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Request for the preparation of a legal opinion on HTA with special consideration of open questions on CEA, CUA and BIA in Switzerland

The text was written by the Swiss Ethics and Medicine Association (www.vems.ch) on behalf of the Foundation for Fairness in Healthcare (www.fairfond.ch).

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Summary

The assessment of the cost-effectiveness of medicines according to WZW criteria is subject to certain conditions. Medicines approved by SwissMedic are generally considered to be cost-effective. However, thanks to research and developments in the pharmaceutical industry, we are seeing a high density of new medicines. The Federal Office of Public Health (FOPH) conducts regular price negotiations with the pharmaceutical industry on behalf of the federal government: The aim is to keep prices in line with the market. However, these can increase healthcare costs, which is why the assessment and approval procedure carried out by SwissMedic involves a retrospective evaluation of these approved medicines. In a so-called Health Technology Assessment (HTA), the social implications of new medicines and the cost-effectiveness for Switzerland (instead of international literature) are reassessed and the expected effect on health insurance premiums is calculated (Budget Impact Analysis). In principle, it can be assumed that new drugs with high efficacy and high cost-effectiveness will not be subject to any limitation by the FOPH, even if they have a relevant effect on health insurance premiums. The calculation of cost-effectiveness is carried out with the help of health economics models. The models used today are reduced exclusively to the effects on patients and compare the quality of life (utility) with the costs (Cost-Utility-Analysis CUA). This ignores numerous efficacy effects of the new drugs that numerically exceed the CUA, in particular the quality of life of relatives, the social costs (absences from work, etc.) and the monetization of lost life years (VSLY), which must also be taken into account in a comprehensive calculation of cost-effectiveness (cost effectiveness analysis, CEA). As a result, these high-priced HTA methods favour cost-effectiveness models that generally minimize the social value of pharmaceutical products. This reduces cost-effectiveness several-fold, with discriminatory implications for the healthcare system in terms of the perception of the costs of pharmaceutical products as relatively less cost-effective at very high prices, a distortion of the real effect of medicines on society and the added value of medical decisions in general. This creates the prerequisite for subjecting the relatively low cost-effectiveness of innovative medicines to a supercritical budget impact analysis, which in turn creates a false legitimization for limitations. From a social point of view, the reduction of cost-effectiveness to the utility of the patient is not desirable. On a legal level, the omission of numerous effects is certainly problematic and hardly in line with the WZW rules. The following comments clarify the situation and end with our questions to the legal community: which effect variables must be used to calculate cost-effectiveness in Switzerland from a legal perspective, is the use of quality of life as an ultimately unmeasurable variable permissible at all, and what conditions must exist for a budget impact analysis with a limitatio consequence?

Introduction

In Switzerland, effective therapies are rationed (limited) by the FOPH due to suspected excessive costs for premium payers. The assumed additional costs of a medical therapy are calculated using the BIA (Budget Impact Analysis) as part of an HTA (Health Technology Assessments) process. The procedure for this was explained by the FOPH in a presentation[1] . These processes involve a comprehensive assessment of a medical effect in terms of value for money, budget impact, social aspects and ethical issues. Unfortunately, the effects for these analyses are practically always focused on the patients when determining the cost-benefit ratio, which means that the cost-effectiveness is often low and the budget impact too high, with consequences for social and ethical issues in society. The problem: If the medical effects are analyzed taking into account social costs, practically every medical therapy approved by Swissmedic is cost-effective and therefore compliant with the WZW. Rationing (limitatio) would then not be justifiable, the medical treatment would have demonstrated a massive improvement in cost-effectiveness and the damage to the reputation of the healthcare system as a cost-ineffective structure would no longer be communicable.

Limitatio justified by BIA (budget impact analysis)

Despite the proven effects of medical treatments, FOPH limits exist in accordance with https://spezialitaetenliste.ch.

Medical effect through LDL reduction

The effect of Leqvio (Inclisiran, Novartis) on LDL is well documented and results in an approximately 50% reduction in LDL cholesterol. For the time being, no data are available on the extent to which this LDL effect has an impact on the reduction of cardiovascular events. The antibodies evolocumab and alirocumab, which have already been shown in studies to significantly reduce cardiovascular events, have similar effects.

Limitatio justified by BIA (budget impact analysis)

Despite these proven effects, there is a FOPH limitation for high-risk patient groups for inclisiran, evolocumab and alirocumab in primary care. Specifically, the following groups of people are excluded: Individuals at high cardiovascular risk with no previous cardiovascular event (setting: primary prevention).
The reason for the limitations is the expected excessively high costs for premium payers (budget impact). The FOPH commissions health economic reports to justify the limitations, which are intended to provide scientific justification for the limitations. These reports carry out cost-effectiveness and budget impact analyses. However, the budget analyses are kept secret by the FOPH with the following justification in a partially granted access[2] : "All information regarding budget impact has been anonymized, as this information is not publicly accessible and must be blacked out in accordance with Art. 7 para. 1 let. g BGÖ for the protection of business secrets. In addition, this information is also not to be edited in accordance with Art. 7 para. 1 let. b BGÖ to protect the implementation of specific official measures in line with the objectives". As a result, such reports show that at the fixed drug prices of around CHF 5,000 per treatment year, the costs for a quality-

