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A METHOD FOR ASSESSING THE COST-EFFECTIVENESS AND THE BREAK-EVEN POINT OF CLINICAL PRACTICE GUIDELINES

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Abstract

Assessing the costs and benefits of developing a clinical practice guideline is important because investments in guidelines compete with investments in other clinical programs. Despite the considerable number of guidelines in many industrialized countries, little is known about their costs and cost-effectiveness. The authors have developed specific measures to determine the cost-effectiveness of guidelines, using a German evidence-based guideline on obesity for the diagnosis and treatment of obese patients as a model. The measures are: the number of people needed to cure, the number of people needed to prevent from developing the disease in question, and the number of people to treat in order to break even.

Keywords: Practice guidelines, Costs, Cost-effectiveness

Clinical practice guidelines are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (19). Alternative interventions that change physician performance include educational materials (other than clinical practice guidelines), formal continuous medical education programs, outreach visits, local opinion leaders, patient-mediated interventions, audit with feedback, and reminders (15). Guideline developers include the government, medical specialty societies, health insurance companies, managed care organizations, academic medical institutions, and commercial organizations. Target groups can be physicians, nonphysician health personnel, patients, caregivers, health planners, payers, or policy makers (37).

Assessing the costs and benefits of developing a clinical practice guideline is important because investments in guidelines compete with investments in other clinical programs. The worldwide investment in guidelines is considerable: the National Health Service of the United Kingdom, for example, was reported to spend 1.5% of its research and development

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budget on guideline development (31). The substantial investment in guidelines is also reflected by the number of guidelines available: as early as in 1993, at least 20,000 guidelines were estimated to exist in the United States alone (36). In addition, the number of guidelines is increasing in many industrialized countries (60). Guidelines not only incur development costs but may also increase treatment costs, since they focus on improving the quality of care (55) and usually do not consider cost-effectiveness (27;38).

In spite of the need for assessments, there is little information about the costs of clinical practice guidelines and, to the best of the authors' knowledge, no information about their cost-effectiveness. Some information exists for guideline development (21;25) and induced disease costs (18), as well as the cost-effectiveness of guidelines disregarding development costs (14;16;41;58).

This study presents a general framework for estimating the cost-effectiveness and the break-even point of guidelines. The break-even point determines the incremental benefit (i.e., the additional benefit of guideline development compared with another intervention or program) that needs to be achieved in order to offset the incremental costs (i.e., the additional costs of guideline development) incurred. The framework was applied to a German evidence-based guideline on obesity that was developed due to a lack of evidence-based recommendations for the diagnosis and treatment of obese patients and published in August 1998 (35).

This article attempts to help guideline developers to assess systematically the incremental costs and benefits of guidelines under development by using the presented framework. Furthermore, the framework helps guideline developers to calculate a break-even point and thus to judge whether the guideline is likely to be cost-effective. In the example used, the framework attempted to answer the question of whether the development of the guideline on obesity was cost-effective.

A FRAMEWORK FOR ESTIMATING THE BREAK-EVEN POINT OF GUIDELINES

To systematically estimate a guideline's break-even point, we suggest that guideline developers follow the sequence below. Costs and benefits should be assessed for developing a guideline as well as for an alternative program to change physician performance (for example, for current practice, i.e., for not developing a guideline). It depends on the perspective of the analysis which of the cost and benefit items below should be included in the analysis.

Estimation of Costs

The costs of a guideline can be divided into product costs and induced disease costs. Product costs result from initiating, developing, pretesting, disseminating, implementing, and operating/maintaining the guideline. For each type of product cost, overhead should be added to salaries of the staff involved. Induced disease costs may result if a decrease in the underuse of services increases the number of services (12) and thus leads to upfront disease costs, or if the improved image of the organization results in additionally enrolled covered lives. Some cost items are intangible, i.e., they are difficult to measure and hence are not included in an economic evaluation of guidelines. An example of such a cost item is a potential decrease of the clinicians' autonomy, which may reduce job satisfaction. If an institution plans to develop more than one guideline, smaller product costs could be anticipated first by the learning curve, and second, by economies of scale. Reasons for the learning curve include an acceleration in searching literature, writing documents, and using databases. The reason for economies of scale are fixed costs, which mainly occur for the first but not for subsequent guidelines. Such fixed costs include the resources for building a database as well as for the decision-making process about how to develop a guideline and to evaluate the literature. Any standardization of these processes reduces the total development costs.

