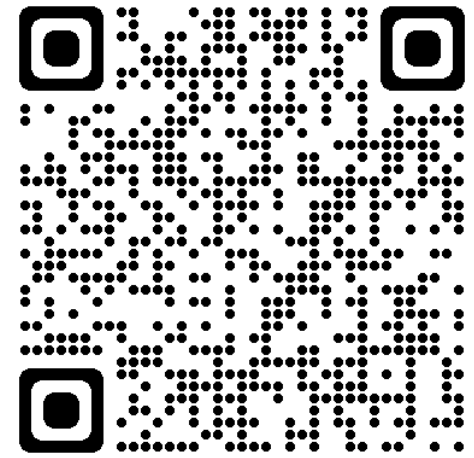


IPECAD Open-Source Model



Framework for Health-Economic Evaluation of Early Treatment in Alzheimer's Disease

Ron Handels

ISPOR conference - Copenhagen (14-11-2023)



IPECAD

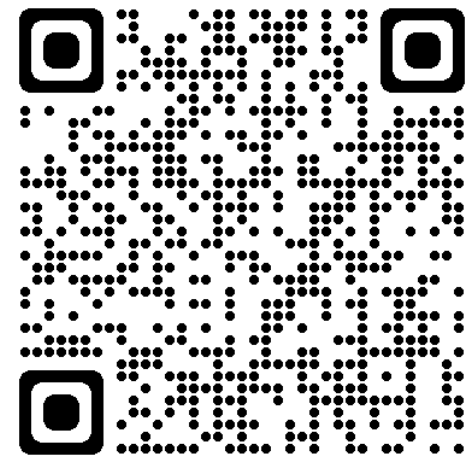
International Pharmaco-Economic Collaboration on Alzheimer's Disease



Maastricht University



Disclosure



Related to this work

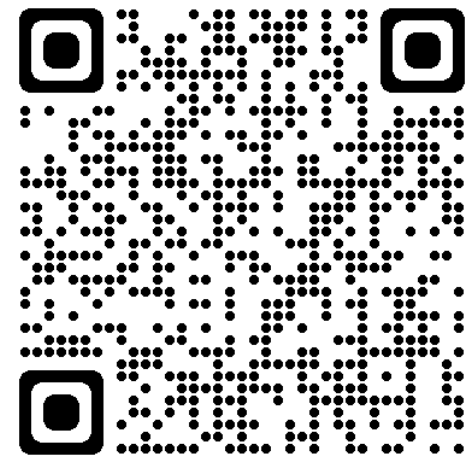
- member of the IPECAD group (un-paid)

Outside this work

- received research **grants** from JPND, ZonMW, IMI, H2020 (paid to institution)
- received **consulting fees** paid to institution in the past 3 years from:
 - Lilly Nederland (2023)
 - iMTA (2023)
 - Biogen (2021)
- member of **ISPOR special interest group** open-source models (un-paid)

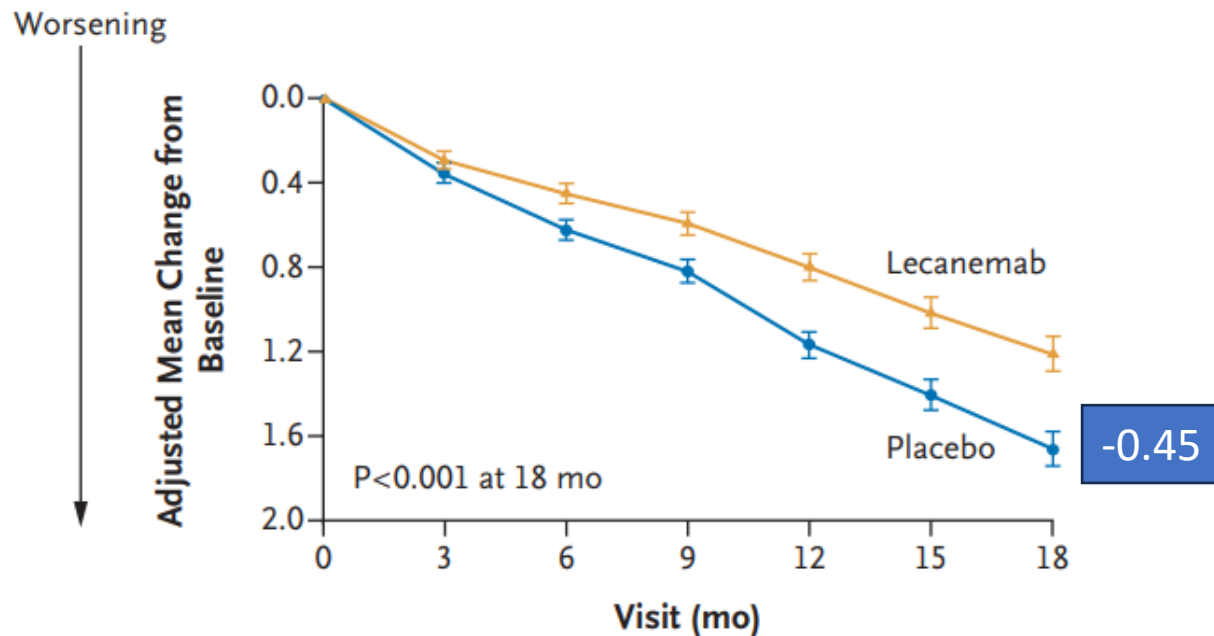
Model developers

- Ron Handels – [Maastricht University](#), [Karolinska Institutet](#)
- Anders Wimo – [Karolinska Institutet](#)
- Anders Sköldunger – [Karolinska Institutet](#)
- Ashley Tate – [Karolinska Institutet](#)
- Bengt Winblad – [Karolinska Institutet](#)
- Daphne Silvertand – [Maastricht University](#)
- Linh Nguyen – [Maastricht University](#)
- Linus Jönsson – [Karolinska Institutet](#)
- Sabine Grimm – [Maastricht University Medical Center](#)
- Sandar Aye – [Karolinska Institutet](#)
- Will Herring – [RTI Health Solutions](#), [Karolinska Institutet](#)

