



# Estimating the potential annual welfare impact of innovative drugs in use in Switzerland

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Expenditures of health care systems are increasing from year to year. Therefore, this study aimed to estimate the difference in costs and benefits of innovative pharmaceuticals launched 2000 onward compared to standard treatment on the national economy of Switzerland in 2010. The approach and formula described in the pilot study by Tsiachristas et al. (1), which analyzed the situation of welfare effects in the Netherlands, served as a model for our own calculations. A literature search was performed to identify cost-utility or cost-effectiveness studies of drugs launched 2000 onward compared to standard treatment. All parameters required for the calculation of welfare effects were derived from these analyses. The base-case threshold value of a quality-adjusted life year was set to CHF 100,000. Overall, 31 drugs were included in the welfare calculations. The introduction of innovative pharmaceuticals since 2000 onward to the Swiss market led to a potential welfare gain of about CHF 781 million in the year 2010. Univariate sensitivity analysis showed that results were robust. Probably because of the higher benefits of new drugs on health and quality of life compared to standard treatment, these drugs are worth the higher costs. The literature search revealed that there is a lack of information about the effects of innovative pharmaceuticals on the overall economy of Switzerland. Our study showed that potential welfare gains in 2010 by introducing innovative pharmaceuticals to the Swiss market were substantial. Considering costs and benefits of new drugs is important.

**Keywords:** welfare impact, cost-effectiveness, innovative drugs, economic evaluation, quality-adjusted life year

## INTRODUCTION

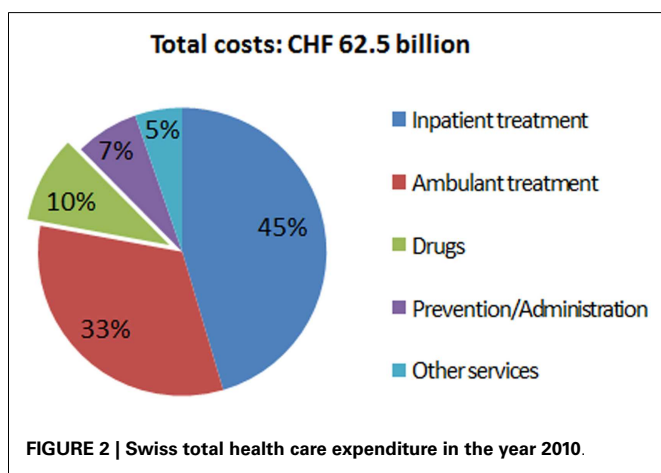
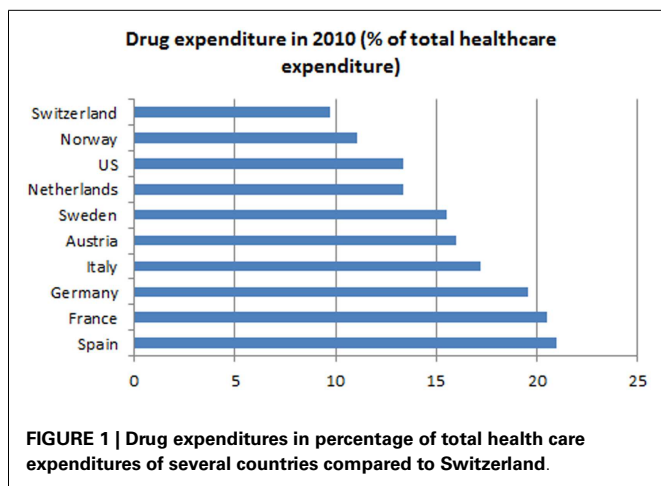
The expenditures of most health care systems, e.g., the US and several European health care systems (2) increased from year to year, the same is true for the Swiss health care system (3). Hence, there is an ongoing debate on how to stop or reduce the increase in health care expenditures and keep the costs on an affordable level. Compared to other countries, such as the US, Germany, France, Austria, etc., Switzerland spent less on drugs in 2010 (Figure 1) (4). Although pharmaceutical expenditure in 2010 only accounted for 9.7% (CHF 6.05 billion) of total health care expenditure in Switzerland (CHF 62.5 billion in 2010) (Figure 2) and even decreased compared to the year 2009 (CHF 6.18 billion or 10.1% of total health care expenditure) (5), health policy and health decision-makers focused mainly on the price of novel and existing medicines.

