more transferable?

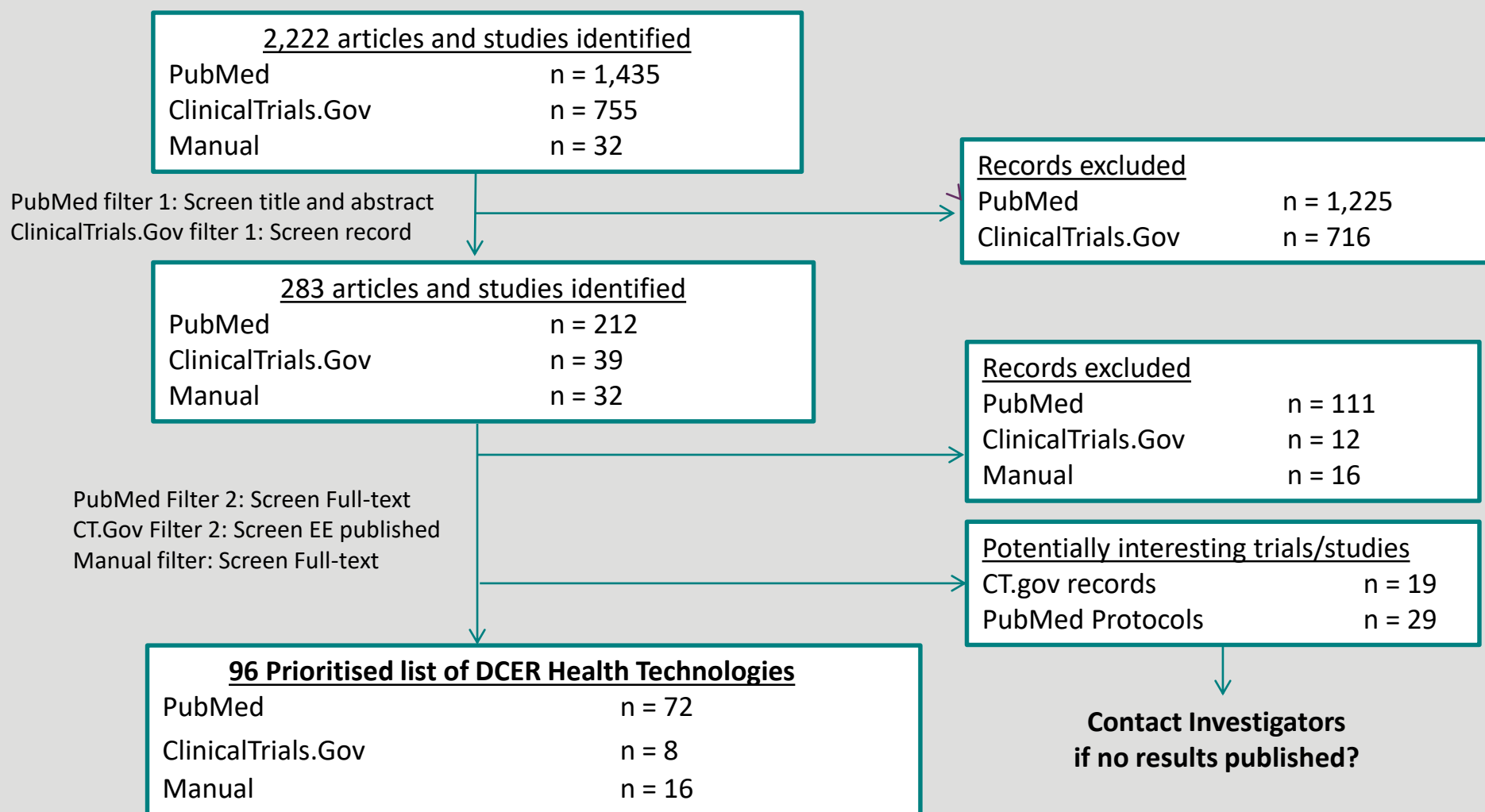
I - Brief on research so far:

