Table 2. Cancers detected by screening and among controls in four European cities

City	Cancers detected per 1000 screened		Cancers detected by screening (%) Dukes' A	Cancers among controls (%) Dukes' A
	1st screen	2nd screen		
Gothenburg	1.9	2.4	34	15
Nottingham	2.3	1.5	51	12
Funen	1.8	0.7	51	9
Burgundy	1.6		52	

COST–BENEFIT ANALYSIS

A cost–benefit analysis cannot be made with any certainty before the final data on mortality are available. The Danish experience with the randomised trial, which began in 1985, suggests that the total cost for screening the Danish population aged 45–74 years (total population, 5 million) every 2 years using Hemoccult-II will be about 800 000 U.S. dollars per year.

Other costs must also be considered, however. A small risk exists of diagnostic and therapeutic colonic perforation, which may be lethal in a very small number of cases. False negative results may result in interval cases, or people may be treated unnecessarily for cancer that would not have been lethal. These drawbacks indicate that a reduction in mortality from the disease must be demonstrated before population screening with Hemoccult-II can be introduced. If no reduction is demonstrated, more complex strategies like flexible sigmoidoscopy with Hemoccult-II may be considered; furthermore, better markers for colorectal cancer must be found both in faeces and in urine and blood. On the basis of the indirect data on colorectal cancer screening so far available, a mathematical model has been used to identify optimal screening strategies in a cost–benefit analysis [3].

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Economics of Cancer Screening: Total Costs and Benefits in Economic Terms

K.M. Pedersen

INTRODUCTION

THE MAIN objective of an economic appraisal of a screening programme is to assist the relevant decision makers in making the best use of the resources available in the health care sector, e.g. screening programmes versus new treatments or, more narrowly, choice of a specific screening programme.

Economics is the study of how to allocate scarce resources to competing ends. Economic appraisals — cost–benefit analysis on the one hand and cost-effectiveness or cost–utility analysis on the other — are useful, relevant tools, as they bring together the two sets of information necessary to evaluate any health-care programme: net consumption of resources and relevant clinical and epidemiological evidence about health-related effects.

An economic appraisal is often added to clinical trials as a last thought, in an attempt to convince decision makers that a screening programme is worthwhile. It should, however, be an integral part of the trials, as it combines results on clinical effectiveness with the resource dimension. It also provides a clear picture of the practical details necessary for the organisation of a 'real life' screening programme, i.e. not only screening frequency and target group but also, for instance, whether a mobile screening unit is to be used in a screening programme for breast cancer and how the screening unit is to be staffed. Such detail is necessary to provide an idea of the expected resource consumption in an actual programme, rather than the often idealised circumstances under which a clinical trial is carried out.

An increasing number of economic appraisals are published and (to a much lesser degree) used when advocating a particular (screening) programme or (even more rarely) for actual decision

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making. At least a superficial knowledge of the scope of economic appraisals is, therefore, necessary, with an understanding of what kind of information and data are used. This article focuses mainly on providing such an overview, with warnings about the pitfalls of the interpretation and use of such analyses.

Analysis of the cost-effectiveness of cancer screening goes back more than a decade. Eddy's book on screening for cancer in 1980 [1] is a landmark; it emphasises modelling of screening for breast cancer, but results are also presented for cervical cancer and cancer of the colon. Several cost-effectiveness analyses were published during the 1980s [2–8], but towards the end of the decade, interest turned to a more general form of cost-effectiveness analysis, namely cost–utility analysis [9–10].

THE TOTAL PICTURE

Often, the main results of an economic appraisal are presented in a very compact form. Some examples, with numerical results, are given in Table 1. Many professionals and decision-makers are in doubt about the exact meaning of such results. How were they calculated? How are they to be interpreted? What is the difference, for instance, between healthy years equivalents and quality-adjusted years of life, and which is the better measure of effectiveness? What are the differences between cost-effectiveness analysis, cost–utility analysis and cost–benefit analysis (in Table 1, examples II, III; I and V, respectively). Are the results applicable to actual screening programmes?

Table 1 is included for illustration and will not be commented upon in detail, but it is worth nothing that whenever years of life and quality-adjusted years of life (healthy years equivalents) are used, costs per year are lower for years of life than for quality-adjusted years of life. If total costs are the same, this means that we get fewer healthy years when adjusting for quality of life than when using the 'raw' years or unadjusted years of life. It is therefore important to understand how and why we adjust for quality of life.