Estimation of Benefits

The duration of the benefit should be assessed and the type of benefit determined. The benefit of an intervention can be measured both in terms of an improvement in clinical outcomes and in terms of an increase in profits.

Improvements in clinical outcomes can be measured as an increase in life expectancy and/or quality of life. If years of life are weighted with the quality of life, quality-adjusted life-years (QALYs) can be used as an aggregated measure.

An increase in profits may result from a decrease in disease and administrative costs as well as from an increase in revenues. A decrease in disease costs may result if a decrease in overuse and/or misuse reduces disease-related upfront costs (12) or if improved clinical outcomes result in a decrease in disease-related downstream costs. A decrease in administrative costs might result, for example, if an organization improves its quality of care and thus reduces its premiums for malpractice insurance. An increase in revenues might result from sales of guideline copies or from an improved image leading to an enhanced demand for medical services.

Intangible benefits (which are difficult to be measured quantitatively) may result from a facilitation of the decision-making process and a heightened confidence in medical decisions. Both of these benefits lead to greater job satisfaction among clinicians. This in turn could lead to a decrease in the labor turnover and therefore in the costs of hiring and training new labor. An additional intangible benefit of the implementation of guidelines is that they may enhance organizational learning.

Relating Costs and Benefits

The total cost and the total benefit of developing the guideline are subtracted from the total cost and the total benefit of the alternative program. Thus, the incremental cost and the incremental benefit of developing a guideline are calculated. The incremental cost and the incremental benefit can be presented separately or in relation to each other. If costs and monetary benefits are presented in relation to each other, a cost analysis is performed. However, a cost analysis is only applicable if monetary benefits are larger than costs. If decision makers are primarily concerned with how to regain the money invested into a guideline, this type of analysis would be preferable. If decision makers consider clinical benefits as well, a cost-effectiveness analysis (CEA) could be performed.

For both types of analyses a break-even point may be calculated at which the incremental product and induced disease costs of the guideline are offset by the incremental benefit. The incremental benefit needed to break even can be expressed in terms of the additional number of patients with the disease in question who need to be cured (BE-NNC) or the additional number of healthy persons who need to be prevented from acquiring the disease (BE-NNP). By multiplying the BE-NNC or the BE-NNP by the additional number of people that need to be treated for a given duration to prevent one target event (NNT), i.e., to cure one patient or prevent one person from acquiring the disease, the additional number of people needed to treat for breaking even (BE-NNT) can be calculated. Any of the break-even points may be judged by the probability that implementation of the guideline is successful.

The following calculations refer to the comparison of developing a guideline to the status quo, which is not developing a guideline. A cost analysis determines the BE-NNC by dividing the annual guideline product cost by the annual per person saving from treatment (Appendix 1). Similarly, the BE-NNP is calculated by dividing the annual guideline product cost by the annual per-person saving from prevention. The net annual per person saving is calculated by subtracting the annual cost per successfully treated/prevented case from the annual saving per successfully treated/prevented case. The annual cost per successfully

treated/prevented case is calculated by multiplying the incremental cost of a person enrolled in a treatment/prevention program by the NNT.

A CEA calculates the BE-NNC and the BE-NNP by dividing the benefit needed to break even (or the costs that need to be offset) by the maximum acceptable cost-effectiveness ratio. If the maximum acceptable cost-utility ratio is used, the total number of QALYs needed to save results. This figure is then divided by the average individual gain in QALYs from improving clinical outcomes and from decreasing induced disease costs. The latter gain in QALYs is calculated by dividing the individual cost saving by the maximum acceptable cost-utility ratio.

The parameters in Appendix 1 can also be used to determine the cost of underusing preventive care that is recommended by a guideline ($Cost_{underuse(px)}$). For each healthy person who does not receive such preventive care, the annual cost is calculated as follows:

$$Cost_{underuse(px)} = (Cost_{ds})/(NNT) - Cost_{px}.$$

Similarly, the cost of underusing treatment according to a guideline can be determined ($Cost_{underuse(tx)}$). For each patient who does not receive treatment, the annual cost is calculated as follows:

$$Cost_{underuse(tx)} = (Cost_{ds})/(NNT) - Cost_{tx}.$$

DEVELOPMENT AND IMPLEMENTATION PROCESS OF THE GERMAN EVIDENCE-BASED GUIDELINE ON OBESITY

Due to a lack of evidence-based recommendations, a group of experts on obesity and on the methods of evidence-based medicine decided in 1997 to develop a German guideline for the treatment of obesity. The target audience for the guideline was primary care physicians, the main providers of obesity care in Germany, as well as obese patients themselves.

