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Cost-effectiveness analysis of a digital health application (DiGA) plus Best Supportive Care (BSC) compared to BSC in German episodic migraine patients

Evelyn Walter[a], Sören Wegner[b], Dominik Burziwoda[b]

[a]IPF Institute for Pharmaeconomic Research, Vienna, Austria [b]Perfood GmbH, Lübeck, Germany

Objectives

sinCephalea is a digital health application (DiGA) and indicated as a prophylactic treatment to reduce migraine days in patients with episodic migraines. The product applies personalized low-glycemic diet as "active ingredient" together with state-of-the-art digital therapeutics technology to address migraines.
To receive preliminary DiGA in Germany, two pilot studies were conducted, out of which the most recent results were applied in this model (AWE II).

The aim of the present cost-effectiveness analysis (CEA) is to analyze a digital health application (DiGA) plus Best Supportive Care (BSC) compared to BSC in patients with episodic migraine.

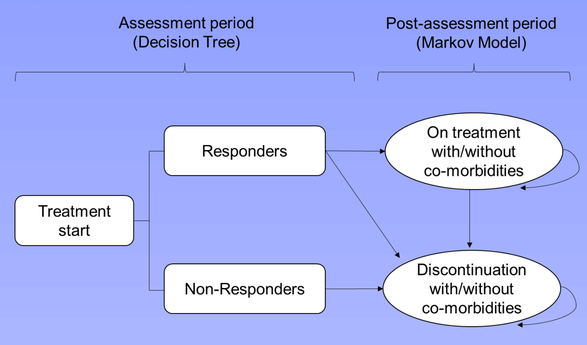
Methods

A decision tree is used to represent a 12-week clinical-trial period, where the probability of treatment response is estimated based on predicted change (at least 30%) in monthly migraine days (MMDs). A Markov structure is then used to represent a post-trial period, where responders and non-responders follow treatment pathways. This modelling approach is predicated upon the assumption that both quality-adjusted life years (QALYs), resource utilization and costs can be estimated based on the MMD frequency being experienced by patients. Direct and indirect costs (2021€) were derived from published sources from the societal perspective. QALYs and costs were discounted (3% p.a.).

Based on the included patient population, the model estimates the following:

- The MMDs distribution for all patients at baseline (week 0)
- The proportion of responders at the endpoint of the trial (week 12)
- The MMDs distributions for responders and non-responders at week 12 = distribution of Markov model in the 1st cycle.
- Within the Markov model patients are adherent or discontinue using sinCephalea. Patients who decide to quit sinCephalea go back to baseline MMDs.

Fig. 1: Model Design



Source: own developed

Tab. 1: Overview of methods applied

Methods	
Type of study	**Cost-effectiveness analysis (CEA) and cost-utility analysis (CUA)**
Type of the model	**Deterministic hybrid model** using • A decision tree and • A Markov-cohort-state-transition model
Perspective	**German societal perspective**
Time horizon Cycle length	**25 years** 12 weeks
Discount rate	**3% for costs & 3% for outcomes**
Population	**Patients with episodic migraines**, a median age of 41, 94% were females. The mean MMDs are 7.7 (median 6 MMDs) at baseline.
Intervention	The DiGA **sinCephalea plus BSC**. BSC is defined as continued treatment with prophylactic and acute medication. Prescription-intervals 3-years.
Comparator	**BSC** (prophylactic and acute medication)
Direct costs	Costs of sinCephalea, prophylactic and acute medication costs, physician visit costs, emergency room visit costs, hospitalization costs, costs treating co-morbidities.
Indirect costs	**Absenteeism and presenteeism costs**
Outcomes	• **Quality-adjusted life-years (QALYs)** based on EQ-5D-5L weighted based on German value sets • **Migraine days avoided**
Results	**Incremental cost utility ratio (ICUR) & incremental cost effectiveness ratio (ICER)**
Timing	**2021**

Source: own developed

Clinical Data

The assessment period of the model is based on clinical trial results of the AWE II analysis. The trial data showed a reduction in MMDs of 2.4 which corresponded to a median reduction of 44%. 30%-Responder Rate was at 58% and 50%-Responder Rate was at 47%. The study showed statistically significant and clinically meaningful improvement on secondary endpoints (MIDAS and HIT-6).