Care must be exercised when using these figures; interpretation is rarely straightforward or clear [14]. The results must be interpreted in context, e.g. compared with ratios for other possible health programmes or those for alternative ways of conducting the screening activity. Most of the numbers in Table 1 are not very informative in isolation, but each ratio of cost-effectiveness or cost–utility ratio is like an iceberg: only the tip shows, and much is hidden and needs to be documented to reveal which cost components have been included and how quality-adjusted years of life were calculated.

To give an impression of how an economic appraisal is not only based on relevant clinical data about effectiveness but also adds important aspects to the organisation of a screening programme, Figure 1 shows the main components of an economic appraisal of a screening programme.

The cost components should include target group, participation rate, activities to increase participation rate, costs of carrying out the screening test, subsequent diagnostic costs (e.g. when the number of true- and false-positive results is known, information about specificity and sensitivity must be integrated and can be used at different levels of sophistication) and the cost of possible treatment subsequent to the detection of early-stage cancers.

In principle, information on costs in the absence of (systematic) screening should also be available, in order to estimate the incremental costs due to the introduction of screening or savings; for instance, a decrease in the number of clinical mammographies required or saved treatment costs for people with cancers in advanced stages. Identification and clarification of a 'zero option' alternative is important, as is the inclusion of several versions of the basic organisation of the screening activity, in order to make a relevant interpretation of the results for both on costs and effects. All too often, such information is lacking.

An attempt must thus be made to calculate the net costs, i.e. the running (operational) costs of the screening programme, depreciation and interest of the relevant investments minus possible savings due to the programme. Costs to the participants should also be included: travel costs and time used at the screening unit. Opinions differ on which savings to include: in many studies (long- and short-term) savings due to decreasing

Table 1. Compact presentation of the results of some recent economic appraisals of cancer screening programmes

I.	An Australian cost–utility analysis of mammographic screening [10]	
1.	Costs per year of life gained	10 560 A$
2.	Costs per healthy years gained	16 930 A$
II.	A Dutch cost-effectiveness analysis of cervical cancer screening [11] (10 invitations per woman, compared with the zero option of no early detection activity)	
1.	Costs per year of life gained	28 000 DFL
2.	Marginal costs per year of life gained	40 800 DFL
III.	A Swedish study of breast cancer screening [12]	
1.	Total costs per life saved	610 000 SKR
2.	Total costs per year of life saved	33 000 SKR
3.	Total costs per quality-adjusted year of life saved	53 000 SKR
IV.	A British report on breast cancer screening [9] (single-view mammography at three-year intervals; assuming that the benefit lasts 15 years after initial screen)	
1.	Costs per year of life gained	£ 3044
2.	Costs per quality-adjusted year of life saved	£ 3309
V.	A US cost–benefit analysis of haemocult screening for colorectal carcinoma [13]	
1.	Saved medical care costs over 5 years (and a projected increase of 22 years in life expectancy)	14 685 US$
2.	Overall costs (saved medical care costs plus costs of screening)	17 438 US$
	or per person-years of increased life expectancy	765 US$

