The Social Impact of Novartis medicines: Two Case Studies from South Africa and Kenya

Results from the Pilot Project

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INTRODUCTION

Social impact, both positive and negative, is a key element of *Novartis´* Financial, Environmental and Social (FES) impact valuation. FES impact valuation is the *Novartis* version of the Triple Bottom Line approach. In 2017, *WifOR* institute was commissioned with conceptualizing and conducting a Social Impact valuation of *Novartis'* products. The aim of this study is to quantify and value the Social Impact of the entire *Novartis* global product portfolio in monetary terms (Figure 1). Separate case studies on other elements of Environmental and Economic Impacts are available elsewhere[1], [2].

Figure 1 Theoretical framework of the Social Impact study

Context and motivation

In the last few decades, healthcare expenditure has been increasing. This has been accompanied by a notable parallel increase in average longevity and quality of life among the global population. As a result, efficient spending in healthcare is increasingly recognized as a direct predictor of better health outcomes and national wealth. Thus, upfront national spending in health systems that is conditionally bound to bringing about better quality of life and wellbeing upon the respective populations could be considered a form of national investment.

Measuring health-related quality of life precisely and reliably has been, nonetheless, a longstanding challenge in public health. Capturing and quantifying a universal unit of increase or decrease in quality of life on the individual and collective patient levels could enable economists to monetize such unit into an economically comprehensible monetary outcome that is compatible with traditional validated economic research techniques. Significant strides in the last few decades were taken to address the conceptual and ethical challenges in this regard, resulting in an increase in the quantity and quality of the body of evidence being published.

WifOR is a research institute based in Germany with a solid track record of economic research and rich expertise in the fields of micro and macroeconomics. In this study, a novel framework that is generalizable and scalable across different countries and medicine portfolios has been developed. This framework capitalizes on a plethora of published medical literature that has been substantially growing in the last few decades. This literature allows for the estimation of health gains generated by *Novartis*' medicines expressed in Quality Adjusted Life Years (QALYs) and Years of Life Saved (YLS). Through the subsequent steps of this approach, health gains are translated into gains in paid and unpaid work activities. Owing to a healthier and more active patient population, those gains eventually contribute "monetary revenue" to the national Gross Domestic Product (GDP). We refer to this monetary revenue as the Social Impact. While the study is still ongoing with an expanding three-dimensional scope (time, geography and medicines covered), until the time of writing this report 63 *Novartis* medicines sold across 11 countries from 3 different portfolios in 2016 and 2017 were assessed (Table 1).

Table 1 Scope of the Social Impact project

Portfolio	Medicine	DE	FR	JP	ZA	CN	MX	EG	US	IT	ES	KE
Innovations	Cosentyx											
	Entresto											
	Onbrez											
	Ultibro											
	Glivec											
	Gilenya											
	Lucentis											
	Tasigna											
	Galvus											
	Jakavi											
	Diovan											
	Votrient											
	Xolair Saa											
	Femara											
	Exforge											
	Tegretol											
	Trileptal											
	Voltaren											
	Neoral											
	Zometa											
	Certican											
	Systane											
	SANDIMMUN											
	SEEBRI											
	DUOTRAV/TRAVATAN											
	EXELON											
Sandoz	Verapamil											
	Valsartan											
	Tramadol											
	Bezafibrate											
	Omeprazole											
	Esomeprazole											
	AMOXICILLIN; CLAVULANIC ACID											
	Celecoxib											
	PIPERACILLIN;TAZOBACTAM											
	ALPRAZOLAM											
	METFORMIN											
	BISOPROLOL											
	SIMVASTATIN											
	RAMIPRIL											
	FUROSEMIDE											
	AMLODIPINE											
	LETROZOLE											
	GLIMEPIRIDE											
	TAMOXIFEN											
	PARACETAMOL											
	IBUPROFEN											
	CETIRIZINE											
	PANTOPRAZOLE											
	LEVOFLOXACIN											
Access	Vildagliptin											
	Glimepiride											
	Metformin											
	Valsartan											
	Amlopidine											
	Bisoprolol											
	HCTZ											
	Furosemide											
	Ramipiril											
	Simvastatin											
	Salbutamol											
	Letrozole											
	Tamoxifen											

Social Impact calculated for 2016
Social Impact calculated for 2017
Social Impact calculated for 2016 and 2017
Social impact not calculated

In the current case study, we present the results from the pilot project for a selection of 34 medicines from 3 different

portfolios, namely: **Novartis Innovative Medicines, Sandoz, and Novartis Access** portfolios delivered in two countries: South Africa in 2017 and Kenya in 2016, where a total of 6,254,710 patients were reached.

