# Cost Effectiveness Analysis in Scientific Herbal Therapy Compared to Conventional Therapy for Dyspepsia

# (Analisis Efektifitas Biaya dalam Terapi Jamu Saintifik dan Konvensional untuk Terapi Dispepsia)

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Abstract: Dyspepsia is a common digestive disorder among global health problems. This study aimed to examine the cost-effectiveness of scientific herbs in the treatment of dyspepsia. This study has used a societal perspective, but the indirect costs are considered equal because the patient is undergoing outpatient care. The analysis was used to determine the cost-effectiveness using the Incremental Cost-Effectiveness Ratio (ICER) method. The results were reported in rupiah currency, which includes categories of direct medical costs and direct non-medical costs. Sensitivity analysis reported changes in results, taking into account various possible influencing variables. A total of 62 patients who were respondents in this study were included in scientific herbal therapy (48.38%) and conventional dyspepsia therapy (51.62%). The cost of scientific herbal therapy was higher than conventional dyspepsia therapy (45.558 $\pm$ 4.351 vs. 39.202 $\pm$ 4.500). However, this difference was not statistically significant on the effectiveness of therapy (96.67% vs. 90.62%; p-value 0.600), the utility index of scientific herbal medicine was greater than conventional dyspepsia therapy (0.85 $\pm$ 0.11 vs. 0.74 $\pm$ 0.14). The ICER value for 1 additional unit of effectiveness was IDR 105,933; while for the addition of 1 unit of quality of life was IDR 57,781. The effectiveness of scientific herbal medicine therapy for dyspepsia was greater than the effectiveness of conventional dyspepsia therapy, where the cost was higher but the effectiveness was better.

Keywords: Cost-effectiveness analysis, ICER, scientific herbal medicine.

Abstrak: Dispepsia adalah gangguan pencernaan umum dalam masalah kesehatan global. Penelitian ini bertujuan untuk memeriksa *cost-effectiveness* dari obat herbal dalam pengobatan dispepsia. Penelitian ini menggunakan *societal perspective*, tetapi biaya tidak langsung dianggap sama karena pasien sedang menjalani rawat jalan. Analisis ini digunakan untuk melihat efisiensi biaya dengan menggunakan metode *Incremental Cost-Efficiency Ratio* (ICER). Hasilnya dilaporkan dalam mata uang rupiah yang mencakup kategori biaya medis langsung dan biaya non-medis langsung. Analisis sensitivitas melapor-kan perubahan dalam hasil dengan mempertimbangkan berbagai variabel yang mungkin berpengaruh. Total 62 responden dalam penelitian ini disertakan dalam terapi pengobatan herbal (48.38%) dan terapi dyspepsia konvensional (51.62%). Biaya terapi pengobatan herbal lebih tinggi daripada terapi dispepsia konvensional (45.558±4.351 vs 39.202±4.500). Namun, perbedaan ini tidak signifikan secara statistik pada efektivitas terapi (96.67% vs 90.62%; p-nilai 0,600), indeks utilitas obat herbal lebih besar daripada terapi dispepsia konvensional (0.85±0.11 vs. 0.74±0.14). Nilai ICER untuk 1 unit efisiensi tambahan adalah RP 105.933; sedangkan untuk tambahan 1 unit kualitas hidup adalah IDD 57.781. Efektivitas terapi obat herbal untuk dispepsia lebih besar daripada efisiensi terapi dispepsi konvensional di mana biayanya lebih tinggi tetapi efektivitas lebih baik.

Kata kunci: Analisis efisiensi biaya, ICER, jamu saintifik.

### INTRODUCTION

THE GLOBAL prevalence of dyspepsia reaches 13-40%<sup>(1)</sup>. Previous studies in Indonesia found the overall prevalence of undiagnosed dyspepsia was 49.75%<sup>(2)</sup>. The prevalence of dyspepsia in Indonesia reaches 40-50%<sup>(3)</sup>. Treatment of dyspepsia involves empirical therapy orally with first-line therapy, namely drugs that suppress gastric acid secretion, such as proton pump inhibitors (PPI) and H2 receptor inhibitors<sup>(4)</sup>. Based on the National Institute For Health And Care Clinic Excellence (NICE) drugs - PPI class of drugs has the main potential for effectiveness in dyspepsia therapy. Long-term use of PPI groups can cause side effects, as well as short-term use, even though there are no side effects but has risks interact with other drugs<sup>(4)</sup>.