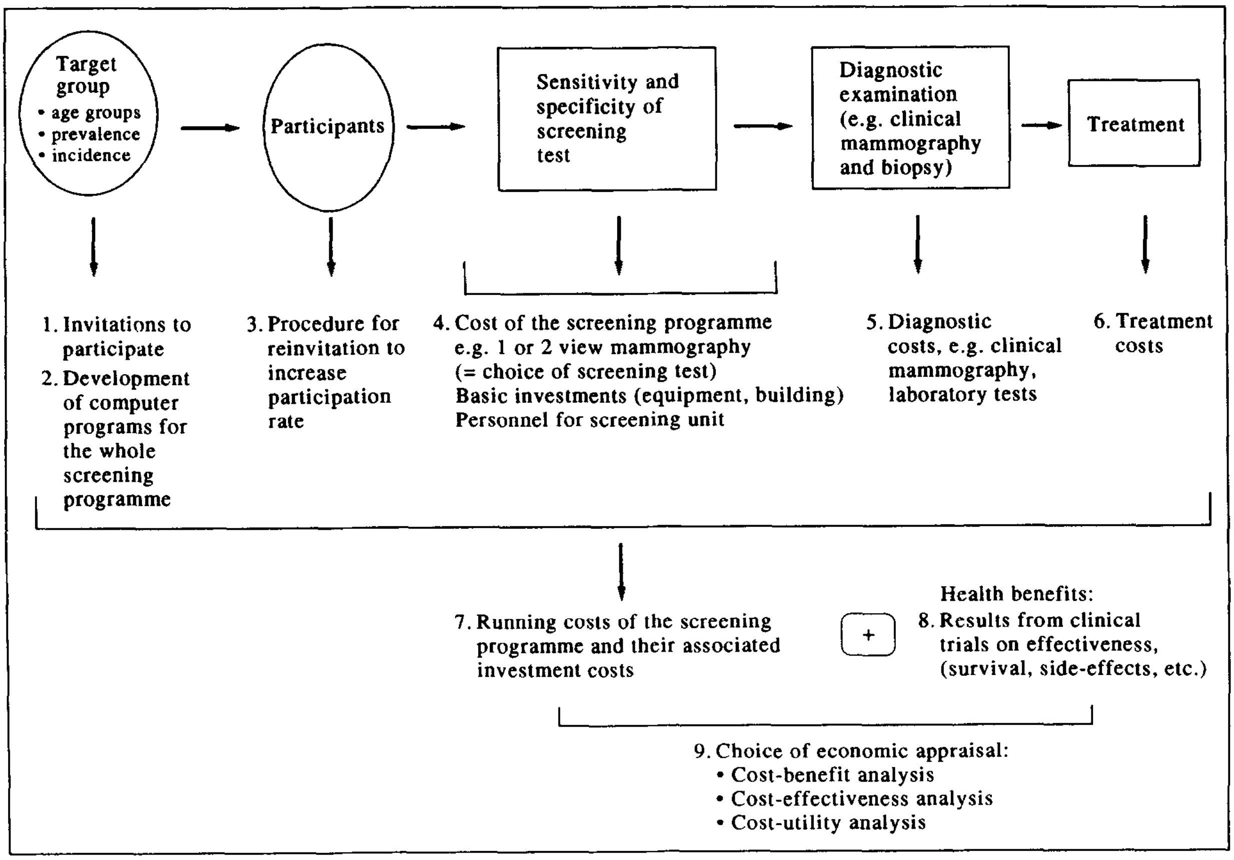

Figure 1. Components of an economic appraisal of a screening programme

total treatment costs for patients with advanced stages of cancer are not included, partly because of the difficulty of tracing such costs precisely, and determining which costs will be absent when the mix of cancer patients changes. Uncertainty about these cost figures can be considerable and is often the reason that they are not included. Furthermore, knowledge about the cost structure of a hospital at the diagnostic level is lacking in most countries or is of very poor quality, often being in reality only a 'guestimate'.

The relevant concept of cost, namely marginal cost, must be used, and costs must not be confused with expenditures—in some cases they are identical, but in other instances they differ. For instance, the 'cost' of drugs is rarely identical to the price that patients pay at the pharmacy, as there are considerable subsidies in most countries. Similarly, sickness benefits, i.e. transfers of money to patients who are unable to work, are not true costs owing to the fact that such transfers are an expression of redistribution, typically between ill and well people or between periods of good and bad health for people who would otherwise be active in the labour market. At a very concrete level, consider an increase in the weekly allowance for children. The family does not become richer: the money available has been redistributed; it is not a cost, but bread-winners probably consider it an expenditure.

Information on costs is combined with the results on the effectiveness ('benefits') of the screening programme in terms of health gains, i.e. increased survival and/or decreased morbidity. Depending on the specific procedure used, one of three different types of economic appraisal can be used.

TYPES OF ECONOMIC APPRAISAL

The basic structures of three common kinds of economic appraisal are shown in Figure 2. The figure should be read from the top left. A screening programme uses resources and (hopefully) in turn 'produces' health gains in terms of increased survival and/or decreased morbidity. The health benefits can be evaluated in three ways. A monetary value can be estimated for, e.g. increased probability of survival (additional years of life) or decreased morbidity; this method is fraught with difficulties [15]. Alternatively, a cardinal utility measure can be used [16, 17], similar to the utility construct used in clinical decision making [18]. Finally, no evaluation at all need be made, i.e. the units in which the health effects are measured are used directly. Combining costs and the three different ways of evaluating health gains results in three types of economic appraisal: cost–benefit analysis, cost–utility analysis and cost-effectiveness analysis.

In cost–benefit analyses, costs and health benefits are evaluated in monetary terms. The main result of this type of analysis is presented in terms of net benefits, i.e. by how much do the monetary benefits exceed costs? If the result is positive, the project should in principle be undertaken. Hence, a cost–benefit analysis assists in answering the question of whether the activity is worthwhile or, put differently, how much, in aggregate, society ought to be spending on better health.