A systematic search of the literature identified relevant clinical articles. The validity of studies was systematically evaluated. The guideline considered the criteria of the U.S. Agency for Health Care Policy and Research (US Agency for Healthcare Research and Quality) (57) and the German Federal Chamber of Physicians (6). Recommendations did not incorporate cost-effectiveness considerations because studies with cost-effectiveness data on obesity were lacking. The guideline was published in August 1998. The resulting total development time was approximately 15 months. The guideline was published in three versions: a comprehensive version for experts, a short version tailored to the needs of primary care physicians, and a version for patients written in lay terms. In addition, translations of the three versions of the guideline have been published in English. The guideline has been implemented through the distribution of copies, announcements in appropriate media channels, presentation at meetings of experts, placement in the World Wide Web, and promotion by opinion leaders.

The three versions of the guideline will be updated no later than 2 years after publication. A more detailed description of the methodology used and the content of the guideline has been published recently (51).

METHODS

The following calculations serve as an example of how the framework might be applied to a real-world problem. The main purpose of the example analysis is to demonstrate the approach taken.

A Break-even Analysis of the Guideline on Obesity

The cost-effectiveness of the guideline was estimated for a population of 50-year-old male Germans. The guideline development was compared with current practice, i.e., not developing a guideline. Since there was little information on cost consequences of treating obesity, we focused on the prevention of obesity and calculated the BE-NNP with the corresponding BE-NNT. The costs and the effectiveness of the English language editions of the guideline were not considered since they were sent abroad and were assumed to have a negligible effect on the German population. Both the cost analysis and the CEA had a third-party payer's viewpoint. Since the guideline was delivered free of charge, revenues were not incorporated.

The analysis was performed using Microsoft Excel 97 (Microsoft Corp., Redmond, WA, USA) and Crystal Ball 4.0 (Decisioneering, Inc., Denver, CO, USA). We identified data sources by searching MEDLINE for articles in English and German published until 2000. In addition, we hand-searched review articles and book chapters for additional sources.

Costs

The annual per person cost of obesity in Germany was calculated by dividing total direct costs of obesity in Germany by the number of obese persons. To calculate total direct costs, costs of diseases that are attributed to obesity were multiplied with the population attributable fraction (PAF). The PAF provides an estimate of the extent to which a disease and its management costs are attributable to an individual factor. The PAF is calculated using the formula $P(RR-1)/[P(RR-1)+1]$, where P is the probability of a person being obese in a given population and RR is the relative risk for the disease in an obese subject (4;5). We calculated the PAF for the eight most expensive nutrition-related diseases (breast cancer, colorectal cancer, coronary heart disease, gallbladder disease, hypercholesterolemia, hypertension, osteoarthritis, type 2 diabetes) (7). PAFs were based on a prevalence rate of obesity (body mass index [BMI] ≥ 30) of 20.0% (3) and the relative risks for the eight nutrition-related diseases shown in Table 1. Preferentially, relative risks for non-Hispanic whites, the major ethnic group in Germany, were taken. All costs were adjusted to 2,000 Deutsch marks (DM).

Several studies have demonstrated the effectiveness of primary prevention of obesity in adults (10;20;33;44;54). Further, a number of frequently cited guidelines on obesity recommend obesity prevention (40;46). Similarly, the German guideline on obesity recommends that persons at risk for obesity, such as those with a familial predisposition, should have preventive advice on a regular basis. We based the cost of a preventive program on the statutory health insurance's price scale (*Einheitlicher Bewertungsmaßstab*) for a biannual visit to a general practitioner. Each visit included a medical history, a clinical examination, and counseling and added up to DM 29.29 (355 points). The NNT over 1 year (4.76) was based on a meta-analysis of studies on educational one-to-one interventions to improve compliance with direct objective measures such as weight change (43). We assumed that persons at risk for obesity would become obese without preventive advice.