One of the alternatives used to overcome side effects and drug interactions with other drugs is to use native Indonesian scientific herbs that have been approved by Minister of Health regulations No.003/ MENKES/PER/I/2010<sup>(5)</sup>. Pre-clinical trials were conducted to compare scientific herbal medicines with conventional therapy for dyspepsia based on the Indonesian herbal medicine formulary in Minister of Health regulationsNo. 6, which proves that *Curcuma domestica* can protect the gastric mucosa with the same level of effectiveness as ranitidine and cimetidine. This means that scientific jamu can be used as an alternative therapy, reinforced by safety tests that show dyspepsia herbal formula does not affect liver and kidney function<sup>(5-7)</sup>.

Herbal medicines are important for dyspepsia because of their safety and toxicity compared to conventional medicines. According to Desi Sukaening's research (2021), the toxicity level of herbal medicines is much lower than conventional medicines. So the role of herbal medicines for dyspepsia is better, especially against the effects of conventional drugs, which cause damage to the gastric mucosal barrier by damaging the gastric defence factors<sup>(8)</sup>.

Dyspepsia in patients has an impact on decreasing productivity because of the influence of symptoms that arise in patients, which make the patient's activities decrease, as well as irregular eating patterns that cause stomach and digestive conditions to be disturpted<sup>(9)</sup>.

Decreased quality of life occurs in patients with dyspepsia. Ineffective therapy for controlling dyspepsia symptoms can interfere with daily activities and increase medical costs. Most patients still feel abdominal pain, so they must stop their daily activities. If pain is not treated immediately, it will cause other symptoms, such as stress, immunity, and metabolic disorders. Eating irregularities can affect gastric acid secretion<sup>(10)</sup>.

The goal of this study was to compare the two types of therapy based on their costs and effectiveness so that the most cost-effective type could be chosen. The ultimate goal was to provide the most effective clinical therapy within the budget.

# MATERIALS AND METHODS

**MATERIALS.** The data used in this research were dyspepsia patients with scientific herbal therapy at the Kalibakung Jamu Health Tour in Tegal, Central Java, Indonesia, and dyspepsia patients with conventional therapy at the Kalibakung Health Centre who came for treatment in January–December 2021.

**Equipments.** Analysis was made using the IBM SPSS version 23.0 statistics software program.

METHOD. Research Design. This research is an observational analytic study to explain the cost-effective comparison of giving scientific herbal medicine for dyspepsia and conventional therapy for dyspepsia. This study has received an ethical clearance from the Universitas Muhammadiyah Purwokerto with number KEPK/UMP/15/XII/2021. Respondent inclusion and exclusion criteria respondents' inclusion criteria were having been diagnosed with dyspepsia and having received therapy at least once; they were at least 18 years old. Respondents were obtained from medical record data in the herbal health tourism and primary health centres. This study excluded respondents who had uncomplete data and passed away during conducting research. This study has used a societal perspective, but the indirect costs are considered equal because the patient was undergoing outpatient care.

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**Research Instruments and Data Collection.** Data collection was carried out retrospectively by tracing patient medical records. The data collected included patient demographic data (gender, age, occupation), data on the cost of treating dyspepsia patients, EQ5D data for interviewing the quality of life of patients before and after examination, data on the effectiveness of therapy for dyspepsia patients using the numeric rating scale (NRS) method, and data on the treatment of dyspepsia patients. The data collected includes characteristics of patients with dyspepsia therapy (gender, age, and occupation). The costs analysed were direct medical costs from the perspective of the finance department or pharmacist and indirect medical costs from the perspective of the patient. Components of direct medical costs include administration fees, doctor consultation fees, medicine fees, pharmacist services fees, embalase fees, health support equipment costs, and others (supplements, honey, or stall medicines) and indirect medical costs include transportation costs, parking fees, and food costs issued during treatment.

Measuring the effectiveness of therapy was done using the numeric rating scale (NRS). Therapy has been said to be much better if, at the baseline NRS, a moderate pain scale >4 to  $\leq$ 7 experienced a decrease in pain with a value of  $\leq$ 2.4 and on a serve scale >8 to  $\leq$ 10 experienced a decrease in pain with a value of  $\leq$ 4.0.

