International Pharmaco-Economic Collaboration on Alzheimer's Disease (IPECAD) Modeling Workshop 2021

21 September 2021 – virtual

Meeting minutes

Introductions

Introductions and/or update on current activities/developments related to decision modeling in AD and related dementias (all IPECAD modeling workshop 2020 participants).

New participants (not part of 2020 workshop) introduced themselves on the chat.

Guest speakers

Anja Schiel (Norwegian Medicines Agency) – presentation – < introduced by Anders Gustavsson >

Theme was around broader regulatory and HTA framework, and the place for and role of cross-model comparisons.

Broad messages included:

- How much uncertainty is acceptable – used an example of a scenario with 3-steps of surrogate endpoints, prior to end outcome.
- HTA Framework, Assessment and Appraisal, with clinical outcomes one of the key inputs but importantly there are a lot of other inputs and considerations.
- TIME – as key consideration, many different dimensions.
- Cross comparisons of modeling may be useful to inform better decisions.

Prof Kit Simpson (Medical University of South Carolina, US) – presentation - < introduced by Will Herring >

Theme was - Challenge of working with surrogate outcomes: learning from research and modeling in the HIV field.

Broad messages included:

- People working in the area of HIV-AIDS (modelers, analysts, other) were not trained for HIV. They came to the important questions in context of HIV-AIDS from many different areas-topics.
- HIV-AIDS modelers learned by making and correcting mistakes, through listening and learning.

- Key model comparison issues are related to natural history and treatment effectiveness. Natural history data, and appropriate use of that data, emphasized as the essential piece (topic).
- Use of surrogate markers a key requirement – but evidence development on surrogate outcomes takes a while (years) to appear / to be available in robust format [for analyst/modelers]. Micro and macro level surrogate markers both considered to be of value.
- Current ICD codes for Alzheimer's disease (dementia) flagged up as not detailed/specific enough, we need more.

Important messages were:

- 'modelers' have a responsibility to teach-explain the models;
- simplicity is King!;
- test models to breaking point;
- use model to assess health system issues-problems;
- explore costing perspective (incl 2-3 year budget impacts);
- document baseline population;
- describe how you translate treatment effects;
- You as the modeler have deep insights!!

Learning from AIDS: [modeling as a] sophisticated mathematical endeavor, but also needs to be simple to explain, if not got face validity it is not useful.

Q&A for external speakers:

Some questions arising:

Q; [JH] -> what sort of communications process amidst HTA [on modeling].

R: [AS] -> good experience within the ROADMAP project where she had the opportunity to 'talk to the modelers' (as often out-sourced by companies). But typically, the distance is too far between HTA agency and the actual modelers.

R: [KS] –> [KS typically] retained the right to be the contact point, so was able to explain modeling. Able to talk directly to the decision-makers. (KS noted that trying to explain a complex model – via email – is very difficult)

Q: [PL] - > importance of design of the model, but in AD a lot of endpoints in trials are not commonly used in clinical practice, need for a perspective on these challenges?

A: [AS] -> Important to get all the data collected, but need both trial and practice-based outcomes and endpoints. We can 'bucket' people in a way that people are seen in practice. Example – MCI stages/states.

Q: [LR] -> challenges for AD modelers as disease is relatively slow, and not seen data on successful interventions, would such data help us a lot?

A: [AS] -> if you have clinically relevant outcome related to move from one stage to the next, that is something we could accept. Biomarkers not as relevant to AD at present (= speculation a long way into the future). Also, HTA agencies have to consider across all patient groups – all conditions.

< HTA agencies could require clinical trial endpoints to be used in practice > < need to collect the right information to confirm effect >

< new financing models may be helpful in terms of taking small steps (what we are willing to pay) >

Q: [RH] -> would lifetime horizon be advised for evaluating early AD drug treatment?

A: [AS] -> lifetime horizon is unlikely to be considered if when data has limited follow-up. Also, for chronic treatment realistic assumptions on adherence are required. 20 years is often applied, and possibly shortened if predictions are unrealistic, which is not optimal.

A: [BT] -> When using short term horizons, we are still making strong assumptions, i.e., there are no differences in costs and benefits after our time horizon. Uncertain data is best account for in the model not by excluding it from the model.

RH (on behalf of organizing Team, and all participants) – extended special thanks to guest speakers.

Looking back and future plans

Ron Handels

Shared brief summary on 2020 workshop: using benchmark scenarios agreed by community we compared across 12 models, with discussion. RH summarized the scenario/s and process, plus brief results and take-aways.

Manuscript in submission (with Editor).

Questions: < nothing arising >

Linus Jönsson and Lars Raket

Proposal for second benchmarking exercise, in 2022 Workshop:

Brief recall on prior benchmarking exercise, specifically on the prior way we introduced treatment effect (i.e., 30% reduction on progression rates).

