

Benefits and Risks of using Whole Disease Models and Pathway Models in Health Economic Research

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ISPOR Europe

Economists building models need to think big!



Various frameworks and guidelines

Not all models are created equal in the level of evidence that can inform decisions

Chloroquine and Hydroxychloroquine: Should these drugs be used to treat COVID-19?

Several in vitro studies report antiviral activity of Chloroquine and Hydroxychloroquine against SARS-CoV-2. At present, there is insufficient in vivo evidence to recommend their use for the current pandemic outside of clinical trials. Further, high-quality studies are urgently needed to provide guidance to clinicians and policy-makers.

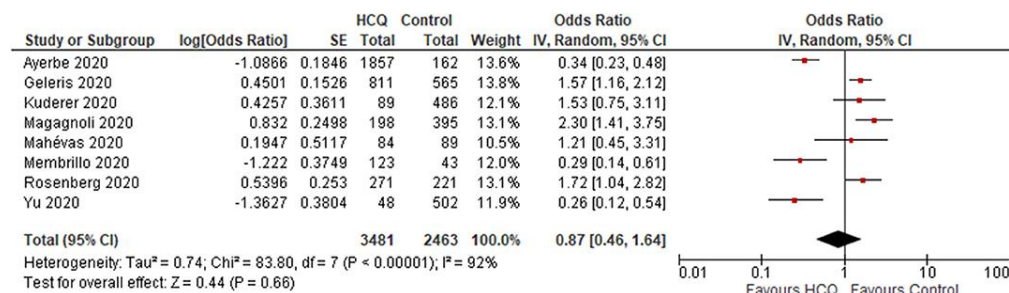
CEBM UNIVERSITY OF OXFORD

#EvidenceCOVID

Kerstin Frie & Kome Gbinigie
25 March, 2020

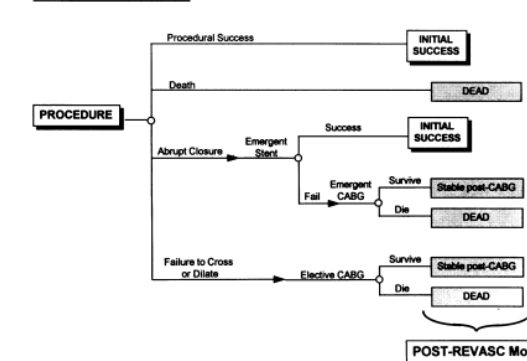


Effect on mortality HCQ vs control July 2020



Front. Med., 29 July 2020 :<https://doi.org/10.3389/fmed.2020.00482>

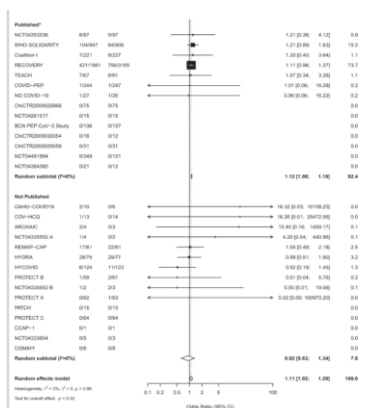
Procedure Sub-tree:



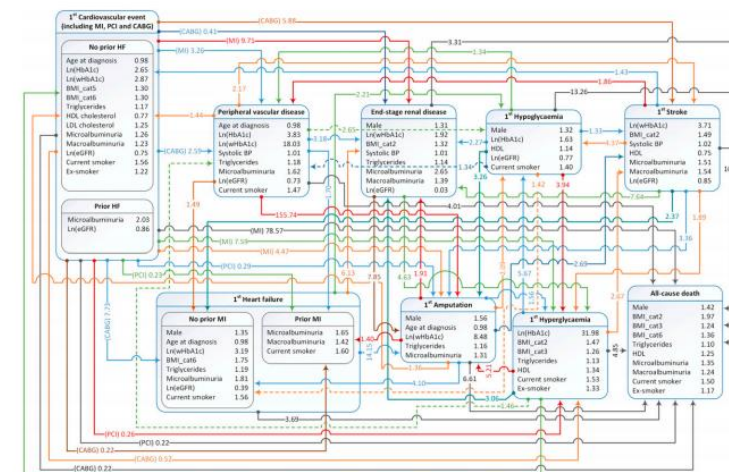
Circulation 1994: <https://doi.org/10.1161/01.CIR.89.4.1859>