In cost–utility analyses, health benefits are measured in terms of usefulness. The inherent difficulties associated with measuring changes in mortality and morbidity in monetary terms, i.e. the problem of cost–benefit analysis, and the need to evaluate

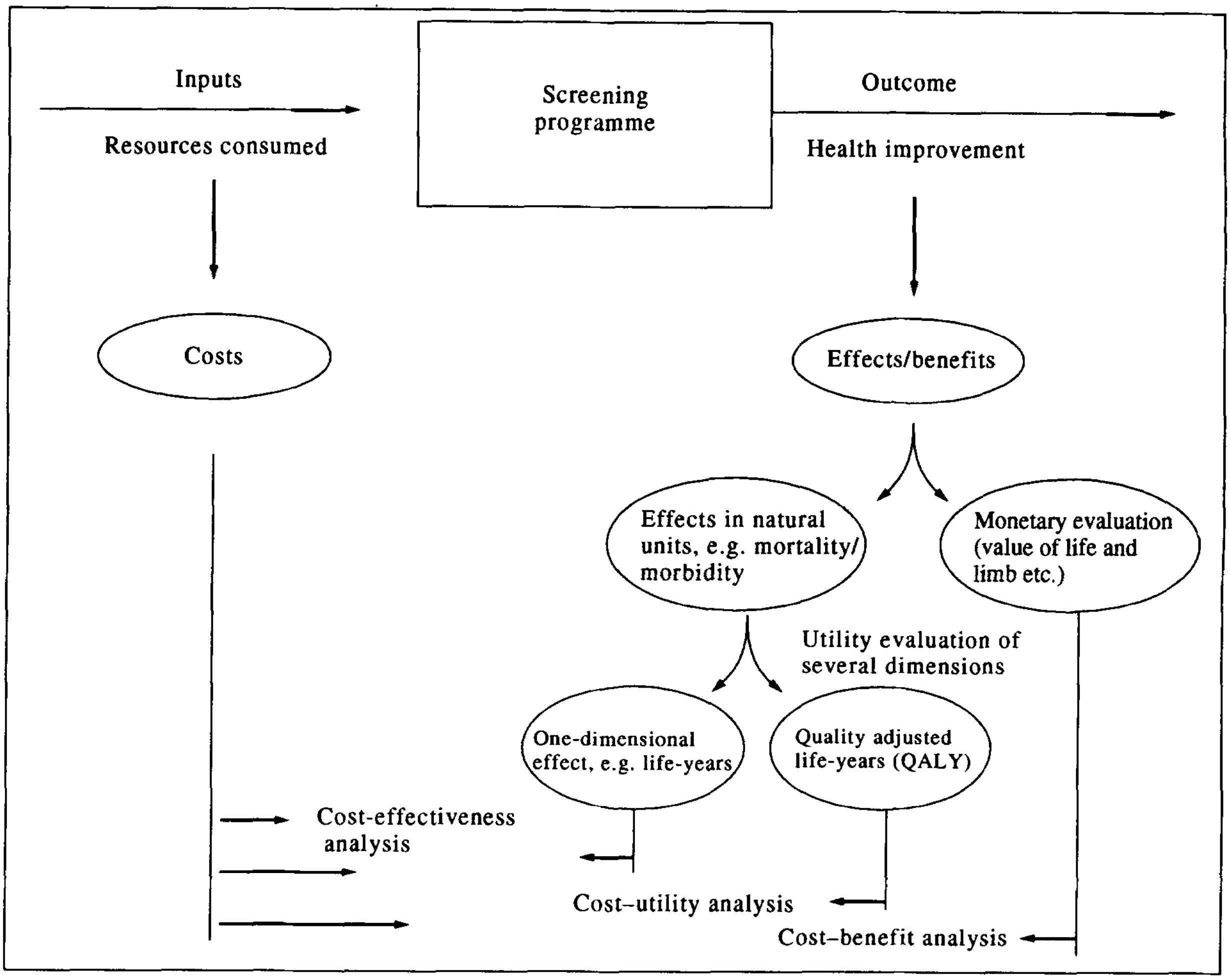

Figure 2. Three types of economic appraisal

the trade-off between quality of life (morbidity) and the length of life (mortality) led to the development of the concept of quality-adjusted years of life or healthy years equivalent [16, 17]. The main result of a cost–utility analysis is presented in thousands of Dkr per quality-adjusted year of life or per healthy years equivalent. In isolation, this number does not help decision makers much: it is of use only when information is available on alternative ways of organising the same activity or when the cost–utility ratio can be compared with those of competing programmes, e.g. other screening programmes or treatment options.