The quality of life scores of dyspeptic patients were taken using the Indonesian version of the European quality of Life-5 Dimension (EQ5D) questionnaire that was taken after the patient underwent therapy. The EQ-5D consists of five questions about mobility, self-care, pain, usual activities, and psychological status, with five possible answers for each item (1 = no problem, 2 = slight problem, 3 = moderate problem, 4 = problem, and 5 = serious problem). The visual analogue scale (VAS) is part of the EQ5D with measurements of the subject's health, with the top points labelled "the best health the patient could imagine" and "the worst health the patient could imagine"

Therapeutic costs have components of direct medical costs and direct non-medical costs. Direct medical costs are calculated in the form of administration fees, doctor consultation fees, drug fees, pharmacist services fees, embassy fees, costs for health support equipment, and others (supplements, honey, or overthe-counter drugs). Direct non-medical costs in the form of transportation costs, parking costs, and food costs incurred while undergoing treatment. Direct medical costs are taken from interviews with the finance department or pharmacists, while non-medical costs are taken directly from interviews with patients.

The cost-effectiveness analysis was calculated using the incremental cost-effectiveness ratio (ICER) formula for the two outcome parameters, namely therapeutic success and utility. The cost-effectiveness assessment is carried out by comparing the ICER value with the willingness to pay (WTP) in Indonesia, which is 3x the value of the gross domestic product per capita in 2021. To find out the parameters that affect the ICER value, sensitivity analysis was used, which is interpreted on a tornado diagram. **Data Analysis.** The Chi-Square test was used to compare patient demographic data and data on the effectiveness of therapy for dyspepsia patients. Statistical analysis was carried out using SPSS, IBM version 23. Pharmacoeconomic analysis was carried out to determine the cost-effectiveness of scientific herbal medicine in the treatment of dyspepsia using the incremental cost-effectiveness ratio (ICER).

## **RESULTS AND DISCUSSION**

Patient Characrasteristics. The total respondents to this study were 62 patients, consisting of 30 patients at the Kalibakung Herbal Health Tourism and 32 patients at the Kalibakung Health Centre. Most of the respondents were dominated by women (67.7%). Women have a higher risk factor for experiencing dyspepsia because gastric secretion is regulated by nervous and hormonal mechanisms. Hormone regulation takes place through the hormone gastrin, which causes an additional flow of a very acidic stomach. The hormone gastrin is influenced by several things, one of which is hormonal factors, where female hormonal factors are more active than men<sup>(12)</sup>. Gastric motility is influenced by emotional factors such as anxiety and depression, which tend to be experienced by women so that they experience gastric emptying and T1/2, which are slower than men. Premenopausal women and postmenopausal women experience hormonal changes such as inhibition of progesterone and oestrogen that affect gastrointestinal motility. Delayed gastric emptying is a clinical feature in the classification of functional dyspepsia, namely dysmotility<sup>(11)</sup>.

The age range of dyspeptic patients was dominated by the age group >55 (27.4%) and 46.8% of the respondents worked as housewives (Table 1). Previous studies have found that several factors affect dyspepsia, namely the tendency towards increasing age. The prevalence of functional and organic dyspepsia will increase due to the influence of the immune system itself; the older the human age, the more vulnerable it will be<sup>(12,13)</sup>. This happens because, with increasing age, the degeneration of organs in the body occurs due to an irregular lifestyle<sup>(14)</sup>. In addition to the characteristics of the age range, the majority of job characteristics are those of housewives (46.8%). This is because housewives have the highest recurrence rate, one of which is due to indirect stress<sup>(15)</sup>.

