Microcosting in Economic Evaluations

Issues of accuracy, feasibility, consistency and generalisability

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Microcosting in Economische Evaluaties

Aspecten van nauwkeurigheid, haalbaarheid, consistentie en generaliseerbaarheid

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Chapter 1

General introduction

The number and variety of treatment options in healthcare have rapidly increased in the past decades. Consequently, healthcare budgets in Western countries are increasingly under pressure, which has raised the awareness that limits must be set to the growth in healthcare costs. As resources – people, time, facilities, equipment and knowledge – are scarce, an organised consideration of the factors involved in a decision to commit healthcare resources to one use instead of another must be made (Drummond et al. 2005; Ritzwoller et al. 2005). In healthcare, the consideration of these factors is commonly performed through economic evaluations, the comparative analysis of alternative treatment options in terms of both their costs and effects (Drummond, Sculpher 2005; Gold et al. 1996).

Even though the effects are at least as important, this thesis will focus on the cost estimation within economic evaluations. Table 1.1 presents the four cost categories which may be relevant. However, which cost categories to include in an economic evaluation remains open to debate because of legitimate differences in values or perspectives (Johnston et al. 1999). Welfare economics adheres to the societal perspective in which all cost categories are considered. Some investigators argue that economic welfare theory alone should dictate which costs are included and which approach is adopted. Others are willing to adopt more pragmatic positions and prioritise the type of costs included, only collecting information on those costs that are relevant to decision makers or to prioritise costs in terms of their importance (Drummond, Sculpher 2005; Gold, Siegel 1996; Johnston, Buxton 1999).

Direct medical costs refer to the sequence of healthcare services (initial treatment and follow up treatments) which relate to the treatment option under consideration. For example, for the treatment option 'stroke', subsequent healthcare services may involve either trombolysis treatment or conservative treatment (*initial treatment*) in combination with visits to healthcare providers (such as the general practitioner and medical specialist), medical imaging services (such as magnetic resonance imaging and X-rays), inpatient stay for the management of treatment related complications and medications (*follow up treatments*). Regardless the perspective chosen for an economic evaluation,

Table 1.1: Distinction of cost categories within economic evaluations

	Medical costs	**Non-medical costs**
Direct costs	Costs of healthcare services which relate to the treatment option under consideration	Patients' out of pocket expenses (e.g. expenses for travel, time and home modifications)
Indirect costs	Costs of healthcare services which do not relate to the treatment option under consideration	Productivity losses due to absence from paid work and reduced efficiency at paid and unpaid work

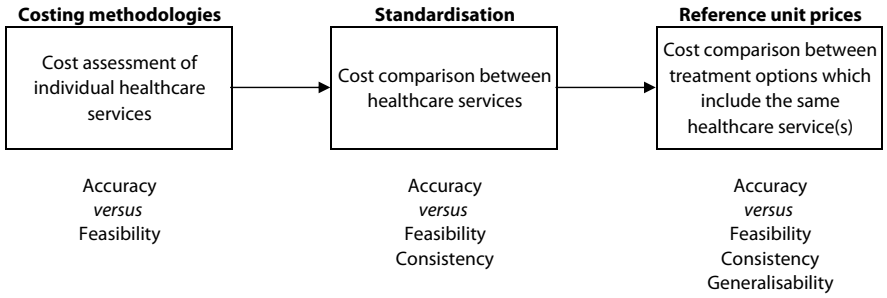
Table 1.2: Definitions of accuracy, feasibility, consistency and generalisability

Accuracy	The extent to which the cost estimate obtained from the costing methodology reflect real costs
Feasibility	The extent to which the costing methodology is applicable in practice
Consistency (*internal validity*)	The extent to which differences between cost estimates are attributable to the healthcare service under consideration, rather than to flaws in the costing methodology
Generalisability (*external validity*)	The extent to which the cost estimate obtained from the costing methodology is reliable for generalisations to other circumstances

the direct medical cost category is always considered. Direct medical costs are relevant in *all* patient populations, where indirect medical costs, patient's out of pocket expenses and productivity losses may be relevant only in *specific* patient populations. For example, productivity losses are assumed to be of minor importance in diseases affecting primarily the elderly. A reliable cost assessment of direct medical costs is therefore crucial. However, the preferred methodology to estimate the costs of healthcare services is still to be determined. This thesis will focus on the accuracy, feasibility, consistency (internal validity) and generalisability (external validity) of the microcosting methodology for the cost estimation of healthcare services within the direct medical cost category (table 1.2).

Figure 1.1 presents the outline of this introduction. The first two sections (section 1.1 and 1.2) will discuss the cost assessment of individual healthcare services. The accuracy of different costing methodologies to determine the costs of healthcare services will be weighted against their feasibility. Section 1.3 will weigh the accuracy of costing methodologies against their consistency which is needed to compare costs between healthcare services. Section 1.4 will demonstrate that the cost comparison between treatment options additionally requires generalisability of cost estimates.

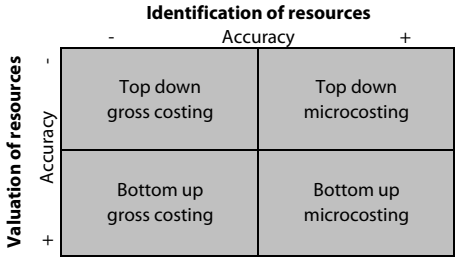
Figure 1.1: Outline of the general introduction



1.1 COSTING METHODOLOGIES

In the cost assessment of individual healthcare services, costs are calculated by multiplying the quantities of resources by the unit costs of resources (Drummond, Sculpher 2005; Jackson 2000; Johnston, Buxton 1999). Resources include direct cost components (such as diagnostic services, consumables, inpatient stay and labour) and indirect cost components (overheads and capital). The stratification of the identification and valuation of cost components by level of accuracy results in four costing methodologies for the cost assessment of healthcare services (figure 1.2).

Figure 1.2: Methodology matrix ~ the level of accuracy at the identification and valuation of cost components



The cost assessment of individual healthcare services aims to help clinical and other decision makers understand whether cost differences between treatment options arise from variations in unit costs or from variation in resource use intensity and to help understand the distributional form of the cost data on which cost estimates are based (Jackson 2000). Bottom up microcosting is particularly appropriate to provide such understanding. The methodology is generally believed to be the gold standard methodology in economic evaluations because it identifies all relevant cost components and values each cost component for all *individual* patients resulting in the most accurate cost estimates (Brouwer et al. 2001; Wordsworth et al. 2005). This allows for the identification of costs directly employed for a patient and for insight in patient subgroups that might have a great share in the total costs. The methodology enables statistical analyses to be made for the detection of cost differences between patients of each single cost component and combination of cost components. However, an important challenge in conducting bottom up microcosting is its feasibility. As this methodology is time consuming, especially when hospital information systems are absent or inadequate, it has not been widely used in assessing the costs of healthcare services.

Table 1.3 presents different definitions of microcosting found in the literature.

Table 1.3: Definitions of microcosting

* Each component of resource use is estimated and a unit cost derived for each (Drummond, Sculpher 2005).
* In microcosting, resource use is identified at a detailed level and a unit cost is attached to each resource (Johnston, Buxton 1999).
* Resources consumed are subject to a detailed inventory and measurement (Gold, Siegel 1996).
* Microcosting is the process of closely examining the actual resources consumed by a particular patient or healthcare service (Finkler et al. 2007).
* A detailed list of each component of a patient's care is created and costed separately for each facet of a patient's hospitalisation (Clement Nee Shrive et al. 2009).
* Microcosting is a 'building block' methodology for determining the 'true' cost of providing specific healthcare services within a healthcare provider. Cost components are individually determined and then combined in order to arrive at the healthcare service costs (Shuman & Wolfe 1992).

Top down microcosting identifies all relevant cost components, but values each cost component for *average* patients (figure 1.2) by separating out costs from comprehensive resources such as annual accounts. Even though the methodology is more feasible compared to bottom up microcosting, the disadvantage of the approach is that it fails to trace costs directly to the specific patients who incur that cost. Therefore, statistical analyses of costs cannot be performed and differences between patients cannot be detected (Clement Nee Shrive, Ghali 2009; Johnston, Buxton 1999).

The accuracy of bottom up and top down microcosting for the cost assessment of healthcare services weighted against their feasibility is depicted in table 1.4.

Table 1.4: Accuracy and feasibility of bottom up and top down microcosting

	Bottom up microcosting	**Top down microcosting**
Accuracy	Ability to trace costs directly to the patients who incur that cost → Allows statistical analyses of costs to be performed: * detection of cost differences of each (combination of) cost component(s) * insight in patient subgroups	Disability to trace costs directly to the patients who incur that cost → Disallows statistical analyses of costs to be performed
Feasibility	Lengthy and expensive	Cheap and 'easy' to apply

Even if it has been decided to follow the microcosting methodology, different levels of accuracy can be applied to different cost components (Finkler, Ward 2007; Johnston, Buxton 1999). Instead of conducting a full bottom up microcosting study, it may be more feasible to apply a confined bottom up microcosting study which restricts the application of bottom up microcosting to those cost components that are believed to have a great impact on the total costs (Drummond, Sculpher 2005).

Although almost all economic evaluations use a mix of the bottom up and top down microcosting methodology in the cost assessment of individual healthcare services (Clement Nee Shrive, Ghali 2009; Wordsworth, Ludbrook 2005), only one previous study has quantified the cost differences resulting from the two approaches or made recommendations on the preferred approach for each cost component. Wordsworth et al. (2005) compared cost estimates of a top down and bottom up methodology and concluded that a full bottom up methodology should be considered for healthcare services with a large component of labour or overheads. However, although their study was conducted in five different countries, it was limited to dialysis therapy in end-stage renal disease (Wordsworth, Ludbrook 2005).

Gross costing

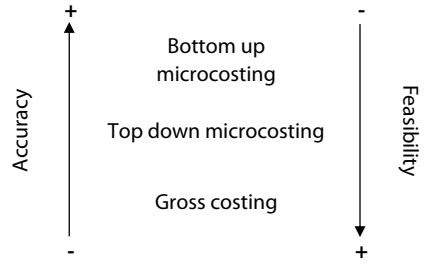
Opposed to microcosting, the gross costing methodology identifies cost components at a highly aggregated level. Generally, gross costing is more feasible compared with microcosting because it identifies only one (or few) cost component which is large relative to the healthcare service being analysed (Gold, Siegel 1996). Often, only inpatient days are identified as a cost component (Jackson 2000). Bottom up gross costing values the cost component for each *individual* patient. Top down gross costing values the cost component per *average* patient by separating out costs from comprehensive sources and is therefore considered to be the least accurate costing methodology (figure 1.2).

The main drawback of gross costing for use in economic evaluations is its inaccuracy, because it fails to trace costs directly to specific cost components. The fewer cost components are distinguished, the more likely it is that dissimilar patients with dissimilar costs will be grouped together (Jackson 2000). For example, when inpatient hospital stay is the only cost component identified for the treatment of stroke, cost differences between stroke patients undergoing trombolysis treatment and stroke patients receiving conservative treatment could only be explained by differences in the number of inpatient hospital days. More evident cost differences, such as those occurring due to the different consumption of medications, would not be detected.

When inpatient days are taken as the only cost component, the gross costing methodology results in an 'all-in' inpatient day cost which supposedly includes the costs of diagnostic services, consumables, inpatient stay and labour. This 'all-in' inpatient day cost should not be confused with the 'net' inpatient day cost which results from the microcosting methodology.

Figure 1.3 presents the levels of accuracy and feasibility for bottom up microcosting, top down microcosting and gross costing.

Figure 1.3: Levels of accuracy and feasibility for the cost estimation of healthcare services



Both economic theory and empirical studies support the observation that gross costing is a poor proxy to microcosting in economic evaluations, particularly when inpatient hospital stay is used as the only cost component (inpatient day allocation; section 1.2). Inpatient hospital stay and its intensity of treatment per inpatient hospital day are changing. Many of the healthcare services formerly provided over a 6-7 day stay are now concentrated in shortened 3-4 day stays. With the increased availability of high cost technologies in operating suites and intensive care units, inpatient hospital days became a relatively poor predictor of cost differences between patients. Patient diagnosis has an important effect on the use of resources which per diem estimates generally do not reflect (Jackson 2000).

A few studies have quantified the cost differences resulting from the microcosting and gross costing (Jackson 2000; Swindle et al. 1999; Whynes & Walker 1995). Whynes & Walker (1995) compared microcosting estimates with gross costing estimates for the treatment of colon cancer. They found that gross costing understated costs by more than 10% for some patient subgroups and overstated costs by more than 13% for others, while the mean for all patients differed by only 1% (Whynes & Walker 1995).

Swindle et al. (1999) investigated the need to combine gross costing with microcosting to reflect resource use variations that are essential to healthcare services. They concluded that microcosting should be applied in healthcare services that are likely to show wide cost variation between patients. However, Swindle et al. (1999) restricted their investigation to healthcare services that refer to the managed care system of the Department of Veterans Affairs in the United States (Swindle, Lukas 1999).

1.2 REIMBURSEMENT FEES

Since the introduction of the system of diagnosis related groups (DRGs) for USA Medicare patients in 1983, case payment mechanisms have gradually become the principal means of reimbursing hospitals in most developed countries (Busse et al. 2006). However, the way in which reimbursement fees for DRGs are calculated differs substantially among countries. Accordingly, the extent to which the actual costs incurred in hospitals are reflected by reimbursement fees differs as well (Schreyogg et al. 2006).

A DRG comprises a series of (subsequent) healthcare services which relate to one diagnosis, but, to a varying degree, also to at least one treatment option (Busse, Schreyogg 2006). In the Netherlands, the series of (subsequent) healthcare services included in a DBC by definition relate to the combination of a diagnosis and a treatment option. The DBC system distinguishes treatment options with fixed fees (list A DBCs) and treatment options with negotiable fees (list B DBCs) (Oostenbrink & Rutten 2006). Reimbursement fees for list B DBCs result from negotiations between hospitals and health insurers, in which case the relationship between actual costs and reimbursement fees is not guaranteed (Oostenbrink, 2006).

Reimbursement fees for DRGs and list A DBCs represent the cost of all healthcare services which are relevant to the considered diagnosis and treatment option. Healthcare services may include inpatient days, outpatient visits, surgical interventions, medical interventions, medical imaging and laboratory services (Beersen et al. 2004). These reimbursement fees result from the assessment of actual costs by means of a variety of approaches to microcosting and / or gross costing. Instead of calculating the costs of healthcare services, many economic evaluations use these reimbursement fees as a proxy to actual costs because they are commonly available at healthcare providers in many countries (Ibbott 1987). However, for several reasons, reimbursement fees based on actual cost assessments are inaccurate for use in economic evaluations (Kosenko et al. 1991; Oostenbrink et al. 2003).

Firstly, adjustment mechanisms are used to deduct reimbursement fees from actual cost estimates (Schreyogg, Stargardt 2006). For example, the actual costs may be adjusted by cost weights to ensure that the reimbursement fees of treatment options are related to the intensity of resources use, by administrative region or hospital type, by regression analyses to account for differences in hospital structure and by price differences among input factors (e.g. local wage level, rental fees) (Ankjaer-Jensen et al. 2006; Bellanger & Tardif 2006; Epstein & Mason 2006; Fattore & Torbica 2006; Sanchez-Martinez et al. 2006; Schreyogg et al. 2006).

Secondly, reimbursement fees have been derided by many economists because accounting conventions frequently distort which costs are included in the fees and such costs often bear little relationship to the resource use in patient care (Jackson 2000; Kosenko, Hill 1991). This situation could create tremendous pressure on the part of the healthcare provider to become more efficient since the healthcare provider's profits for healthcare services are based on maximalising the difference between the established reimbursement fees and actual costs (Kosenko, Hill 1991).

Finally, although healthcare has long contended that every patient is unique and standards are not possible, the reality of reimbursement systems is that patients are grouped together. Some reimbursement fees represent a mixture of clinical codes more than others. The rarer the healthcare service, the more likely it will be included with other healthcare services in the same reimbursement group rather than forming its own reimbursement fee. High volume treatments and very high costs treatments (even when rare) are more likely to have their own reimbursement fee. Clinical costing has shown that the dispersion around the mean costs varies greatly between reimbursement groups, with highly variable reimbursement groups most likely combining different healthcare services (Jackson 2000).

Several earlier studies have compared the differences between microcosting estimates and reimbursement fees, reaching contradicting conclusions (Chumney et al. 2004; Cohen et al. 1993; Heerey et al. 2002; Skeie et al. 2002). Heerey et al. (2002) compared the available microcosting and reimbursement fees of DRGs representing acute myocardial infarction, heart failure and human immunodeficiency virus at one healthcare provider in Ireland. They observed significant differences between the two different costing approaches, the largest reported difference being the DRG representing 'percutaneous cardiac procedures for acute myocardial infarction' with the microcosting mean cost being 66% higher than the reimbursement fee (Heerey, McGowan 2002).

A study by Chumney et al. (2004), carried out in the United States, has examined how the use of costs derived using a DRG-based or microcosting methodology impacts the results of an economic evaluation. Contrary to the conclusion of Heerey et al. (2002), they found no significant difference in the resulting cost effectiveness ratio when using the different costing approaches for treatments of human immunodeficiency virus- and acquired immunodeficiency syndrome therapies. It was concluded that the costing approach has little effect on the outcome of a decision model in heterogeneous conditions (Chumney, Biddle 2004).

1.3 STANDARDISATION

Economic evaluations can provide healthcare decision makers with valuable information on the relative efficiency of alternative healthcare services, healthcare services at different healthcare providers and healthcare services in different countries. However, due to the wide range of costing methodologies applied and omission of certain costs, cost estimates of different healthcare services are often not readily comparable or cannot be adjusted to a different context (Hoffmann & Graf von der Schulenburg 2000; Kolaczinski & Hanson 2006; Oostenbrink et al. 2002).

The standardised application of a costing methodology ensures that all healthcare services under consideration adhere to the same costing methodology. This way the cost estimates resulting from using the costing methodology can be attributed to the healthcare service under consideration, rather than to flaws in the methodology (Drummond, Sculpher 2005; Gold, Siegel 1996). Thus, standardised application encourages comparability and enables a meaningful comparison of actual cost differences between healthcare services, e.g. medical practice patterns, patient case-mixes, financial incentives, relative and absolute price differences between countries and quality of care (Hirth et al. 1999; Johnston, Buxton 1999; Raikou et al. 2000).

In the cost comparison between healthcare services, the accuracy of the costing methodology is challenged by the need for consistency (internal validity). Microcosting provides the most accurate cost estimates, but its consistency is restricted by the availability and quality of data (Drummond, Sculpher 2005; Gold, Siegel 1996). More than in the top down approach, this restriction is present in the bottom up approach because more detailed data is needed for the resource use valuation of individual patients (Shuman & Wolfe 1992). Resource use information for individual patients and cost components is generally not available with the same level of precision, even within a single healthcare provider's clinical costing system and systems vary markedly between healthcare providers (Jackson 2000).

Despite the disability of top down microcosting to perform statistical analyses to explore cost differences between patients receiving the same healthcare service (*patient level*; section 1.1), statistical analyses between healthcare providers providing the same healthcare service (*hospital level*) is feasible when resource use data is available for at least 2 healthcare providers per healthcare service.

Published guidelines on the conduct of economic evaluations provide little guidance regarding the standardised use and potential bias of the different costing methodologies for

the cost comparison between healthcare services (Clement Nee Shrive, Ghali 2009; Krauth et al. 2005; Oostenbrink, Koopmanschap 2002). In general, guidelines are rather global with respect to costing and large differences between these guidelines exist (Johnston, Buxton 1999; Oostenbrink, Koopmanschap 2002). In 2000, the 'Dutch Manual for Costing: Methods and Standard Costs for Economic Evaluations in Health Care' has been published. This Manual provides guidelines and recommendations on the preferred standardised costing approach and data source for each cost component in the Netherlands. However, apart from the Dutch Manual, only few studies have made recommendations on the preferred standardised costing approach or data source to be used in economic evaluations.

Jackson (2000) proposed five criteria for evaluation of several costing approaches and data sources of healthcare provider cost data with detailed consideration of the way resource use and unit costs are derived: accuracy of cost component identification, accuracy of cost component valuation, lengthiness of the costing exercise, generalisability of study results and affordability of the data collection. She concluded that economic evaluations should defend the feasibility of the costing methodology and data source for the decision context (Jackson 2000). However, Jackson (2000) did not make explicit recommendations on the use of specific data sources for single cost components.

Clement Nee Shrive et al. (2009) compared the standardised application of microcosting and gross costing for sirolimus-eluting stents. They concluded that the standardised costing methodologies produced markedly different cost estimates and that the difference in cost effectiveness produced by each standardised costing methodology was of a magnitude that could influence the results of an economic evaluation (Clement Nee Shrive, Ghali 2009). Clement Nee Shrive et al. (2009) neither made recommendations on the preferred data source for each cost component.

In order to compare the healthcare utilisation of smokers, former smokers and never smokers, Ritzwoller et al. (2005) attempted to create comparable measures of resource use and unit costs from the hospital information systems of seven healthcare providers. They found a substantial variation in both the content and capture of data across all healthcare providers and across all cost components (Ritzwoller, Goodman 2005). The cost component which was captured most consistently across healthcare providers and hospital information systems included 'inpatient days'. Contrary, the availability of 'labour' varied across all healthcare providers. Ritzwoller et al. (2005) only recommended on hospital information systems as the data source for the extraction of data.

1.4 REFERENCE UNIT PRICES

Reference unit prices are predetermined estimates of what it is expected to cost or what it should cost to produce one unit of a healthcare service (Finkler, Ward 2007; Jones 1995). They are particularly useful for healthcare services which have a great share in the total costs of the alternative treatment options (sequences of healthcare services; section 1.1). Reference unit prices are important in economic evaluations, because they encourage comparability between treatment options (Drummond et al. 1993; Ferguson 2001; Jones 1995; Oostenbrink, Koopmanschap 2002; Viens-Bitker et al. 1986). The lack of a reference unit prices is often considered a weakness of economic evaluations that hinders the interpretation and comparison of treatment options (Drummond et al. 1997; Ferguson 2001; Hoffmann & Graf von der Schulenburg 2000). However, three major barriers limit the establishment of reference unit prices from the standardised application of microcosting (Drummond, Jonsson 1997; Oostenbrink, Koopmanschap 2002). The methodology is time consuming and expensive to perform (section 1.1), its accuracy is challenged by its need for consistency (section 1.3) and by its need for generalisability to other populations, other healthcare providers and other countries. Despite these disadvantages, the standardised application of microcosting is recommended for those healthcare services which resource use and / or unit costs are relatively high compared to those of the other healthcare services within the treatment option, because their costs can markedly affect the results of an economic evaluation (Oostenbrink, Koopmanschap 2002; Sculpher et al. 2004).

To guarantee generalisability (external validity), the ideal reference unit prices are established from large, diverse populations, which require data from multiple sources (Ritzwoller, Goodman 2005). However, reference unit prices are often based on the resource use information of the healthcare providers in which the economic evaluation is performed (Adam & Evans 2006; Johnston, Buxton 1999; Oostenbrink, Buijs-Van der Woude 2003). Healthcare providers participating in economic evaluations may not be representative of the costs of the same healthcare service in the wider universe of healthcare providers (Jackson 2000). A study of Raikou et al. (2000) has shown that the use of healthcare provider specific unit costs results in statistically different conclusions compared with the use of average unit costs. The use of healthcare provider specific unit costs would tend to overestimate the cost per patient, as by using the average unit costs, it fails to take into account the substitution of relatively less expensive resources for more expensive ones (Oostenbrink, Koopmanschap 2002; Raikou, Briggs 2000).

Reference unit prices are currently available, among other countries, in Germany, the United Kingdom and the Netherlands. Krauth et al. (2005) have proposed empirical reference unit prices for primary healthcare services from the direct medical and indi-

rect non-medical cost categories in Germany (table 1.1). Healthcare services included, among others, outpatient and inpatient care. The gross costing methodology was applied to determine regional specific, medical specialty specific or diagnosis specific unit costs based on administrative charges and rates or on official statistics (Krauth, Hessel 2005). However, little is known about the application of these empirical reference prices in the conduct of economic evaluations.

The reference cost database of the United Kingdom contains a wide range of reference prices for acute care interventions which are systematically classified into categories that are clinically distinct and have similar implications for resources (Raftery et al. 2005). Due to the 'fast track' activity and cost information collection from all National Health Service Trusts, Ferguson (2001) has argued that the database is severely flawed for application in economic evaluations. Nevertheless, the reference prices are used to support development of health improvement programmes, service and financial frameworks and service agreements, to monitor efficiency targets and to calculate the national tariff, utilised in payment by results policy implementation (Curtis & Netten 2008; Ferguson 2001; Raftery, Roderick 2005). The reference prices are partly presented in an annual report, the 'Unit Costs of Health and Social Care', which aims to 'improve unit cost estimates over time, drawing on material as it becomes available, including ongoing and specially commissioned research' and is widely used for application in economic evaluations (Curtis & Netten 2008).

The Dutch Manual provides reference prices of the healthcare services most often used in economic evaluations and do not take into account any differences between patient groups. Healthcare services include e.g. inpatient days, outpatient visits, visits to the general practitioner and physiotherapist, daycare treatments, laboratory and medical imaging services. Reference prices are determined from either the top down microcosting or the gross costing methodology. The manual has contributed to standardisation and uniformity of costing studies (Oostenbrink, Buijs-Van der Woude 2003).

1.5 AIMS OF THIS THESIS

The nature of costs is such that the more refined the analysis, generally the more costly it is (Finkler, Ward 2007; Johnston, Buxton 1999). In economic evaluations, decision makers must consider whether the benefits of more reliable cost information justify the additional costs and complexity incurred in obtaining accurate and detailed information (Gold, Siegel 1996; Shuman & Wolfe 1992). Jackson (2000) has suggested that economic evaluations emphasise the economic concepts underlying cost measurements, but

are pragmatic in their acceptance of the poor quality of available data and offer little study design advice on the selection of costing methods to optimise data quality. The choice between costing methodologies should reflect the importance of accurate cost estimates, feasibility and costs (Clement Nee Shrive, Ghali 2009; Gold, Siegel 1996; Oostenbrink, Koopmanschap 2002).

This thesis aims to determine and compare the costs of individual healthcare services and to draw general methodological conclusions regarding the application of the microcosting methodology. Drawing general methodological conclusions, special attention will be paid to the following research areas:

- The accuracy and feasibility of bottom up and top down microcosting estimates in the cost assessment of individual healthcare services
- The accuracy and feasibility of reimbursement fees in the cost assessment of individual healthcare services
- The consistency of the standardised application of the microcosting methodology for the cost comparison of alternative healthcare services
- The generalisability of reference unit prices established from the standardised application of microcosting estimates for the cost comparison of alternative treatment options (sequences of healthcare services)

The methodology will be applied to various healthcare services in a variety of medical specialties, including oncology, haematology, intensive care medicine, dentistry, general practitioner medicine, cardiology and neurosurgery.

1.6 OUTLINE OF THIS THESIS

Chapter 2 and 3 assess the accuracy of different costing methodologies for the cost assessment of individual healthcare services. Chapter 2 explores the extent to which the application of bottom up microcosting, top down microcosting and gross costing produce different cost estimates. For the cost assessment of overheads and capital, the microcosting methodology is not applicable, because it is often not possible to identify a strong relationship between these indirect cost components and the healthcare service under consideration. Chapter 3 investigates the degree to which the application of different allocation alternatives produce different cost estimates. The healthcare services appendectomy, normal delivery, hip replacement, cataract, stroke and acute myocardial infarction serve as illustrations, on the basis of which an attempt is made to formulate general methodological recommendations.

Chapter 4 and 5 mean to establish reference unit prices from the standardised application of microcosting for the Netherlands. Chapter 4 aims to determine the reference prices for inpatient hospital days, outpatient visits and daycare treatments in the field of haematology and oncology. Chapter 5 estimates the reference price of intensive care unit days.

Chapters 6-11 address the standardised application of the microcosting methodology to detect actual cost differences between healthcare services in different countries (chapter 6 and 7), between healthcare services at different healthcare providers (chapter 6 and 8) and between alternative treatment options (chapters 8-11). Chapters 7 and 8 additionally compare microcosting estimates with reimbursement fees. Where applicable, the reference unit prices obtained from chapter 4 and 5 are employed to be able to truthfully compare treatment options. Healthcare services investigated include intensive care unit days, tooth fillings, diagnostic tests for the detection of coronary artery disease, treatments of benign (WHO grade I) meningioma, treatments of stage III colon cancer and the patellofemoral pain syndrome.

Finally, chapter 12 will draw general methodological conclusions regarding the application of the microcosting methodology by means of accuracy, feasibility, consistency and generalisability.

Chapter 2

Comparing methodologies for the cost estimation of healthcare services

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Leona Hakkaart-van Roijen

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2.1 ABSTRACT

The aim of the study was to determine whether the total cost estimate of a healthcare service remains reliable when the cost components of bottom up microcosting were replaced by the cost components of top down microcosting or gross costing. Total cost estimates were determined in representative general hospitals in the Netherlands for appendectomy, normal delivery, stroke and acute myocardial infarction for 2005. It was concluded that restricting the use of bottom up microcosting to those cost components that have a great impact on the total costs (i.e. labour and inpatient stay) would likely result in reliable cost estimates.

Keywords: Microcosting – Cost comparison – Cost calculation – Methodology – Healthcare service

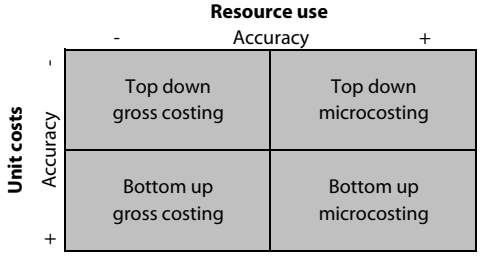
2.2 INTRODUCTION

Economic evaluations are increasingly used in the decision making of registration, reimbursement and pricing of healthcare services (Hoffmann & Graf von der Schulenburg 2000). The decision making is often hindered by the wide cost variations that are observed between economic evaluations that consider the same healthcare service. These variations are not a problem as long as they reflect actual differences, e.g. medical practice patterns, patient case-mixes, financial incentives and relative and absolute price differences between countries (Johnston et al. 1999; Raikou et al. 2000). However, Drummond et al. (2005) have suggested that some of the observed costs differences arise because of differences in costing methodology rather than because of actual differences in the performance of the healthcare services being evaluated.

An important cause for methodological differences concerns the level of accuracy that is addressed (figure 2.1). The level of accuracy is determined by the identification of cost components (gross costing versus microcosting) and valuation of cost components (top down versus bottom up costing). In gross costing cost components are defined at a highly aggregated level (e.g. inpatient days only), whereas in microcosting all relevant cost components are defined at the most detailed level (Drummond et al. 2005; Swindle et al. 1999). In the top down approach cost components are valued by separating out the relevant costs from comprehensive sources (e.g. annual accounts), resulting in average unit costs per patient. In the bottom up approach cost components are valued by identifying resource use directly employed for a patient, resulting in patient specific unit costs (Brouwer et al. 2001; Wordsworth et al. 2005).

Only a few studies have quantified the cost differences that are caused by methodological differences. Swindle et al. (1999) investigated the need to combine gross costing with microcosting to reflect resource use variations that are essential to the healthcare services. They concluded that microcosting should be applied in cost components that

Figure 2.1: Methodology matrix ~ the level of accuracy at the identification and valuation of cost components



are likely to show wide cost variation between patients (Swindle, Lukas 1999). However, Swindle et al. (1999) restricted their investigation to healthcare services that refer to the managed care system of the Department of Veterans Affairs in the United States and did not distinguish between the top down and bottom up approach.

In contrast, Wordsworth et al. (2005) compared cost estimates of a top down and bottom up methodology, but did not explore the gross costing methodology. In addition, although their study was conducted in five different countries, it was limited to dialysis therapy in end-stage renal disease. Wordsworth et al. (2005) concluded that a *full* bottom up methodology should be considered for healthcare services with a large component of labour or overheads (Wordsworth, Ludbrook 2005).

Economic evaluations do not have a systematic effect on the decision making process in healthcare, partially due to the application of different costing methodologies (Drummond, Sculpher 2005; Hoffmann & Graf von der Schulenburg 2000). Therefore, the establishment of standard or recommended methodologies is relevant in economic evaluations as well as in price setting for hospital management and health insurance purposes. Drummond et al. (1993) have argued that standard methodologies encourage scientific quality of economic evaluations, comparability between economic evaluations and assistance in the interpretation of results from setting to setting.

The combination of the bottom up and microcosting methodology (bottom up microcosting; figure 2.1) is generally believed to be the gold standard methodology for the costing of healthcare services. The methodology is reliable because all relevant cost components are identified and valued at the most detailed level (Drummond, Sculpher 2005). This allows for the identification of costs per individual patient and for insight in sub-populations that might have a great share in the total costs. However, bottom up microcosting is very time consuming, especially when hospital information systems are absent or inadequate. Consequently, an important challenge in conducting costing studies is the financial burden of the costing exercise (Wordsworth, Ludbrook 2005).

Decision makers must consider whether the benefits of more reliable cost data justify the additional costs incurred in obtaining accurate and detailed data. Instead of conducting a full bottom up microcosting study, it may be more efficient to restrict the application of bottom up microcosting to those cost components that are believed to have a great impact on the total costs (Drummond, Sculpher 2005). Therefore, the aim of the present study was to determine whether the total cost estimate of a healthcare service remains reliable when the cost components of bottom up microcosting were replaced by the cost components of top down microcosting or (bottom up) gross costing. Total cost

estimates were determined in representative general hospitals in the Netherlands for appendectomy, normal delivery, stroke and acute myocardial infarction (AMI) for 2005. These healthcare services serve as illustrations, on the basis of which we attempt to formulate general methodological recommendations.

2.3 METHODS

Total cost estimates for appendectomy, normal delivery, stroke and AMI were determined using bottom up microcosting, top down microcosting and (bottom up) gross costing. Resource use and unit costs were collected in representative general hospitals in the Netherlands for 2005. The hospital perspective was taken and all costs incurred from hospital admission to discharge of the patient were assessed. Direct costs involved diagnostic procedures (medical imaging services, laboratory services and other diagnostic procedures), medications, labour (direct patient time of medical specialists, residents, nurses and other staff), inpatient stay (hotel and nutrition and the indirect patient time of nurses) and devices. Indirect costs (overheads) included general expenses, administration and registration, energy, maintenance, insurance and the personnel costs of supportive departments. All costs were based on 2005 cost data. Where necessary, costs were adjusted using the general price index (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

Bottom up microcosting

The bottom up microcosting was characterised by the identification of patient specific resource use and hospital specific unit costs. The microcosting was performed as part of the EU funded research project *Health*BASKET (full title: Health Benefits and Service Costs in Europe, contract no. FP6 501588) (Busse et al. 2006; Schreyogg et al. 2005). Retrospective cost analyses were conducted in fifteen general hospitals for appendectomy (n=100), normal delivery (n=70), stroke (n=70) and AMI (n=60). The patient samples contained patients without co-morbidities or complications. Direct costs were determined by combining resource use with the unit costs of direct cost components. Resource use was available per individual patient. Unit costs of diagnostic procedures and devices were obtained from (financial) hospital databases. Medication costs were derived from the administration of the hospital pharmacies. Labour costs were based on standardised costs per day or per minute, which equalled the normative income divided by the number of workable days or minutes per year. Normative incomes were based on the fees agreed on in collective labour agreements. Annual costs on inpatient stay were taken from the annual accounts for the year 2005 and divided by the annual number

of patient days to calculate costs per inpatient day. Overheads were also taken from the annual accounts of 2005 and appointed to direct costs by raising the direct costs with a mark-up percentage (marginal mark-up allocation). The mark-up percentage was determined by dividing annual indirect costs by annual direct costs.

Top down microcosting

The top down microcosting was characterised by the identification of patient specific resource use and national tariffs as unit costs. The microcosting was conducted in twenty-three general hospitals, where prospective cost analyses for appendectomy (n=528), normal delivery (n=1,821), stroke (n=1,216) and AMI (n=690) were performed in 2004. The patient samples contained patients without co-morbidities or complications. Resource use was now available for an average patient only, e.g. a norm-time (the time in which a specialist is expected to be able to perform his tasks) was used for the treatment time. Unit costs were based on national tariffs. Overheads were allocated using hourly rate allocation in which the service time of the primary treatment serves as a proxy for resource consumption, yielding a cost per treatment minute.

Gross costing

The gross costing was characterised by the identification of resource use of inpatient days only and hospital specific unit costs. Retrospective cost analyses at twenty-five general hospitals were performed in 2007. The patient samples contained all patients that presented at the hospital with appendectomy (n=660), normal delivery (n=2,114), stroke (n=1,484) or AMI (n=780) including those who had co-morbidities and complications. The methodology just distinguished inpatient stay and overheads, which were appointed to patients on the basis of inpatient days only using a bottom up approach. Direct and indirect annual costs were taken from the annual accounts for the year 2005 and divided by the annual number of inpatient days to calculate direct and indirect costs per inpatient day. The mean costs per patient were then determined by multiplying the length of stay (LOS) with the total costs per inpatient day. The mean LOS of the bottom up microcosting was used in order to correct for the inclusion of patients that had co-morbidities and complications.

Comparison of total cost estimates

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 13.0. In addition to descriptive statistics, tests for normal distribution of the total cost estimates were performed using the Kolmogorov–Smirnov test. Total

cost estimates of the top down microcosting and gross costing were compared with those of the bottom up microcosting by means of cost differences, 95% confidence intervals, two-sample T tests and non-parametric Mann-Whitney U test. In all cases $P < 0.05$ was taken as statistically significant. Finally, cost differences between the bottom up microcosting and bottom up microcosting in which the cost components were individually or simultaneously replaced by top down microcosting or gross costing were examined by means of percentage.

2.4 RESULTS

Appendectomy

The bottom up microcosting resulted in total costs of € 1,796 (SD 220; table 2.1). Labour contributed to half of the total costs, mainly due to costs for the diagnostic laparoscopy that was performed in three quarters of the patients. The LOS ranged from 1.5 to 3 days between hospitals. The total cost estimates obtained using top down microcosting (€ 2,025; SD 341) and gross costing (€ 2,278; SD 480; table 2.2) were somewhat higher than the bottom up microcosting.

Table 2.1: Total cost estimates of the bottom up microcosting (Euro 2005)

	Appendectomy	Normal delivery	Stroke	Acute myocardial infarction
Diagnostic procedures				
Medical imaging services	42.75	0.57	162.10	100.67
Laboratory services	53.68	20.11	56.12	77.46
Other	35.34	36.17	38.17	171.58
Medications	34.40	0.78	14.86	423.89
Labour				
Medical specialist	627.96	45.83	797.13	233.15
Resident	52.49	25.07	107.40	75.46
Nurse	115.06	118.61	21.56	179.09
Other	60.56	207.57	236.85	209.86
Inpatient stay				
Hotel and nutrition	90.22	32.21	675.67	249.60
Normal ward	285.63	0.00	1,959.10	511.97
Intensive care	0.00	0.00	503.57	1,431.08
Devices	0.00	0.00	0.00	1,395.33
Overheads	397.32	146.66	1,691.49	278.49
TOTAL	**1,795.42**	**633.58**	**6,264.02**	**5,337.63**

Table 2.2: Total cost estimates of bottom up microcosting, top down microcosting and gross costing (Euro 2005)

	Bottom up microcosting	Top down microcosting	Gross costing
Appendectomy	**1,796**	**2,025**	**2,278**
Diagnostic procedures + medications	166	173	
Labour	856	757	1,662
Inpatient stay + devices	376	755	
Overheads	397	340	616
Normal delivery	**634**	**711**	**718**
Diagnostic procedures + medications	58	18	
Labour	397	475	506
Inpatient stay + devices	32	55	
Overheads	147	163	212
Stroke	**6,264**	**7,235**	**12,154**
Diagnostic procedures + medications	271	537	
Labour	1,163	729	7,605
Inpatient stay + devices	3,138	4,217	
Overheads	1,691	1,752	4,549
Acute myocardial infarction	**5,338**	**5,738**	**10,842**
Diagnostic procedures + medications	774	771	
Labour	698	660	7,256
Inpatient stay + devices	3,588	3,417	
Overheads	278	890	3,586

Normal delivery

Total costs in the bottom up microcosting equalled € 634 (SD 243; table 2.1). Labour was responsible for two thirds of the total costs. All normal deliveries concerned outpatient admissions with a LOS ranging from 0.5 to 1.0 days between hospitals. The total cost estimate obtained using top down microcosting was very similar to the estimate using bottom up microcosting. That obtained using gross costing was slightly higher than the bottom up microcosting (€ 718; SD 201; table 2.2).

Stroke

Total costs in the bottom up microcosting summed up to € 6,264 (SD 3,704; table 2.1). Conservative (drug) treatment and trombolysis were performed in 71% and 29% of the patients respectively. Inpatient stay contributed to half of the total costs with a LOS ranging from 5 to 18 days between hospitals. Approximately 20% of the inpatient days were spent at a stroke unit. The total cost estimate obtained using top down microcost-

ing was somewhat higher (€ 7,235; SD 2,886) and that obtained using gross costing even two times higher (€ 12,154; SD 2,801; table 2.2) than the bottom up microcosting.

Acute myocardial infarction

The bottom up microcosting resulted in total costs of € 5,338 (SD 1,299; table 2.1). Percutaneous transluminal coronary angioplasty (PTCA), conservative (drug) treatment and trombolysis were performed in 91%, 7% and 2% of the patients respectively. Inpatient stay accounted for 67% of the total costs, mainly due to costs for the stent that was implanted in all PTCA patients. The LOS ranged from 5 to 7 days between hospitals. About one third of the inpatient days was spent at the intensive care unit. The total cost estimate obtained using top down was virtually equal to the bottom up microcosting (€ 5,738; SD 2,223), whereas that using gross costing was two times higher than the bottom up microcosting (€ 10,842; SD 2,788; table 2.2).

Comparison of total cost estimates

Table 2.3 presents the descriptive statistics of the total cost estimates using bottom up microcosting, top down microcosting and gross costing. The total cost estimates were clearly normally distributed ($0.423 < P < 0.886$), except for that of the gross costing for normal delivery ($P = 0.047$).

The estimates according to the top down were generally higher than the bottom up microcosting, albeit only slightly. Two-sample T tests showed that the cost estimates of the bottom up and top down microcosting were not significantly different for normal delivery, stroke and AMI ($P > 0.478$). However, the estimates of the two methodologies were significantly different for appendectomy ($P = 0.033$; table 2.3). Fairly reliable total cost estimates were obtained when the cost components of the bottom up microcosting were *individually* replaced by the cost components of top down microcosting (table 2.4). Nevertheless, top down microcosting provided a relatively weak alternative to cost components with a large impact on the total costs. That is, labour in normal delivery (63%) and inpatient stay in appendectomy (21%) and stroke (50%). Overall, comparable results were obtained when two or three cost components were *simultaneously* replaced by the cost components of top down microcosting.

The total costs for stroke and AMI using the gross costing were substantially higher than the bottom up microcosting (stroke 94% higher, AMI 103% higher). Replacing either the direct or indirect cost component of the bottom up microcosting with that of the gross costing reinforced this finding (table 2.4). Significant differences between the estimates

Table 2.3: Descriptive statistics of the total cost estimates for the bottom up microcosting, top down microcosting and gross costing

	Hospital sample, n	Patient sample, n	Hospital sample, mean	SD	Mean Difference compared to Bottom up	95% Confidence Interval for Mean Difference		Two samples Test T	Sig. (2-tailed)
						Lower Bound	Upper Bound		
Bottom up microcosting									
Appendectomy	10	100	1,796	220	-	-	-	-	-
Normal delivery	7	70	634	243	-	-	-	-	-
Stroke	7	70	6,264	3,704	-	-	-	-	-
Acute myocardial infarction	6	60	5,338	1,299	-	-	-	-	-
Top down microcosting									
Appendectomy	21	528	2,025	341	229	29	429	2.25	0.033
Normal delivery	21	1,821	711	266	77	136	290	0.71	0.478
Stroke	21	1,216	7,235	2,886	971	2,038	3,980	0.63	0.558
Acute myocardial infarction	21	690	5,738	2,223	400	1,009	1,809	0.56	0.591
Gross costing									
Appendectomy	25	660	2,278	480	482	158	806	3.03	0.005
Normal delivery	25	2,114	718	201	84	63	231	1.16	0.254
Stroke	25	1,484	12,154	2,801	5,890	3,267	8,513	4.59	0.000
Acute myocardial infarction	25	780	10,842	2,788	5,504	3,093	7,915	7.15	0.000

SD = standard deviation

Sig. = significance

Table 2.4: Total cost estimates of bottom up microcosting in which one cost component was estimated using top down microcosting or gross costing (Euro 2005)

	Total costs ~ bottom up microcosting			
	Appendectomy	**Normal delivery**	**Stroke**	**Acute myocardial infarction**
Base case	**1,796**	**634**	**6,264**	**5,338**
Diagnostic procedures + medications				
Top down microcosting	1,802	594	6,530	5,335
Labour				
Top down microcosting	1,696	*711	5,830	5,300
Inpatient stay				
Top down microcosting	**2,175	656	*7,343	5,167
Gross costing ▲	*2,059	653	***9,296	***7,534
Overheads				
Hourly rate allocation	1,738	650	6,325	*5,949
Inpatient day allocation	*2,014	*699	***9,122	***8,645

▲ = including diagnostic procedures + medications and labour
* = deviation from base case > 10%
** = deviation from base case > 20%
*** = deviation from base case > 30%

of the bottom up microcosting and gross costing were observed for appendectomy, stroke and AMI (two-sample T test, $P < 0.005$; Mann-Whitney U test, $P < 0.005$). These cost differences were consistently greater than those of the bottom up and top down microcosting (table 2.3).