METHODS

We used a phased approach to calculate the global social impact of the Novartis medicines in scope. We first calculated the drugs´ *Health Benefits* through the incremental gains in QALYs and YLS on the relevant patients. We then aggregated and translated these in activity gains comprising paid and unpaid work. Last, we calculated the *Socioeconomic Benefits* as monetary contributions to the national GDP in US dollars. The following lines describe the study methods in more detail.

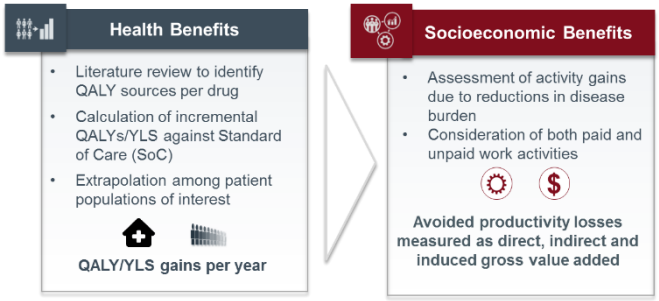

Figure 2 Steps towards calculating the Social Impact

The Health Benefits

Comprehensive literature searches in MEDLINE (accessed through PubMed) and Google Scholar were conducted. The objective was to identify published economic evaluations quantifying QALYs as the utility/effectiveness measure for every medicine and sub-indication included in the study. QALYs/YLS were selected as they allow to demonstrate health outcomes across diverse diseases. The incremental undiscounted QALY/YLS gains compared to the Standard of Care (SoC) were then calculated for the average patient for one year. For medicines with multiple authorization labels, the epidemiological weight based on prevalence estimates from the Global Burden of Disease (GBD) study [3] was used. This facilitated deriving an average indication-weighted QALY estimate for an average patient receiving the medicine.

Furthermore, the proportion of patients in the working age (under 60 years of age) were also derived from the GBD study to later differentiate between economic gains from paid and unpaid work activities. Whenever literature reporting QALYs was not available, Years of Life Saved (YLS) were used as an alternative metric of health gains. Similarly, when QALYs and YLS were not found for a specific medicine, the Anatomical Therapeutic Chemical (ATC) classification system was used to derive QALYs/YLS for proxy medicines that were nearest in classification to the medicine in question.

On the other hand, when multiple suitable publications were available for one medicine and indication, selection of the best match was based on ten a priori criteria that aimed at arriving at the best available evidence. Those criteria (listed below) prioritized, in an ordinal fashion, the literature providing an overall closer match to the country and disease indication of interest when comparing competing sources:

1. Disease indication and medicine label
2. Medicine comparator
3. Patients' demographic and disease characteristics at baseline
4. Time horizon of study
5. Country investigated in the study
6. Medicine dose
7. Medicine dosage form
8. Discounting rate
9. Publication date
10. Health outcome investigated

Subsequently, the QALY estimates for every medicine were multiplied by the number of patients reached for the corresponding medicine sold in the country and year of interest. The latter figures on patients reached were provided by *Novartis*. Figure 3 illustrates the calculation steps with the example of letrozole in Kenya.

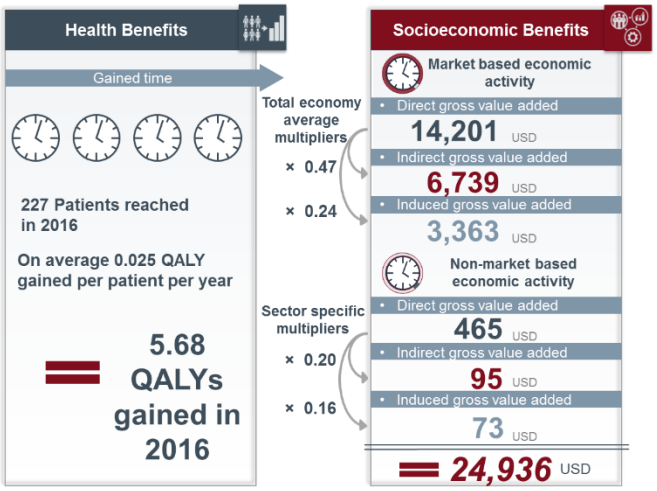

Figure 3 The example of letrozole in Kenya in 2016

The Socioeconomic Benefits

In a second step, activity gains associated with improved health were quantified from a macroeconomic perspective. This was achieved through linking QALY gains with a measure of patient's paid and unpaid work activities. Country specific parameters from macroeconomic databases by the International Labour Organization (ILO), United Nations (UN) or the World Bank were used.

