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Institute for Quality and Efficiency in Health Care

Technical Document

Cost Estimation

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1 Basic Principles of Cost Estimation

1.1 Cost Definitions

1.1.1 Opportunity Costs

Opportunity cost is the basic theoretical cost concept in health economic evaluation [1-4]. It defines the value of scarce resources in the production of health care interventions. Opportunity costs refer to the benefit of resources from the next best alternative use. As is shown in micro-economic theory, opportunity costs are reflected in the market prices of a perfectly competitive market [2,5]. However, most markets in the health care sector are imperfect: prices are regulated by public institutions, or negotiated between associations of providers and payers, or even do not even exist, which means prices are often no adequate indicators of opportunity costs. For example, hospital charges may deviate from social opportunity costs if a hospital has a local monopoly or if it cross-subsidizes some interventions from others [4].

1.1.2 Marginal versus Average Costs

A basic decision in cost estimation is whether to base calculation on average cost or marginal cost [1,3,4,6,7]. Average costs are the costs per output unit, marginal costs are the extra costs when production is increased by one (infinitesimal) output unit, i.e., one additional patient treated or one additional (infinitesimal) unit of intervention produced (see Table 1). One difference between the assessment of average costs and marginal costs is that fixed costs (as buildings and equipment) are included in average costs, but are not considered in marginal costs. However, costs often increase more than proportionally when production output is expanded, and marginal costs will exceed average costs. For example, the extra cost of performing an additional operation in a hospital might be more than the average operation cost (for example, due to overtime premiums).

Which cost concept should be applied in cost estimation – average cost or marginal cost – depends on the specific research question. In general, health economic evaluation supports decision making on investment decisions (adoption, licensing or coverage of new technologies), which means that *long-term* costs (and effects) are relevant (in which all costs, including the short-term fixed costs, are variable). Moreover, the basic question in health

economic evaluation is what will be the *additional* costs (and effects) when output is slightly increased or decreased. Accordingly, the concept of *long-term marginal* cost is favoured in health economic evaluation.

Table 1: Definition of costs

Total costs	TC	All costs associated with the production of output *q* $TC(q) = FC + VC(q)$
Fixed costs	FC	Costs which do not vary with the production output q Example: building, equipment
Variable costs	VC	Costs which vary with the production output q Example: (personnel), material
Average costs	AC	Cost per output unit (at production level q) $AC(q) = TC(q)/q$
Marginal costs	MC	Extra costs associated with producing one extra output unit (at production level q) $MC(q) = dTC(q)/dq$
Incremental costs	IC	Cost difference between two intervention alternatives A and B $IC_{AB} = TC_A - TC_B$

Source: Kristensen [8, p. 147]

Nevertheless, it will usually be sufficient to estimate average costs. In the long term, when all resources are variable (including the short-term fixed costs: buildings, equipment and overheads), it can be assumed that providers of health care services will produce at an optimal plant size (or efficient scale, i.e., in the long-term average cost minimum where long-term marginal costs equal long-term average costs – and where long-term average costs and short-term average costs are equal, as is shown in micro-economic theory). Then average costs are a good predictor for long-term marginal costs. (It should be noted that the estimation of average costs is usually easier than the estimation of marginal costs.)

Innovations and/or regulative changes may induce shifts of capacity utilization, i.e., a large decrease in demand (and capacity utilization) for some health care services and a large

increase in demand (and capacity utilization) for others. Costs of adaptation to a new long-term equilibrium (with all short-termed fixed resources in a new optimal combination) are not usually calculated in health economic evaluation. Nevertheless, it is recommended to give a qualitative description and a rough estimation of short-term costs and adaptation costs if changes in (fixed) resource consumption are substantial [3].

1.1.3 Incremental Costs

Incremental cost is another fundamental concept in health economic evaluation [4,6,9]. The difference to the marginal cost concept is that incremental cost denotes the cost difference between two alternative technologies, while marginal cost relates to the extra costs of producing one extra (infinitesimal) output unit.

Thus, in the incremental cost concept, two discrete alternatives are compared. Sometimes, comparisons are between entirely different programmes (e.g., pharmaceutical intervention versus surgical intervention), sometimes they are between different intensity levels of one programme (e.g., different doses of a pharmaceutical). In the case of different intensity levels, there is no clear differentiation between incremental costs and marginal costs in the literature. For example, in a multi-test screening programme for colon cancer [10], some authors denote costs of an additional test marginal, while others term it incremental [4,11]. According to the above definition, the example describes incremental comparisons. Incremental cost refers to the intervention alternatives compared in health economic evaluation studies and forms part of the core result of a health economic evaluation, the incremental cost-effectiveness ratio.

1.2 Perspective of the Economic Analysis

Health economic evaluation can be performed from different perspectives, e.g., the societal perspective, the payers' perspective or the providers' perspective [1,3,4,6,7,9,12-14]. The perspective of an economic analysis determines the entire process of cost estimation: not only identification of the relevant resource consumption (expenses or opportunity costs from a specific perspective), but also quantification and valuation of the identified resource consumption (see Chapters 2 and 3).

According to the Social Code Book V, an economic evaluation must be performed from the perspective of the citizens insured by the Statutory Health Insurance (SHI). This definition is

not unambiguous and allows for a certain range of perspectives from SHI perspective to societal perspective. The range includes (1) the SHI perspective, (2) the combined SHI plus patients' perspective, (3) extensions to other social insurances (Statutory Long-term Care Insurance, Statutory Pension Insurance, Statutory Accident Insurance) and public sectors, (4) societal perspective (Table 2). The societal perspective is the broadest perspective. All costs are included, regardless of who will incur them: statutory health insurance, other social insurances and public sectors (e.g., incapacity to earn an income, education in special schools for hearing-impaired children), the patients and their families (e.g., time and travel expenses), or the rest of the society (e.g., production losses). In contrast, the SHI perspective is restricted to expenses of the SHI (for health care services and sick pay, but also loss of revenue is considered).

Table 2: Perspectives

<table>
<tr><th colspan="4">Perspective</th><th>Cost categories</th></tr>
<tr><td></td><td rowspan="5">Public sectors</td><td rowspan="2">Social insurance</td><td>Statutory Health Insurance</td><td>Transfers</td></tr>
<tr><td rowspan="6">Society</td><td>Direct health care costs</td></tr>
<tr><td rowspan="5"></td><td>Costs to other social insurances</td></tr>
<tr><td rowspan="2"></td><td>Costs to other public sectors</td></tr>
<tr><td rowspan="2"></td><td>Direct costs to patients and their families</td></tr>
<tr><td>Time costs to patients and their families</td></tr>
<tr><td></td><td></td><td></td><td>Productivity costs</td></tr>
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Source: Adapted from CADTH [13], Kristensen [8, p. 146]

The perspective of an economic evaluation will be defined according to specific research question. Though it might be possible to extend the perspective including the societal perspective.

In the following chapters, at first the societal perspective (Chapter 2), and subsequently the perspective of the Statutory Health Insurance (Chapter 3) will be discussed in more detail. The structure of the next chapters follows a deductive approach, deriving the specific perspective (Statutory Health Insurance) from the general perspective (society).

1.3 Time Horizon for the Cost Estimation

The time frame should be long enough to capture all, for the decision on reimbursement, relevant cost differences (and outcome) differences between the programmes compared in the health economic analysis. For chronic conditions, a time horizon spanning a lifetime is possibly required (particularly if lifespan gains are expected) [1,4,9,13,15]. However, the time horizon in cost estimation should not exceed the time horizon in outcome estimation.

Often, the appropriate time horizon exceeds the available primary data (from prospective studies), because prospective studies mostly examine intermediate outcomes. Thus, it is appropriate to use several time horizons in economic evaluations: a short-term analysis that is based only on data from prospective studies and a long-term analysis that includes modelled data [9,16].

1.4 Cost Classification in Health Economic Evaluations

1.4.1 Cost Classification from the Societal Perspective

From a societal perspective, costs in health economic evaluations are commonly classified into [1,3,4,9,13,16,17]:

- direct medical costs (or direct health care costs);
- direct non-medical costs (or direct non-health care costs); and
- indirect costs (or productivity costs).