Decremental Cost-Effective Interventions (DCEIs)

First results

Meryl Darlington, URC-éco

Economic systematic review results – PRISMA CHART

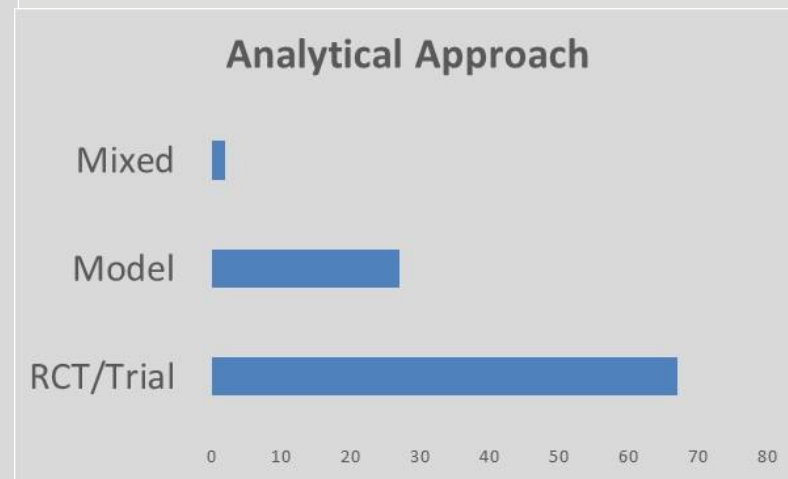
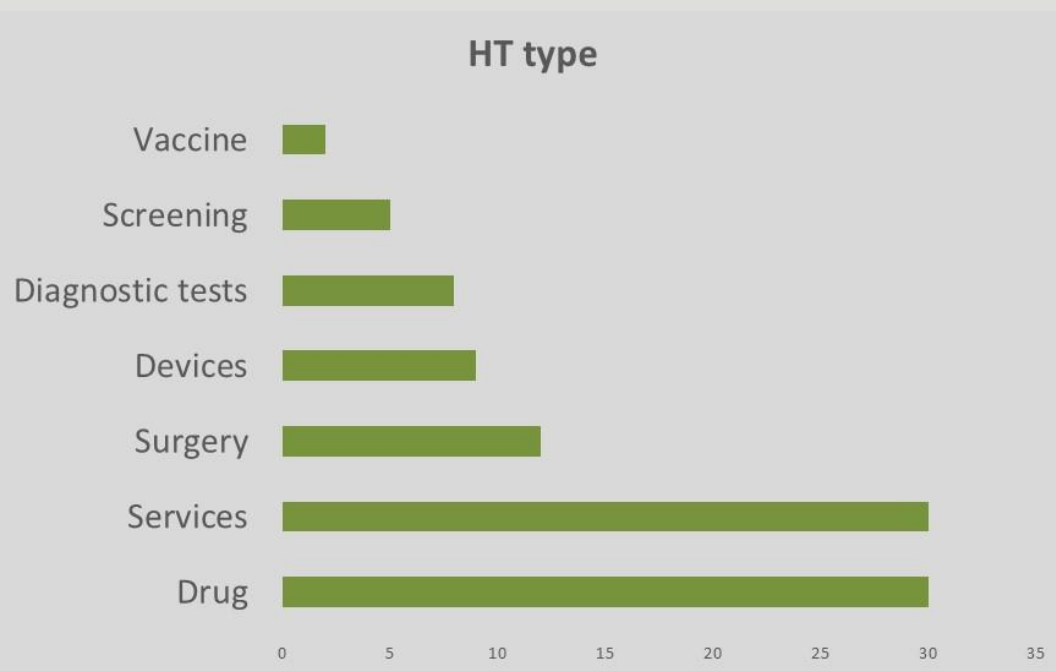