**Patient's Symptoms.** On the side of the patient's symptoms before therapy, as listed in Table 2, the symptoms experienced by dyspeptic patients mostly included heartburn or epigastric pain. The pain can be used as a parameter of the success of therapy by

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Characteristics	Herbal Therapy		Conventional Therapy		Total		P Value
	Ν	%	Ν	%	N	%	
Gender							
Man	10	33.3%	10	31.3%	20	32.3%	0.861
Woman	20	66.7%	22	68.8%	42	67.7%	0.801
Age							
15 - 25	1	3.3%	5	15.6%	6	9.7%	
25 - 35	3	10%	6	18%	9	14.5%	
35-45	6	20%	9	28.1%	15	24.2%	0.012
45 - 55	13	43.3%	2	6.%	15	24.3%	
>55	7	23.3%	10	31.3%	17	27.4%	
Work							
Housewife	14	46.7%	15	46.9%	29	46.8%	
Entrepreneur	12	40 %	11	34.4%	23	37.1%	
Farmer	1	3.3%	3	9.4%	4	6.5%	0.794
Teacher	2	6.7%	1	3.1%	3	4.8%	
Student College	1	3.3%	2	6.3%	3	4.8%	

Table 1. Characteristics of dyspepsia therapy patients.

 Table 2. Symptoms of dyspepsia patients before therapy.

Symptoms of Dyspepsia	Herbal Health Tourism		Public health Centers		Total	
- j j	N	%	N	%	N	%
Bloated						
Yes	24	80%	28	87.5%	52	83.87%
No	6	20%	4	12.5%	10	16.12%
Heartburn						
Yes	30	100%	32	100%	62	100%
No	0	0%	0	0%	0	0%
Nauseous						
Yes	7	23.33%	13	40.62%	20	32.25%
No	23	76.67%	19	59.37%	42	67.75%
Quick Satisfaction						
Yes	27	90%	30	93.75%	57	92.93%
No	3	10%	2	6.25%	5	8.07%
Fullness						
Yes	30	100%	31	96.87%	61	98.38%
No	0	0	1	3.13%	1	1.62%
Lose appetite						
Yes	27	90%	23	71.87%	50	80.65%
No	3	10%	9	28.13%	12	19.35%
Limp						
Yes	8	26.67%	10	31.25%	18	29.03%
No	22	73.33%	22	68.75%	44	70.97%

looking at the degree of pain reduction. The symptoms experienced by dyspeptic patients mostly included heartburn or epigastric pain. Dyspepsia is a general term used for a syndrome or a collection of symptoms in the form of pain or discomfort in the pit of the stomach, nausea, bloating, vomiting, belching, fullness quickly, and a feeling of fullness in the stomach. The effect of one of the factors is that feelings of depression, anxiety and sadness will cause stomach acid levels to rise sharply, which will causes ulcers and pain in the stomach. Likewise, excessive fear and worry, as well as negative feelings, especially when eating, will stimulate the sympathetic nervous system, resulting in reduced pancreatic enzymes and causing difficulties in digesting food. These all lead to flatulence, gas, heartburn, and other digestive problems<sup>(16,17)</sup>.

**Efectiveness of Theraphy.** Table 3 showed that the effectiveness of therapy or the success of therapy for dyspepsia patients was scientific herbal therapy for dyspepsia. The percentage of success for scientific herbal therapy was higher than that for those receiving conventional therapy (96.67% vs. 90.62%; p value = 0.600). The effectiveness of therapy or the success of therapy for dyspepsia patients was scientific herbal therapy for dyspepsia.

Information	Herbal Therapy	Conventional Therapy	P Value
Succeed	29 (96.67%)	29 (90.62%)	0.600
Not Succeed	1 (3.33%)	3 (9.38%)	0.000

Table 3. Effectiveness of therapy for dyspepsia patients.

In the Indonesian herbal medicine formulary, a pre-clinical trial study resulted in Curcuma domestica being able to protect the gastric mucosa, which has the same effectiveness as ranitidine, and Cinnamomi *burmanii*<sup>(5,15)</sup>. This study is similar to the previous study that found that herbal medicine can be considered an appropriate treatment for functional dyspepsia  $(p<0.001)^{(18)}$ . A previous study conducted by Dian Safitri (2020) regarding the administration of turmeric water for pain due to dyspepsia has a p value of 0.000, which means that there was an influence between the squeeze of turmeric water and a decrease in pain intensity and pain scale among gastritis patients who have dyspepsia<sup>(19)</sup>. Turmeric extract can protect the gastric mucosa by increasing mucus secretion and having a vasodilator effect, so turmeric can increase the defence of the gastric mucosa. The results of previous studies indicate p = 0.0998 in the correlation test, which means that there is a relationship between turmeric production and stomach acid with a value of  $r \ge 0.5^{(20)}$ . Previous research has shown that Chinese herbal medicine can be a more effective and safer substitute for therapy than conventional medicine. This

is proven by the fact that Chinese herbal medicines are superior to prokinetic drugs in reducing global symptoms of dyspepsia for 4 weeks<sup>(21)</sup>.