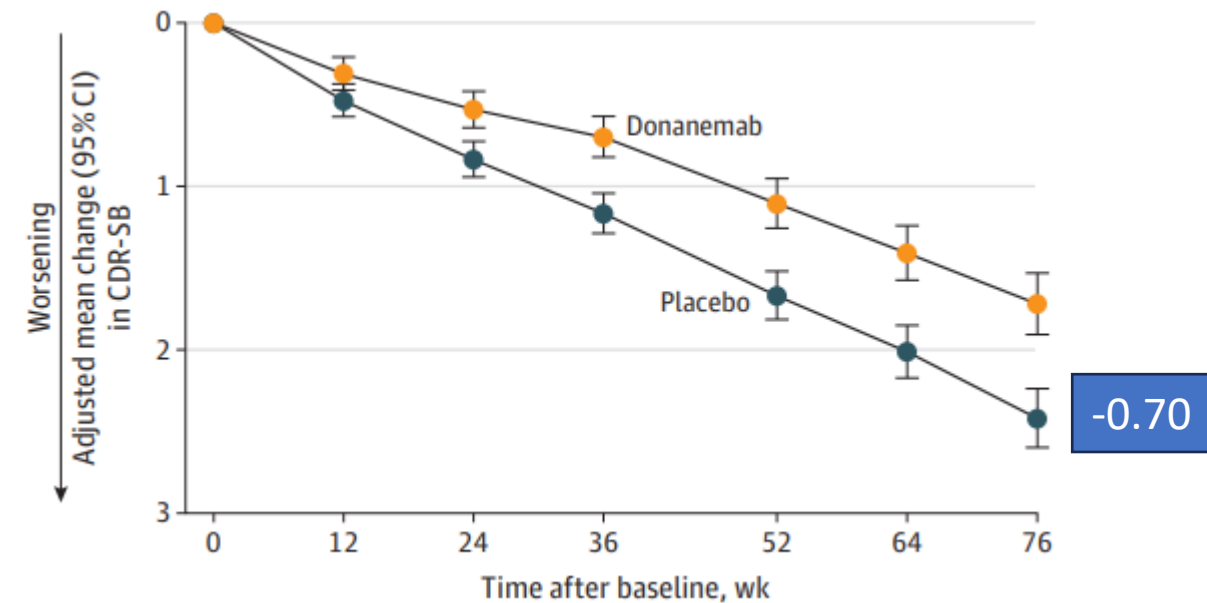


AD drug trials in MCI and mild dementia with abnormal amyloid (Clinical Dementia Rating, CDR)

Lecanemab (2023)



Donanemab (2023)

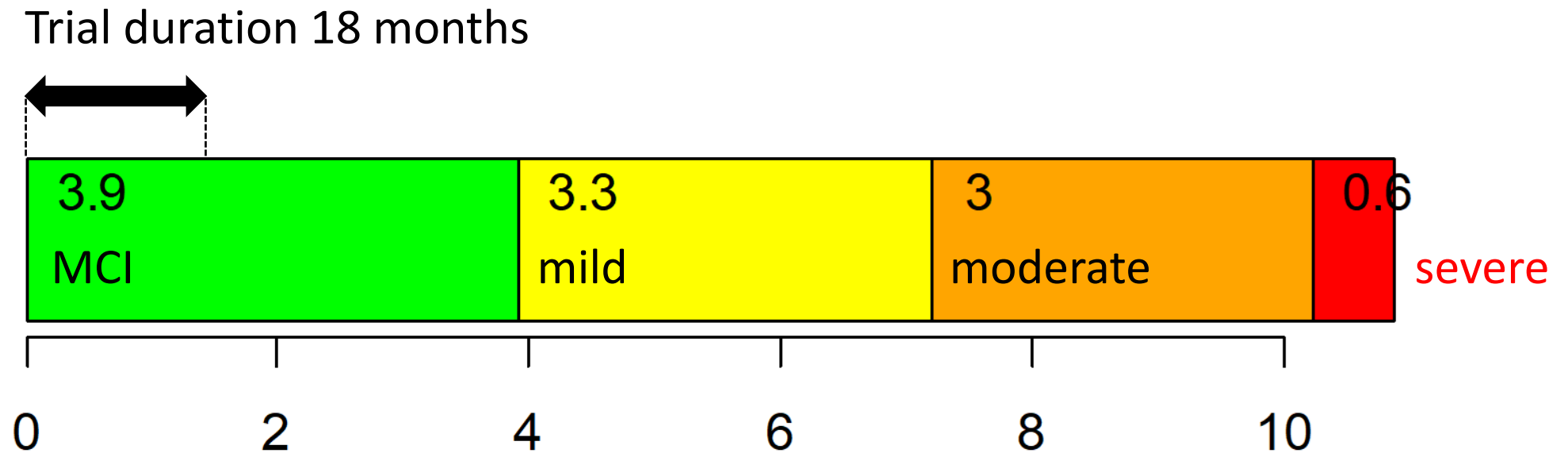


CDR: cognition and function (range: 0-18)

Lecanemab, graph copied from publication [van Dycke et al., 2023: <https://doi.org/10.1056/NEJMoa2212948>]

Donanemab, graph copied from publication [Sims et al., 2023: <https://doi.org/10.1001/jama.2023.13239>]