Co-morbidities

The term comorbidity is used to refer to the statistical association of two distinct diseases in the same individual at a rate higher than expected by chance. Many illnesses are reported to be comorbid with migraine. The following comorbidities were identified based on a systematic literature review and were integrated in the model in addition to AWE II trial data: chronic pain, cardiometabolic disorders (hypertension, pre-diabetes and type 2 diabetes), mental health-related comorbidities (major depression, anxiety), chronic migraine and obesity. The incidences of comorbidities depend on the MMDs.

Resource Use (RU) and Costs

RU to calculate direct costs were derived from the clinical AWE II trial and was supplemented by RU data from the literature for emergency room visits and hospitalizations. Direct medical-costs were calculated based German reimbursement prices/tariffs/G-DRGs for the year 2021 (€).
Indirect cost calculations are based on the MIDAS questionnaire and the documented number of days of activity limitations due to migraine. Days absent from work and days with reduced work productivity by at least half was multiplied with the gross earning.
RU and lost working days depend on the number of MMDs.

Results

DiGA plus BSC is associated with direct costs of 64,203 € (SD, 2,279 €) and indirect costs of 145,557 € (SD, 10,593 €) compared to 65,129 € (SD, 2,565 €) of direct costs and 158,458 € (SD, 11,685 €) of indirect costs when only BSC is used. DiGA plus BSC had a higher QALYs estimate at 13.81 (SD, 0.43) compared to 13.55 QALYs (SD, 0.40). The utility benefit corresponds to over 3 months in perfect health. DiGA plus BSC is the dominant strategy.

Institut für Pharmaökonomische IPF Forschung

CONTACT:
Dr. Evelyn Walter
IPF Institute for Pharmaeconomic Research
Wolfengasse 4/7
1010 Vienna, Austria
Tel +43-1-5132007-13
Fax +43-1-5132007-15
Email: e.walter@ipf-ac.at
Web: www.ipf-ac.at

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Tab. 2: Results, 2021

Costs	Intervention sinCephalea plus BSC	Control BSC	Incremental
Direct:	**64,203.39 €**	**65,128.87 €**	**-925.48 €**
Indirect:	**145,556.52 €**	**158,458.37 €**	**-12,901.85 €**
TOTAL COSTS	209,759.92 €	223,587.24 €	-13,827.32 €
Outcomes			
QALYs	13.811	13.550	0.261
ICUR		DOMINANT	
Migraine Days	1.608	1.812	-204
ICER		DOMINANT	

Source: own calculations

The DiGA plus BSC strategy marked as "dominant" saves money and improves outcome compared to BSC alone (table 2).
A closer examination of direct costs shows that DiGA plus BSC is associated with costs savings (-925 €) in all cost components and offset DiGA costs (see table 2 and figure 2a).
A look at the indirect cost components shows that there are considerable savings, especially in the area of presenteeism (- 8,910 €). The reduced sick days contribute 3,992 € to the total savings (figure 2b).

Fig. 2a: Direct cost components

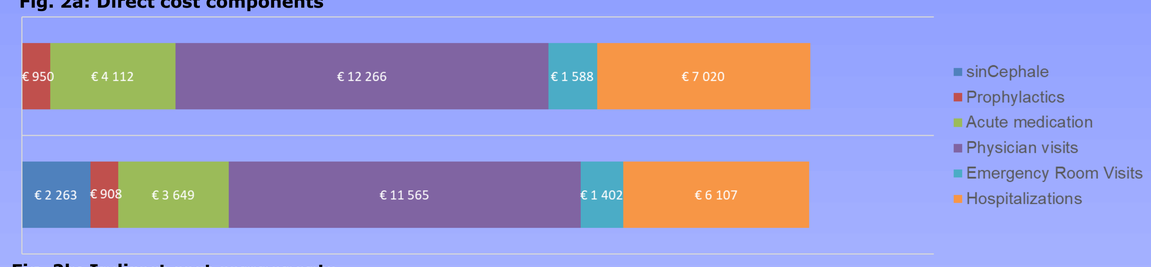
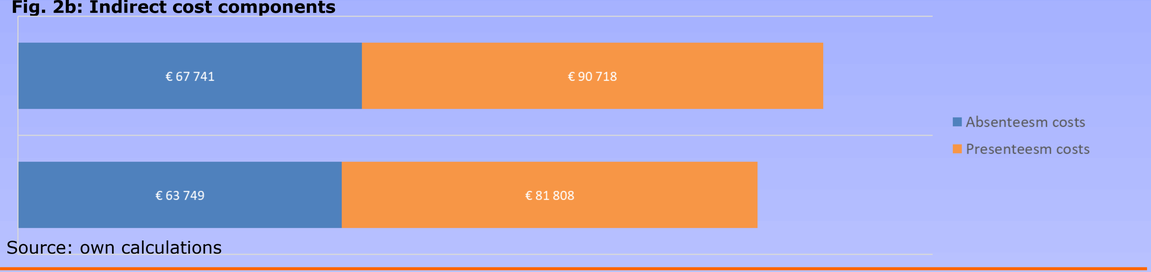