New or innovative medicines are often more expensive than well-established drugs. This supports the common opinion that the expenditures on drugs are too high and should be reduced. For this reason, politicians and decision-makers often focus on the price of a new drug when there are negotiations about introducing a new drug to the Swiss market. Seldom is attention paid to the fact that a new drug may have additional effects on the health state or the quality of life of a patient compared to the standard drug, i.e., the currently most prescribed drug for a given indication. For example, the new drug costs more than the standard therapy. Without considering additional costs or benefits, we would conclude that medical treatment of the patient with the new drug is more

expensive than treating the patient with the standard drug. Suppose that the new drug reduces hospital length of stay or number of physician visits compared to the standard therapy (6). This could result in reduced resource use by the patient, which could save costs in patients' care (7). These additional benefits including externalities may outweigh the drug expenditures, and in the end we may generate welfare gains due to the prescription of new drugs. There is also evidence in international literature that health care expenditure positively effects on outcomes (8, 9) and increase in drug spending leads to cost savings in other health care expenditures and these savings often outweigh the spending (10–12). Others argue that over the past 50 years, the majority of new products (up to 90%) have provided only few benefits, but also considerable harms that have added to national healthcare costs (13).

The timeliness of this topic is supported by a ruling of the Swiss Federal Court of Justice in 2010 which stated that the treatment of Morbus Pompe, which is a very rare disease, at CHF 500,000 per year is too expensive given its only small health effects and that health insurers are not required or forced to pay for such treatments beyond the proposed threshold of CHF 100,000/QALY (14, 15). This is the first time that a formal and in this case legally binding cost-effectiveness threshold has been suggested in Switzerland.

To evaluate the health economic impact of a new pharmaceutical, it is required to conduct a cost-effectiveness analysis that considers not only the additional costs a new drug has compared to an alternative, but also the additional benefits. Ideally, the result of the cost-effectiveness analysis is presented as the ratio



of the differences of costs and QALYs (incremental cost–utility ratio, ICUR) for the new drug compared to standard treatment, because ICURs are not indication-specific and therefore, ICURs of different diseases can be compared to each other.

The aim of this analysis was to show the importance of considering the costs of a new drug as well as its benefits from a Swiss perspective and to evaluate the total potential annual welfare impact due to the implementation of new drugs for the Swiss economy in 2010.

## MATERIALS AND METHODS

To the best of our knowledge, we are the first to assess the welfare effects of innovative drugs in Switzerland. Another such evaluation has already been performed in the Netherlands, which revealed great potential welfare gains of introducing new pharmaceuticals to the market (1). This evaluation and published report by Tsiachristas et al. (1) provided the methodological basis for our own calculations. The aim of the exploratory study was to establish knowledge in the welfare impact of innovative drugs introduced to the Dutch market after 1997 to reflect a 10-year time horizon. The authors mainly used pharmacoeconomic studies collected by the Dutch Health Care Insurance Board (CVZ), the British National

Institute for Health and Clinical Excellence (NICE), and the Canadian Agency for Drugs and Technologies in Health (CADTH). A limited number of studies have been also collected from the scientific literature and in total, 52 studies were included. The heterogeneous and foreign studies have been roughly adjusted to the Dutch situation by using purchasing power parities (PPP) and the deflator of the gross domestic product (GDP) as it is difficult to adjust for varying cost calculation methods and other country-specific aspects of a pharmacoeconomic evaluation. The welfare gains amounted to € 1.7 billion based on a QALY valuation of € 50,000. Further details of the methodology have already been extensively described in the report (1).

Our approach was to estimate the welfare impact of a basket of novel and innovative drugs in Switzerland for the year 2010, which were launched 2000 onward. The parameters needed for these calculations were derived from published literature.