Direct costs refer to the resource consumption in the provision of health care interventions. They encompass the entire current resource use (e.g., the costs of a mammography screening programme) as well as future resource use attributable to the programme (e.g., validation of test results and diagnostics, costs or cost savings associated with breast cancer or prevented breast cancer). Future costs can span a lifetime in some indications.

Direct costs are differentiated into direct medical and direct non-medical costs. Direct medical costs refer to the resource consumption in the health care sector associated with the production of health interventions. Resource consumption includes, for example, the costs of hospital stays, outpatient visits, pharmaceuticals and devices. Direct non-medical costs refer to resources supporting the medical production in the health care sector. These are, for example, transportation costs to medical interventions, child care costs for an ill parent, time of patients in the co-production of medical interventions, and time of family members (or volunteers) in informal care for ill or disabled patients.

Indirect costs denote the production losses due to

- unfitness for work (in the case of illness);
- early retirement/incapacity for work (in the case of long-term illness or disability);
- premature death.

In the literature, there are controversial opinions whether morbidity costs (due to unfitness for work or early retirement) should be presented on the cost side or on the outcome side of a cost-effectiveness ratio. The US Panel on Cost-Effectiveness in Health and Medicine [18] advocates integrating productivity costs into a quality-of-life measure (which implies consideration of production losses on the outcome side) [3]. However, the literature predominantly recommends consideration of production losses on the cost side [4,13,19-21].

Concerning mortality costs (due to premature death), the literature agrees not to present those production losses on the cost side when mortality is also considered on the outcome side (e.g., through QALYs or life years gained), as otherwise double-counting would occur – at least in part (as far as the individual is concerned). However, costs to the rest of the society (represented by loss of taxes and contributions to social insurance) must be considered on the

cost side [21]. For more details on morbidity costs and mortality costs see Sections 2.1.4 and 2.3.3.

Drummond et al. [22] suggested an alternative cost classification from the societal perspective: (1) resource use in the health care sector, (2) resource use in other sectors, (3) patient and family resources, (4) productivity losses. In this alternative classification, cost implications for other sectors (e.g., education in special schools for hearing-impaired children) are explicitly considered by separating non-medical costs into resource consumption in other sectors and costs to patients and their families. A problem of this alternative classification is that cost categorization is partly based on expenses and not on social opportunity costs. In particular, this is true for patients' co-payments.

1.4.2 Intangible Costs

A cost category used in the past, but seldom nowadays, is that of intangible costs. These costs refer to items difficult to measure and value in cost terms, e.g., pain and suffering associated with a treatment. However, parts of intangible costs are actually not costs (i.e., no resources are denied to alternative uses), and overall they are not strictly intangible, as they can actually be valued through quality-of-life measures (through generic or disease-specific instruments to measure quality of life), or willingness-to-pay (an approach that will not be pursued in this technical document) [4]. In summary, intangible items should be reported on the outcome side.

1.4.3 Insured versus not Insured Costs

The classification into insured and not-insured costs is perfectly suited to a combined SHI plus patients' perspective in health economic evaluation. Insured costs are covered by the Statutory Health Insurance, while not-insured costs accrue to the patients and their families. Insured costs encompass in particular expenses for health care services, but also – in the German health care system – sick pay and contribution losses after a defined period of unfitness for work. Not-insured costs to patients and their families are, for example, out-of-pocket expenses and co-payments for pharmaceuticals, devices and physician visits, moreover time costs and loss of net income due to illness.

2 Processing Cost Estimations from a Societal Perspective

Cost estimation is based on a four-step process:

- identification of the relevant cost items;
- measuring resource use;
- valuation of resource units;
- calculating total costs of the intervention alternatives.

In principle, all four steps could be integrated deriving total costs in a single step. However, the four-step process is recommended because executing separate steps is more likely to support comprehensive cost estimations [3] (although sometimes collecting cost data is easier than separating into quantification of resource use and valuation of unit costs).

As mentioned above (Section 1.2), the perspective of an economic analysis determines the entire costing process. Following a deductive approach, the processing of cost estimations is presented first from the societal perspective (Chapter 2) and then from the perspective of the Statutory Health Insurance (Chapter 3).

2.1 Identification of Resource Consumption

2.1.1 Methods for the Identification of Resource Use

A comprehensive identification of cost items relevant to the intervention alternatives should be generated [1,4,13], even if not all cost items are finally measured and valuated, for example, because some cost items only have a minor impact on total costs, or on the cost difference (cost increments) between the intervention alternatives (see Section 2.2.1). An overview of common resource items in health economic evaluations is listed in Table 3.

The identification of the relevant resource inputs starts with the description of the production function of the health care intervention [1,3]. The production function combines knowledge of the intervention alternatives, the natural course of the disease, impact of treatments on the disease (including productivity changes) and the interactions of patient subpopulations and the health care system.

Table 3: Items of resource use in health economic evaluations

Cost categories	Resource consumption
Direct medical costs	Outpatient visits - general practitioner - specialist Procedures and diagnostics - tests - diagnostic imaging - surgical interventions Pharmaceuticals Physiotherapy Medical devices Hospital stays Rehabilitation Services - home care - nursing care
Direct non-medical costs	Patient time - in treatment - in health activities - time expenditure due to illness Informal care

(continue)

Table 3: Items of resource use in health economic evaluations (Continue)

Cost categories	Resource consumption
	Services Devices and investments Transportation
Indirect costs	Reduced work productivity Sick leave / unfitness for work Early retirement due to illness Premature death

Source: Adapted from Kobelt [14, p. 31]

Developing a decision tree of the therapeutic pathways which contains all relevant downstream events is recommended to ensure a broad identification of resource consumption [23]. Sources of information on relevant resources and production function will include [24]:

- review of studies;
- textbook knowledge of the disease course and treatment alternatives;
- guidelines,
- administrative and accounting data (e.g., data of sickness funds and private health insurances);
- expert opinion.

2.1.2 Intervention Costs, Follow-up Costs and Cost Offsets

In health economic evaluations, a mere comparison of technology costs between new and existing health technologies is not sufficient. New technologies are frequently more cost-intensive than existing health technologies, which is particularly true for pharmaceuticals.

However, in general, health interventions not only differ in mere technology costs, but also in their impact on (follow-up) costs for other health care services (and, of course, on health effects). Thus, the increased cost of a new technology may be offset by savings in other health care sectors. Cost offsets will be achieved when the new technology (e.g., new drug A) results in a cost reduction for other health care services (e.g., hospital stays and outpatient visits) compared to the alternative technology (e.g., existing drug B).

Thus, as mentioned above (Section 1.3), it is necessary that the time frame of health economic evaluations is long enough to capture all relevant cost differences (and outcome differences) between the programmes compared in the health economic analysis. For chronic conditions, a time horizon spanning a lifetime might be required (particularly if lifespan gains are expected).

If a cost-offset claim is obtained in a decision model extrapolating the clinical effects from a randomized controlled trial (by using, for example, observational studies), the impact of the cost offset should be investigated in comprehensive sensitivity analyses.

2.1.3 Future Costs (Costs in Life Years Gained)

In health economic literature, a differentiation is often suggested between

- related versus unrelated costs, and
- costs in normal life years versus costs in life years gained [1,2,4].

Health economic guidelines agree that cost estimation in normal life years can be limited to related costs (i.e., costs for diseases related to the intervention). The rationale is that unrelated costs in normal life years should be identical for all intervention alternatives assessed in an economic analysis and therefore can be neglected in incremental cost-effectiveness analyses [1,2,4]. Differences between treatment arms are only accidental. Thus, the neglect of unrelated costs will reduce estimation errors. On the other hand, it should be ensured that neglected costs are, in fact, unrelated.

Future costs may be subdivided into (1) related health care costs, (2) unrelated health care costs and (3) net consumption of a patient (consumption minus production) in added life years. Most authors agree that related costs in added life years (related future costs) should be

included in health economic evaluations [1,2,4]. For example, a cholesterol-lowering intervention may expand lifespan. Then, costs of the lifelong medication (including treatment of side effects) and costs of cardio-vascular diseases occurring during the added life years will be included in the cost estimation.