2.5 DISCUSSION

The extent to which bottom up microcosting is reflected by total cost estimates using top down microcosting or gross costing seems to differ between healthcare services. Our results suggest that top down microcosting can be a strong alternative to bottom up microcosting. However, relatively poor total cost estimates are obtained when the cost components with a large impact on the total costs are obtained using top down microcosting. Specifically, in line with the results of Wordsworth et al. (2005), bottom up microcosting may be preferred over top down microcosting for labour with respect to labour intensive healthcare services (such as normal delivery). Additionally, bottom up microcosting may result in more favourable cost estimates for inpatient stay with respect to healthcare services with a long LOS (such as stroke). Basically, the costs of an inpatient day consist of the costs of hotel and nutrition, normal ward and intensive care

(table 2.1) which unit costs vary widely between hospitals. In our hospital sample, the unit costs of hotel and nutrition varied between € 22 and € 85 per day and those of the normal ward between € 80 and € 154 per day.

Our results further imply that gross costing might be a weak alternative to bottom up microcosting. In agreement with the study of Swindle et al. (1999), this is particularly true for healthcare services that show wide cost variation between patients (such as stroke and AMI). Generally, our study revealed a wide cost variation for healthcare services with a long LOS. The total costs for stroke and AMI (with mean LOS of 9.2 and 5.7 days respectively) were two times higher using gross costing than using bottom up microcosting. Contrary, the gross costing estimate for normal delivery (with a mean LOS of 0.8 days) did not significantly differ from the bottom up microcosting estimate (two-sample T test, $P = 0.254$; table 2.3).

Our study showed two remarkable results. Hourly rate allocation was a good proxy to marginal mark-up allocation, with the exception of AMI. However, the share of overheads for AMI (5%) was considerably lower compared to those for appendectomy (22%), normal delivery (23%) and stroke (27%). This can be explained by the fact that only one hospital (1/6) of the bottom up microcosting for AMI was able to provide a mark-up percentage. This relatively very low mark-up percentage was subsequently imputed to the other hospitals.

Another remarkable result was the fact that a significant deviation from the bottom up microcosting was observed when the *inpatient stay* component for appendectomy was obtained using top down microcosting. However, *labour* had a greater impact (48%) than inpatient stay (24%) on the total costs of the healthcare service. The deviation of the inpatient stay component was probably due to a relatively high inpatient stay estimate in the top down microcosting.

This study has several limitations. Firstly, the study meant to consider all costs incurred from hospital admission to discharge of the patient. However, hospital financial databases do not capture capital costs because hospitals receive separate funding to cover these costs (Oostenbrink et al. 2002). As a result, the total costs of the three methodologies were compared excluding capital costs.

The original patient samples used for the gross costing calculations included patients with and without co-morbidities and complications, while the samples used for the bottom up and top down microcosting calculations included patients without co-morbidities and complications only. Not surprisingly, no significant differences were

found between the LOS of the bottom up and top down microcosting samples (P = 0.776). However, the mean LOS of the gross costing samples was on average 37% higher than that of the microcosting samples. To prevent that the cost comparisons between the methodologies were confounded by actual differences (i.e. patient case-mixes), the LOS of the bottom up microcosting was used for the gross costing calculations. In general it is known that costs of healthcare services are skewed and a few patients with co-morbidities and complications may have a considerable impact on the average costs per inpatient day. Future studies could determine whether our conclusions are generalisable to patient populations with and without co-morbidities and complications.

Even though different databases were used for the three methodologies, we believe that the hospital samples are sufficiently representative of the target population of all hospital admissions. The average number of beds per hospital in our sample was 492 beds, which is close to the average number of beds per hospital in the Netherlands (453 beds) (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007). Moreover, the hospitals in our study were located at different regions in the Netherlands.

To determine the uncertainty of the obtained microcosting estimates, one-way sensitivity analyses were carried out by varying the resource use and unit cost values of individual cost components between 50% and 150%. The greatest deviation in the total costs was found when treatment time was altered, but the deviation was limited to ± 6-28%. Changing the mark-up percentage for the calculation of the overhead costs resulted in a deviation in the total costs of only ± 4-17%.

In practice, other factors play a role in the decision on which costing methodology is best applied. One consideration lies in the aim of the cost calculation. Bottom up microcosting is preferably performed as part of economic evaluations, because the methodology allows for the calculation of actual cost per individual patient or sub-population. Top down microcosting is generally performed to support budgetary decisions, for which an average cost measure per patient from the hospital (management) perspective is employed. Other considerations are the availability of time and data. The application of microcosting is lengthy and expensive, because resource use and unit costs are often not available or inaccurately registered. Only when the cost calculation aims to provide a cost estimate short term or when data is not available, gross costing could be considered. However, gross costing should always be interpreted with caution because the methodology is often not reliable and thus sensitive to wrong conclusions. Gold et al. (1996) have suggested earlier that the choice between costing methodologies should reflect the importance of precise cost estimates, feasibility and costs.

Economic evaluations are a prerequisite for reimbursement or implementation of healthcare services in many countries, because they can provide healthcare decision makers with valuable information on the relative efficiency of different services. However, the use of standard methodologies is required to ensure comparability and relevance to health policy makers (Drummond, Sculpher 2005; Hoffmann & Graf von der Schulenburg 2000). Even though bottom up microcosting is generally believed to be the gold standard methodology for the costing of healthcare services, it has not been widely used in economic evaluations of healthcare services. The methodology is very time consuming and, therefore, decision makers must trade off data reliability and the cost of collecting accurate and detailed data. The present study suggests that restricting the use of bottom up microcosting to those cost components that have a great impact on the total costs (i.e. labour and inpatient stay) would likely result in reliable total cost estimates.

2.6 ACKNOWLEDGEMENTS

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Chapter 3

Comparing methodologies for the allocation of overhead and capital costs to healthcare services

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3.1 ABSTRACT

Typically little consideration is given to the allocation of indirect costs (overheads and capital) to healthcare services, compared to the allocation of direct costs. Weighted service allocation is believed to provide the most accurate indirect cost estimation, but the method is time consuming. The aim of this study was to determine whether hourly rate, inpatient day and marginal mark-up allocation are reliable alternatives for weighted service allocation. We compared the cost approaches independently for appendectomy, hip replacement, cataract and stroke in representative general hospitals in the Netherlands for 2005. Our results suggest that hourly rate allocation and inpatient day allocation produce estimates that are not significantly different from weighted service allocation. Hourly rate allocation may be a strong alternative to weighted service allocation for healthcare services with a relatively short inpatient stay. The use of inpatient day allocation would likely most closely reflect the indirect cost estimates obtained by the weighted service method.

Keywords: Indirect cost allocation – Cost comparison – Overheads – Healthcare service – Methodology

3.2 INTRODUCTION

Economic evaluations are a prerequisite for the reimbursement and implementation of healthcare services in many countries, because they can provide healthcare decision makers with valuable information on the relative efficiency of different services (Drummond et al. 2005; Hoffmann & Graf von der Schulenburg 2000). To be able to support management decisions, direct and indirect cost estimations should therefore be associated as closely as possible with the patients who cause them to be incurred (Roberts et al. 1999). However, the assessment of *actual* resource use is lengthy and expensive, especially when hospital information systems are absent or inadequate (Drummond, Sculpher 2005; Finkler et al. 2007).

Indirect cost components generally concern overheads (general expenses, administration and registration, energy, maintenance, insurance and the personnel costs of non patient services, like management and administration) and capital (depreciation of buildings and inventory and interest). They often comprise a large proportion of the overall costs of healthcare services (Finkler, Ward 2007; Roberts, Frutos 1999). In a study of St-Hilaire et al. (2000) carried out in Canada, indirect costs were estimated to represent between 35% and 40% of the total costs of healthcare services. More recently, Oostenbrink et al. (2002) have estimated the proportion of indirect costs to be 24% in the Netherlands. However, compared to the allocation of direct cost components, usually little consideration is given to the allocation of indirect cost components to healthcare services (Finkler, Ward 2007; St-Hilaire & Crepeau 2000). St-Hilaire et al. (2000) have suggested that the lack of interest and theoretical support for the estimation of indirect costs is mainly due to their arbitrary nature. An invalid estimation of indirect costs may completely wipe out the time and effort spent on the cost determination of the direct costs. In order to generate valuable information for decision making, it is therefore recommended to gain a better understanding of the distribution of indirect cost components (Roberts, Frutos 1999).

There are two types of indirect cost allocation (Finkler, Ward 2007). Firstly, the allocation of indirect costs from the supporting departments to the medical departments within the hospital should be considered, using e.g. cost center allocation or activity based costing (Drummond, Sculpher 2005; Finkler, Ward 2007; St-Hilaire & Crepeau 2000). However, the present paper will focus on the second type of allocation, which allocates indirect costs within the medical department to specific patient(-group)s. Cost center allocation and activity base costing are not applicable to this type of allocation, because these methods assume that the indirect costs have a cause and effect relationship with the department rather than with patients. Therefore, no allocation base or cost driver

can trace indirect costs to the *actual* resource utilisation of patients in an economically feasible way (Finkler, Ward 2007; Oostenbrink et al. 2002).

Finkler et al. (2007) have described four basic methods for the distribution of indirect costs within the medical department to specific patient(-group)s. The first method is weighted service allocation, which establishes the relative costs of each patient by assigning relative value units. The method is believed to most closely reflect *actual* resource consumption. However, it is very time consuming to observe the *actual* resource use of each patient and to convert the various resource use components into units suitable for assessing relative value units (Finkler, Ward 2007). Therefore, most economic evaluations apply hourly rate allocation, inpatient day allocation or marginal mark-up allocation. The hourly rate method employs service time of the primary treatment as a proxy for resource consumption, yielding a cost per treatment minute. In inpatient day allocation, all patients are assumed to have the same indirect costs per inpatient day regardless of their *actual* resource use. Marginal mark-up allocation distributes indirect costs to direct costs by raising the direct costs with a mark-up percentage.

Cost estimates based on *actual* resource use are relevant for both economic evaluations as well as price setting for hospital management and health insurance purposes (Hoffmann & Graf von der Schulenburg 2000). Decision makers must consider whether the benefits of more reliable cost data justify the additional costs incurred in obtaining accurate and detailed data (Finkler, Ward 2007; St-Hilaire & Crepeau 2000). However, even though indirect cost often represent a large share of the total cost of healthcare services, no studies have quantified the cost differences that result from the application of the different methods for the allocation of indirect costs within the medical department to patient(-group)s. Hence, the aim of the present study was to determine whether hourly rate, inpatient day and marginal mark-up allocation are reliable alternatives for weighted service allocation. We report the results of a costing exercise designed to collect and compare the indirect cost allocation approaches independently for appendectomy, hip replacement, cataract and stroke in representative general hospitals in the Netherlands for 2005. These healthcare services represent large burden of disease measured as number of people affected or costs related in many developed and developing countries. The healthcare services serve as illustrations, on the basis of which we attempt to formulate general methodological recommendations.

3.3 METHODS

The costing exercise was conducted as part of the EU funded research project *Health*-BASKET (full title: Health Benefits and Service Costs in Europe, contract no. FP6 501588) (Busse et al. 2006; Schreyogg et al. 2005). Retrospective cost analyses were conducted at eighteen general hospitals in the Netherlands for appendectomy (n=100), hip replacement (n=70), cataract (n=70) and stroke (n=70), from the hospital perspective. The study included 100 males between 14 and 25 years of age who presented at the hospital with acute abdominal pain, 70 females between 65 and 75 years of age with hip osteoarthritis requiring hip replacement because of considerable impairment, 70 males between 70 and 75 years of age who were diagnosed with Cataracta Senilis and 70 otherwise healthy females of between 60 and 70 years of age with severe hemiparesis, aphasia and dependency.

Direct cost estimates were determined using the microcosting methodology, in which all relevant cost components from hospital admission to discharge of the patient were defined at the most detailed level. Direct costs included diagnostic procedures (medical imaging services, laboratory services and other diagnostic procedures), medications, labour (direct patient time of medical specialists, residents, nurses and other staff), inpatient stay (hotel and nutrition and the indirect patient time of nurses) and devices. Details of the direct cost analyses are described in detail elsewhere (Epstein et al. 2008; Fattore & Torbica 2008; Schreyogg 2008; Stargardt 2008).

Indirect cost components included overheads and capital and were appointed to healthcare services using weighted service allocation, hourly rate allocation, inpatient day allocation and marginal mark-up allocation. *Annual* direct and indirect costs were taken from the annual accounts of the participating hospital departments. All costs were based on 2005 cost data. Where necessary, costs were adjusted using the general price index of the Dutch Central Bureau of Statistics (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

Weighted service allocation

The weighted service method establishes the relative cost of each patient, by assigning a base value to the elementary resource use of the healthcare service and adding relative values to this base value when the patient incurred additional resource use (Finkler, Ward 2007). For each healthcare service, all participating hospitals were included in an ordinary least squares (OLS) regression analysis. OLS regression was chosen because the technique means to disentangle the relationship between an outcome variable (also

called dependent variable) and predictor variables (also called independent variables). Direct costs were taken as the dependent variable and department and treatment characteristics as explanatory variables. Department characteristics consisted of the number of beds per department, bed occupation and the number of surgeons per department. Treatment characteristics comprised inpatient stay, medication costs, treatment time and use of additional interventions (cemented hip, yes/no for hip replacement; thrombolysis, yes/no for stroke). Data on treatment characteristics were analyzed at the hospital level since individual patient data were not available. A full model was assembled using backward regression. The β_0- coefficient of the model was considered the elementary resource use of each healthcare service. Subsequently, the corresponding β-coefficients of the explanatory variables that were significantly associated with the direct costs were assumed to add a relative value. Based on the weighted service method, the predicted indirect costs per patient were estimated by dividing *annual* direct costs by the product of the predicted direct costs and *annual* indirect costs.

Hourly rate allocation

The hourly rate method employs service time of the primary treatment as a proxy for resource consumption, yielding a cost per treatment minute. The unit costs per treatment minute were determined by dividing the *annual* indirect costs by the total number of workable minutes of the medical specialists of the corresponding hospital departments in 2005.

Inpatient day allocation

In inpatient day allocation, all patients are assumed to have the same indirect costs per day regardless of their *actual* resource use. The *annual* indirect costs were divided by the total number of inpatient days in 2005 to calculate the unit costs per inpatient day.

Marginal mark-up allocation

In marginal mark-up allocation, indirect costs are distributed to direct costs by raising the direct costs with a mark-up percentage. The mark-up percentage was determined by dividing *annual* indirect costs by *annual* direct costs.

Comparison of methodologies

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 13.0. In addition to descriptive statistics, the Friedman test was per-

formed to detect cost differences between the four methods for each of the healthcare services. Indirect cost estimates of hourly rate, inpatient day and marginal mark-up allocation were compared with those of weighted service allocation by means of cost differences and the Wilcoxon signed ranks test Z.

3.4 RESULTS

Appendectomy

The weighted service method resulted in overhead costs of € 647 (SD 201) and capital costs of € 237 (SD 100; table 3.1). The indirect costs contributed to 39% of the total costs. Treatment time and medication costs were considered to add relative value to the base value (table 3.2). The overhead estimate based on hourly rate allocation was somewhat higher compared to weighted service allocation (€ 738; SD 615), whereas the estimate obtained using marginal mark-up allocation was somewhat lower (€ 397; SD 32; table 3.1). The indirect cost estimates obtained using the inpatient day method were virtually equal to those using the weighted service method.

Hip replacement

The weighted service method resulted in overhead costs of € 1,733 (SD 658) and capital costs of € 618 (SD 256; table 3.1). The bed occupation, number of surgeons and treatment time were considered to add relative value to the base value (table 3.2). Hourly rate, inpatient day and marginal mark-up allocation resulted in slightly lower indirect costs than weighted service allocation (table 3.1).

Cataract

The overhead and capital costs in the weighted service method totalled € 203 (SD 66; table 3.1) and were responsible of 29% of the total costs. Although the model explained 81% of the direct costs, there was only a weak significance between the direct costs and inpatient stay and between the direct costs and treatment time ($0.10 < P < 0.20$). The indirect cost estimates obtained using hourly rate allocation were more than twice as high as the estimates using weighted service allocation. Inpatient day and marginal mark-up allocation resulted in somewhat lower indirect costs compared to weighted service allocation (table 3.1).

Table 3.1: Total cost estimates using weighted service, hourly rate, marginal mark-up and inpatient day allocation (Euro 2005)

	Weighted service allocation		Hourly rate allocation		Inpatient day allocation		Marginal mark-up allocation	
	mean	SD	mean	SD	mean	SD	mean	SD
Appendectomy	**2,282**	**322**	**2,431**	**246**	**2,278**	**297**	**2,002**	**246**
Direct costs	1,398	125	1,398	125	1,398	125	1,398	125
Indirect costs	884	242	1,033	865	880	230	604	54
Overheads	647	201	738	615	643	191	397	32
Capital	237	100	295	260	237	100	207	29
Hip replacement	**6,421**	**1,812**	**6,247**	**1,792**	**6,312**	**1,362**	**6,378**	**1,792**
Direct costs	4,070	1,031	4,070	1,031	4,070	1,031	4,070	1,031
Indirect costs	2,351	868	2,177	1,391	2,241	521	2,307	848
Overheads	1,733	658	1,667	1,201	1,658	460	1,706	686
Capital	618	256	510	229	583	148	601	236
Cataract	**690**	**180**	**969**	**166**	**668**	**146**	**630**	**166**
Direct costs	487	127	487	127	487	127	487	127
Indirect costs	203	66	482	540	181	23	143	58
Overheads	147	49	350	390	131	20	104	47
Capital	56	20	132	154	50	10	39	14
Stroke	**11,589**	**8,439**	**7,527**	**4,064**	**10,447**	**4,477**	**6,874**	**4,064**
Direct costs	4,573	2,371	4,573	2,371	4,573	2,371	4,573	2,371
Indirect costs	7,017	7,483	2,954	3,961	5,874	2,263	2,301	1,243
Overheads	5,917	7,375	2,538	3,807	4,609	2,315	1,692	942
Capital	1,100	849	416	494	1,265	667	609	302

SD = standard deviation

Stroke

The weighted service method resulted in overhead costs of € 5,917 (SD 7,375) and capital costs of € 1,100 (SD 849; table 3.1). The proportion of indirect cost components was 60% of the total costs. Inpatient stay and treatment time were considered to add relative value to the base value, albeit with a weak significance ($0.10 < P < 0.20$; table 3.2). The capital estimate of the inpatient day method was a bit higher than that of the weighted service method. All other estimates were considerably lower than those of weighted service allocation, ranging from 22% lower (overhead estimate of the inpatient day method) to 71% lower (overhead estimate of the marginal mark-up method) (table 3.1).

Table 3.2: Regression models used to define relative value units for the weighted service method

	Appendectomy $R^2 = 0.674$		Hip replacement $R^2 = 0.752$		Cataract $R^2 = 0.809$		Stroke $R^2 = 0.874$	
	Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**
Constant	1,065.77	***97.00	11,663.71	**4,678.90	32.70	*114.49	264.52	*1,395.45
Department characteristics								
Bed occupation (%)			132.48	*74.73				
Number of medical specialists (fulltime units)			166.42	*187.25				
Treatment characteristics								
Inpatient stay (days)					646.02	*447.55	186.57	*123.72
Treatment time (minutes)	1.96	***1.14	7.10	*13.69	0.78	*4.61	3.48	*3.23
Medication costs (Euro 2005)	7.45	**2.66						

SE = standard error
* P < 0.20
** P< 0.10
*** P < 0.05

Comparison of methodologies

Table 3.3 presents the descriptive statistics of the indirect cost estimates using weighted service, hourly rate, inpatient day and marginal mark-up allocation. The Friedman test showed significant differences between the four methods for appendectomy ($P = 0.006$) and stroke ($P = 0.029$), whereas no significant differences were found for hip replacement ($P = 0.845$) and cataract ($P = 0.418$).

The extent to which the hourly rate estimates reflected the weighted service estimates varied between healthcare services. Although cost differences ranged from –58% for

Table 3.3: Indirect cost estimates for the weighted service, hourly rate, marginal mark-up and inpatient day allocation (Euro 2005)

	Hospital sample, n	Patient sample, n	Indirect cost, mean	SD	Mean Difference compared to weighted service	Wilcoxon signed ranks test Z Exact Sig. (2-tailed)
Appendectomy						
Weighted service allocation	10	100	884	242	-	-
Hourly rate allocation	10	100	1,033	865	149	1.000
Inpatient day allocation	10	100	880	230	-4	0.922
Marginal mark-up allocation	10	100	604	54	-280	0.002
Hip replacement						
Weighted service allocation	7	70	2,351	868	-	-
Hourly rate allocation	7	70	2,177	1,391	-174	0.813
Inpatient day allocation	7	70	2,241	521	-110	0.688
Marginal mark-up allocation	7	70	2,307	848	-44	1.000
Cataract						
Weighted service allocation	7	70	203	66	-	-
Hourly rate allocation	7	70	482	540	278	0.469
Inpatient day allocation	7	70	181	23	-22	0.938
Marginal mark-up allocation	7	70	143	58	-60	0.297
Stroke						
Weighted service allocation	7	70	7,017	7,483	-	-
Hourly rate allocation	7	70	2,954	3,961	-4,062	0.219
Inpatient day allocation	7	70	5,874	2,263	-1,143	0.688
Marginal mark-up allocation	7	70	2,301	1,243	-4,716	0.031

SD = standard deviation
Sig. = significance

stroke to +137% for cataract, there were no statistically significant differences, likely because of the relatively large standard deviations ($P > 0.219$; table 3.3).

The indirect cost estimates according to the inpatient day method were generally slightly lower than the estimates according to the weighted service method. Wilcoxon signed ranks Z tests showed that the cost estimates of weighted service and inpatient day allocation were not significantly different for any of the healthcare services ($P > 0.688$; table 3.3).

The indirect costs using the marginal mark-up method were substantially lower than the weighted service method, with the exception of hip replacement. These cost differences were consistently greater than those between the weighted service and inpatient day method ($P < 0.297$; table 3.3).

Finally, differences between hourly rate allocation and inpatient day allocation, between hourly rate and marginal mark-up allocation and between inpatient day allocation and marginal mark-up allocation were explored. Wilcoxon signed ranks Z tests only observed

Figure 3.1: Relationship between the total cost estimates using weighted service and hourly rate allocation for the estimation of indirect costs (Euro 2005)

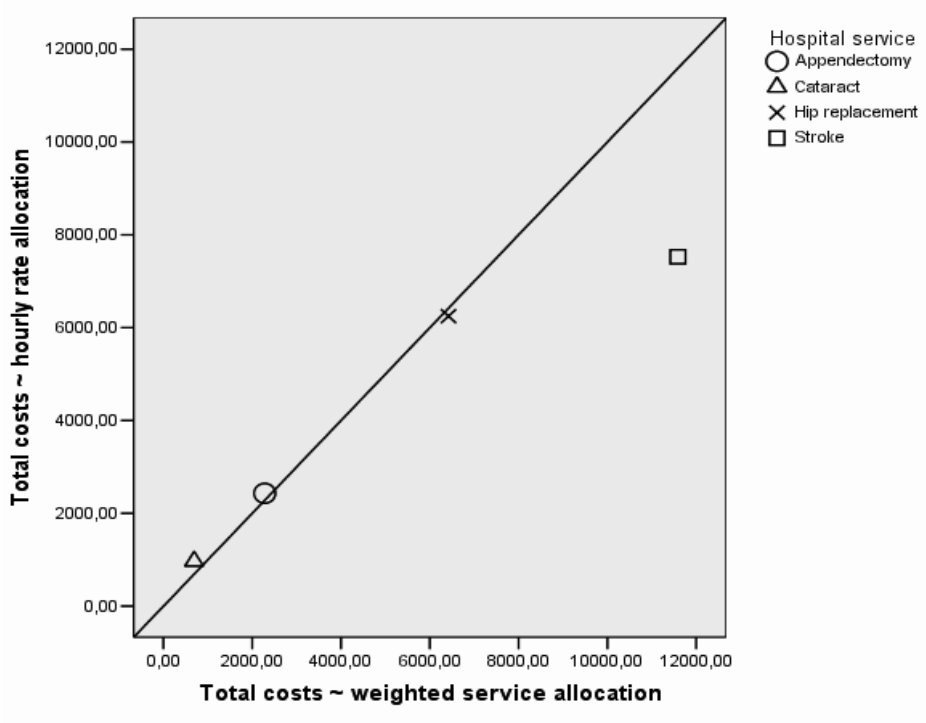
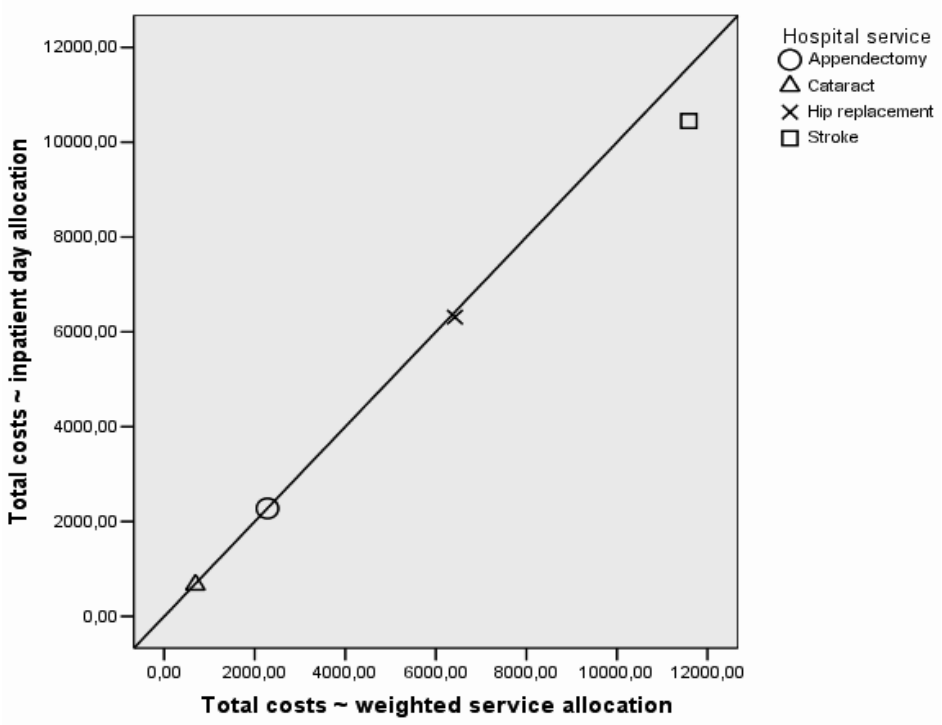


Figure 3.2: Relationship between the total cost estimates using weighted service and inpatient day allocation for the estimation of indirect costs (Euro 2005)



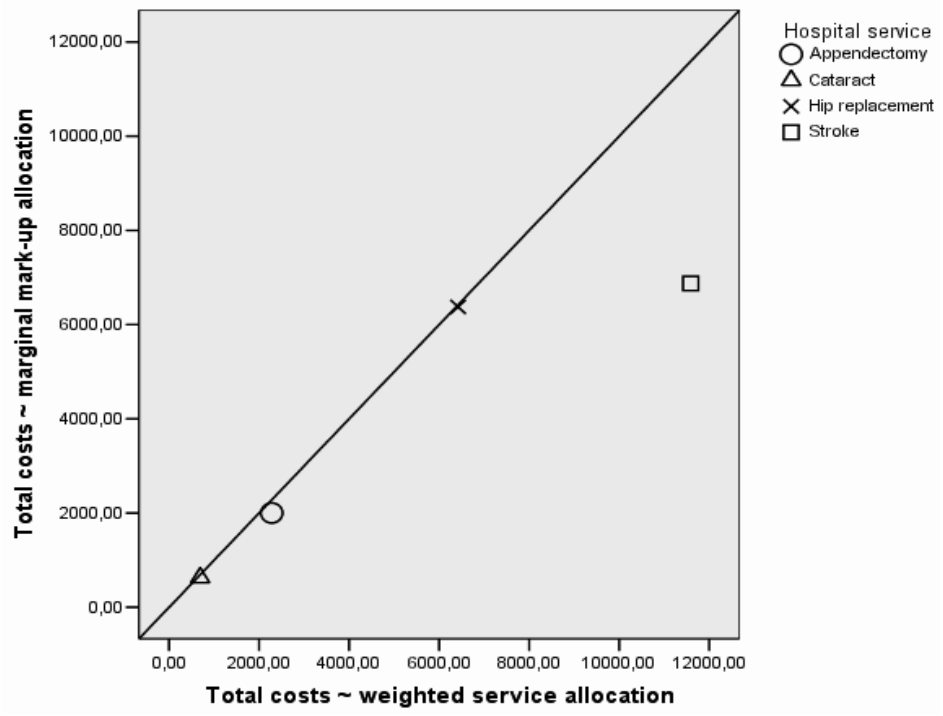
significant differences between inpatient day allocation and marginal mark-up allocation for appendectomy ($P = 0.002$) and stroke ($P = 0.016$).

Despite the differences in indirect cost estimates, the total (direct and indirect) cost estimates are similar. Figures 3.1, 3.2 and 3.3 show that the only important deviations between total cost estimate using the weighted service estimate and the total cost estimates using the other indirect cost methods are found with stroke.

3.5 DISCUSSION

Even though weighted service allocation is believed to most closely reflect *actual* resource use consumption, our results suggest that hourly rate allocation and inpatient day allocation produce estimates that are not significantly different from weighted service allocation. One particular allocation method does not necessarily produce indirect cost estimates that are always higher than those obtained using another method. For example, where indirect costs for appendectomy and cataract were lower using mar-

Figure 3.3: Relationship between the total cost estimates using weighted service and marginal mark-up allocation for the estimation of indirect costs (Euro 2005)



ginal mark-up allocation, they were higher using hourly rate allocation in comparison to weighted service allocation.

Generally, our study revealed that inpatient stay has a great impact on the indirect cost estimates of the allocation methods. The use of inpatient day allocation would likely most closely reflect the indirect cost estimates obtained by the weighted service method (table 3.3). However, inpatient day allocation may underestimate the proportion of indirect costs in healthcare services with a short inpatient stay, because the costs incurred during treatment are allocated evenly to all inpatient days (the inpatient day on which the treatment took place as well as the subsequent inpatient days). Furthermore, the inpatient day method fails to trace costs directly to the patients who incur that cost. The result is that costs are allocated by averaging (Drummond, Sculpher 2005; Finkler, Ward 2007; Oostenbrink, Koopmanschap 2002).

Hourly rate allocation might be a weak alternative to weighted service allocation for healthcare services with a long inpatient stay (such as stroke; table 3.3). The logic of the hourly rate method is that longer primary treatments consume more resources.

Therefore, hourly rate allocation may overestimate the share of indirect costs in healthcare services with a short inpatient stay, because the costs incurred by patients that are admitted are allocated evenly to the treatment time of all patients (including those that are not admitted). The method does not distinguish identical healthcare services performed at different moments (e.g. week or weekend, daytime or night-time). Additionally, the approach assumes the primary treatment (i.e. thrombolysis time) to be the most important cost driver, which is not the case for all healthcare services (Finkler, Ward 2007).

Compared to weighted service allocation, marginal mark-up allocation resulted in 30% lower indirect costs for appendectomy and cataract (with average inpatient stay of 2.4 and 0.5 days respectively) and even 67% lower indirect costs for stroke (with average inpatient stay of 15.9 days; table 3.3). This finding reflects the main disadvantage of the method, specifically the explicit assumption of linearity between direct and indirect costs (Finkler, Ward 2007; Oostenbrink, Koopmanschap 2002).

In practice, many factors play a role in the decision about which indirect cost method is most appropriate. One consideration lies in the aim of the indirect cost calculation. Weighted service allocation is preferably performed as part of economic evaluations, because the methodology allows for the calculation of actual cost per individual patient(-group)s (Finkler, Ward 2007). However, there may conceivably be evaluations for which one of the simpler methods will suffice, since the result is unlikely to change irrespective of the estimation assumed for the cost of hospital care. Inpatient day allocation is generally performed to support budgetary decisions, for which an average cost measure per patient from the hospital (management) perspective is employed (Drummond, Sculpher 2005).

Another consideration lies in the feasibility of the indirect cost method. The feasibility of an indirect cost method may be associated with the availability of time and data. For example, the choice for weighted service allocation depends on the presence and adequacy of the standard relative value units in a particular institution (Finkler, Ward 2007).

Finally, the type of healthcare service plays a role in the decision about which indirect cost methods is most appropriate. Hourly rate allocation is obviously less appropriate for healthcare services in which the primary treatment is not the most important cost driver. Marginal mark-up allocation may not be sufficiently accurate for healthcare services that incur a wide direct cost variation between patient(-group)s. The overriding principle to bear in mind in considering approaches for the allocation of indirect costs is that all

approaches are inherently arbitrary (Finkler, Ward 2007). Moreover, the method used to estimate the indirect costs may reflect political, economical or administrative trends, which make the estimation highly subjective (St-Hilaire & Crepeau 2000).

A lack of time and data prevented us from assessing the indirect cost differences of other healthcare services than appendectomy, hip replacement, cataract and stroke. Additionally, for some medical departments it was necessary to rely on annual direct and indirect cost *estimates* rather than on concrete data because cost information was difficult to obtain. In some cases imputation from the hospital level to the department level was used. Future studies could determine whether our conclusions are generalisable to other healthcare services, hospital (department)s and countries.

Lack of certain data forced us to make important choices about the units of measurement used, namely for the weighted service method. We determined the relative value units of the weighted service method on the basis of direct cost components that were sometimes only poorly significantly associated with the direct costs ($P > 0.10$; table 3.2). Besides, no characteristics at the patient level were available for the determination of relative value units.

Medical practice and severity of illness within each healthcare service might vary across hospitals, which may have affected the resource use and total costs of our patient sample. Although our conclusions were based on the information obtained from a sample of hospitals, we believe that this sample was sufficiently representative of all Dutch hospitals. The average number of beds per hospital in our sample was 497 beds, which is close to the average number of beds per hospital in the Netherlands (453 beds) (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007). Moreover, the hospitals in our study were located in different regions in the Netherlands.

Little consideration is usually given to the allocation of indirect cost components to healthcare services. This is reflected by the poor information that is provided regarding indirect costs in publications that report on economic evaluations. To ensure quality and comparability of costing approaches in costing studies, it is important for each economic evaluation to report on the indirect cost components included and the indirect cost allocation method used.

To our knowledge, no previous studies have ever compared the cost estimates resulting from different allocation methods for the distribution of indirect costs within the medical department to patient(-group)s. However, some studies have assessed the cost

differences arising from different allocation methods for the distribution of indirect costs from the supporting departments to the medical departments within the hospital (amongst others: (Berlin & Smith 2004; St-Hilaire & Crepeau 2000)). Other studies have compared indirect cost allocation methods for the distribution of cost components that were regarded as direct cost components in our study, e.g. indirect patient time of nurses (amongst others: (Peden & Baker 2002)). Considering the fact that indirect costs often comprise a large proportion of the overall costs of healthcare services (Oostenbrink, Koopmanschap 2002; St-Hilaire & Crepeau 2000), a better understanding of the distribution of indirect cost components at the department level seems justified.

Within a decision theory framework, erroneous estimation of the indirect costs could lead to incorrect assessment of research priorities and inappropriate allocation of resources. Even though the weighted service method is believed to be the most objective measurement of distributing indirect costs at the medical department level to individual healthcare services as well as the key method to reimbursement, the present study generally found no statistically significant relationship between the allocation method employed and the indirect costs produced. The use of inpatient day allocation would likely most closely reflect the indirect cost estimates obtained by the weighted service method. Besides, hourly rate allocation may be a strong alternative to weighted service allocation for healthcare services with a relatively short inpatient stay.

3.6 ACKNOWLEDGEMENTS

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Chapter 4

The unit costs of inpatient hospital days, outpatient visits and daycare treatments in the field of oncology and haematology

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4.1 ABSTRACT

Background: Many economic evaluations are conducted in the field of oncology and haematology, partially owing to the introduction of new expensive drugs in this field. Even though inpatient days, outpatient visits and daycare treatments are frequently the main drivers of total treatment costs, their unit costs often lack generalisability. **Objective:** To determine the unit costs of inpatient hospital days, outpatient visits and daycare treatments specifically for oncological and haematological diseases in the Netherlands. **Design:** Unit costs were collected from 30 oncological and haematological departments of 6 university and 24 general hospitals. Costs included direct labour and indirect labour, hotel and nutrition, overheads and capital. OLS regression models were constructed to examine the degree of association between unit costs and hospital and hospital department characteristics. All costs were based on Euro 2007 cost data. **Results:** At university hospitals, the unit costs per inpatient day were determined at € 633 in oncological and € 680 in haematological departments. At general hospitals the mean costs per inpatient day were € 400. Unit costs for inpatient hospital days, outpatient visits and daycare treatments equalled the relative ratio 100:21:44. Direct labour costs were the major cost driver and the type of hospital (university, yes/no) was a strong predictor of unit costs. **Conclusions:** The present study provided unit costs for inpatient hospital days, outpatient visits and daycare treatments in the field of oncology and haematology. The results may be used as Dutch reference unit prices in economic evaluations assessing oncological and haematological diseases.

Keywords: Unit cost ~ Inpatient hospital day ~ Daycare treatment ~ Outpatient visit ~ Reference price

4.2 INTRODUCTION

Because oncological and haematological diseases are among the highest causes of death in the developed world, the number and variety of treatment options have rapidly increased in the past decades. The introduction of new expensive drugs in this field has caused hospital budgets in Western countries to be continuously under pressure. Therefore, the need arose to assess these drugs in terms of their costs and benefits (Dumarcet 2008; Groot et al. 2006; Jefford et al. 2005; Rodenburg-van Dieten 2005; Uyl-de Groot & Giaccone 2005). In the Netherlands, pharmacoeconomic evidence is required after three years of initial usage in daily practice in order to receive additional funding for expensive inpatient drugs on top of the fixed hospital budget (Groot, Huijgens 2006; Rodenburg-van Dieten 2005). Consequently, many economic evaluations are conducted in the field of oncology and haematology.

Inpatient hospital days, outpatient visits and daycare treatments have proven to be important cost drivers in economic evaluations determining the costs of alternative treatment options in the management of oncological and haematological diseases. Their unit costs should be accurate because they can markedly affect the results of an economic evaluation (Drummond 2005; Oostenbrink et al. 2003). However, clear public disseminated information on the unit costs of inpatient hospital days, outpatient visits and daycare treatments is lacking (Adam & Evans 2006; Oostenbrink, Buijs-Van der Woude 2003; Oostenbrink et al. 2002). In the current practice of economic evaluations, unit costs are usually calculated from the specific healthcare providers at which the economic evaluation is performed (among others: (Hale et al. 2002; Hieke et al. 2004; Maroun et al. 2003)). These unit costs often lack generalisability because healthcare providers participating in economic evaluations may not be representative of the overall treatment patterns in a country (Adam & Evans 2006; Oostenbrink, Buijs-Van der Woude 2003; Oostenbrink, Koopmanschap 2002). To guarantee generalisability, the ideal unit prices are established from large, diverse populations, which require data from multiple sources (Ritzwoller et al. 2005).

One earlier study has determined the unit costs of inpatient hospital days in the Netherlands (Oostenbrink, Buijs-Van der Woude 2003). Oostenbrink et al. (2003) (Oostenbrink, Buijs-Van der Woude 2003) collected unit costs from 22 hospital departments of 10 university and 12 general hospitals, including ear-nose-throat specialty - (3/22), internal medicine - (7/22), gynaecology - (1/22), haematology - (2/22), oncology - (4/22), pulmonary - (2/22) and surgery (3/22) departments. These unit costs were determined to be € 396 in university hospitals and € 282 in general hospitals (adjusted to 2007). The results of this study were used to develop reference prices for inpatient hospital days in

the Netherlands and contribute to the comparability and generalisability of economic evaluations (Oostenbrink, Buijs-Van der Woude 2003; Oostenbrink, Koopmanschap 2002).

However, the reference prices developed by Oostenbrink et al. (2003) (Oostenbrink, Buijs-Van der Woude 2003) may not be sufficiently distinctive for use in the field of oncology and haematology because they are determined for use at any medical specialty. Factors influencing the potential differences between the unit costs at any medical specialty and the unit costs in the field of oncology and haematology may include the patient case-mix and medical practice patterns (e.g. number of beds and the employment of an intensive care unit) (Adam & Evans 2006; Coutet et al. 2004; Friedman et al. 2006; Hale, Cohen 2002; Oostenbrink, Buijs-Van der Woude 2003). Therefore, the primary aim of the present study was to determine the unit costs of inpatient hospital days, outpatient visits and daycare treatments specifically for oncological and haematological diseases in the Netherlands.

The results of the obtained unit costs may give rise to the question which factors are responsible for the differences in costs between hospital departments. Therefore, the current study additionally aimed to identify associations between collected descriptive hospital and hospital department characteristics and the obtained unit costs.

4.3 METHODS

Total costs of inpatient hospital days, outpatient visits and daycare treatments were determined separately for university and general hospitals. For university hospitals, a further distinction was made between oncology and haematology departments. For general hospitals, no distinction was made between oncology and haematology unit costs because oncology and haematology patients are often admitted to general internal medicine departments.

Total cost estimates were determined by the identification of resource use and unit costs of the following cost components: direct labour of medical specialists, residents, nurses and administrative staff, indirect labour of clinical and non-clinical departments (e.g. laundry and cleaning), hotel and nutrition, overheads (general expenses, maintenance and energy, rent and leasing) and capital (depreciation of inventory and interest). Costs of medical imaging services, laboratory services and medications were explicitly excluded from this study, because they are considered to be highly dependent on the

disease and treatment strategy under consideration and often explain total cost differences between alternative treatments in economic evaluations.

Unit costs were calculated using the microcosting methodology, because this methodology provides cost estimations that most accurately reflect actual costs by identifying all relevant cost components at the most detailed level (Drummond et al. 2005). All costs were based on Euro 2007 cost data. Where necessary, costs were adjusted to 2007 using the general price index from the Dutch Central bureau of Statistics (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

Recruitment of hospitals

A sample of university and general hospitals was identified which was representative of the overall practice setting and treatment patterns in the Netherlands. For oncology, this concerned departments which participated in the randomised phase III clinical trial investigating sequential versus combination chemotherapy with capecitabine, irinotecan and oxaliplatin (CAIRO) in advanced stage III / IV colorectal cancer carried out by the Dutch Colorectal Cancer Group (DCCG) (Koopman et al. 2007). The haematological departments were involved in the randomised phase III study on the effect of thalidomide combined with adriamycin, dexamethasone (AD) and high dose melphalan performed by the Dutch haemato-oncology association (HOVON) in patients <65 years old with previously untreated multiple myeloma (HOVON 50) (HOVON).

Standardised reporting templates

At each of the qualified hospital departments, one medical specialist was asked personally by the investigators whether they would like to participate in the study. Using standardised reporting templates, the participating medical specialists were asked to provide resource use information separately for inpatient hospital days, outpatient visits and daycare treatments. Resource use information included the direct labour minutes spent by medical specialists, residents, nurses and administrative staff attributable to an average patient. Resource use of direct labour was valued with standardised unit costs per minute, which equalled the normative income (including social premiums, fees for irregular working hours and the costs of replacement during illness) divided by the number of workable minutes per year. Normative incomes were based on collective labour agreements. Because medical specialists of general hospitals work in independent corporations and are not on the payroll of the hospital, the normative income for these medical specialists are based on a national rate that also includes overhead costs. Subsequently, their unit costs are substantially higher than those for medical special-

ists of university hospitals (€ 2.50 versus € 1.46 per minute). Therefore, the normative income of university hospitals (€ 1.46 per minute) was used to value medical specialists' time at both university and general hospitals.

Annual accounts

The annual accounts of the year 2006 of the hospital departments were acquired to obtain input data for the cost calculation of indirect labour, hotel and nutrition, overheads and capital. Annual costs of hotel and nutrition were divided by the annual number of inpatient hospital days to be able to appoint hotel and nutrition use to inpatient hospital days. Annual costs of indirect labour, overheads and capital were divided by the annual costs of patient related care. Subsequently, this 'mark-up percentage' was multiplied by the summed daily costs of direct labour and hotel and nutrition.

Missing values

Missing values were replaced by mean values after correction for the number of available beds.

Sensitivity analyses

To determine the uncertainty of the obtained cost estimates for university as well as general hospitals, one-way sensitivity analyses were carried out by varying the resource use and unit cost values of the individual cost components between 50% and 150%. Furthermore, at 6 (random) general hospital departments, one nurse was additionally asked to provide resource use data on daycare treatments to verify the information obtained from medical specialists.

Statistical analyses

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 15.0. In addition to descriptive statistics, one way analyses of variance with and without post hoc testing (type Bonferroni) were used to investigate cost differences between hospitals. Besides, all hospital departments were included in an ordinary least squares (OLS) regression analysis to explore the degree of association between total costs (dependent variable) and collected hospital and hospital department characteristics (explanatory variables). Hospital characteristics included 'type of hospital' (university, yes/no), 'number of beds at the hospital' and 'number of inpatient days per year'. Department characteristics involved 'number of medical specialists' in

combination with 'number of beds at the department' and 'number of patients per day' for inpatient hospital days, 'number of visits per day' and 'mean duration of a visit' for outpatient visits and 'number of beds at the daycare treatment' and 'number of patients per day' for daycare treatments.

4.4 RESULTS

For university hospitals, the medical specialists of 3 oncology departments (UH1-3) and 3 haematology departments (UH3-5) were willing to cooperate. For general hospitals, a total of 24 departments (GH1-24) agreed to contribute. During the course of the data collection, one department (GH-24) was unable to provide detailed resource use information on inpatient hospital days. Furthermore, three departments (GH-9, GH-13, GH-24) were unable to provide detailed resource use information on outpatient visits and three departments (GH-7, GH-14, GH-22) on daycare treatments.