[1] https://docfind.ch/HTAKlazienMatter.pdf
[2] https://docfind.ch/LEQVIO_BudgetImpactAnalysis_BAG_Offenlegung_122023.pdf

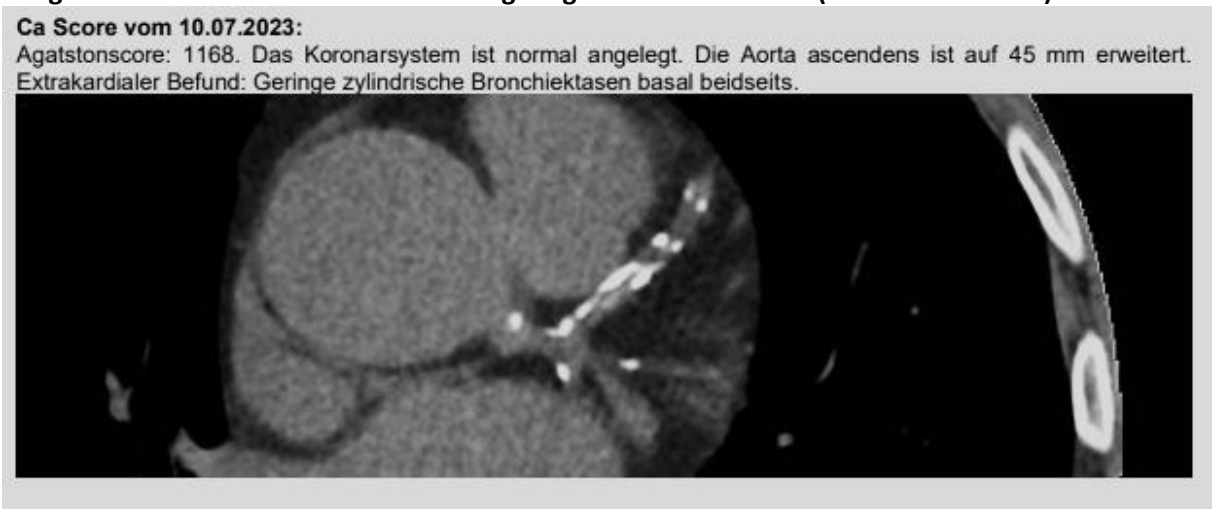
adjusted life year (QALY) amount to over CHF 200,000. The "Willingness To Pay/QALY Threshold" is generally set at CHF 100,000/QALY.

Limitatio violates fundamental medical rights (Kieser legal opinion)

These limitations represent a violation of the basic principles of healthcare, according to which high-quality medical care must be guaranteed at the lowest possible price (see the comments in the Kieser report on Sovaldi, 2015[3]): The limitation of the aforementioned lipid-lowering drugs deprives patients of an effective therapy. This also legally conflicts with the medical care mandate.

Casuistry

In one case, the health insurer Concordia refused to cover the costs of Leqvio[4] . The reason given on 24.07.2023: Prerequisite for OKP not fulfilled.
Concordia health insurance subsequently received a letter[5] with a request to grant the cost approval after all. On 04.09.2023, the Concordia health insurance company granted the cost approval after all[6] . Below is the reason why Concordia health insurance decided in the patient's interest:
Patient with pronounced coronary calcifications. Age 68 years. Male. Non-smoker. HbA1c 5.7%. Cholesterol 3.0. HDL 0.9. LDL 1.9. TG 1.0. Basic lipid therapy: Atozet 10/80 mg 1-0-0 for several years. Blood pressure 135 mm Hg.
SCORE2-OP risk: High pre-test risk of heart attack and stroke of 7.9% in 10 years. Night test risk: Very high night test risk: 19.8%. Calcium score result: Agatston score 1 168. sensitivity 54.0%, specificity 86.0% for ASCVD [1], [2].
Bayes theorem: PTP for positive calcium score test: (PV x SE)/[PV x SE + (1 - PV) x (1 - SP)] [3].
Image source: Praxis Kardiolab and Rodiag Diagnostic Center Olten (Michel Romanens)



[3] http://docfind.ch/Kieser052015.pdf
[4] https://varifo.ch/wp-content/uploads/2023/09/LeqvioKOGUAbgelehnt.png
[5] https://varifo.ch/wp-content/uploads/2023/09/VarifoBriefLimitatioLeqvio082023.pdf
[6] https://varifo.ch/wp-content/uploads/2023/09/KoGuLeqvioConcordia04092023.png

Limitation according to specialty list[7] : Temporary limitation until 31.12.2025:
LEQVIO (as well as alirocumab and evolocumab) is reimbursed in addition to a diet and a maximum tolerated dosage of an intensified LDL-C lowering therapy:
- in secondary prevention in patients after a clinically manifest atherosclerotic, ischemic cardiovascular event and an LDL-C level of > 1.8 mmol/L.
- In patients with heterozygous familial hypercholesterolemia and an LDL-C level of > 2.6 mmol/L.