96 Prioritised list of DCER Health Technologies

PubMed search	n = 72
ClinicalTrials.Gov	n = 8
Manual search	n = 16

- 36 Top score studies in terms of all factors
- 42 with some quality/transferability/bias issue
- 18 Medium/Low quality (transferability and bias not assessed)

Economic systematic review – Results



Economic systematic review – Example of DCEI

Clinical and epidemiological research

EXTENDED REPORT

Disease activity-guided dose optimisation of adalimumab and etanercept is a cost-effective strategy compared with non-tapering tight control rheumatoid arthritis care: analyses of the DRESS study

Wietske Kievit,¹ Noortje van Herwaarden,² Frank HJ van den Hoogen,^{2,3} Ronald F van Vollenhoven,⁴ Johannes WJ Bijlsma,⁵ Bart JF van den Bemt,^{6,7} Aatke van der Maas,² Alfons A den Broeder²

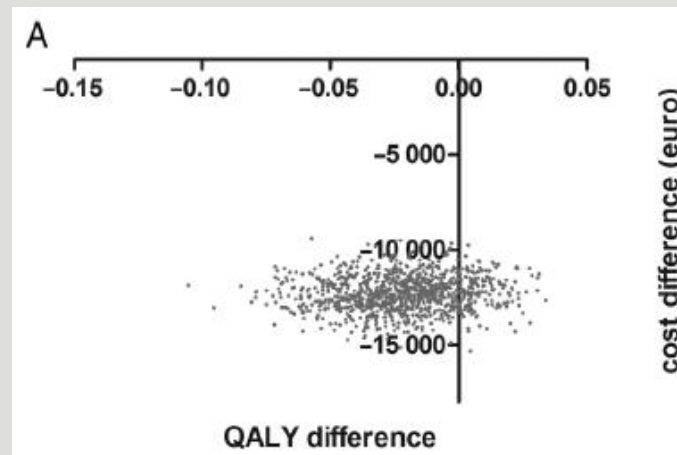


Table 3 Mean QALYs and costs for both strategies as a result of 1000 bootstrapped replication

Group	QALY	Incremental QALY	Costs	Incremental costs
Optimisation	1.23 (1.20; 1.26)		€16 633 (€27 604; €30 074)	
Control	1.25 (1.22; 1.29)	-0.02 (-0.07; 0.02)	€28 913 (€15 316; €17 944)	€12 280 (€10 502; €14 104)

Data are presented as means with 95 percentile resulting from the 1000 bootstrapped replications.
QALYs, quality adjusted life years.

The DCER was €390 493 of savings per QALY lost.

Economic systematic review – Example of DCEI: Non-inferior & cost saving

[Lancet](#). 2016 Jul 16;388(10041):239-47. doi: 10.1016/S0140-6736(16)00380-9. Epub 2016 May 17.

Tumour necrosis factor inhibition versus rituximab for patients with rheumatoid arthritis who require biological treatment (ORBIT): an open-label, randomised controlled, non-inferiority, trial.

Porter D¹, van Melckebeke J², Dale J³, Messow CM⁴, McConnachie A⁴, Walker A², Munro R³, McLaren J⁵, McRorie E⁶, Packham J⁷, Buckley CD⁸, Harvie J⁹, Taylor P¹⁰, Choy E¹¹, Pitzalis C¹², McInnes IB².