To estimate a measure of paid work for individuals in the working age, gained QALYs were valuated against the average annual labour productivity, i.e. the country specific gross value added (GVA) per employee. [4], [5]. Thus, it was assumed that all patients who are younger than 60 years of age are economically active (either on full or part time basis) and that no children were among the patients reached.

To quantify the activity gains beyond employment, information on the average time use in hours per day [6], [7], reported separately for males and females, was used as a basis to attach a monetary value for unpaid work to each QALY. Data on unpaid work activities was only available in highly aggregated form for most of the country portfolio. On this account, the amount of unpaid work in terms of GDP contributions was approximated in two steps. First, built on the assumption that GDP per capita [8] reflects the amount of paid work per capita, the measure was

	Paid work		Unpaid work activities			
	< 60y	Average annual labor productivity GVA / employee	all ages	Average annual productivity of the population GVA / capita	× Time use - hours per day: h of unpaid work / h of paid work	× Value of unpaid work - Derived from sector specific labor productivity: Average GVA per employee (Household sector) / Average GVA per employee (Total economy)
South Africa		18,566 USD		5,165 USD	0.96 (Ratio)	0.61 (Ratio)
Kenya		3,652 USD		1,231 USD	0.57 (Ratio) proxy value Tanzania	0.12 (Ratio)

Figure 4 Parameters used in deriving the Socioeconomic Benefits

multiplied by the ratio of time use for paid and unpaid work per capita. This/The ratio can be interpreted as people spending a factor of the amount of time for paid work additionally on unpaid work. In a second step, the resulting product was multiplied by an estimated factor, which was intended to reflect that unpaid work activities have a lower labour productivity than average across all sectors of the economy (Figure 4).

In addition, the wider economic indirect and induced effects initiated by an increase in economic activity were taken into account by using country-specific value-added multipliers.

For Kenya and South Africa, some special features had to be considered during implementation. In the case of Kenya, there was no data on time use available from the United Nations time use portal or any other source. Therefore, it was necessary to identify a country whose values could be used as best proxy. The choice of Tanzania as best representative was based on proximity of place as well as highest convergence in GDP per capita [8] and Human Development Index (HDI) [9]. Additionally, information from national accounts by economic sector were retrieved from the Kenya National Bureau of Statistics (KNBS) [10], since other sources did not contain all the data needed. Data for South Africa was available. Thus, no proxies were needed to complete the parameter set.

RESULTS

Table 2 presents the findings from the Health Benefits literature review. Overall, 46 publications were used to derive QALY estimates for 33 medicines and YLS estimate for one medicine (amlodipine).

Total patients reached per medicine varied widely, and therefore the number of patients reached per medicine and country along with the country specific economic parameters influenced the total Social Impact of a drug portfolio in the corresponding country.

For the year 2017 in South Africa and 2016 in Kenya, based on the calculatory numbers of patients reached, a total of 56,711 QALYs and 59 YLS were generated through the use of the 34 medicines. This amounted to a total of USD 1.95 billion as monetized Social Impact (Figure 5).

Epidemiological data were used to estimate the average proportion of patients in the working age for the target population of each medicine. The calculated Social Impact per medicine reflects the age structure of the underlying patient population when examining the proportional contribution of the two components of the Social Impact: The GVA due to paid and unpaid work activities (Figure 6).

DISCUSSION

In contrast to other methods, this framework allows for considering not only the economic contributions of a healthier population due to paid work, but also the contributions of individuals outside the labour market. This is especially important as it highlights the social value of healthier individuals even if they are not active participants in the labour force. This practically means that no implicit conclusions about favouring medicines for younger individuals or arguments for "leaving out" older individuals could be drawn from the study results. This has been a classical ethical debate among health economists for the so-called productivity studies[11].