Risk category according to AGLA[8] : Very high cardiovascular ASCVD risk is defined as follows: ESC SCORE2/SCORE2-OP 10-year risk in persons <50 years: ≥7.5% or in persons 50-69 years: ≥10 % or in persons ≥70 years: ≥15 % or existing ASCVD: clinically or clearly demonstrated by imaging (Clinical: history of acute MI, ACS, coronary revascularization, other arterial revascularization, stroke, TIA, aortic aneurysm, PAD. Imaging techniques: Plaque detection by coronary angiography, carotid ultrasonography, coronary CT, but not intima-media thickness IMT of the carotids).
The following risk groups can be categorized.

A) Secondary prevention risk group: Limitatio for LDL ≤1.80 mmol/l
B) Risk group primary prevention heterozygous familial hypercholesterolemia: Limitatio LDL ≤2.60 mmol/l
    a. Homozygous hypercholesterolemia: Limitatio for all patients
C) Risk group Primary prevention heterozygous familial hypercholesterolemia with very high post-test risk[9] according to atherosclerotic plaque detection by imaging according to AGLA criteria: Limitatio LDL ≤2.60 mmol/l
D) Risk group Primary prevention with very high night test risk according to atherosclerotic plaque detection by imaging according to AGLA criteria: Limitatio 100%.
E) Risk group Primary prevention with very high risk according to SCORE2/-OP: Limitatio 100%.

The effect of treatment with evolocumab and alirocumab: absolute risk reduction in 10 years
Base case: risk of ASCVD in 10 years 20%. Relative risk reduction through LDL reduction per 1 mmol/l in primary prevention: 30% [4]. Expected LDL reduction: 1.3 mmol/l. Effect relative risk reduction: 39%. Absolute risk reduction: 7.8%, NNT 12.8.
Cost-effectiveness for 1,000 people treated in 10 years: Costs: Basic therapy per pack CHF 2,538. Annual costs CHF 5,076. Total costs: 1,000 people x 10 years x CHF 5076 = CHF 50.76 million (excluding medical monitoring). Expected events: 36 deaths. 164 non-fatal events. 200 events. Effect of therapy over 10 years of avoided events: fatal: 14.2, non-fatal: 64.0, total avoided events: 78. Cost/QALY according to SMB formula 2013: Cost/QALY = - 197 902 Fr. (134.94 QALY gained)[10] . Cost of a year of life lost (VSLY): CHF 260,000[11] . Years of life lost: per death: 20 years. Cost of years of life lost: CHF 73.8 million Return on investment: CHF 23.1 million.
Legal aspects [5]:

[7] www.spezialitaetenliste.ch
[8] https://agla.ch/de/rechner-und-tools/cvrisk-determination
[9] Post-test risk refers to the calculation of the risk of cardiovascular events based on SCORE2/-OP as the pre-test risk and the risk calculated using Bayes' theorem from imaging procedures for atherosclerosis [3], [7]-[10].
[10] In the SMB model[11] assumes a QALY loss per non-fatal event of 20% over 5 years. Calculation tool available online [12]. Not included in these calculations are the QALY losses of relatives due to cardiovascular events, e.g. 200 events at 10% quality of life loss over 10 years for 4 relatives = 800 QALY, which would have to be added to the 134.94 QALY[13]. Furthermore, the social costs were also not taken into account in this model, which according to Schwenkglenks are roughly the same as the medical treatment costs [14].
[11] According to Schleiniger 2006, the WHO recommends calculating the value of life with the GDP per person and year using the formula GDP/Px3=approx. 260,000 Fr.[15].

"If, however, the limitation set by the Federal Office of Public Health means that certain insured persons do not receive treatment that is in itself part of high-quality medical care, the corresponding design principle is violated.
Sufficient justification by the Federal Office of Public Health (FOPH): The decision to include a preparation with a restricted limitation in the list of specialties is a decision of considerable significance. A very large number of people are affected, and at the same time very large sums are involved, which may or may not be borne by Swiss health insurance. In this situation, it is to be expected that the Federal Office will justify its decision with particular care and in a coherent and comprehensible manner."

Discrimination of risk groups: While risk groups A-C fortunately do not fall under the limitatio in part due to their very high risk, groups D-E, which also have a very high risk, fall completely under the limitatio. Furthermore, people with homozygous hypercholesterolemia are not mentioned at all.
The selective limitation of cost-effective medical treatments for people at very high cardiovascular risk, at least planned until December 21, 2025, is unacceptable without further justification on the part of the FOPH, especially since the cost-effectiveness of these high-priced treatments for hyperlipidemia, as we have shown here for Leqvio, is demonstrable.
In addition, some patients with a very high cardiovascular risk fall within the defined limit, although there may be no medical reasons for this, while others are not granted a limit. This discriminates against patients and can also have legal consequences, especially as people in primary prevention with advanced atherosclerosis have the ASCVD risk of people in secondary prevention after a cardiovascular event [6].
Requests to the BAG:

1. We ask the FOPH to disclose the reasons for the limitation, in particular the basis and results of any budget impact analysis[12] .
2. The current discriminatory limit should be restricted to <1.4 mmol/l LDL as soon as possible if a person has a very high cardiovascular risk.
3. The risk assessment from the imaging of atherosclerosis must be taken into account in official decisions.
4. Limitations must be adapted to the new AGLA guidelines, in particular with regard to SCORE2/-OP risk categories (formerly: PROCAM-based risk assessment).
    a. "According to AGLA risk category" is now obsolete and all statements by the authority in this regard must be corrected immediately (SCORE2/OP).
5. In future, cost-effectiveness calculations must be designed in such a way that the VSLY is taken into account and QALY models are considered obsolete for ethical and methodological reasons[13] .