## LITERATURE SEARCH

A restrictive literature search based on the results of Tsiachristas et al. (1) was conducted using the databases PubMed, the Cost-Effectiveness Analyses (CEA) Registry, and data from the Centre for Review and Dissemination (CRD). The search focused on cost-effectiveness and cost–utility analyses, respectively. References from the beginning of the study up to 31st October 2010 were included. The included studies were restricted to English and German language. The search focused on publications reporting CEA of new drugs launched 2000 onward in Switzerland. Titles, abstracts, and finally full-texts of the articles found within the search were screened to assess the eligibility of those cost-effectiveness, respectively, cost–utility analyses. Studies that fulfilled the following pre-defined inclusion criteria were considered:

- Costs were reported transparently and the reference price year was presented
- The outcome measure was expressed in QALYs (preferred outcome measure) or life years gained (LYG)
- At least, an incremental cost-effectiveness ratio (ICER, additional costs per additional effects, e.g., LYG, blood pressure reduced by one unit, etc.) was reported (an ICUR was preferred)
- the time horizon was clearly stated.

For our analysis, it would have been more accurate to consider only studies from a societal perspective (16). The societal perspective includes not only the direct cost such as drug costs, hospitalization costs, or costs for a physician visit, but also considers the indirect cost, e.g., the costs of productivity losses, work absences, or informal care by family members. The literature search identified only few studies from a societal perspective that met the inclusion criteria. Hence, several studies from a health care payer perspective had to be included in our analysis as well.

## CALCULATING THE WELFARE IMPACT

The cost-effectiveness of a drug is not only influenced by its costs and effects, but also by the society's willingness-to-pay (WTP) for a QALY or by the determined cost-effectiveness threshold of a country. The cost-effectiveness threshold commonly used in the US varies between US\$ 50,000 and US\$ 100,000 per QALY

(17). NICE acceptable cost-effectiveness thresholds for the UK are set at £ 20,000–30,000 per QALY (18). There is no official cost-effectiveness threshold in Switzerland, but as mentioned above, there was recently a discussion on this health topic initiated by a ruling of the Federal Court of Justice in 2010 that one life year saved is worth about CHF 100,000 (14, 15). Accordingly, we assumed that in Switzerland the commonly used and accepted cost-effectiveness threshold is CHF 100,000/QALY. However, in Switzerland this threshold is still arguable and there will be further discussions on this in the future.

To calculate the potential welfare impact of a new drug, it is required to know the ICER, respectively, ICUR of this drug compared to the standard treatment. Whereas the ICER is the ratio between the additional costs of a drug compared to an alternative treatment and the additional effects gained, respectively, effects lost with the drug compared to an alternative ( $\Delta\text{costs}/\Delta\text{effects}$ ), the ICUR is the ratio between the additional costs of a drug compared to an alternative treatment and the additional QALYs gained, respectively, QALYs lost ( $\Delta\text{costs}/\Delta\text{QALYs}$ ). One possibility to get the ICERs/ICURs of innovative drugs would have been to perform several CEA of the respective drugs on our own, but as these analyses have to be performed comprehensively and are therefore very time-consuming, we decided to derive the ICERs/ICURs from already published cost-effectiveness studies of the respective drugs.

The more patients benefit from a drug, the more attractive is it not only from a healthcare point of view but also economically. Hence, the number of patients possibly benefiting from the drug was needed to calculate the welfare impact. The potential number of users includes all patients who could possibly be treated with a drug, but that is not always the same as actual users as not all people affected by a disease get treated. Therefore, the best way to assess the potential number of users is the estimated number of customers from the manufacturer. Because the number of all patients potentially benefiting of the respective drug was difficult to obtain, the actual number of users had to be used in most cases. Only for four different drugs, namely conjugated vaccine, ibandronate, atorvastatin, and memantine, the information about the potential number of users was directly provided from the manufacturer. For risperdal and mimpara, the number of drug packages sold in 2010 was provided by the pharmaceutical manufacturer (IMS Health sales figures) and the number of actual users was calculated indirectly based on the usual dosage prescribed (19). For the other drugs, the number of actual users was provided by the largest health insurance group in Switzerland, Helsana. These numbers were not presented in the results due to confidentiality reasons. The benefit from a drug also depends on the duration of the effect, in this case approximately the time horizon (which was either 1 year, as long as the duration of the treatment or longer) used in the cost-effectiveness models, which was also retrieved from the published literature.