Early health economic models were simple, but find it hard to capture complex diseases like diabetes

Effect on mortality HCQ vs control: May 2021



Combined OR on all-cause mortality for hydroxychloroquine is 1.11 (95% CI: 1.02, 1.20)
Dominated by two large RCTs RECOVERY and SOLIDARITY



Diabetes models require several years of development & large data sets (such recently developed Type 1 model)

Diabetes Care 2020 Jun; dc192249: <https://doi.org/10.2337/dc19-2249>

Using meta-analysis to better understand simulation models



Search of the diabetes model-based economic evaluations literature produced 124 comparisons from 76 papers;

- Extracted information on baseline change & LE/QALY;
- Looked at the association between changes in incremental QALYs and changes in HbA1c (measure of blood glucose);
- Provided a calculator to “check” if individual models are outliers;

Pharmacoeconomics (2017) 35:319–329
DOI 10.1007/s40273-016-0466-0

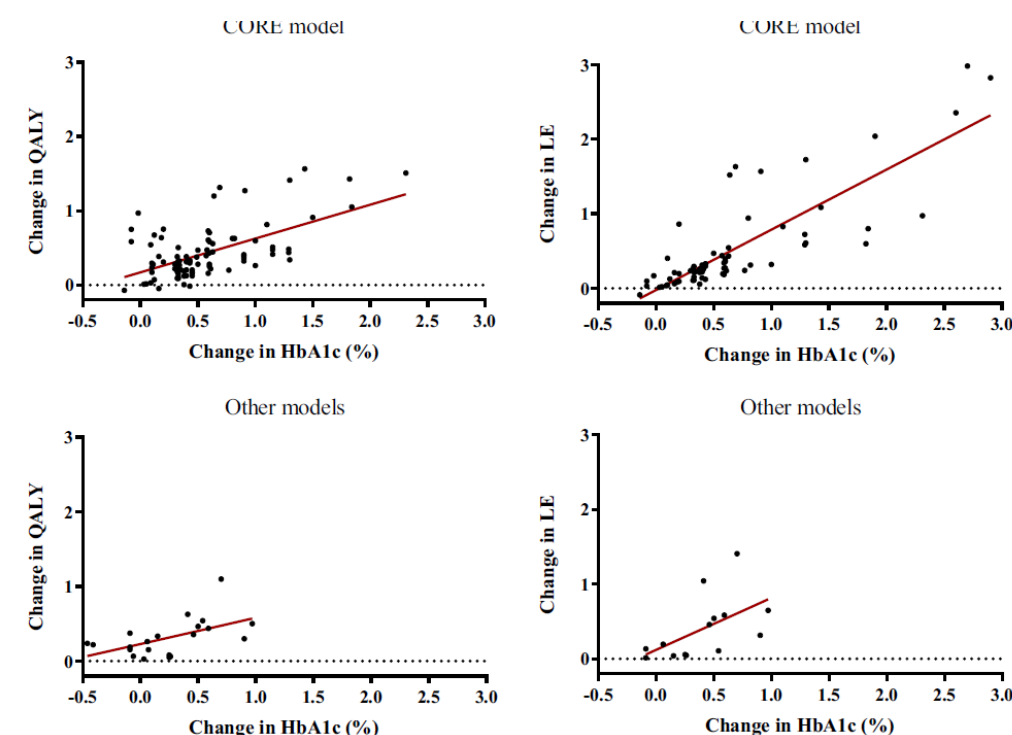


SYSTEMATIC REVIEW

How Consistent is the Relationship between Improved Glucose Control and Modelled Health Outcomes for People with Type 2 Diabetes Mellitus? a Systematic Review