Literature on casuistry

[1] E. F. Gudmundsson *et al*, "Carotid plaque is strongly associated with coronary artery calcium and predicts incident coronary heart disease in a population-based cohort," *Atherosclerosis*, vol. 346, pp. 117-123, Apr. 2022, doi: 10.1016/j.atherosclerosis.2022.01.018.

[12] https://www.bag.admin.ch/dam/bag/de/dokumente/kuv-aufsicht/rakv2/ks-07-02-boe-vbgoe.pdf.download.pdf/ks-7-2-boe-vbgoe.pdf

[13] Our observations on the use of QALY as a rationing tool in healthcare have been described elsewhere [16]. In health economics models in Switzerland, the loss of quality of life due to illness is calculated unilaterally for the sick person, while the loss of quality of life for relatives is not calculated. For this reason alone, numerous therapies with demonstrable cost-effectiveness appear as not cost-effective in the QALY calculations. If QALYs are used, relatives should not be discriminated against. Further information: https://qaly.ch/

[2] F. Ackermann, "BayesCalcTab." https://www.kardiolab.ch/BayesCalcTab.html (accessed Jul. 30, 2023).
[3] M. Romanens *et al*, "Improvement of cardiovascular risk prediction: time to review current knowledge, debates, and fundamentals on how to assess test characteristics," *Eur J Cardiovasc Prev Rehab*, vol. 17, no. 1, pp. 18-23, 2010.
[4] Cholesterol Treatment Trialists' Ctt Collaborators, "The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomized trials," *Lancet*, vol. 6736, pp. 1-10, May 2012.
[5] U. Kieser, "Expert opinion provided to the Association Ethics and Medicine (VEMS) on questions of reimbursement of drugs against hepatitis C," pp. 1-19, 2015, Accessed: Jul. 30, 2023, [Online]. Available: www.docfind.ch/GutachtenKieserRationierung032015.pdf
[6] A. C. Razavi *et al*, "*! Very-High-Risk Atherosclerotic Cardiovascular Disease Status Among Patients with CAC >1000: Implications for Intensive Lipid-Lowering Therapy," *J Clin Lipidol*, vol. 17, no. 4, pp. e12-e13, Jul. 2023, doi: 10.1016/J.JACL.2023.05.020.
[7] M. Romanens and R. Darioli, "Risk markers from imaging techniques," in *Atherosclerosis Prevention*, E. Battegy, G. Noseda, and W. Riesen, Eds, Huber Verlag, 2007 [Online]. Available: https://docfind.ch/Romanens2007.pdf
[8] M. Romanens, F. Ackermann, W. Riesen, J. D. Spence, and R. Darioli, "Imaging as a cardiovascular risk modifier in primary care patients using predictor models of the European and international atherosclerosis societies," *Cardiovascular Medicine*, vol. 10, no. 04, pp. 139-150, 2007, doi: https://doi.org/10.4414/cvm.2007.01242.
[9] M. Romanens *et al*, "Prediction of cardiovascular events with traditional risk equations and total plaque area of carotid atherosclerosis: The Arteris Cardiovascular Outcome (ARCO) cohort study," *Prev Med (Baltim)*, vol. 147, Jun. 2021, doi: 10.1016/j.ypmed.2021.106525.
[10] M. Romanens, A. Adams, W. Bojara, S. Balint, and W. Warmuth, "Cost-Effectiveness-Analysis of Statins in primary care. Results from the Arteris Cohort Study (in press)," *Swiss Med Wkly*, 2021.
[11] S. Felder, P. Jüni, C. A. Meier, and et al, "SMB Statin Recommendation," 2014 [Online]. Available: https://www.swissmedicalboard.ch/fileadmin/public/news/2013/bericht_smb_statine_primaerpraevention_lang_2013.pdf
[12] M. Romanens, "Cost Effectiveness Spreadsheet." 2023. Accessed: Jul. 30, 2023 [Online]. Available: http://qaly.ch/wp-content/uploads/2023/05/QALYExpert.xlsx
[13] F. Gutzwiller *et al*, "Methoden zur Bestimmung von Nutzen bzw. Wert medizinischer Leistungen," *SAMS Study*, 2012, [Online]. Available: https://www.samw.ch/dam/jcr:bac6f456-0baf-4422-bbac-61ea067b6bbd/studie_samw_gutzwiller_schwenkglenks.pdf
[14] S. Wieser *et al*, "The cost of non-communicable diseases in Switzerland," 2014. doi: 10.5167/uzh-103453.
[15] R. Schleiniger, "The Value of Life: Methods, Empiricism, Applications," *ZHAW*, no. August, 2006, [Online]. Available: https://digitalcollection.zhaw.ch/bitstream/11475/16911/3/DerWertdesLebens.Bericht_2006_SC3.4.pdf
[16] M. Romanens, A. Adams, W. Bojara, S. Balint, and W. Warmuth, "Cost-effectiveness analysis of statins in primary care: results from the Arteris cohort study," *Swiss Med Wkly*, vol. 151, no. 1516, 2021, doi: 10.4414/smw.2021.20498.