Finally, the potential Swiss welfare impact in 2010 of a new drug was calculated by using the following equation developed by Tsiachristas et al. (1):

$$\text{Welfare impact} = [\text{QALY}_{\text{value}} - \text{cost}/\text{QALY}] \\ \times [\Delta \text{QALY}/\text{time horizon}] \times [\text{number of users}]$$

As explained in the original publication (1),  $\text{QALY}_{\text{value}}$  in this context meant QALY threshold and for cost/QALY, the ICER or ICUR derived from published CEA was used. First, the ICER/ICUR was subtracted from the QALY threshold mentioned above. Second, the result was multiplied with the additional QALYs gained or lost by the new drug divided by the time horizon to get the additional QALYs gained or lost in 1 year and last, the result was multiplied with the number of users.

Uncommonly, some new drugs do not only have better outcomes, i.e., more LYs or QALYs are gained, but are also cheaper than the alternative drugs. In this situation, where the resulting ICER/ICUR is negative it is called dominant and usually, no ICER/ICUR is reported. But for the purpose of this study, it was necessary to express all results as ICERs/ICURs, even if they were negative. Hence, in these cases where the new drug had better outcomes and was also cheaper than the standard treatment, a negative ICER/ICUR was presented. This influenced the equation in such a way, that in these cases the first part of the equation turned into  $\text{QALY}_{\text{value}} + \text{cost}/\text{QALY}$ , which led to a higher potential welfare gain.

#### ADJUSTMENT OF THE DATA TO THE SWISS SITUATION IN 2010

Including only cost-effectiveness studies performed from a Swiss perspective would have been preferred. Due to the fact that only few cost-effectiveness studies have been conducted in a Swiss setting, most cost-effectiveness studies included in our analysis were studies from foreign countries. Accordingly, there was a need to adjust the data to Switzerland before running the equation. The ICERs/ICURs were first adjusted to the year 2010 of the original country by using the deflator of GDP (20–25, 30). Then, PPPs were used to convert the foreign ICER/ICUR results to Swiss francs (27).

#### UNIVARIABLE SENSITIVITY ANALYSIS

A univariate sensitivity analysis was conducted. Costs/QALY, i.e., the ICER or ICUR adjusted to Switzerland, the QALY effect itself, and the time horizon were varied between 80 and 120% of the original values ( $\pm 20\%$ ). The formula shows that varying the QALY effect and the number of users to the same extent would lead to the same welfare impact. Therefore, the number of users was varied between 50 and 150% of the original values ( $\pm 50\%$ ). In addition, the calculation was performed using a QALY threshold of CHF 50,000 reflecting also lower QALY thresholds such as in the US and the UK and using a very high QALY threshold of CHF 150,000.

## RESULTS

#### LITERATURE SEARCH

Our search identified 175 citations found in PubMed, CEA, and in CRD. Titles and abstracts of all references were screened to identify cost-effectiveness and cost-utility analyses. Full-texts were considered for the final inclusion of 31 studies (Table 1), of which 29 were conducted in foreign settings and only two studies that also met the inclusion criteria were conducted in a Swiss setting. There was no need for adjustment of the data of these two studies (28, 29). Articles were mainly excluded because they did not report an ICER/ICUR or they did not fulfill other pre-defined inclusion criteria.

**Table 1 | Drugs included in the welfare basket.**

Number	Drug	Brand	Company
1	Bosentan monohydrate (34)	Tracleer®	Actelion
2	Peginterferon alfa 2a (35)	Pegasys®	Roche
3	Conjugated vaccine (36)	Prevenar®	Wyeth
4	Ezetimibe (37)	Ezetrol®	Merck Sharp & Dohme
5	Sirolimus (38)	Rapamune®	Wyeth
6	Interferon beta-1a (39)	Avonex®	Biogen
7	Ibandronate (40)	Bonviva®	Roche
8	Rizatriptan (41)	Maxalt®	Merck Sharp & Dohme
9	Linezolid (42)	Zyvoxid®	Pfizer
10	Rivastigmine (43)	Exelon®	Novartis
11	Rosiglitazone (44)	Avandia®	GlaxoSmithKline
12	Oseltamivir (45)	Tamiflu®	Roche
13	Clopidogrel (46)	Plavix®	Bristol-Myers Squibb
14	Memantine (47)	Ebixa®	H. Lundbeck
15	Risperidone (48)	Risperdal®	Janssen-Cilag
16	Atomoxetine (49)	Strattera®	Eli Lilly
17	Atorvastatin (50)	Lipitor®	Pfizer
18	Orlistat (51)	Xenical®	Roche
19	Natalizumab (52)	Tysabri®	Elan Pharma
20	Oxaliplatin (53)	Eloxatin®	Sanofi-Aventis
21	Rosuvastatin (54)	Crestor®	AstraZeneca
22	Trastuzumab (55)	Herceptin®	Roche
23	Cinacalcet (56)	Mimpara®	Amgen Europe
24	Sitagliptin (57)	Januvia®	Merck Sharp & Dohme
25	Rimonabant (58)	Acomplia®	Sanofi-Aventis
26	Pimecrolimus (59)	Elidel®	Novartis
27	Human papillomavirus vaccine (28)	Gardasil®	Merck Sharp & Dohme
28	Fulvestrant (60)	Faslodex®	AstraZeneca
29	Erlotinib (61)	Tarceva®	Roche
30	Eplerenone (62)	Inspra®	Pfizer
31	Raltegravir (29)	Isentress®	Merck Sharp & Dohme