The inclusion of unrelated health care costs is more controversial [1-4]. On the one hand, future costs are a direct consequence of life-prolonging interventions. On the other hand, life-prolonging technologies (e.g., hypertension screening) are not linked with future therapeutic decisions (e.g., chemotherapy for advanced stages of cancer).

Garber and Phelps [2] show that, under certain assumptions, the inclusion of unrelated cost does not change the ranking of incremental cost-effectiveness ratios (cost per life year gained). For all interventions, the cost per life year gained will increase by a fixed amount. Thus, accepting the (somewhat restrictive) assumptions of the Garber-Phelps-model, inclusion or exclusion of unrelated cost does not matter. In contrast, Meltzer [25] argues (based on a less restrictive model) that all unrelated future cost, including impact on the individual's production and consumption, should be considered in health economic evaluations. Only then, will decisions consistent with lifetime utility maximisation be taken.

Weinstein and Manning [26] indicate that both models adhere to welfare economics and that a decision-maker's approach, in contrast, leaves more degrees of freedom to the analysis (which allows both, inclusion or exclusion of unrelated costs). Similarly, most guidelines leave it to the individual analyst, whether or not to include unrelated health care costs [1,4,23,27].

Summing up the controversial discussion on future costs, the recommendations are twofold

- In a base case, only related future costs should be considered.
- In sensitivity analyses, (1) total health care costs (i.e., related and unrelated health care costs) in life years gained and (2) total future costs (including net consumption of the patient) should be calculated. Age- and gender-specific data on average health care costs are most appropriate, when health care costs in added life years are calculated.

2.1.4 Time Costs

Diseases, in particular chronic diseases, often tie up a substantial part of patient time. As presented above (see Table 3) patient time is spent in treatment (including travel and waiting time) and their own health activities (particularly in chronic diseases), or time expenditures arise due to illness (e.g., when a patient is confined to bed). Similarly, family and volunteers spend time caring for the patient. Thus, patients and volunteers forgo other activities (i.e., opportunity costs arise). Time costs encompass parts of the direct non-medical costs (patient time and informal caregivers' time) and indirect costs (productivity losses).

Measurement and valuation of time expenditures may depend on the activities given up:

- paid work (production losses);
- unpaid work (e.g., house work or voluntary activities outside the home);
- leisure.

Concerning paid work, opinions differ as to whether production losses due to unfitness for work or early retirement ("morbidity costs") should be presented on the cost side or on the outcome side of a cost-effectiveness ratio (see Section 1.4.1). The US Panel on Cost-Effectiveness in Health and Medicine [18,28] advocates integrating productivity costs into a quality of life measure (which implies consideration of production losses on the outcome side) [3], assuming patients will consider loss of income due to illness in their quality of life.

However, the large majority of the literature recommends consideration of production losses on the cost side [4,13,19-21,29]. It is argued that the usual quality-of-life approaches focus on pure health effects. None of the existing quality-of-life instruments ask patients to consider income effects due to inability to work [30], rather, the Health Utility Index (HUI), a widespread quality-of-life instrument, asks individuals actively to ignore income effects [31]. Moreover, for the German context (with substantial sickness benefits), unfitness to work is associated with only partial income losses, which means that consideration of income losses due to unfitness for work would only have a minor impact on quality of life estimates. Thus, it is recommended to present production losses due to inability to work on the cost side.

The literature agrees not to present production losses due to premature death ("mortality costs") on the cost side when mortality is also considered on the outcome side (e.g., through QALYs or life years gained), as otherwise double-counting would occur, as far as the individual is concerned. However, costs to the rest of the society (loss of taxes and contributions to social insurances) must be considered on the cost side [19,21,30].

Unpaid work (e.g., housework or voluntary activities outside home) will be treated like paid work, i.e., mortality costs will be presented on the outcome side (through QALYs or life years gained) and morbidity costs on the cost side, although valuation may be different (see Section 2.3.3). In contrast, the literature recommends that the patients' lost leisure time should be considered on the outcome side, when a quality-of-life measure is included in health economic studies [1,19,28,32]. It is expected that patients consider effects on leisure time in quality-of-life estimates. Where possible, patients should be instructed to value loss of leisure in terms of quality of life. Nevertheless, as it is not certain that lost leisure is considered in quality of life estimates (especially when a representative population sample is valuating health states), sensitivity analyses with presentation of lost leisure time on the cost side should be conducted (when no quality-of-life measure is utilized in health economic studies, costs of lost leisure should be presented on the cost side anyway). Moreover, as informal caregivers' quality of life is definitely not considered in health economic evaluations, their lost leisure time should be calculated on the cost side. It is conceded that, in most applied studies, impact on patients' and informal caregivers' leisure time is not considered.

2.2 Quantification of Resource Use: Micro-costing versus Macro-costing

For cost estimations, there is a range of costing approaches with micro-costing and macro-costing defining the ends of the range [1,3,4,6,13,32]. In macro-costing, composite intermediate products and services (e.g., inpatient days) are identified and measured. Micro-costing, on the other hand, starts with a detailed identification and measurement of services (e.g., a hospital stay split into components like consultation, operation, medication, diagnostics, nursing, housing, food, cleaning, overheads, etc.), and determines the required resource use (personnel, material, equipment, building, overheads etc.). Hospital costing is given as an example for different precision grades of costing in Figure 1.

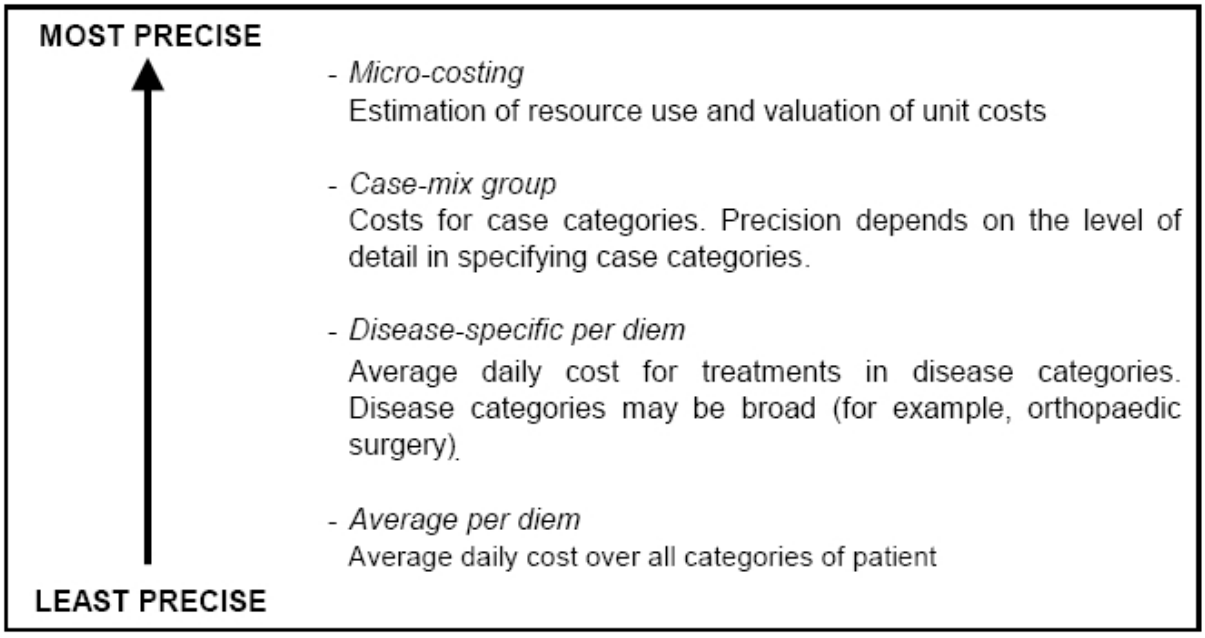

Figure 1: Grades of precision in hospital costing. Source: Drummond [22, p. 71]

The grade of precision required in an economic analysis is an important determinant for the selection of costing methods. It determines the entire process of identification, quantification and valuation of the resource consumption [1]. Factors influencing the precision of cost estimations are:

- cost of products and services;
- frequency of utilization (or probability of occurrence): products and services that are cost-intensive and often utilized (by nearly all patients) should be measured in a micro-costing approach;
- time in the course of a chronic disease: for events in the far future, macro-costing may be sufficient due to the impact of discounting;
- variations between patients: when cost variations are small between patients, macro-costing may be sufficient (e.g., a hospital ward with a relatively homogeneous production);
- variations between intervention alternatives: similarly, when cost variations are small between adjuvant and follow-up intervention, macro-costing will be sufficient [24].