Which utility (CUA)?

In the language of health economics, utility is understood to mean quality of life. In CUA analyses (cost-utility analysis), the effect of the medical measure on the quality of life of the patient is recorded and compared with the medical costs, although quality of life can hardly be measured objectively[14] .

What effects (CEA, ROI)?

Of course, a medical measure has concrete effects such as preventing death, heart attacks or strokes (CEA=cost effectiveness analysis). In the cost-effectiveness analysis, these successes are compared with the medical costs. Which effects are quantified in a health economics report depends on which cost-effectiveness result is to be achieved. The fewer effects are taken into account, the lower the cost-effectiveness. The following five effects can be included in health economics models:

Table 1: Effect variables as a result of medical treatment

1. QALY of patients
2. QALY of relatives
3. Direct costs
4. Indirect costs
5. VSLY (value of a statistical life year)

In a presentation on the cost-effectiveness of drugs in medicine[15] , it was calculated how the cost-effectiveness result changes depending on the five effects taken into account. As a result, the company receives money back (ROI=return on investment) taking the five effects into account.

Normative effects of cost-effectiveness in society

In principle, drugs approved by Swissmedic are cost-effective if all five effects are taken into account in the health economics models. The fact that health economics, sometimes also directly commissioned by the FOPH, only considers the utility effect in the models leads to a hidden implicit normativity of economics and its effects on the healthcare system and society, as can be read in a report[16] by the Swiss Association for Ethics and Medicine: if a medical measure is described as less cost-effective at the level of the patient, where the same measure can be described as very cost-effective at the societal level, questions arise that require a societal solution. In our view, the mathematical separation of patients from their social and societal environment by the health economics models is problematic. This is a construct, just as the question of guilt in the WZW procedures is not derived from a specific clinical offense, but is constructed mathematically and statistically.

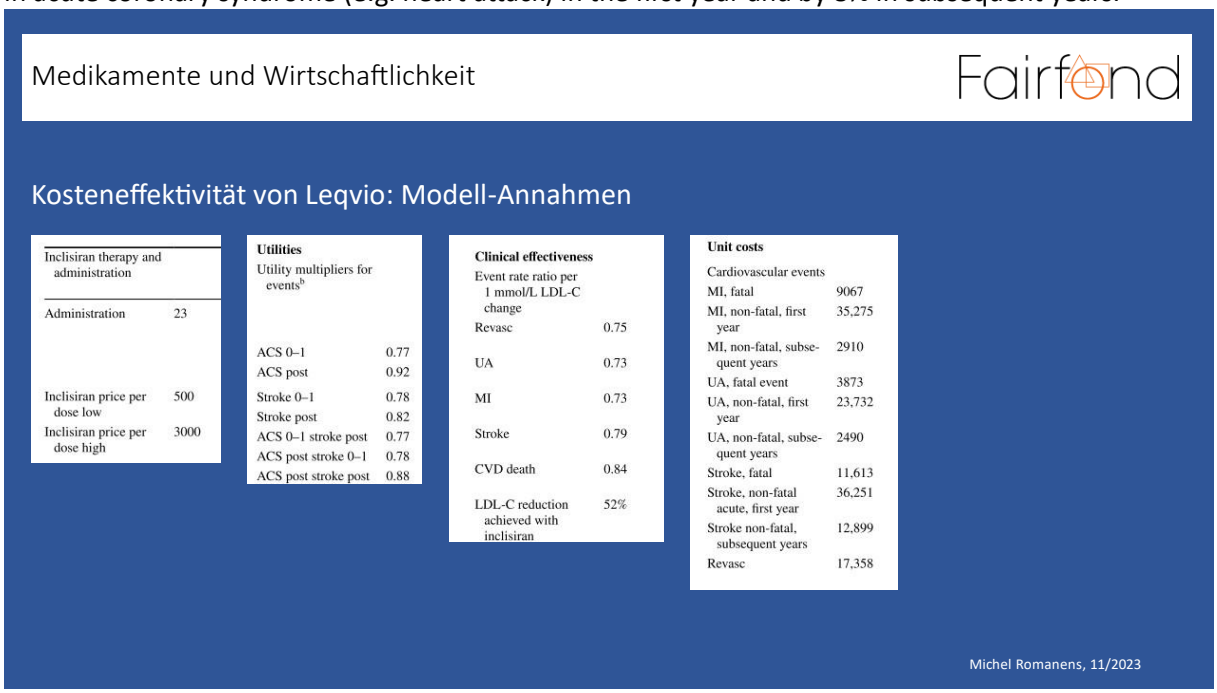
It is clear that this seems to be the real reason why the FOPH has massively blacked out the budget impact analysis section on Leqvio. Society in Switzerland should not realize how high-quality medical care is being rationed with the help of CUA purely for cost reasons. For physicians, another effect of CUA is unacceptable: if the health economy models highly effective treatment as non-effective,

[14] https://smw.ch/index.php/smw/article/view/2989
[15] https://docfind.ch/MedicinesAndCostefficiencyTraining23112023.pdf
[16] English: https://docfind.ch/VEMSReportCEA.pdf German: https://docfind.ch/VEMSBerichtCEA.pdf

medicine suffers massive reputational damage. The rehabilitation of medicine in today's cost narratives regarding unaffordable and ultimately useless medicine can only be achieved by taking into account the five effects of medical measures.