The future cost of prolonged survival from prevention was calculated by subtracting lifetime costs without prevention from lifetime costs with prevention, disregarding the net saving during the period of normal weight. Lifetime costs were calculated by multiplying age-specific relative direct costs per year (1) by age-specific healthcare expenditures per year (8;9). Costs were discounted at an annual rate of 5% (26).

Effectiveness

To calculate the number of QALYs gained from prevention, we added the gain from maintaining a normal weight for 1 year (quality of life without obesity (45) minus quality of life

Table 1. Base Case Values and Ranges Used in the Sensitivity Analysis

Parameter	Base case value, DM (range)	Reference no.	Comment
Cost data			
Total health care expenditures in Germany	551,565,428,000	48	
Directs costs of breast cancer	2,290,195,122	49	
Directs costs of colorectal cancer	2,364,804,878	49	
Directs costs of coronary heart disease	41,708,800,000	34	
Directs costs of gallbladder disease	1,253,734,266	7	
Directs costs of hypercholesterolemia	1,656,000,000	7	
Directs costs of hypertension	7,854,750,583	7	
Directs costs of osteoarthritis	11,469,357,724	49	
Directs costs of type 2 diabetes mellitus	6,573,227,642	49	
Cost of a visit for obesity prevention	29.29	32	
Guideline product costs	652,000 (598,000–716,000)		
Epidemiologic data			
Prevalence rate of obesity	0.20	3	
Relative mortality rate (BMI > 31)	2.69 (2.30–3.08)	56	
Relative risk of breast cancer (BMI > 31)	0.89 (0.73–1.09)	30	Pooled risk of pre- and postmenopausal women using the general variance-based method (42)
Relative risk of colorectal cancer (BMI ≥ 29)	1.74 (1.17–2.58)	22;23	Pooled risk using the general variance-based method (42)
Relative risk of coronary heart disease (BMI ≥ 29 (59), ≥30)	2.99 (2.56–3.50)	47;59	Pooled risk using the general variance-based method (42)
Relative risk of gallbladder disease (men: BMI > 30; women: BMI ≥ 28.1)	1.75 (1.48–2.08)	17	Pooled risk of men and women using the general variance-based method (42)
Relative risk of hypercholesterolemia (BMI ≥ 30)	1.48 (1.42–1.55)	39	Pooled risk of men and women using the general variance-based method (42); blood cholesterol ≥240 mg/dL
Relative risk of hypertension (BMI ≥ 30)	2.04 (1.97–2.11)	39	Pooled risk of men and women using the general variance-based method (42); systolic blood

(Continued)

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Table 1. *(Continued)*

Parameter	Base case value, DM (range)	Reference no.	Comment
			pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg
Relative risk of osteoarthritis (BMI upper tertile)	2.94 (1.81–4.77)	29	Pooled risk of men and women using the general variance-based method (42); lower bound of upper BMI tertile was assumed to be ≥30
Relative risk of type 2 diabetes (BMI ≥ 31)	58.52 (53.72–63.74)	11;13	Pooled risk using the general variance-based method (42)
Other data			
Preference weight of 45- to 54-year-old males	0.814 (0.800–0.828)	45	Rating scale; range estimate
Preference weight of 45- to 54-year-old obese males	0.718 (0.691–0.744)	Thomas Evers, Institute of Health Economics, Cologne, personal communication, April 16, 2000	Rating scale
Guideline utilization time, years	4 (3–7)	Estimate	See text
Maximum acceptable cost-utility ratio, DM/QALY	30,000 (20,000–40,000)	Estimate	See text
Annual discount rate, %	5 (0–10)	26	

with obesity; Thomas Evers, Institute of Health Economics, Cologne, personal communication, April 16, 2000) to the gain due to an increase in life expectancy. For calculating the latter gain, the average quality-adjusted life expectancy with and without successful prevention was obtained by applying the relative risk of dying to the life table of German males (50) and discounting QALYs at an annual rate of 5% (26). It was assumed that the mortality rate stayed constant throughout the lifetime.

Guidelines on obesity, such as the one by the Scottish Intercollegiate Guidelines Network (46), and the German guideline on obesity are updated 2 years after publishing, implying that the guidelines will be outdated thereafter. Based on this expert consensus, we made the conservative assumption for the base-case that the guideline will not be used 2 years beyond update, i.e., 4 years after initial publishing.