Inpatient hospital days

Table 4.1 presents the cost distribution for inpatient hospital days per oncology and haematology department at university hospitals. Unit costs at haematology departments varied between € 630 and € 734 (n=3) and those at oncology departments between € 540 and € 704 (n=3; $P = 0.469$). Both the number of beds and the number of patients per inpatient day were slightly, but not significantly, higher at oncology departments. No significant cost differences of individual cost components were found between the oncology and haematology departments.

Table 4.2 shows the cost distribution for inpatient hospital days at general hospitals. Unit costs at general hospitals amounted to € 400 (range: from € 296 to € 556; n=23) and were about 39% lower than those at university hospitals ($P < 0.001$). In all hospitals, direct labour costs were the major cost component and ranged from 45% to 59%. Nurses were the greatest attributors to the direct labour costs (between 25% and 67% of direct labour costs).

Outpatient visits

Table 4.3 presents the unit costs of outpatient visits at university hospitals separately for oncology and haematology. Total costs per outpatient visit ranged from € 99 to € 132 at oncology departments (n=3) and from € 125 to € 158 at haematology departments

(n=3; P = 0.212). The number of outpatient visits per day per medical specialist was slightly, but not significantly, higher at oncology departments.

Table 4.4 summarises the unit costs of outpatient visits at general hospitals. Unit costs at general hospitals were € 86 (range: from € 45 to € 193; n=21) and were about 34% lower than those at university hospitals (P = 0.008). At all hospitals, direct labour costs were the most important cost driver with medical specialists as the greatest contributor (between 50% and 89% of direct labour costs).

Table 4.1: Inpatient hospital day: cost distribution per university hospital (Euro 2007)

	Oncology					Haematology				
Hospital ID	**UH-1**	**UH-2**	**UH-3**	**Mean**	**SD**	**UH-3**	**UH-4**	**UH-5**	**Mean**	**SD**
Number of beds at the hospital	953	882	1,221	1,019	179	1,221	1,042	733	999	247
Annual number of inpatient days at the hospital (*1,000)	213	138	306	219	84	306	238	164	236	71
Number of medical specialists at the department	12	8	21	14	7	13	9	6	9	3
Number of beds at the inpatient department	20	16	42	26	14	16	16	19	17	2
Number of patients per day at the inpatient department	18	16	32	22	9	16	15	19	17	2
Direct labour	**281**	**293**	**370**	**314**	**48**	**351**	**343**	**295**	**330**	**30**
Medical specialist	83	79	169	110	51	136	90	110	112	23
Resident	58	65	65	63	4	65	59	46	57	10
Nurse	126*	132	123	128	6	142	178	125	148	27
Administrative worker	14	16	12	14	2	8	17	13	13	4
Indirect labour	**101**	**163**	**134**	**133**	**31**	**128**	**141**	**123**	**131**	**9**
Hotel and nutrition	**64**	**74**	**85**	**74**	**11**	**85**	**111**	**98**	**98**	**13**
Overheads	**59**	**87**	**80**	**76**	**14**	**77**	**90**	**79**	**82**	**7**
Capital	**34**	**40**	**35**	**36**	**3**	**34**	**49**	**35**	**39**	**8**
TOTAL COSTS	**540**	**656**	**704**	**633**	**85**	**675**	**734**	**630**	**680**	**52**

UH = university hospital
SD = standard deviation
* missing value

Table 4.2: Inpatient hospital day: cost distribution per general hospital (Euro 2007)

Hospital ID	GH-1	GH-2	GH-3	GH-4	GH-5	GH-6	GH-7	GH-8	GH-9	GH-10	GH-11	GH-12	GH-13	GH-14	GH-15	GH-16	GH-17	GH-18	GH-19	GH-20	GH-21	GH-22	GH-23	Mean	SD
Number of beds at the hospital	600	1,014	627	367	410	541	233	726	582	516	339	369	242	397	745	754	673	1,035	390	275	925	613	576	563	231
Annual number of inpatient days at the hospital (*1,000)	14	242	137	72	90	166	61	185	151	132	77	68	50	71	171	184	144	253	115	53	167	129	135	125	62
Number of medical specialists at the department	3	5	2	4	2	2	1	2	3	7	2	2	2	3	4	7	5	4	1	2	4	6	3	3	2
Number of beds at the inpatient department	22	36	18	28	8	26	12	25	24	21	19	29	24	15	19	25	30	28	11	22	16	28	29	22	7
Number of patients per day at the inpatient department	20	34	18	24	8	26	12	25	24	21	19	25	24	13	16	20	10	25	10	22	16	25	26	20	6
Direct labour	**189**	**224**	**180**	**318**	**194**	**199**	**248**	**164**	**160**	**221**	**186**	**250**	**169**	**260**	**203**	**244**	**215**	**180**	**237**	**185**	**260**	**201**	**197**	**212**	**38**
Medical specialist	41	77	58	131	37	40	175*	28	27	62*	110	128	29	75	31	68	55	20	22	22	81	51	16	55	35
Resident	53	47	39	0	55	44	0	46	48	55	0	0	44	55	44	53	42	46	71	52	44	46	44	40	20
Nurse	89	96*	76	181	90	105	63	85	78	97	69	116	91	116	120	112*	105	105	134	99	127	95	132	103	27
Administrative worker	6	4	7	5	12	10	10	5	7*	6	7	5*	5	14	8	11	14	10	9	11	8	10	5	8	3
Indirect labour	**58**	**82**	**47**	**85**	**56**	**75**	**114**	**61**	**44**	**56**	**57**	**83**	**60**	**83**	**52**	**76**	**85**	**77**	**85**	**47**	**87**	**70**	**60**	**70**	**17**
Hotel and nutrition	**40**	**34**	**29**	**36**	**37**	**64**	**39**	**24**	**36**	**24**	**36**	**42**	**37**	**29**	**37**	**37**	**54**	**31**	**46**	**30**	**22**	**41**	**37**	**37**	**9**
Overheads	**40**	**51**	**41**	**48**	**36**	**46**	**53**	**26**	**26**	**34**	**38**	**41**	**32**	**39**	**33**	**63**	**47**	**48**	**60**	**30**	**41**	**28**	**39**	**41**	**10**
Capital	**63**	**4**	**45**	**69**	**46**	**44**	**40**	**35**	**30**	**41**	**40**	**37**	**34**	**50**	**42**	**50**	**50**	**29**	**51**	**31**	**53**	**14**	**41**	**41**	**14**
TOTAL COSTS	**390**	**394**	**342**	**556**	**370**	**429**	**493**	**309**	**296**	**374**	**357**	**452**	**333**	**462**	**367**	**470**	**451**	**366**	**480**	**323**	**463**	**354**	**374**	**400**	**67**

GH = general hospital
SD = standard deviation
* missing value

Table 4.3: Unit cost of inpatient hospital day, outpatient visit and daycare treatment at university hospitals (Euro 2007)

	Inpatient day				Outpatient visit				Daycare treatment			
	Oncology (n=3)		Haematology (n=3)		Oncology (n=3)		Haematology (n=3)		Oncology (n=3)		Haematology (n=3)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Number of beds at the hospital	1,019	179	999	247	1,019	179	999	247	1,019	179	999	247
Annual number of inpatient days at the hospital (*1,000)	219	84	236	71	219	84	236	71	219	84	236	71
Number of medical specialists at the department	14	7	9	3	14	7	9	3	14	7	9	3
Number of beds at the inpatient department	26	14	17	2								
Number of patients per day at the inpatient department	22	9	17	2								
Number of outpatient visits per day per medical specialist					17	5	14	2				
Average duration of an outpatient visit					14	4	15	0				
Number of beds at the daycare treatment									19	4	12	6
Number of patients per day at the daycare treatment									27	20	28	18
Direct labour	**314**	**48**	**330**	**30**	**74**	**10**	**89**	**11**	**133**	**31**	**143**	**20**
Medical specialist	110	51	112	23	56	11	58	7	50	21	43	18
Resident	63	4	57	10	0	0	0	0	12	6	11	1
Nurse	127	5	148	27	11	4	19	11	55	13	59	14
Administrative worker	14	2	13	4	7	2	12	6	15	6	30	17
Indirect labour	**133**	**31**	**131**	**9**	**25**	**7**	**27**	**3**	**57**	**9**	**59**	**5**
Hotel and nutrition	**74**	**11**	**98**	**13**	**0**	**0**	**0**	**0**	**37**	**5**	**49**	**6**
Overheads	**76**	**14**	**82**	**7**	**14**	**3**	**17**	**2**	**33**	**4**	**37**	**3**
Capital	**36**	**3**	**39**	**8**	**7**	**2**	**8**	**1**	**16**	**4**	**18**	**4**
TOTAL COSTS	**633**	**85**	**680**	**52**	**120**	**19**	**142**	**17**	**276**	**34**	**305**	**28**

SD = standard deviation

Table 4.4: Unit cost of inpatient hospital day, outpatient visit and daycare treatment at general hospitals (Euro 2007)

	Inpatient day (n=23)		Outpatient visit (n=21)		Daycare treatment (n=21)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Number of beds at the hospital	563	231	577	231	623	284
Annual number of inpatient days at the hospital (*1,000)	125	62	127	62	137	70
Number of medical specialists at the department	3	2	3	2	3	2
Number of beds at the inpatient department	22	7				
Number of patients per day at the inpatient department	20	6				
Number of outpatient visits per day per medical specialist			21	6		
Average duration of an outpatient visit			15	6		
Number of beds at the daycare treatment					13	8
Number of patients per day at the daycare treatment					19	8
Direct labour	**212**	**38**	**54**	**24**	**91**	**38**
Medical specialist	60	42	38	20	19	16
Resident	40	20	0	0	5	7
Nurse	103	26	10	6	49	23
Administrative worker	8	3	5	3	18	11
Indirect labour	**70**	**17**	**15**	**6**	**30**	**14**
Hotel and nutrition	**37**	**9**	**0**	**0**	**18**	**5**
Overheads	**41**	**10**	**9**	**4**	**18**	**8**
Capital	**41**	**14**	**9**	**5**	**19**	**9**
TOTAL COSTS	**400**	**67**	**86**	**36**	**176**	**68**

SD = standard deviation

Daycare treatments

Table 4.3 also presents the unit costs of daycare treatments at university hospitals separately for oncology and haematology. Unit costs at haematology departments were € 305 (range: from € 276 to € 328; n=3) and approximately 11% higher than those at oncology departments (€ 276; range: from € 250 to € 314; n=3; $P = 0.310$). The number of beds at the daycare treatment was slightly, but not significantly, higher at oncology departments.

Table 4.4 summarises the unit costs of daycare treatments at general hospitals. Unit costs at general hospitals amounted to € 176 (range: from € 96 to € 382; n=21) and were about 39% lower than those at university hospitals ($P = 0.001$). At all hospitals, direct and indirect labour costs accounted for about 50% and 18% of the total costs. Nurses were the greatest attributors to the direct labour costs (50% of direct labour costs). The share of medical specialist costs was higher at university (34% of direct labour costs) than at general hospitals (21% of direct labour costs; $P = 0.001$).

Sensitivity analyses

For all unit costs, the greatest variation in the total costs was found when direct labour minutes of either medical specialists or nurses was altered, but the deviation was limited to ± 4-23%. For the cost calculation of hotel and nutrition, changing the number of inpatient hospital days per year resulted in a variation in the total costs of ± 5-8%. For the cost calculation of indirect labour, overheads or capital, total costs deviated to only ± 3-11% when the respective mark-up percentages were altered. At 6 general hospital departments, one nurse was additionally asked to provide resource use data on daycare treatments to verify the information obtained from medical specialists. No significant differences were found between the resource use acquired from medical specialists and nurses ($P = 0.530$).

OLS regression

Table 4.5 shows the models of the OLS regression that were constructed to examine the degree of association between total costs and hospital and hospital department characteristics. For inpatient hospital days, model 1a included all associated characteristics, of which only 'type of hospital' ($P = 0.002$) and 'number of patients per day' ($P = 0.107$) were associated with total costs. When the non-significant variables were left out (model 1b), using a cut-off value of $P > 0.200$, 'number of patients per day' lost its significance. Model 1c included 'type of hospital' only and was able to explain 72% of total costs. The university hospital type was associated with an increase in costs of € 256 ($P < 0.001$).

For outpatient visits, model 2a included all associated characteristics, of which only 'type of hospital' ($P = 0.037$) and 'mean duration of a visit' ($P < 0.001$) were associated with total costs. When only these variables were included in the OLS regression (model 2b), the university hospital type was associated with a cost increase of € 46 ($P = 0.001$) and one additional minute of duration of a visit with a cost increase of € 4 ($P = 0.001$). Model 2b was able to explain only 54% of total costs.

Table 4.5: Regression models to explain total costs (hospital department n=30)

	Inpatient hospital days						Outpatient visits				Daycare treatments			
	Model 1a $R^2 = 0.766$		Model 1b $R^2 = 0.732$		Model 1b $R^2 = 0.718$		Model 2a $R^2 = 0.728$		Model 2b $R^2 = 0.539$		Model 3a $R^2 = 0.679$		Model 3b $R^2 = 0.643$	
	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE
Hospital characteristics														
Type of hospital	217.37	***63.59	254.40	***30.73	256.22	***30.94	49.84	***22.03	46.29	***12.47	79.00	*55.13	117.80	***30.71
Number of beds at the hospital	-0.03	0.12					0.05	0.05			-0.05	0.10		
Number of inpatient days	-0.03	0.43					-0.05	0.15			0.48	*0.36	0.29	**0.17
Inpatient hospital day characteristics														
Number of medical specialists	6.31	6.93												
Number of beds at the department	3.33	3.75												
Number of patients per day	-6.46	*3.84	-2.41	2.01										
Outpatient visit characteristics														
Number of medical specialists							-3.21	3.16						
Number of visits per day							0.23	0.89						
Mean duration of a visit							6.36	***1.29	4.00	***1.03				
Daycare treatment characteristics														
Number of medical specialists											5.18	6.40		
Number of beds at the daycare treatment											4.01	***1.60	3.78	***1.52
Number of patients per day											-5.78	***1.65	-4.61	***1.25

SE = standard error
* $0.10 \leq P < 0.20$
** $0.05 \leq P < 0.10$
*** $P < 0.05$

For daycare treatments, model 3a included all associated characteristics, of which only 'number of beds at the hospital' (P = 0.621) and 'number of medical specialists' (P = 0.429) were not associated with total costs. When these non-significant variables were left out (model 3b), using a cut-off value of $P > 0.200$, the regression analysis showed cost increases for 'type of hospital', 'number of inpatient days' and 'number of beds at the daycare treatment' and a cost decrease for 'number of patients per day'. The latter analysis explained 64% of total costs.

4.5 DISCUSSION

Including a total of 30 hospital departments, this study is the most extensive cost assessment of unit costs for inpatient hospital days, outpatient visits and daycare treatments in the field of oncology and haematology in the Netherlands thus far. With respect to inpatient hospital days at university hospitals, total costs were € 633 ± 85 for oncology and € 680 ± 52 for haematology. Unit costs at haematology departments were approximately 7% higher than those at oncology departments (P = 0.469). For general hospitals, no distinction was made between oncology and haematology unit costs because oncology and haematology patients are often admitted to general internal medicine departments. Total costs at general hospitals were € 400 ± 67 with direct labour costs contributing to about half of the total costs.

Oostenbrink et al. (2003) determined the unit costs of inpatient hospital days at any medical specialty. Even though they additionally included medication and blood products, Oostenbrink et al. (2003) found the unit costs of inpatient hospital days to be substantially lower than those found in our study. Total costs in their sub-sample of haematology (n = 2) and oncology departments (n = 4) amounted to € 327 and € 303 respectively (adjusted to 2007) (Oostenbrink, Buijs-Van der Woude 2003). The methodology used to derive the direct labour cost estimates of residents and nurses may partly explain this difference. Whilst medical specialists were asked to estimate the direct labour minutes spent per inpatient hospital day in our study, Oostenbrink et al. (2003) divided the annual costs of residents and nurses by the annual number of inpatient hospital days. The higher cost estimations in our study directly influenced overhead and capital costs, because these were determined using a marginal mark-up percentage. Nevertheless, in agreement with our results, Oostenbrink et al. (2003) found total haematology costs to be 8% more expensive than total oncology costs and observed direct labour costs to contribute to about 51% of total costs.

Our results further suggest that total costs for inpatient hospital days, outpatient visits and daycare treatments equalled the relative ratio 100:21:44 (tables 4.3-4), which is fairly in line with the results of other studies. Oostenbrink et al. (2002) found the relative ratio in general hospitals to be 100:17:46 (€ 282, € 49, € 128; adjusted to 2007) (Oostenbrink, Koopmanschap 2002). Van Agthoven et al. (2004), who performed an economic evaluation in patients with stage II / III multiple myeloma at the haematology departments of 2 university and 6 general hospitals, observed a relative ratio of 100:25:45 (€ 463, € 109, € 207; adjusted to 2007) (van Agthoven et al. 2004). Ward et al. (2006), who compared the cost effectiveness of different treatment options in patients with metastatic colorectal cancer in the United Kingdom, used unit costs with a relative ratio of 100:20:30 (€ 632, € 131, € 191; adjusted to 2007) (Ward et al. 2006).

Our OLS regression may give some indications on the factors responsible for the differences in costs between hospital departments. It was concluded that the 'type of hospital' (university, yes/no) was able to predict up to 72% of the total costs for inpatient hospital days. The 'type of hospital' was also a strong predictor with respect to outpatient visits, in combination with 'mean duration of a visit', and regarding daycare treatments, combined with 'number of inpatient days', 'number of beds at the daycare treatment' and 'number of patients per day'. Oostenbrink et al. (2003) have also performed regression analyses but none of their independent variables showed a relationship with total costs that came near to significance.

Next to the variables included in our OLS regression, other variables may have been able to explain the cost variation between hospitals and the difference between university and general hospitals, such as the patient case-mix of the individual hospital departments. Although we did not acquire information on the patient case-mix, it is likely that the patients admitted to the university hospitals were relatively more severely ill and in need of more resources than patients admitted to the general hospitals. However, as these differences reflect daily practice, they encourage the establishment of generalisable unit costs.

The cost calculations on oncology and haematology each were based on data of the hospital departments of 3 of 8 university hospitals in the Netherlands. There are indications that the included departments may be accurate representatives to Dutch university hospitals. In 2006, 36% and 39% of inpatient hospital days at university hospitals were attributable to the oncology and haematology departments of our university hospitals respectively. The average number of beds per university hospital in our sample was 966 beds, which is close to the average number of beds per university hospital in the Netherlands (997 beds) (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid

Welzijn en Sport 2007). Besides, the university hospitals in our study were located at different regions of the country.

Although we faced some missing data during the course of the data analyses, the extent to which data were missing was limited. Because hospitals in the Netherlands are obliged to give details on a predetermined list of cost components by means of their publicly available annual accounts, no data was missing on indirect labour, hotel and nutrition, overheads and capital. Regarding direct labour minutes, six hospitals (GH-7, GH-9, GH-13-14, GH-22 and GH-24) were unable to provide detailed resource use information on inpatient hospital days and/or outpatient visits and/or daycare treatments and were therefore excluded from the analyses. Of the remaining oncology departments, 7.8% of the required items in university hospitals and 5.6% of those in general hospitals were missing. Sensitivity analyses have also demonstrated that our study resulted in fairly robust cost estimates.

The microcosting methodology is ideally combined with the bottom up approach, in which cost components are valued by identifying resource use directly employed for a patient (Wordsworth et al. 2005). However, our study applied the top down approach in which cost components are valued by separating out the relevant costs from comprehensive sources (e.g. annual accounts). Additionally, lack of detailed data prevented us from assessing the costs of overheads and capital by means of more conventional methods, such as cost center allocation or inpatient day allocation (Oostenbrink, Koopmanschap 2002). Alternatively, marginal mark-up allocation was used for the cost estimation of overheads and capital. Previous studies concluded that the top down approach may be a good proxy to the bottom up approach and that marginal mark-up allocation may be sufficiently accurate for hospital services which are not expected to vary widely between patients (Oostenbrink, Koopmanschap 2002; Wordsworth, Ludbrook 2005). This was the case in the present study, as the costs of medical imaging services, laboratory services and medications were explicitly excluded to ensure truthful comparability of alternative treatments in economic evaluations. Costs of medical imaging services, laboratory services and medications are considered to be highly dependent on the disease and treatment strategy and often explain total cost differences between alternative treatments. Therefore, we believe that the use of a top down approach and marginal mark-up allocation did not markedly affect the results of the present study.

Inpatient hospital days, outpatient visits and daycare treatments form important cost drivers in economic evaluations, but information on their unit costs is often lacking (Adam & Evans 2006; Oostenbrink, Buijs-Van der Woude 2003; Oostenbrink, Koopmanschap 2002). The present study provided unit costs for inpatient hospital days, outpatient

visits and daycare treatments in the field of oncology and haematology. The results may be used as reference unit prices in economic evaluations assessing new expensive drugs for oncological and haematological diseases.

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Chapter 5

A microcosting study of intensive care unit stay in the Netherlands

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5.1 ABSTRACT

The primary objective of this paper was to estimate the actual daily costs of intensive care unit (ICU) stay using a microcosting methodology. As a secondary objective, the degree of association between daily ICU costs and some patient characteristics was examined. This multicenter, retrospective cost analysis was conducted in the medical-surgical adult ICUs of one university and two general hospitals in the Netherlands for 2006, from a hospital perspective. A total of 576 adult patients were included, consuming a total of 2,868 nursing days. The mean total costs per ICU day were € 1,911, with labour (33%) and indirect costs (33%) as the most important cost drivers. An ordinary least squares regression analysis including 'age', 'NEMS/TISS-28 score', 'mechanical ventilation', 'blood products' and 'renal replacement therapy' was able to predict 50% of the daily ICU costs.

Keywords: Intensive care – Microcosting – Cost analysis – ICU stay – Mechanical ventilation

5.2 INTRODUCTION

Although intensive care unit (ICU) beds comprise less than 10% of hospital beds, ICUs consume 22% of total hospital costs in the United States (Halpern et al. 1994). Also the costs of ICUs in Netherlands have been estimated to represent approximately 20% of the total hospital budget (van Dijk & van der Werken 1998), with the cost per nursing day in between 3- and 5-fold more than in general wards (Oostenbrink et al. 2003). Therefore, insight in the costs and cost drivers of ICU stay seems justified.

Several studies have assessed the costs of ICU services, but cost estimations on an ICU day vary extensively (Dasta et al. 2005; Edbrooke et al. 1997; Flaatten & Kvale 2003; Graf et al. 2002; Moran et al. 2004; Oostenbrink, Buijs-Van der Woude 2003; Rechner & Lipman 2005). From a multicenter Australian study, Moran et al. (2004) reported the mean costs per nursing day to be € 1,489 (adjusted to 2006). At the other extreme, the daily treatment costs in a Norwegian university hospital ICU were found to be € 3,097 (adjusted to 2006) (Flaatten & Kvale 2003).

Many studies have tried to explain the wide variations in actual differences between ICUs (Bertolini et al. 2003; Edbrooke et al. 2001; Oostenbrink, Buijs-Van der Woude 2003). The patient case-mix is considered to have an important effect on the costs of ICU stay. Other potential factors influencing the differences in actual costs of ICU stay include medical practice patterns (e.g. number of beds and the presence of a high dependency unit), financial incentives and relative and absolute prices between countries (Bertolini, Rossi 2003; Dasta, McLaughlin 2005; Edbrooke, Ridley 2001; Jacobs et al. 2001). However, it has been argued that some of the observed differences are more related to methodological differences than to actual cost differences (Elliott 1997; Moran, Peisach 2004; Rechner & Lipman 2005).

An important cause for methodological differences concerns the level of accuracy that is addressed. In gross costing cost components are defined at a highly aggregated level (e.g. inpatient days only), whereas in microcosting all relevant cost components are defined at the most detailed level (Drummond 2005). The latter methodology allows for the identification of costs per individual patient and for insight in patient subgroups that might have a great share in the total costs of the ICU. As this methodology is time consuming, especially when hospital information systems are absent or inadequate, it has not been widely used in assessing the costs of ICU stay.

Microcosting studies have been carried out in Australia (Moran, Peisach 2004) and the United Kingdom (Edbrooke, Stevens 1997). However, a microcosting study for the Neth-

erlands has not yet been performed. Therefore, the primary aim of the present study was to calculate the actual daily costs of ICU stay in the Netherlands using a microcosting methodology.

Critically ill patients require therapies that can vary considerably in type, duration and cost (Jacobs, Edbrooke 2001). Therefore it is desirable to have insight in the variables that are able to predict the daily cost of individual patients. Because the microcosting methodology is particularly appropriate to provide such an insight, the secondary objective of the current study was to examine the degree of association between daily ICU costs and the following routinely collected patient characteristics: 'age', 'gender', 'ICU length of stay', 'NEMS/TISS-28 score', 'mechanical ventilation', 'blood products', 'renal replacement therapy' and 'sepsis'. ICU length of stay and the NEMS/TISS-28 score were included in the analysis to control for the severity of illness of the patient. Mechanical ventilation, blood products, renal replacement therapy and sepsis were included because several recent studies suggest that these variables are associated with increased costs (Bakker et al. 2004; Berbece & Richardson 2006; Burchardi & Schneider 2004; Dasta, McLaughlin 2005; Manns et al. 2003).

5.3 METHODS

This microcosting study was conducted in three hospitals in the Netherlands for 2006, from a hospital perspective. A retrospective cost analysis of patients admitted to a 32-bed medical-surgical adult ICU was performed at a university hospital during a period of 7 weeks in 2006: from 16 April to 15 May and from 5 June to 23 June. Besides, data was collected in two medical-surgical adult ICUs at general university affiliated hospitals. The first concerned a 10-bed ICU. Because of capacity problems in the summers of 2005 and 2004, it was decided to retrospectively collect data for a period of 6 months in 2003: from 1 January to 1 July (general hospital 1). The second adult ICU involved a 22-bed ICU at which data was prospectively collected for a period of one week: from 4 November 2006 to 10 November 2006 (general hospital 2).

Total population

Total costs for individual patients were determined by the identification of resource use and unit costs of direct and indirect cost components. Direct cost components involved diagnostic procedures (medical imaging services and laboratory services), consumables (medications, fluids and disposables), hotel and nutrition and labour. Indirect cost components concerned overheads (general expenses, administration and registration,

energy, maintenance, insurance and the personnel costs of non patient services, like management and administration) and capital (depreciation of buildings and inventory and interest).

Direct cost components
Total direct costs were determined by multiplying *resource use* by the corresponding *unit prices* for 2006.

Resource use
Data on resource use of diagnostic procedures, medications, fluids and hotel and nutrition was acquired from either computerised Patient Data Management Systems (PDMS; the university hospital and general hospital 1) or from patient records (general hospital 2). Annual resource use of disposables was divided by the annual number of nursing days to be able to appoint disposable use to nursing days. Resource use of ICU specialist time and indirect nursing time per nursing day were estimated by dividing the number of workable days per year by the number of nursing days per year. To estimate direct nursing time per single nursing day either the Therapeutic Intervention Scoring System score (TISS-28; general hospitals) or a simplified version of the TISS-28 score, the Nine Equivalent of Nursing Manpower Use score (NEMS; the university hospital), were used. Time for consultations of non-ICU medical staff attributable to each individual nursing day was either prospectively collected using patient record forms (the university hospital and general hospital 2) or computerised PDMS (general hospital 1).

Unit prices
Unit costs of diagnostic procedures and disposables were obtained from (financial) hospital databases. Unit costs of medications and fluids were derived from the administration of the hospital pharmacies. Annual costs on hotel and nutrition were taken from the annual accounts 2005 and divided by the annual number of nursing days to calculate unit costs per nursing day. Table 5.1 presents the unit costs of labour per minute. Unit costs of labour were based on standardised costs per day or per minute, which equalled the normative income divided by the number of workable days or minutes per year. Because medical specialists in general hospitals work in independent corporations and are not on the payroll of the hospital, the normative income for these medical specialists were based on a national rate that also includes some overhead costs. Normative incomes of other staff categories were based on collective labour agreements.

Table 5.1: Unit costs of labour (Euro 2006 per minute)

	Unit costs at university hospital	Unit costs at general hospitals
Labour ~ ICU		
- ICU specialist	1.10	2.46
- ICU resident	0.48	0.54
- ICU nurse	0.41	0.41
Labour ~ Consultations		
- Medical specialist	1.10	2.46
- Resident	0.48	0.54
- Pharmacist	1.05	1.05
- Physiotherapist	0.64	0.64
- Laboratory technician	0.48	0.51
- Nutrition specialist	0.48	0.48

ICU = intensive care unit

Indirect cost components

Annual overhead and capital costs were taken from the annual accounts 2005 and divided by the direct costs, excluding medical specialist costs in general hospitals. Thus, indirect costs were allocated to patients using a marginal mark-up percentage.

In addition to descriptive statistics, analyses of variance were used to investigate cost differences between hospitals.

Patient subgroups

Total costs of four patient subgroups were compared with those of the total population by means of two-sample T tests: patients requiring mechanical ventilation, patients requiring blood (derived) products, patients requiring renal replacement therapy and patients with sepsis.

OLS regression

Patients of all hospitals were included in an ordinary least squares (OLS) regression analysis to explore the degree of association between daily ICU costs and routinely collected patient characteristics. Total costs were taken as the dependent variable and 'age', 'gender' (male, yes/no), 'ICU length of stay', 'NEMS/TISS-28 score', 'mechanical ventilation' (yes/no), 'blood products' (yes/no), 'renal replacement therapy' (yes/no) and 'sepsis' (yes/no) as explanatory variables. Pearson's correlation coefficients, obtained from simple

binomial regression analyses, investigated the ability of the patient characteristics to predict daily costs of ICU stay.

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 13.0. In all cases $P < 0.05$ was taken as statistically significant. All costs were based on Euro 2006 cost data. Where necessary, costs were adjusted to 2006 using the general price index (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

Table 5.2: Patient characteristics of the hospital patient samples

	University hospital (n=242)	**General hospital 1 (n=304)**	**General hospital 2 (n=30)**
Age, years, mean ± SD	54 ± 15	64 ± 18	58 ± 16
Sex, male/female, n (%)	133/109 (55/45)	176/128 (58/42)	16/14 (53/47)
ICU stay, days, mean ± SD (min-max)	6.0 ± 5.6 (1-30)	5.9 ± 12.2 (1-148)	3.8 ± 5.7 (1-8)
NEMS / TISS-28, mean ± SD	27 ± 8	29 ± 9	29 ± 9
Mechanical ventilation, n (%)	180 (74)	177 (58)	19 (63)
Blood (derived) products, n (%)	93 (38)	181 (60)	12 (40)
Renal replacement therapy, n (%)	9 (4)	18 (6)	1 (3)
Sepsis, n (%)	12 (5)	41 (13)	1 (3)
Admission diagnosis, n (%)			
Cardiovascular	27 (18)	146 (47)	10 (33)
Gastrointestinal	26 (18)	54 (17)	6 (20)
Haematological	0 (0)	2 (1)	0 (0)
Metabolic	1 (1)	8 (3)	0 (0)
Neurological	33 (22)	22 (7)	4 (13)
Renal	2 (1)	8 (3)	1 (3)
Respiratory	27 (18)	67 (22)	9 (30)
Unknown	32 (22)	3 (1)	0 (0)

SD = standard deviation
NEMS = nine equivalents of nursing manpower use score
TISS = therapeutic intervention scoring system

5.4 RESULTS

The patient characteristics of the hospital patient samples are summarised in table 5.2. A total of 576 admissions of age mean ± SD 62 ± 15 years with 56% male were recorded, of which 242 at the university hospital and 304 and 30 at the general hospitals 1 and 2, respectively. These admissions related to 2,868 nursing days (1,000 at the university hospital and 1,750 and 118 at the general hospitals respectively).

Total population

An overview of descriptive statistics at the hospital level is given in table 5.3. The mean total costs per ICU day were € 1,805 in the university hospital compared to € 2,176 and € 1,753 in the general hospitals resulting in average daily costs of € 1,911 ± 230 ($P <$ 0.001). A substantial cost variation was found in the total costs obtained for individual patients (range: € 751 to € 11,116). Even though the distribution of costs varied by cost component, labour and overheads and capital were the most important cost drivers in all patients.

Direct cost components

Labour costs accounted for a third of the total costs (€ 635 ± 117; table 5.3). Although the labour costs of ICU specialists were lower in the university hospital compared to the general hospitals, their resource use appeared to be very similar (71 versus 77 and 67 minutes) because the cost variation of ICU specialists between hospitals was primarily caused by a difference in unit costs (€ 1.10 per minute in the university hospital versus € 2.46 per minute in the general hospitals; table 5.1).

The distribution of labour costs by the other ICU staff categories was somewhat different in general hospital 1 compared to the other hospitals. While the university hospital and general hospital 2 employed 20 and 9 ICU residents respectively, general hospital 1 employed only one. This was reflected in the resource use of ICU residents which was a manifold lower in general hospital 1 than in the other hospitals (37 minutes versus 149 and 157 minutes). Conversely, the share of costs for ICU nurses in general hospital 1 was considerably higher (€ 541 versus € 382 and € 330; table 5.3).

The share of patients receiving medical imaging services and laboratory services amounted to 88% and 93% respectively. Medical imaging services were double the costs in general hospital 2 (€ 119) compared to the other hospitals (€ 58 and € 67 respectively; table 5.3). Laboratory services were much higher in the university hospital (€ 188), in comparison with the other hospitals (€ 125 and € 120 respectively; table 5.3).

Hotel and nutrition represented only 4% of the daily ICU costs (€ 71 ± 25; table 5.3).

Indirect cost components

In all three hospitals, the proportion of overheads and capital accounted for a third of the total costs (€ 669 ± 141; table 5.3).

Table 5.3: Mean total costs of cost components of a patient day at a medical-surgical intensive care unit (Euro 2006)

				Total population	
				Hospital sample (n=3)	
	University hospital	General hospital 1	General hospital 2	Mean	SD
Diagnostic procedures					
- Medical imaging services	58	67	119	81	33
- Laboratory services	188	125	120	144	38
Consumables					
- Medications	140	145	137	141	4
- Fluids	127	141	145	138	9
- Disposables	3	32	62	32	29
Hotel and nutrition	87	83	42	71	25
Labour					
~ ICU					
- ICU specialist	74	188	163	142	60
- ICU resident	70	20	84	58	34
- ICU nurse	382	541	330	418	110
~ Consultations					
- Medical specialist	9	9	8	9	1
- Resident	6	5	4	5	1
- Pharmacist	1	1	0	1	1
- Physiotherapist	0	1	1	1	0
- Laboratory technician	1	2	3	2	1
- Nutrition specialist	0	1	1	0	0
Overheads	561	494	419	491	71
Capital	96	322	115	177	125
TOTAL	**1,805**	**2,176**	**1,753**	**1,911**	230

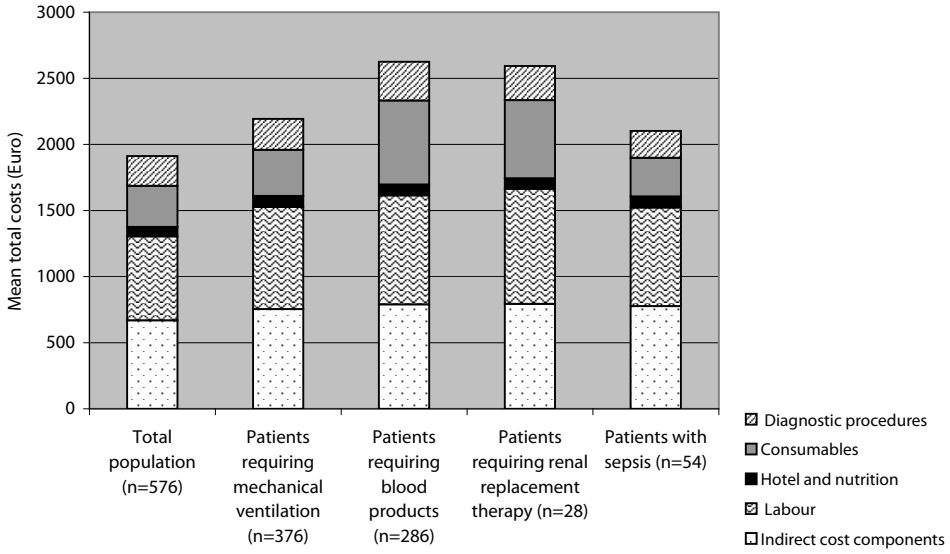
SD = standard deviation
ICU = intensive care unit

Patient subgroups

Figure 5.1 presents the distribution of cost components for the total population and four patient subgroups. The cost estimates for patients requiring mechanical ventilation (€

2,110 ± 204; $P < 0.001$), blood products (€ 2,625 ± 968; $P < 0.001$) and renal replacement therapy (€ 2,594 ± 1.004; $P = 0.006$) were significantly higher than those of the total population. However, no significant cost differences were found for patients with sepsis ($P = 0.304$).

Figure 5.1: Distribution of cost components for the total population and sub-populations (Euro 2006)



OLS regression

Table 5.4 shows two models of the OLS regression that were constructed to examine the degree of association between total costs and the patient characteristics. Model 1 included all patient characteristics, of which 'gender' ($P = 0.425$), 'ICU length of stay' ($P = 0.060$) and 'sepsis' ($P = 0.317$) were not significantly associated with daily ICU costs. When these variables were left out (model 2), 'age', 'NEMS/TISS-28 score', 'mechanical ventilation', 'blood products' and 'renal replacement therapy' remained significantly related to total costs. Overall, this analysis explained 50% of the average daily ICU costs. Requirement of mechanical ventilation was associated with a *de*crease in costs of € 132.82 ($P < 0.001$), while one additional year of age corresponded to a *de*crease of € 3.45 ($P < 0.001$). However, when the 'NEMS/TISS-28 score' was not included as a control variable, cost *in*creases in 'age' and 'mechanical ventilation' were observed. The latter finding was reinforced by the superior ability of the 'NEMS/TISS-28 score' to predict total costs ($R^2 = 0.373$; figure 5.2) over 'mechanical ventilation' ($R^2 = 0.125$) and 'age' ($R^2 = 0.012$). Binomial

regression analyses showed cost increases of € 451.66 ($P < 0.001$) for 'mechanical ventilation' and € 4.42 ($P < 0.001$) for 'age'.

Finally, a positive correlation of daily ICU costs with the use of 'blood products' (R^2 = 0.232) was demonstrated. No substantial correlation was found between daily costs and any of the other variables.

Table 5.4: Regression models to explain mean total costs (n=576)

	Model 1 $R^2 = 0.503$		**Model 2** $R^2 = 0.501$	
Independent variable	**Coefficient**	**SE**	**Coefficient**	**SE**
Patient characteristics				
Age	-3.06	**0.84	-3.45	**0.82
Sex	19.49	24.42		
ICU length of stay	-0.59	*0.31		
TISS score	43.47	**1.77	43.65	**1.74
Mechanical ventilation	-115.71	**32.11	-132.82	**31.06
Blood (derived) products	441.36	**27.93	447.67	**27.86
Renal replacement therapy	193.76	**52.89	207.44	**52.60
Sepsis	-29.51	29.51		

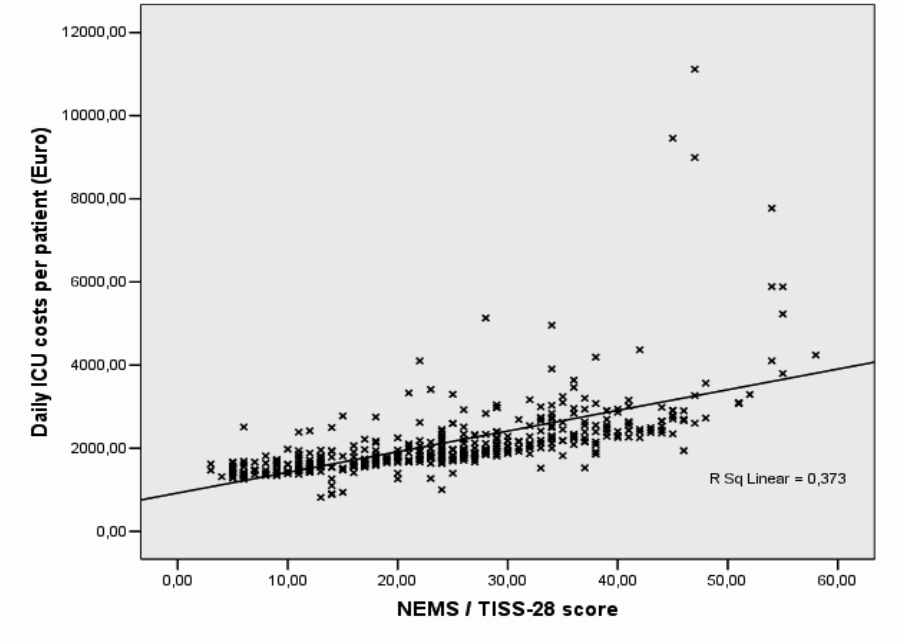
SE = standard error
ICU = intensive care unit
TISS = therapeutic intervention scoring system
* $0.05 < P < 0.10$
** $P < 0.01$

5.5 DISCUSSION

This is the second microcosting study on the costs of ICU stay in Europe following the study of Edbrooke et al. (1997). Average daily direct costs were € 1,243 ± 108. Indirect costs were € 669 ± 141, which made the daily ICU costs of one ICU day € 1,911 ± 230. These results are in agreement with the costs of ICU stay as calculated by Edbrooke et al. (1997). They found the daily ICU costs to be € 2,074 (adjusted to 2006), with labour contributing to 24% of the mean costs (versus 33% in our study). Furthermore, Edbrooke et al. (1997) also observed substantial cost variation in the cost components obtained for individual patients.

Compared to the daily costs of *patients not requiring mechanical ventilation*, those of patients requiring mechanical ventilation were 29% more costly ($P < 0.001$). This finding is similar to that of Dasta et al. (2005) who found a cost increase of 32% (increases of

Figure 5.2: Relationship of NEMS / TISS-28 score and daily ICU costs per patient (Euro 2006)



62% on the first day, 37% on the second day and 25% on subsequent days of admission). Compared to the daily costs of *the total population*, those of patients requiring mechanical ventilation were 15% more costly ($P < 0.001$). Similarly, blood products, renal replacement therapy and sepsis in critically ill patients were associated with cost increases of 37% ($P < 0.001$), 36% ($P = 0.006$) and 10% ($P = 0.304$) respectively.

The OLS regression analyses indicate that daily NEMS / TISS-28 scores are able to predict 37% of the daily costs. This percentage is similar to that observed by de Keizer et al. (1998) (40%), but surprisingly low compared to studies carried out by Graf et al. (2002) (92%) and Moran et al. (2004) (81%). Despite the high correlations found in these studies, Edbrooke et al. (2001) suggested that high variance in patient specific daily costs makes the predictive power of the TISS score poor.

The regression analyses further suggest that ICU length of stay is unable to predict *daily* ICU costs ($R^2 = 0.004$). However, ICU length of stay showed a strong power to predict *total* ICU costs for an individual patient ($R^2 = 0.984$), comparable to other adult ICU studies (Graf, Graf 2002; Moran, Peisach 2004; Rapoport et al. 2003; Stricker et al. 2003).

This study has several limitations. Firstly, because of capacity problems in the summers of 2005 and 2004, resource use data of general hospital 1 was derived from 2003 whereas

that of the other hospitals was obtained in 2006. After application of the general price index, mean costs of general hospital 1 were € 147 ± 1,108 ($P = 0.002$) higher than those of the total population. However, this cost increase might have been caused by the introduction of e.g. newer therapies and changes in staff occupation.

Secondly, because of time constraints, daily ICU costs of general hospital 2 were based on only one week in 2006. However, of all 1,427 admissions in this hospital in 2006, the mean age (56 ± 21 years), the percentage of males (55%), the average length of ICU stay (4.5 ± 7.6 days), the average TISS-score (27 ± 12), the percentage of mechanical ventilation days (52%) and average number of mechanical ventilation days per patient (7.0 ± 11.2 days) were comparable to corresponding figures of this one week (table 5.2).

Lastly, analyses on renal replacement therapy were conducted for the general hospitals only, as the databases of the university hospital were insufficiently adequate to provide information on renal replacement therapy.

Even though our study included the ICUs of only three hospitals, there are indications that these ICUs may be fairly accurate representatives to Dutch ICUs. A national survey, carried out by the Dutch Association for Intensive Care (NVIC) to investigate the supply and demand of ICU services in the Netherlands in 2002, showed that approximately 35% of the available ICU beds were concentrated in university hospitals (33% in our study). Additionally, the survey revealed that the overall TISS score of Dutch ICUs varied between 14 and 35 (between 24 and 29 in our study) and that the average length of ICU stay amounted to 5.5 days in university hospitals and 3.6 days in general hospitals (6.0 and 4.9 days respectively in our study). More than 45% of the nursing days were mechanical ventilation days in a majority of Dutch ICUs (65% in our study). Besides, the three hospitals in our study were located at different regions in the Netherlands.

In conclusion we found the average daily ICU costs to be € 1,911 ± 230 for the total population, with significant cost increases in patients requiring mechanical ventilation, blood products or renal replacement therapy. The derived costs were comparable to the reference costs of € 1,779 (adjusted to 2006) (Oostenbrink et al. 2002) for an ICU day in the Netherlands.

5.6 ACKNOWLEDGEMENTS

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Chapter 6

The costs of intensive care unit stay for patients with and without mechanical ventilation in Europe

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6.1 ABSTRACT

Purpose: to determine and compare the true costs of ICU stay at seven randomly selected ICUs from four European countries. Additionally, the costs of ICU stay for patients with and without mechanical ventilation (MV) were determined. **Methods**: The retrospective cost analyses were performed at the adult ICUs of one German hospital (400 patients), two Italian hospitals (1,204 patients), three Dutch hospitals (576 patients) and one British hospital (549 patients). A standardised bottom up microcosting methodology was employed to ensure that the identified cost differences would reflect only actual cost differences. **Results**: Total costs per ICU day amounted to € 1,766 ± 445 (range: 1,317 to € 2,503). With the exception of the British hospital, *direct* costs were of the same magnitude at all hospitals (range: € 1,124 to € 1,360). Cost increases for MV varied between 20% and 72%. Labour was the key cost driver and contributed to increased direct costs at the British hospital (compared with the other hospitals) and for patients requiring MV (compared with patients not requiring MV). **Conclusions**: Total costs of ICU stay vary widely between the seven hospitals resulting mainly from differences in labour and *indirect* costs.