Whereas cost–benefit analyses address the general question of the social desirability of an activity, cost–utility analyses (and cost-effectiveness analyses, see below) address a much more limited problem: to achieve a given objective at least cost or to maximise a given output from a fixed budget. Whether the objective is worthwhile is not open to question.

Cost-effectiveness analyses differ from cost–utility analyses only with respect to the measure used. In a cost-effectiveness analysis, a one-dimensional measure is used, and there is no explicit evaluation of this measure. As for cost–utility analysis, the main results are typically presented in thousands of Dkr per year of life gained.

Different economic analyses answer different questions. For a decision maker, a cost–benefit analysis addresses the question of how worthwhile a health care project is—whether it should be undertaken at all. The only necessary condition is that the net result be positive. Cost-effectiveness and cost–utility analyses have a much narrower focus: assuming that it has been decided in principle that some kind of screening programme should be undertaken, what is the most cost-effective way of doing this, i.e. how can the highest effectiveness (health gain) be obtained per cost unit?

THEORETICAL BASES OF COST–BENEFIT, COST-EFFECTIVENESS AND COST–UTILITY ANALYSES

Without entering into the question in detail, it should be noted that cost–benefit analysis is based on a different economic theory than cost-effectiveness and cost–utility analyses. This explains why these analyses address different questions.

Cost–benefit analysis is based on (normative) welfare economics, in which one is concerned on normative grounds with how welfare is increased by allocating (scarce) resources according to certain principles [19]. Very few good cost–benefit analyses have been done in health care in general and in screening in particular, owing mainly to the inherent difficulty in practical use of a monetary evaluation of health. The term cost–benefit analysis is often used loosely by non-economists, as illustrated by example V in Table 1 [13], which is a cost-effectiveness analysis with several flaws.

Cost-effectiveness and cost–utility analyses are based on a much looser theoretical basis, the latter having a better theoretical foundation (found in the literature on expected utility: [16, 18, 20]), as it is based on reasoning with regard to utility.

These theoretical issues are mentioned only in passing to give the reader an idea of why economists have different opinions about the relevance and usefulness of cost–benefit, cost-effectiveness and cost–utility analyses, why they are executed differently and address different questions. The relevant economic theory provides answers to questions like: how to measure the monetary value of life, how to measure costs, whether to include 'saved pensions' or 'saved sickness pay', whether quality-adjusted years of life is a better measure of utility than healthy years equivalents. Readers with no background in economics often get the impression that the ever-increasing number of economic appraisals is based on a firmer practical and theoretical basis than is in fact the case. This situation is somewhat worrying in view of the fact that such analyses are gaining in importance.

SOME UNRESOLVED ISSUES IN COST–UTILITY ANALYSIS

The main feature of the utility side of cost–utility analysis is that separate (i.e. non-comparable) dimensions of changes in health status over time are combined into a single score, based on individual preferences, to generate a measure of quality-adjusted years of life or healthy years equivalents. Many cost–utility analyses are published, but there remain important, unresolved, theoretical and practical problems.

Any type of weighting to combine non-comparable dimensions involves judgement about who is to pass such judgements and how the weighting should be done. Who should be asked to evaluate quality of life and increased years of life? Should it be patients, their families, the general population (in a sample survey), politicians or professionals like doctors and nurses? In the Australian study mentioned in Table 1, groups of 40 women over the age of 40 and 60 women who had breast cancer were involved in the process of deriving utility weights. Are these the relevant groups? Similar questions could be asked about the Swedish and British studies shown in Table 1. In the British study [9], a weighting scheme developed in another context was adopted, and no attempt was made to make an explicit preference assignment or weighting for the study. The ratio based on quality-adjusted years of life in Table 1 is thus purely illustrative (as pointed out by the authors). This is often overlooked, however, and such illustrative numbers take on a life of their own—they become 'real'.

In view of the fact that cost–utility analysis is used for making decisions about the future use of resources for a screening programme which is to be put at the disposal of future users one could argue that the general population should be asked, by means of a sample survey, to estimate the relevant utility weights. If utility weights are elicited from physicians and nurses, their personal and professional judgements would be decisive but would not necessarily reflect the judgements of the general population or patients. We will leave the issue here, having pointed out a difficult problem that should be considered carefully [16, 20].