Both costing approaches are often combined in a health economic analysis: The micro-costing approach is used for resource consumptions that are central to the health economic analysis, whereas resource consumptions that are less central will be determined by the macro-costing approach [6]. In general, costs of the intervention alternatives assessed in the economic analysis will be derived in a micro-costing estimation.

An (often implicit) assumption in micro-costing is that the cost estimates (derived from one or several locations) are representative for the entire system [3]. This assumption should be verified. For macro-costing, deviations from the true societal opportunity costs will often occur when valuation is based on regulated “prices” [1]. Macro-costing data may be robust against geographical and institutional variations [3].

Again, as for the identification of resource consumptions (see Section 2.1.1), a decision tree of the therapeutic pathways is useful to differentiate into central and less central cost items. Sources of information on the required precision of cost estimations will include [13,24]:

- studies and reviews;
- clinical practice guidelines;
- administrative and accounting data (e.g., data of sickness funds and private health insurances);
- modelling exercises (combining data from various sources);
- (expert opinion).

2.3 Resource Valuation

2.3.1 Valuation of Health Care Services

Cost estimation in health economic evaluations should reflect societal opportunity costs. As mentioned above (Section 1.1.1), prices of perfectly competitive markets indicate opportunity costs. However, most markets in the health care sector are imperfect as prices are regulated by public institutions (e.g., Uniform Value Scale for outpatient services and DRGs for inpatient services), or negotiated between associations of providers and payers (e.g., outpatient and inpatient budgets).

In micro-costing, quantification is based on the resource utilization (personnel, material, equipment, building, overheads, etc.) for health care services. As most resources are negotiated on competitive markets, it is recommended to take resource prices for valuation.

Also, when cost estimation is focussing on medical procedures (e.g., examination, lab test, diagnostic imaging), it is recommended using market prices, if available, unless there are good reasons for adjustment to societal opportunity costs [4,13]. Reasons for adjustment to opportunity costs are as follows:

- Market prices do not cover all costs. An example is, if investment costs are financed separately. German hospital prices (DRGs) do not include investment costs but these are financed by the federal states. Thus, an adjustment is justified, as in, for example, a mark-up for the estimated capital (i.e., equipment and building) utilization (see Section 2.3.5).

- Excess profit is observed in a health market. A common adjustment is the determination of cost-to-charge ratios to remove excess profits [4,13].

- Different prices exist for identical services, depending on who is paying (e.g., sickness funds, Statutory Accident Insurance, private health insurances). For example, in Germany, physician fees for ambulatory health care services differ between Statutory Health Insurance (based on Uniform Value Scale) and private health insurances (based on Medical Fee Scale), with higher compensations in private health insurance. Assuming that on average physicians earn a fair income (compared to other professions), a weighted average fee could be applied (see Section 2.3.5).

- Prices only form a charging unit, independent of actual resource use (e.g., costs per inpatient day) and/or substantial cross-subsidisation is observed.

When macro-costing methods are applied (focussing on composite intermediate products and services, such as inpatient days), similar adjustments to societal opportunity costs can be justified (but may be less urgent, since less precise cost estimates are accepted in macro-costing due to the minor impact on incremental costs).

2.3.2 Valuation of Pharmaceuticals

The difference between market price and societal opportunity cost is probably largest for patent-protected pharmaceuticals. Innovative pharmaceuticals require substantial investment for research and development (R&D) which must be refinanced as long as the pharmaceutical is patent-protected. During the period of patent protection the pharmaceutical enterprise may set monopoly prices. Thus, during the period of patent protection market prices will be clearly above social opportunity costs.

Estimating opportunity costs for innovative pharmaceuticals is difficult due to enormous information requirements. First, it should be decided whether long-term or short-term opportunity costs should be referred to [3,33]. As mentioned above (Section 1.1.2), health economic evaluations commonly support decision making on investment decisions, which means that *long-term marginal* costs will be favoured. However, in the literature on pharmaceutical opportunity costs, both approaches, short-term and long-term marginal costs are discussed [3,33].

In the short term, only costs of production and distribution of the pharmaceutical will be considered. A substantial part of total costs to society will not be included, i.e., R&D investments, which are fixed costs (and thus sunk costs) in the short-term. In long-term decisions R&D investments are part of social opportunity costs. R&D costs should be allocated to the periods of the pharmaceutical's life expectancy. Allocation of R&D cost could be performed, applying for example a user cost of capital approach.

Another problem from a national societal perspective is which part of R&D investment should be borne by a specific country (or: how R&D costs should be allocated to different

countries). Possible approaches might be: (1) the (expected) country's share on the global market of the specific drug, or (2) the country's willingness to pay for the specific drug

Recommendations for the valuation of pharmaceuticals are as follows:

- A rough estimation of long-term opportunity costs (on the basis of "market shares") might be performed.
- For other pharmaceuticals (other than the intervention and the comparator technologies of the health economic evaluation), adjusted market prices will often be sufficient for the estimation of opportunity costs as (1) the impact on total and incremental costs might be lower and (2) for non-patented pharmaceuticals, the difference between market price and opportunity cost might be small(er).
- In the case of considering R&D costs, those should be reported separately. In addition, an analysis without considering R&D costs should be conducted.

2.3.3 Valuation of Lost Time

Valuation of time expenditures depends on the activities given up due to illness (see Section 2.1.4):

- paid work (production losses),
- unpaid work (e.g., house work or voluntary activities outside home) or
- leisure.

As delineated above (Section 2.1.4), lost time at paid and unpaid work (due to inability to work) should be presented on the cost side, while loss of leisure time should be presented on the outcome side (should a quality-of-life measure be included in health economic evaluations). However, in sensitivity analyses, valuation of lost leisure time on the cost side is feasible. Moreover, lost leisure time of informal caregivers is in principle be valuated on the cost side (if it is valuated in applied studies at all).

For the valuation of productivity costs, there are two fundamental methods, the human capital approach and the friction cost approach. The human capital approach (HCA) suggests that

health care interventions are a kind of investment in an individual's human capital (similar to education). HCA rests on neoclassical theory of the firm. According to neoclassical theory, profit-maximising firms expand their labour input until marginal revenue product of labour equals unit labour costs (gross wage plus payroll-related costs), assuming diminishing marginal productivity of labour. Thus, according to the human capital approach (HCA), valuation of production losses is based on labour costs. All future productivity losses (up to retirement age) will be considered in HCA.

The friction cost approach (FCA) was developed to overcome some unrealistic assumptions of the HCA, particularly the assumption of perfectly competitive labour markets, which implies the existence of full employment (in contrast to the empirical experience of substantial unemployment in many countries) [34,35]. FCA suggests that, for long-term incapacity for work, costs of production loss are limited to a "friction period", i.e., until a patient is replaced by a previously-unemployed individual and the former production level is restored (whereby time is needed to search for and train the previously-unemployed person). Costs in the FCA encompass production loss in the friction period and transaction costs (searching for and training the previously-unemployed individual). Concerning short-term unfitness for work (within the friction period), FCA argues that part of the workload might be performed by colleagues of the patient or made up by the patient upon his/her return to work. Thus, short-term production losses might be less than labour costs (according to HCA). Empirical studies in the Netherlands found that short-term costs are about 80 percent of labour costs [34].

Thus, the cost difference between HCA and FCA may be small for short-term absence from work but will increase markedly for long-term absence from work as HCA considers all future productivity losses, whereas FCA is limited to the friction period.

There is an ongoing debate in the literature whether HCA or FCA is better to represent productivity costs [34,36-38]. As mentioned above, the human capital approach rests on some unrealistic assumptions (particularly full employment in the labour market). HCA shows potential rather than real production losses. In contrast, FCA is focussed on real production losses. Nevertheless, FCA has been criticized, too. In particular, the assumption of zero opportunity costs of labour after the friction period has implications for the calculation of direct medical costs. Then, it is argued, opportunity costs of labour inputs in health care are

nearly zero, too, because health care workers could be replaced by a previously-unemployed individual at nearly zero cost as– only transaction costs for searching for and training the previously-unemployed individual would accrue [19,38]. Furthermore, the FCA implicitly assumes that the previously-unemployed individual valuates opportunity costs near to zero. If that were true, the unemployed would work at a wage slightly above unemployment benefits – a behaviour that is not often found empirically.