Challenge: cost-effectiveness lifetime horizon



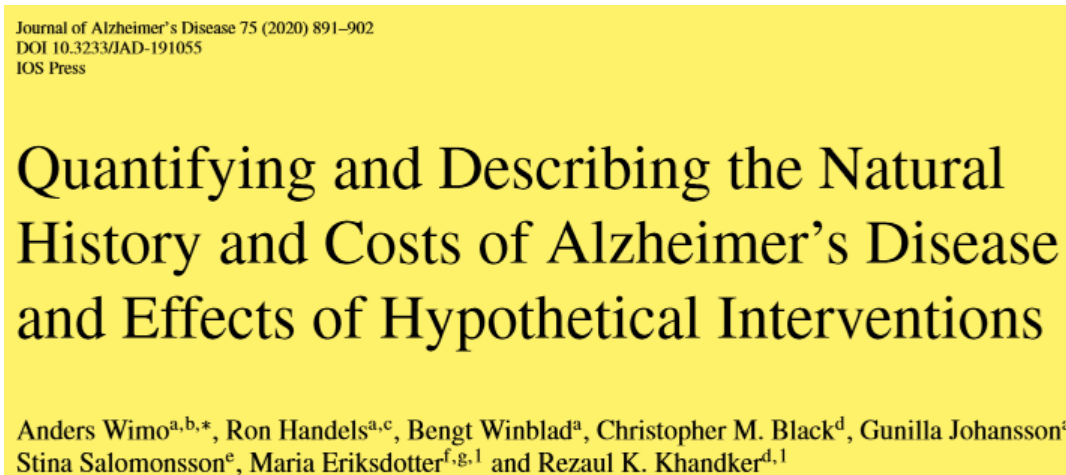
Aim

- **Reimbursement decision:** need for transparent and credible model
- **Aim:** develop updated open-source decision-model framework for health-economic evaluation of future Alzheimer's disease treatments

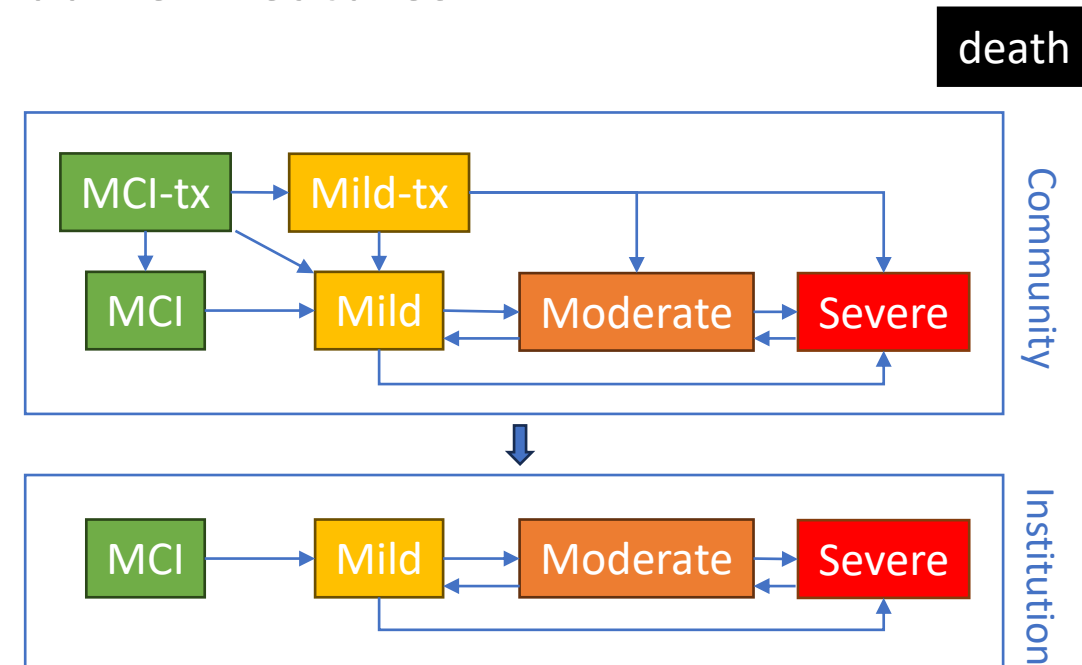
Replicate and update existing model

Replicate existing model

- MMSE-based Markov model [Wimo, 2020]
- Natural disease progression SveDem registry
- Internal validity replication (<0.6% deviation)



Add new features



Waning, discontinuation, living setting,
European region mortality/utility/cost estimates,
(probabilistic) uncertainty analysis

Hypothetical intervention

Natural history

- Transition probabilities disease severity and death [Wimo, 2020]
- Utilities and costs by state [same as Green, 2019]

Target population

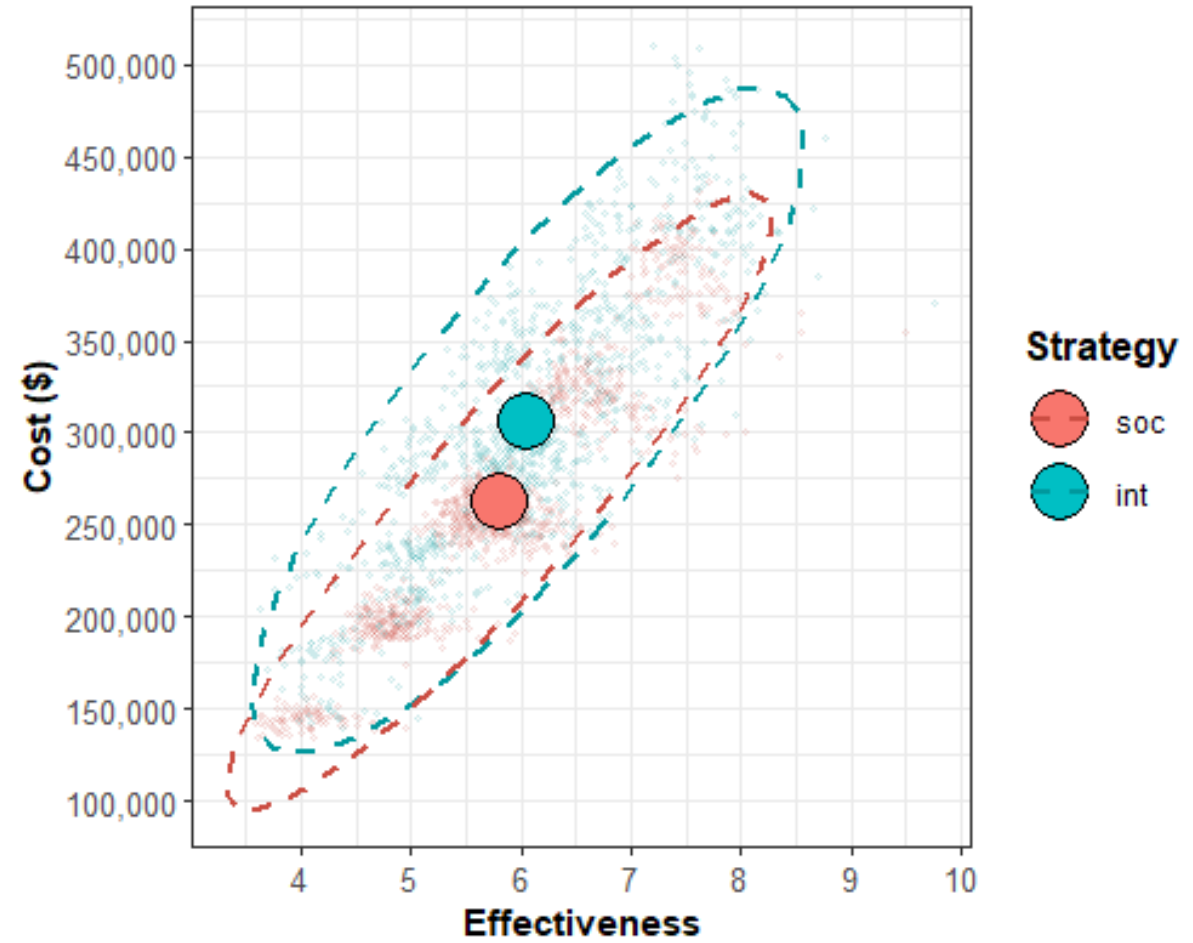
- MCI
- Abnormal amyloid
- Age 70 years
- Diagnosis in clinical setting