**Comparison of EQ-ED Response Dimensions.** The value of EQ-5D VAS of scientific herbal medicine was higher than conventional therapy  $(64.06\pm7.56 \text{ vs})$ 63.67±8.09). The score of utility value in scientific herbal medicine was higher than conventional therapy (0.85±0.1 vs. 0.74±0.14) as shown in Table 4. The conventional therapy prescribed for dyspeptic patients at the Kalibakung health centre consisted of first-line therapy for dyspepsia, such as omeprazole from the proton pump inhibitor (PPI) class and ranitidine from the H2 group. The prescription of scientific herbal therapy recipes was carried out by the herbal medicine doctor, and the compounding of the prescription in the form of simplicia was carried out by the herbal medicine scientists. Recipes in the form of dry simplicia, which are generally used with turmeric (Curcuma domestica), ginger (Zingiber officinale), black cumin (Nigella sativa), and sembung (Blumea alsamidera), have different prescribing patterns depending on the patient's condition or history of the patient's disease<sup>(22)</sup>.

Dimensions	Levels	Herbal Therapy	Conventional Therapy	Total
Dimensions	(Problem)	(N=30)	(N=32)	(N = 62)
Mobility (%)	No	27 (90.00)	22 (69.00)	49 (79.00)
Moonity (70)	Yes	3 (10.00)	10 (23.00)	13 (20.97)
Solf core $(9/)$	No	29 (97.00)	26 (91.00)	55 (89.00)
Self-care (70)	Yes	1 (3.00)	6 (19.00)	7 (11.29)
Daily activities (%)	No	22 (73.00)	17 (53.00)	37 (60.00)
	Yes	8 (27.00)	15 (47.00)	25 (40.32)
Pain / Discomfort (%)	No	0 (0.00)	0 (0.00)	0 (0.00)
Tall / Disconnon (70)	Yes	30 (100.00)	32 (100.00)	62 (100.00)
Anviety / Demossion (0/)	No	30 (67.00)	18 (56.00)	34 (55.00)
Anxiety / Depression (%)	Yes	10 (33.00)	14 (44.00)	28 (45.16)
EQ – 5D VAS, mean $\pm$ SD		64.06±7.56	63.67±8.09	
$EQ - 5D$ Index, mean $\pm$ SD		0.85±0.11	$0.74{\pm}0.14$	

Table 4. Comparison of EQ-ED response dimensions of dyspepsia patients.

In both treatments for dyspepsia patients, conventional therapy was used for three days. Giving therapy for three days has the same effective therapeutic outcome as the two-day therapy range of PPI therapy which was the first-line therapy in dyspeptic patients, with the result that it can reduce gastric acid secretion<sup>(23)</sup>. In scientific herbal therapy, therapy was used for 1 week. Giving therapy for one week has a therapeutic outcome of reducing the degree of pain, has no side effects, and does not show liver and kidney function abnormalities<sup>(5-7)</sup>. The range of conventional therapy and scientific herbal therapy has a different duration of therapy, but both have the same outcome, reducing pain relief by reducing gastric acid secretion. Dyspepsia patients have a significant impact on the patient's quality of life because the measurement of quality of life has become one of the clinical goals in addition to being measured by the success of therapy<sup>(24)</sup>.

In dyspeptic patients, the success of therapy can be seen in the measurement of the patient's quality of life as an evaluation of clinical outcomes. This study found data on the quality of life of dyspeptic patients for each decrease in the quality of life of patients who feel pain (100%) and anxiety or depression (55%). The existence of a relationship between anxiety or depression affects the severity of dyspepsia. Based on research data, it showed that dyspepsia affects the quality of life, with pain being the dominant influence on the quality of life of dyspepsia patients<sup>(25)</sup>.