An advantage of HCA from an economic point of view is, that it can be transferred to unpaid work and leisure (see below), while FCA is limited to paid work. Thus, with HCA, all components of time costs are derived from a common cost concept. Moreover, in contrast to FCA, the human capital approach is based on economic theory. In conclusion, it might be argued that HCA is overestimating and FCA is underestimating opportunity costs of paid work. Thus, sensitivity analyses are recommended. Base case should be the human capital approach.

As mentioned above, the human capital approach can also be applied to unpaid work (including informal caregiving) and leisure time. Individuals' time can alternatively be allocated to either paid work or leisure (and unpaid work). As is shown in neoclassical consumer theory, individuals will expand their paid working time until the marginal benefit of leisure (and unpaid work) equals the net wage rate (or the marginal consumption foregone that could have been financed by the net wage rate from an additional paid work hour). Thus, opportunity costs of leisure and unpaid work is the net wage rate.

An alternative method for the valuation of unpaid work, replacement cost estimate, is based on the market price (i.e., gross wage rate) of, for example, housekeeping or nursing care professionals (depending on the unpaid activities). It should be noted that informal work is often less efficient than formal work (e.g., more time might be taken due to lack of training). Thus, replacement costs might overvalue unpaid work.

In the literature, it is assumed that opportunity costs generate a lower bound and replacement costs an upper bound estimation of unpaid work. Otherwise it would be expected that individuals buy in the services rather than produce it themselves [21]. In the base case opportunity costs of leisure should be determined. In a sensitivity analysis the replacement cost approach might be applied.

In health economic analyses, valuation of lost time could be based on individual labour costs, i.e., gross wage rates plus wage supplements (in Germany, employer contributions to social insurance) or, alternatively, average labour costs. In the literature, age-sex adjusted wage rates are also suggested. In the base case average labour costs should be determined.

2.3.4 Inflation and Discounting

Health economic evaluation studies often require a long time horizon to capture all relevant cost and outcome differences between the programmes compared. Thus, different timing of costs is usually observed.

When price data utilized in health economic evaluations come from different time periods, adjustments to inflation should be performed. In principle, health care specific inflation rates should be applied. As these specific inflation rates are not available for most health care services in Germany, it is recommended to use the general price index for the national economy (published by the Federal Statistical Office).

There is a broad consensus in the literature that costs (and outcomes) should be discounted to their present value to adjust for differential timing [4,39,40]. Discounting reflects the positive time preference of individuals, i.e., individuals prefer present to future benefits, as it leaves more options.

Reasons for a positive time preference are:

- diminishing marginal utility of consumption, combined with expected increasing future incomes (assuming positive economic growth);
- risk of lifespan, i.e., risk whether future consumptions will be available.

As is shown in neoclassical theory, assuming perfect markets with certain information about the future (i.e., no risk) and absence of taxation, the time preference will equal the market interest rate (i.e., the opportunity cost of capital), thus indicating the social discount rate. Individuals will only forgo present consumption, if future consumption (based on investment) exceeds present consumption.

The proper discount rate is controversial. Often 5 or 3 percent are suggested in international guidelines (both for costs and outcomes) [41]. Also, it is often argued that the real interest rate of low-risk long-term government bonds is a good indicator for the social time preference. In this case, the discount rate would oscillate at around 3 percent [39,42,43]. Thus, in the base case, a discount rate of 3 percent is recommended. Sensitivity analyses should apply 0 and 5 percent [4,13].

2.3.5 Potential for Standardization

To improve comparability of health economic evaluations, standardization of costing methods is recommended, including the development of standard cost lists. Countries like Australia [44], Canada [23,45] and the Netherlands [32,46] have presented standard cost lists that supplement guidelines for health economic evaluation. Standard cost lists present average valuations for common services and resource consumptions.

In the Netherlands, for example, hospital costs (cost per inpatient day, differentiated between general and academic hospitals), physician visits to general practitioners and specialists (costs per visit), valuation of medical staff time, costs of paid work (including friction period), costs of unpaid work and travel costs are determined.

Similarly, in Germany, the working group “Methods in Health Economic Evaluation” (AG Methoden der gesundheitsökonomischen Evaluation – AG MEG) of the German Society of Social Medicine and Prevention has derived standard costs for the most important health services and resource consumptions [47]. Examples for standard costs are presented in Table 4.

Table 4: Standard costs (2002)

	Standard cost (EUR)
Inpatient days[1]	Costs per day
Internal medicine	284
Surgery	329
Gynaecology	344
Paediatrics	363
Psychiatry	260
Intensive care	908
Average inpatient day	380
Ambulatory practice visits[2]	Costs per visit
General practitioner	15.24
Internist	32.92
Cardiologist	58.75
Gynaecologist	25.56
Paediatrician	18.19
Radiologist	79.43
Psychiatrist	14.60
Average physician visit	21.89
Physiotherapist visit	14.34

(continue)

Table 4: Standard costs (2002) (continue)

	Standard cost (EUR)
Paid and unpaid work	Costs per day/hour
Labour costs[3] (per working day)	156
Friction costs[3] (per working day)	125
Friction period[3] (calendar days)	72 days
(Adjusted) net wage rated (per hour)[4]	17.80

Source: Based on Krauth et al. [47]

Notes on the calculation of standard costs

1 Inpatient costs contain running costs (financed by SHI or private health insurance) and capital utilization costs (financed by the federal states). Capital utilization costs are modelled based on investment costs for new hospitals, assumptions about life span and utilization rates of equipment/buildings and assumptions about the proper interest rate.

2 Costs per physician visit are a weighted average of SHI and private insurance costs (with higher compensations in private health insurance). The calculation is based on the assumption that, on average, physicians earn a fair income (compared to other professions).

3 Labour costs encompass gross wage plus employer contributions to social insurance. The calculation of average labour costs per day is based on the weighted average labour costs of full-time and part-time working individuals in Germany. Friction costs are assumed to be 80 percent of labour costs (as in the Netherlands). The friction period was derived from an enterprise survey on job vacancies [48].

4 The (adjusted) net wage rate is the opportunity cost to unpaid work (see Section 2.3.2). It includes contributions to Statutory Pension Insurance and Statutory Unemployment Insurance, as these insurances show characteristics of income, in contrast to Statutory

Health Insurance, which is merely based on the ability-to-pay principle (Krauth et al. [47], and similarly Posnett and Jan [49]).

The literature assumes that a weighted average price of inpatient and outpatient prices might be a good predictor for opportunity costs of pharmaceuticals [47]. As no information on inpatient sales and prices is available, an adjusted outpatient price was recommended. This could be, for example, pharmacy price net of discounts and rebates to sickness funds. Rebates are now substantial in the German health care system as rebate contracts between pharmaceutical enterprises and sickness funds are promoted by the legislator. An alternative might be to calculate the average price of the three lowest priced pharmaceuticals of a reference price group.

3 Processing Cost Estimation from the Perspective of the Statutory Health Insurance

As mentioned above (Section 1.2) a certain range of perspectives, from SHI perspective to societal perspective, is compatible with the definition in the Social Code Book V (perspective of the citizens insured by the Statutory Health Insurance). In Chapter 3, the processing of cost estimations from the perspective of the Statutory Health Insurance is presented.

3.1 Definition of the SHI Perspective

Measurement and valuation of resource use is determined by objectives of the Statutory Health Insurance. For example, the objectives of a single sickness fund (acting in a competitive insurance market) and the objectives of the SHI system at large might have different implications for expense estimation (for more details see Krauth et al. [47]).

In this technical document, the SHI system perspective (based on the legal mandate of the Social Code Book V – SGB V) is applied. Among other specifications, the efficiency demand of the SGB V states that health care services, provided for persons insured by sickness funds, are adequate, sufficient and efficiently produced.