Intervention

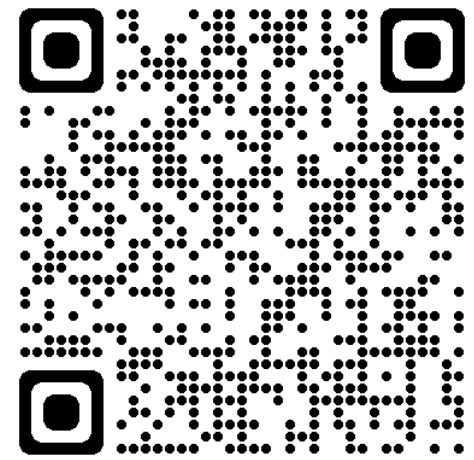
- 25% reduction in transition:
 - from MCI to mild dementia
 - From mild to moderate dementia
- Treat: 7 years
- Waning: 5%
- Discontinuation: 10%
- \$10,000/year

ICER

- \$146,449/QALY



Road to transparency & credibility

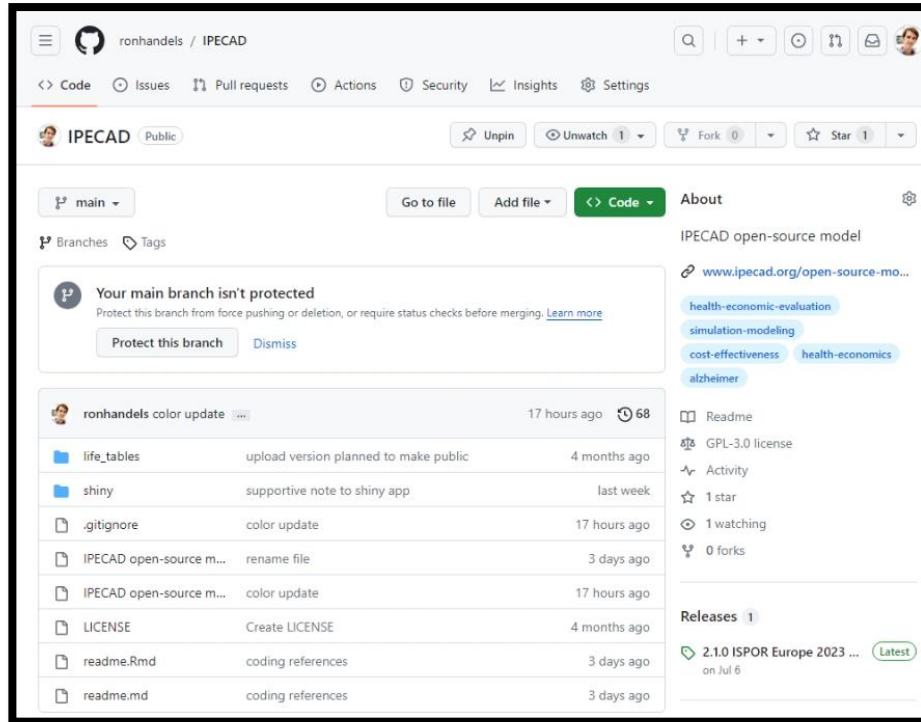


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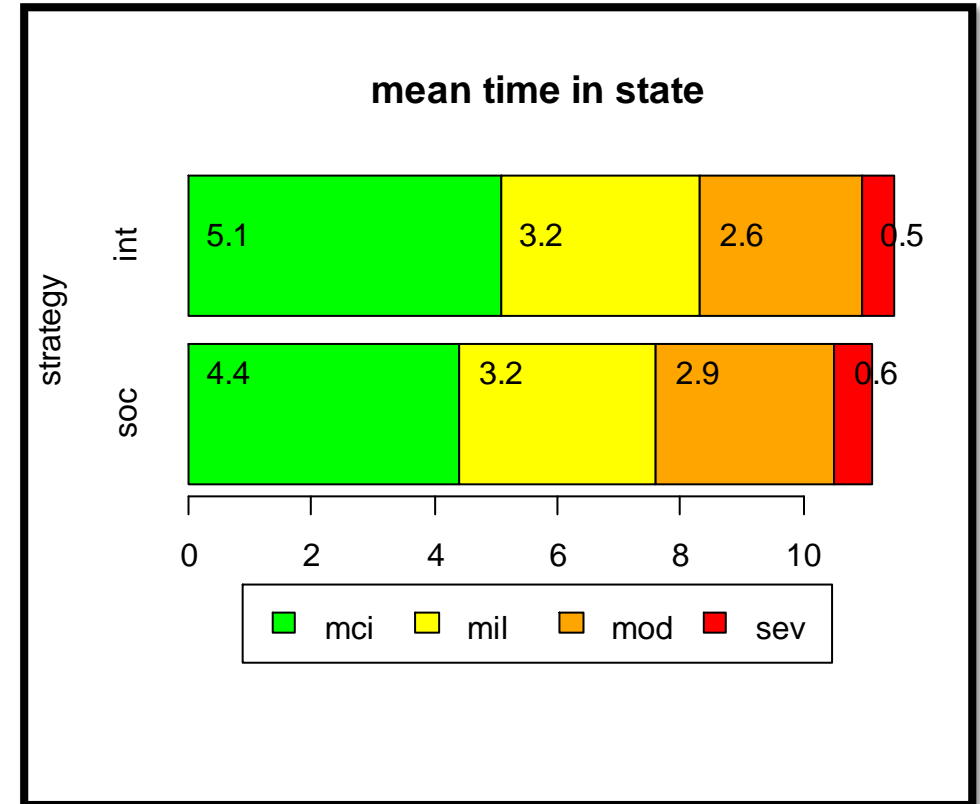