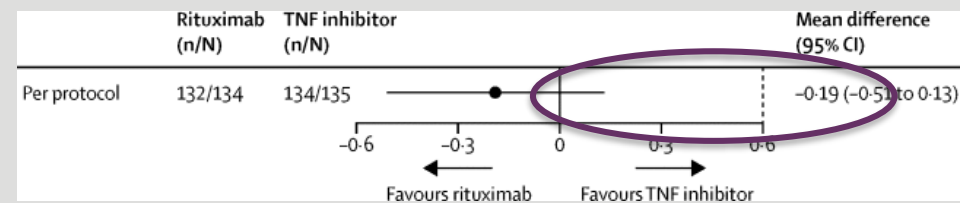


Table 5. Health-care costs and QALYs over 12 months

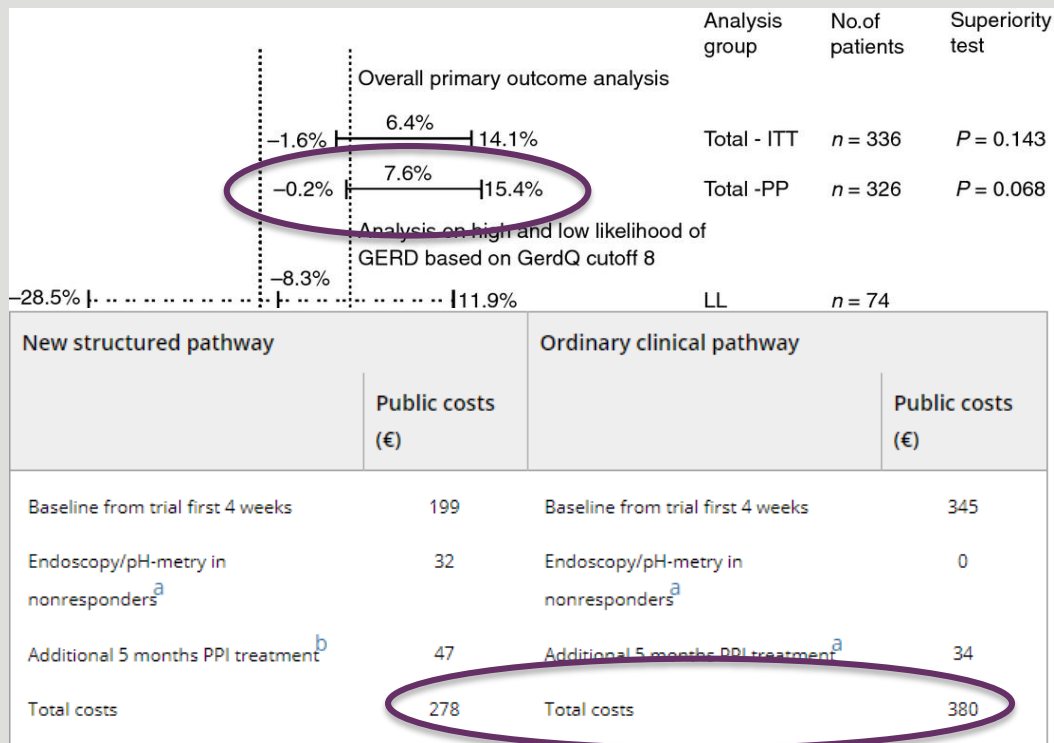
	Rituximab	TNF inhibitor
Health-care costs		
Medicines, infusions, clinics	£8391	£10 356
Primary care	£366	£370
Blood tests, radiograph	£141	£163
Total	£9405	£11 523
QALYs (EQ-5D AUC)	0.454	0.481

Bootstrap estimated mean cost difference £1999 (95% CI 2755 to 1440). Bootstrap estimated mean difference 0.028 (-0.041 to 0.094). QALY=quality-adjusted life-years. TNF=tumour necrosis factor. EQ-5D=EuroQol questionnaire. AUC=area under the curve.