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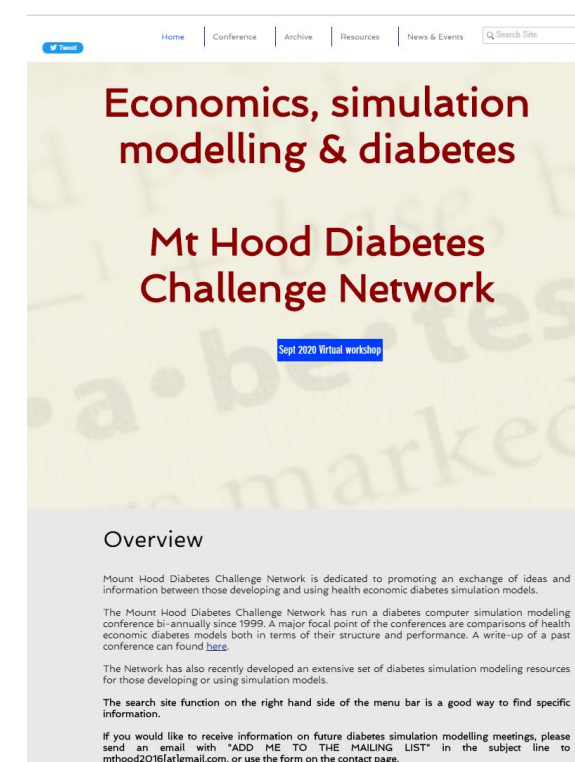
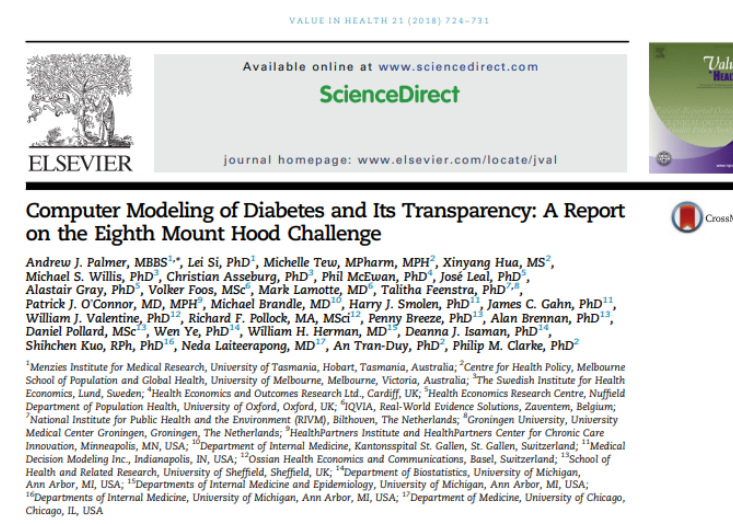


Whole disease modelling community: Mt Hood challenge network



Set up in 1999 when two modelling groups compared their diabetes simulation models:

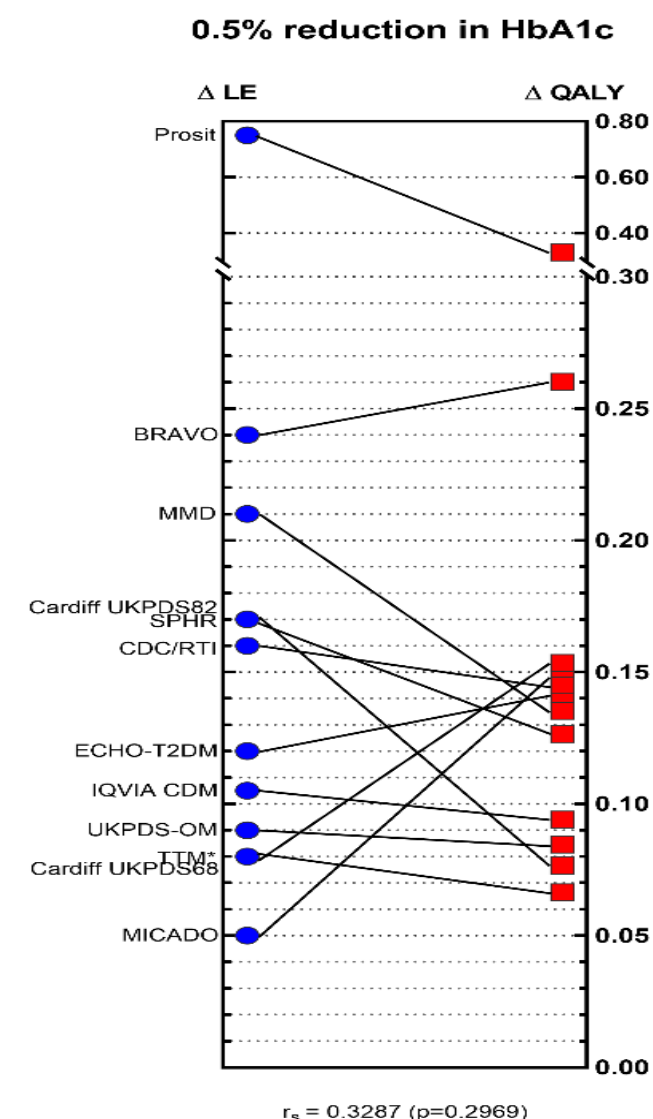
- Held 10 international conferences, where up to a dozen modelling groups have undertaken challenges and compared results;
- Have a website with resources and information;
- Maintain a diabetes simulation model registry;
- Have defined standards for transparency in simulation modelling
- Awarded a prize for applied paper that best implements the guidelines
- Network provides both “peer review” and a way of disseminating information