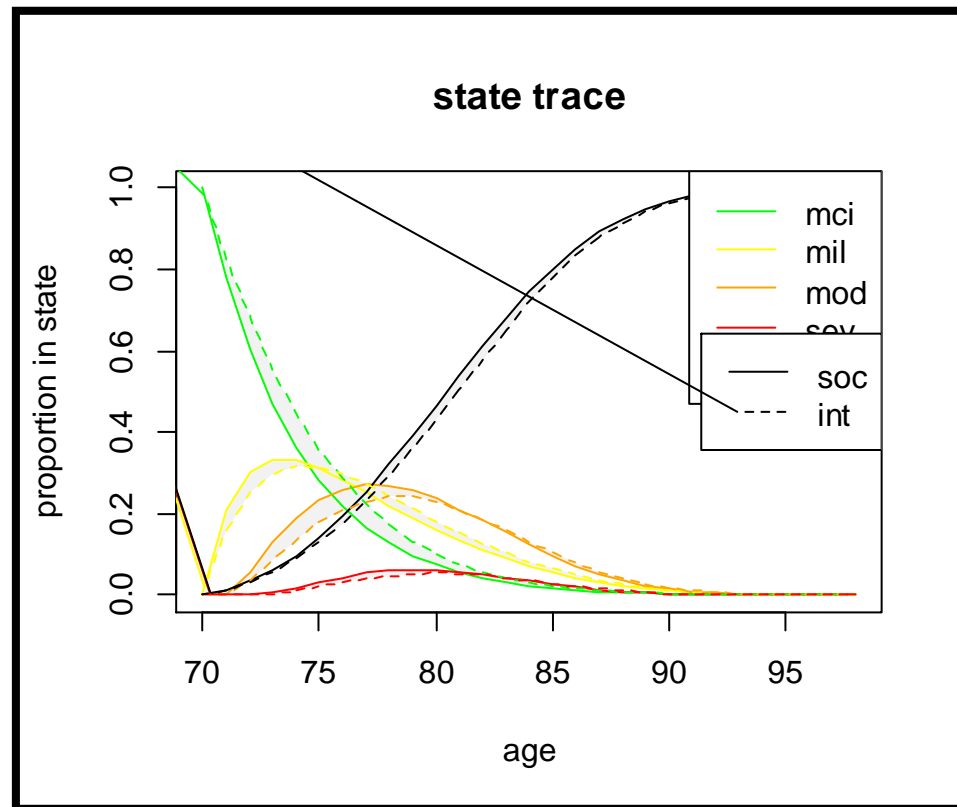
Code: <https://github.com/ronhandels/IPECAD/>



R base and annotated code, user-friendly inputs list, guiding readme, GitHub version control

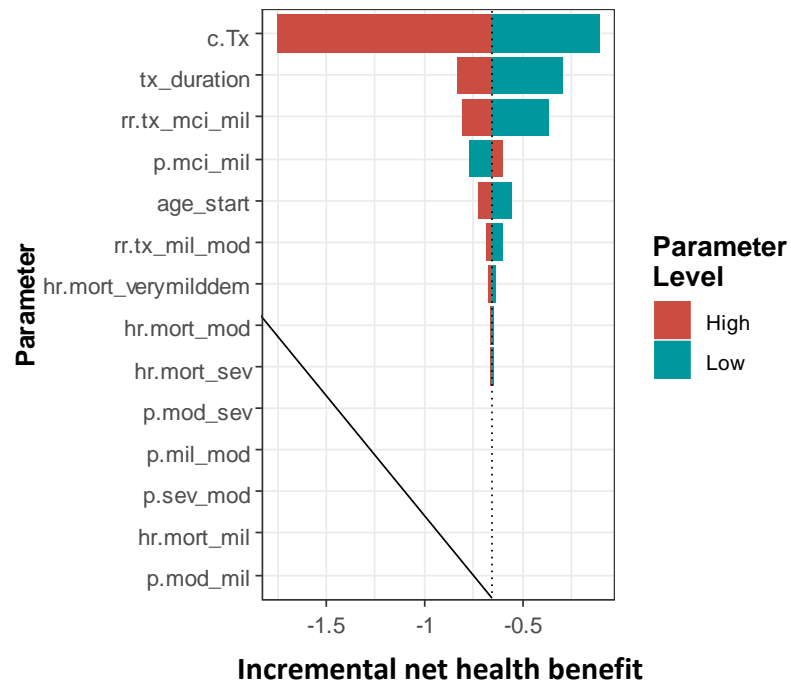
Additional outcomes

	QALY	COST	LY	NHB
soc	5.69	322,291	10.61	-2.37
int	5.94	351,695	10.97	-2.85
incremental	0.25	29,404	0.36	-0.48