Key words: Intensive care – Microcosting – Cost analysis – ICU stay – Mechanical ventilation

6.2 INTRODUCTION

Although intensive care unit (ICU) beds comprise less than 10% of hospital beds, ICUs consume 22% of total hospital costs in the United States (Halpern et al. 1994). Also the costs of ICUs in the Netherlands have been estimated to represent approximately 20% of the total hospital budget (van Dijk & van der Werken 1998), with the costs per day between 3- and 5-fold greater in ICUs than that in general wards (Oostenbrink et al. 2003). Therefore, insight into the costs of ICU stay seems justified.

Several studies have assessed the costs of ICU services, but cost estimations of an ICU day vary extensively. From a multicenter German study, Moerer et al. (2007) reported the total costs per ICU day to be € 823 (adjusted to 2006) (Moerer et al. 2007). At the other extreme, the total costs per day at ICUs in the United States were found to be € 3,100 (adjusted to 2006) (Cooper & Linde-Zwirble 2004). A number of studies have tried to explain the wide variations in actual cost differences between ICUs (Bertolini et al. 2003; Edbrooke et al. 2001; Oostenbrink, Buijs-Van der Woude 2003). The patient case-mix is considered to have an important effect on the costs of ICU stay. Other potential factors influencing the differences in actual costs include variations in staff composition and medical practice, the availability of health care resources, relative and absolute prices between countries and the quality of care (Drummond & Pang 2001; Edbrooke, Ridley 2001). Owing to these factors, large variability between ICUs has been demonstrated previously (Rothen et al. 2007; Treggiari et al. 2007; Wunsch et al. 2008).

To be able to compare actual cost differences between ICUs in a straightforward way, the use of a standardised costing methodology is required (Elliott 1997; Negrini et al. 2006; Pines et al. 2002). However, a systematic literature review by Elliot et al. (1997) demonstrated that the costing methodologies employed to calculate costs of ICU stay are diverse and make comparative analyses between studies difficult (Elliott 1997). In their narrative review, Pines et al. (2002) have argued that, despite considerable progress in costing methodologies, critical care studies have not adequately implemented these techniques (Pines, Fager 2002).

A first attempt at developing a methodology for standardised costing of individual ICUs was made by Edbrooke et al. (1999) (Edbrooke et al. 1999). Their methodology values cost components, grouped into six cost blocks (equipment, estates, nonclinical support services, clinical support services, consumables and staff) by means of *top down* microcosting, in which relevant costs are separated out from comprehensive sources resulting in unit costs per *average patient* (Drummond et al. 2005). To examine whether it was applicable to different countries, Negrini et al. (2006) used the methodology to

determine the costs of ICU stay in France, Germany, Hungary and the United Kingdom (UK). A recognised limitation of their study was that estimates of costs instead of true costs were permitted for some cost components, because cost data was not always available at the ICUs under consideration (Negrini, Sheppard 2006).

The *bottom up* microcosting methodology, in which cost components are valued by identifying resource use directly employed for *individual patients*, is generally considered to be the gold standard methodology for costing hospital services (Drummond, Sculpher 2005). Different accounting and financing systems between and within countries present difficulties with standardisation in the collection of cost data. Further, cost data is not always available in the same detail. To minimise cost variations caused by differences in accounting systems, it is crucial to identify and value all relevant direct cost components at the most detailed level. As the bottom up microcosting methodology is particularly amenable for identifying and valuing components at this detailed level, it may be the most reliable and valid methodology to ensure comparability of the true costs of ICUs between different countries. Therefore, the primary objective of the present study was to determine and compare the true costs of ICU stay at seven randomly selected ICUs from four European countries using a standardised bottom up microcosting methodology.

Several recent studies suggest that mechanical ventilation (MV) is associated with increased costs in the ICU (Dasta et al. 2005; Jacobs et al. 2001; Ridley et al. 1991). Patients who require MV represent approximately 33% of all patients admitted to the ICU and incur a disproportionately high share of the total cost of ICU treatment (Dasta, McLaughlin 2005). As the bottom up microcosting methodology is particularly appropriate for gaining insight into sub-populations that might contribute to a larger share of the total costs (Drummond, Sculpher 2005), the secondary objective of the current study was to determine the costs of ICU stay for patients with and without MV.

6.3 METHODS

A retrospective cost analysis of ICU patients was performed at the adult ICUs of seven hospitals, of which one in Germany, two in Italy, three in the Netherlands and one in the UK. The hospitals were randomly selected and based on willingness to participate. The German hospital involved the focused care (level III) hospital 'Klinik am Eichert' in Göppingen (hospital G), at which anaesthesiological adult ICU (12 beds) all patients admitted between January and October 2006 were recruited. In Italy, data was collected at the medical-surgical adult ICUs of the 'San Paolo Hospital' in Milan (hospital I1; 6

beds) and of the 'Azienda Ospedaliera' in Padova (hospital I2; 18 beds), at which departments all patients admitted from January 2006 to January 2007 were included. In the Netherlands, costing studies were performed at the medical-surgical adult ICUs of the 'Erasmus MC University Medical Center' in Rotterdam (hospital N1; 32 beds; April to July 2006), the general university affiliated hospital 'Gelre Hospitals' in Apeldoorn (hospital N2; 10 beds; January to July 2003) and the general university affiliated hospital 'Isala clinics' in Zwolle (hospital N3; 22 beds; November 2006). The latter three hospitals are representative of the overall setting and treatment patterns in the Netherlands. The UK hospital concerned the 'Royal Berkshire NHS Trust Hospital' in Reading (hospital U), at which medical-surgical adult ICU (9 beds) all patients admitted from April 2006 to April 2007 were recruited.

Total costs were determined from the hospital perspective and comprised direct as well as indirect costs. Direct cost components included diagnostic procedures (medical imaging and laboratory services), consumables (medications, fluids and disposables), hotel and nutrition and labour (ICU specialists, ICU nurses, consulted specialists such as medical specialists, residents, pharmacists, physiotherapists, laboratory technicians and nutrition specialists). ICU specialists were defined as any physician directly employed at the ICU department. Likewise, ICU nurses comprised any nurse directly employed at the ICU department. Consequently, wide variability exists in terms of training of both ICU specialists and ICU nurses. The indirect cost components generally included general expenses, administration and registration, energy, maintenance, insurance and the personnel costs associated with non patient services (e.g. management and administration), the depreciation of buildings and inventory and interest.

A standardised bottom up microcosting methodology was employed to ensure that the identified cost differences would reflect only actual cost differences. Resource use and unit costs of the cost components were collected using uniform reporting templates. Resource use of diagnostic procedures, consumables, hotel and nutrition was derived from computerised Patient Data Management Systems (PDMS) or from patient records. Labour time spent by ICU specialists, ICU nurses and consulted specialists per ICU day was determined by dividing the number of workable days per year by the number of ICU days per year.

Unit costs represented the true costs to the hospital rather than wholesale prices. The unit costs of diagnostic procedures, consumables, hotel and nutrition were primarily obtained from hospital administrative databases. The unit costs of labour were based on normative incomes and allocated to patients according to the time spent per ICU

day. Annual indirect costs were taken from hospital financial databases or accounting systems.

In some instances, we were unfortunately not able to employ the bottom up approach. Although the total costs of the 25 most expensive medications and disposables in terms of total expense were determined using the bottom up approach at hospital 1, the top down approach was used for the cost assessment of the remaining medications and disposables. At hospitals I1 and I2, total costs of medical imaging services were determined using the bottom up approach from January 2006 to April 2006. These total costs were considered representative for the patients recruited from April 2006 to January 2007. At hospital U, all direct cost components were valued using a top down approach with ICU days as the cost distributor.

All costs were based on Euro 2006 cost data. Where necessary, costs were adjusted to 2006 using the general price index from the Dutch Central Bureau of Statistics (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007). Mean exchange rates for 2006 were used. Additionally, total costs were adjusted for purchasing power parity (PPP) to control for differences in price levels between the countries. These were derived from the Eurostat purchasing power parities and comparative price level indices for the ESA95 aggregates that were developed to compare price levels with the EU-25.

6.4 RESULTS

The patient characteristics of the hospital patient samples are summarised in table 6.1. A total of 2,729 admissions of age 61 ± 19 years with 60% male were recorded, with an average of 390 ± 232 per hospital. These admissions related to 16,791 ICU days (2,407 ± 1,607 on average per hospital). The patient case-mix differed somewhat from hospital to hospital. The SAPS II score ranged from 27 ± 15 in hospital I2 to 42 ± 20 in hospital U. There was a higher proportion of patients with gastrointestinal diseases at hospital G (31%), of cardiovascular diseases at hospitals I2 (30%), N2 (47%) and N3 (33%) and of respiratory diseases at hospitals I1 (37%) and N3 (30%).

Total population

An overview of descriptive statistics at the hospital level is given in table 6.2. Mean total costs varied between € 1,317 (hospital G) and € 2,503 (hospital U). With the exception of hospital U, mean direct costs per ICU day were of the same magnitude at all hospitals

Table 6.1: Patient characteristics of the patient samples

	hospital G	hospital I1	hospital I2	hospital N1	hospital N2	hospital N3	hospital U
	n=400	n=448	n=756	n=242	n=304	n=30	n=549
Age, years, mean ± SD	66 ± 16	61 ± 19	65± 21	54 ± 15	64 ± 18	58 ± 16	55 ± 20
Sex, male/female, n (%)	214/186 (54/46)	267/181 (60/40)	489/267 (65/35)	133/109 (55/45)	176/128 (58/42)	16/14 (53/47)	341/208 (62/38)
ICU stay, days, mean ± SD (min-max)	7.8 ± 12.6 (2-98)	5.2 ± 7.4 (1-117)	7.0 ± 5.8 (1-158)	6.0 ± 5.6 (1-30)	5.9 ± 12.2 (1-148)	3.8 ± 5.7 (1-8)	5.0 ± 5.1 (1-40)
SAPS II, mean ± SD	28 ± 15	41 ± 22	27 ± 15	*	34 ± 16	*	42 ± 20
Mechanical ventilation, n (%)	155 (39)	366 (82)	248 (33)	180 (74)	177 (58)	19 (63)	384 (70)
Admission diagnosis, n (%)							
Cardiovascular	21 (5)	69 (15)	225 (30)	27 (18)	146 (47)	10 (33)	83 (15)
Gastrointestinal	125 (31)	40 (9)	150 (20)	26 (18)	54 (17)	6 (20)	58 (11)
Metabolic	12 (3)	31 (7)	5 (1)	1 (1)	8 (3)	0 (0)	10 (2)
Neurological	20 (5)	73 (16)	39 (5)	33 (22)	22 (7)	4 (13)	40 (7)
Renal	38 (10)	20 (5)	97 (13)	2 (1)	8 (3)	1 (3)	28 (5)
Respiratory	27 (7)	164 (37)	114 (15)	27 (18)	67 (22)	9 (30)	132 (24)
Unknown/Other	157 (39)	51 (11)	126 (17)	32 (22)	5 (1)	0 (0)	198 (36)

SD = standard deviation
ICU = intensive care unit
SAPS = simplified acute physiology score
* not available

ranging from € 1,124 (hospital I1) to € 1,360 (hospital N2). The higher direct costs for hospital U were entirely due to the higher share of labour costs (€ 1,568 compared to on average of € 684 at the other hospitals). The cost differences between hospitals decreased slightly when costs were adjusted for PPPs. However, the relative ranking of total costs by hospital persisted.

Even though the distribution of costs varied by cost component, labour was the most important cost driver at all hospitals. Labour costs accounted for half of the total costs (810 ± 349; table 6.2). The higher labour costs at hospital U were predominantly explained by the higher unit costs of ICU nurses (€ 0.82 versus € 0.43 per minute), but also unit costs of ICU specialists were somewhat higher (€ 1.48 versus € 1.06 per minute at the other hospitals; table 6.3) and Furthermore, the labour costs of consulted specialists were a manifold higher at hospital U compared to the other hospitals (€ 202 versus € 36 in on average at the other hospitals). Non-ICU medical specialists were responsible for the greatest share of the labour costs of consulted specialists, but also physiotherapists accounted for a considerable proportion (27% at hospital U versus on average 16% at the other hospitals).

Table 6.2: Mean total costs of cost components of a patient day at the intensive care units (Euro 2006)

								Total population	
	hospital G	hospital I1	hospital I2	hospital N1	hospital N2	hospital N3	hospital U	Hospital sample (n=7)	
	n=400	n=448	n=756	n=242	n=304	n=30	n=549	Mean	SD
Diagnostic procedures									
- Medical imaging services	47	43	31	58	67	119	41	58	29
- Laboratory services	127	154	124	188	125	120	54	127	41
Consumables									
- Drugs	111	109	202	140	145	137	109	136	33
- Fluids	57	49	38	127	141	145	54	87	48
- Disposables	71	74	68	3	32	62	113	60	35
Hotel and nutrition	77	37	24	87	83	42	11	52	31
Labour									
- ICU specialist	189	247	274	144	208	246	285	228	50
- ICU nurse	428	355	540	382	541	330	1,081	522	260
- Consulted specialist	77	56	32	18	19	17	202	60	67
Total direct costs	**1,184**	**1,124**	**1,333**	**1,148**	**1,360**	**1,219**	**1,949**	**1,331**	**287**
Total indirect costs	133	210	139	657	816	534	554	435	273
TOTAL	**1,317**	**1,334**	**1,472**	**1,805**	**2,176**	**1,753**	**2,503**	**1,766**	**445**
Total (PPP adjusted)	**1,270**	**1,308**	**1,443**	**1,718**	**2,070**	**1,668**	**2,227**	**1,672**	**369**
	0.96	*0.98*	*0.98*	*0.95*	*0.95*	*0.95*	*0.89*	*0.95*	*0.03*

SD = standard deviation
ICU = intensive care unit
PPP = purchasing power parity

The share of consumables varied between 11% of the total costs at hospital U and 21% at hospital I2 (table 6.2). The absolute costs of fluids were almost three times higher at hospitals N1, N2, N3 compared to the other hospitals. The cost component predominantly represented blood (derived) products at hospitals G, I1, I2 and U, whereas at hospitals

Table 6.3: Resource use and unit costs of the cost component labour

	hospital G	hospital I1	hospital I2	hospital N1	hospital N2	hospital N3	hospital U
	n=400	n=448	n=756	n=242	n=304	n=30	n=549
ICU specialist	**189**	**247**	**274**	**144**	**208**	**246**	**285**
FTE per inpatient day	0.45	1.17	2.09	0.00	0.00	0.82	0.78
Resource use (minutes)	201	187	208	212	213	221	192
Unit costs (Euro 2006 per minute)	0.94	1.32	1.32	0.68	0.98	1.12	1.48
ICU nurse	**428**	**355**	**540**	**382**	**541**	**330**	**1,081**
FTE per inpatient day	3.72	6.77	4.97	5.84	4.60	2.86	6.04
Resource use (minutes)	793	871	1,325	923	1,305	797	1,318
Unit costs (Euro 2006 per minute)	0.54	0.41	0.41	0.41	0.41	0.41	0.82

ICU = intensive care unit
FTE = fulltime equivalent

N1, N2 and N3 it additionally comprised medications which were administered to the patient intravenously.

Diagnostic procedures were responsible for about 10% of the total costs (table 6.2). Absolute costs of laboratory services were much lower at hospital U (€ 54 compared to on average € 140 at the other hospitals).

Indirect costs amounted to € 435 ± 273 (table 6.2), but its proportion in the total costs varied widely between hospitals (from 9% at hospital I2 to 37% at hospital N2).

Patients requiring mechanical ventilation

Approximately 56% of identified patients were mechanically ventilated at some point during their ICU stay. Hospital I2 had the lowest share of mechanically ventilated patients, whereas hospital I1 had the highest share (table 6.1).

Table 6.4 presents the cost distribution by cost component for patients requiring MV and for patients not requiring MV. Mean daily ICU costs for the seven hospitals were € 1,986 ± 494 for patients requiring MV and € 1,490 ± 389 for those not requiring MV. Patients requiring MV were between 20% (hospitals G and N1) and 72% (hospital I2) more expensive than patients not requiring MV. The absolute costs of labour were much higher for patients requiring MV (€ 970 versus € 601; table 6.4). The absolute costs of the other cost components were also higher for patients requiring MV, albeit to a minor extent.

Table 6.4: Mean total costs of cost components of a patient day at the intensive care units for patients requiring mechanical ventilation and patients not requiring mechanical ventilation (Euro 2006)

								Total population	
	hospital G	hospital I1	hospital I2	hospital N1	hospital N2	hospital N3	hospital U	Hospital sample (n=7)	
	n=155	n=366	n=248	n=180	n=177	n=19	n=384	Mean	SD
Patient requiring mechanical ventilation									
Diagnostic procedures	139	187	241	262	220	207	123	197	51
Consumables	239	406	283	296	374	427	276	329	73
Hotel and nutrition	102	24	37	87	83	42	11	55	35
Labour	839	920	802	632	841	850	1,908	970	423
Indirect costs	136	139	210	657	816	534	554	435	273
TOTAL	**1,455**	**1,676**	**1,573**	**1,934**	**2,334**	**2,060**	**2,872**	**1,986**	**494**
Patient not requiring mechanical ventilation									
	n=245	n=82	n=508	n=62	n=127	n=11	n=165		
Diagnostic procedures	200	138	122	222	134	275	74	166	69
Consumables	239	318	143	233	208	255	276	239	55
Hotel and nutrition	57	24	37	87	83	42	11	49	29
Labour	581	728	405	409	622	320	1,144	601	279
Indirect costs	132	139	210	657	816	534	554	435	273
TOTAL	**1,209**	**1,347**	**917**	**1,608**	**1,863**	**1,426**	**2,059**	**1,490**	**389**

SD = standard deviation

6.5 DISCUSSION

The primary objective of the present study was to determine and compare the true costs of ICU stay at seven randomly selected ICUs from four European countries using a standardised bottom up microcosting methodology. Mean total costs of ICU stay were € 1,766 ± 445 but varied widely between the seven hospitals (table 6.2). Owing to the higher unit costs and total costs of labour, mean direct costs per ICU day were almost two times higher at hospital U (table 6.2-3). Because mean direct costs were fairly similar

between the other hospitals, total cost differences between these hospitals were mainly resulting from diverging indirect costs. PPP adjustment had a minimal overall impact on the results, particularly since the PPPs for the four countries were fairly similar.

Large variability between ICUs has been demonstrated previously (Rothen et al. 2007; Treggiari et al. 2007; Wunsch et al. 2008). Because we applied a standardised costing methodology, differences between hospitals are assumed to be solely due to actual cost differences. The country of origin was clearly the most important factor to explain the cost differences observed in this study. Labour costs have previously been demonstrated to be higher in the UK compared to other European countries. Also Negrini et al. (2006) found the proportion of labour to be 67% of the direct costs (compared to 61% in our study) with British hospitals being far more costly than the hospitals in France, Germany and Hungary (Negrini, Sheppard 2006).

Furthermore, the variety of healthcare systems in the different countries coincides with different parties being responsible for the same cost item. For example, where most capital costs of public hospitals are paid for by the state in Germany and do not represent any costs to the hospital, this was not the case in Italy, the Netherlands or the UK. Therefore, as we always applied the hospital perspective, cost items included in the indirect costs varied somewhat from country to country.

Actual differences between the ICUs may further be explained by the country of origin in combination with other factors, such as different patient case-mixes (table 6.1) and variations in staff composition. The German patient sample included a higher proportion of patients with gastrointestinal diseases (31% compared to 12% on average in the other countries), because ICUs in Germany are used for post-surgery care. In addition, even though not necessarily in Göppingen, the density of acute care beds per 1,000 inhabitants is relatively high in Germany (6.4 compared to on average 2.9 in the other countries). Similarly, it is likely that patients admitted to the ICU in the UK are more severely ill and in need of more intensive care (density of acute care beds: 2.3) which was reflected by the higher SAPS II score at hospital U (42 ± 20). As a result, actual differences might partly explain the lower costs at hospital G and the higher costs at hospital U.

In Italy, there is a relative shortage of ICU technicians and specialised nurses and, thus, ICU specialists generally have more responsibilities compared to ICU specialists in the other countries. Even though this suggests that costs were not estimated under ideal circumstances, i.e. staff deficiency, the Italian costs resulting from our study provide costs as occurring in daily practice. The number of FTE ICU specialists amounted to 1.17 per inpatient day at hospital I1 and to 2.09 at hospital I2 (versus 0.74 on average at the

other hospitals; table 6.3). Furthermore, in contrast to the other countries, ICU specialists included ICU residents in the Netherlands which may have affected the resource use and unit costs of labour for ICU specialists. Brazzi et al. (2002) have earlier suggested that, given the wide variation in the number of activities performed and in the proportion of working time spent performing activities, data comparing costs between different ICUs should be interpreted with caution (Brazzi et al. 2002).

Other actual differences may have arisen due to differences in medical practice and the availability of health care resources. The decision to mechanically ventilate a patient and the presence and use of high dependency units differed between hospitals. Besides, hospital G represented a focused care hospital, whereby the most severely ill patients are admitted to maximal care hospitals. In contrast, the highest available level of care was provided at the other hospitals. Lastly, it should be kept in mind that increased resource use consumption is not necessarily associated with better outcomes.

As a secondary objective, the costs of ICU stay for patients with and without MV were determined. In line with the findings of earlier studies (Dasta, McLaughlin 2005; Jacobs, Edbrooke 2001), MV was associated with increased costs of on average 33%. Labour was the main cause of the much higher direct costs for patients requiring MV (compared to patients not requiring MV). Dasta et al. (2005), who performed a costing study to determine the incremental costs of MV at ICUs in the United States, found an average cost increase of 62% on the first day, 37% on the second day and 25% on subsequent days of admission (Dasta, McLaughlin 2005). Based on regression modelling, Jacobs et al. (2001) have estimated the increase in average daily costs per patient requiring MV to be € 236 (adjusted to 2006), which includes the additional resources and increased workload of the nursing staff (Jacobs, Edbrooke 2001).

The microcosting approach is ideally combined with a bottom up methodology, in which cost components are valued by identifying resource use directly employed for a patient. Even though bottom up microcosting result in more accurate costs compared with top down microcosting, the methodology has two major limitations. Firstly, bottom up microcosting is often hindered by the absence or inadequacy of hospital information systems. Therefore, for some occasions in the present study, we applied the top down microcosting methodology instead (Drummond, Sculpher 2005). For example, resource use data at hospital U was only available per average patient, which may have led to a slight overestimation of the cost difference observed between the hospitals.

Secondly, bottom up microcosting is lengthy and expensive (Drummond, Sculpher 2005). Therefore, our study included only a small sample of hospitals. In order to make

cross country comparisons, cost assessments from a larger sample of ICUs per country are needed. Besides, random sampling within and between countries could enhance the reliability of our results. However, cross country cost comparisons are scarce and thus we believe that our study provides valuable insight into the relative costs of ICU stay in different European countries.

Our study is the second to determine and compare the costs of ICU stay across European countries following the study of Negrini et al. (2006). Because Negrini et al. (2006) employed the top down approach, they were able to include many more hospitals than was possible for our study (19 in France, 222 in Germany, 13 in Hungary and 75 in the UK). Our results may be viewed as preliminary data to support the funding of a future studies to determine their generalisability to other ICUs within and beyond our sample of countries.

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Chapter 7

Costs and prices of single dental fillings in Europe: A microcosting study

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7.1 ABSTRACT

Dental fillings represent an established procedure to treat tooth decay. The present paper provides a cost comparison of dental filling procedures across nine European countries. More specifically, the paper aims to estimate the costs and prices (i.e. reimbursement fees) of a single dental filling procedure in an approximately 12-year-old child with a toothache in a lower molar who presents at a dental practice, as described in a case vignette. Both amalgam and composite fillings were examined. Total costs were determined by identifying resource use and unit costs for the following cost components: diagnostic procedures, labour, medications, disposables and overheads. Altogether, 49 practices provided data for the cost calculations. Mean total costs per country varied considerably, ranging from € 8 to € 156. Labour costs were the most important cost driver in all practices, comprising 58% of total costs. Overhead costs were the second-most important cost component in the majority of countries. Actual cost differences across practices within countries were relatively small. Cost variations between countries were due primarily to differences in unit costs, especially for labour and overheads and only to a lesser extent to differences in resource use. Finally, cost estimates for a single dental filling procedure based on reimbursement fees led to an underestimation of the total costs by approximately 50%.

Keywords: Dentistry – Dental filling – Europe – Cost comparison – Health care costs

7.2 INTRODUCTION

Dental fillings represent an established procedure to treat tooth decay. Dental filling procedures involve assessing the cavity, preparing the filling, excavating decayed material and filling the tooth. The procedure is usually carried out by dentists, with or without the assistance of dental nurses, and is generally provided at independent dental practices.

Dental fillings are one of the services explored as part of work package 9 of the EU *Health*BASKET project. More specifically, the case vignette in question concerns 'an approximately 12-year-old child with a toothache in a lower molar who presents at a dental practice. After diagnosis, the dentist decides to place an amalgam filling.' The vignette was defined in detail to ensure that the same case was considered in each country and dental practice. Dental fillings performed as an inpatient procedure were excluded from the study.

The aim of the present paper was to estimate resource use, total costs and prices (i.e. reimbursement fees) for a single dental filling procedure in nine participating EU member states: Denmark, England, France, Germany, Hungary, Italy, the Netherlands, Poland and Spain. Dental fillings allow for relatively straightforward cost calculation and comparison, because they involve a relatively homogeneous procedure that is performed in a small organisational unit in primary care.

Background

A dental filling is indicated when a caries lesion is found in a molar tooth. Assessment by a dentist determines whether treatment is required and may include diagnostic procedures such as medical imaging services, vitality testing, cold testing and percussion testing. Therapy involves preparing the filling, excavating decayed material from the affected tooth and placing the filling into the cavity. Dental amalgam has been used as a restorative material in dentistry for more than a century and is made by combining elemental mercury, silver, tin, copper and possibly other metallic elements. Although a second visit is desirable to polish the amalgam after placement, amalgam fillings are quick and easy to apply (Rateitschak 1994).

In recent years, a shift from dental amalgam to adhesive dentistry with resin composites has taken place in many countries. Composite fillings are a mixture of glass or quartz filler in a resin medium that produces a tooth-coloured filling. Applying a composite filling is more time consuming (Rateitschak 1994), but has a variety of obvious advan-

tages. Many dentists prefer composites for aesthetic, toxicological, or ecological reasons (Lehmann & Hellwig 1993). Composites require removing less tooth structure, cause less sensitivity to hot and cold, have a strengthening effect on the remaining tooth and allow for individual colour nuances (Opdam 2005). In Germany and the Netherlands, the use of dental amalgam has ceased almost entirely, particularly among younger patients (Lehmann & Hellwig 1993; Opdam 2005).

To our knowledge, no publications over the past decade have explored the costs of single dental filling procedures in Europe. However, Oscarson et al. (1998) assessed the relative impact of cost components on the total costs of dental care in Sweden. In that study, labour turned out to be the major cost driver, comprising 67% of total costs. Overheads accounted for 25% of the total costs (Oscarson et al. 1998).

Some studies have evaluated the long-term costs of different filling materials (Mjor et al. 1997; Sjogren & Halling 2002) and the cost effectiveness of different types of dental treatments for caries prevention (Griffin et al. 2002; Jokela & Pienihakkinen 2003; Kervanto-Seppala et al. 2000), large substance loss (Bragger et al. 2005; Kelly & Smales 2004; Kolker et al. 2006), class II restorations (Tobi et al. 1999; Yip et al. 2002) and asymptomatic disease-free third molars (Edwards et al. 1999). Even though treatment time was recognised by most papers as crucial for explaining cost variation, it was included as a cost estimate in only three studies (Jokela & Pienihakkinen 2003; Kervanto-Seppala, Lavonius 2000; Tobi, Kreulen 1999). The other economic evaluations used general service fees to approximate costs.

7.3 METHODS

A standardised microcosting methodology was used to ensure that the identified cost differences would reflect only actual cost differences. Cost components included diagnostic procedures, labour, medications, disposables and overheads. In each country, a sample of dental practices was identified that was representative of the overall practice setting and treatment patterns in that country. Dentists in Denmark, France, Hungary, Italy, the Netherlands, Poland and Spain were asked personally by the investigators whether they would like to participate in the study. In England and Germany, 20 and 175 randomly selected dentists, respectively, were asked by (e-)mail if they would like to participate. In addition, a request was placed in the dental information bulletin published by the German Dental Association.

Information on resource use and the unit costs of cost components was collected from between 3 and 15 representative dental practices per country. Dentists were asked to provide information on the last 10 patients who matched the vignette description or to estimate resource use and unit cost data based on an average patient. Although the case vignette restricted the use of restorative materials to amalgam, the decision was ultimately made to examine both amalgam and composite fillings, as some practices no longer used amalgam. Using standardised reporting templates, data were collected by means of face-to-face interviews (France, Germany, Italy, Poland and Spain), telephone interviews (Denmark, France, Germany, Hungary and the Netherlands) and questionnaires (England, France, Germany, Hungary, the Netherlands and Poland). Alternative sources were used to gather additional information, including national/local health registries (Denmark, England, France and the Netherlands) and manufacturers (Germany).

Labour costs for dentists and dental assistants were based on treatment time (length of session) and multiplied by standardised costs per time unit. Costs per time unit were determined on the basis of gross income (including social security costs) and either the number of workable hours (Denmark, England, France, Germany, Hungary and the Netherlands) or the number of hours dedicated to direct patient care only (Italy, Poland and Spain). Labour not directly involved in the treatment process was included in overheads.

Although the cost items included in the overheads varied somewhat from practice to practice, these generally included the costs of rent, utilities (electricity, heat and water), cleaning and waste management, insurance, telecommunication, equipment and administration. Overhead costs were based on average treatment time, total overhead costs per year and either the number of workable hours (England, Germany, Hungary and the Netherlands) or the number of hours dedicated to direct patient care only (France, Italy, Poland and Spain). In Denmark, Italy and Poland, some estimations of overhead costs were provided directly by the dentists.

In addition to descriptive statistics, analyses of variance were used to evaluate variations in variables between and within countries. Normal distribution of total costs in the different practices was assessed using the Kolmogorov-Smirnov test ($P = 0.085$).

The dental practices in all participating countries were included in an ordinary least squares (OLS) regression analysis, taking mean total costs as the dependent variable and practice, treatment and country characteristics as explanatory variables. Practice characteristics consisted of the 'type of practice' (independent practice, yes/no), the 'number of dentists per practice' and the 'number of dental assistants per dentist'. These variables served as a proxy to control for the type and the size of the practices.

Treatment characteristics consisted of the 'percentage of patients receiving amalgam', the 'percentage of patients receiving medical imaging services' and 'treatment time'. These variables served as a proxy for treatment decisions taken at a particular practice. Country variables were included to control for differences between countries. As a supplement, random effects regression modelling was applied to take into account the fact that data originated from patients seen in various countries and practices (Singer 1998). In this analysis, both countries and practices were included as random effects, whereas practice, treatment and country characteristics were included as fixed effects. Finally, purchasing power parities (PPPs) were included in the random effects model to control for differences in price levels between the countries. PPPs were based on the latest Organisation for Economic Co-operation and Development (OECD) statistics on PPPs and comparative price levels.

Reimbursement fees are supposed to cover all aspects of the dental filling procedure, including assessment of the cavity, preparation of the filling, excavation of decayed material and placement of the filling. Therefore, the last analysis involved calculating Pearson's correlation coefficients to investigate whether reimbursement fees represent a good cost estimate for mean total costs.

Statistical analyses were conducted with the statistical software programmes SPSS for Windows version 13.0 and SAS version 8.02. *P* values less than 0.05 were considered statistically significant. The perspective of the study was that of the practitioner and all costs were measured in values of 2005. Mean exchange rates for 2005 were used.

7.4 RESULTS

Data for the cost calculations were provided by a total of 49 practices, 15 of which (31%) were located in Germany. In most countries, it was difficult to recruit dentists who were willing to participate. However, no association was found between the way in which dentists had been approached (i.e. personally or through random selection) and mean total costs ($P = 0.162$).

Practice characteristics

Practice characteristics per country are summarised in table 7.1. Most participating practices were independent dental practices. Although independent practices are generally private, all practices in Poland (5/5) and one practice in Italy (1/5) were affiliated with public institutions. In Denmark, dental care is provided through public municipal

Table 7.1: Practice characteristics per country

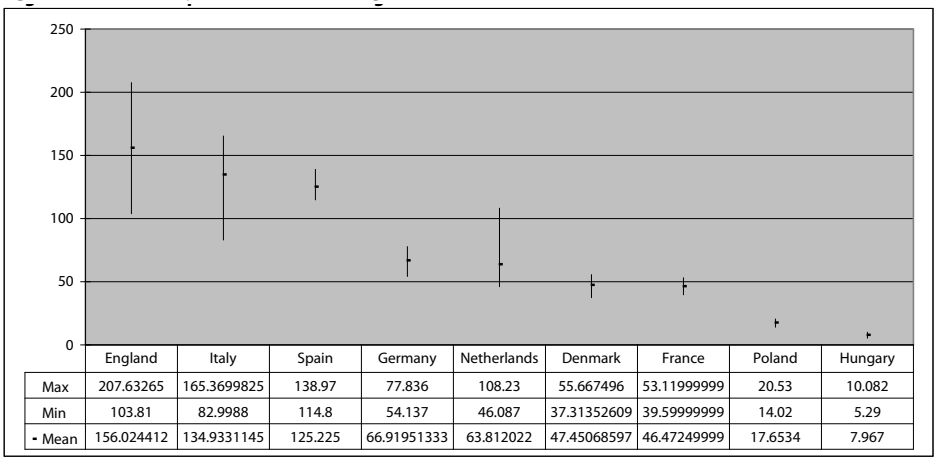
	Number of practices included	% Independent practice	% Community based practice	% Outpatient department of hospital	% Private	% Public	Number of dentists per practice	Number of dental assistants per practice	Number of other supporting staff per practice
England*	4	0	100	0	0	100	*	*	*
Italy	5	100	0	0	80	20	1.0	1.0	0.0
Spain	4	100	0	0	100	0	1.5	2.5	1.0
Germany	15	100	0	0	100	0	1.7	3.7	0.7
Netherlands	5	100	0	0	100	0	2.0	1.4	0.0
Denmark	4	0	100	0	0	100	26.3	46.5	12.1
France	4	100	0	0	100	0	1.3	0.5	0.3
Poland	5	100	0	0	0	100	2.6	*	*
Hungary	3	67	0	33	67	33	1.0	1.0	0.7

* not available

dental care organisations, which generally have more dentists (26.3 dentists) and dental assistants (46.5 assistants) per practice (compared to an average of 1.6 dentists and 1.7 assistants in the other countries). Overall, mean total costs did not differ significantly between single and group practices ($P = 0.675$).

Cost comparison between countries

Figure 7.1: Cost comparison of tooth filling between countries



	England	Italy	Spain	Germany	Netherlands	Denmark	France	Poland	Hungary
Max	207.63265	165.3699825	138.97	77.836	108.23	55.667496	53.11999999	20.53	10.082
Min	103.81	82.9988	114.8	54.137	46.087	37.31352609	39.59999999	14.02	5.29
- Mean	156.024412	134.9331145	125.225	66.91951333	63.812022	47.45068597	46.47249999	17.6534	7.967

An overview of mean total costs per country is given in figure 7.1 and table 7.2. The mean total costs for all countries were € 74 (SD 53), ranging from € 8 in Hungary to € 156 in England. Variations were caused by large differences in the mean total costs of labour ($P < 0.001$), consumables ($P < 0.001$), medical imaging services ($P < 0.001$) and overheads ($P < 0.001$).

Without exception, labour costs were the most important cost driver in all countries and practices. Labour costs accounted for 58% of total costs (€ 43; SD 33) on the average and for as much as 77% and 70% of total costs in Denmark and England, respectively. The large differences in labour costs between countries were essentially caused by wide variations in unit costs, especially for the dentist ($P < 0.001$). Dentist costs per minute ranged from € 0.09 in Hungary to € 2.88 in England (table 7.2). However, the relatively high dentist costs in England are also assumed to include disposable costs which makes straightforward comparisons difficult.

Although there appeared to be consensus among dentists on treatment time ($P = 0.309$), length of session was relatively long in Spain (64 minutes versus an average of 35

minutes in the other countries; table 7.2). Dentists spent as much time with the patients as did dental assistants on the average (i.e. 37 minutes), but dentists' unit costs were four times higher (€ 0.92 versus € 0.22 per minute). As a result, 81% of labour costs in our sample were attributable to dentist costs.

Overhead costs were the second-most important cost component in most countries (mean € 18; SD 17). Overhead covered 24% of the total costs, ranging from 7% in England to as much as 40% in Spain and 41% in Germany. This wide variation was due, for the most part, to large differences in unit costs, ranging from € 0.07 in Hungary to € 1.01 in Italy ($P = 0.003$; table 7.2). The number of hours on which labour and overheads were based (i.e. workable hours or hours dedicated to direct patient time only) did not have an impact on mean total costs ($P_{labour} = 0.123$ and $P_{overheads} = 0.618$).

The remaining costs consisted primarily of the costs of diagnostic procedures (€ 8; SD 13) and consumables (€ 5; SD 6). Diagnostic procedures represented a high share of total costs in England (23%) and the Netherlands (33%). Medical imaging costs ranged from € 0.11 in Germany to € 35 in England. A significant difference was found for the percentage of patients who underwent diagnostic procedures ($P = 0.012$; table 7.2). On average, 7 out of 10 patients underwent medical imaging services (i.e. X-ray and bitewing radiographs). However, this proportion was only 2 out of 10 in Germany. Also, unit costs for medical imaging services varied widely, ranging from € 0.30 in France to € 39 in the Netherlands ($P = 0.001$; table 7.2), which may reflect different mixes of medical imaging services.

Consumable costs played an important role in Hungary and Italy. Hungary showed a high relative share of consumable costs (20% versus an average of 7% in the other countries), whereas a high absolute level was observed in Italy (€ 20 versus an average of € 2 in the other countries). The latter finding was due primarily to the high costs of the filling material (€ 15 versus an average of € 1 in the other countries).

In total, 59% of patients received an amalgam filling (table 7.2). The lowest percentages of amalgam fillings were found in Germany (27%) and the Netherlands (10%). On average, unit costs for amalgam fillings were more than 2 times lower than those for composite fillings; in Germany and the Netherlands, however, they were 8 times lower (table 7.2). Nevertheless, the percentage of patients receiving amalgam had no significant influence on mean total costs ($P = 0.661$).

No significant differences between countries were observed with regard to resource use or the unit costs of anaesthetics ($P = 0.264$ and $P = 0.111$ respectively; table 7.2).

Table 7.2: Resource use and unit costs of the cost components

	England*	Italy	Spain	Germany	Netherlands	Denmark*	France	Poland*	Hungary*	Mean	SD
DIAGNOSTIC PROCEDURES											
Medical imaging services	**35**	**11**	**3**	**0**	**21**	**1**	**0**	**1**	**0**	**8**	**12**
Resource use (no. of units)	0.88	0.70	1.00	0.20	0.54	0.78	1.00	0.40	0.60	0.68	0.27
Unit costs (Euro 2005/6 per unit)	40.35	16.00	2.51	0.53	39.00	0.81	0.30	3.73	0.53	11.53	16.70
LABOUR											
Dentist	**97**	**48**	**61**	**26**	**24**	**21**	**24**	**8**	**2**	**35**	**30**
Resource use (minutes)	33.75	36.00	63.75	33.93	31.93	33.75	32.50	47.82	23.50	37.44	11.68
Unit costs (Euro 2005/6 per unit)	2.88	1.32	0.96	0.78	0.74	0.63	0.75	0.16	0.09	0.92	0.82
Dental assistant	**11**	**18**	**7**	**8**	**9**	**15**	**1**	**2**	**2**	**8**	**6**
Resource use (minutes)	42.36	44.00	63.75	33.93	25.08	41.50	10.75	40.50	33.50	37.26	14.48
Unit costs (Euro 2005/6 per unit)	0.27	0.41	0.12	0.25	0.34	0.37	0.10	0.05	0.06	0.22	0.14
CONSUMABLES											
Amalgam	***	**3**	**3**	**0**	**0**	**0**	**0**	**	**1**	**0**	**0**
Resource use (no. of units)	1.00	0.40	1.00	0.27	0.10	0.38	0.75	1.00	0.45	0.59	0.35
Unit costs (Euro 2005/6 per unit)	****	8.40	3.00	0.30	0.33	0.45	0.45	****	1.30	2.03	2.97
Composite	****	**12**	****	**2**	**2**	**1**	**0**	****	**1**	**3**	**5**
Resource use (no. of units)	0.00	0.60	0.00	0.73	0.90	0.63	0.25	0.00	0.55	0.41	0.35
Unit costs (Euro 2005/6 per unit)	****	20.00	****	2.25	2.73	0.85	1.36	****	1.30	4.75	7.50
Disposables	***	**5**	**1**	**2**	**0**	**0**	**4**	**2**	**0**	**2**	**2**

MEDICATIONS											
Anaesthetic	**1**	**3**	***	**0**	**0**	**1**	**0**	**	**0**	**1**	**1**
Resource use (no. of administrations)	1.00	0.97	****	0.71	0.78	0.95	1.00	****	0.85	0.89	0.12
Unit costs (Euro 2005/6 per administration)	0.57	2.90	****	0.46	0.51	0.85	0.24	****	0.30	0.83	0.93
OVERHEADS	**11**	**36**	**51**	**27**	**7**	**9**	**14**	**4**	**2**	**18**	**17**
Resource use (minutes)	34	36	64	34	32	34	33	48	24	37.44	11.68
Unit costs (Euro 2005/6 per unit)	0.31	1.01	0.80	0.80	0.22	0.27	0.43	0.08	0.07	0.44	0.34
TOTAL	**156**	**135**	**125**	**67**	**64**	**47**	**46**	**18**	**8**	**74**	**53**
Patient co-payment	0	19	0	11	0	****	14	0	0	5	8
Reimbursement	27	19	50	66	61	****	32	9	7	34	23

SD = standard deviation

* Denmark Krone (kr) 1 = € 0.1342, Great Britain Pound (£) 1 = € 1.463, 1 Hungarian Forint (Ft) = € 0.004047 and Polish Zloty (zł) 1 = € 0.2500

** subsumed in disposables

*** subsumed in labour

**** not applicable

Within-country cost comparisons

Overall, variations in mean costs between practices within individual countries were relatively small. Analyses of variance revealed within-country variations for the treatment time of dental assistants ($P = 0.001$), as well as for the unit costs and total costs of amalgam ($P_{\text{unit costs amalgam}} = 0.005$ and $P_{\text{total costs amalgam}} = 0.001$). Furthermore, broad within-country variations were found for the total costs of medical imaging services (Germany and Hungary); for treatment time and the unit costs of dental assistants (France); for resource use and unit costs of amalgam (Denmark, Germany, Italy and the Netherlands); for the unit costs and total costs of composites (France); for the total costs of consumables (Italy): for the use of anaesthetics (Poland); and for the unit costs and total costs of anaesthetics (France).

Although practice characteristics likely influenced differences in the unit costs of overheads, our sample was too small to draw reliable conclusions on possible associations. Even so, in Hungary, unit costs were 3 times higher in private practices than they were in public practices. In Spain, urban practices reported higher rental rates than rural practices.

In Italy, the mean costs of public practices were much lower than those of private practices (€ 83 versus an average of € 148). This disparity was attributable primarily to the lower unit costs of medical imaging services, labour and consumables in public practices. Mean costs in the one outpatient department in Hungary included in our sample were much lower than the costs seen in the independent practices in that country (€ 5 versus an average € 9). This was due to lower cost estimates of all cost components except for overheads. In the Netherlands, the mean costs in one practice were considerably higher than those seen in the other practices (€ 108 versus an average € 53). These higher mean costs were due primarily to longer sessions.

OLS regression

Table 7.3 shows the results of the different regression models that were constructed to examine the degree of association between total costs and practice characteristics. In all cases, the dependent variable was total costs. The first set of models, labelled as model 1, included practice characteristics, treatment characteristics and countries. Of the practice and treatment characteristics included in these analyses, only 2 were significantly associated with mean total costs: use of medical imaging services and treatment duration. Specifically, use of medical imaging services was associated with an increase in mean total costs of € 25.80 ($P < 0.001$) and 1 extra minute of treatment was associ-

ated with an additional € 1.14 increase in mean total costs ($P < 0.001$). Use of a random effects regression model (model 1b) led to regression coefficients and standard errors that were very similar to those seen in the OLS model (model 1a). The combination of PPP-adjusted total costs and a random effects regression model (model 1c) also resulted in similar values.

Model 2 contained only practice characteristics and treatment characteristics. Unlike model 1, the number of dentists per practice was significantly associated with total costs when OLS regression was used (model 2a). Practices with more dentists showed lower total costs than practices with fewer dentists ($P < 0.10$). Independent practices and number of assistants per dentist were not associated with total costs. As with model 1, the use of medical imaging services and longer treatment duration were associated with higher costs, while the use of amalgam was not significantly associated with total costs. When a random effects model (model 2b) was estimated instead of OLS regression, three changes were noticed. Firstly, the number of dentists per practice was not significantly associated with total costs. Secondly, the coefficients for medical imaging services and treatment duration were slightly smaller. Lastly, the standard errors were approximately half the size of those seen using OLS regression. Use of PPP-adjusted total costs in a random effects model (model 2c) resulted in coefficients and standard errors that were similar to those seen with unadjusted total costs and random effects (model 2b).