Health economics models in reality using the example of Leqvio (the results for alirocumab and evolocumab are comparable)

In the study on the cost-effectiveness of Leqvio[17] , the utility in the event of illness is reduced by 33% in acute coronary syndrome (e.g. heart attack) in the first year and by 8% in subsequent years.



Inclisiran therapy and administration	
Administration	23
Inclisiran price per dose low	500
Inclisiran price per dose high	3000

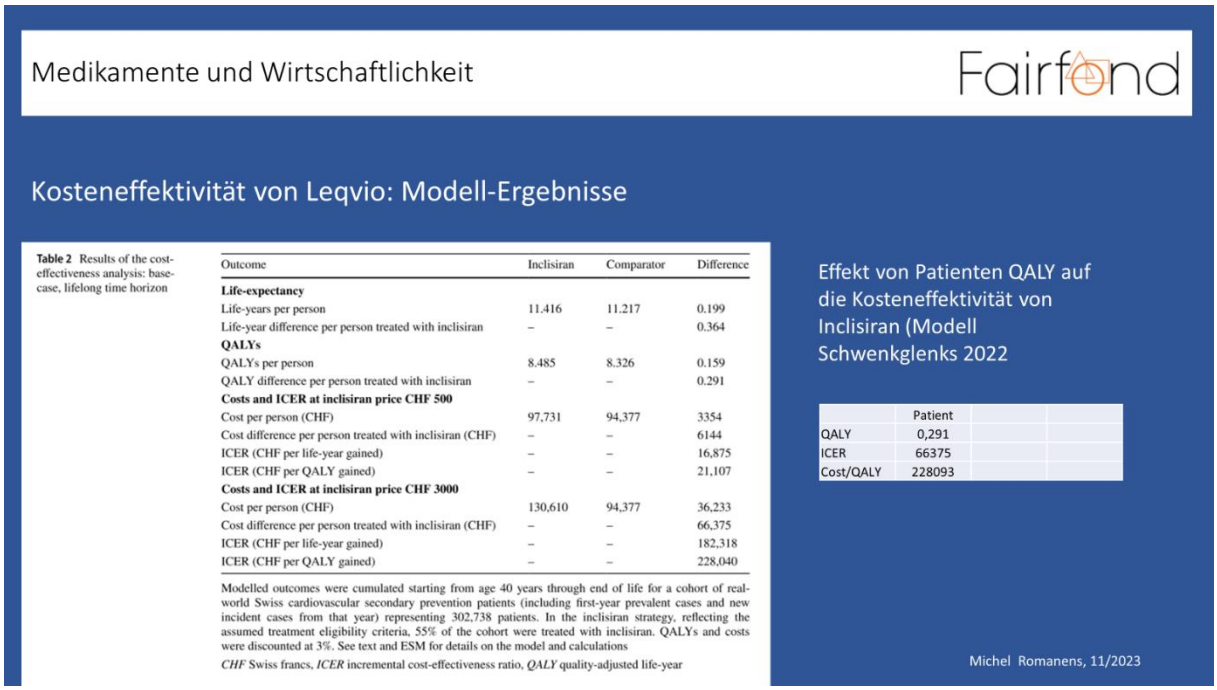
Utilities	
Utility multipliers for events[b]	
ACS 0–1	0.77
ACS post	0.92
Stroke 0–1	0.78
Stroke post	0.82
ACS 0–1 stroke post	0.77
ACS post stroke 0–1	0.78
ACS post stroke post	0.88

Clinical effectiveness	
Event rate ratio per 1 mmol/L LDL-C change	
Revasc	0.75
UA	0.73
MI	0.73
Stroke	0.79
CVD death	0.84
LDL-C reduction achieved with inclisiran	52%

Unit costs	
Cardiovascular events	
MI, fatal	9067
MI, non-fatal, first year	35,275
MI, non-fatal, subsequent years	2910
UA, fatal event	3873
UA, non-fatal, first year	23,732
UA, non-fatal, subsequent years	2490
Stroke, fatal	11,613
Stroke, non-fatal acute, first year	36,251
Stroke non-fatal, subsequent years	12,899
Revasc	17,358

The costs per QALY are estimated at CHF 228,040 according to the model used.

[17] https://pubmed.ncbi.nlm.nih.gov/35723806/



However, only the utility of the patients is taken into account here[18] , but not that of their relatives, and other effects such as social costs and VSLA were not considered either. If we calculate these effects on cost-effectiveness, we obtain the following results:
By taking into account the QALY of relatives, the cost-effectiveness improves to CHF 134,183.