Better understanding models: role of reference cases & model registries



- One way to compare models is to simulate a reference case. This involves a pre-defined treatment effect (eg change in HbA1c in the case of diabetes models) on a standard patient;
- Recent comparisons by the Mt Hood network indicates wide variation in incremental LE and QALYs;
- A major challenge for health economics is to find ways of resolving or accounting for these differences across models;
- A model registry and reference case also provides a way to track changes in a model over time – one positive step would be for journals and payers to require a reference case to be run and reported when a model is used to evaluate an intervention;

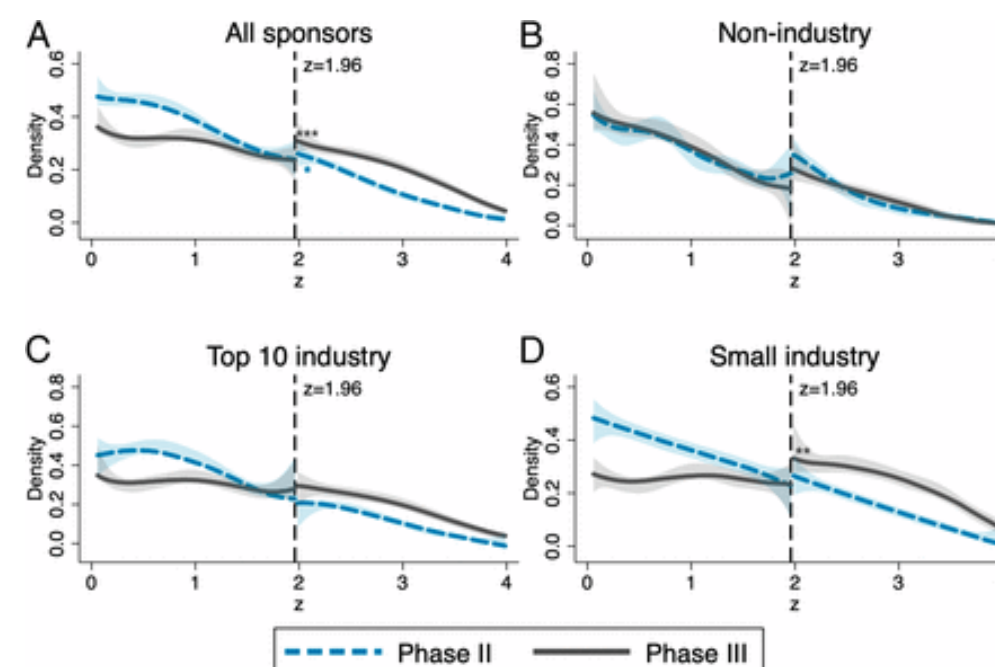


Tew M. Forthcoming in MDM

Using registries to stop “WTP threshold hacking”



- Selective reporting and publication of results deemed statistically significant (i.e. $P < 0.05$) is a significant problem in science;
- Trial registries (ClinicalTrials.gov) requiring pre-specification of primary endpoints has reduced the problem of “P-hacking” in reporting of RCTs;
- We face the same problem in health economics- as cost-effectiveness is determined against a WTP threshold;
- “WTP threshold hacking” involves adapting a model until it produces a ICER below a threshold;
- The solution to this problem probably also will involve use of registries of models



Adda J. P-hacking in clinical trials and how incentives shape the distribution of results across phases
PNAS 2020; <https://doi.org/10.1073/pnas.1919906117>

Reference simulation

The values below are simulated Quality Adjusted life Years (QALYs) for a set of reference simulations

Model	Sex	Control	0.5% red. HbA1c	10mmHg in SBP	0.5mmol/l red. LDL	1-unit red BMI	All combined	Date
UKPDS Outcomes Model	Male	11.9	11.99	12.08	12.13	11.92	12.41	5/10/2018
UKPDS Outcomes Model	Female	13.57	13.64	13.74	13.69	13.59	13.95	5/10/2018