Difference in exchange rates between the different national currencies and USD along with other country specific economic parameters, such as GDP per capita and average time use, are the main socioeconomic parameters that influence the final Social Impact. Therefore, the underlying heterogeneity between

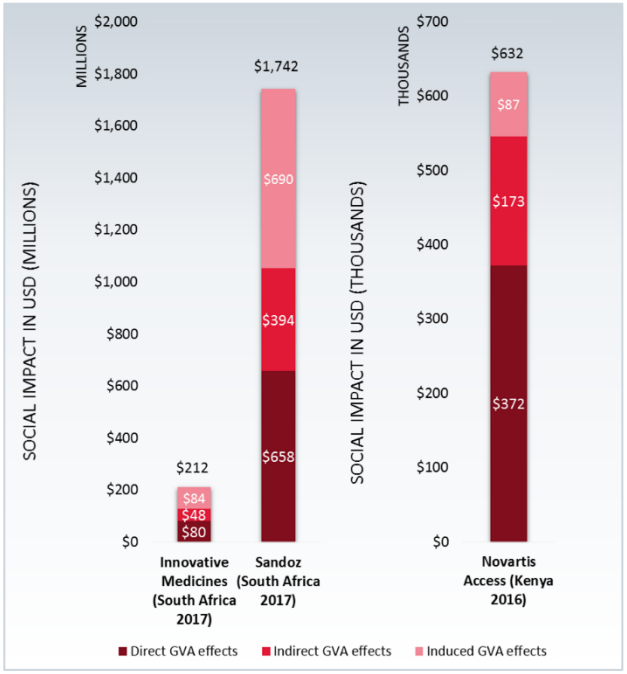

Figure 5 The Social Impact per Drug Portfolio

the economies of the different countries should be considered when interpreting the reported results.

Limitations

WifOR, in close cooperation with *Novartis,* had a priori defined and well-agreed-upon study concept and methodological framework in place. Nevertheless, due to the novelty of this approach, this pilot study was conducted while having to frequently solve problems on an ad-hoc fashion.

The current report arguably delivers ground-breaking analyses that provide insights and visibility on value aspects for medicines on an unprecedented global scale. Having said that, however, in this section we list the main set of assumptions that we expect to have compromised the certainty of our estimates. For the most part, we believe that the uncertainty brought about by those assumptions are acceptable given the bird's eye perspective this study intends to deliver and the explorative nature of the pilot project. Therefore, as more experience and knowledge become accumulated, *WifOR* is committed to improve and refine the methods and assumptions made in future implementations of the project. The main assumptions of the study are the following:

1. The health gains reported for a studied population in the literature did not always coincide perfectly with the target population of the country, drug and indication in question. The degree of precision to which a piece of literature depicted the health outcomes upon the intended target population depended on the extent of their resemblance with regards to the ten characteristics listed in the methods section (see: Methods: The Health Benefits).
2. While QALY is an aggregate metric of survival and quality of life, we assumed that one QALY is equivalent to one person-year of full capability of performing paid and unpaid activities.
3. Economic evaluations that only reported discounted QALYs/YLS were still included in the study. In the absence of the full economic markov models, information on the actual undiscounted QALY gains per year could not be precisely reproduced. We used the conventional discounting formula [12] together with the reported discount rate and half the reported time horizon to derive an estimate of the undiscounted QALY. This method, however imperfect, was validated using economic evaluations reporting both discounted and undiscounted QALYs and was found to be conservative.

$$P = \frac{F}{(1+r)^t}$$

The discounting formula, where P is the discounted value, F is the undiscounted value, r is the discount rate, and t is the time horizon.

4. Except for information on the age structure derived from GBD study, further details on the patients' characteristics were not pursued. It was assumed that an average patient shares the same economic profile of the population's average person, e.g. the amount of time spent working.
5. Expressing the Social Impact in USD (not the national currency) unties the relation between the monetary gains to the living costs in the respective country.
6. For Kenya and South Africa: Since both are developing countries, it is expected that the informal economic sector plays an important role in those countries' economies. Not taking the informal sector into account in our calculations might have biased our estimates when calculating the GVA generated due to unpaid work.

CONCLUSION

Our approach to quantifying the productivity-related economic gains of medicines helps demonstrating an important aspect of their value across geographies and disease indications. Although built on several assumptions, this approach helps express value and communicate in simple monetary terms.