Model 3 was the simplest of the 3 models and contained only treatment characteristics. The associations seen between treatment characteristics were very similar to those seen in model 2. As with model 2, medical imaging services and longer treatment duration were associated with higher costs, whereas the use of amalgam was not significantly associated with total costs. The coefficients for medical imaging services and treatment duration were slightly smaller. Also, the use of a random effects model (model 3b) resulted in standard errors that were approximately half the size of those seen using OLS regression (model 3a). Finally, the use of PPP-adjusted total costs in a random effects model (model 3c) resulted in coefficients and standard errors that were similar to those seen with unadjusted total costs and random effects (model 3b).

Reimbursement: Pearson's correlation coefficient

Table 7.2 also presents the fees charged by dental practices to patients and their healthcare insurers. There was a surprisingly weak positive linear relationship between reimbursement (including patient co-payment) and the total costs of dental filling per country (Pearson's correlation coefficient: R = 0.280).

Table 7.3: Regression models to explain mean total costs per practice (n=49)

	Model 1a Without random effects Without PPP		Model 1b With random effects Without PPP		Model 1c With random effects With PPP		Model 2a Without random effects Without PPP	
Independent variable	**Coefficient**	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**
Practice characteristics								
Independent practices	-19.69	18.29	-19.77	19.32	-23.73	20.71	-22.37	22.05
Dentists per practice	-0.32	0.33	-0.31	0.34	-0.27	0.37	-1.56	*0.80
Assistants per dentist	-3.52	4.20	-2.86	3.61	-2.97	3.90	10.10	6.63
Treatment characteristics								
Amalgam	-6.41	6.36	-7.20	7.12	-7.78	7.63	-23.32	14.60
Medical imaging	25.80	***9.20	25.83	**9.65	28.52	***10.35	42.01	**16.39
Treatment time	1.14	***0.30	1.18	***0.30	1.27	***0.33	1.62	***0.54
Countries								
Denmark	-46.66	*23.17	-48.02	*24.47	-41.90	26.23	-	-
France	-42.85	***14.15	-42.47	***13.92	-45.32	***14.95	-	-
Hungary	-67.53	***13.75	-67.30	***14.16	-78.32	***15.2	-	-
Netherlands	-16.01	10.13	-16.28	10.14	-17.73	10.89	-	-
Poland	-73.23	***14.58	-73.08	***13.77	-88.77	***14.82	-	-
England	87.01	***29.06	86.84	***29.92	100.20	***32.1	-	-
Italy	48.90	***10.41	48.50	***10.41	49.98	***11.18	-	-
Spain	6.58	15.91	4.78	16.10	-12.83	17.28	-	-

Germany served as a reference country and was therefore not included in this table.
PPP = purchasing power parities
SE = standard error
* P < 0.10
** P< 0.05
*** P < 0.01

Dental practices were generally more likely to make a loss than a profit when performing dental filling procedures. Amongst countries incurring costs in excess of reimbursement, the magnitude of the mean loss incurred was € 52, with figures ranging from less than € 1 in France and Hungary to € 129 in England. However, the € 27 reimbursement fee in England (table 7.2) reflected National Health Service (NHS) reimbursement to community dentists for placing an amalgam filling and was considerably lower than the national reimbursement rate for a child's first outpatient visit for orthodontic treatment (€ 208), which most closely reflected the vignette description.

Model 2b With random effects Without PPP		Model 2c With random effects With PPP		Model 3a Without random effects Without PPP		Model 3b With random effects Without PPP		Model 3c With random effects With PPP	
Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**
-25.36	17.54	-31.35	18.94	-	-	-	-	-	-
-0.37	0.34	-0.31	0.37	-	-	-	-	-	-
-2.89	3.55	-2.98	3.85	-	-	-	-	-	-
-6.59	7.03	-7.31	7.55	-9.03	14.62	-5.20	8.09	-6.06	8.87
28.16	***9.34	31.25	***10.04	38.85	**16.77	22.83	**9.45	25.06	**10.36
1.24	***0.30	1.31	***0.32	1.13	**0.56	1.44	***0.30	1.57	***0.33
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-

7.5 DISCUSSION

This study is the first to compare the costs of single dental filling procedures in Europe. The mean costs of a single dental filling amounted to € 74, which was much higher than the average sum of patient co-payment and reimbursement (€ 39). According to this comparison, using fees as a cost estimate for a dental filling would have led to a 50% underestimation of total costs. This disparity was due almost completely to relatively low reimbursement rates in England, Italy and Spain. Charges by dental practices to patients and their healthcare insurers vary widely between countries, because charges are highly dependent on national health payment systems, as well as on political and economical factors. A fairly strong direct correlation appears to exist between reimbursement (including patient co-payment) and gross domestic product per capita, with less wealthy countries providing lower levels of reimbursement (R = 0.767).

As expected, treatment time was clearly very important in determining the total costs of episode of care described in the vignette. This was particularly true if we consider that the two most important cost drivers (i.e. labour and overheads) were based on this estimate. However, absolute cost differences between countries were attributable primarily to differences in unit costs. These differences in unit costs were partly reflected in differences in gross domestic product per capita (R = 0.617).

Our regression analyses revealed a number of interesting findings. The between-country differences in total costs were evident throughout the analyses. These differences did not change and were not sensitive to the presence or absence of any practice or treatment characteristics in the model. With one exception, the practice characteristics that were examined in this study were never significantly associated with total costs. This one exception involved a negative and marginally significant association ($P = 0.058$) between total costs and the number of dentists. However, once information about the country was included in the analysis, this association disappeared. Two treatment characteristics were consistently associated with higher total costs: use of medical imaging services and longer treatment time. The use of medical imaging services and an additional minute of treatment time were associated with extra costs that ranged from approximately € 23 to € 42 and from € 1.18 to € 1.62, respectively, depending on the structure and contents of the regression model. Lastly, PPP adjustment had a minimal overall impact on the results, particularly since the PPPs for most of these countries were fairly similar.

Oscarson et al. (1998) conducted a microcosting study to determine the relative impact of cost components on the total costs of dental care in Sweden. Different methods for the valuation of treatment time and for allocating the unit costs of overheads were used. The results of their study were very similar to those of the present study. Labour and overheads contributed to 67% and 25% of the total costs, respectively (versus 58% and 23% in our study). Furthermore, total costs were highly sensitive to changes in length of session. Decreasing treatment time by 10% and 30% reduced the average costs of treatment time by approximately 10% and 40%, respectively. The study also confirmed sensitivity to the unit costs of labour, although this sensitivity was not as high as that of length of session (Oscarson, Kallestal 1998).

Our study confirmed that the unit costs of amalgam are considerably lower than those of composites (€ 2.03 versus € 4.75; table 7.2). Tobi et al. (1999) assessed the incremental cost effectiveness of the use of composite resins and amalgam for the restoration of amalgam class II restorations. Treatment time was prospectively measured and used to approximate treatment costs. It was concluded that amalgam restorations were associated with about half the treatment time required for composite restorations (Tobi,

Kreulen 1999). Other studies have also demonstrated favourable costs for amalgam, albeit over the long term. Mjör et al. (1997) compared the relative costs of direct class II restorations for different filling materials in England over a patient's lifetime. Their study illustrated the relatively low life-long costs of amalgam restorations and the relatively high costs of treatment using a resin-based composite (Mjor, Burke 1997). A comparable conclusion was drawn by Sjögren et al. (2002), who evaluated the theoretical long-term treatment costs of class II molar restorations in Sweden. Use of composite fillings was twice as costly over 10 years as the use of amalgam fillings (Sjogren & Halling 2002).

Even though several studies have assessed the cost effectiveness of dental treatments, only few address the use of amalgam or composites using fees as a proxy for actual costs. In a study by Sjögren et al. (2002), the mean initial costs of amalgam and composite direct class II molar restorations were € 60 and € 77, respectively (base year: 2006). Kolker et al. (2006) assessed the costs of large amalgam fillings and crowns in the United States for restoring teeth that had been severely compromised due to a loss of tooth structure. Initial average costs for teeth with crowns were € 641, while the initial costs assigned to teeth with large amalgam fillings were € 104 (Kolker, Damiano 2006). A study by Kelly et al. (2004) that assessed the relative cost effectiveness in Australia of alternative methods for restoring large tooth substance loss determined that the discounted costs of amalgam class I, cusp overlay amalgam class II and multi surface resin composite class IV restorations were € 40, € 91 and € 65, respectively (base year: 2006) (Kelly & Smales 2004).

Our case vignette described an approximately 12-year-old child, mainly to exclude any complications that might have occurred in the case of older patients. However, some dentists participating in our study pointed out that 12-year-old children usually do not need a filling, as children lose their milk teeth between the ages of 10 and 12. These dentists argued that milk teeth are typically removed as a preferred treatment and that adult teeth rarely show cavities in this age group because they are relatively new. Furthermore, dental problems in 12-year-old children are rare in Denmark due to the free preventive dental care that is offered to children up to the age of 18. Nevertheless, earlier studies have demonstrated that 12-year-old and even younger children can very well have fillings (Guelmann & Mjor 2002; Honkala et al. 1989; Pair et al. 2004; Tran & Messer 2003).

Other limitations of our study are due to methodological issues. Firstly, although special attention was paid to selecting representative practices in the participating countries, our study reflects the results of only small number of practices. Secondly, the extent of the cavity was not specified in the vignette, thus ignoring the possibility that longer

treatment times might be required to restore an occlusal cavity as compared to cavities affecting two or more surfaces around the tooth. Thirdly, cost information was difficult to obtain, as dentists generally do not record costs per item. As a result, for some practices it was necessary to rely on estimates rather than concrete data. In some cases imputation was used. Another difficulty occurred in collecting overhead costs since the method for allocation of overhead costs varied somewhat from practice to practice.

In conclusion, the mean total costs of a dental filling in a lower molar of an approximately 12-year-old child ranged from € 8 to € 156 in the 9 European countries participating in this study. Labour was by far the most important cost driver. Actual differences in costs between countries were due primarily to differences in unit costs and only to a lesser degree to differences in resource use.

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Chapter 8

A microcosting study of diagnostic tests for the detection of coronary artery disease in the Netherlands

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8.1 ABSTRACT

Objective: The primary aim of the present study was to calculate the actual costs of four diagnostic tests for the detection of coronary artery disease in the Netherlands using a microcosting methodology. As a secondary objective, the cost effectiveness of eight diagnostic strategies was examined, using microcosting and reimbursement fees subsequently as the cost estimate. **Design**: A multicenter, retrospective cost analysis from a hospital perspective. **Setting**: The study was conducted in three general hospitals in the Netherlands for 2006. **Interventions**: Exercise electrocardiography (exECG), stress echocardiography (sECHO), single-photon emission computed tomography (SPECT) and coronary angiography (CA). **Results**: The actual costs of exECG, sECHO, SPECT and CA were € 33, € 216, € 614 and € 1.300 respectively. For all diagnostic tests, labour and indirect cost components (overheads and capital) together accounted for over 75% of the total costs. Consumables played a relatively important role in SPECT (14%). Hotel and nutrition only applied to SPECT and CA. Diagnostic services were solely performed for CA, but their costs were negligible (2%). Using microcosting estimates, exECG-sECHO-SPECT-CA was the most and CA the least cost effective strategy (€ 397 and € 1.302 per accurately diagnosed patient). Using reimbursement fees, exECG-sECHO-CA was most and SPECT-CA least cost effective (€ 147 and € 567 per accurately diagnosed patient). **Conclusions**: The use of microcosting estimates instead of reimbursement fees led to different conclusions regarding the relative cost effectiveness of alternative strategies.

Keywords: Diagnostic strategy – Diagnostic test – Microcosting – Cost analysis – Cost effectiveness

8.2 INTRODUCTION

Diagnostic strategies for the detection of coronary artery disease (CAD) are known to vary widely between and within countries. However, the gold standard strategy for the detection of CAD is coronary angiography (CA), an invasive procedure that is believed to be associated with a 100% diagnostic accuracy (Dewey & Hamm 2007; Hernandez & Vale 2007). CA is a relatively expensive strategy and is associated with well known procedure-related morbidity and mortality compared to non-invasive tests (Hachamovitch et al. 2002). Therefore, diagnostic strategies may include one or more of the following non-invasive diagnostic tests prior to CA: exercise electrocardiography (exECG), stress echocardiography (sECHO) and single-photon emission computed tomography (SPECT).

Advantages of exECG include the low costs and high accessibility. However, exECG is a poor diagnostic test, especially in low risk populations, owing to its low positive predictive value (Hernandez & Vale 2007; Marwick et al. 2003; Sabharwal et al. 2007). sECHO is associated with better sensitivity and specificity than exECG and is a well recognised method for the detection of prognostically significant CAD (Jeetley et al. 2007; Marwick, Shaw 2003). Finally, even though the diagnostic accuracy of sECHO and SPECT is almost similar (Heijenbrok-Kal et al. 2007; Imran et al. 2003), sECHO has a significantly higher specificity whereas SPECT has a significantly higher sensitivity. This may make each diagnostic test useful in different settings (Heijenbrok-Kal, Fleischmann 2007). However, SPECT is more costly and not as widely available as exECG and sECHO (Sabharwal, Stoykova 2007; Tardif et al. 2002)

Accuracy of diagnostic testing is also considered to be dependent on the pre-test likelihood for CAD defined by different cardiovascular risk factors, such as age and gender (Dewey & Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch et al. 2004; Sabharwal, Stoykova 2007). In 2003, the prevalence of CAD in the Netherlands was estimated to be 4.2% in the general population and 15.6% in the age group of 60 years and older. The relative prevalence was greater in men than women: 5.1% versus 3.3% in the general population and 18.2% versus 13.1% in the age group of 60 years and older. Besides, the diagnostic accuracy of diagnostic tests is generally believed to vary between men and women (Hernandez & Vale 2007; Redberg & Shaw 2003; Sabharwal, Stoykova 2007).

Economic evaluations have become increasingly important to examine the cost effectiveness of alternative strategies (Dewey & Hamm 2007; Drummond et al. 2005). This is reflected in the great amount of economic evaluations of diagnostic strategies for the detection of CAD carried out in the past five years (amongst others: (Dewey &

Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch, Hayes 2004; Hernandez & Vale 2007; Jeetley, Burden 2007; Marwick, Shaw 2003; Mowatt et al. 2004; Redberg & Shaw 2003; Sabharwal, Stoykova 2007; Sharples et al. 2007; Tardif, Dore 2002)). Some of these studies have compared the costs of different strategies per accurately diagnosed patient (Jeetley, Burden 2007). Strategies *in*cluding sECHO were generally found to be more cost effective than strategies *ex*cluding sECHO (Jeetley, Burden 2007). Other studies have evaluated the long-term costs (e.g. total disease costs) of different diagnostic strategies (Dewey & Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch, Hayes 2004; Hernandez & Vale 2007; Marwick, Shaw 2003; Sharples, Hughes 2007). Without exception, these long-term studies determined CA to be the most cost effective strategy (Dewey & Hamm 2007; Hernandez & Vale 2007).

The microcosting methodology provides cost estimations that most accurately reflect actual costs, because all relevant cost components are identified at the most detailed level (Drummond et al. 2005). As this methodology is time consuming, it has not been widely used in assessing the costs of diagnostic tests for the detection of CAD. Instead, most economic evaluations have used reimbursement fees or general service charges to approximate the costs (Dewey & Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch, Hayes 2004; Jeetley, Burden 2007; Marwick, Shaw 2003; Mowatt, Vale 2004; Redberg & Shaw 2003; Sharples, Hughes 2007; Tardif, Dore 2002).

To our knowledge, no publications in the past five years have calculated the costs of diagnostic tests for the detection of CAD using a microcosting methodology. However, Hernandez & Vale (2007) as well as Sabharwal et al. (2007) have explored the cost effectiveness of different diagnostic strategies based on microcosting estimates that were determined by Underwood et al. (1999) in the United Kingdom. These estimates date back to 1999. Therefore, the primary aim of the present study was to calculate the up-to-date actual costs of four diagnostic tests (exECG, sECHO, SPECT and CA) for the detection of CAD in the Netherlands using a microcosting methodology. As a secondary objective, in order to demonstrate that the use of microcosting estimates instead of reimbursement fees might result in different conclusions regarding the relative cost effectiveness of diagnostic strategies, the cost effectiveness of eight diagnostic strategies (exECG–SPECT–CA, exECG–CA, SPECT–CA, CA, exECG–ECHO–SPECT–CA, exECG–ECHO–CA, sECHO–SPECT–CA and sECHO–CA) was examined, using microcosting and reimbursement fees subsequently as the cost estimate.

8.3 METHODS

The microcosting study

The microcosting study was conducted at three general hospitals in the Netherlands for 2006, from a hospital perspective. Data was collected at the cardiology departments of general hospital 1 (exECG, sECHO and CA), general hospital 2 (exECG and CA) and general hospital 3 (sECHO). The cardiology department of general hospital 1 concerned a university-affiliated teaching department. The cost analysis of SPECT was performed at the nuclear departments of general hospital 1, which was run by radiologists and cardiologists, and general hospital 2, which was run by nuclear specialists. Overall, the general hospitals were representative of the overall setting and treatment patterns in the Netherlands.

Actual costs per diagnostic test were determined by the identification of resource use and unit costs of direct and indirect cost components. Direct cost components involved diagnostic procedures that were performed prior to the diagnostic test (medical imaging services and laboratory services), consumables (medications and disposables), hotel and nutrition and labour. Indirect cost components concerned overheads (general expenses, administration and registration, energy, maintenance, insurance and the personnel costs of non patient services, like management and administration) and capital (depreciation of buildings and inventory and interest).

Total direct costs were determined by multiplying resource use by the corresponding unit prices for 2006. Resource use was collected by means of eight face-to-face interviews, i.e. one interview per hospital department and diagnostic test combination. At each interview, one medical specialist, one laboratory technician and one administrative worker participated. Using standardised reporting templates, the medical specialist, laboratory technician and administrative worker were asked to estimate resource use based on an average patient. Alternative sources were used to gather resource use information on equipment (number of tests per year, purchasing value and maintenance costs), including hospital information systems and manufacturers.

Unit costs of diagnostic procedures and disposables were obtained from (financial) hospital databases. Unit costs of medications were derived from the administration of the hospital pharmacies. Annual costs on hotel and nutrition were taken from the annual accounts 2005 and divided by the annual number of nursing days to calculate unit costs per nursing day. Unit costs of direct labour were based on standardised costs per day or per minute, which equalled the normative income divided by the number of

workable days or minutes per year. Because medical specialists work in independent corporations and are not on the payroll of the hospital, their normative income was based on a national rate that also includes some overhead costs. Normative incomes of other staff categories were based on collective labour agreements.

Annual overhead and capital costs were taken from the annual accounts 2005 and divided by the direct costs, excluding the costs of medical specialist. Thus, indirect costs were appointed to patients using a marginal mark-up percentage.

The cost effectiveness analysis

The cost effectiveness of eight diagnostic strategies was examined, in order to demonstrate that the use of microcosting estimates instead of reimbursement fees might result in different conclusions regarding the relative cost effectiveness of diagnostic strategies. The cost estimate was subsequently based on the actual costs of the diagnostic tests that were obtained from the microcosting study and reimbursement fees that currently apply in the Netherlands (€ 18, € 74, € 335 and € 496 for exECG, sECHO, SPECT and CA respectively).

The following diagnostic strategies were included: exECG–SPECT–CA, exECG–CA, SPECT–CA, CA, exECG–ECHO–SPECT–CA, exECG–ECHO–CA, sECHO–SPECT–CA and sECHO–CA. The decision-tree model that was used to assess the cost effectiveness of these diagnostic strategies was copied from Mowatt et al. (Mowatt, Vale 2004). However, the model was modified to allow for the inclusion of sECHO as a diagnostic test (figure 8.1). The diagnostic strategies were considered as sequences of diagnostic tests rather than individual strategies. A subsequent diagnostic test within a diagnostic strategy was only performed in case of a true-positive or indeterminate diagnostic test outcome. Because CA was believed to be associated with 100% sensitivity and specificity, a false-positive test result was not a possible outcome in the model. For each diagnostic strategy, the model provided information about the number of accurately diagnosed patients (i.e. the number of patients with a true-positive or true-negative test outcome) and the costs per accurately diagnosed patient.

The cost effectiveness of two cohorts of 1,000 hypothetical patients newly presenting with possible CAD was examined, stratified by gender. The age of both cohorts was 60 years with corresponding prevalences of 18.2% and 13.1% for men and women respectively. The sensitivity, specificity, rate of indeterminacy and mortality of all diagnostic tests were taken from literature and summarised in table 8.1 (Mowatt, Vale 2004; Redberg & Shaw 2003).

Figure 8.1: Decision-tree model used for the assessment of the cost-effectiveness of eight diagnostic strategies

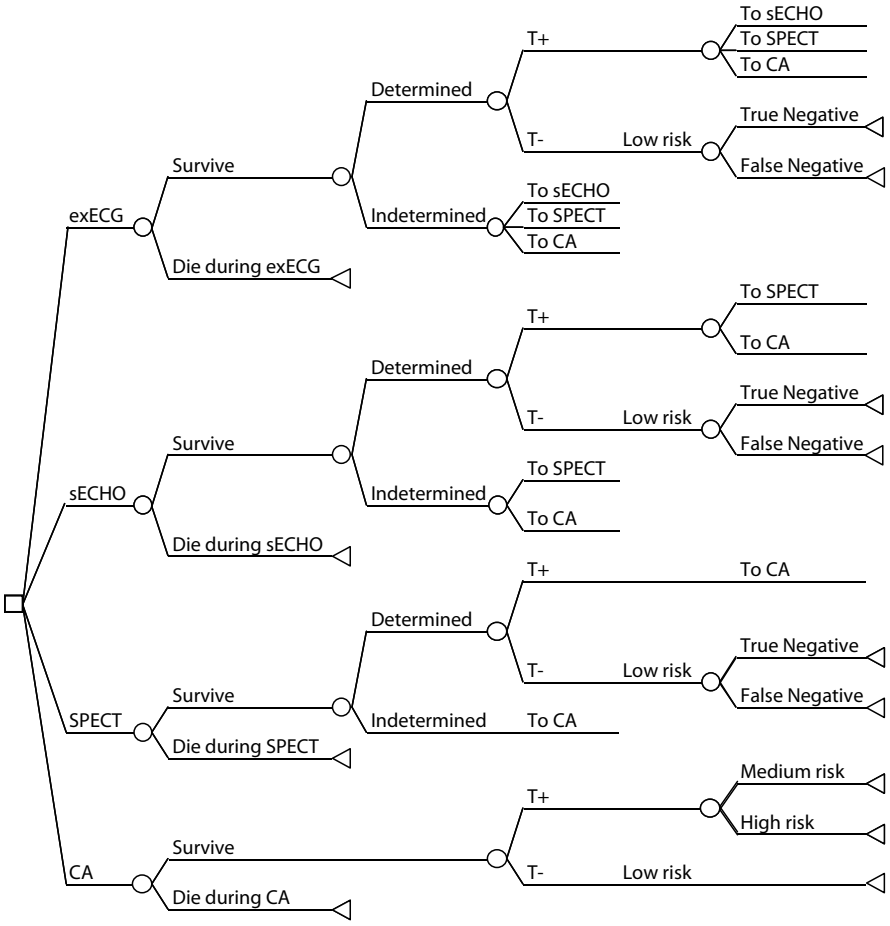

Table 8.1: Model parameters of the decision-tree model regarding diagnostic test performance

	Sensitivity (%)		Specificity (%)			
	Men	Women	Men	Women	**Indeterminacy (%)**	**Mortality (%)**
Exercise ECG	66	67	60	65	18	0
Stress ECHO	78	76	89	86	15	0
SPECT	83	90	59	80	9	0
CA	100	100	100	100	0	0

The sensitivity, specificity, rate of indeterminacy and mortality of exercise ECG and SPECT were determined on the basis of cumulated data from 16 studies assessing patients with a suspicion or a history of CAD, which were identified by Mowatt et al. (2004). The accuracy of stress ECHO was derived from Redberg et al. (2003) who performed a meta-analysis of pharmacological stress testing in men and women of mixed disease severity. CA as the golden standard was set to have 100% accuracy.

Statistical analyses were conducted with the Microsoft Corporation software programme Microsoft Office Excel 2003. All costs were based on Euro 2006 cost data. Where necessary, costs were adjusted to 2006 using the general price index (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

8.4 RESULTS

The microcosting study

An overview of the actual costs per diagnostic test is given in table 8.2. The actual costs of exECG amounted to € 33. A difference between the hospitals was found in the amount of time spent on the patient (5 minutes in general hospital 2 and 15 minutes in general hospital 1). Overall, labour accounted for 51% of the total cost. Other costs comprised indirect cost components (34%) and consumables (15%).

The actual costs of sECHO were € 216 and concerned the weighted average of a sECHO for which activity was induced by performing a bicycle test and a pharmacological sECHO with dobutamine and atropine. The proportion of labour costs varied between 51% in general hospital 1 and 63% in general hospital 3. Two thirds of the labour costs occurred during the examination. About 35% of the total costs consisted of indirect cost components, with an echographic device being responsible for 80% of the capital costs. Consumables constituted 8% of the total cost.

SPECT was performed as an inpatient procedure with an admission of on average 0.5 days. The actual costs added up to € 614. Labour costs accounted for 32% of the total cost. Two thirds of the labour costs occurred during examination. A great share of consumable costs was assigned to radiopharmaca (62%). Costs for indirect cost components and hotel and nutrition were responsible for 45% and 5% of the total costs respectively. Most of the capital costs were attributable to a gamma camera.

CA was performed as an inpatient procedure with an admission of on average one day. The actual costs of CA amounted to € 1.300. A wide difference between hospitals was found in the total costs (€ 932 in general hospital 1 and € 1.667 in general hospital 2), mainly due to the different composition of staff categories and the different application of diagnostic procedures (e.g. X-thorax, blood group AB0, urine screening). Labour accounted for one quarter of the total cost. Other costs consisted of indirect cost components (51%), consumables (14%), hotel and nutrition (7%) and diagnostic procedures (2%). Costs for the contrast agent amounted to € 46 but only represented 4% of the total cost.

Table 8.2: Total costs of the cost components per diagnostic test (Euro 2006)

	Exercise ECG			Stress ECHO			SPECT			CA		
	Mean	**General hospital 1**	**General hospital 2**	**Mean**	**General hospital 1**	**General hospital 3**	**Mean**	**General hospital 1**	**General hospital 2**	**Mean**	**General hospital 1**	**General hospital 2**
Diagnostic procedures												
Medical imaging services	**0**	0	0	**0**	0	0	**0**	0	0	**20**	0	40
Laboratory services	**0**	0	0	**0**	0	0	**0**	0	0	**3**	2	5
Consumables												
Medications	**0**	0	0	**1**	0	2	**87**	83	92	**47**	47	47
Disposables	**5**	7	3	**16**	22	10	**23**	23	23	**141**	147	134
Hotel and nutrition	**0**	0	0	**0**	0	0	**20**	24	16	**40**	48	31
Labour												
Medical specialist	**6**	8	4	**78**	56	100	**75**	25	125	**218**	174	261
Resident	**0**	0	0	**0**	0	0	**0**	0	0	**19**	0	39
Laboratory technician	**8**	11	5	**44**	52	35	**114**	125	103	**41**	49	33
Nurse	**0**	0	0	**0**	0	0	**8**	0	17	**94**	76	113
Administrative worker	**3**	4	2	**3**	4	2	**10**	9	11	**9**	7	11
Indirect cost components												
Overheads	**9**	9	9	**38**	43	33	**189**	134	245	**452**	205	698
Capital	**2**	3	2	**37**	39	34	**88**	96	79	**217**	178	256
TOTAL	**33**	41	25	**216**	216	216	**614**	519	709	**1,300**	932	1667

The cost effectiveness analysis

Table 8.3 and figure 8.2 summarise the costs of the diagnostic strategy, the number of accurately diagnosed patients and the costs per accurately diagnosed patient based on our microcosting estimates. The costs per diagnostic strategy were on average 18% higher in men than in women, but up to 64% higher for exECG-sECHO-SPECT-CA. Diagnostic strategies including sECHO were cheaper than strategies excluding sECHO. The diagnostic strategy that included CA only was the most expensive strategy, being two times more expensive than sECHO-CA and three times more expensive than exECG-sECHO-CA.

The number of accurately diagnosed patients was generally slightly lower in men than in women. Mean numbers at the point of diagnosis ranged from 908 (exECG-sECHO-SPECT-CA) to 971 (SPECT-CA) in men and from 945 (exECG-sECHO-CA) to 988 (SPECT-CA) in women. As expected, the strategy that included CA only, being defined as perfectly sensitive and specific, diagnosed the highest number of patients (998,5 patients with 1,5 patients who died during diagnosis).

Table 8.4 and figure 8.2 present the costs of the diagnostic strategy, the number of accurately diagnosed patients and the costs per accurately diagnosed patient based on reimbursement fees that currently apply in the Netherlands. Using microcosting

Table 8.3: Results from the decision-tree model: costs of the diagnostic strategy, number of accurately diagnosed patients and costs per accurately diagnosed patient ~ based on microcosting estimates

	exECG-SPECT-CA	exECG-CA	SPECT-CA	CA	exECG-sECHO-SPECT-CA	exECG-sECHO-CA	sECHO-SPECT-CA	sECHO-CA
Costs of the diagnostic strategy (Euro 2006)								
Men *(n=1,000)*	763,400	744,147	1,306,353	1,299,980	457,219	421,679	711,578	667,244
Women *(n=1,000)*	597,531	685,094	1,075,991	1,299,980	279,201	382,397	629,361	655,399
Mean	**680,466**	**714,621**	**1,191,172**	**1,299,980**	**368,210**	**402,038**	**670,470**	**661,322**
Number of accurately diagnosed patients								
Men *(n=1,000)*	928	948	971	999	908	924	943	965
Women *(n=1,000)*	955	964	988	999	946	945	963	973
Mean	**942**	**956**	**979**	**999**	**927**	**935**	**953**	**969**
Costs per accurately diagnosed patient (Euro 2006)								
Men	822	785	1,345	1,302	504	456	755	691
Women	625	711	1,090	1,302	295	405	653	674
Mean	**722**	**747**	**1,216**	**1,302**	**397**	**430**	**703**	**682**

Figure 8.2: Average costs per accurately diagnosed patient: the use of microcosting estimates versus reimbursement fees (Euro 2006)

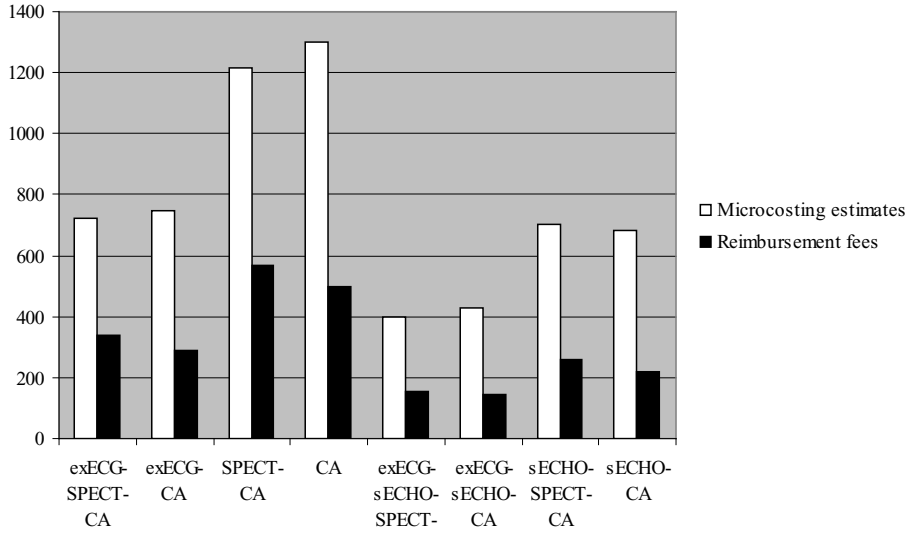

Table 8.4: Results from the decision-tree model: costs of the diagnostic strategy, number of accurately diagnosed patients and costs per accurately diagnosed patient ~ based on reimbursement fees

	exECG-SPECT-CA	**exECG-CA**	**SPECT-CA**	**CA**	**exECG-sECHO-SPECT-CA**	**exECG-sECHO-CA**	**sECHO-SPECT-CA**	**sECHO-CA**
Costs of the diagnostic strategy (Euro 2006)								
Men *(n=1,000)*	351,637	289,200	599,186	496,000	178,030	143,525	265,068	213,177
Women *(n=1,000)*	283,773	266,669	511,293	496,000	110,331	130,418	232,780	208,658
Mean	**317,705**	**277,935**	**555,240**	**496,000**	**144,181**	**136,972**	**248,924**	**210,918**
Number of accurately diagnosed patients								
Men *(n=1,000)*	928	948	971	999	908	924	943	965
Women *(n=1,000)*	955	964	988	999	946	945	963	973
Mean	**942**	**956**	**979**	**999**	**927**	**935**	**953**	**969**
Costs per accurately diagnosed patient (Euro 2006)								
Men	379	305	617	497	196	155	281	221
Women	297	277	518	497	117	138	242	215
Mean	**337**	**291**	**567**	**497**	**156**	**147**	**261**	**218**

estimates, exECG-sECHO-SPECT-CA was the most and CA the least cost effective strategy (€ 397 and € 1.302 per accurately diagnosed patient). Using reimbursement fees, exECG-sECHO-CA was most and SPECT-CA least cost effective (€ 147 and € 567 per accurately diagnosed patient). Overall, diagnostic strategies including sECHO were more cost effective than strategies excluding sECHO.

8.5 DISCUSSION

This is the second microcosting study on the costs of diagnostic tests for the detection of CAD in Europe following the study of Underwood et al. (1999). Even though the distribution of costs by cost component varied, labour and indirect cost components together accounted for over 75% of the total costs of all diagnostic tests. Consumables played a relatively important role in SPECT (14%). Hotel and nutrition only applied to SPECT and CA, as these diagnostic tests were performed as an inpatient procedure with admissions of on average 0.5 and 1.0 days respectively. Diagnostic procedures were solely performed for CA, but their costs were negligible (2%).

Underwood et al. (1999) conducted a microcosting study to determine the costs of diagnostic tests in patients newly presenting with possible CAD in three hospitals from the hospital perspective. The study included 396 patients with a mean age of 57 years (versus 60 years in our study) and with 63% men (versus 50% in our study). Cost components included consumables, labour, some overheads and capital. The costs of exECG, *rest* ECHO, SPECT and CA were calculated to be € 132, € 188, € 413 and € 2.067 respectively (adjusted to 2006; versus € 33, € 216, € 614 and € 1.300 in our study). Furthermore, the costs of four diagnostic strategies (exECG– SPECT –CA, exECG–CA, SPECT –CA, CA) were determined to be € 921, € 768, € 864 and € 2.354 respectively (adjusted to 2006; versus € 680, € 715, € 1.191 and € 1.300 in our study) (Underwood et al. 1999). Because no distribution of costs by cost component was specified, it is unclear which cost components caused the cost differences between the study of Underwood (1999) and our study. However, cost differences may partly be explained by the difference in pre-test likelihood for CAD between the two studies.

Our study confirmed that strategies including sECHO were more cost effective than strategies excluding sECHO. Jeetley et al. (2007) compared the cost effectiveness of sECHO with that of exECG as a first line test in the assessment of patients attending hospital with suspected CAD, non-diagnostic ECG and negative troponin in the United Kingdom. Their study illustrated the superiority of initial sECHO compared to exECG, on the cost side (€ 538 versus € 756) as well as on the effectiveness side (risk stratification, diagnostic

certainty and referrals for further investigation) (Jeetley, Burden 2007). A comparable conclusion was drawn by Tardif et al. (2002), who compared the cost effectiveness of *contrast* sECHO with that of SPECT as a first line test in the treatment of patients with suspected CAD in Canada. sECHO had a similar success rate to SPECT, but had 28% lower costs and had the potential of additional cost savings through the elimination of further diagnostic tests (Tardif, Dore 2002).

Other studies have evaluated the long-term costs (e.g. total disease costs) of different diagnostic strategies (Dewey & Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch, Hayes 2004; Hernandez & Vale 2007; Marwick, Shaw 2003; Sharples, Hughes 2007). These long-term studies reinforced CA to be the most cost effective strategy, particularly in patients that are at high risk of CAD (Dewey & Hamm 2007; Hernandez & Vale 2007). However, there seems to be disagreement on the relative cost effectiveness of the other diagnostic strategies. This disagreement can partly be explained by actual differences between studies, e.g. the pre-test likelihood of the target population, medical practice patterns (e.g. whether the strategy is performed as an outpatient or inpatient procedure and the type of radiopharmaca used) and relative and absolute price differences between countries. However, it is clear that some of the observed differences were more related to methodological differences (e.g. study perspective, outcome measures and time horizons), which complicated the comparison of the relative cost effectiveness found by the studies in a straightforward way.

Our study demonstrated that also the use of different cost methodologies might lead to different conclusions concerning the relative cost effectiveness of alternative strategies. Replacing the microcosting estimates with the reimbursement fees resulted in a worse relative cost effectiveness of SPECT-CA compared to CA and a better relative cost effectiveness of exECG-sECHO-CA compared to exECG-sECHO-SPECT-CA (tables 8.3 and 8.4). Even though the microcosting methodology is believed to provide cost estimates that most accurately reflect actual costs (Drummond, Sculpher 2005), most economic evaluations have used reimbursement fees or general service charges to approximate costs (Dewey & Hamm 2007; Hachamovitch, Berman 2002; Hachamovitch, Hayes 2004; Jeetley, Burden 2007; Marwick, Shaw 2003; Mowatt, Vale 2004; Redberg & Shaw 2003; Sharples, Hughes 2007; Tardif, Dore 2002).

The microcosting methodology is ideally combined with a bottom up approach, in which cost components are valued by identifying resource use directly employed for a patient. This allows for the identification of costs per individual patient and for insight in sub-populations that might have a great share in the total costs. However, bottom up microcosting is often hindered by the absence or inadequacy of hospital information

systems. Therefore, in the present study a top down approach, in which cost components are valued by separating out the relevant costs from comprehensive sources (e.g. annual accounts), was used instead.

Another limitation of our study concerned the inclusion of only a small number of general hospitals, although special attention was paid to selecting representative general hospitals. Nonetheless, there are indications that our study resulted in fairly reliable and accurate estimates. To determine the uncertainty of the obtained microcosting estimates, one-way sensitivity analyses were carried out by varying the resource use and unit cost values of individual cost components between 50% and 150%. The greatest deviation in the total costs was found when treatment time was altered, but the deviation was limited to ± 13-29%. Changing the mark-up percentage for the calculation of the overhead costs resulted in a deviation in the total costs of only ± 9-17%.

A last limitation of our study was the exclusion of costs and effects of CAD that incur during the disease course. There is a consensus amongst health economists that the cost effectiveness of a strategy must include the estimation of costs and effects of the disease diagnosed. However, the aim of our cost effectiveness analysis was to demonstrate that the use of microcosting estimates instead of reimbursement fees might result different conclusions regarding the relative cost effectiveness of diagnostic strategies. An analysis of costs and effects that incur during the disease course would have required a more sophisticated model that would go beyond the scope of the illustrative aim of the cost effectiveness analysis presented.

In conclusion, the actual costs of exECG, sECHO, SPECT and CA were € 33, € 216, € 614 and € 1.300 respectively, with labour and indirect cost components as the most important cost drivers. The incorporation of microcosting estimates may result in different conclusions regarding the cost effectiveness of a diagnostic strategy.

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Chapter 9

A microcosting study of microsurgery, LINAC radiosurgery and gamma knife radiosurgery in meningioma patients

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9.1 ABSTRACT

Background: The aim of the present study was to determine and compare initial treatment costs of microsurgery, LINAC radiosurgery and gamma knife radiosurgery in meningioma patients. Additionally, the follow up costs in the first year after initial treatment were assessed. **Materials and methods**: Cost analyses were performed at two neurosurgical departments in the Netherlands from the healthcare providers' perspective. A total of 59 patients were included, of which 18 microsurgery patients, 15 LINAC radiosurgery patients and 26 gamma knife radiosurgery patients. A standardised microcosting methodology was employed to ensure that the identified cost differences would reflect only actual cost differences. **Results**: Initial treatment costs, using equipment costs per fraction, were € 12,288 for microsurgery, € 1,547 for LINAC and € 2,412 for gamma knife radiosurgery. Higher initial treatment costs for microsurgery were predominantly due to inpatient stay (€ 5,321) and indirect costs (€ 4,350). Follow up costs were slightly, but not significantly, higher for microsurgery compared to LINAC and gamma knife radiosurgery. Annual total costs using equipment costs per fraction, amounted to € 14,329 for microsurgery, € 3,060 for LINAC and € 3,966 for gamma knife radiosurgery. LINAC and gamma knife radiosurgery were equally expensive when equipment was valued per treatment (€ 2,198 and € 2,412 respectively). **Conclusions**: Even though initial treatment costs were a manifold higher for microsurgery compared to both radiosurgical treatments, our study gives indications that the relative cost difference may decrease when follow up costs occurring during the first year after initial treatment are incorporated. This reinforces the need to consider follow up costs after initial treatment when examining the relative costs of alternative treatments.

Keywords: Microcosting – Meningioma – Radiosurgery – Cost comparison – Microsurgery

9.2 INTRODUCTION

Meningiomas are common tumors of the central nervous system that originate from the meningeal coverings of the spinal cord and the brain, and account for up to 30% of all primary brain tumors (Riemenschneider et al. 2006). Intracranial meningiomas are most commonly reported in adults in their fourth through sixth decades of life and are more common in women with a female preponderance of about 2:1 (Rockhill et al. 2007). The incidence of meningiomas is climbing and may indicate more sensitive diagnostic modalities or increased exposure to environmental risk factors (Campbell et al. 2009). Meningiomas are generally slow-growing and benign tumors with a broad spectrum of clinical characteristics. According to the World Health Organisation (WHO) classification, the most commonly used grading system for meningiomas, there are three malignancy grades: benign (WHO grade I), atypical (WHO grade II) and anaplastic or malignant (WHO grade III) (Louis et al. 2007).

The gold standard procedure for the treatment of meningioma is microsurgery. Even though advances in microsurgical approaches have greatly improved patient outcomes for meningioma once thought to be unresectable, long term cure remains a desirable but elusive goal (D'Ambrosio & Bruce 2003). Besides, microsurgery is costly, because it concerns a labour intensive inpatient procedure (Banerjee et al. 2008; Bennett et al. 2007; Wellis et al. 2003). Therefore, stereotactic radiosurgery, the delivery of a high single dose of radiation to a discrete tumor volume, is increasingly accepted as an alternative to conventional microsurgery in selected patients (Elia et al. 2007; Wellis, Nagel 2003).

Radiosurgery, either with linear accelerator (LINAC) or gamma knife, is able to target surgically inaccessible or difficult lesions and has a decreased risk of complications related to surgery and anaesthesia (Bennett, Tigue 2007; D'Ambrosio & Bruce 2003; Griffiths et al. 2007; Yano & Kuratsu 2006). Radiosurgical patients may experience a higher quality of life than microsurgical patients, especially in the short term, because radiosurgery concerns a minimally invasive outpatient procedure (Banerjee, Moriarty 2008; Cho et al. 2006; Myrseth et al. 2005). Advantages of LINAC radiosurgery include the relatively low costs and high accessibility. Gamma knife radiosurgery has been suggested to be more accurate, but its costs are higher and accessibility lower than LINAC radiosurgery, particularly due to its high equipment costs (Griffiths, Marinovich 2007; Perks et al. 2003).

Only few studies have earlier compared the treatment costs of alternative treatments in intracranial tumor patients, such as acoustic neuromas and vestibular schwannomas, but most of them are outdated (Mehta et al. 1997; Ott 1996; Porter et al. 1997; Rutigliano et al. 1995; van Roijen et al. 1997). Of the studies performed in the past 5 years, three com-

pared microsurgery with gamma knife radiosurgery (Banerjee, Moriarty 2008; Cho, Tsao 2006; Wellis, Nagel 2003). Another study made a cost comparison between LINAC and gamma knife radiosurgery (Griffiths, Marinovich 2007). However, these studies neither compared the initial treatment costs of microsurgery, LINAC radiosurgery and gamma knife radiosurgery, nor compared alternative treatments in meningioma. Therefore, the aim of the present study was to calculate initial treatment costs of microsurgery, LINAC radiosurgery and gamma knife radiosurgery in meningioma patients from a healthcare providers' perspective. Because the microcosting methodology identifies all relevant cost components at the most detailed level (Drummond et al. 2005), it was used to provide cost estimations that most accurately reflect actual costs.

The healthcare providers' perspective also includes follow up costs which occur after initial treatment. Ignoring these follow up costs could result in unjust conclusions regarding the relative costs of alternative treatments (Banerjee, Moriarty 2008; Drummond 2005). Therefore, this study additionally aims to calculate the follow up costs in the first year after initial treatment with microsurgery, LINAC radiosurgery and gamma knife radiosurgery.

9.3 METHODS

To be able to make a truthful comparison between microsurgery, LINAC and gamma knife radiosurgery patients, only patients with a radiologically confirmed benign (WHO grade I) meningioma with diameter ≤ 3.0 cm were recruited. Atypical (WHO grade II) and anaplastic or malignant (WHO grade III) patients, patients with meningioma diameter > 3.0 cm, patients receiving fractionated radiotherapy and patients of whom follow up cost data was unavailable were excluded from this study. Recruitment took place at the department of neurosurgery of the Erasmus MC University Medical Center in Rotterdam (microsurgery and LINAC radiosurgery) and at the department of neurosurgery of the St. Elisabeth hospital in Tilburg (gamma knife radiosurgery). Enrolment took place retrospectively in September 2008. All costs were based on Euro 2007 cost data. Where necessary, costs were adjusted to 2007 using the general price index from the Dutch Central Bureau of Statistics (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

The microcosting study

Initial treatment costs of microsurgery, LINAC and gamma knife radiosurgery were based on a detailed microcosting study, in which resource use and unit costs of direct and

indirect cost components were identified. Direct cost components involved diagnostic procedures (medical imaging and laboratory services), consumables (medications and disposables), inpatient stay (at the normal ward and intensive care unit), labour (including neurosurgeons, anaesthesiologists, radiation oncologists, residents, physicists, radiation technicians, operation assistants and nurses) and equipment. Indirect cost components concerned overheads (general expenses, administration and registration, energy, maintenance, insurance and the personnel costs of non patient services, like management and administration) and capital (depreciation of buildings and inventory and interest).