[18] In principle, quality of life cannot be scientifically determined, see our peer-reviewed article on the cost-effectiveness of statins: Should we "QALY"?
https://smw.ch/index.php/smw/article/view/2989/4941 Health economists like to "qaly" medicine. In this context, "I qaly" the healthcare system is the expression of an evolving mathematical machinery [34] that aims to give answers to the question of whether a medical therapy is indicated or not. Health economists claim that the QALY is a reliable metric like body size or weight. However, QALYs are influenced by cultural, social, individual, extrinsic or intrinsic observations and factors, and experience of life quality based upon physical, psychological, interpersonal, socioeconomic and spiritual dimensions that are never constant over time. The constancy of the multiplicative utility function over time is not evidence-based, and can never be evidence-based at the individual level. Too many variables influence utility and, therefore, QALYs are expressing a fixed utility over time [35], which creates an axiomatic expression [27] of what is claimed to be real and is completely unrelated to human life quality, despite the claims of health economists who measure life quality. QALYs are not reproducible as a metric, being hampered by several biases (especially response shift and recall bias), and they lack a gold standard [36, 37].

Medikamente und Wirtschaftlichkeit

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Kosteneffektivität von Leqvio: Modell-Ergebnisse

Table 2 Results of the cost-effectiveness analysis: base-case, lifelong time horizon

Outcome	Inclisiran	Comparator	Difference
Life-expectancy			
Life-years per person	11.416	11.217	0.199
Life-year difference per person treated with inclisiran	–	–	0.364
QALYs			
QALYs per person	8.485	8.326	0.159
QALY difference per person treated with inclisiran	–	–	0.291
Costs and ICER at inclisiran price CHF 500			
Cost per person (CHF)	97,731	94,377	3354
Cost difference per person treated with inclisiran (CHF)	–	–	6144
ICER (CHF per life-year gained)	–	–	16,875
ICER (CHF per QALY gained)	–	–	21,107
Costs and ICER at inclisiran price CHF 3000			
Cost per person (CHF)	130,610	94,377	36,233
Cost difference per person treated with inclisiran (CHF)	–	–	66,375
ICER (CHF per life-year gained)	–	–	182,318
ICER (CHF per QALY gained)	–	–	228,040

Modelled outcomes were cumulated starting from age 40 years through end of life for a cohort of real-world Swiss cardiovascular secondary prevention patients (including first-year prevalent cases and new incident cases from that year) representing 302,738 patients. In the inclisiran strategy, reflecting the assumed treatment eligibility criteria, 55% of the cohort were treated with inclisiran. QALYs and costs were discounted at 3%. See text and ESM for details on the model and calculations

CHF Swiss francs, *ICER* incremental cost-effectiveness ratio, *QALY* quality-adjusted life-year

Effekt von Patienten QALY auf die Kosteneffektivität von Inclisiran (Modell Schwenkglenks 2022

	Patient	4 Relatives	
QALY	0,291	0,2	0,491
ICER	66375		66375
Cost/QALY	228093		135183

Michel Romanens, 11/2023

This can also be recalculated using a simpler calculation model from the Swiss Medical Board for statins in 2014. The result is CHF 57,563/QALY.

Medikamente und Wirtschaftlichkeit

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Kosteneffektivität von Leqvio: Einschluss QALY Verwandte

Input Variables for Population of 1'000	Your Choice
Time of treatment in years	10
QALY loss due to disease (default 20%)	20
VSL (cost of death per year)	8500
Expected years of lost life per person (e.g. 30 years for a 50 year old)	5
Fatal risk per year in %	0,363
Non fatal risk per year in %	1,6335
Relative Risk Reduction of Treatment in %	39
Cost of disease first year	25000
Cost of disease subsequent years	8000
Cost of therapy per year in CHF	3500
Include Social cost in the model (1=no, 2=yes)	1
Results	
Qaly gained in 1000 persons treated	534,49
Cost / QALY (Cost-Effectiveness)	57 563
Return on investment (cost vs VSLY)	
Avoidable fatal heart attacks	14,2
Years Lost	5
Cost of therapy	35 000 000
VSLY (not discounted)	601 673
Return on investment (cost vs VSLY)	-34 398 328
Return on investment (cost vs VSLY) for 1 000 000 treated persons	-34 398 327 500
Patient Risk	200