Cost-effectiveness

We derived a maximum threshold for a cost-effective treatment (DM 30,000 per QALY) from the costs per life-year saved from several well-accepted medical interventions in Germany (2;52;53). This threshold is rather conservative because many other well-accepted interventions in Germany, such as hemodialysis treatment, presumably have much higher cost-effectiveness ratios. In addition, the value of a QALY is generally larger than the value of a life-year saved.

Sensitivity Analysis

A multivariate sensitivity analysis was performed to determine the robustness of the cost-effectiveness results. The analysis was performed using a Monte Carlo simulation with

10,000 iterations. For this purpose the parameters listed in Table 1 were simultaneously varied. Ranges were entered as four standard errors of the mean or, if unavailable, as reasonable estimates covering the complete distribution. Distributions were assumed to be either normal or log-normal. Uncertainty ranges containing 95% of replicated results were reported.

A univariate sensitivity analysis was performed to determine parameters with a major impact on the cost-effectiveness. The uncertainty ranges either represented estimates (Table 1) or contained 95% of replicated results from a Monte Carlo simulation with 10,000 iterations.

RESULTS

The costs of developing and disseminating the guideline were estimated to be DM 737,918 (Table 2). This represents the annual salary of approximately seven full-time research fellows. The main cost driver was the time for searching the literature and writing the documents. The median time for evaluating one article was about 15 minutes.

Using the formula in Appendix 1, the BE-NNP in the cost analysis was calculated as:

$$\begin{aligned}\text{BE-NNP} &= \text{DM737918}/[(4\text{ yrs})(\text{DM }846.35 - ((\text{DM}58.58)(4.76))] \\ &= 325.07.\end{aligned}$$

In the CEA the BE-NNP was calculated as:

$$\begin{aligned}\text{BE-NNP} &= \text{DM}737\ 918/[(4\text{ yrs})((\text{DM}30\,000/\text{QALY})(0.17\,\text{QALYs}) \\ &\quad + (\text{DM}846.35 - (\text{DM}58.58)(4.76)))] \\ &= 33.16.\end{aligned}$$

In other words, the CEA revealed that in order to break even, 326 additional 50-year-old nonobese males would have to be prevented from becoming obese for 4 years (34) (Table 3). Alternatively, each year for a total of 4 years, 326 additional 50-year-old nonobese males would have to be prevented from becoming obese (34). Based on an NNT of 4.76 (43), 1,548 additional persons would need to be enrolled in a prevention program over 4 years in order to break even (cost analysis). According to the CEA, the figure is 128.

Using the formula for calculating the cost of underusing preventive care, the annual cost of each healthy person who does not receive preventive care according to the guideline is:

$$\text{Cost}_{\text{underuse(px)}} = (\text{DM}846.35)/(4.76) - \text{DM}58.58 = \text{DM}119.22.$$

The results of the univariate sensitivity analysis of key parameters are shown in Table 3. All parameters except for guideline product costs had a major impact on the break-even points.

DISCUSSION

Assessing the costs and benefits of developing a clinical practice guideline is important because investments in guidelines compete with investments in other clinical programs. This article attempts to help guideline developers to assess systematically the incremental costs and benefits and to calculate the break-even points of guidelines under development by using the presented framework. The break-even points are presented as the number of patients needed to prevent getting the disease (BE-NNP), the number of patients needed to cure the disease (BE-NNC), and the number of people needed to treat (BE-NNT). The framework, including the break-even analysis, was applied to the German evidence-based guideline on obesity. The cost-analysis revealed costs of DM 680,000 to DM 800,000 for

Table 2. List of Cost Items (Market Values) for the Guideline on Obesity and Their Estimated Monetary Values (DM 1 = EUR 0.51)