3.2 Identification of Resource Consumption

3.2.1 Classification of Expenses from the SHI Perspective

The SHI perspective differs from the societal perspective in the classification of costs/expenses. A suitable classification for the German Statutory Health Insurance might be:

- expenses for health care services,
- transfers,
- (loss of) contributions to social insurances.

Table 5: Expenses and (lost) revenues of the Statutory Health Insurance

Cost categories	Resource consumption
Expenses for health care services	Ambulatory practice visits - general practitioner - specialist Procedures and diagnostics - tests - diagnostic imaging - surgical interventions Dental care Pharmaceuticals Physiotherapy Medical devices Hospital stays Rehabilitation (non-employed population) Short-term nursing care at home
Transfers	Sick pay
Contributions	Loss of contributions to SHI Contributions to pension insurance Contributions to long-term care insurance Contributions to unemployment insurance

Concerning health care services, only products and services covered by the Social Health Insurance are considered in health economic evaluations from the SHI perspective. Table 5 presents an overview of SHI-financed health care services. Areas of health care, covered by other social insurances are long-term care (covered by the Statutory Long-term Care

Insurance), rehabilitation for the working population (covered by the Statutory Pension Insurance), occupational accidents and occupational disease (covered by the Statutory Accident Insurance).

Transfer benefits of the Statutory Health Insurance refer to sick pay. Sick pay is given to employed members of sickness funds after six weeks of unfitness for work – but no longer than 78 weeks during a period of 36 month (during the first six weeks of illness salary payment by the employer is continued). Sick pay accounts for 70 percent of the gross wage (but a maximum of 90 percent of the net wage). In addition to sick pay to the sick member, sickness funds cover part (about half) of the contributions to pension insurance, long-term care insurance and unemployment insurance. Moreover, patients are exempt from contributions to the Statutory Health Insurance while receiving sick pay.

3.2.2 Methods for the Identification of Resource Use

As in the societal perspective, a comprehensive identification of expense items relevant to the intervention alternatives should be generated (see Section 2.1.1). Again, it is recommended to develop a decision tree of the therapeutic pathways which contains all relevant downstream events for a broad identification of resource consumptions. Even events not covered by the Statutory Health Insurance should be considered in the decision tree, as SHI-relevant subsequent resource consumptions might be induced by these events.

As in the societal perspective, a mere comparison of technology expenses between new and existing health technologies is not sufficient. The time horizon of a health economic evaluation should be long enough to capture all relevant expense differences (and outcome differences relevant to the Statutory Health Insurance) between intervention alternatives. Future expenses, i.e., expenses in life years gained, should be differentiated into related and unrelated expenses. As in the societal perspective, recommendations are as follows: In a base case, only related future expenses should be derived. In a sensitivity analyses all future expenses and all future expenses (related and unrelated expenses in life years gained) should be included.

It should be noted that future expenses have more impact on the SHI system perspective than on the perspective of a single sickness fund as individuals may change to another sickness fund in the future (e.g., because of lower contribution rates). Thus, it is not certain that future

costs will accrue to a sickness fund (but might be covered by another sickness fund the patient has changed to). From the perspective of the SHI system, it is certain that future costs will be covered by the SHI system.

3.3 Measuring Health Services Utilization

As in the societal perspective, the grade of precision required in an economic analysis is an important determinant for the selection of costing methods, i.e., for the decision whether micro-costing or macro-costing methods should be applied. Factors influencing the precision of expense estimations are (see also Section 2.2.1):

- expenses of products and services;
- frequency of utilization (or probability of occurrence);
- time in the course of a chronic disease;
- variations between patients;
- variations between intervention alternatives.

In addition, the proper grade of precision in measuring health services utilization is also influenced by the price system, i.e., the units of health care services on which prices are based (for more details, see Section 3.4). For example, in the hospital sector, prices are based on a DRG-system. Thus, diagnoses according to the DRG-system should be identified and measured, while detailed measurement of medical procedures would not be adequate.

Both costing approaches, micro-costing and macro-costing, are often combined in a health economic analysis: The micro-costing approach is used for health care services that are central to the health economic analysis, whereas health care services that are less central will be determined by the macro-costing approach [6, p. 152]. Again, as for the identification of medical procedures (see Section 3.2.2), a decision tree of the therapeutic pathways may be useful to differentiate into central and less central cost items.

3.4 Prices and Expenditures

Health economic evaluations from the SHI perspective should refer to expenses (and/or loss of revenues). In general, administered and negotiated prices on health care markets determine expenses, representing opportunity cost to SHI. Thus, in contrast to cost estimation from the societal perspective, there will commonly be no adjustments of (administered and negotiated) market prices.

Nevertheless, some sector-specific budgets might impact on opportunity costs to SHI. For example, in the hospital sector, a target hospital budget is negotiated between the hospital and sickness funds. Hospital care is remunerated by DRGs, but once the target budget is reached, remunerations and thus opportunity costs to sickness funds decrease to 35 percent of the usual remuneration. Alternatively, an increase in hospital care services to some patients (i.e., patients from the evaluation studies) might induce a decrease in hospital care services to other patients (e.g., through early discharge) because the hospital might want to avoid an excess of target budget.

Early discharge of other patients will or will not induce opportunity costs to SHI, i.e., additional expenses in other sectors (e.g., ambulatory practice care, short-term nursing care, pharmaceuticals), or through later readmissions due to complications – depending on medical reasons. Thus, there might even be zero opportunity costs (if early discharge will not induce additional expenses). In sensitivity analyses, the impact of lower opportunity costs (e.g., 0, 35 or 50 percent) could be calculated. In other health care sectors there are similar impacts of sector-specific budgets on opportunity costs (for more details, see Krauth et al. [47]).

As mentioned above (Section 3.3), the price system defines the maximum grade of precision in expense calculation (i.e., micro-costing versus macro-costing). For example, in hospital care, prices are base on a DRG-system. Thus, DRG is the most precise expense valuation (for hospital care) in health economic evaluation studies from the SHI perspective. Less precise valuations (e.g., expenses per inpatient day) might be derived (see Section 3.5). In the ambulatory practice sector, there is a detailed price system (Uniform Value Scale), specifying prices for a broad range of medical procedures (e.g., examination, lab test, diagnostic imaging etc.). Again, less precise valuations (e.g., expenses per ambulatory practice visit) might be derived.

Finally, it should be mentioned that in expense estimation from the SHI perspective expenses should be adjusted by co-payments by the patients (resulting in a decrease in expenses for the Statutory Health Insurance). In fact, for most health care services, patients have to pay co-payments.

3.5 Potential for Standardization

Standardization of costing methods from the SHI perspective is recommended, including the development of standard expenditure lists. As for the societal perspective, AG MEG has derived standard expenditures from the perspective of the Statutory Health Insurance [47,50]. Examples for standard expenses are presented in Table 6.

Table 6: Standard costs (2002)

	Societal perspective (EUR)	SHI perspective (EUR)
Inpatient days	Costs per day	
Internal medicine	284	229
Surgery	329	264
Gynaecology	344	289
Paediatrics	363	308
Psychiatry	260	205
Intensive care	908	853
Average inpatient day	380	325
Ambulatory practice visits	Costs per visit	
General practitioner	15.24	13.72
Internist	32.92	29.63
Cardiologist	58.75	52.88
Gynaecologist	25.56	23.01

(continue)

Table 6: Standard costs (2002) (continue)

	Societal perspective (EUR)	SHI perspective (EUR)
Ambulatory practice visits	Costs per visit	
Paediatrician	18.19	16.37
Radiologist	79.43	71.50
Psychiatrist	14.60	13.14
Average physician visit	21.89	19.71
Physiotherapist visit	14.34	13.55
Paid and unpaid work	Costs per day	
Labour costs (per working day)	156	
Labour costs/sick pay (per calendar day)	89	59

Source: Based on Krauth et al. [50], Krauth et al. [47]

4 Data Sources

4.1 Data Sources for Health Economic Evaluations

Health economic analyses combine data (and knowledge bases) from a broad variety of sources. Table 7 categorizes data sources and gives examples.