Resource use of diagnostic procedures, consumables, inpatient stay and equipment (number of treatments per year) was available per individual patient and were acquired from hospital information systems (bottom up microcosting). Resource use of labour was collected by means of two face-to-face interviews, i.e. one interview per hospital department (top down microcosting). Using standardised reporting templates, two medical specialists per hospital department were asked to estimate resource use of labour of an average meningioma patient matching the inclusion criteria.

Resource use of medical imaging services was valued using the fees as issued by the Dutch Healthcare Authority. Unit costs of laboratory services and medications were taken from (financial) hospital databases. Annual costs of disposables were obtained from hospital information systems and divided by the annual number of inpatient days to calculate unit costs per inpatient day. Resource use of inpatient stay was valued using reference unit prices (Oostenbrink et al. 2004). Unit costs of labour were based on standardised costs per minute, which equalled the normative income divided by the number of workable minutes per year. Normative incomes were based on collective labour agreements. Unit costs of health care utilisation are presented in table 9.1.

Equipment was valued using replacement and maintenance costs with a discount rate of 4% and an anticipated life expectancy of 10 years. The LINAC considered in our study was used for fractionated (multiple fraction) as well as stereotactic (single fraction) treatments where the gamma knife only performed stereotactic treatments. To be able to determine the influence of alternative calculation methods, equipment costs were determined both per fraction and per treatment. As patients receiving fractionated treatments were excluded from this study, the alternative calculation methods were expected to have a substantial impact on the results.

Annual overhead and capital costs were taken from the annual accounts 2006 and divided by direct costs. Thus, indirect costs were appointed to patients using a marginal mark-up percentage.

Table 9.1: Unit costs of health care utilisation ~ initial treatment (Euro 2007)

Medical imaging services (a)	
Computed tomography	207.50
Magnetic resonance imaging	269.90
Inpatient stay (b)	
Inpatient hospital day	386.28
Labour (per minute) (c)	
Medical specialist	1.46
Resident	0.56
Laboratory technician	0.56
OP-assistant	0.50
Nurse	0.43
Equipment (replacement costs) (d)	
Gamma knife	3,000,000.00
LINAC	2,500,000.00

Source:
(a) Dutch Healthcare Authority
(b) Oostenbrink, 2004
(c) Collective labour agreements
(d) (financial) Hospital databases

Follow up costs

Follow up costs included visits to healthcare providers (including the general practitioner, medical specialist, physiotherapist, social worker and company physician), medical imaging services, inpatient stay, medications and medical aids (such as wheelchairs, rolling walkers and walking-canes). Follow up costs involved all resource use occurring during the first year after treatment, including resource use which was unrelated to the meningioma treatment.

Resource use of medical imaging services was based on an established protocol, prescribing one magnetic resonance imaging (MRI) at 13 weeks and one at 52 weeks after initial treatment. Other resource use was obtained from standardised questionnaires which were sent to the home addresses of the recruited patients 4, 26 or 52 weeks after initial treatment. The recall period was 4 weeks. Annual follow up resource use and costs were determined by adding up the values per recall period. The values for the

time between the measurement periods (week 5-22 and week 27–48) were established through linear interpolation. However, resource use of medications was not linearly interpolated when interpolation would lead to unrealistic regimens. For example, patients may receive flucloxacillin during the 4 week recall period. As flucloxacillin is generally given during a course of 5-10 days, its costs would be included in the calculations, but not linearly interpolated.

Resource use of visits to healthcare providers and inpatient stay was valued using reference unit prices (Oostenbrink, Bouwmans 2004). Resource use of medical imaging services was valued using the fees as issued by the Dutch Healthcare Authority. Wholesale prices were used to value resource use of medications and medical aids. Because patients were asked whether they made use of medical aids at every measurement moment, we assumed a once only purchase with a life expectancy of 5 years. Unit costs of health care utilisation are presented in table 9.2.

Table 9.2: Unit costs of health care utilisation ~ follow up (Euro 2007)

General practitioner (one visit)	21.35
Medical specialist (one visit)	59.20
Physiotherapist (one visit)	24.05
Social worker (one visit)	24.05
Company physician (one visit)	59.20
Magnetic resonance imaging	269.90
Inpatient hospital day	386.28
Walking-cane	10.00
Rolling walkers	125.00
Wheelchair	200.00
Daisy player	400.00

Source: Oostenbrink, 2004

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 15.0. In addition to descriptive statistics, differences between the treatment groups and between follow up scores were assessed by means of the one-way analysis of variance (ANOVA) test for variables showing a normal distribution, the Kruskal-Wallis and Mann Whitney U tests for variables not normally distributed and Pearson Chi-square test for variable fractions. To adjust for multiple testing, one way analyses of variance with post hoc testing (type Bonferroni) were additionally performed.

9.4 RESULTS

A total of 143 benign meningioma patients were treated at our two hospital sites between August 2007 and August 2008. These included 5 atypical (WHO grade II) patients, 31 patients with meningioma diameter > 3.0 cm, 34 patients receiving fractionated radiotherapy and 14 patients whose follow up cost data were unavailable. Thus, a total of 59 patients were recruited, of which 18 microsurgery patients, 15 LINAC radiosurgery patients and 26 gamma knife radiosurgery patients. Table 9.3 presents the general characteristics at baseline of the patients. The tumor volume of microsurgery patients was significantly higher than that of LINAC and gamma knife radiosurgery patients (ANOVA test: $P < 0.001$). Besides, LINAC radiosurgery patients reported a lower current health state (measured on a visual analog scale, 0 being worst imaginable health and 100 being best imaginable health) compared with microsurgery and gamma knife radiosurgery patients. No significant differences between the treatment groups were observed in any of the other general characteristics.

In the remainder of this chapter, values for the LINAC group are provided using equipment costs per fraction (with values using equipment costs per treatment between brackets).

The microcosting study

An overview of initial treatment costs per group, using equipment costs per fraction, is given in table 9.4. Initial treatment costs were € 12,288 for microsurgery, € 1,547 (€ 2,198) for LINAC and € 2,412 for gamma knife radiosurgery. The higher costs for microsurgery were predominantly due to inpatient stay (€ 5,321) and indirect costs (€ 4,350).

The share of inpatient stay in total treatment costs accounted for 43% in microsurgery, 25% (18%) in LINAC and 16% gamma knife radiosurgery. Microsurgery patients were admitted for an average of 11.3 (SD 5.8) inpatient days. Sixty-one % of the microsurgery patients were admitted to the intensive care unit for an average of 1.0 day. LINAC and Gamma knife radiosurgery concerned outpatient procedures. Therefore, costs for inpatient stay were over ten times higher in microsurgery than in the other two groups (€ 5,321 versus € 386). A substantial cost variation was found in inpatient stay costs obtained for individual microsurgery patients (range: € 2,318 to € 11,201).

The proportion of labour in total treatment costs was responsible for 15%, 14% (10%) and 10% for microsurgery, LINAC and gamma knife radiosurgery. Labour was also a manifold more expensive in microsurgery compared with the other two groups (€ 1,901 compared to € 211 and € 246). This was reflected by resource use of medical specialists,

Table 9.3: General characteristics of the patients at baseline

		Microsurgery	LINAC radiosurgery	Gamma Knife radiosurgery
n		18	15	26
Age	<31 years	0%	7%	0%
	31-50 years	44%	20%	35%
	51-70 years	44%	67%	42%
	>70 years	11%	7%	23%
Sex	Males	16.7%	26.7%	11.5%
	Females	83.3%	73.3%	88.5%
Current health state *		75.0 (SD 5.8)	66.7 (SD 15.3)	80.0 (SD 11.1)
Location of meningioma	Parasagittal	11%	33%	0%
	Convexity	11%	33%	15%
	Tuberculum sellae	28%	0%	0%
	Sphenoid ridge	22%	0%	0%
	Olfactory groove	11%	13%	0%
	Falcine, tentorial and petroclival	17%	20%	42%
	Cavernous sinus	0%	0%	15%
	Cerebellopontine angle	0%	0%	27%
Tumour volume	<5 cm^3	6%	60%	46%
	6-10 cm^3	6%	33%	42%
	11-15 cm^3	35%	7%	8%
	16-20 cm^3	24%	0%	0%
	21-25 cm^3	6%	0%	4%
	26-30 cm^3	18%	0%	0%
	31-35 cm^3	6%	0%	0%
Initial treatment duration	minutes	348 (SD 115)	20 (SD **)	60 (SD 26)
Inpatient hospital days	days	11.3 (SD 5.8)	1.0 (SD **)	1.0 (SD **)

SD = standard deviation

* self-reported by the patients, measured on a visual analog scale with scores ranging from 0 (worst imaginable health) to 100 (best imaginable health)

** not available

Table 9.4: Initial treatment costs of microsurgery, LINAC radiosurgery and gamma knife radiosurgery (using equipment costs per fraction) (Euro 2007)

	Microsurgery (n=18)	LINAC radiosurgery (n=15)	Gamma Knife radiosurgery (n=26)
Diagnostic procedures			
Medical imaging services	289	351	280
Laboratory services	231	0	0
Consumables			
Medications	134	1	5
Disposables	62	18	18
Inpatient stay			
Normal ward	4,142	386	386
Intensive care unit	1,180	0	0
Labour			
Medical specialist	888	102	146
Resident	328	0	0
Physicist	0	8	11
Radiation technician	0	101	90
OP-assistant	297	0	0
Nurse	388	0	0
Equipment	0	50	963
Overheads and capital	4,350	530	513
Initial treatment costs	**12,288**	**1,547**	**2,412**

which amounted to 610 minutes in microsurgery (neurosurgeons and anaesthesiologists), 70 minutes in LINAC and to 100 minutes in gamma knife radiosurgery (neurosurgeons and radiation oncologists). Besides, the microsurgical treatment required the involvement of residents (580 minutes), operation assistants (600 minutes) and nurses (900 minutes), where the radiosurgical treatments only required radiation technicians (180 minutes for LINAC and 161 minutes for gamma knife radiosurgery) and physicists (11 minutes for LINAC and 15 minutes for gamma knife radiosurgery).

Accounting for 40% of total treatment costs, equipment was a relatively important cost driver in gamma knife radiosurgery. The replacement cost of the gamma knife (€ 3,000,000) resulted in an annuity of € 369,873. With maintenance costs of € 160,000 per year and an average of 550 fractions or treatments per year, equipment costs per fraction or treatment were estimated to be € 963. Similar calculations for the LINAC resulted in equipment costs of € 50 per fraction and of € 701 per treatment.

The share of diagnostic procedures in initial treatment costs ranged from 4% in microsurgery to 23% (16%) in LINAC radiosurgery. However, absolute costs of medical imaging services were comparable between treatment groups. At least one MRI or computed tomography was performed for each individual patient. Laboratory services were only carried out in microsurgery patients (€ 231; SD 139).

Costs for consumables accounted for less than 2% of initial treatment costs in all treatment groups. Fenytoinenatrium and nadroparin were among the most cost substantial medications administered in microsurgery and lidocaine and alfentanil in gamma knife radiosurgery patients. Another cost substantial medication was dexamethason, which was administered in all groups on indication.

The proportion of overheads and capital represented 35%, 34% (24%) and 21% of initial treatment costs in the three treatment groups

Follow up costs

A questionnaire was completed by each of the recruited patients. For the microsurgery group, 22% (4/28) of the questionnaires were returned at 4 weeks, 44% (8/18) at 26 weeks and 34% (6/18) at 52 weeks after treatment. These percentages amounted to 20% (3/15), 40% (6/15) and 40% (6/15) for the LINAC radiosurgery and to 42% (11/26), 31% (8/26) and 27% (7/26) for the gamma knife radiosurgery group.

The fractions of patients visiting any medical specialist were 61% for microsurgery, 20% for LINAC and 38% for gamma knife radiosurgery (Pearson Chi-square test: $P = 0.054$). For patients visiting the medical specialist, the annual number of visits amounted to 3, 6 and 4 respectively (ANOVA test: $P = 0.565$).

The fractions of patients visiting the physiotherapist were 28% for microsurgery, 40% for LINAC and 19% for gamma knife radiosurgery (Pearson Chi-square test: $P = 0.366$). Two LINAC radiosurgery patients, with a relatively low current health state at baseline, each received 8 physiotherapist visits during the 4 week recall period. These visits were included in the calculations, but not linearly interpolated. As a result, the annual number of physiotherapist visits for patients visiting the physiotherapist amounted to 9 for microsurgery, 6 (instead of 10) for LINAC and 6 for gamma knife radiosurgery (ANOVA test: $P = 0.848$).

Statistical differences were neither found in the fractions of patients visiting the general practitioner, social worker and company physician, nor in the corresponding numbers of visits per year. Resource use of medical imaging was identical in the three groups

according to the established protocol. None of the patients was admitted for inpatient stay. Medications were used by about 72% of the patients in microsurgery and 73% and 65% in LINAC and gamma knife radiosurgery respectively. In each treatment group, about 1 out of 6 patients made use of a medical aid. A summary of follow up costs (4 weeks per measurement moment) is given in table 9.5.

Table 9.5: Follow up costs (4 weeks per measurement moment) (Euro 2007) (median)

	Microsurgery			**LINAC radiosurgery**			**Gamma Knife radiosurgery**		
	4 weeks	26 weeks	52 weeks	4 weeks	26 weeks	52 weeks	4 weeks	26 weeks	52 weeks
	(n=4)	(n=8)	(n=6)	(n=3)	(n=6)	(n=6)	(n=11)	(n=8)	(n=7)
General practitioner	5 (0)	19 (21)	25 (0)	7 (0)	11 (0)	0 (0)	6 (0)	21 (21)	3 (0)
Medical specialist	44 (59)	67 (59)	20 (0)	99 (59)	0 (0)	30 (0)	27 (0)	30 (30)	34 (0)
Physiotherapist	0 (0)	20 (0)	36 (36)	16 (0)	14 (12)	20 (0)	9 (0)	8 (0)	0 (0)
Social worker	0 (0)	0 (0)	4 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0)	0 (0)
Company physician	15 (0)	15 (0)	10 (0)	39 (0)	10 (0)	0 (0)	22 (0)	7 (0)	0 (0)
Medical imaging services	0 (0)	49 (49)	42 (42)	0 (0)	49 (49)	42 (42)	0 (0)	49 (49)	42 (42)
Inpatient stay	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Medications	16 (13)	19 (5)	5 (3)	35 (52)	18 (13)	24 (15)	10 (4)	14 (4)	13 (1)
Medical aids	1 (0)	1 (0)	0 (0)	0 (0)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)
Total	82 (73)	189 (183)	141 (123)	197 (192)	212 (175)	134 (114)	74 (24)	161 (132)	92 (101)
SD	29	64	101	38	175	81	86	105	45
25 percentile	59	131	45	162	53	62	22	68	42
75 percentile	112	261	238	*	368	221	127	231	130

SD = standard deviation

* = not available

Annual follow up costs for treatment related and unrelated resource use consumption were € 2,041 for microsurgery, € 1,514 for LINAC radiosurgery and € 1,553 for gamma knife radiosurgery (Kruskal-Wallis test: $P = 0.120$).

Annual total costs are presented in table 9.6 and amounted to € 14,329 for microsurgery, € 3,060 (€ 3,711) for LINAC and € 3,966 for gamma knife radiosurgery (Kruskal-Wallis test: $P < 0.001$). When multiple testing was not taken into account, the annual total costs of LINAC and gamma knife radiosurgery were not significantly different (Mann Whitney U test: $P = 0.096$). Using one way analyses of variance with post hoc testing, the latter *P*-value was no longer significant ($P = 0.006$)

Table 9.6: Annual total costs of microsurgery, LINAC radiosurgery and gamma knife radiosurgery (using equipment costs per fraction) (Euro 2007)

	Microsurgery	LINAC radiosurgery	Gamma Knife radiosurgery	Kruskal-Wallis Asymp. Sig.
Initial treatment costs	12,288	1,547	2,412	
Relative to microsurgery	*100*	*13*	*20*	
Follow up costs	2,041	1,514	1,553	0.120
General practitioner	270	66	143	0.212
Medical specialist	539	291	410	0.072
Physiotherapist	344	222	207	0.429
Social worker	26	0	17	0.675
Company physician	160	94	62	0.826
Medical imaging services	540	540	540	0.331
Inpatient stay	0	0	0	1.000
Medications	156	290	172	0.308
Medical aids	6	11	3	0.582
Relative to microsurgery	*100*	*74*	*76*	
Total costs	14,329	3,060	3,966	0.000
Relative to microsurgery	*100*	*21*	*28*	

Asymp. Sig. = asymptomatic significance

9.5 DISCUSSION

This study is the first to compare total costs of alternative procedures in the treatment of meningioma patients. With initial treatment cost of € 12,288, microsurgery was the most expensive treatment option. Most important cost drivers were inpatient stay (43%), indirect costs (35%) and labour (15%). This finding is in agreement with the study of Wellis et al. (2003), who found initial treatment costs of microsurgery in patients harbouring an arteriovenous malformation, acoustic neuromas, meningiomas or brain metastasis potentially amenable to radiosurgery (diameter < 0.3 cm) to be € 12,979 in Germany (adjusted to 2007). Inpatient stay, indirect costs and labour accounted for 33%, 39% and 13% of initial treatment costs in their study respectively (Wellis, Nagel 2003). Banerjee et al. (2008) determined initial treatment costs for vestibular schwannoma patients in the United States (diameter > 3.0 cm) at € 22,332. However, they used general service charges rather than actual costs which may make comparison misleading (Banerjee, Moriarty 2008). The study of Cho et al. (2006) found treatment costs for intracranial base tumors (diameter < 3.0 cm) to be € 4,628 (adjusted to 2007) in Taiwan (Cho, Tsao 2006).

The two alternative methods for the calculation of equipment costs have proven to substantially impact our results. Initial treatment costs for gamma knife radiosurgery were € 866 more expensive using equipment costs per fraction and € 262 more expensive using equipment costs per treatment compared with LINAC radiosurgery. Even though the replacement values of the LINAC and gamma knife are of the same magnitude (€ 2,500,000 versus € 3,000,000; table 9.2), the average number of LINAC procedures per year was about 9,200 compared to 550 for the gamma knife. The results of our cost analysis suggest that LINAC and gamma knife radiosurgery are equally expensive when equipment is valued per treatment. This finding confirms the results of Griffiths et al. (2007) who compared the equipment costs of the LINAC and gamma knife in Australia. Griffiths et al. (2007) estimated gamma knife radiosurgery to cost up to € 1,057 more per fraction and to € 132 more per treatment over LINAC radiosurgery (adjusted to 2007).

Our results further imply that follow up costs in the first year after initial treatment affected the relative costs of the alternative treatment options. Initial treatment costs for microsurgery, LINAC and gamma knife radiosurgery equalled the relative ratio 100:13(18):20. However, the relative ratio decreased to 100:21(26):28 when follow up costs were included (table 9.6). The latter finding is not in agreement with the results of Banerjee et al. (2008). With follow up costs in the first year after initial treatment of approximately € 5,200 for microsurgery patients and € 900 for gamma knife radiosurgery patients (adjusted to 2007), they observed an increased relative ratio when follow up costs were added (Banerjee, Moriarty 2008). Because Banerjee et al. (2008) did not report resource use of individual cost components, it is unclear which factors have caused their different conclusion.

One limitation of our study was the inclusion of resource use which was unrelated to the meningioma treatment in the follow up costs. As LINAC radiosurgery patients reported a lower current health state compared with patients in the other two treatment groups, follow up costs of LINAC radiosurgery patients may have relatively overestimated costs occurring if only resource use related to the meningioma treatment would have been considered. For example, 73% of the medication costs were not related or possibly but not definitely related to the meningioma treatment for the LINAC radiosurgery group. These percentages amounted to 67% in the microsurgery group and 68% in the gamma knife radiosurgery group. Medications directly related to the meningioma treatment involved dexamethason (often in combination with a proton pump inhibitor or histamine H2-receptor antagonist) and anticonvulsants. Costs for medical aids were exclusively related to the meningioma treatment for all three patient groups. Unfortunately it was not possible to assess the differences between resource use related and resource use

unrelated to the meningioma treatment for the other cost components (visits to health-care providers, medical imaging services and inpatient stay).

Our inclusion criteria restricted the recruitment of a greater amount of patients. To be able to make a truthful comparison with gamma knife patients, only patients with a radiologically confirmed benign (WHO grade I) meningioma patients with meningioma diameter ≤ 3.0 cm were recruited. However, at the Erasmus MC University Medical Center, microsurgery and LINAC radiosurgery were not commonly performed in meningioma with diameter ≤ 3.0 cm. Besides, microsurgery was unlikely to be applicable in meningiomas which were difficult or precarious to access.

Consequently, our study included only a small sample of patients, especially for the calculation of follow up costs in which the microcosting patient samples were further divided into three subgroups to be able to detect follow up costs at 4, 26 and 52 weeks. In addition, follow up costs for the time between the measurement periods (week 5-22 and week 27–48) were established through linear interpolation which may have affected the results. Our results may therefore not be representative for the clinical treatment patterns in the Netherlands. However, costing studies which assess follow up costs are scarce and thus we believe that our study provides valuable insight in the relative costs of alternative procedures for the treatment of meningioma.

Meningioma may be treated with procedures other than microsurgery, LINAC and gamma knife radiosurgery. Yano et al. (2006) suggested that a conservative treatment with close monitoring may be the best therapeutic strategy in asymptomatic meningioma patients to avoid surgery-related incidences of morbidity (Yano & Kuratsu 2006). Furthermore, a combination therapy of microsurgery and radiosurgery may be beneficial (Bennett, Tigue 2007; Black et al. 2001). When meningioma does not respond favourably to microsurgery and / or radiosurgery, alternative procedures may include chemotherapy, immunotherapy, hormone therapy, gene therapy and / or toxins (D'Ambrosio & Bruce 2003). However, cost information on these treatment options is not yet available.

Earlier studies of others suggested radiosurgery to be more cost effective than microsurgery (Banerjee, Moriarty 2008; Cho, Tsao 2006; Myrseth, Moller 2005). Rutigliano et al. (1995) concluded that radiosurgery resulted in favourable costs per life year compared with surgical resection in solitary metastatic brain tumors. Myrseth et al. (2005) observed significantly favourable post treatment facial nerve function, hearing, complication rates and quality of life for gamma knife radiosurgery over microsurgery in unilateral vestibular schwannoma patients. However, our study did not weigh the costs of meningioma treatment against outcome measures, which prevented us from drawing conclusions

regarding the relative cost effectiveness of the three investigated treatments. To be able to better assist clinical decision making for meningioma patients, future studies should determine the cost effectiveness of microsurgery, LINAC and gamma knife radiosurgery by including clinical outcome measures and quality of life.

Furthermore, future studies should consider productivity costs due to absence from work and reduced efficiency at paid and unpaid work. As our study was conducted from the healthcare providers' perspective, it disregarded productivity costs. However, as radiotherapy is a minimally invasive outpatient procedure, a productivity cost reduction over microsurgery may be expected. Therefore, productivity costs could significantly affect the cost effectiveness of microsurgery, LINAC and gamma knife radiosurgery in meningioma patients (Cho, Tsao 2006; Drummond 2005; Wellis, Nagel 2003).

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Chapter 10

Real-world costs of adjuvant treatment for stage III colon cancer patients in the Netherlands

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10.1 ABSTRACT

This study aimed to examine the costs of adjuvant treatment in stage III colon cancer based on real-world resource use. Data were gathered from a representative patient sample in the Netherlands (n=206). Mean costs per patient amounted to € 9,029 for 5-FU/LV, € 9,909 for capecitabine, € 32,634 for 5-FU/LV with oxaliplatin and € 23,468 for capecitabine with oxaliplatin. The administration of chemotherapy (including inpatient hospital days, daycare treatments, outpatient visits and chemotherapy) was the most important cost driver. Lower treatment costs for capecitabine with oxaliplatin compared to 5-FU/LV with oxaliplatin may in part relieve the economic burden of stage III colon cancer in the future.

Keywords: Stage III colon cancer – Cost analysis – Real-world resource use – Oxaliplatin – Capecitabine – Economic burden

10.2 INTRODUCTION

Colorectal cancer is one of the most prevalent malignancies in the Western world. In the Netherlands, about 10,000 patients per year are newly diagnosed with colorectal cancer. With 14% of tumors, the incidence of colon cancer ranks third for men, after prostate cancer (21%) and lung cancer (16%). For women colorectal cancer has the second highest incidence (13%) after breast cancer (33%) (Lemmens & Coebergh 2006; Poos et al. 2005). In 2005, costs of colorectal cancer in the Netherlands were estimated at € 273.3 million, which equals 10% of the total health expenditures of cancers and 0.4% of total health expenditures (Poos, Smit 2005). Annual costs of colorectal cancer are expected to rise as the number of patients diagnosed with colorectal cancer is expected to increase to about 14,000 by the year 2015, owing to an increasing incidence (especially for men) as well as to the growth and ageing of the population (Lemmens & Coebergh 2006).

For colon cancer, surgery to remove the primary tumor is the principal first-line treatment for about 80% of patients, after which almost half will eventually develop local or distant recurrence (Cassidy et al. 2006; Krol et al. 2007; Young & Rea 2000). The benefit of chemotherapy has been clearly demonstrated in patients with stage III colon cancer. Therefore, the use of adjuvant chemotherapy following surgery has become the standard therapy in stage III colon cancer (Eggington et al. 2006; Pandor et al. 2006). For many years, treatment with 5-fluorouracil and leucovorin (5-FU/LV) was the only effective treatment available. However, during the past decade, new drugs, such as capecitabine, have demonstrated at least equivalent clinical benefit (Cassidy, Douillard 2006; Reddy 2004; Twelves 2006). Some new drugs, such as oxaliplatin, have even proven to significantly improve survival (Andre et al. 2004; Kuebler et al. 2007).

As of 2005, national guidelines in the Netherlands recommend the use of 5-FU/LV in combination with oxaliplatin as the primary treatment option for stage III colon cancer. Capecitabine is the preferred treatment option when oxaliplatin is not indicated (Committee Pharmacotherapeutical Aid (CFH) & Health Care Insurance Board (CVZ) 2009; Punt et al. 2005). The Dutch Association for Medical Oncology (NVMO) further supports the use of capecitabine in combination with oxaliplatin, as this treatment option has proven to be beneficial in stage IV colon cancer (Punt, Richel 2005).

In general, the diversity of treatment agents and regimens applied in daily practice results in a wide cost variation between patients (Ferro et al. 2008). Especially new expensive drugs, such as oxaliplatin, have placed a serious economic burden on the healthcare system, not only because of higher costs per drug but also because of their expanded use (Ferro, Myer 2008; Krol, Koopman 2007). Previous studies examining the

costs of stage III colon cancer treatment based their cost assessment on resource use obtained from published data, expert opinion, randomised controlled trials (RCTs) or a combination of these (among others: (Aballea et al. 2007; Aballea et al. 2007; Cassidy, Douillard 2006; Di Costanzo et al. 2008; Douillard et al. 2007; Eggington, Tappenden 2006; Gorner & Riemer-Hommel 2008; Maniadakis et al. 2009; Pandor, Eggington 2006; Twelves 2006)). However, the potentially limited generalisability of RCT-based economic evaluations may seriously restrict their relevance to policy-making. This could result in a greater focus on real-world pharmacoeconomics which allows for the evaluation of treatment outcomes in daily clinical practice. The primary aim of the present study was to examine the costs of stage III colon cancer treatment based on real-world resource use. In addition, the economic burden of stage III colon cancer patients in the Netherlands was determined.

10.3 METHODS

This retrospective cost analysis was performed in conjunction with a population-based clinical outcomes study, which aimed to provide insight in the use of oxaliplatin in daily clinical practice. Details of the study design of this clinical outcomes study will be published in a forthcoming publication. In short, all patients newly diagnosed with stage III colon cancer (pTanyN1,2M0, ICD-O C18-C19.9) who received adjuvant chemotherapy in the Netherlands in 2005 and 2006 were eligible for the study. Patients were identified from the Dutch Cancer Registry, a database containing detailed information on demographics, tumor characteristics and survival outcomes of more than 95% of all new cancer cases in the Netherlands. More specific information was retrospectively gathered from the medical records of all patients treated in a subset of 19 hospitals, which reflect the diversity of clinical practice. Patients were excluded if the medical record revealed that the patient had stage IV clinical disease, did not receive any chemotherapy or did not receive chemotherapy in the selected hospital. As the study aimed to examine the real-world situation, patients were additionally excluded when they participated in RCTs. Furthermore, the few additional patients treated with bevacizumab and uracil/tegafur (UFT) were disregarded as well as patients with second malignancies and patients who had received radiotherapy for rectal cancer. Based on minimal case reports, a random representative sample was selected from the remaining patients, of whom detailed information on resource use associated with each treatment and follow up was additionally collected.

The present paper describes the results of the cost analysis which was conducted from a hospital perspective. Resource use data were drawn from the individual patients

recruited for the clinical outcomes study. Mean costs per patient were calculated for the four most common treatment groups seen in daily practice: 5-FU/LV, capecitabine, 5-FU/LV with oxaliplatin and capecitabine with oxaliplatin. Total costs for individual patients were determined by the identification of resource use and unit costs of the following cost components: inpatient hospital days, intensive care days, outpatient visits, consultations by telephone, daycare treatments, emergency room visits, radiotherapy, surgical procedures, laboratory services, medical imaging services, chemotherapy and concomitant medications.

Resource use was divided into two time periods. Period 1 began on day 1 of the first administration of adjuvant chemotherapy. To capture resource use resulting from treatment related toxicity, period 1 ended one month after the last administration of chemotherapy. Period 2 started one month after the last administration of chemotherapy and lasted until disease progression (or end of follow up).

Table 10.1 presents the unit costs of inpatient hospital days, intensive care days, outpatient visits, consultations by telephone, daycare treatments and emergency room visits. The unit cost calculations were based on detailed microcosting studies reflecting full hospital costs, including overhead costs, and will be reported in a second forthcoming publication. Some unit costs were weighted for their origin: 33% of the unit costs were based on data from the university hospitals and 67% on those from general hospitals. These shares reflect the distribution of patients among hospitals in Dutch daily practice.

The resource use of surgical procedures, laboratory services and medical imaging services was valued using the fees as issued by the Dutch Healthcare Authority. Unit costs of chemotherapy are shown in table 10.1. Unit costs of chemotherapy and concomitant medications were acquired from the Committee Pharmacotherapeutical Aid (Committee Pharmacotherapeutical Aid & Health Care Insurance Board 2009). The cost assessment of chemotherapy was performed including and excluding the waste occurring as the consequence of an inappropriate disposal of unused or partially used ampoules, vials or syringes of drugs (Fasola et al. 2008).

To determine the uncertainty of the obtained cost estimates, one-way sensitivity analyses were carried out by varying the unit cost values of inpatient hospital day, outpatient visit and daycare treatment unit costs between 50% and 150%. Unit costs other than those of hospital days were considered to be fairly stable or of less influence and were therefore not subjected to sensitivity analyses.

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 15.0. In addition to descriptive statistics, differences between the four treatment groups were assessed by means of the one-way analysis of variance (ANOVA) test for variables showing a normal distribution, the Kruskal-Wallis test for variables not normally distributed and the Pearson Chi-square test for variable fractions. The paired sample T test was used to examine cost differences occurring due to the inclusion or exclusion of waste. To adjust for multiple testing, one way analyses of variance with post hoc testing (type Bonferroni) were additionally performed. In all cases $P < 0.05$ was taken as statistically significant. All costs were based on Euro 2007 cost data. Where necessary, costs were adjusted to 2007 using the general price index from the Dutch Central bureau of Statistics (Centraal Bureau voor de Statistiek & Ministerie voor Volksgezondheid Welzijn en Sport 2007).

Table 10.1: Unit costs (Euro 2007)

Oncology regular inpatient hospital day *	400
Oncology university inpatient hospital day	633
Intensive care unit day	1,940
Oncology regular outpatient visits *	86
Oncology university outpatient visits	120
Consultations by telephone	13
Oncology regular daycare treatment *	176
Oncology university daycare treatment	276
Emergency room visits	191
5-Fluorouracil (mU)	0.0068
Leucoforin (mg)	0.3282
Capecitabine (mg)	0.0069
Oxaliplatin (mg)	5.1889
Uracil/tegafur (mg)	0.0556

mU = milli international unit (IU); 1 mU = 0.001 IU
mg = milligram
* Weighting factor 33:67 for university and general hospitals applied

10.4 RESULTS

A patient flowchart is provided in figure 10.1. A total of 463 patients were treated at one of the 19 hospitals included in our study during the years 2005 and 2006, of which 391 met our inclusion criteria. Detailed information on resource use associated with each treatment and follow up was collected for a random representative sample of 206 patients, of which 17 received 5-FU/LV, 89 received capecitabine, 37 received 5-FU/LV with oxaliplatin and 65 received capecitabine with oxaliplatin.

The patient characteristics of the total population (n=391) as well as those of the four treatment groups at baseline are summarised in table 10.2. Patients receiving oxaliplatin are significantly younger (Pearson Chi-square test: $P < 0.001$) and have fewer comorbidities ($P = 0.014$) than patients who did not receive oxaliplatin containing regimens.

Table 10.2: Patient characteristics at baseline for the total population as well as for the 5-FU/LV, capecitabine and oxaliplatin treatment groups

	Total	No oxaliplatin		Oxaliplatin		Pearson Chi-square test Asymp. Sig. (2-sided)
	population	5-FU/LV	Capecitabine	5-FU/LV	Capecitabine	
Baseline Characteristics	**n=391**	**n=15**	**n=89**	**n=37**	**n=65**	
Age - years						
Median	64	71	73	60	60	0.000
Range	22-85	41-79	58-85	34 - 76	22-82	
Age group - no. (%)						
< 70	279 (71.4)	6 (40.0)	29 (32.6)	31 (83.8)	54 (83.1)	0.000
≥ 70	112 (28.6)	9 (60.0)	60 (67.4)	6 (16.2)	11 (16.9)	
Sex - no. (%)						
male	209 (53.5)	11 (73.3)	67 (75.3)	31 (83.8)	59 (90.8)	0.571
female	182 (46.5)	4 (26.7)	22 (24.7)	6 (16.2)	6 (9.2)	
No. of comorbid conditions - no. (%)						
< 2	332 (84.9)	9 (60.0)	44 (49.4)	20 (54.1)	36 (55.4)	0.014
≥ 2	59 (15.1)	6 (40.0)	45 (50.6)	17 (45.9)	29 (44.6)	
Depth of invasion - no. (%)						
T2 -T3	336 (86.2)	13 (86.7)	78 (88.6)	34 (91.9)	55 (84.6)	0.811
T4	54 (13.8)	2 (13.33)	10 (11.4)	3 (8.1)	10 (15.4)	
Unknown	1		1			
No. of nodes involved - no. (%)						
N1	242 (61.9)	10 (66.7)	59 (66.3)	23 (62.2)	38 (58.5)	0.331
N2	149 (38.1)	5 (33.3)	30 (33.7)	14 (37.8)	27 (41.5)	
Histological appearance - no. (%)						
Well differentiated	322 (86.3)	10 (66.7)	71 (80.7)	29 (78.4)	55 (90.2)	0.191
Poorly differentiated	51 (13.7)	5 (33.3)	17 (19.3)	8 (21.6)	6 (9.8)	
Unknown	18		1		4	
CEA level - no.						
< 5 ng/ml (ULN)	278 (84.5)	9 (90.0)	66 (93.0)	22 (78.6)	45 (77.6)	0.008
≥ 5 ng/ml (ULN)	51 (15.5)	1 (10.0)	5 (7.0)	6 (21.4)	13 (22.4)	
Unknown	62	5	18	9	7	

Asymp. Sig. = asymptomatic significance
CEA = carcinoembryonic antigen
ULN = upper limit of normal

Furthermore, carcinoembryonic antigen levels were significantly lower in the patients treated without oxaliplatin ($P = 0.008$).

Mean costs per patient for periods 1 and 2 amounted to € 9,029 for 5-FU/LV, € 9,909 for capecitabine, € 32,634 for 5-FU/LV with oxaliplatin and € 23,468 for capecitabine with oxaliplatin.

Period 1: from the first administration until one month after the last administration of chemotherapy

The mean follow up durations for period 1 were 5.8 ± 2.3 months for patients receiving 5-FU/LV (range: 5.2 to 44.2 months), 6.0 ± 1.3 for patients receiving capecitabine (range: 1.0 to 47.6 months), 5.9 ± 1.0 months for patients receiving 5-FU/LV with oxaliplatin (range: 7.3 to 46.6 months) and 6.4 ± 1.4 months for patients receiving capecitabine with oxaliplatin (range: 3.6 to 44.2 months).

Table 10.3 presents the distribution of cost components for period 1 of the four treatment groups, taking the waste of chemotherapy into account. Mean costs per patient amounted to € 5,939 for 5-FU/LV, € 6,159 for capecitabine, € 28,159 for 5-FU/LV with oxaliplatin and € 20,710 for capecitabine with oxaliplatin (Kruskal Wallis test: $P < 0.001$). Mean costs for 5-FU/LV with oxaliplatin and capecitabine with oxaliplatin were significantly different ($P < 0.001$), where mean costs for 5-FU/LV and capecitabine were not significantly different ($P = 0.073$). A substantial cost variation was found in the total costs obtained for individual patients within treatment groups as well as in each individual cost component. The administration of chemotherapy (including inpatient hospital days, daycare treatments, outpatient visits and chemotherapy) was the most important cost driver.

Inpatient stay costs were € 988 in 5-FU/LV, € 1,924 in capecitabine, € 9,716 in 5-FU/LV with oxaliplatin and € 2,070 in capecitabine with oxaliplatin. Of the inpatient admissions, 3% related to other than oncology departments, such as surgery and pulmonary departments. Inpatient hospital days were especially important in the 5-FU/LV with oxaliplatin group, as the administration of 5-FU/LV and oxaliplatin concerned inpatient procedures. Patients treated with 5-FU/LV with oxaliplatin were admitted for an average of 20.3 (SD 16.9) inpatient days, compared to 2.1 (SD 4.7), 4.1 (SD 20.2) and 4.3 (SD 9.4) days in the other three treatment groups (ANOVA test: $P < 0.001$; table 10.3). Only one patient was admitted to the intensive care unit. This patient was treated with capecitabine and developed sepsis during her admission for dehydration from diarrhoea.

Table 10.3: Distribution of cost components in period 1 for 5-FU/LV, capecitabine and oxaliplatin treatment groups

	No oxaliplatin				Oxaliplatin			
	5-FU/LV		Capecitabine		5-FU/LV		Capecitabine	
	n=15		n=89		n=37		n=65	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Resource use (numbers)								
Inpatient hospital days	2.1	4.7	4.1	20.2	20.3	16.9	4.3	9.4
Intensive care unit days	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
Outpatient visits	10.9	13.3	8.4	4.1	10.0	6.4	8.1	6.2
Consultations by telephone	0.8	1.4	1.4	2.3	1.0	3.1	2.0	3.2
Daycare treatments	10.1	12.6	0.8	2.2	6.8	12.1	5.8	3.7
Emergency room visits	2.1	7.7	0.6	1.5	0.2	0.8	0.3	0.8
Costs (Euro 2007)								
Inpatient hospital days	988	2,238	1,924	9,633	9,716	8,077	2,070	4,495
Intensive care unit days	0	0	22	206	0	0	0	0
Outpatient visits	1,060	1,299	821	399	973	625	786	603
Consultations by telephone	10	18	17	29	12	39	25	41
Daycare treatments	2,122	2,629	176	455	1,434	2,530	1,211	769
Emergency room visits	406	1,470	111	290	44	148	61	159
Radiotherapy	0	0	0	0	0	0	47	371
Intravenous access	0	0	0	0	218	393	25	195
Colonoscopy	113	438	62	163	76	165	97	257
Other surgical	35	131	20	62	36	99	44	129
Laboratory	308	205	169	99	247	99	232	136
X-ray	21	33	25	37	44	58	30	57
CT scan	14	54	40	88	74	139	48	94
PET scan	94	364	48	449	0	0	23	178
Ultrasound	17	36	34	53	31	64	52	66
Other radiological	0	0	6	38	8	44	10	49
5-Fluorouracil (bolus)	5	14	0	1	112	73	4	17
5-Fluorouracil (infusion)	110	63	2	15	160	60	6	23
Leucovorin	480	341	18	127	3,210	1,353	141	532
Capecitabine	0	0	2,491	926	190	516	2,334	852
Oxaliplatin	0	0	0	0	9,791	3,747	13,141	41,513
Uracil/tegafur	0	0	10	99	0	0	30	235
Concomitant medications	154	384	163	740	1,782	4,985	295	251
Total costs (Euro 2007)	5,939	2,694	6,159	9,656	28,159	12,025	20,710	41,694
Median	6,690		4,508		27,462		15,809	
Minimum	994		357		3,114		1,979	
Maximum	9,424		91,254		66,972		343,292	

SD = standard deviation
CT = computed tomography
PET = positron emission tomography

Daycare treatments were of minor importance in the capecitabine treatment group (€ 176; SD 455), because capecitabine is administered orally during outpatient visits. In contrast, costs for daycare treatments were much higher in the other three treatment groups (€ 2,122 for 5-FU/LV, € 1,434 for 5-FU/LV with oxaliplatin and € 1,211 for capecitabine with oxaliplatin; Kruskal Wallis test: $P = 0.016$). Using one way analyses of variance with post hoc testing, the latter *P*-value is no longer significant. A substantial variation was found in number of daycare treatments per individual patient (range: 0-46).

The number of outpatient visits was of the same magnitude in the four treatment groups (ANOVA test: $P = 0.239$). The proportion of outpatient visits in total treatment costs was responsible for 18% in 5-FU/LV, 13% in capecitabine, 3% in 5-FU/LV with oxaliplatin and 4% capecitabine with oxaliplatin.

When waste was included, mean costs for chemotherapy amounted to € 596 for 5-FU/LV, € 2,521 for capecitabine, € 13,463 for 5-FU/LV with oxaliplatin and € 15,655 for capecitabine with oxaliplatin. For the 5-FU/LV with oxaliplatin treatment group, oxaliplatin alone accounted for 73% of the chemotherapy costs and 35% of the total treatment costs. For the capecitabine with oxaliplatin group, these proportions equalled 84% and 64%.

Table 10.4 presents the distribution of chemotherapy costs with and without waste for 5-FU/LV, capecitabine and oxaliplatin treatment groups. Cost differences between total chemotherapy costs including and excluding waste were significantly different for all four treatment groups (paired sample T test: $P = 0.001$; $P = 0.044$; $P < 0.001$; $P < 0.001$ respectively). The cost differences between oxaliplatin chemotherapy costs including and excluding waste were € 893 for 5-FU/LV with oxaliplatin and € 482 for capecitabine with oxaliplatin. Total chemotherapy costs were not significantly different for the capecitabine group when multiple testing was taken into account.

Period 2: from one month after the last administration of chemotherapy until progression or end of follow up

The mean follow up durations period 2 were 25.0 ± 8.7 months for patients receiving 5-FU/LV (n=17), 22.1 ± 9.6 for patients receiving capecitabine (n=89), 22.7 ± 12.4 months for patients receiving 5-FU/LV with oxaliplatin (n=37) and 19.4 ± 8.8 months for patients receiving capecitabine with oxaliplatin (n=65). Resource use was collected until disease progression for 22% of the patients (n=46) and until the end of follow up for 78% of the patients (n=160).

Table 10.4: Distribution of chemotherapy costs with and without waste for 5-FU/LV, capecitabine and oxaliplatin treatment groups (Euro 2007)

	No oxaliplatin		Oxaliplatin	
	5-FU/LV	Capecitabine	5-FU/LV	Capecitabine
	n=15	n=89	n=37	n=65
Cost including waste				
5-Fluorouracil (bolus)	5	0	112	4
5-Fluorouracil (infusion)	110	2	160	6
Leucovorin	480	18	3,210	141
Capecitabine	0	2,491	190	2,334
Oxaliplatin	0	0	9,791	13,141
Uracil/tegafur	0	10	0	30
Total costs	596	2,521	13,463	15,655
Cost excluding waste				
5-Fluorouracil (bolus)	5	0	98	4
5-Fluorouracil (infusion)	100	2	148	5
Leucovorin	434	17	3,207	141
Capecitabine	0	2,491	190	2,332
Oxaliplatin	0	0	8,897	12,659
Uracil/tegafur	0	10	0	30
Total costs	539	2,521	12,541	15,171
Cost difference				
5-Fluorouracil (bolus)	1	0	14	1
5-Fluorouracil (infusion)	10	0	12	0
Leucovorin	46	0	3	0
Capecitabine	0	0	0	1
Oxaliplatin	0	0	893	482
Uracil/tegafur	0	0	0	0
Total difference	57	0	922	484

Table 10.5 presents the distribution of cost components for period 2 considering all patients within the four treatment groups (n=206). Mean costs per patient amounted to € 3,090 for 5-FU/LV, € 3,750 for capecitabine, € 4,475 for 5-FU/LV with oxaliplatin and € 2,758 for capecitabine with oxaliplatin (Kruskal Wallis test: $P = 0.379$). Mean costs for patients whose resource use was collected until progression were not significantly different from patients whose resource use was collected until the end of follow up ($P_{\text{5-FU/LV}} = 0.167$; $P_{\text{capecitabine}} = 0.691$; $P_{\text{5-FU/LV with oxaliplatin}} = 0.743$; $P_{\text{capecitabine with oxaliplatin}} = 0.072$).