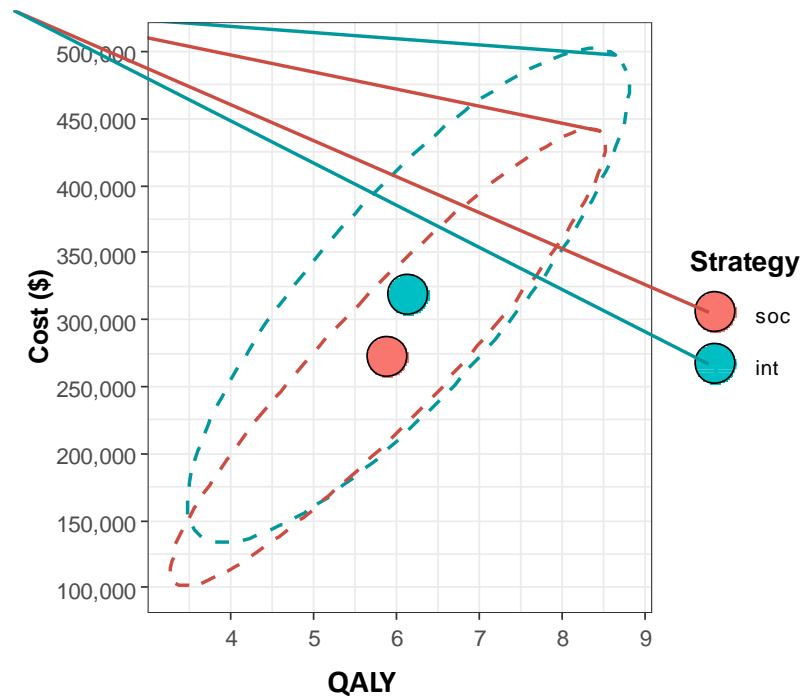


Sensitivity analyses: R package dampack

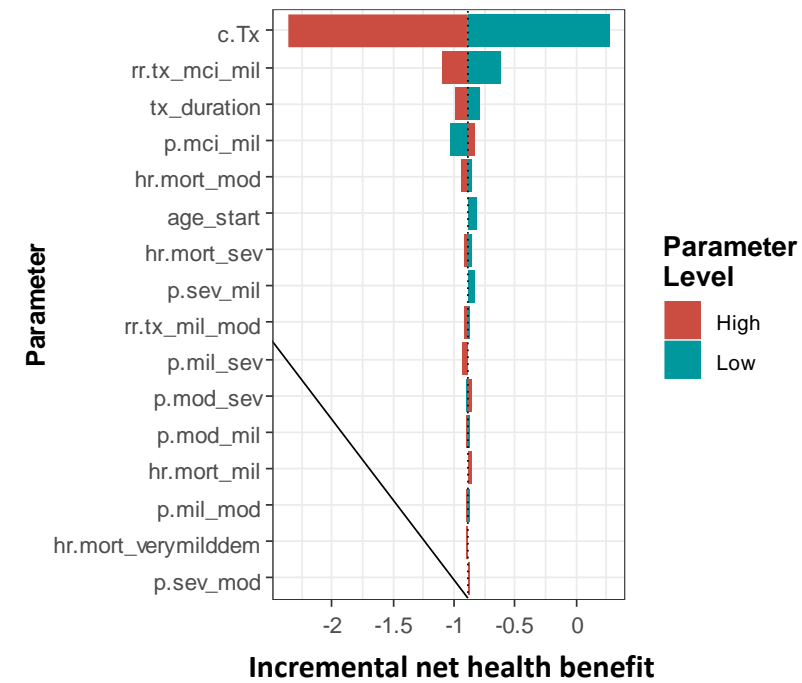
Deterministic



Probabilistic



Probabilistic



Headroom analysis

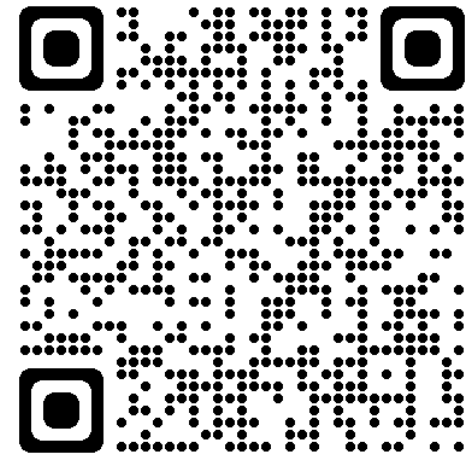
European region	Intervention costs at 40,000 Euro/QALY
British Isles	€4444
East	€3170
North	€4692
South	€5385
West	€3943

EU region-specific costs per disease state [Jönsson, 2023]

Spreadsheet

[illegible]

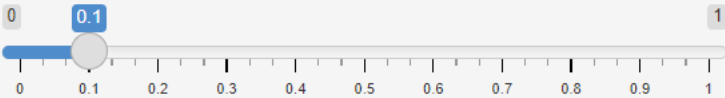
state trace															check	QALYs		
		mcon	mclof	milon	mllof	mod	sev	mcl_i	mil_i	mod_j	sev_j	dth				mcon	mclof	milon
		0.00	4.40	0.00	2.80	1.95	0.29	0.00	0.41	0.95	0.32	17.89						
		3.64	1.44	1.16	1.69	1.78	0.26	0.00	0.39	0.85	0.28	17.53						
1	0	1	0	0	0	0	0	0	0	0	0		TRUE			0.00	0.73	0.00
2	0	0.779	0	0.207	0	0	0	0	0	0	0	0.014	TRUE			0.00	0.57	0.00
3	0	0.605	0	0.296	0.056	2E-04	0	0.005	0.002	8E-06	0.035		TRUE			0.00	0.44	0.00
4	0	0.47	0	0.322	0.117	0.005	0	0.012	0.011	9E-04	0.062		TRUE			0.00	0.34	0.00
5	0	0.364	0	0.314	0.164	0.013	0	0.018	0.025	0.004	0.098		TRUE			0.00	0.27	0.00
6	0	0.281	0	0.289	0.192	0.022	0	0.024	0.041	0.009	0.142		TRUE			0.00	0.21	0.00
7	0	0.217	0	0.256	0.203	0.028	0	0.028	0.057	0.016	0.194		TRUE			0.00	0.16	0.00
8	0	0.167	0	0.222	0.201	0.031	0	0.031	0.071	0.023	0.254		TRUE			0.00	0.12	0.00
9	0	0.128	0	0.188	0.188	0.032	0	0.033	0.081	0.029	0.32		TRUE			0.00	0.09	0.00
10	0	0.098	0	0.157	0.169	0.031	0	0.034	0.088	0.033	0.391		TRUE			0.00	0.07	0.00
11	0	0.075	0	0.129	0.147	0.028	0	0.034	0.089	0.035	0.464		TRUE			0.00	0.05	0.00
12	0	0.057	0	0.104	0.124	0.024	0	0.032	0.087	0.034	0.538		TRUE			0.00	0.04	0.00
13	0	0.043	0	0.082	0.101	0.02	0	0.03	0.081	0.032	0.611		TRUE			0.00	0.03	0.00
14	0	0.032	0	0.064	0.08	0.016	0	0.027	0.073	0.028	0.68		TRUE			0.00	0.02	0.00
15	0	0.024	0	0.049	0.061	0.012	0	0.024	0.062	0.023	0.745		TRUE			0.00	0.02	0.00