Economic systematic review – Example of DCEI: Non-inferior & cost saving

Randomised clinical trial: a comparison between a GerdQ-based algorithm and an endoscopy-based approach for the diagnosis and initial treatment of GERD

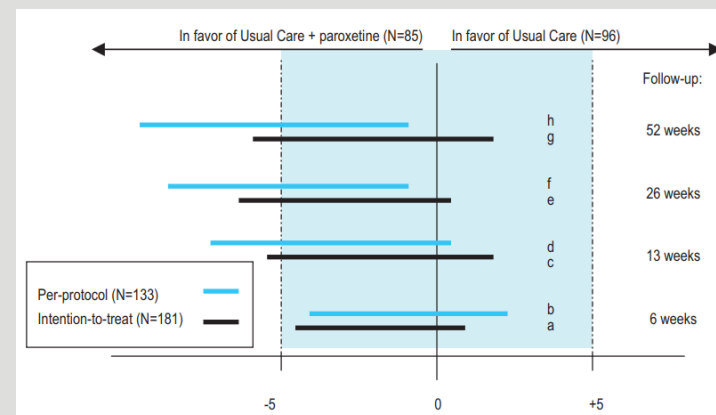
C. Jonasson*, B. Moum†, C. Bang†, K. R. Andersen§ & J. G. Hatlebakk*



Economic systematic review – Equivalence trials

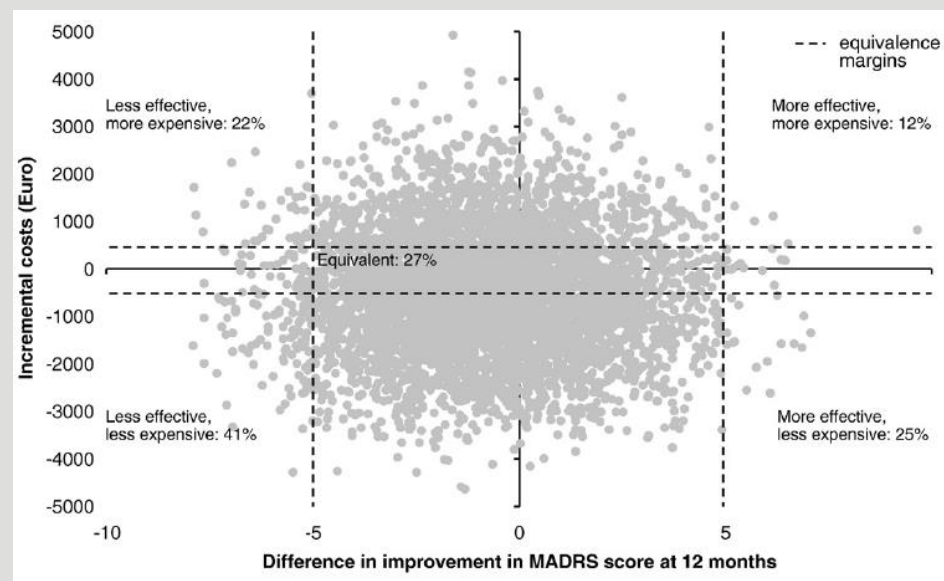
Clinical effectiveness of usual care with or without antidepressant medication for primary care patients with minor or mild-major depression: a randomized equivalence trial

Marleen LM Hermens¹, Hein PJ van Hout^{*1}, Berend Terluin¹, Herman J Adèr², Brenda WJH Penninx³, Harm WJ van Marwijk¹, Judith E Bosmans⁴, Richard van Dyck³ and Marten de Haan¹



Cost-effectiveness of usual general practitioner care with or without antidepressant medication for patients with minor or mild-major depression

Judith E. Bosmans^{a,b,*}, Marleen L.M. Hermens^c, Martine C. de Bruijne^a, Hein P.J. van Hout^c, Berend Terluin^c, Lex M. Bouter^d, Wim A.B. Stalman^c, Maurits W. van Tulder^{a,b}



I - Brief on research so far:
***First results on Non Pharmacological
Interventions (NPIs)***
Hospinnomics

NPIs' evaluation by type (physical activity):

Systematic literature review

- Pathologies: rheumatology (53%), cardiology (26%), respiratory disorders, diabetes, mental health, cancer
- study designs: RCTs (83%), models/simulation (11%), CTs, retrospective studies (2%)

Publication: Guillon M., Rochaix L., Dupont JCK, (2018) "Cost-effectiveness of interventions based on physical activity in the treatment of chronic conditions: a systematic literature review", *International Journal of Health Technology Assessment in Health Care*, Oct 9:1-17.