But aware RCT type results will not fit directly with this type of effectiveness input in models.

So, focus currently (2022 Workshop) is on deriving treatment effectiveness from trial data. How to bring trial findings (input findings) to modeling framework?

Future workshop (2022) – proposal is on estimating and incorporation of treatment effects in AD cost-effectiveness modeling. Using a simulated trial dataset. Context proposed of ‘mild-moderate’ AD (based on convenience in data availability). Data provided to workshop participants be similar to a short version of a clinical study report.

One question [from LJ/Team] = how much data would people want/need? We can provide more data to those who are keen to get into the detail of the challenge.

Proposal is aligned with producing-reporting a set of results/outcomes similar to the last modeling workshop.

Q: From -> Anja Schiel: Suggests important to start with modeling in earlier stages of AD, prior to mild AD dementia. Most studies are moving away from the later stages of disease. So, suggest energy is put into early stages of disease. [agreement with this on chat]

Response: From -> Lars Raket: pointed to other potentially encouraging trial results in tau-based interventions in mild AD setting.

Discussion that working within mild-moderate AD can also overlap with similar questions in MCI and early AD.

Q: what utility, cost and mortality inputs to use? A: idea is to provide U.S. life table, and inputs for costs and utilities.

Discussion around replicating trial and/or real-world evidence, as a method to determine the validity of model predictions.

Discussion on possible drivers of variability, and how to reduce them; being: different ways of specifying treatment effect, different natural progression rates, sub-group-specific benefits of treatment, non-drug/drug interventions, levels of benefit (costing perspective). Models must justify their choices, and would be valuable to understand their consequences for model predictions/outcomes.

Discussion on replacing natural history data with trial data, and risk of overfitting the model with that data.

IPECAD Team -> Asked for initial indication from participants whether the proposal for 2022 workshop was on the right track – 'thumbs up' for example. Response online indicated: Wide range of interest and positive signs to move ahead on this.

LJ – explained this was proposing the concept for the next workshop and, given level of support we will then take things to the next stage by setting out the plans in more detail, prior to agreeing a longer timeline for activities leading to a provisional date in Sept 2022 for the next workshop.

AOIB

(none raised)

Closing remarks

In closing LJ thanked all for their input and support.

RH explained all on call would continue to receive updates from the workshop. Request for people to advise (RH) if updates no longer wanted.

Participant list

First name	Last name	Organization	model
Colin	Green	University of Exeter	IPECAD
Ron	Handels	Maastricht University; Karolinska Institutet	IPECAD
Linus	Jönsson	Karolinska Institutet	IPECAD
Anders	Gustavsson	QuantifyResearch; Karolinska Institutet	IPECAD
Anders	Wimo	Karolinska Institutet	SveDem; IPECAD
Anders	Sköldunger	Karolinska Institutet	KP; IPECAD
Bengt	Winblad	Karolinska Institutet	IPECAD
Will	Herring	RTI Health solutions	Herring et al.
Lars	Raket	Novonordisk	
Eldon	Spackman	University of Calgary	Spackman et al.
Eric	Jutkowitz	Brown	Jutkowitz et al.
Mauricio	Lopez Mendez	Brown	Jutkowitz et al.
Peter	Shewmaker	Brown	Jutkowitz et al.
Jakub	Hlávka	University of Southern California	FEM
Bryan	Tysinger	University of Southern California	FEM
Paige	Lin	Tufts Medical Center	
Ali	Tafazzoli	Evidera	ADACE
Jorgen	Moller	Evidera	ADACE
Mark	Belger	Lilly	CEM
Michael	Happich	Lilly	CEM
Javier	Mar Medina	Osakidetza / Hospital Basque	BASQDEM
Myriam	Soto-Gordoa	Mondragon Unibertsitatea	BASQDEM
Inge	de Kok	Erasmus Medical Center Rotterdam	MISCAN
Chiara	Brück	Erasmus Medical Center Rotterdam	MISCAN
Rob	Espinosa	Medicus Economics	Davis et al.
Scott	Johnson	Medicus Economics	Davis et al.
Robert	Anderson	London School of Economics	CPEC
Anja	Schiel	Norwegian Medicines Agency	
Kit	Simpson	Medical University of South Carolina	
Peter	Neumann	Tufts Medical Center	
Hana	Broulikova	Vrije Universiteit Amsterdam	
Jeroen	Jansen	University of California San Francisco	
Peter	Pemberton-Ross	Biogen	
Amber	Werbrouck	HICT	
Chelsea	Stellick	University of Alberta	Spackman et al.
Adam	Kasle	BresMed	
Montserrat	Chivite	Grifols	
Stephanie	Cline	Acumen Pharmaceuticals	
Javier Sanchez	Alvarez	Roche	