### WELFARE IMPACT (BASE-CASE)

For every drug, the welfare impact was calculated separately according to the formula described before. Generally, the results of the individual drugs differed broadly (Table 2). There were some drugs which did not generate much potential welfare gain over 1 year compared to the standard treatment, e.g., peginterferon alfa 2a (CHF 658,144), risperidone (CHF 996,206), rimonabant (7,759), HPV vaccine (22,157), and others. Then, there were drugs

where the evidence of potential welfare gains with the introduction of these drugs was much higher, e.g., bosentan monohydrate (CHF 10,717,090), clopidogrel (CHF 257,359,200), pimecrolimus (CHF 54,412,070), etc. Nevertheless, each of the 31 reviewed drugs generated a positive result, meaning a clear welfare gain, except one of the drugs. The introduction of cinacalcet (mimpara) to the Swiss market resulted in a monetary loss compared to the standard treatment. To obtain the total welfare impact for the Swiss economy due to the introduction of innovative drugs to the Swiss market, all results were summed up, which led to a total potential welfare gain of CHF 781.39 million for the year 2010 (Table 2). This amounted to about 0.0014% of the GDP in Switzerland in 2010 (30).

### SENSITIVITY ANALYSIS

All results of the univariate sensitivity analysis showed the robustness of the base-case findings, meaning that for every variation of the input parameters, there was a potential welfare gain. The most influential parameter was the QALY threshold followed by the number of users (Figure 3), which were both varied by 50%. When using a QALY threshold of CHF 50,000, the potential welfare gain was only CHF 260.77 million, which was the lowest calculated. In the sensitivity analysis, the potential welfare gain ranged from CHF 260.77 million to CHF 1.30 billion (Figure 3).

### DISCUSSION

To the best of our knowledge, this study is the first attempt to calculate the welfare impact of innovative drugs in a Swiss setting. Although the costs of the most innovative drugs often surpass the costs of previous or existing pharmaceuticals, prescribing newer drugs is still reasonable, at least in most cases due to more benefits. Our base-case results showed that introducing innovative drugs to the Swiss market led to potential welfare gains in 2010 accounting for approximately CHF 781.39 million, which accounts for 13% of total drug expenditure in 2010 in Switzerland (5). There was only one drug included in our study that led to additional costs per QALY gained compared to the standard treatment, i.e., which decreased the potential welfare gained for the Swiss economy. The sensitivity analysis showed that results were robust.

Some of the general limitations specific to the calculation approach used in this study have already been discussed by the original report published by Tsiachristas et al. (1). We are aware that the formula created by the authors has not been utilized widely; further validation is deemed necessary. Nevertheless, there do not seem any *a priori* reasons to assume that the derived model would not perform sufficiently adequate for our study question. Other limitations include inconsistencies in the economic evaluation, international differences in health care systems and health determinants, limited data availability and lack of agreement about the appropriate valuation of a QALY. Therefore, in the next section, we will focus on limitations specific to our study.