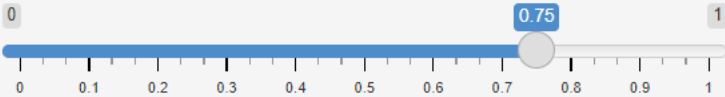
<https://github.com/ronhandels/IPECAD/>

0.28 = amyloid positive & injury positive [Vos, 2015]
0.25 = amyloid positive & injury undetermined [Vos, 2015]

Discontinuation (proportion per year):

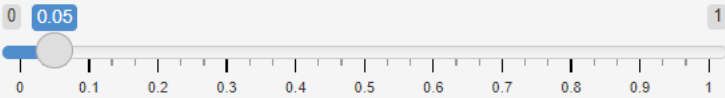


Treatment effect (RR):



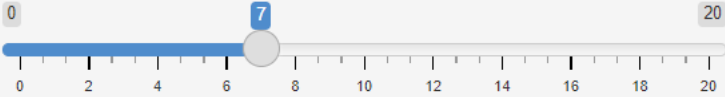
applied to transition MCI to mild dementia and to mild to moderate dementia

Treatment waning:

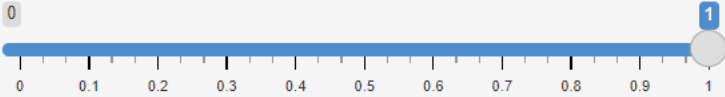


proportion per year treatment no longer effective

Treatment duration (years):

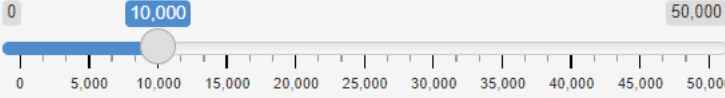


Starting state MCI (proportion):



1 minus this proportion starts in mild dementia

Costs treatment (USD):

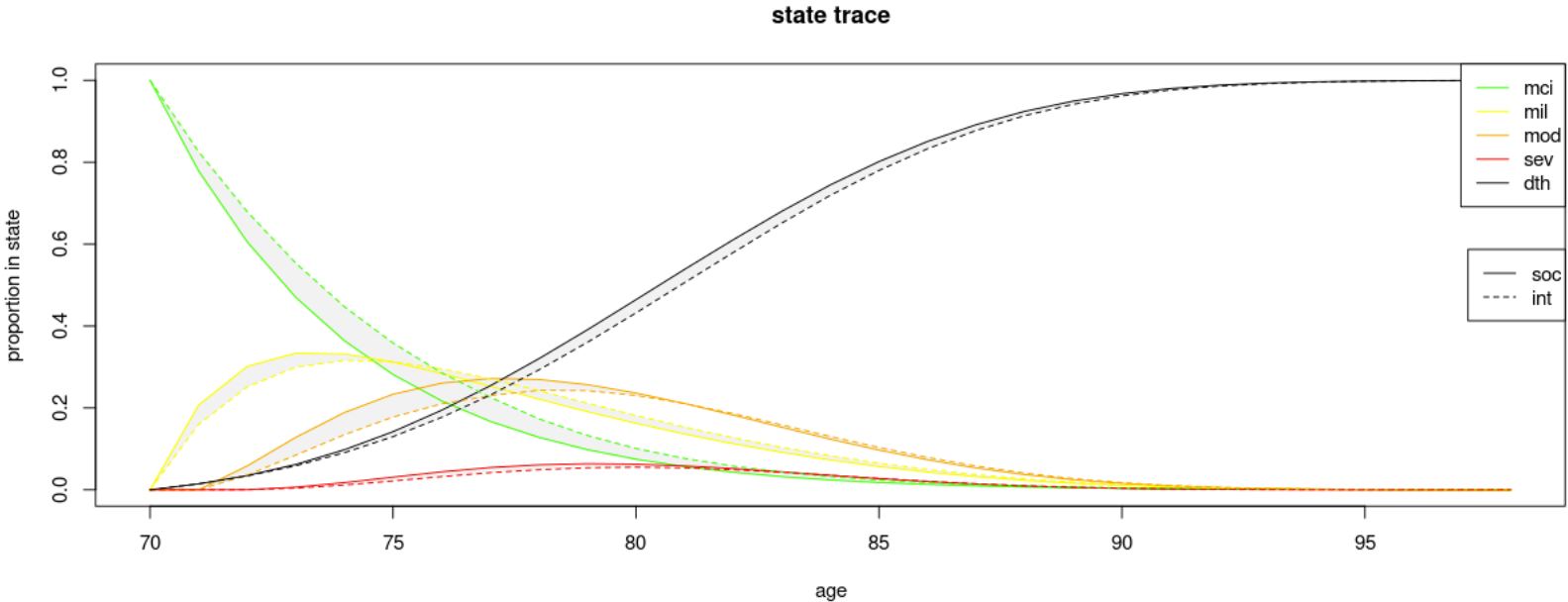


when on treatment

Health-economic outcomes

	QALY	COST	LY	NHB
soc	5.69	322,291	10.61	-2.37
int	5.94	351,695	10.97	-2.85
incremental	0.25	29,404	0.36	-0.48