... to reimbursement decision

Policy brief: 'Should physical activity be reimbursed? Evidence from selected countries', Guillon M., Rochaix L., Dupont JCKD, March 2019

GPs could prescribe bingo and dancing after English trial's success

One practice prescribing activities saw 20% cut in hospital outpatient admissions



Non pharmacological interventions (NPIs) : Example on brain diseases



705 articles in 218 journals of which 198 in SCIMAGO
Journals' ranking by Impact Factor

Pubmed search of RCTs on NPIs
 (("2011"[Date - Publication] :
 "3000"[Date - Publication])) AND
 ("Brain Diseases"[MesH]) AND
 ("Complementary Therapies"[MesH]
 OR "Nondrug"[MesH])) AND
 Randomized Controlled Trial[ptyp]



Step 1: Following completion of systematic reviews and typologies, identification of candidate interventions.

Step 2: Setting up of 'specialist forum' with representatives from up to 4 European health authorities to assess evidence on DCEIs and NPIs and provide additional insights (6M delay; no impact on other MS/Ds)

Step 3: DCE: Identify the conditions (such as reversibility of symptoms) under which HTA bodies will agree to encourage DCEIs or NCIIs by providing the relevant guidance for prescribers

III Collaborations

Time planned from WP11 for collaborations

WP 2 (3 M)

Time planned for collaborations (no funding)

WP 8 on hospital performance

WP10 on rare diseases

Collaborations hoped from other Member countries on stakeholders' meeting (June 2019) and on DCE

Thank-you



Economic systematic review – Results (some top score studies)

Database	Author	Year	Country	Disease/Condition	Intervention	Comparator	Type of EE	Analytical approach	Effects	Cost	DCER
PubMed	<i>Kievit et al</i>	2016	Netherl.	Rheumatoid arthritis	Dose optimisation for TNFi	TNFi	CEA	RCT	-0.02 QALYs	- € 12 280	€ 390 493/QALY Lost
PubMed	<i>Oddershed et al</i>	2016	UK	HIV	Protease inhibitor	On-going triple therapy	CEA	Mixed	-0.0227 QALYs	- £ 6 417	£ 282 641/QALY Lost
CT.Gov	<i>Brown et al</i>	2018	UK	Rheumatoid arthritis	Alternative TNFi	Abatacept	CEA	RCT	-0.02 QALY	- £ 3 768	£ 253 967/QALY Lost
Manual	<i>Stroupe et al</i>	2006	US	Inguinal hernia	Watchful waiting	Tension-free surgical repair	CEA	RCT	-0.0140 QALY	- \$ 2 721	\$ 194 331/QALY Lost
Manual	<i>Manca et al</i>	2006	UK	Neck pain	Brief physiotherapy intervention	Usual physiotherapy management	CEA	RCT	-0.0010 QALY	- \$ 122	\$ 122 278/QALY Lost
PubMed	<i>Howard et al</i>	2017	UK	Leukaemia	FCM-miniR	FCR	CEA	RCT	-0.059 QALYs	- £ 6 619	£ 112 193/QALY lost
PubMed	<i>Vanier et al</i>	2017	France	Rheumatoid Arthritis	Spacing arm	Maintenance arm	CEA	RCT	-0.158 QALYs	- € 8 440	€ 53 417/QALY Lost
PubMed	<i>Westwood et al</i>	2014	UK	Lung cancer	EGFR PCR Kit	Exon 19–21	CEA	Markov	-0.286 QALYs	- £ 9 194	£ 32 196/QALY Lost
PubMed	<i>Goorden et al</i>	2013	Netherl.	Major depressive disorder	Collaborative care	Care as usual	CUA	RCT	-0.05 QALYs	- € 709	€ 14 589/QALY Lost