Table 7: Data sources

Data source	Examples
Studies	Clinical studies
	Observational studies
	Reviews
Administrative data	Sickness funds
	Private health insurance
	Statutory pension insurance
	Statutory long-term care insurance
	Federal association of SHI physicians
	German hospital organization
	Hospitals
Supplementary data	Official statistics (e.g., Federal Statistical Office)
	Registries (e.g., AMI, cancer)
	Guidelines
	Surveys
	Expert opinion (for identification of relevant resources)

4.2 Transferability of Cost Data

In general, health economic assessments will include study results from foreign countries. As is documented by the increasing amount of literature on transferability of cost data (e.g., [22,51-55]), the transfer of cost data from one country to another (i.e., from the studied countries to the target country) should be performed with care.

Welte et al. [56] developed a framework to examine the transferability of cost data from foreign studies. This framework describes (1) factors influencing transferability of cost data, (2) key determinants influenced, (3) efforts to check correspondence between studied and target country, and (4) adjustments to improve transferability to the context of the target country.

A selection of factors that might affect the transferability of study results are [51,53,56]:

- population characteristics (examples)
    - incidence / prevalence of diseases
    - case-mix
    - life expectancy
- health care system characteristics (examples)
    - absolute and relative prices
    - clinical practice variation
- methodological characteristics (examples)
    - perspective
    - discount rate
    - productivity cost approach

There are knock-out criteria (general and specific) that will preclude transferability of cost data

- The intervention, evaluated in foreign countries, or the comparators are not relevant to the target country (e.g., a comparator drug is not licensed in the target country).
- The study quality does not meet the methodological standards of the target country.
- Each transferability factor can become a (specific) knock-out criterion.

Modelling adjustments are definitely necessary when there are large differences between studied and target country in (1) incidence / prevalence, (2) practice variation, or (3) relative prices. However, every other transferability factor might lead to adjustments as well. Adjustments may concern the structure of the decision model (to adapt to different health care processes) or the resource utilization. Adjustments of valuation (unit prices) should always be carried out. Furthermore, adjustments for inflation (see also Section 2.3.3) and different currencies should be performed. For currency conversion, purchasing power parities are recommended. For more details see Welte et al. [56].

5 Example: Patient Education Programme for Ankylosing Spondylitis

In the example, a cost estimation is presented for an education programme for patients with ankylosing spondylitis (AS). AS is an inflammatory rheumatoid disease with a chronic progressive course involving pain and functional limitations of the spine and thorax, and in part also of the joints. In Europe, conservative estimates show a prevalence of AS of 0.1 to 0.5 %. The onset of disease usually occurs between the ages of 20 and 40; 75 % of patients with AS are male [57,58].

The education is part of a complex inpatient rehabilitation scheme. In six 90-minute modules, the structured education programme addresses the following points: (1) clinical picture, (2) physiotherapy, (3) pain and coping with pain, (4) pharmaceutical and surgical therapies, (5) everyday behaviour that is appropriate for the spine, and (6) coping with everyday life and the disease. The education takes place in the form of seminars with 6 to 10 patients per education group, and is implemented by an education team (physician, psychologist, physiotherapist, occupational therapist). Module No. 6 is conducted together with a representative of the AS self-help group. The education aims to change patient behaviour; in particular, the aim is to increase treatment compliance and optimize the self-management of patients.

5.1 Methods

5.1.1 Study Design

The evaluation of the education programme is based on a randomized, controlled, prospective, multi-centre study design [59]. A total of 323 patients were recruited from 3 rheumatologic rehabilitation clinics. 140 complete data sets were available for the intervention group (IG), and 119 complete sets were available for the control group (CG) – the response rate was not significantly different. The analysis was performed from the societal perspective and from the SHI perspective. In the following text the cost estimation from a societal perspective is described and differences between the SHI and the societal perspective are discussed.

5.1.2 Education Programme Costs

From an economic perspective, the education programme consisted of the following components: (1) preliminary talks with patients, (2) conduct of the education courses,

(3) preparation and coordination of the courses, (4) education of the course instructor (proportionate costs), and (5) development of the education programme (proportionate costs).

The estimation of the education programme costs was performed on the basis of the resource utilisation (staff, material, room, and overhead costs). The time expenditure for the education programme was determined through written and personal questioning of the instructors. The time expenditure for the representative of the self-help group was estimated. An additional estimated 20 % for common time was allotted to the staff's direct time expenditure for the education (physicians, psychologists, and physiotherapists/occupational therapists). The estimation of the use of resources for staff was orientated towards staff expenditure following the German civil service pay scale (approx. €36/h for physicians and psychologists and approx. €26/h for physiotherapists/occupational therapists). The time expenditure for the representative of the AS self-help group was estimated by means of the average opportunity costs for leisure time (€16.3/h).

Material costs (education materials and expendable items) were estimated following the cost record of the "Working Group Patient Education" of the German Society for Rheumatology. The room costs were estimated to be €15/course hour. This is inferred from a fictive monthly rent of €10/m^2, an estimated space requirement of 120m^2 (100m^2 course room and 20m^2 proportionate circulation area), and a total use of the course rooms for about 4 hours/working day. In a simplified approach, the overhead costs of the clinic were allotted to the staff costs at 20 %.

5.1.3 Follow-up costs

The direct and indirect follow-up costs were recorded in patient surveys at the start of rehabilitation, as well as 6 and 12 months after the end of rehabilitation. In addition to the patient survey, administrative data of the patients' sickness funds were obtained. In the patient survey, a list of different physicians groups was used for the assessment of contacts with physicians, and AS-related contacts were described: (1) back/joint pain, (2) stomach and intestinal diseases, (3) urinary tract infections, (4) iritis, and (5) skin diseases. Physiotherapeutic and balneophysical services, which are key therapeutic elements in AS, were recorded in a differentiated manner. Regarding non-medical cost parameters, the following items were considered: (1) patients' time expenditure for treatment, (2) patients'

own therapy-relevant activities (independent performance of physiotherapy, physical exercise for patients with rheumatic disease, and relaxation exercises), and (3) AS-related increase in time expenditure in everyday life, in particular in the morning due to morning stiffness. Concerning indirect costs, the duration of incapacity to work was recorded.

In the patient survey, for most cost parameters, measuring the resource utilisation was limited to a 4-week period for each of the 3 time points (start of rehabilitation, as well as 6 and 12 months after the end of rehabilitation). In order to represent the costs in 12-month periods, the corresponding patient data were interpolated. Regarding incapacity to work, 12-month data (at the start of rehabilitation and 12 months after the end of rehabilitation) were recorded in addition to the 4-week data of patients. The evaluation of indirect costs was conducted according to the human capital approach (basic analysis) and the friction cost approach (sensitivity analysis). Cost analysis parameters (including valuation of the cost parameters) are presented in Table 8.

Table 8: Cost parameters in the health economic evaluation

Cost parameters	**Valuation (in euros)**
Direct medical costs	
GP contacts AS	15.7 / contact
Specialist contacts AS	25.8 / contact
Group physiotherapy	4.1 / contact
Individual physiotherapy	13.8 / contact
Massages	9.5 / contact
Medical baths	12.3 / contact
Packages	6.4 / contact
Electrotherapies	4.1 / contact
Relaxation exercises	3.3 / contact
Hospital stays AS	365 / day of care

(continue)

Table 8: Cost parameters in the health economic evaluation (continue)

Cost parameters	Valuation (in euros)
Direct non-medical costs	
Time expenditure for treatments – GP contact – Specialist contact – Physiotherapy – Massages and baths	16.3 / hour
Time expenditure for patients' own activities – Physiotherapy – Physical exercise – Relaxation exercises	16.3 / hour
Additional time expenditure for everyday life	16.3 / hour
Indirect costs	
Incapacity to work (human capital approach)	88 / calendar day
Incapacity to work (friction cost approach)	70 / calendar day

5.2 Results

5.2.1 Programme Costs

The costs of an education course were largely independent of the number of participants. The AS education programme was designed for 6 to 10 course participants. As presented in Table 9, the programme costs per participant lay between €117 (for 10 participants) and €186 (for 6 participants); with an average utilization by 8 participants, the programme costs were €143.