### LIMITATIONS OF THE STUDY

The main limitation of this study was probably the lack of Swiss-specific data and when interpreting the welfare impact results, it must be considered that in this study the obtained cost-effectiveness data for Switzerland, i.e., the obtained ICERs/ICURs for our calculations were in almost all the cases adjusted from

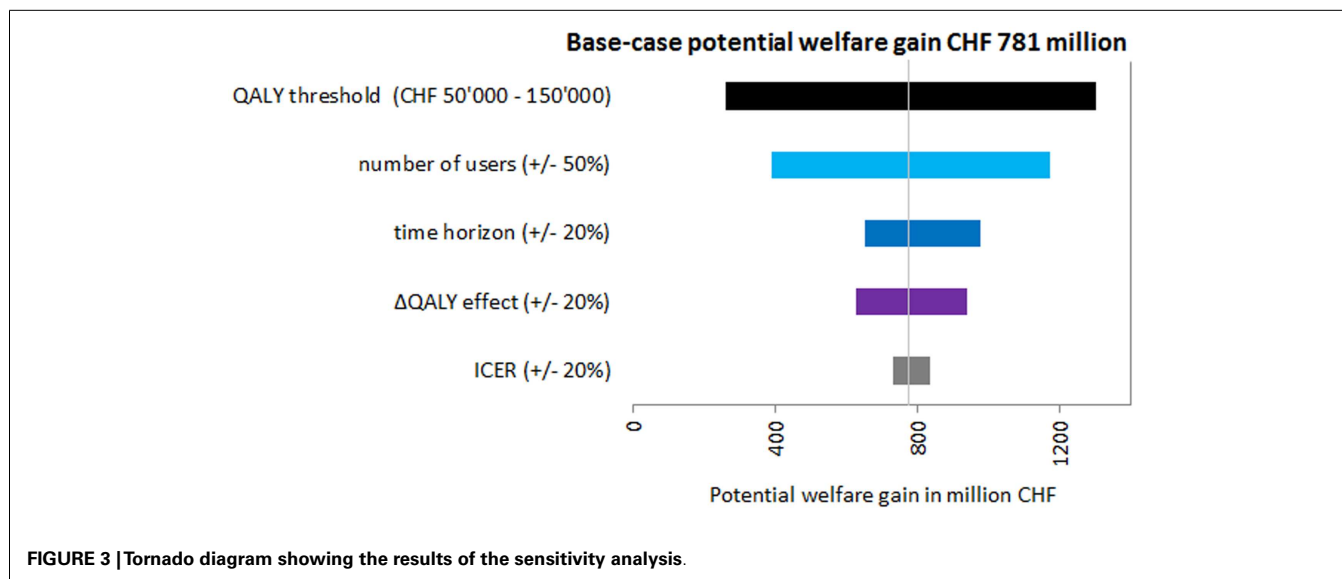
**Table 2 | Input parameters used for the welfare impact calculations.**