Item	Volume	Unit cost, DM	Base case cost, DM (range)
Development			
Phase I: Development of the draft			
Work station (bottom-up calculation)	3.98 years (research fellows + senior scientists)	4,300/year	17,114
Evaluation of the literature (295 publications)	0.125 years (research fellow)	110,000/year	13,750
Literature search and writing the draft	3.48 years (research fellows)	110,000/year	382,800
Salary of senior scientists	0.5 years (4 scientists)	130,000/year	65,000
Overhead (top-down allocation)	3.98 years (research fellows + senior scientists)	8,600/year	34,228
Phase II: Design and printing			
Design and printing, including overhead	3,000, 8,000, and 11,000 copies of the expert, short, and patient versions, respectively		78,000
Dissemination			
Distribution of copies including overhead; estimate 110% of distribution costs until 11/99 (100%; 120%)	18,603 copies (16,912; 20,294)		8,448 (7,680–9,216)
Implementation			
Education of physicians and patients (time spent by opinion leaders, physicians, and patients)	NA		
Operation and maintenance			
Revision of the draft, including overhead; estimate 20% (10%; 30%) of phase I costs			102,578 (51,289–153,868)
Design and printing, including overhead (estimate)	3,000, 4,000, and 5,000 copies of the expert, short, and patient versions (3,000, 3,000, 3,000; 3,000, 8,000, 11,000)		32,000 (30,000–40,000)
Distribution of copies, including overhead (estimate)			4,000 (2,000–8,000)
Costs not allocable			
Travel (estimate)			<1,000
Total			737,918 (681,861–801,976)

NA = not assessable.

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Table 3. Sensitivity Analysis

Parameters	Cost analysis		Cost-effectiveness analysis	
	BE-NNP for 1 year	BE-NNT for 1 year	BE-NNP for 1 year	BE-NNT for 1 year
Base case (interval containing 95% of simulation replications)	325.07 (176.34–569.97)	1,547.34 (839.37–2,713.07)	33.16 (19.87–43.02)	127.54 (76.44–165.45)
Annual per person saving from prevention, DM				
298.26	618.52	2,944.15	34.85	134.03
820.60	224.81	1,070.10	31.72	121.99
Guideline product costs, DM				
681,861	300.38	1,429.79	30.64	117.86
801,976	353.29	1,681.66	36.04	138.62
Guideline utilization time, years				
3	433.43	2,063.12	44.22	170.06
7	185.76	884.19	18.95	72.88
Increase in QALYs from prevention				
0.13	NA	NA	41.29	158.82
0.20	NA	NA	28.09	108.04
Maximum acceptable cost-utility ratio, DM/QALY				
20,000	NA	NA	47.33	182.03
40,000	NA	NA	25.52	98.16

NA = not applicable.

developing, printing, and disseminating the guideline on obesity, which equals EUR 350,000 to EUR 410,000 and is the opportunity cost of about 70 hip replacements.

The cost analysis, considering the monetary benefits of developing a guideline, suggested that each year for a total of 4 years, 326 additional 50-year-old males would need to be prevented from becoming obese (BE-NNP). Based on a CEA and a maximum acceptable cost-utility ratio of DM 30,000/QALY, the BE-NNP was 34. The CEA revealed smaller break-even numbers because it not only considers monetary but also clinical benefits. In addition, our analysis revealed that for each healthy person who does not receive preventive care on obesity, annual costs totaling DM 119 result. These considerable costs may be balanced against the cost of enforcing the recommendations on prevention.

To the best of our knowledge, this is the first article that presents a detailed cost analysis of a clinical practice guideline. Other developers that use a similar development process may multiply the presented volumes of resources consumed by their unit costs to calculate their own total cost.

The advantage of the framework is its systematic approach, which is particularly useful for less-experienced decision makers assessing the costs and benefits of a pioneer guideline. Although we used complex modeling to derive estimates including uncertainty ranges, simpler calculations may suffice and may provide a quick orientation on the cost-effectiveness of a guideline, particularly if the benefit needed to break even were extremely low or high. Moreover, the concepts of the BE-NNP and the BE-NNC may show a high acceptance among decision makers and clinicians, particularly among those familiar with the concept of the NNT. Similar to the concept of the NNT, the concepts of the BE-NNP and the BE-NNC may be fairly easy to understand.

Our findings should be interpreted in the context of the estimates and assumptions stated in the Methods section. In addition, the following limitations apply. First, maximum acceptable cost-utility ratios such as the DM 30,000/QALY used for calculating the

break-even points of the CEA are not without criticism (e.g., see Gold et al. [24]) because they depend on ethical values. We believe that for obesity prevention and treatment, our choice of a threshold value represents real circumstances better than using no threshold at all. Further, compared with the range of threshold values suggested in the literature (28), we used a conservative value. Moreover, we varied the value in the sensitivity analysis.