Table 10.5: Distribution of cost components in period 2 for 5-FU/LV, capecitabine and oxaliplatin treatment groups

	No oxaliplatin				Oxaliplatin			
	5-FU/LV		Capecitabine		5-FU/LV		Capecitabine	
	n=15		n=89		n=37		n=65	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Resource use (numbers)								
Oncology hospital days	2.3	5.1	2.7	6.6	4.3	9.8	1.8	4.3
Intensive care unit days	0.0	0.0	0.2	2.2	0.0	0.0	0.0	0.0
Oncology outpatient visits	9.3	10.9	6.8	5.4	8.9	5.7	6.7	4.5
Consultations by telephone	0.5	0.9	0.6	1.3	0.7	1.3	0.6	1.4
Daycare treatments	0.3	1.0	0.4	0.9	0.2	0.6	0.4	0.9
Emergency room visits	0.1	0.5	0.4	1.0	0.2	0.5	0.1	0.3
Costs (Euro 2007)								
Oncology hospital days	1,063	2,340	1,248	3,068	2,007	4,533	818	1,963
Intensive care unit days	0	0	458	4,319	0	0	0	0
Oncology outpatient visits	904	1,065	665	523	870	559	654	443
Consultations by telephone	7	12	7	16	8	17	7	17
Daycare treatments	70	219	81	180	50	122	82	196
Emergency room visits	25	98	84	195	40	89	17	52
Radiotherapy	0	0	0	0	0	0	0	0
Intravenous access	0	0	0	0	123	369	0	0
Colonoscopy	367	477	405	419	621	1,477	466	547
Other surgical	0	0	37	116	92	310	23	89
Laboratory	165	188	209	406	167	131	164	208
X-ray	97	98	79	106	82	99	65	80
CT scan	97	375	139	252	261	292	114	213
PET scan	94	364	128	660	0	0	138	550
Ultrasound	201	177	158	143	135	166	178	153
Other radiological	0	0	50	197	18	65	31	175
5-Fluorouracil (bolus)	0	0	0	0	0	0	0	0
5-Fluorouracil (infusion)	0	0	0	0	0	0	0	0
Leucovorin	0	0	0	0	0	0	0	0
Capecitabine	0	0	0	0	0	0	0	0
Oxaliplatin	0	0	0	0	0	0	0	0
Uracil/tegafur	0	0	0	0	0	0	0	0
Concomitant medications	0	0	0	0	0	0	0	0
Total costs (Euro 2007)	3,090	3,411	3,750	6,570	4,475	6,016	2,758	3,046
Median	1,701		1,987		2,285		1,932	
Minimum	0		0		216		0	
Maximum	9,283		53,727		33,871		18,384	

SD = standard deviation
CT = computed tomography
PET = positron emission tomography

Inpatient hospital days, outpatient visits and colonoscopies were the most important cost drivers. Patients receiving 5-FU/LV with oxaliplatin received more computer tomographies ($P = 0.002$) than patients in the other three groups. Patients having their port-a-cath removed only concerned patients treated with 5-FU/LV with oxaliplatin ($P = 0.001$). None of the other cost components reached statistical significance.

Sensitivity analyses

The sensitivity of the total costs to varying the unit costs of inpatient hospital days, daycare treatments and outpatient visits between 50% and 150% was tested, as described before. The influence of this variation appeared to be rather modest: total costs in periods 1 and 2 varied by 6-18% when inpatient hospital day unit costs were varied, by 3-11% when daycare treatment unit costs were varied and by 1-12% when outpatient visit unit costs were varied.

Economic burden

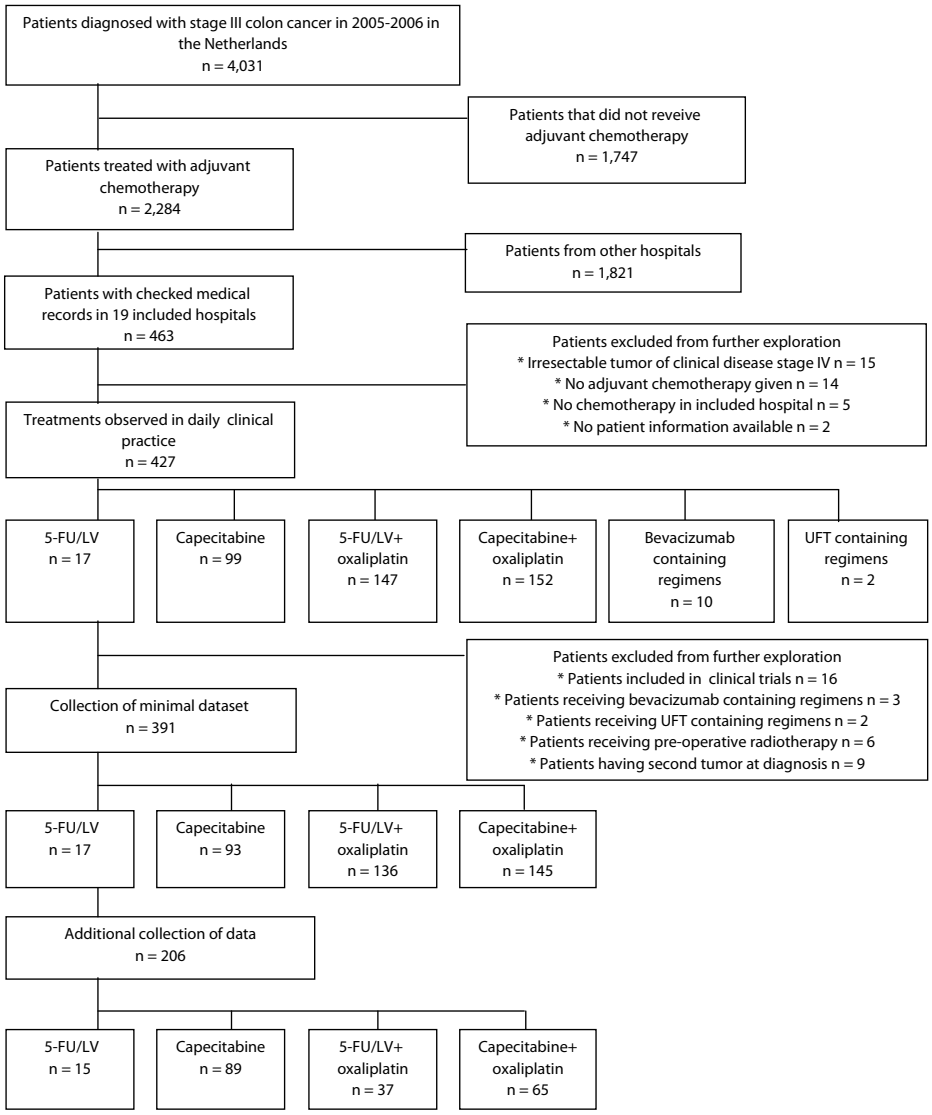
In 2005 and 2006, 2,284 newly diagnosed with stage III colon cancer patients in the Netherlands received adjuvant chemotherapy (figure 10.1). Of these, 4% received 5-FU/LV, 24% received capecitabine, 35% received 5-FU/LV with oxaliplatin and 37% received capecitabine with oxaliplatin. Extrapolating the obtained mean treatment cost per treatment group resulted in an economic burden of € 26.1 million per year.

10.5 DISCUSSION

To our knowledge, this is the first cost assessment of stage III colon cancer treatment based on real-world resource use. The combination of 5-FU/LV and oxaliplatin was observed to be the most expensive treatment option. Treatment costs of 5-FU/LV with oxaliplatin in periods 1 and 2 were € 23,605 more expensive than 5-FU/LV without oxaliplatin (Kruskal Wallis test: $P < 0.001$), predominantly owing to the inpatient administration of chemotherapy. Earlier studies, most of which based on the MOSAIC trial, have also demonstrated favourable costs for 5-FU/LV without oxaliplatin over 5-FU/LV with oxaliplatin, although to a varying degree (Aballea, Boler 2007; Aballea, Chancellor 2007; Gorner & Riemer-Hommel 2008; Pandor, Eggington 2006).

Furthermore, treatment costs of 5-FU/LV with oxaliplatin in periods 1 and 2 were € 9,166 more expensive than that of capecitabine with oxaliplatin (Kruskal Wallis test: $P < 0.001$). Maniadakis et al. (2009), whose study was carried out in Greece, determined total treat-

Figure 10.1: Patient distribution



ment cost of 5-FU/LV with oxaliplatin as an adjuvant treatment for high risk colon cancer patients to be € 4,955 more expensive than that of capecitabine with oxaliplatin ($P <$ 0.001; follow up duration: ≈13 months). The higher costs for 5-FU/LV with oxaliplatin were almost entirely due to higher hospitalisation costs. The 5-FU/LV with oxaliplatin group was hospitalised for an average of 10.7 inpatient days (versus 20.3 in our study) where the capecitabine with oxaliplatin group was hospitalised for an average of 2.2 inpatient days (versus 4.3 in our study) (Maniadakis, Fragoulakis 2009).

Treatment costs of capecitabine and 5-FU/LV were not statistically different (Kruskal Wallis test: $P = 0.073$). However, studies based on the X-ACT trial have estimated the cost of capecitabine to be about € 5,400 lower (adjusted to 2007) than those of 5-FU/LV (Cassidy, Douillard 2006; Douillard, Tilleul 2007; Eggington, Tappenden 2006; Pandor, Eggington 2006; Twelves 2006). Both in our study and in the X-ACT trial, the costs of chemotherapy were about € 2,000 lower for 5-FU/LV compared to capecitabine. In our study, these lower costs were compensated for by the higher cost of daycare treatments during which the study drugs were administered (cost difference: € 1,891 in favour of capecitabine). In contrast, the lower chemotherapy costs for 5-FU/LV in the X-ACT trial were not able to compensate for the higher cost of daycare treatments (cost difference: € 7,311 in favour of capecitabine).

The inclusion or exclusion of waste resulting from the consequence of an inappropriate disposal of unused or partially used ampoules, vials or syringes of drugs, was demonstrated to have only a modest influence on the total cost results. The economic loss due to the waste of chemotherapy equalled 3.4% of the total chemotherapy costs. As expected, the influence was greatest in patients receiving oxaliplatin (table 10.4). The share of waste amounted to 7.2% of the total costs for oxaliplatin, which is fairly similar to the results of Fasola et al. (2008) who determined the economic loss at the medical oncology department of an Italian hospital to be 6.7% of their annual oxaliplatin expenditure (Fasola, Aita 2008).

In addition, this study examined the economic burden of stage III colon cancer patients in the Netherlands. By means of extrapolation, the economic burden was determined at € 26.1 million per year, which equals around 10% of the costs of colorectal cancer in the Netherlands (Poos, Smit 2005). This figure still holds when solely the patients whose resource use was collected until disease progression were considered (n=46), as there are indications that their costs were not significantly different from those of the patients whose resource use was collected until the end of follow up.

Economic evaluations are designed to provide clinicians and healthcare decision makers with valuable information on the cost effectiveness of pharmaceutical therapies. Economic evaluations piggy-backed on RCTs are believed to provide the most scientifically valid evidence for cost effectiveness. However, conventional RCTs have recognised limitations for determining cost effectiveness of new treatments (Drummond 2005; Rothman & Greenland 1998), resulting in a greater focus on real-world pharmacoeconomics which allows for the evaluation of treatment outcomes in daily clinical practice. For example, of the patients receiving 5-FU/LV with oxaliplatin in our study (n=37), only 13% fully met the treatment scheme as prescribed by the MOSAIC trial (Aballea, Boler

2007; Aballea, Chancellor 2007; Eggington, Tappenden 2006; Pandor, Eggington 2006). Maniadakis et al. (2009) have concluded that cost analyses carried out alongside RCTs should be interpreted in the specific context in which they were undertaken (Maniadakis, Fragoulakis 2009).

However one should be cautious in directly using real-world resource use for the cost comparisons between treatment groups, because the treatment groups may not be comparable. From our sample, patients receiving oxaliplatin were significantly younger, had fewer comorbidities and higher carcinoembryonic antigen levels than patients not receiving oxaliplatin. Clearly, the medical specialist did not randomly assign the different treatment options. Consequently, the prognosis of patients receiving oxaliplatin may be different from patients who did not receive oxaliplatin. These imbalances regarding prognostic factors may have led to invalid cost comparisons. Adjusting for patient characteristics via regression techniques is one method to correct for these imbalances and might be the objective of a future study.

Stage III colon cancer patients may be treated with chemotherapies other than 5-FU/LV, capecitabine and oxaliplatin. Other treatment options applied in daily practice are UFT and bevacizumab. The National Adjuvant study of colorectal cancer in Japan, an RCT of surgery with UFT for stage III rectal cancer, showed survival gains compared with surgery alone (Hisashige et al. 2008). However, no studies have compared UFT treatment with other adjuvant chemotherapies. The Dutch guidelines refer to UFT as a treatment option for the elderly and for patients with comorbidities. The angiogenesis inhibitor bevacizumab is not referred to in the Dutch guidelines, but has shown activity when combined with 5-FU/LV-based regimens as first-line treatment of stage IV colon cancer. Bevacizumab is currently being evaluated as part of adjuvant therapy in stage III colon cancer in the National Surgical Adjuvant Breast and Bowel Project C08 trial and the AVANT (AVastin adjuvANT) trial (De Gramont et al. 2006).

Even though the effects are at least as important in economic evaluations, this study has focussed on the cost estimation of the treatment for stage III colon cancer. The effects may be particularly important in oncology in which prolonged survival and quality of life play a substantial role. Earlier studies have suggested that capecitabine offers at least equivalent clinical benefit as conventional 5-FU/LV (Cassidy, Douillard 2006; Reddy 2004; Twelves 2006). In addition, oxaliplatin containing regimens have shown superior clinical outcomes over 5-FU/LV (Andre, Boni 2004; Kuebler, Wieand 2007). To be able to better assist clinical decision making for stage III colon cancer patients in the Netherlands, cost effectiveness results will be reported in our forthcoming publication on the

clinical outcomes study, which will allow us to draw conclusions regarding the relative cost effectiveness of alternative treatment options.

The current distribution of patients suggests a trend towards the use of capecitabine and oxaliplatin containing regimens as the first line treatment for stage III colon cancer patients in the Netherlands. This trend is in agreement with the recommendations of the national guidelines (Committee Pharmacotherapeutical Aid & Health Care Insurance Board 2009; Punt, Richel 2005). The lower treatment costs for capecitabine with oxaliplatin compared to 5-FU/LV with oxaliplatin may in part relieve the economic burden of stage III colon cancer patients in the future.

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Chapter 11

Cost-utility of exercise therapy in adolescents and young adults suffering from the patellofemoral pain syndrome

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11.1 ABSTRACT

The objective of this paper was to determine the cost effectiveness of exercise therapy (intervention group) compared to 'usual care' (control group) in adolescents and young adults with the patellofemoral pain syndrome in primary care. This multicenter prospective randomised clinical trial with cost-utility analysis was conducted at 38 general practices and 3 sport medical advice centers in the Netherlands for 2007. A total of 131 patients were included. The annual direct medical costs per patient were significantly higher for the intervention group (€ 434) compared to the control group (€ 299) mainly caused by additional physiotherapy visits. The average annual societal costs per patient were significantly lower in the intervention group (€ 1,011 versus € 1.166). Productivity costs were the largest cost component, in particular costs due to reduced efficiency at paid work which were responsible for 47% and 56% of the total costs in the intervention and control group respectively. Patients in the intervention group experienced a slightly, but not significantly, higher quality of life (0.8722 versus 0.8617). With a cost effectiveness ratio of - € 14,738 per quality adjusted life year, exercise therapy appears to be cost effective as compared to 'usual care'.

Keywords: Exercise therapy – Patellofemoral pain syndrome – Cost effectiveness – Physiotherapy – Cost analysis

11.2 INTRODUCTION

Patellofemoral pain syndrome (PFPS) is a common complaint in adolescents and younger adults. The incidence of PFPS increases from age 14 with a peak incidence around age 25 and is higher for women than for men (Arendt 2007; van Linschoten et al. 2006). The most typical symptom of PFPS is a diffuse peripatellar and retropatellar localised pain, typically provoked by ascending or descending stairs, squatting, cycling and sitting with flexed knees for prolonged periods of time (Arroll et al. 1997; Cutbill et al. 1997).

Clinical guidelines of the Dutch College of General Practice recommend a conservative treatment for PFPS by informing the patient about the background of the condition and its favourable prognosis (usual care) (Cirkel et al. 1998). General practitioners do not always adhere to these guidelines. From a pilot study on patients with PFPS visiting the general practitioner it was shown that 35% of patients were referred to exercise therapy by a physiotherapist at the first visit. After 12 months of follow up, 64% of the patients were referred to exercise therapy (van Linschoten, van Middelkoop 2006).

Economic evaluations are a prerequisite for the reimbursement and implementation of treatments in many countries, because they can provide healthcare decision makers with valuable information on the relative efficiency of alternative treatments. Costs are preferably determined from a societal perspective in which all relevant costs are included (Drummond 2005). However, many economic evaluations only include direct medical costs. As productivity costs may account for more than 50% of the total costs, disregarding these costs may significantly effect the cost effectiveness (CE-)ratio (Tranmer et al. 2005). As PFPS frequently occurs in young (working) patients, a productivity cost reduction due to absence from paid work and reduced efficiency at paid and unpaid work may be expected. These productivity cost reductions might partially compensate for the additional cost of exercise therapy.

A few studies have previously evaluated the effectiveness of exercise therapy. A Cochrane review by Heintjes et al. (2003) summarised the evidence for treatment efficacy in reducing anterior knee pain and improving knee function in patients with PFPS. They found one high and two low quality studies which used a control group not receiving exercise therapy. One high and one low quality study observed exercise therapy to be more effective in treating PFPS with respect to pain reduction. Additionally, one low quality study reported significantly greater functional improvement with exercise. However, the quality of the trials was such that further research was necessary to confirm this conclusion (Heintjes et al. 2003).

No earlier studies have yet assessed the cost(-effectiveness) of exercise therapy in patients with PFPS. Because of the lack of information on the costs as well as on the effectiveness of exercise therapy, general practitioners lack the knowledge to apply the most cost effective treatment to patients with PFPS. Therefore, the aim of the present study was to determine the cost effectiveness of exercise therapy (intervention group) compared to 'usual care' (control group) in adolescents and young adults dealing with PFPS in primary care.

11.3 METHODS

This cost-utility study was performed in conjunction with a randomised clinical trial. More details of the study design can be read in the protocol published in 2006 (van Linschoten, van Middelkoop 2006). In short, adolescents and young adults between 14 and 40 years of age presenting with symptoms of PFPS and no history of previous active treatment with exercises within the last 6 months were eligible for enrolment by the general practitioner or sport physician. The complaints should have persisted for longer than 2 months but no longer than 2 years. Furthermore, at least 3 of the following symptoms should have been present: pain when walking stairs, pain when squatting, pain when running, pain when cycling, pain when sitting with knees flexed for a prolonged period of time, grinding of the patella, and a positive clinical patellar test (such as Clarke's test or "signe du rabot") (Malanga et al. 2003; Nijs et al. 2006). Patients were excluded when suffering from radiologically confirmed knee osteoarthrosis / arthritis, patellar tendinopathy, Osgood-Schlatter disease or other defined pathological conditions of the knee, or had previous knee injuries and / or surgery. The patients were randomised to exercise therapy (intervention group) or 'usual care' (control group), stratified for clinical setting (general practitioner / sport physician) and age (<18 years / ≥18 years). The randomisation was done by an independent researcher using a computer-generated list.

Patients in the intervention group received advice and information on the background of PFPS by a physician and were appointed to a standardised exercise program, supervised by physiotherapists (9 sessions during 6 weeks), with continuation of home exercises. Patients in the control group only received advice and information on the background of PFPS by a physician, similar to the advice given by general practitioners and sport physicians in a normal care situation. As this is a pragmatic trial using the intention to treat principle, a minority of patients in the control group might have received a small amount of exercise therapy. Recruitment took place in the 38 HONEUR practices (a research network of general practices allied with the Department of General Practice of Erasmus MC University Medical Center) and at the sport medical advice centers in

Rotterdam, Leidschendam and Gorinchem. Enrolment commenced in August 2005 and finished in May 2007. The follow up period was one year.

The primary outcome measures of the randomised clinical trial included pain, knee function and perception of recovery. These clinical results will be reported in a forthcoming publication. The present paper will focus on the cost-utility study and is based on an intention to treat analysis.

The cost-utility study was primarily conducted from a societal perspective, but the healthcare perspective was also appraised. Data on direct medical costs, productivity costs and quality of life was collected using standardised questionnaires which were sent to the home addresses of the patients at baseline and 6, 13, 26, 39 and 52 weeks after randomisation. The recall period was 6 weeks. Annual costs were determined by adding up the costs per period. The costs for the time between the measurement periods (week 6-7, week 14–20, week 27-33 and week 40–46) were established through linear interpolation. The last observation carried forward (LOCF) method was applied in case of missing values. All costs were based on Euro 2007 cost data. Where necessary, costs were adjusted to 2007 using the general price index from the Dutch Central Bureau of Statistics.

Direct medical costs

Total direct medical costs for individual patients were determined by multiplying resource use by the corresponding unit prices. Data on resource use of visits to healthcare providers (including the general practitioner, physiotherapist and medical specialist), medical imaging services (magnetic resonance imaging, computed tomographies and X-rays), medications and disposables (including cold and hot compresses, orthopaedic insoles, elastic bandages, braces and tape) was acquired from the questionnaires. Resource use of visits to the physiotherapist was additionally obtained from the physiotherapist. Resource use of medical imaging services which were used to exclude patients with other diagnoses than PFPS were not incorporated in the direct medical costs because they took place prior to enrolment. Such resource use is normally excluded in an economic evaluation (Drummond 2005).

Unit costs of visits to the general practitioner and physiotherapist were based on a detailed microcosting study. Using standardised reporting templates, seven general practitioners and eight physiotherapists were each individually asked to estimate the time spent by the general practitioner / physiotherapist and the assistant on an average patient. Unit costs were based on the normative income for free labour practitioners,

the collective labour agreement of general practitioner care and the number of workable hours per year (Oostenbrink et al. 2002). Annual overhead costs were allocated to patients using a marginal mark-up percentage.

The resource use of visits to other healthcare providers was valued using reference unit prices (Oostenbrink, Koopmanschap 2002). The resource use of medical imaging services was valued using the fees as issued by the Dutch Healthcare Authority. Wholesale prices were used to value the resource use of medications and disposables. Because patients were asked whether they made use of disposables at every measurement moment, we assumed that cold and hot compresses were used once monthly. Orthopaedic insoles, elastic bandages and braces were assigned a life expectancy of 4 years, whereas tape was assumed to be purchased each year.

Productivity costs

The productivity costs involved productivity losses resulting from absence from paid work and reduced efficiency at paid and unpaid work.

Absence from paid work
The number of absent days from paid work due to PFPS problems was valued using the overall average net value added per employee to avoid differences in productivity losses between the intervention and control group would be caused by (income) differences which are related to age, gender and educational level but not to PFPS problems.

Reduced efficiency at paid work
Reduced efficiency at paid work was also valued using the overall average net value added per employee. The efficiency loss was established by means of the quality- and quantity method as developed by Brouwer et al. (1999) and incorporated in the PRODISQ instrument (Brouwer et al. 1999; Koopmanschap 2005). The patients gave their mark for the quality of their work on the last working day of each 6 weeks on a visual analog scale from 0 (worst quality) to 10 (best quality). The same question was posed for the quantity of their work on their last working day. These marks were assumed to be representative for the overall recall period. The efficiency loss during paid work in terms of hours lost was then determined to be (1−(quality/10)×(quantity/10))×working hours per day.

Reduced efficiency at unpaid work
Patients were asked to indicate how many hours of housekeeping tasks were taken over by their family, other people and paid aid due to PFPS problems. The number of hours

housekeeping tasks that were taken over was valued using the current price of simple professional home care (Oostenbrink, Koopmanschap 2002).

Quality of life

The quality of life was measured by means of the EQ-5D instrument. The EQ-5D has five dimensions: mobility, self-care, activity, pain and anxiety. Each dimension has three levels: no problems (level 1), some problems (level 2) and serious problems (level 3). Hence, EQ-5D has 243 possible health states. Utility values for these health states were measured with the time trade-off technique on a random sample of the general adult population of the Netherlands (Lamers et al. 2006). The scores range from −0.329 (worst situation) to 1.0 (perfect health).

Patients were also asked to indicate how they experienced their current health state on a visual analog scale, 0 being worst imaginable health and 100 being best imaginable health. Furthermore, patients were asked to indicate how they experienced the severity of their PFPS problems at rest during the last week on a scale from 0 (no pain) to 10 (worst imaginable pain).

Statistical analyses were conducted with the statistical software programme SPSS for Windows version 15.0. In addition to descriptive statistics, tests for normal distribution of the total cost estimates were performed using the Kolmogorov–Smirnov test. Differences between the intervention and control group and between baseline and follow up scores were assessed by means of the independent sample T test (for variables showing a normal distribution), the Mann Whitney U test (for variables not normally distributed) or Pearson Chi-square test (for variable fractions). To adjust for multiple testing, one way analyses of variance with post hoc testing (type Bonferroni) was additionally performed for direct medical cost values. Using non parametric bootstrapping (drawing 2,500 observations at random from the available patient sample), the degree of uncertainty for costs and health effects and the cost-utility ratio was examined on the so-called CE-plane. In addition, an acceptability curve was generated to indicate the probability that the intervention has lower incremental costs per quality adjusted life year (QALY) gained than various thresholds for the maximum willingness to pay for an extra QALY.

11.4 RESULTS

A patient flowchart is provided in figure 11.1. A total of 163 patients consulted our HONEUR practices or sport medical advice centers during the year 2005, of which 16 did

not meet our inclusion criteria, 10 did not receive informed consent and 6 experienced diminished complaints. Thus, 131 patients were recruited, of which 65 in the intervention and 66 in the control group. For the intervention group, 100% of the questionnaires were returned at baseline, 86% after 6 weeks, 79% after 13 weeks, 83% after 26 weeks, 74% after 39 weeks and 83% after 52 weeks. For the control group, 100% of the questionnaires were returned at baseline, 91% after 6 weeks, 89% after 13 weeks, 78% after 26 weeks, 66% after 39 weeks and 88% after 52 weeks.

Figure 11.1: Patient flowchart

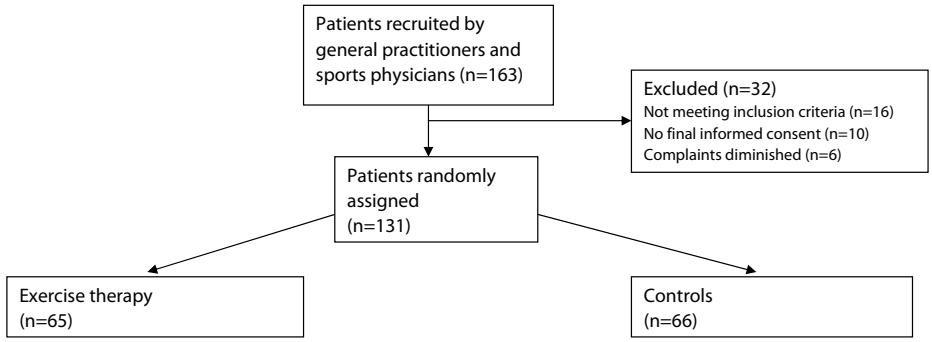


Table 11.1 presents the general characteristics at baseline of the patients in the two groups. Two thirds of the patients were females. Even though there were no significant differences between the groups, the mean age of the patients, the proportion of patients with paid work as their primary occupation, the number of working hours per week and the income per hour were slightly higher in the intervention group than in the control group.

Direct medical costs

Tables 11.2 and 11.3 provide a detailed summary of the medical consumption of both groups. Around 83% of all patients visited the general practitioner at baseline. For the intervention group, the shares of patients visiting the general practitioner went down to 25% at 6 weeks and to 6% at 13 weeks. For the control group, the percentages amounted to 20% and 14% respectively.

In the intervention group, the fraction of patients visiting a physiotherapist showed a fast increase to 88% at 6 weeks and a decrease from 13 weeks onwards to 26% at 39 weeks. The average number of visits was 4 per patient at 6 weeks and 2 at 13 weeks. At the other measurement moments, the number of visits per patient was around one. In

Table 11.1: General characteristics of the respondents at baseline

		Intervention group (n=65)	Control group (n=66)
Average age		24.7 (med 24.0; SD 8.6)	23.4 (med 22.0; SD 7.8)
Sex	Men	35.4%	36.4%
	Women	64.6%	63.6%
Body mass index (*)		23.2 (med 22.5; SD 3.9)	23.0 (med 22.8; SD 3.4)
Primary occupation	School	40.6%	45.5%
	Paid work	50.0%	42.4%
	Other	9.4%	12.1%
Paid work		70.8%	69.7%
Average hours of work per week		29.1 (med 34.0; SD 21.3)	24.8 (med 25.5; SD 17.5)
Average income per hour (Euro 2007)		15.35 (med 13.5; SD 10.8)	12.39 (med 12.8; SD 6.5)
Sports		76.6%	78.1%
Average hours of sports per week		4.9 (med 4.0; SD 3.5)	5.1 (med 4.0; SD 3.6)

med = median
SD = standard deviation
(*) Body mass index = weight / (length)^2

Table 11.2: Healthcare utilisation in 6 weeks for the intervention group, n = 65 (median)

		Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
General practitioner	Contact	83.3%	24.6%	6.2%	6.6%	3.1%	7.7%
	Mean	1.05 (1.0)	0.35 (0.0)	0.08 (0.0)	0.09 (0.0)	0.05 (0.0)	0.09 (0.0)
Sport physician	Contact	16.9%	4.7%	3.1%	1.5%	0.0%	1.5%
	Mean	0.28 (0.0)	0.05 (0.0)	0.12 (0.0)	0.02 (0.0)	0.00 (0.0)	0.02 (0.0)
Physiotherapist	Contact	3.1%	87.7%	58.5%	36.9%	26.2%	20.0%
	Mean	0.38 (0.0)	4.38 (4.0)	2.04 (0.0)	0.92 (0.0)	0.79 (0.0)	1.12 (0.0)
Medical specialist	Contact	3.1%	1.5%	1.5%	1.5%	3.1%	3.1%
	Mean	0.02 (0.0)	0.00 (0.0)	0.02 (0.0)	0.05 (0.0)	0.09 (0.0)	0.03 (0.0)
Company physician	Contact	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	Mean	0.02 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)
MRI / CT	Contact	0.0%	0.0%	0.0%	3.1%	3.1%	0.0%
	Mean	0.05 (0.0)	0.00 (0.0)	0.00 (0.0)	0.05 (0.0)	0.05 (0.0)	0.00 (0.0)
X-ray	Contact	6.2%	0.0%	3.1%	1.5%	1.5%	0.0%
	Mean	0.11 (0.0)	0.00 (0.0)	0.05 (0.0)	0.05 (0.0)	0.03 (0.0)	0.00 (0.0)
Medications		13.8%	6.2%	6.2%	7.7%	6.2%	4.6%
Prescription		7.7%	3.1%	1.5%	1.5%	3.1%	1.5%
Over the counter		6.2%	3.1%	4.6%	6.2%	3.1%	3.1%
Disposables		52.4%	56.6%	73.4%	67.2%	73.4%	71.9%

MRI = magnetic resonance imaging
CT = computed tomography

Table 11.3: Healthcare utilisation in 6 weeks for the control group, n = 66 (median)

		Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
General practitioner	Contact	84.4%	19.7%	13.6%	13.8%	9.1%	7.6%
	Mean	1.05 (1.0)	0.21 (0.0)	0.17 (0.0)	0.15 (0.0)	0.11 (0.0)	0.12 (0.0)
Sport physician	Contact	25.0%	3.0%	1.5%	1.5%	0.0%	1.5%
	Mean	0.18 (0.0)%	0.11 (0.0)	0.09 (0.0)	0.03 (0.0)	0.00 (0.0)	0.02 (0.0)
Physiotherapist	Contact	12.5%	16.7%	13.6%	13.6%	10.6%	3.0%
	Mean	0.03 (0.0)	0.55 (0.0)	0.61 (0.0)	0.92 (0.0)	0.52 (0.0)	0.55 (0.0)
Medical specialist	Contact	1.6%	0.0%	1.5%	4.5%	4.5%	1.5%
	Mean	0.05 (0.0)	0.00 (0.0)	0.02 (0.0)	0.06 (0.0)	0.06 (0.0)	0.05 (0.0)
Company physician	Contact	1.6%	1.5%	3.0%	3.1%	0.0%	1.5%
	Mean	0.00 (0.0)	0.03 (0.0)	0.05 (0.0)	0.05 (0.0)	0.00 (0.0)	0.02 (0.0)
MRI / CT	Contact	4.7%	0.0%	0.0%	1.5%	1.5%	3.0%
	Mean	0.00 (0.0)	0.00 (0.0)	0.00 (0.0)	0.02 (0.0)	0.02 (0.0)	0.03 (0.0)
X-ray	Contact	10.9%	6.1%	6.1%	7.7%	3.0%	3.0%
	Mean	0.06 (0.0)	0.06 (0.0)	0.06 (0.0)	0.09 (0.0)	0.03 (0.0)	0.05 (0.0)
Medications		10.6%	10.6%	9.1%	7.6%	10.6%	13.6%
Prescription		1.5%	1.5%	3.0%	4.5%	3.0%	6.1%
Over the counter		9.1%	9.1%	6.1%	3.0%	7.6%	7.6%
Disposables		50.0%	62.1%	59.1%	60.6%	60.6%	60.6%

MRI = magnetic resonance imaging
CT = computed tomography

the control group, the fraction of patients visiting a physiotherapist showed a more or less continuous pattern of around 13% during the entire follow up. The average number of visits was always lower than one per patient, caused by a few patients with a relatively high number of visits.

Medication was used by about 6% of the patients in the intervention group and 11% in the control group during follow up. In both groups, one third of the medications was prescribed by a physician. The medications most frequently used were paracetamol, naproxen, nurofen, diclofenac, glucosamine and tramadol.

A summary of the direct medical costs per 6 weeks is given in table 11.4. The unit costs of medical consumption are shown in tables 11.5 and 11.6. At 6 and 13 weeks the medical costs per patient were higher for the intervention group than for the control group (Mann Whitney U test: $P6 < 0.001$; $P13 = 0.023$), which coincided with higher costs for physiotherapy ($P6 < 0.001$; $P13 < 0.001$). At 6 weeks, the costs for X-rays were significantly lower for the intervention group than for the control group ($P6 < 0.045$). No significant cost differences for any of the other cost components (visits to healthcare

providers, medical imaging services, medications and disposables) were found 26, 39 and 52 weeks after randomisation.

Annual direct medical costs for both the intervention and the control group are presented in table 11.7. The direct medical cost estimates for the intervention and control group were € 434 (SD 786) and € 299 (SD 732) respectively (Mann Whitney U test: $P <$

Table 11.4: Mean direct medical costs per respondent for the past 6 weeks per measurement moment (Euro 2007) (median)

	Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks	One year
Intervention group							
General practitioner	15 (15)	5 (0)	1 (0)	1 (0)	1 (0)	1 (0)	**13**
Sport physician	16 (0)	3 (0)	7 (0)	1 (0)	0 (0)	1 (0)	**16**
Physiotherapist	9 (0)	100 (91)	47 (23)	21 (0)	18 (0)	26 (0)	**296**
Medical specialist	1 (0)	0 (0)	1 (0)	3 (0)	5 (0)	2 (0)	**23**
Company physician	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**0**
MRI / CT	12 (0)	0 (0)	0 (0)	12 (0)	12 (0)	0 (0)	**52**
X-ray	5 (0)	0 (0)	2 (0)	2 (0)	1 (0)	0 (0)	**9**
Medications	2 (0)	2 (0)	1 (0)	0 (0)	1 (0)	1 (0)	**8**
Disposables	2 (0)	2 (0)	2 (0)	2 (0)	2 (0)	2 (0)	**17**
Total	63 (24)	112 (114)	61 (46)	43 (4)	41 (3)	32 (3)	**434**
SD	96	68	87	119	142	104	
25 percentile	15	49	3	0	0	0	
75 percentile	74	162	76	46	16	11	
Control group							
General practitioner	15 (15)	3 (0)	2 (0)	2 (0)	2 (0)	2 (0)	**18**
Sport physician	11 (0)	6 (0)	5 (0)	2 (0)	0 (0)	1 (0)	**18**
Physiotherapist	1 (0)	12 (0)	14 (0)	21 (0)	12 (0)	12 (0)	**126**
Medical specialist	3 (0)	0 (0)	1 (0)	4 (0)	4 (0)	3 (0)	**25**
Company physician	0 (0)	2 (0)	3 (0)	3 (0)	0 (0)	1 (0)	**14**
MRI / CT	0 (0)	0 (0)	0 (0)	4 (0)	4 (0)	8 (0)	**35**
X-ray	3 (0)	3 (0)	3 (0)	4 (0)	1 (0)	2 (0)	**22**
Medications	2 (0)	1 (0)	1 (0)	3 (0)	3 (0)	3 (0)	**22**
Disposables	2 (1)	2 (1)	2 (1)	2 (1)	2 (1)	2 (1)	**17**
Total	37 (17)	30 (4)	32 (4)	45 (3)	28 (3)	34 (1)	**299**
SD	38	62	76	108	92	158	
25 percentile	15	0	0	0	0	0	
75 percentile	55	25	20	15	13	8	

MRI = magnetic resonance imaging
CT = computer tomography
SD = standard deviation

Table 11.5: Unit costs of health care utilisation (Euro 2007)

General practitioner (one visit)	14.77
Sport physician (one visit)	59.20
Physiotherapist costs (one visit)	22.86
Medical specialist (one visit)	59.20
Company physician (one visit)	59.20
MRI / CT	263.00
X-ray	47.20
Paracetamol (500 mg)	0.04
Naproxen (250 mg)	0.16
Nurofen (200 mg)	0.10
Diclofenac (25 mg)	0.13
Glucosamine (400 mg)	0.22
Tramadol (100 mg)	0.32
Cold compress	2.00
Hot compress	2.00
Orthopaedic insoles	150.00
Elastic bandage	30.00
Brace	60.00
Tape	5.00

MRI = magnetic resonance imaging
CT = computed tomography
Mg = milligram

Table 11.6: Resource use and unit costs of the general practitioner and physiotherapist

	General practitioner		Physiotherapist	
	Mean	**SD**	**Mean**	**SD**
LABOUR				
General practitioner / physiotherapist	**9.67**	**0.81**	**20.08**	**13.39**
Resource use (minutes)	10.33	0.87	45.00	30.00
Unit costs (Euro 2007 per minute)	0.94	0.00	0.45	0.45
Assistant	**1.24**	**1.97**		
Resource use (minutes)	3.44	5.47		
Unit costs (Euro 2007 per minute)	0.36	0.00		
OVERHEADS	**3.86**	**0.71**	**2.78**	**2.28**
Marginal mark-up percentage	36%	5%	14%	40%
TOTAL	**14.77**	**2.87**	**22.86**	**16.70**

SD = standard deviation

0.001). When multiple testing is not taken into account, the annual costs of visits to the physiotherapist ($P < 0.001$) and X-rays ($P = 0.007$) were significantly different. Using one way analyses of variance with post hoc testing, the *P*-value is no longer significant. No significant differences were found for any of the other cost components.

Table 11.7: Annual direct medical costs with descriptive statistics (Euro 2007)

	Mean number of visits per patient year	Mean costs per patient	Median costs per patient	SD	Mann-Whitney U Asymp. Sig. (2-tailed)
Intervention group					
General practitioner	0.94	13.94	0.00	38.23	-
Sport physician	0.26	15.18	0.00	69.38	-
Physiotherapist	12.94	295.74	205.74	334.83	-
Medical specialist	0.38	22.77	0.00	121.79	-
Company physician	0.00	0.00	0.00	0.00	-
MRI / CT	0.20	52.60	0.00	314.10	-
X-ray	0.22	10.41	0.00	60.49	-
Medications	-	7.52	0.00	25.63	-
Disposables	-	15.77	0.00	22.79	
Total	-	433.92	228.60	786.01	-
Control group					
General practitioner	0.60	18.13	0.00	40.56	0.442
Sport physician	0.31	18.39	0.00	81.07	0.737
Physiotherapist	5.52	126.19	0.00	385.58	0.000
Medical specialist	0.38	22.42	0.00	107.23	0.728
Company physician	0.21	12.71	0.00	68.83	0.083
MRI / CT	0.13	34.54	0.00	169.59	0.688
X-ray	0.49	23.24	0.00	66.31	0.007
Medications	-	22.89	0.00	81.43	0.106
Disposables	-	20.90	7.50	27.83	0.256
Total	-	299.41	58.59	732.46	0.000

SD = standard deviation
Asymp. Sig. = asymptomatic significance
MRI = magnetic resonance imaging
CT = computer tomography

Productivity costs

Absence from paid work

Table 11.8 presents the productivity costs per 6 weeks due to absence from paid work. Patients in the intervention group were slightly, but not significantly, more absent from paid work in comparison to the control group. In both groups, the highest absence from work was observed at 6 weeks (15% and 17%), with a decrease up until 39 weeks (5% and 12%). At 52 weeks, 9% of the patients in the intervention and 4% of the patients in the control groups were absent from work.

The annual costs due to absence from paid work per patient were € 72 (SD 269) and € 113 (SD 349) for the intervention and control group respectively (Mann Whitney U test: $P = 0.729$).

Table 11.8: Productivity costs due to absence from paid work in the past 6 weeks per measurement moment (Euro 2007)

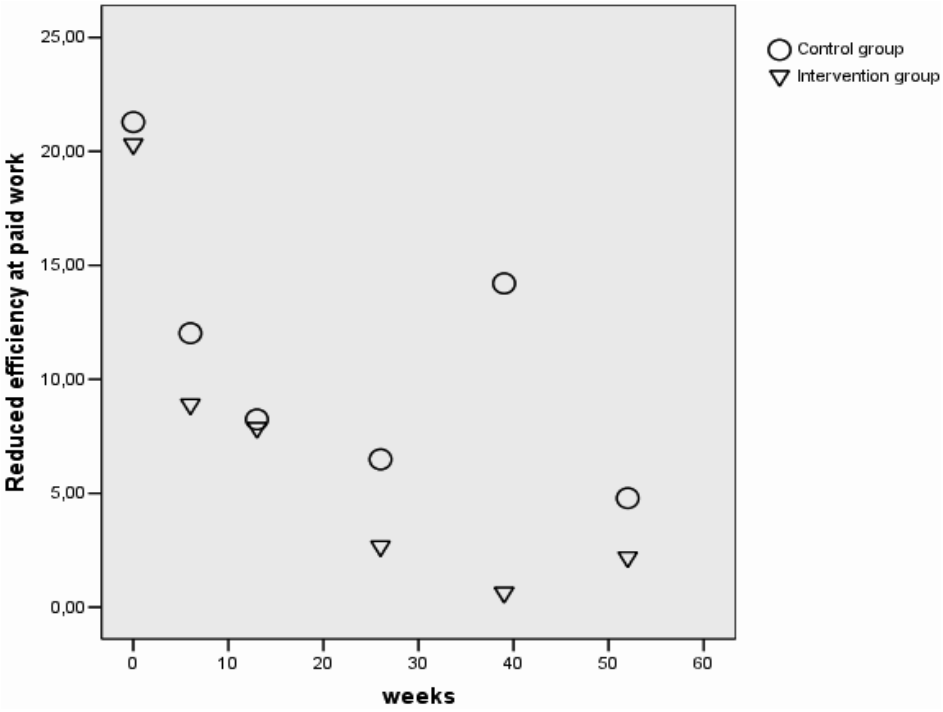
	Baseline	6 weeks	13 weeks	26 weeks	39 weeks	52 weeks
Intervention group						
Number of respondents with a paid job	45	40	42	44	44	46
Share of respondents absent	11%	15%	7%	5%	5%	9%
Number of days absent, mean (SD)	3.8 (1.3)	6.5 (1.2)	1.0 (*)	1.0 (*)	1.0 (*)	1.6 (0.3)
Costs due to absence from work, mean (SD)						
Per respondent with a paid job	37.61 (113.12)	86.84 (212.60)	6.36 (23.22)	4.05 (18.77)	4.05 (18.77)	12.59 (41.63)
Per respondent	26.03 (95.41)	53.44 (171.34)	4.11 (18.83)	2.74 (15.50)	2.74 (15.50)	8.91 (35.38)
Control group						
Number of respondents with a paid job	45	46	44	43	42	49
Share of respondents absent	11%	17%	14%	12%	12%	4%
Number of days absent, mean (SD)	1.5 (1.0)	7.8 (4.7)	1.0 (*)	1.0 (*)	1.9 (2.3)	1.3 (0.4)
Costs due to absence from work, mean (SD)						
Per respondent with a paid job	23.75 (89.87)	121.01 (312.91)	12.15 (30.92)	10.36 (28.89)	23.33 (98.47)	4.54 (22.72)
Per respondent	16.19 (74.78)	84.34 (266.32)	8.10 (25.80)	6.75 (23.70)	14.84 (79.00)	3.37 (19.62)

SD = standard deviation
* = not available

Reduced efficiency at paid work

Figure 11.2 shows the scores on reduced efficiency at paid work for the intervention and the control group over time. The efficiency loss during paid work in terms of hours lost was lower in the intervention in comparison to the control group at baseline and during follow up. Seventy-nine % of the patients in the intervention group and 71% in the control group indicated that the reduced efficiency was caused by PFPS problems. The efficiency loss for both groups was highest at baseline (21% and 20%) and lowest at 52 weeks (5% and 2%), with a continuous decrease from 6 weeks onwards. The intervention group had a peak (14%), whereas the control group had a small dip (1%) in efficiency loss at 39 weeks. However, the differences between both groups were never significantly different (Pearson Chi-square test: $P > 0.206$).