Drug	Cost/QALY or LYG	ICER for CH 2010	QALY effect <sup>a</sup>	Time horizon (years)	Year	Valuta	Perspective	Welfare impact (CHF)
Bosentan monohydrate (Tracleer®)	55,927/LYG	63,562.2	3.87 LY	15	2004	AUD	Health care payer	10,717,086
Peginterferon alfa 2a (Pegasys®)	10,444/QALY	17,337.2	0.3 QALY	47.1	2005	GBP	NHS	658,144
Conjugated vaccine (Prevenar®)	28,156/LYG	49,606.73	0.0033 LY	10	2001	GBP	Direct cost + cost of work loss	1,026,706
Ezetimibe (Ezetrol®)	27,475/LYG	44,746.56	0.134 LY	24.1	2006	GBP	Health care payer	6,234,995
Sirolimus (Rapamune®)	-27,047/LYG	-33,372.4	1.8 LY	20	2003	GBP	NHS	18,005,274
Interferon beta-1a (Avonex®)	44,789/MLY	49,449.91	1.21 MLY	12	2002	CAD	Societal	1,778,900
Ibandronate (Bonviva®)	-20,316/LYG	-25,067.27	0.019 LY	1.19	2003	GBP	NHS	3,935,835
Rizatriptan (Maxalt®)	-6,625/QALY	-7,185.73	0.00048 QALY	0.0027	2002	CAD	Societal	268,926,615
Linezolid (Zyvoxid®)	29,945/QALY	34,533.36	6.73 QALY	9	2001	CAD	Third-party payer	10,769,990
Rivastigmine (Exelon®)	7,249/QALY	7,561.74	0.0077 QALY	0.46	2004	CAD	Societal	13,303,996
Rosiglitazone (Avandia®)	5,137/QALY	9,147.21	0.1464 QALY	20	2000	GBP	NHS	3,486,152
Oseltamivir (Tamiflu®)	-6,182/QALY	-5,226.96	0.0034 QALY	1	2006	USD	Societal	3,630,309
Clopidogrel (Plavix®)	25,100/QALY	28,618.51	0.55 QALY	14.2	2002	USD	Societal	257,359,176
Memantine (Ebixa®)	-6,613/QALY	-5,322.69	0.0276 QALY	2	2005	USD	Societal	4,550,762
Risperidone (Risperdal®)	39,890/QALY	40,619.47	0.0509 QALY	5	2006	USD	Health care payer (Brazil)	996,206
Atomoxetine (Strattera®)	15,224/QALY	25,688.75	0.046 QALY	1	2004	GBP	NHS	4,430,139
Atorvastatin (Lipitor®)	43,667/QALY	59,662.96	0.033 QALY	4.8	2005	EUR	Societal (Sweden)	55,463,430
Orlistat (Xenical®)	13,125/QALY	18,141.37	0.0304 QALY	1	2003	EUR	Health care system (Sweden)	25,768,442
Natalizumab (Tysabri®)	-11,265/QALY	-12,799.14	0.34 QALY	20	2005	EUR	Societal (Sweden)	1,961,690
Oxaliplatin (Eloxatin®)	4,805/QALY	8,082.99	0.68 QALY	50	2003	GBP	Health care payer	3,725,213
Rosuvastatin (Crestor®)	36,548/QALY	49,426.78	0.08 QALY	23.5	2006	EUR	Health care payer (Finland)	15,291,792
Trastuzumab (Herceptin®)	35,975/QALY	49,153.24	0.262 QALY	25.4	2005	EUR	Societal (Sweden)	1,216,275
Cinacalcet (Mimpara®)	61,890/QALY	104,433.05	0.34 QALY	24.1	2004	GBP	Health care payer	-59,101
Sitagliptin (Januvia®)	11,547/QALY	15,729.13	0.095 QALY	14.2	2006	EUR	Health care payer (UK)	7,543,994
Rimonabant (Acomplia®)	71,973/QALY	73,289.18	0.0581 QALY	5	2006	USD	Third-party payer	7,759
Pimecrolimus (Elidel®)	35,000/QALY	38,642.23	0.03 QALY	0.5	2002	CAD	Societal	54,412,070
HPV vaccine (Gardasil®)	26,005/QALY	26,885	0.020 QALY	70.55	2006	CHF	Health care payer	22,157
Fulvestrant (Faslodex®)	-33,571/QALY	-40,140.15	0.021 QALY	10	2007	EUR	Health care payer (Germany)	316,366
Erlotinib (Tarceva®)	-212,700/QALY	-184,240.96	0.01 QALY	2	2007	USD	Health care payer	956,471
Eplerenone (Inspra®)	20,579/QALY	23,732.24	0.0676 QALY	12.8	2001	USD	Health care payer	511,542
Raltegravir (Isentress®)	45,687/QALY	46,906	3.73 QALY	50	2007	CHF	Health care payer	4,440,071 781,388,456

QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; LYG, life year gained; NHS, National Health Service; MLY, monosymptomatic life year. For reasons of confidentiality, the number of actual users is not declared.

<sup>a</sup> QALY effect means difference in quality-adjusted life years between treatment and comparator strategy.





foreign cost-effectiveness data. As the costs of drugs, the life expectancy, the national economy, and other factors affecting the ICER/ICUR estimate differ between countries, the ICERs/ICURs from another country might not be applicable to Switzerland without further adjustments in addition to GDP and PPP conversions. For example, the comparative standard treatment used in the country, the cost-effectiveness analysis was performed for might differ from the standard treatment used in Switzerland. In an economic analysis, the new treatment should always be compared with the most relevant comparator in that setting or country. Therefore, the ICER/ICUR of a new treatment in a foreign country compared to the county-specific relevant standard treatment might not be exactly transferable to the Swiss setting. Because a QALY is calculated by multiplying the utility weight of a given state with the life years being in this state (31) and these utilities are not the same among countries, the QALYs gained or lost with the new drug compared to the standard treatment might differ among countries. For these reasons, it would have been desirable to use only Swiss data for our calculations to get a more reliable estimate of the welfare impact of innovative drugs in Switzerland.