State trace: plot



State trace:

Standard of care strategy

mci	mil	mod	sev	dth
1.00	0.00	0.00	0.00	0.00

Discussion

- **Open-source** model framework
- **Alzheimer's disease** drug treatments
- **Transparency and credibility** of health-economic outcomes

Anticipated users

- Reimbursement agency: external validation of submitted model
- Academia: early HTA / add features (e.g., diagnostics)
- Industry & consultancy: validated model as starting point

Advantages

- Stack knowledge (not re-invent wheel)
- Single user / small research group

Domains of transparency

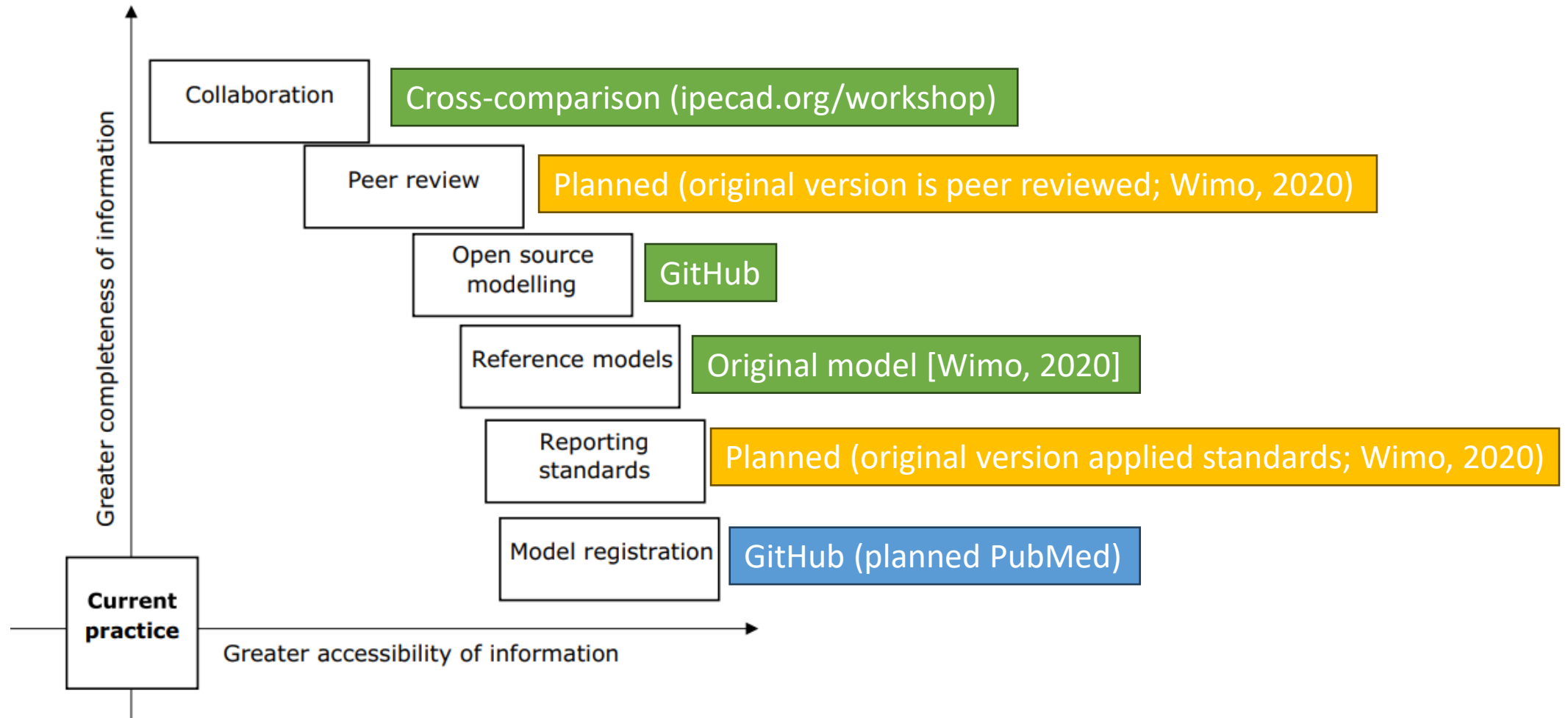


Figure copied from Sampson et al., 2019: <https://doi.org/10.1007/s40273-019-00819-z>

Wimo et al., 2020: <https://doi.org/10.3233/jad-191055>

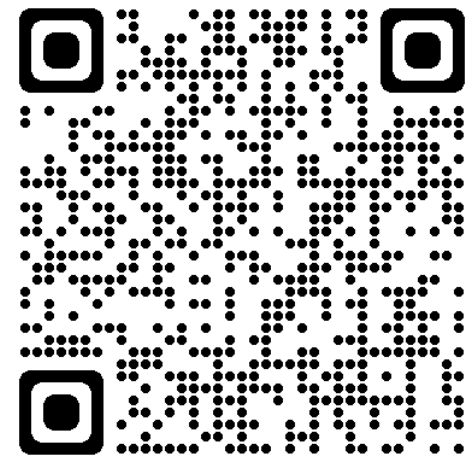
Take home message

- IPECAD **open-source** model for Alzheimer's disease
- Transparency and credibility
- www.ipecad.org/open-source-model



IPECAD

International Pharmaco-Economic Collaboration on Alzheimer's Disease



- **Cross-comparison** of 9 international models
 - Poster MSR136 Wednesday 9.00 - 11:30h
 - www.ipecad.org
- **ISPOR SIG** open-source modeling
 - Dialog on open-source cost-effectiveness and comparative effectiveness models
 - OpenSourceSIG@ispor.org

Questions?

ron.handels@maastrichtuniversity.nl