Table 9: Costs of the education programme

Programme components	**Costs per participant (in euros)**		
	6 participants	8 participants	10 participants
Preliminary talks	11	11	11
Conduct of the course	108	81	66
Preparation and coordination	43	32	25
Instructor education	12	9	8
Programme development	12	9	7
Total	**186**	**143**	**117**
Resource use	**Costs per participant (in euros)**		
	6 participants	8 participants	10 participants
Staff	133	102	83
Materials	4	3	3
Room (incl. technical equipment)	23	18	15
Overhead	26	20	16
Total	**186**	**143**	**117**

5.2.2 Follow-up costs

The education programme costs were compared with potential savings in follow-up costs. Table 10 presents (1) the follow-up costs per economically active patient in the control group (CG); (2) the follow-up costs per economically active patient in the intervention group (IG), in each case in the 12-month periods before the start of rehabilitation (PRE) and after the end of rehabilitation (POST); and (3) the cost differences per patient between the intervention and control groups (IG - CG) in the 12-month periods before the start of rehabilitation (PRE) and after the end of rehabilitation (POST). The total follow-up costs are differentiated in (1) direct medical costs (use of medical services); (2) direct non-medical costs (patients' time expenditure for restoration of health); and (3) indirect costs (patients' disease-related absence from work). The indirect costs were derived from the 12-month data of patients (at the start of rehabilitation and 12 months after the end of rehabilitation).

As seen in Table 10, the total costs in the 12-month period before the start of rehabilitation amounted to about €13 900 per patient (€13 400 in the control group and €14 400 in the intervention group). The costs for health services (direct medical costs) amount to €2000 (or only 14 % of the total costs). In contrast, the evaluated time expenditure of patients for treatments, patients' own activities, and AS-related burdens due to morning stiffness (direct non-medical costs) dominated the total costs at about €7400 per patient (or 54 % of the total costs). The average time expenditure of patients with AS was about 9.4 hours per week (or 81 minutes per day), which corresponded to about 25% of the weekly working time of a fully employed person. The incapacity-to-work days, which were estimated with labour costs according to the human capital approach (indirect costs), amounted to about €4500 per economically active patient, or 32 % of the total costs in the 12-month period before the start of rehabilitation (i.e., about 50 incapacity-to-work days [calendar days] in the 12-month period before the start of rehabilitation). The cost differences between control and intervention group before the start of rehabilitation were not statistically significant.

In the 12-month period after the end of rehabilitation, the total costs in the control group increased by about €500 per patient compared with the 12-month period before the start of rehabilitation. In contrast, in the intervention group the costs decreased clearly by €3400 per patient. The direct medical costs decreased in both patient groups; however, only by about €100 per patient in the control group, but by over €900 per patient in the intervention group. The more notable savings in the intervention group were caused particularly by the greater reduction in inpatient days of care (0.1 days of care in the control group versus 2.3 days of care in the intervention group). In contrast, the cost reductions in services provided by physicians were nearly identical. The costs for services for physical and medical therapies increased slightly in the control and intervention group in the 12-month period after the end of rehabilitation compared with the 12-month period before the start of rehabilitation (which, in line with the aim of the rehabilitation programme and particularly of the education programme, was caused by the expansion of active treatments).

The direct non-medical costs increased slightly in the control group by about €100 per patient in the 12-month period after the end of rehabilitation (compared with the 12-month period before the start of rehabilitation); in the intervention group, they decreased by about €400 per patient. The cost reduction in the intervention group was caused by the lower time

expenditure for contacts with physicians as well as by the reduction in physical exercise activities (with simultaneous, but non-compensating expansion of physiotherapy under therapeutic supervision and independently performed physiotherapy).

Regarding indirect costs, clear differences between both patient groups were shown (based on the 12-month patient data). In the control group, the indirect costs increased by about €400 in the 12-month period after the end of rehabilitation compared with the 12-month period before the start of rehabilitation (with about 5 incapacity-to-work days more), and decreased by about €2100 in the intervention group (with 24 incapacity-to-work days less).

There was a significant time effect in the intervention group for indirect costs and total follow-up costs; in the control group, the cost differences (after rehabilitation compared with before rehabilitation) were not significant. In the base case, a total of €3900 per patient was saved in 12 months by the patient education programme (difference in the reduction in costs of €3400 in the intervention group compared with the increase in costs of €500 in the control group). The cost savings were divided into about €800 for direct medical costs, €500 for direct non-medical costs, and €2600 for indirect costs (see Table 10). The interaction effects were significant for the indirect follow-up costs and the total follow-up costs. The savings for the follow-up costs clearly more than compensated for the costs of the patient education programme (€117 to €186). The net savings amounted to about €3700 to €3800.

Table 10: Total follow-up costs (in euros): societal perspective

	(1) Control group				(2) Intervention group				(3) IG - CG			
	PRE	**POST**	**Δ**	**p ***	**PRE**	**POST**	**Δ**	**p ***	**PRE**	**POST**	**Δ**	**p ***
Direct medical costs						(in euros)						
Physicians' services	835	689	-146		577	403	-174		-258	-286	-28	
Physical medicine	465	543	78		553	601	48		88	58	-30	
Other	454	400	-54		1088	273	-815		634	-127	-761	
Total	**1754**	**1632**	**-122**	.97	**2218**	**1277**	**-941**	.49	**464**	**-355**	**-819**	.67
Direct non-medical costs												
Time for treatment	2072	2196	124		2101	2046	-55		29	-150	-179	
Time for patients' own activities	3190	3207	17		3889	3572	-317		699	365	-334	
Additional time for everyday life	1785	1785	0		1785	1785	0		0	0	0	
Total	**7047**	**7188**	**141**	.51	**7775**	**7403**	**-372**	.71	**728**	**215**	**-513**	.71
Indirect costs												
Incapacity to work	**4612**	**5048**	**436**	.90	**4315**	**2196**	**-2119**	.00	**-297**	**-2852**	**-2555**	.03
Total costs	**13413**	**13868**	**455**	.37	**14308**	**10876**	**-3432**	.01	**895**	**-2992**	**-3887**	.02

* Wilcoxon test
PRE: 12-month period before the start of rehabilitation
POST: 12-month period after the end of rehabilitation
Δ: POST minus PRE

5.3 Sensitivity Analyses

A number of sensitivity analyses were conducted for the cost estimation of the AS education programme. Among other things, (1) the time costs of patients were excluded from the analysis; (2) alternative data approaches for indirect costs were investigated (SHI data as well as interpolated 4-week data of patients); and (3) a valuation of indirect costs was undertaken with the friction cost approach.

Cost savings persisted when time costs were not considered in the health economic analysis. For the alternative data approaches on incapacity-to-work times, cost savings were confirmed by the SHI data. In contrast, for the interpolated 4-week data of patients, cost savings were no longer significant (about €1100 for indirect costs and €2400 for total costs were reported). When the assessment of indirect costs was conducted by means of the friction cost approach, cost savings decreased to about €500 (indirect costs) and about €1700 (total costs), but were also no longer significant.

5.4 SHI Perspective

From the SHI perspective, the costs of the patient education are not relevant for decisions, as the education programme is a component in a rehabilitation programme that is (largely) financed by the pension insurance. However, the SHI system perspective can be interpreted as an extract of the general social insurance perspective. From the perspective of the general social insurance, the costs of the education programme must be considered. It is assumed that the (additional) costs of rehabilitation incurred by the patient education programme are considered in the negotiations between the rehabilitation clinics and the pension insurance regarding the daily rate for patient care. The change in the daily rate for patient care will then be orientated towards the societal opportunity costs (excluding the time costs of the representative of the self-help group).

In the example presented, the clearest differences between the societal and the SHI perspective concern the indirect costs/transfer payments. In addition, the time costs for patients are irrelevant from the SHI point of view. In the 12-month period before the start of rehabilitation, payments for sickness benefits were €600 (compared with about €4500 for total absence-from-work costs and about €2200 for AS-related absence-from-work costs). In the control group, payments for sickness benefits increased after rehabilitation by about €500 per

patient per 12 months (an average of 10 sickness benefit days more than before rehabilitation). In the intervention group, payments for sickness benefits decreased after rehabilitation by about €150 (an average of 3 sickness benefit days less than before rehabilitation). However, this did not cause a significant interaction effect. Thereby from the SHI perspective, no significant savings for total costs were achieved in general.

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