Another limitation of the study and its findings resulted from the fact that many included studies were from a third-party payer perspective and not from a societal perspective. Studies from a third-party payer perspective only include direct costs, such as hospitalization costs, drug costs, physician costs, etc. To assess the welfare impact of innovative drugs, also indirect costs, e.g., productivity losses, work absences, informal care by family members, etc., should be considered as these can have a substantial effect on the resulting ICER/ICUR of a new drug compared to standard treatment. Because the majority of the included cost-effectiveness studies were from a third-party payer perspective and those studies from a societal perspective did not always met the other pre-defined inclusion criteria, we decided to also include studies from a third-party payer perspective. Otherwise, our basket of innovative drugs available to calculate the welfare impact in Switzerland in 2010 would have been much smaller and might not

have been representative of innovative drugs in Switzerland. Bearing in mind that we only included 31 drugs in our calculations and in Switzerland approximately 700 new drugs were registered since 2000 onward (32), the inclusion of studies was very restrictive and the potential welfare gain could even be higher.

A further limitation is the number of users derived for our calculations. Very often there was not much information available about the potential users and therefore, we had to use the number of actual users in the year 2010 as an approximate estimate for the number of potential users (except for Conjugated vaccine, ibandronate, atorvastatin, and memantine), which is not always consistent. Furthermore, it was not possible to obtain the number of actual users directly from the manufacturers for every drug. For risperidone and cinacalcet, an estimate had to be made based on data from the number of sold packages in Switzerland (information was provided from the manufactures who had this number from IMS Health sales figures) and the standard dose for the specific drug (19). All other numbers of actual users were provided by the Helsana Group, the largest health insurer in Switzerland. With 1.8 million Swiss people insured (33), we think that Helsana is representative enough to estimate the actual users in Switzerland. As actual users might differ from potential users and the welfare impact calculations depend on the number of users, we were aware that the result could differ substantially.

It must be mentioned that not all of the cost-effectiveness studies measured the clinical effects expressed in QALYs, which was the preferred outcome measure. Instead, for five drugs (bosentan monohydrate, conjugated vaccine, ezetimibe, sirolimus, and ibandronate) the effect was measured in LYG which does not take into account the quality of life during the additional LYG by the new drug. The equivalent QALY estimate could be much lower, e.g., the patient gained one life year by the new treatment but the quality of life was as bad as 0.2 and therefore, the new drug would only have a benefit of 0.2 QALYs gained instead of one LYG meaning that the calculated welfare impact of these five drugs might be lower when calculated by using QALYs. The same applied for the welfare

impact calculations of interferon beta-1a. The authors of this study used monosymptomatic life years (MLY) as the measure of effect.

Some drugs included in our study (bosentan monohydrate, peginterferon 2a, ibandronate, risperidone, oxaliplatin, trastuzumab, cinacalcet, and erlotinib) are used for more than one indication. In all cases, the cost-effectiveness study was conducted for one indication only. The information about volume of users we got from the manufacturers of the drug or Helsana, or we calculated based on the number of sold packages made no difference between the diverse indications. But it is very likely that the QALY gain of the drug is not the same for every indication. For these particular drugs, we might have overestimated the welfare impact by using the total number of volume users independent from indication and the QALY effect of the drug measured for only one indication.

Nevertheless, our calculations were conservative and included only a small portion of the total number of innovative drugs launched 2000 onward in Switzerland. The potential welfare gain generated by the introduction of new drugs in Switzerland in 2010 was substantial and the sensitivity analysis showed that using a lower QALY threshold of CHF 50,000 also led to a potential welfare gain in 2010. Together with the fact that the prices of many new drugs in Switzerland have decreased, the total potential welfare gain might be even greater. As one drug (Mimpara) showed negative welfare effects, we cannot generally conclude that there is a positive welfare effect of new drugs compared to standard treatment. But this finding should effect that health decision makers do not only discuss the price of a new pharmaceutical but also its benefit, ideally expressed in QALYs. For this purpose, there is an urgent need for performing CEA of novel pharmaceuticals, if possible prior to the introduction to the market.

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