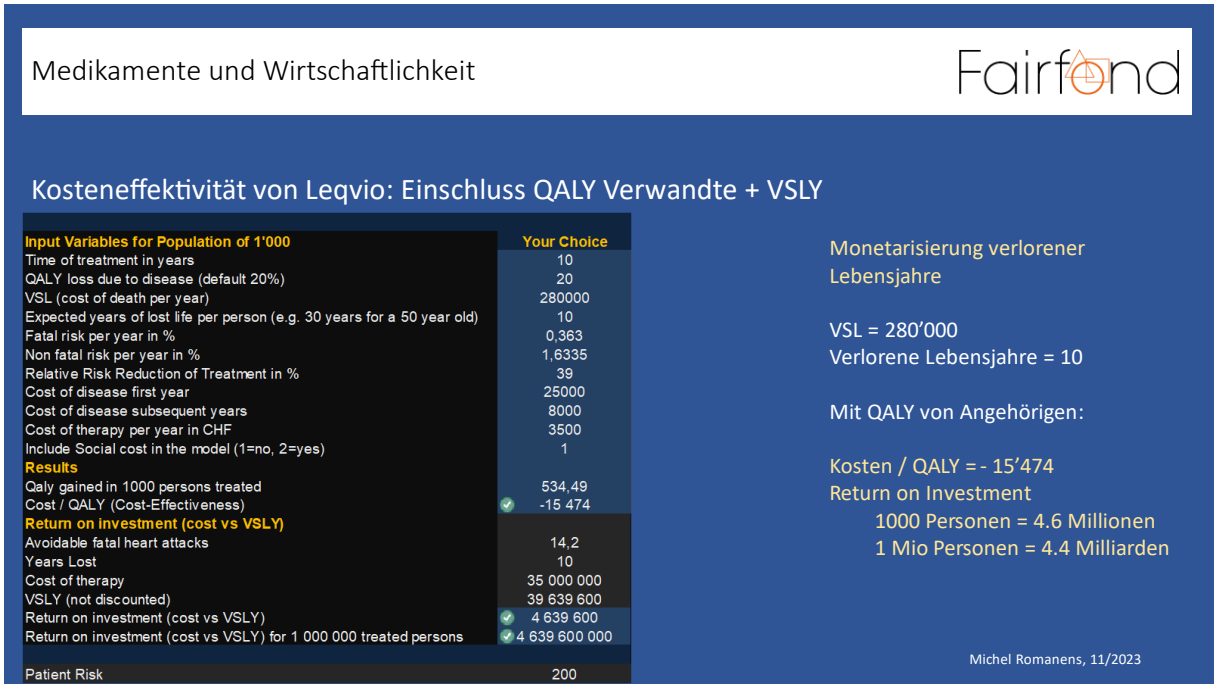
Verwandten / Angehörigen-Modell
4 Verwandte erleiden in 10 Jahren eine verminderte Lebensqualität von 5 Jahren.
Anzahl Personen mit Ereignissen: 200
Anzahl Personen mit verminderter Lebensqualität = 4x200=800
QALY Verlusts 10% pro Jahr über 5 Jahre

Therapie ergibt zusätzliche 400 QALY

Kosten/QALY = 57'563 Fr!

Michel Romanens, 11/2023

Including the VSLY calculated over 20 years, the return on investment for 1,000 people treated is CHF 4.6 million.



The cost-effectiveness of drugs is influenced by the choice of model components. Complex Markov models or simple SMB models (Statin Report 2014) deliver similar results. The decisive factor is therefore not the complexity of the model, but the choice of model components. When calculating cost-effectiveness without QALY dependents and without VSL = costs / QALY > CHF 200,000. When calculating cost-effectiveness with QALY dependents and without VSL = costs / QALY < CHF 100,000. When calculating cost-effectiveness with QALY dependents and with VSL = costs / QALY negative QALY / ROI. The omission of cost-effectiveness variables creates a false picture of unaffordable medicine. The calculation details can be found here: https://varifo.ch/wp-content/uploads/2023/12/QALYExpert.xlsx.

Legal issues:

The evaluation of the cost-effectiveness of medical interventions by health economics is subject to numerous biases. Neither the quality of life (with QALY) can be scientifically objectified[19] , nor are socially relevant effects of medical interventions correctly mapped, particularly with regard to VSLY[20] . This leads to a distorted perception of the added value of medical effects and affects numerous aspects of law, ethics and the rules of value creation.

In view of the high costs of medical services, today's health economics models offer the opportunity for the FOPH to impose rationing effects on society by setting limits. However, the effect models take into account reduced effects that reduce the impact of medical measures on patients. However, much greater effects are achieved by reducing the social and societal damage caused by illness. As a result, today's health economics models are suspected of using reduced effect models to turn effective, appropriate and economical medicine into the opposite, an unacceptable process. From a legal perspective, a comprehensive assessment is therefore necessary, with the following questions to be answered:

[19] https://www.ajmc.com/view/is-the-qaly-fit-for-purpose-
[20] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8201370/

1. Do legal definitions of cost-effectiveness exist?
2. Is the quality of life of patients (QALY effect) legally sufficient for assessing medical effects?[21]
3. In addition to the cost-effectiveness effects for the patients (reduced quality of life due to the disease), to what extent should the monetization of avoidable deaths, avoidable social costs (e.g. loss of work), avoidable suffering (quality of life of relatives, QALY effect on relatives) and avoidable treatment costs be taken into account?
4. Concerning the WZW rule: is the sole consideration of effects (QALY effect) for patients sufficient or must the QALY effects on relatives and the social costs of medical services also be taken into account when fulfilling WZW criteria?[22]
5. What requirements must budget impact analyses fulfill in order to be able to justify a limitation in a legally sufficient manner?
6. Is the reduction of the models for calculating cost-effectiveness to the sick individual instead of calculating cost-effectiveness for society at best legally actionable?

[21] Numerous countries, including the USA and Germany, do not use QALY by law. Further background information on QALY https://qaly.ch and https://www.physicianprofiling.ch/VEMSRationierung2014.pdf

[22] The FOPH defines "economic efficiency: Benefits and costs, taking into account the cost impact (budget impact)." This statement is therefore not centered on patients; the broader budget impact on society can also be included. Slide 23: explicit mention of working days gained. https://docfind.ch/HTAKlazienMatter.pdf