In principle, the relevant method for weighting increased years of life and, for instance, negative side-effects (quality of life) to get a utility measure like quality-adjusted years of life is based on the theory of expected utility. The literature is relatively uninformative, however, in practice. Several practical ways of carrying out the exercise have been developed, including the time trade-off method, standard gamble methods and category rating. These methods are not interchangeable [16, 21]: risk ('lottery') is an important part of the standard gamble method but not of the time trade-off or category scaling methods. Attitude and reaction to risk can also influence results obtained by different methods. Under certain conditions, the time trade-off method can be justified by the axioms of expected utility theory, as can the standard gamble method under more general conditions. This is not the case for category scaling.

Which method should be used? There is no 'correct' answer. The standard gamble method is preferable but is difficult to use in practice; category rating is relatively easy to use but theoretically suspect. As in much applied science, it is like sailing between Scylla and Charybdis. Similarly, framing and context of questions (description of possible health states) is known to influence respondents' answers heavily [20, 22]. The method of aggregating the preferences of a group of respondents is a further complicating problem [23]: should one simply calculate an average for the group or take the median or some other measure, or is there no 'correct' answer? Unfortunately, the latter is the case, but in practice the mean and the median are used.

It is not unusual to see utility weights developed in the U.S.A. applied to European studies or to another type of study. Even if the weights had been derived flawlessly, such procedures are wrong. U.S. judgements about quality of life do not necessarily coincide with European preferences. National utility weights must always be developed for specific national studies.

These unresolved issues emphasise the need to document cost–utility analyses carefully, so that readers can evaluate the quality of a study for themselves. The number of unresolved issues must not, however, discourage development of the use of utility measurement.

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To Screen or Not to Screen. How do we Decide on Which Cancer Screening Activities to Embark Upon?

J.D.F. Habbema and G.J. van Oortmarssen

THE PUBLIC HEALTH PERSPECTIVE

SCREENING, i.e. early detection before a clinical diagnosis is made on the basis of symptoms, has been proposed for cancers at many sites (see [1] for an overview). The goal of population screening is to reduce the burden of the cancer in terms of morbidity and mortality. In this respect, it is just one of several possible interventions and should be compared with the other alternatives: primary prevention, early case finding, treatment, rehabilitation and terminal care. In judging screening, however, adverse effects should be considered especially carefully, because inevitably a number of apparently healthy persons will be subjected to medical tests, and possibly to treatment, with no real long-term improvement in health or longevity.

The comparison should be based primarily on the favourable and adverse effects and risks of the interventions. In making choices about (re)allocation of funds between types of intervention, their costs should be weighted against their health effects. Cost-effectiveness analysis, cost–utility analysis and cost–benefit analysis are the methodologies which may be applied in investigating the decision problems [2–4]. A consideration that is often overlooked is that of (re)distribution of health over the population. For example, cervical cancer is typically a disease of women in lower socioeconomic strata, while breast cancer is one of the few examples of a disease that occurs more frequently in people in higher socioeconomic strata. In view of the present inequality in the distribution of health demonstrated in many countries, cervical cancer screening should deserve some extra attention, but also taking into account that it has a less favourable cost-effectiveness ratio than breast cancer screening.

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AN ILLUSTRATION OF BREAST CANCER SCREENING

Table 1 shows the predicted favourable and adverse effects of two-yearly breast cancer screening of women aged 50–70 years in the Netherlands [5]. Nationwide screening between 1990 and 2017 is expected to result in a reduction of 6000 breast cancer deaths and a gain of 16 500 years of life per million screening examinations.

Adjustment of the years of life because of changes in quality of life brought about by other effects of screening will have only a small impact: 16 000 quality-adjusted years of life would be gained.

Health effects should be considered in relation to the resources required for establishing those effects. For example, the total cost of 15.8 million screenings for breast cancer in the 27-year period will be 489 million ECU (1 ECU = 2.30 Dfl), i.e. 31 ECU per examination. These costs are partly compensated, since screening will result in a decrease in the costs of management of breast cancer (−249 million ECU), mainly because of the

Table 1. Favourable and adverse effects of breast cancer screening in the Netherlands: implications for differences in quality-adjusted years of life per million screening examinations (no discounting)

	Number	Quality-adjusted years of life
Screening examinations	1 000 000	− 115
Years of life gained	16 500	+ 15 700
Advanced and terminal cancer	1 080	+ 730
Lead time (earlier diagnosis)	17 500	− 500
Breast conserving therapy instead of mastectomy	750	+ 40
Others		+ 145
Total		16 000