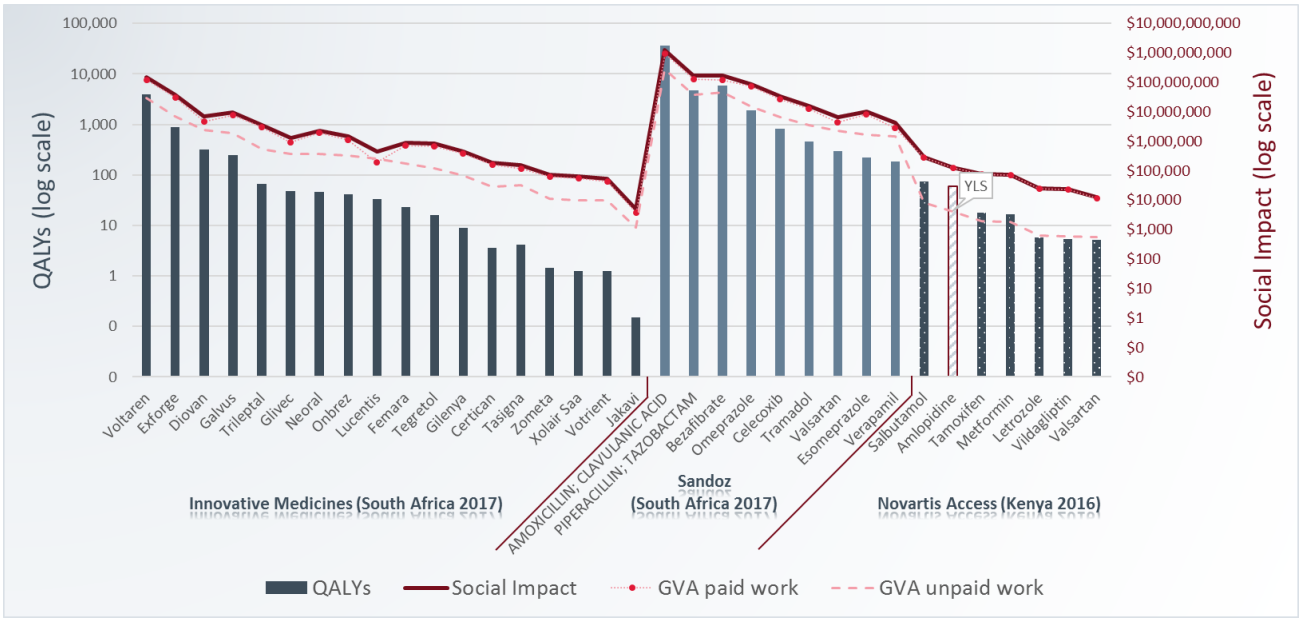

Figure 6 Health gains (left Y-axis) and Social Impact (right Y-axis), broken down by medicine

Table 2 Literature Review of Health Benefits

Portfolio	Medicine	Indication(s)	Indication weight (GBD)	Patients reached (Provided by Novartis)	Health gains per patient year	% Under 60 years of age (GBD)	Source
Innovative Medicines (South Africa)	Onbrez	COPD	100%	5,711	0.01 QALYs	55%	[13]
	Glivec	Chronic myeloid leukemia	51%	315	0.17 QALYs	40%	[14]
		Gastrointestinal Stromal Tumour	49%				[15]
	Gilenya	Multiple sclerosis	100%	69	0.08 QALYs	84%	[16]
	Lucentis	Age-related macular degeneration (AMD)	100%	500	0.05 QALYs	12%	[17]
	Tasigna	Chronic myelogenous leukemia (imatinib-resistant)	100%	216	0.02 QALYs	59%	[18]
	Galvus	Add‑on to metformin for the treatment of DM-II	100%	15,695	0.01 QALYs	62%	[19]
	Jakavi	Myelofibrosis	100%	4	0.03 QALYs	51%	[20]
	Diovan	Post-Myocardial infarction	3%	124,479	0.003 QALYs	30%	[21]
		Moderate hypertension	95%				[22]
		Chronic heart failure	3%				[23]
	Votrient	Renal Cell Carcinoma	50%	34	0.02 QALYs	70%	[24]
		Soft-tissue sarcoma	50%				
	Xolair Saa	Severe persistent allergic asthma	100%	26	0.04 QALYs	90%	[25]
	Femara	Advanced Breast Cancer	70%	974	0.03 QALYs	61%	[26]
		Extended adjuvant therapy in early breast cancer	15%				[27]
		Initial adjuvant therapy in early invasive breast cancer	15%				[28]
	Exforge	Hypertension	100%	68,314	0.01 QALYs	70%	[29]
	Tegretol	Epilepsy	100%	27,832	0.0007 QALYs	88%	[30]
	Trileptal	Epilepsy	100%	2,390	0.02 QALYs	88%	[30]
	Voltaren	Osteoarthritis / Rheumatoid Arthritis	100%	418,503	0.01 QALYs	61%	[31]