The higher the value of QOL presented, the better the health condition felt by the patient<sup>(26)</sup>. Dyspepsia disorders can reduce a patient's quality of life. Data from Jamu Registry 2014-2018 stated that dyspepsia was the top diagnosis, followed by diabetes mellitus, hypertension, haemorrhoids, and arthritis. More than 50% of functional dyspepsia patients are on medication all the time, requiring a lot of medical expenses, and approximately 30% of patients take time off from work and school due to recurrence of disease symptoms, this certainly reduces the quality of  $life^{(14,27)}$ .

**Theraphy Cost.** Table 5 showed that data on the cost of scientific herbal therapy  $(45,558 \pm 4,351)$  was higher than conventional dyspepsia therapy  $(39,202 \pm 4,500)$ . The biggest cost difference between the two groups was in transportation because the average dyspepsia patient who received therapy at the Kalibakung Health Centre lived closer than the patient at Kalibakung Herbal Tour. The medical device category has a significant comparison because in scientific herbal therapy, when patients receive herbal medicine at Griya Jamu Wisata Kesehatan Kalibakung, some of these patients buy tools to boil herbs, such as "kendil" and a spatula. This shows where herbal therapy (<sup>28</sup>).

**ICER Effectiveness.** The results of the calculations in Table 6 showed that the ICER of effectiveness was IDR 105,933 per therapy effectiveness. These results showed that the cost of scientific herbal therapy for dyspepsia was higher (IDR 6,356) and more effective (0.06) than the cost of conventional dyspepsia therapy. In addition, the ICER quality of life was obtained (IDR 57,781 per quality of life) and showed that the cost of scientific herbal therapy was higher than the cost of conventional therapy. The results of the quality of life among patients using scientific herbal therapy were greater than the quality of life among patients using conventional dyspepsia therapy with the difference of effectiveness was 0.11 (Table 6).

The tornado diagram, as seen in Figure 1, for sensitivity analysis has several variables, with the maximum ICER value on the dark green bar and the minimum ICER value on the light green bar for each variable. The results of the sensitivity analysis aimed at the top bar and the longest range are the variables that have the most influence on changes in the ICER value, namely the services of herbal medicine pharmacists.

Table 5. Therapy cost.							
C = = t	Herbal Tł	nerapy	Conventional Therapy				
Cost	Means	SD	Means	SD			
Direct Medical Cost							
Administration	3,200	0	10,000	0			
Doctor Consultation	4,800	0	4,000	0			
Drug	4,058	1,200	4,583	1,704			
Pharmacist Services	9,000	0	1,400	0			
Imbalace	1,200	0	250	0			
Direct Non-Medical Cost							
Transportation	15,833	5,843	10,500	4,522			
Parking	0	-	1,000	0			
Eat	2,633	5,411	2,688	6,918			
Medical devices	2,167	11,867	0	0			
Etc	2,667	8,519	4,781	12,746			
Total	45,558	4,351	39,202	4,500			

Table 5. Therapy cost

<b>T</b> 1	Q	Juantity	D	ICED	
Пегару	Cost (IDR)	Effectiveness	Cost (IDR)	Effectiveness	ICER
Effectiveness					
Scientific Herb	45,558	96.67%	6,356	0.06	105,933
Conventional Therapy	39,202	90.62%	-	-	-
Quality of Life Scientific Herb	45,558	0.85	6,356	0.11	57,781
Conventional Therapy	39,202	0.074	-	-	-

Table 6. ICER dyspepsia therapy.



Figure 1. Tornado diagram sensitivity analysis.

Based on these results, it shows that scientific herbal medicine therapy for dyspepsia is cost-saving compared to conventional therapy. However, it is acceptable for medical therapy because the ICER value produced is far below the WTP value, which is IDR 186.6 million. The value of WTP (willingness to pay) obtained is set to be three times the gross domestic product (GDP) per capita of Indonesia in 2021, based on the recommendations of the WHO Macroeconomic and Health Commission in 2000<sup>(29,30)</sup>.

# **CONCLUSION**

The value of the cost of therapy with the ICER method concluded that scientific herbal medicine therapy for dyspepsia was cost-saving compared to conventional dyspepsia therapy. The effectiveness of scientific herbal medicine therapy for dyspepsia was greater than the effectiveness of conventional dyspepsia therapy, where the cost was higher but the effectiveness was better. The quality of life of patients receiving scientific herbal therapy is better than that of patients receiving conventional therapy. Output value using utilities instead of QALYs.

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