Second, the evidence-based guideline on obesity was the first evidence-based guideline developed by our institute. Therefore, the resulting costs may only be representative for pioneering guidelines. Currently, our institute is developing an evidence-based guideline on diabetes mellitus. The present process suggests smaller unit costs through learning and economies of scale.

Third, total guideline costs did not include the costs of implementation. These costs may be considerable given the time spent by opinion leaders, physicians, and patients for educating physicians and patients.

Fourth, the target population consisted of 50-year-old males. Thus, the results may not apply to other population groups.

The cost of our guideline is difficult to compare with estimates of other guidelines because details on the cost components included (for example, implementation costs) are not reported. Estimates for other guidelines range from US $100,000 (Dutch College of General Practitioners [21]) to US $1,000,000 (U.S. Agency for Health Care Policy and Research [25]).

The above break-even points of the guideline on obesity have to be judged by the probability that guideline implementation has been successful. Feedback already obtained shows that the estimated break-even points of the guideline on obesity may be attainable even without a major implementation effort. This may also be true for the upper bounds of the uncertainty ranges. Eighteen-thousand copies (all three versions) have been mailed out, most of them by request. Additional guideline copies have most likely been downloaded from the Internet. Further, it is assumed that the copies have a spillover effect, i.e., primary care physicians and patients internalizing the guideline content influence their peers. Thus, we conclude that the development of the guideline on obesity could be cost-effective.

To estimate the break-even point of a guideline, developers should try to precisely estimate individual savings, guideline utilization time, and increases in preference weights. All of these parameters had a major impact on the cost-effectiveness of the guideline on obesity.

Further research on the cost-effectiveness of guidelines is strongly recommended. Particularly, the clinical and economic benefits of guidelines need to be measured to obtain better prior estimates for assessing the break-even points of guidelines under development. In addition, the acceptance of the proposed measures of a break-even point should be evaluated among decision makers. If acceptance were high, break-even points could be used as a criterion for funding of new guidelines.

POLICY IMPLICATIONS

Assessing the costs and benefits of developing a clinical practice guideline is important because investments in guidelines compete with investments in other clinical programs. Despite the considerable number of guidelines in many industrialized countries, little is known about their costs and cost-effectiveness. Total costs may be considerable: the authors estimate that the cost of a German evidence-based guideline on obesity equals the opportunity cost of about 70 hip replacements. For determining the cost-effectiveness of guidelines, the authors developed specific measures. Policy makers may demand estimates for these measures prior to funding of new guidelines. Also, the authors propose a way of calculating the cost of underusing a guideline's recommendations that policy makers may balance against the cost of enforcing a guideline's recommendations.

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APPENDIX 1

HOW TO CALCULATE THE NUMBER NEEDED TO PREVENT AND THE NUMBER NEEDED TO CURE TO BREAK EVEN FOR DEVELOPING A GUIDELINE

Abbreviations

BE-NNP = the number needed to prevent to break even;
BE-NNC = the number needed to cure to break even;
N_{pop} = population figure;
$Rate_{dx}$ = prevalence rate of the population;
NNT = additional number of people needed to treat to prevent one target event;
$Cost_{gu}$ = guideline product costs;
$Cost_{px}$ = annual per person incremental cost of prevention;
$Cost_{tx}$ = annual per person incremental cost of treatment;
$Cost_{ds}$ = per person saving of downstream costs;
$Time_{val}$ = duration of the guideline usage;
$Ratio_{CU}$ = maximum acceptable cost-utility ratio; and
$QALYs_{gained}$ = QALYs gained per person by improving clinical outcomes and decreasing induced disease costs.

Cost Analysis

$$\text{BE-NNP} = Cost_{gu}/[(Time_{val})(Cost_{ds} - (Cost_{px})(NNT))]$$
$$\text{BE-NNC} = Cost_{gu}/[(Time_{val})(Cost_{ds} - (Cost_{tx})(NNT))]$$

Cost-effectiveness Analysis

$$\text{BE-NNP} = Cost_{gu}/[(Time_{val})((Ratio_{CU})(QALYs_{gained}) + Cost_{ds} - (Cost_{px})(NNT)))]$$
$$\text{BE-NNC} = Cost_{gu}/[(Time_{val})((Ratio_{CU})(QALYs_{gained}) + Cost_{ds} - (Cost_{tx})(NNT)))]$$