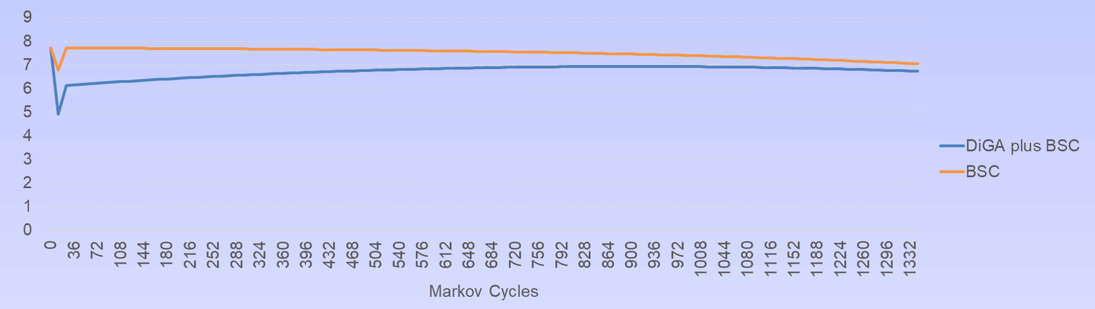
Fig. 2b: Indirect cost components



Source: own calculations

Using DiGA plus BSC leads to the fact that patients are able to reduce 204 migraine days. The total number of MMDs in the DiGA plus BSC group is always below the number of those with BSC alone (Fig. 3).

Fig. 3: MMDs over 25 years

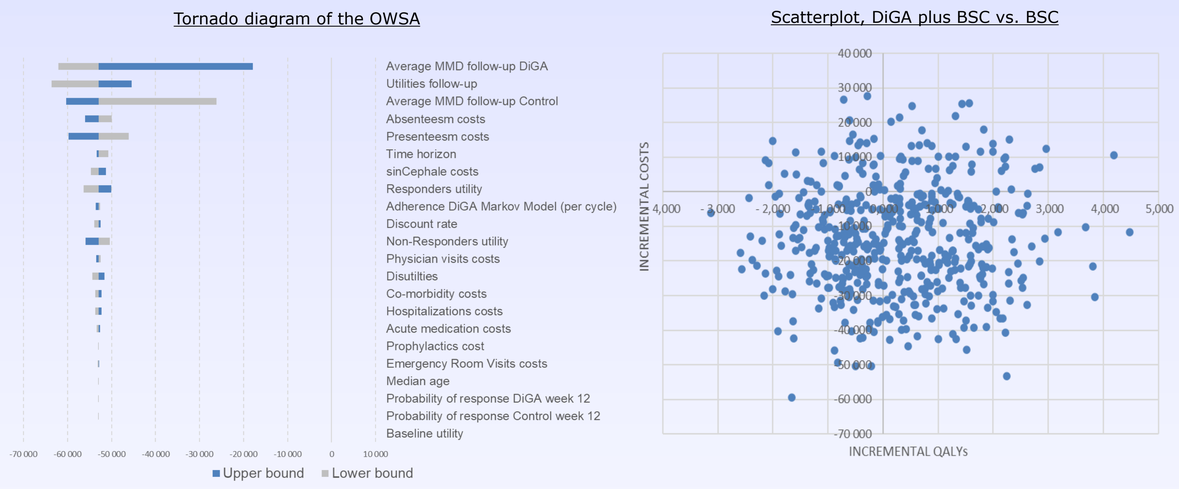


Source: own calculations

Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) and deterministic one-way sensitivity analysis (OWSA) were carried out to examine the robustness of the model.

Fig. 4: Sensitivity Analysis



Source: own calculations

The Monte-Carlo PSA results of 500 second-order simulations plotting incremental costs versus incremental effects (Figure 4).
A deterministic OWSA confirms the results. At a willingness-to-pay threshold of 25,000 €, 99% of simulation are in the cost-effective range.
Deterministic one-way sensitivity analysis confirms probabilistic results.

Conclusion

In patients with episodic migraine, the use of DiGA plus BSC is highly cost-effective and associated with savings for the German healthcare system.

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Additional literature with the author