Portfolio	Medicine	Indication(s)	Indication weight (GBD)	Patients reached (Provided by Novartis)	Health gains per patient year	% Under 60 years of age (GBD)	Source
Innovative Medicines (South Africa)	Neoral	Ulcerative colitis	0.2%	1,218	0.04 QALYs	86%	[32]
		Dry Eye Syndrome	81%				[33]
		Moderate to severe psoriasis	18%				[34]
	Zometa	Osteorporosis	96%	959	0.002 QALYs	86%	[35]
		Skeletal metastases in hormone-refractory prostate cancer patients	2%				[36]
		Breast cancer patients with bone metastases	2%				[37]
	Certican	Kidney transplantation	100%	319	0.01 QALYs	89%	[38]
Sandoz (South Africa)	Verapamil	Hypertension	95%	17,806	0.01 QALYs	30%	[39]
		Coronary heart disease	5%				[40]
	Valsartan	Post-Myocardial infarction	3%	18,964	0.003 QALYs	30%	[21]
		Moderate hypertension	95%				[22]
		Chronic heart failure	3%				[23]
	Tramadol	Osteoarthritis	100%	326,306	0.001 QALYs	54%	[41]
	Bezafibrate	Prevention of major cardiovascular events	100%	191,049	0.03 QALYs	42%	[42]
	Omeprazole	Upper GIT symptoms	79%	355,410	0.01 QALYs	76%	[43]
		Erosive Reflux Esophagitis	1%				[44]
		Chronic low back pain	11%				[45]
		Prevention of Myocardial infarction	3%				[46]
		Rheumatoid arthritis	1%				[47]
		Osteoarthritis	6%				[48]

Portfolio	Medicine	Indication(s)	Indication weight (GBD)	Patients reached (Provided by Novartis)	Health gains per patient year	% Under 60 years of age (GBD)	Source
Sandoz (South Africa)	Esomeprazole	Gastroesophageal reflux disease	93%	327,156	0.0007 QALYs	76%	[49]
		Osteoarthritis	7%				[50]
	AMOXICILLIN; CLAVULANIC ACID	Prophylaxis in haematogenous bacterial arthritis	100%	3,463,180	0.01 QALYs	54%	[51]
	Celecoxib	Rheumatoid arthritis	3%	139,721	0.004 QALYs	64%	[52]
		Osteoarthritis	34%				[53]
		Chronic low back pain	63%				[45]
	PIPERACILLIN; TAZOBACTAM	Prophylaxis in haematogenous bacterial arthritis	100%	596,397	0.01 QALYs	54%	[51]
Novartis Access (Kenya)	Vildagliptin	Add-on to metformin for the treatment of type 2 Diabetes Mellitus	100%	386	0.01 QALYs	70%	[19]
	Metformin	Treatment of overweight type 2 Diabetes Mellitus	100%	371	0.04 QALYs	70%	[54]
	Valsartan	Post-Myocardial infarction	10%	684	0.01 QALYs	37%	[21]
		Moderate hypertension	85%				[22]
		Chronic heart failure	5%				[23]
	Amlopidine	Hypertension	9%	1,977	0.03 YLS	53%	[39]
		Coronary heart disease	91%				[40]
	Salbutamol	Chronic obstructive pulmonary disease	100%	2,834	0.03 QALYs	62%	[55]
	Letrozole	Advanced Breast Cancer	70%	227	0.03 QALYs	69%	[26]
		Extended adjuvant therapy in early breast cancer	15%				[27]
		Initial adjuvant therapy in early invasive breast cancer	15%				[28]
	Tamoxifen	Advanced Breast Cancer	70%	86	0.21 QALYs	69%	[56]
		Postmenopausal women with early breast cancer	15%				[57]
		Breast cancer prevention	15%				[58]

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