Figure 11.2: Reduced efficiency at paid work for the intervention and the control group as measured by the visual analogue scale (in %)



The annual costs due to reduced efficiency at paid work were € 473 (SD 2,371) and € 648 (SD 2,066) for the intervention and control group respectively (Mann Whitney U test: $P = 0.223$).

Reduced efficiency at unpaid work

At baseline about 3% of the patients in the intervention group and 10% of the patients in the control group had housekeeping tasks taken over (Pearson Chi-square test: P = 0.090). These fractions remained stable during follow up and were significantly different only at 6 weeks (P = 0.025). Virtually all hours were taken over by family members. None of the patients made use of paid aid.

The annual costs of taking over housekeeping tasks were € 32 (SD 251) and € 105 (SD 529) for the intervention and control group respectively (Mann Whitney U test: P = 0.228).

Quality of life

Figure 11.3 shows the scores on the EQ-5D over time for the intervention and the control group. The quality of life scores on the EQ-5D were never significantly different between the intervention and the control group. However, the quality of life for both groups was lowest at baseline and highest at 52 weeks, with a slight increase in quality of life from 13 weeks onwards. The scores on the EQ-5D at baseline were 0.8191 (SD = 0.1422) in the intervention group and 0.8073 (SD = 0.1706) in the control group. At 52 weeks the scores were respectively 0.8973 (SD = 0.1719) and 0.8812 (SD = 0.2046). The intervention group had a small dip in quality of life score at 6 weeks, 0.8223 (SD = 0.1571), compared to the control group, 0.8609 (SD = 0.1249; P = 0.121). The intervention group had a peak quality of life score at 39 weeks, 0.8632 (SD = 0.1967), compared to the control group, 0.8287 (SD = 0.2194; P = 0.346).

Inspecting each EQ-5D dimension, the intervention group only had significantly less problems on activity at 26 weeks (Pearson Chi-square test: P = 0.019) and only significantly more problems on mobility at 39 weeks (P < 0.022).

The EQ-5D VAS scores on the current health state and the severity of PFPS problems at rest are shown in figures 11.4 and 11.5 for the intervention and the control group over time. During follow up, the intervention group experienced slightly higher current health, albeit not significant (P > 0.099). For both groups, the current health state was virtually lowest at baseline (78.62 versus 79.95) and highest at 52 weeks (84.03 versus 83.62), with a slight increase from 6 weeks onwards. The intervention group experienced a lower severity of their PFPS problems during treatment follow up (P < 0.042). The severity was highest at baseline (4.14 versus 4.03) and lowest at 52 weeks (0.302 versus 0.358), with a continuous decrease from baseline onwards.

Figure 11.3: Quality of life (utility values) for the intervention and the control group as measured by the EO-5D

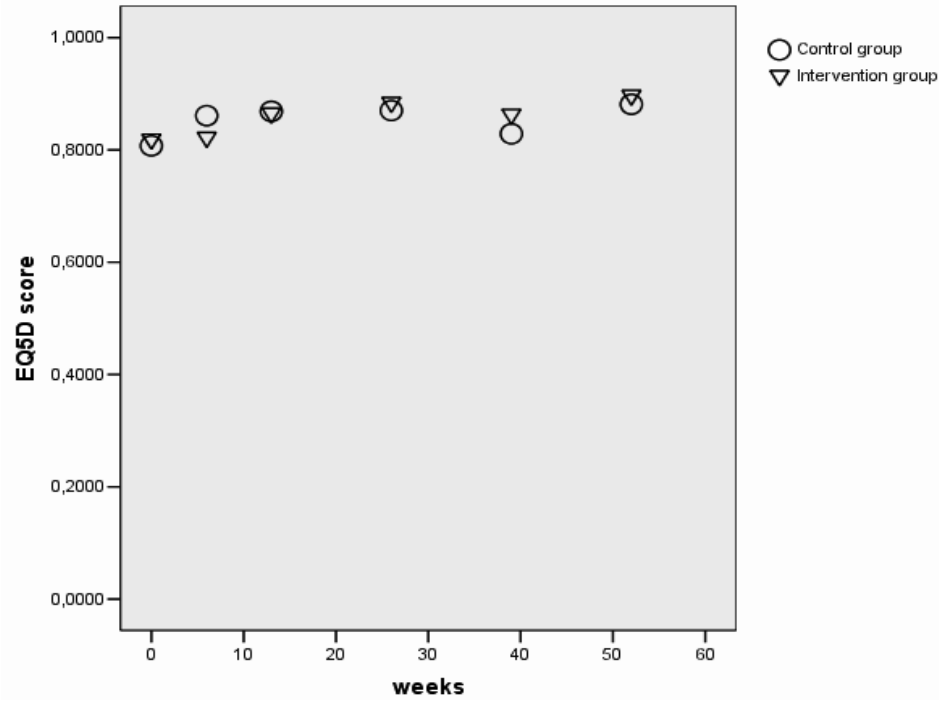


Figure 11.4: Current health state for the intervention and the control group as measured by the EUROQOL visual analogue scale

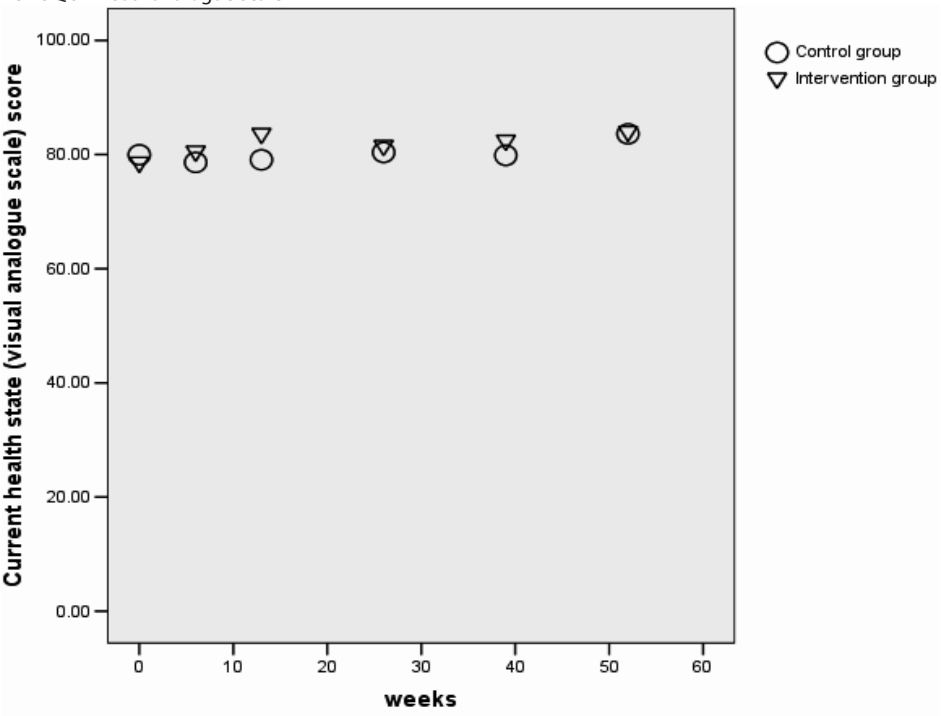
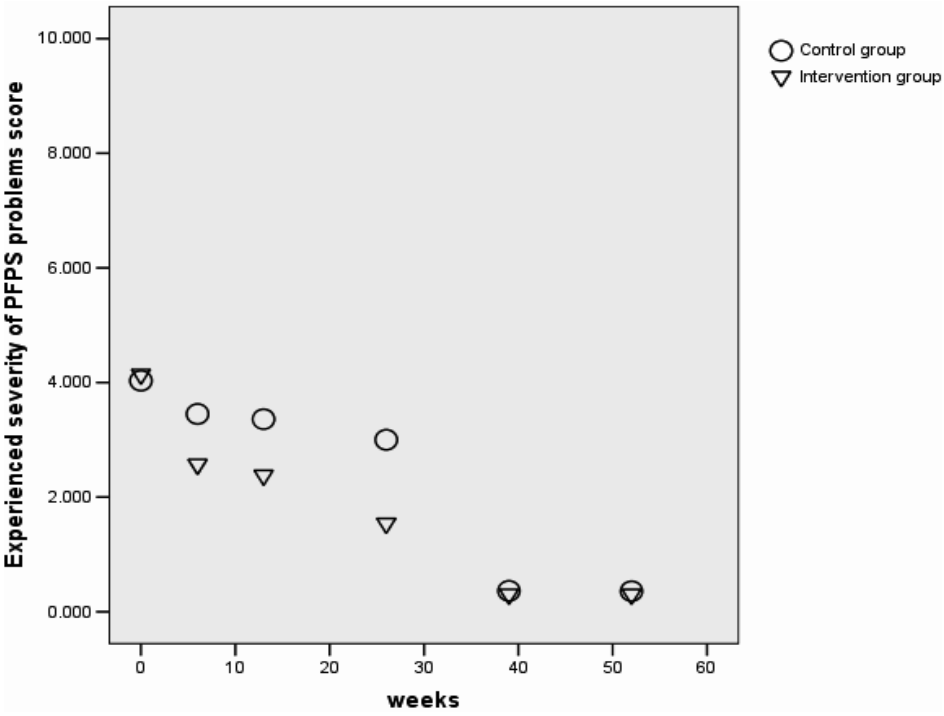


Figure 11.5: Severity of PFPS problems in rest in the past week for the intervention and the control group measured on a scale from 0 (no pain) to 10 (worst imaginable pain)



Cost effectiveness

Table 11.9 provides the total annual costs and quality of life per patient in the intervention and control group. The total annual costs per patient were € 155 lower for the intervention group compared to the control group (€ 1,011 versus € 1.166; Mann Whitney U test: $P = 0.030$). Furthermore, an average patient gained 0.0105 QALY due to the intervention (independent sample T test: $P = 0.666$), which resulted in a societal average CE-ratio of - € 14,738 per QALY. However, the variance around this CE-ratio was substantial. Using non parametric bootstrapping (2,500 draws), the simulated 95% confidence interval for the CE-ratio ranged from - € 210,206 to + € 178,822. The CE-plane (figure 11.6) showed that the intervention was dominant in 52% of the cases (positive health effects and cost savings) and for 14% it was inferior. The probability that the intervention had positive health effects was about 70%, the probability for cost savings was about 68%. The acceptability curve showed a probability of 73% that the cost per QALY were lower than € 20,000.

When only direct medical costs were included, average incremental costs per patient were € 135 and the average cost per QALY € 12,754. The bootstrapped confidence interval

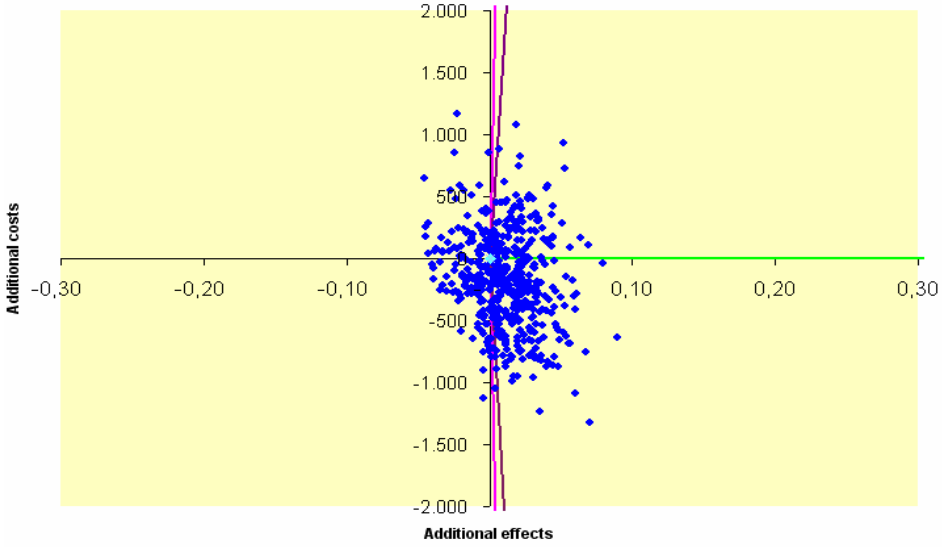
for the CE-ratio was again wide, ranging from - € 114,042 to + € 122,151. The probability for cost savings was about 17%. The acceptability curve showed a probability of 57% that the cost per QALY was lower than € 20,000 and 66% that it was lower than € 80,000.

Table 11.9: The total annual costs and quality of life per respondent in the intervention and the control group (Euro 2007) (SD)

	Intervention group	Control group	Incremental	Mann-Whitney U Asymp. Sig. (2-tailed)
Direct medical costs	434 (786)	299 (732)	135	0.000
Productivity costs	577 (2,384)	867 (2,192)	-290	0.113
Absence from paid work	72 (269)	113 (349)	-41	0.729
Reduced efficiency at paid work	473 (2,371)	648 (2,066)	-175	0.223
Reduced efficiency at unpaid work	32 (251)	105 (529)	-73	0.228
TOTAL COSTS	1,011 (2,453)	1,166 (2,462)	-155	0.030
Quality of life (QALY)	0.8722 (0.1413)	0.8617 (0.1381)	0.0105	0.533

SD = standard deviation
Asymp. Sig. = asymptomatic significance
QALY = quality adjusted life years

Figure 11.6: CE-plane which examined the degree of uncertainty for costs and health effects and the cost-utility ratio



11.5 DISCUSSION

This is the first economic evaluation on exercise therapy in adolescents and young adults with PFPS. The annual direct medical costs per patient were significantly higher for the intervention group (€ 434; SD 786) compared to the control group (€ 299; SD 732) mainly caused by additional physiotherapy visits. Productivity costs amounted to € 577 (SD 2,384) and € 867 (SD 2,192) for the two groups respectively, even though the difference in productivity cost between the two groups was not significant. From the societal perspective, the annual total costs per patient were significantly lower for the intervention group (€ 1,011) compared to the control group (€ 1,166) (borderline significance when taking into account multiple testing). This finding confirms that the inclusion of productivity costs considerably affects the total costs and the CE-ratio.

Economic evaluations are preferably determined from a societal perspective in which all relevant costs are included (Drummond 2005). Our results suggest that productivity costs are the most important cost component, even more so than direct medical costs. Particularly costs which occurred due to reduced efficiency at paid work were substantial. The latter result reinforces the conclusions of earlier studies in e.g. low back pain that productivity losses are significant despite the relatively young (working) patient sample (Hoeijenbos et al. 2005).

Quality of life appears to correlate well with the health state and experienced severity of PFPS problems. Exercise therapy resulted in a significant lower experienced severity, especially at 6, 13 and 26 weeks (figures 11.4 and 11.5). This finding is in agreement with that of Timm (1998), who concluded that exercise therapy almost halves the pain-scores and drastically improves functional ability after 4 weeks (Timm 1998). In contrast, the randomised controlled trial carried out by Clark et al. (2000) concluded that exercise therapy resulted in significantly greater pain reduction only after 52 weeks (Clark et al. 2000). Other randomised studies that compared exercise therapy with non-exercise therapy in PFPS studied outcomes after exercise therapy versus brace treatment (Lun et al. 2005), or studied the effect of multi-modal physiotherapy including exercises (Collins et al. 2008; Crossley et al. 2002) and are therefore not directly compare to the present study.

Regarding the expected time period, it is very speculative whether continued exercise therapy would raise health effects and improve cost effectiveness. This should be subject of another study. However, it can be concluded that when the positive health effects of the current exercise therapy would sustain in the longer run, with low or zero medical costs, the cost effectiveness will improve.

Although our study excluded patients with clearly defined other anterior knee pain syndromes than PFPS, all different entities within PFPS were included (e.g. maltracking problem, strength problem, bone abnormality). Possibly the results would be different in certain sub-entities of PFPS, but subgroup analysis could not be performed for such sub-entities as they were not defined in our study. However, given the fact that diagnoses of such sub-entities is hardly feasible in primary care settings, the results presented here apply to the whole group of PFPS and are relevant for the primary care setting.

Resource use of medical imaging services which were used to exclude patients with other diagnoses than PFPS were not incorporated in the direct medical costs because they took place prior to enrolment. Even though the physician's preference in using imaging studies or braces may be important to explain differences between patients in general, it does not explain the difference between the patients of our intervention and control group because the indications for the imaging studies of PFPS patients in the intervention group did not differ from those in the control group.

Remarkably, eight patients in the intervention group reported to have visited the physiotherapist zero times. In these cases, the number of visits as provided by the physiotherapist was used in the cost calculations. Additionally, only 14% of the patients reported exactly the same number of physiotherapy visits as the physiotherapist. Of the remaining patients, 47% reported less and 39% more visits per year than the physiotherapist. The average numbers of visits per year were 7.9 and 7.4 according to the patients and physiotherapists respectively, which was slightly lower than the projected 9.0 visits. Even though the use of two independent sources for the cost calculation generally provokes inconsistency, it takes advantage of more accurate and complete data.

Furthermore, only 88% of the patients in the intervention group visited a physiotherapist at 6 weeks. This implies that at least some of the intervention patients did not meet the terms of the standardised exercise program they were appointed to. However, these patients were not excluded from the analyses because our study was set up on an intention to treat basis which more accurately reflects reality.

This study has several limitations. Direct medical unit costs are ideally based on the microcosting methodology. Because all relevant cost components are identified at the most detailed level, the microcosting methodology provides cost estimations that most accurately reflect actual costs. As this methodology is time consuming, especially when administrative information systems are absent or inadequate, it has not been widely used in economic evaluations. Therefore, we restricted the use of microcosting estimates to visits to the general practitioner and physiotherapist. Compared to Dutch

reference unit prices, the use of microcosting estimates did likely not result in different conclusions regarding the relative costs of exercise therapy and 'usual care' (Oostenbrink, Koopmanschap 2002). The resource use of visits to the general practitioner was virtually equal between the exercise therapy and 'usual care' groups. The difference between the microcosting estimate and reference unit price was negligible for visits to the physiotherapist, particularly when productivity costs were considered. Dutch reference unit prices were used as a proxy to the other medical unit costs.

Another limitation of our study concerned the inclusion of only a small number of patients, although special attention was paid to selecting representative practices and sport medical advice centers. The variance in quality of life between patients was limited, but the variance for all cost categories was substantial (table 11.9). This resulted in wide confidence intervals for the CE-ratio's, implying considerable uncertainty for decision makers whether to adopt exercise therapy. Our uncertainty analysis indicated that there is a probability of 70% that exercise therapy produces positive health effects, 73% that the cost per QALY gained is lower than € 20,000 and 68% that exercise therapy saves societal costs. Whether these results are sufficiently acceptable to use exercise therapy instead of the conservative strategy is up to the decision maker (e.g. policy maker, general practitioner or patient).

During the course of our study we faced some other methodological challenges. We applied a naive method to deal with missing observations (LOCF) compared to, for instance, multiple imputation (Oostenbrink et al. 2003). However, the influence of the imputation method was limited as the number of missings was small. The variable 'income' had the lowest response rate (71%). As a result, the average net value added per employee (€ 89.06) was based on a limited number of responses. With respect to absence from paid work, we had many missing data on the duration of absence. Therefore, we imputed values for the missing data based on the overall average duration of absence per measurement moment.

This study was conducted in the Netherlands. However we believe that our resource use findings could be representative of other countries, especially those in which the general practitioner operates as the gatekeeper of health care.

Clinical guidelines of the Dutch College of General Practice recommend a conservative treatment for PFPS (Cirkel, Klaassen 1998). However, with a CE-ratio of - € 14,738 per QALY, our study revealed a considerable probability that exercise therapy is cost saving or cost effective as compared to the conservative strategy. Although there seems to be a rationale to question the current guidelines, an efficient policy concerning phys-

iotherapy requires treatment consensus and an optimal interaction with other health providers such as general practitioners and medical specialists. Therefore, future studies should investigate the possibilities to further implement this exercise therapy.

11.6 ACKNOWLEDGEMENTS

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Chapter 12

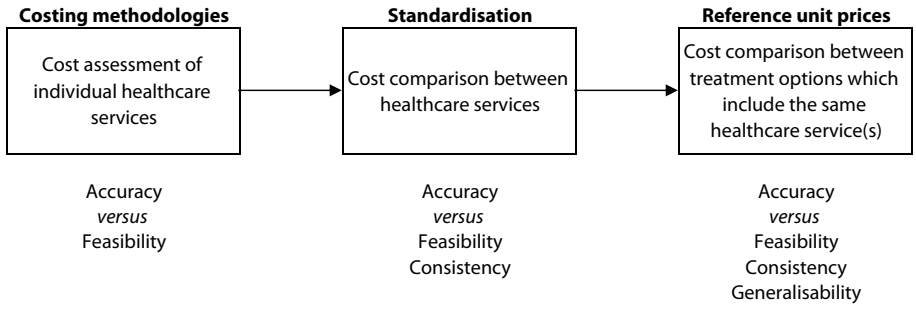
General discussion

The introduction of this thesis has defined four criteria for evaluating costing methodologies: accuracy, feasibility, consistency and generalisability (chapter 1). The relative importance of the different criteria obviously varies with the decision context and with the magnitude and dispersion in the cost components (Jackson 2000; Johnston et al. 1999). In some decision contexts, a cost estimate can be very imprecise without seriously affecting the decision. Even though bottom up microcosting is considered to be the gold standard methodology in economic evaluations, it may not be the best costing methodology to support budgetary decisions or in payment policy in which knowing the specific accurate cost of each healthcare service is relatively irrelevant (Johnston, Buxton 1999). Almost inevitably, the need to understand the costs of healthcare services arises in the context of a practical decision at the clinical or policy level and this decision context shapes the costing methodology which is most relevant (Jackson 2000).

Previous chapters aimed to determine and compare the costs of individual healthcare services, reaching healthcare service specific conclusions. This chapter will discuss general methodological conclusions regarding the application of the microcosting methodology for the cost assessment of individual healthcare services (section 12.1 and 12.2), for the cost comparison between healthcare services (section 12.3) and for the cost comparison between treatment options (section 12.4). Figure 12.1 presents the outline of this general discussion.

The hospital setting may be the most complex setting for the cost calculation of healthcare services, because its healthcare services comprise various cost components which resource use and unit costs are not always easy to reveal (as will be discussed below). As most of the chapters in this thesis refer to the hospital setting, the recommendations regarding the application of the microcosting methodology may also apply to other relatively straightforward settings, such as primary care and mental health, which predominantly exploit the cost component labour.

Figure 12.1: Outline of the general discussion



12.1 COSTING METHODOLOGIES

This thesis has confirmed that bottom up microcosting provides the most precise and fine-grained estimates of the costs of care for an identified group of patients. However, chapter 2 quantified the cost differences resulting from the two approaches and concluded that top down microcosting may be a strong alternative to bottom up microcosting. Total cost estimates using bottom up and top down microcosting were not significantly different for normal delivery, stroke and acute myocardial infarction.

Moreover, top down microcosting was proven to be more feasible. Because of its time consuming data collection, none of the studies in this thesis applied the bottom up approach in all individual cost components. Nevertheless, the bottom up microcosting methodology was used for all cost components except 'disposables' in the cost calculation of intensive care unit days (chapter 5) and for all cost components with the exception of 'disposables' and 'labour' in the cost assessment of microsurgery and neurosurgery in meningioma patients (chapter 9). These two chapters provide indications on the preferred costing methodology for individual cost components and illustrated the obstacles faced in conducting bottom up microcosting.

Inpatient stay
In healthcare services with a relatively long length of stay (such as stroke; chapter 2), bottom up microcosting was particularly recommendable compared with top down microcosting for 'inpatient stay'. Information on the resource use of inpatient days was structurally available in the hospital information systems. Thus, the application of the bottom up approach appeared to be accurate as well as feasible for 'inpatient days'.

Labour
Bottom up microcosting was also especially recommendable compared with top down microcosting for 'labour' in healthcare services which are labour intensive (such as normal delivery; chapter 2). This finding is in agreement with the results of Wordsworth et al. (2005), who compared cost estimates of a top down and bottom up microcosting methodology in dialysis therapy in end-stage renal disease. Wordsworth et al. (2005) found slightly poorer total cost estimates for healthcare services with a large component of 'labour'. However, whilst the bottom up approach was able to provide the most accurate cost estimates for 'labour', the time consuming data collection made its application hardly feasible. Chapter 5 illustrated the poor feasibility when applying bottom up microcosting in 'labour'. Information on the resource use of labour was not available at any of the healthcare providers. In order to attain information on direct labour minutes, 32 intensive care unit beds at one healthcare provider were permanently monitored

by research students for 21 days (24/7) to score each minute of medical specialists' and consulting specialists' time. This lengthy and expensive procedure restricted the data collection to 32*21 bed days which equalled 20% of the patient sample. Jackson (2000) has suggested that recording of staff time may make cost estimates flawed by low response rate or incomplete recording of information and that the collection effort may entail delays affecting the lengthiness of the costing study.

Diagnostic procedures and consumables

Fairly accurate total cost estimates were obtained when the bottom up microcosting estimates of 'diagnostic procedures', 'medications' and disposables' were either individually or simultaneously replaced by top down microcosting estimates (chapter 2). In chapter 5 and 9, resource use data on 'diagnostic procedures', 'medications' and disposables' per individual patient was available from hospital information systems of most healthcare providers. However, where the cost component 'inpatient stay' only records the cost item 'inpatient days' (either or not stratified to medical specialty), the cost components 'diagnostic procedures', 'medications' and disposables' comprise a wide variety of numerous cost items. For example, for the cost assessment of intensive care unit days (chapter 5), 202 cost items were recorded for 'diagnostic procedures' and 3,547 cost items for 'medications'. Because the systems were designed for other purposes than cost calculation, information systems containing resource use information were without exception incompatible with systems containing unit costs. Therefore, information from the systems needed to be hand matched. This obstacle was present to a greater extent in chapter 5, which included 576 patients with relatively complex resource use, compared with chapter 9, which included only 59 patients whose resource use was relatively straightforward. Thus, with respect to feasibility, top down microcosting may be preferred over bottom up microcosting for the cost components 'diagnostic procedures', 'medications' and disposables' in studies including a relatively great patient sample or with a rather complex resource use. Of course, other factors also play a role in the choice which methodology to use, such as decision-context, the sensitivity of de decision to estimation errors and the availability of time and data (see also section 12.3). These factors may be decisive in case of borderline magnitude sample sizes.

Table 12.1 summarises the recommended costing methodology per cost component based on accuracy and feasibility.

The advantages of restricting the use of bottom up microcosting to key cost components are that it limits the data collection effort, reduces the likelihood of the accuracy of the data being affected and may reduce research expenditure. The aim would be to minimise data collection while maximising the ability to measure the difference in costs

between patients (Johnston, Buxton 1999). Chapter 2 has demonstrated that fairly accurate total cost estimates are obtained when the cost components of the bottom up microcosting are *individually* or *simultaneously* replaced by the cost components of top down microcosting.

Table 12.1: Recommended costing methodology per cost component for the cost assessment of healthcare services

Cost component	Recommended methodology	
	Bottom up microcosting	**Top down microcosting**
Inpatient days	Especially for healthcare services with a relatively long length of stay	Only when patient level resource use data is not available
Labour	Only for labour intensive healthcare services and only in studies including a small patient sample or with rather straightforward resource use	Especially for labour indigent healthcare services and in studies including a great patient sample or with rather complex resource use
Diagnostic procedures and consumables	Only in studies including a small patient sample or with rather straightforward resource use	Especially in studies including a great patient sample or with rather complex resource use

Gross costing

Chapter 2 additionally explored the accuracy of gross costing and confirmed that gross costing may be weak alternative to microcosting. This is in agreement with the study of Whynes & Walker (1995), who compared microcosting estimates with gross costing estimates for the treatment of colon cancer. Therefore, gross costing should only be considered for economic evaluations when the cost calculation aims to provide a cost estimate short term or when data is not available. Swindle et al. (1999), who investigated the need to combine gross costing with microcosting to reflect resource use variations that are essential to healthcare services, concluded that microcosting should be applied in healthcare services that are likely to show wide cost variation between patients. Either way, gross costing estimates should always be interpreted with caution because its inaccuracy is sensitive to wrong conclusions (Clement Nee Shrive et al. 2009; Swindle et al. 1999).

12.2 REIMBURSEMENT FEES

Reimbursement fees were also confirmed to be a weak alternative to serve as a proxy to actual costs of healthcare services. Two studies of this thesis compared top down microcosting estimates with reimbursement fees and found a weak positive linear relationship between microcosting estimates and reimbursement fees. For dental filling procedures, microcosting estimates of nine European countries were generally higher than reimbursement fees (chapter 7). Similarly, microcosting estimates were generally higher for diagnostic tests for the detection of coronary artery disease in the Netherlands (chapter 8). These results are similar to those of Heerey et al. (2002) who compared the available microcosting and reimbursement fees of diagnostic related groups (DRGs) representing acute myocardial infarction, heart failure and human immunodeficiency virus at one healthcare provider in Ireland.

Chapter 8 additionally determined whether the noted cost differences impacted the outcome of an economic evaluation. The use of microcosting estimates instead of reimbursement fees led to different conclusions regarding the relative cost effectiveness of alternative strategies. Contrary to our conclusion, Chumney et al. (2004), whose study was carried out in the United States, found no significant difference in the resulting cost effectiveness ratio when using the different costing approaches and concluded that, the costing approach has little effect on the outcome of a decision model in heterogeneous conditions.

The availability of reimbursement fees facilitates their use in economic evaluations, but reimbursement fees, particularly for healthcare services with high treatment costs, may not always be an accurate reflection of actual costs. For the Netherlands, table 12.2 presents the comparison between top down estimates and reimbursement fees of some healthcare services dealt with in this thesis. Half of the healthcare services incur costs in excess of reimbursement, most of which are the diagnostic tests for the detection of coronary artery disease (chapter 8). Amongst healthcare services that incurred costs below reimbursement levels, the mean level of 'profit' was € 1,229 (range: € 25 for stroke to € 2,984 for acute myocardial infarction). These findings suggest that the reimbursement fees used in the respective studies do not reflect actual costs in the Netherlands.

In 2005, a DRG-like case-mix system based on 'diagnosis treatment combinations' (DBCs) was introduced in the Netherlands. The DBC system distinguishes treatment options with fixed fees (list A DBCs) and treatment options with negotiable fees (list B DBCs) (Oostenbrink & Rutten 2006). In 2008, list A DBCs covered 80% of the hospital budgets and their reimbursement fees were based on actual costs. Each list A DBC includes all

relevant healthcare services, such as inpatient days, outpatient visits, surgical interventions, medical interventions, medical imaging, laboratory services and medications (Beersen et al. 2004). Resource use of these healthcare services are provided by 23 volunteering front-runner (general) hospitals. Unit costs of these healthcare services are determined from a variety of approaches to microcosting or gross costing by the Dutch Healthcare Authority (Oostenbrink & Rutten 2006).

Resource use and unit costs of the healthcare services at the 23 front-runner hospitals are collected in a national database which is controlled and maintained by DBC Onderhoud and used to determine national reimbursement fees for list A DBCs. This national database may serve as an important data source for the conduct of future economic evaluations. Although the national reimbursement fees are publicly available, at present, limited actors have access to the detailed resource use and unit cost information of healthcare services included in list A DBCs. Besides, upcoding and cream skimming have been described as a potential risk to undermine the relationship between reimbursement fees and actual costs (Steinbusch et al. 2007).

The reimbursement fees used in this thesis originate from the time in which the new reimbursement system was still under development. Future studies, such as the EU funded research project EuroDRG (full title: Diagnosis-Related Groups in Europe: towards Efficiency and Quality, January 2009—December 2011), need to determine the extent to which the reimbursement fees of the DBC case mix system reflect actual costs and can be used as reference unit prices for economic evaluations (Oostenbrink & Rutten 2006).

Table 12.2: Comparison between the top down microcosting estimate and Dutch reimbursement fee

Healthcare service	Top down microcosting estimate (Euro 2007)	Reimbursement fee (Euro 2007)	Cost difference (Euro 2007)
Appendectomy	2,071	4,382	-2,311
Normal delivery	727	727	0
Hip replacement	6,522	6,997	-474
Cataract	644	1,065	-420
Stroke	7,399	7,424	-26
Acute myocardial infarction	5,868	8,919	-3,051
Tooth filling	65	62	3
Exercise electrocardiography	33	18	15
Stress echocardiography	219	75	144
SPECT	623	340	283
Coronary angiography	1,320	503	816

SPECT = Single-photon emission computed tomography

12.3 STANDARDISATION

This thesis has confirmed that the standardised application of top down microcosting is the preferred costing methodology for the comparison of alternative healthcare services. The methodology was sufficiently accurate compared with bottom up microcosting and fairly consistent compared with gross costing. Nevertheless, the consistency of the top down microcosting methodology was restricted by the availability and quality of data. To guarantee consistency, the ideal standardised methodology derives resource use and unit cost data from identical data sources at each healthcare provider. For the standardised application of top down microcosting, this thesis generally used three data sources for the extraction of data: hospital information systems, annual accounts and expert opinion.

Hospital information systems were able to provide the most accurate cost estimates for the cost comparison between healthcare services. The advantage of hospital information systems is that they are inexpensive to use because they are present for both clinical and financial purposes. However, resource use information for individual cost components was generally not available with the same level of precision even within a single healthcare provider's clinical costing system and systems varied markedly between healthcare providers. Although providing fairly detailed information, hospital information systems are constrained by limits of the coding systems in place (Johnston, Buxton 1999; Ritzwoller et al. 2005).

Annual accounts were structurally available and particularly consistent but its accuracy is poor due to the aggregated level in which data is available. Cost estimates derived from annual accounts are not specific to a particular patient and measures of costs will not normally reflect variability between patients (Jackson 2000).

Owing to its inconsistency, expert opinion was only considered when no other data source was available. Expert opinion is the simplest method to obtain resource use data (Budd 1988). However, more than the other two data sources, expert opinion is subject to potential bias, including recall bias, evasive answer bias, non-response bias and question format. Besides, the limitations of basing resource use on panel estimates is that it may be an inaccurate method if recollection is poor and if estimates relate to ideal service rather than what happens in practice (Johnston, Buxton 1999). Therefore, it may be recommendable to define a glossary of terms before starting the data collection from hospital information systems at different providers (Budd 1988; Jackson 2000).

Of course, other data sources may be used for the collection of data. When economic evaluations are conducted alongside clinical trials, the opportunity arises to collect comprehensive and detailed information on resource use quantities by means of e.g. interviews, questionnaires, patient records or case record forms (Johnston, Buxton 1999). Also published literature could serve as a data source (Jackson 2000), but it needs to be kept in mind that the data acquired from literature is representative for the study under consideration.

Evidently, different cost components may require data extraction from different data sources (Johnston, Buxton 1999; Ritzwoller, Goodman 2005). Jackson (2000) has argued that the choice of the data source should depend on the decision-context and the sensitivity of de decision to estimation errors. For the cost calculation of healthcare services from the hospital perspective, the standardised application of top down microcosting in this thesis (chapters 4-11) provided indications on the preferred data source for individual cost components and illustrated the obstacles faced in deriving resource use information from identical data sources.

Inpatient stay

Resource use data for 'inpatient stay' was available in hospital information systems as well as in annual accounts. Hospital information systems provided the most accurate and consistent resource use data for 'inpatient stay' and are therefore the preferred data source for this cost component. This finding is in agreement with that of Ritzwoller et al. (2005) who concluded that 'inpatient days' was captured most consistently across healthcare providers and hospital information systems.

Labour

The resource use of 'labour' was not available at the patient level in the hospital information systems of any of the healthcare providers. This finding is partly in line with that of Ritzwoller et al. (2005) who observed a varying availability of 'labour' across healthcare providers in the United States. Where annual accounts were able to provide consistent resource use data on *indirect* labour, they did not contain resource use information on *direct* labour. Consequently, all of the studies of this thesis made use of expert opinion to obtain direct labour minutes (chapters 4 and 7-9). Using standardised reporting templates, medical specialists were asked to provide the direct labour minutes spent per average patient. Due to the missing values which are inherent to and undermine the accuracy of the expert opinion, the consistency of the data source proved to be weak. For example, 5-8% of the required resource use data on direct labour minutes appeared to be missing in the study regarding inpatient hospital days, outpatient visits and day-care treatments in the field of haematology and oncology (chapter 4). Therefore, data

provided by medical specialists were validated by consulting the annual accounts, e.g. data on 'number of medical specialists' and 'number of beds'. Additionally, some nurses were asked to provide resource use data on daycare treatments to verify the information obtained from medical specialists.

Diagnostic procedures and consumables

The three studies which included relatively few healthcare providers used hospital information systems to obtain resource use data on 'diagnostic procedures', 'medications' and disposables' (chapters 5-6 and 9). Chapter 5 illustrated the poor consistency of hospital information systems. Resource use of intramural 'medications' was registered by drug category at some healthcare providers and by drug name in others, both either or not in combination with drug doses and administration form (e.g. tablet, injection). Also, the definition of categories varied at different healthcare providers. For example, blood (derived) products were categorised as an independent category at some healthcare providers but incorporated to the category fluids at others. Besides, the same variable, with the same name, at two different healthcare providers often represented two entirely different concepts. Owing to the creation of healthcare provider specific resource use codes, hospital information systems led to a reduced consistency for the cost comparison between healthcare services compared with other data sources. Therefore, hospital information systems may only be preferred in studies including relatively few healthcare providers or with a rather straightforward resource use. Because annual accounts were not able to provide resource use information on 'diagnostic procedures', 'medications' and disposables', the three studies which included relatively many healthcare providers used expert opinion to collect data (chapters 4 and 7-8).

Table 12.3 summarises the recommended data source per cost component based on accuracy and consistency.

The obstacles faced in the standardisation of the data collection were particularly present in the studies comparing the costs of healthcare services in different countries (chapter 6 and 7). Therefore, it turned out to be impossible to fully exclude some methodological differences. With different sources of costing data available in many jurisdictions, it is important to understand how the different sources affect the outcomes of economic evaluations. Without a clear understanding of the different data sources and the potential bias in the resulting estimates from each costing methodology, the limitations of economic evaluations are not explicitly acknowledged (Clement Nee Shrive, Ghali 2009).

Ritzwoller et al. (2005) suggested performing a detailed data inventory and generating detailed data dictionaries for the creation comparable measures of resource use and

unit costs. The data inventory seeks to find out how, and in what detail, resource use information the cost components inpatient services, outpatient services and outpatient pharmacy can be identified at each of the seven participating healthcare providers. The data dictionaries generate comparable measures of resource use from the data inventory to derive consistent estimates of cost. Ritzwoller et al. (2005) emphasise the importance of ascertaining, cataloguing and addressing the within- and between- data source differences in resource use and argue that the difficulty is in making the data comparable across different healthcare providers.

Table 12.3: Recommended data source per cost component for the standardised application of top down microcosting

Cost component	Recommended data source
Inpatient days	Hospital information systems
Labour	Expert opinion for direct labour minutes and annual accounts for indirect labour minutes
Diagnostic procedures and consumables	Hospital information systems, especially in studies including few healthcare providers or with rather straightforward resource use

12.4 REFERENCE UNIT PRICES

The 'Dutch Manual for Costing: Methods and Standard Costs for Economic Evaluations in Health Care' (Oostenbrink et al. 2002) provides guidelines and recommendations on the preferred costing approach for each cost component in the Netherlands which are principally in line with the recommendations of this thesis (section 12.1). Reference unit prices of the Dutch Manual are determined from the standardised application of either top down microcosting or gross costing. However, from this thesis it can be concluded that the top down microcosting should be the preferred costing methodology to establish reference prices. The methodology resulted in fairly accurate cost estimates compared with bottom up microcosting. Moreover, in chapter 4, the standardised application of top down microcosting resulted in cost estimates which are equally reliable in terms of generalisability compared with gross costing, because it was possible to include a large sample of healthcare providers (n=30).

For the Netherlands, three studies of this thesis determined reference unit prices from the standardised application of microcosting (chapters 4-5 and 11). Chapter 4 determined reference unit prices for inpatient hospital days, outpatient visits and daycare treatment in the field of oncology and haematology. Chapter 5 assessed reference unit price for intensive care unit days. Finally, chapter implicitly 11 determined the reference

unit prices of general practitioner visits and physiotherapist visits. The reference prices are presented in table 12.4 and were employed where applicable in this thesis (chapter 9-11). Besides, the table shows the corresponding reference prices of the Dutch Manual and those of the 'Unit Costs of Health and Social Care' which annual report is widely used for application in economic evaluations in the United Kingdom (Curtis & Netten 2008).

Table 12.4: Reference unit prices based on the standardised top down microcosting methodology

Healthcare service	Reference unit prices determined in this thesis (Euro 2007)	Reference unit prices of the Dutch Manual (Euro 2007)	Reference unit prices of the Unit Costs of Health and Social Care, UK (Euro 2007)
Inpatient hospital day		406	
▪ Haematology	493		
▪ Oncology	478		
▪ Psychiatry			398
Outpatient visit		75	104
▪ Haematology	105		
▪ Oncology	97		
Daycare treatment		243	205
▪ Haematology	219		
▪ Oncology	209		
Inpatient ICU day	1,940	1,786	
▪ Psychiatry			778
General practitioner visit	10	21	53
Physiotherapist visit	20	24	58

UK = United Kingdom
ICU = intensive care unit

For inpatient hospital days, outpatient visits and inpatient intensive care unit stay, the prices determined in this thesis (chapter 4 and 5) are somewhat higher than those obtained from the Dutch Manual and the 'Unit Costs of Health and Social Care'. Still, the prices of this thesis and those of the Dutch Manual were both derived from the standardised application of top down microcosting. The deviation in costs for inpatient hospital days, outpatient visits and daycare treatments could be explained by the fact that this thesis aimed to determine reference prices at the relatively labour intensive haematology and oncology departments where the reference unit prices of the Dutch Manual were determined at any medical specialty. Another explanation may be the use of different data sources for the extraction of labour data for residents and nurses.

Chapter 4 used expert opinion for the calculation of direct labour and annual accounts for indirect labour costs. Because Oostenbrink et al. (2002) did not distinguish direct and indirect labour costs as they solely used annual accounts.

For general practitioner and physiotherapist visits, the prices determined in this thesis (chapter 11) are lower than those obtained from the Dutch Manual and the 'Unit Costs of Health and Social Care'. The cost differences are most likely explained by the application of a different costing methodology. Where the standardised application of the top down microcosting methodology was used in chapter 11, the Dutch Manual simply divided the total annual expenditures by the annual number of visits (gross costing) (Oostenbrink, Koopmanschap 2002).

Reference unit prices are important in economic evaluations because they encourage comparability between treatment options (Drummond et al. 1993; Ferguson 2001; Jones 1995; Oostenbrink, Koopmanschap 2002; Viens-Bitker et al. 1986). Updating reference unit prices should be done periodically because they have to fit with current clinical practice and the availability of data (Budd 1988). The reference unit prices of the Dutch Manual were established in 2000 and updated in 2004. A new update is due in 2010. This update should ideally base its reference prices on the standardised application of top down microcosting.

12.5 GENERAL METHODOLOGICAL CONCLUSIONS

For the cost assessment of individual healthcare services, this thesis provided study design advice on the selection of costing methods per individual cost component to optimise data quality. Bottom up microcosting gives the most accurate approximation of true costs, but its low feasibility forms a challenge for application in economic evaluations. However, top down microcosting has proven to be a strong alternative to bottom up microcosting with respect to accuracy and the approach is fairly feasible in terms of data availability, costs and complexity. The standardised application of top down microcosting resulted in sufficiently accurate cost estimates for the cost comparison between healthcare services and for the establishment of reference unit prices. However, the consistency of the top down microcosting methodology was restricted by the availability and quality of data. This thesis recommended on the preferred data source per individual cost component. Hospital information systems are generally the favoured data source, but are often not able to provide information on the resource use of 'labour'. Instead, annual accounts and expert opinion are recommended to derive 'labour' minutes.

In answering certain research and policy questions, this thesis has provoked many suggestions for future research of which two were explicitly discussed. Future studies need to determine the extent to which the reimbursement fees of the DBC case mix system reflect actual costs and can be used for economic evaluations. Also, there are challenges in updating, extending and improving existing reference unit prices in the Netherlands.

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SUMMARY

As resources – people, time, facilities, equipment and knowledge – are scarce, an organised consideration of the factors involved in a decision to commit healthcare resources to one use instead of another must be made. The consideration of these factors is commonly performed through economic evaluations which compare alternative healthcare services in terms of both their costs and effects. This thesis focussed on the cost side of economic evaluations. More specifically, this thesis aimed to determine and compare the costs of individual treatment options (sequences of healthcare services), healthcare services and cost components (parts of the healthcare service) and to draw general methodological conclusions regarding the application of the microcosting methodology. General methodological conclusions were based on the extent to which microcosting estimates reflected real costs (accuracy), the extent to which the methodology was applicable in practice (feasibility), the extent to which differences between microcosting estimates were attributable to the healthcare service under consideration rather than to flaws in the methodology (consistency) and the extent to which microcosting estimates were reliable for generalisations to other circumstances (generalisability). The methodology was applied to a variety of medical specialties, including oncology, haematology, intensive care medicine, dentistry, general practitioner medicine, cardiology and neurosurgery.

Bottom up versus top down microcosting

The preferred methodology to estimate the costs of healthcare services is still to be determined. In economic evaluations, decision makers must consider whether the benefits of more reliable cost information justify the additional costs and complexity incurred in obtaining accurate and detailed information. Owing to its accuracy, bottom up microcosting is generally believed to be the gold standard methodology. The methodology identifies and values all relevant cost components at the individual patient level. This allows for the identification of costs directly employed for a specific patient and for insight in patient subgroups that might have a great share in the total costs. However, an important challenge in conducting bottom up microcosting is its feasibility. As this methodology is time consuming, especially when hospital information systems are absent or inadequate, it has not been widely used in assessing the costs of healthcare services.

Although top down microcosting identifies all relevant cost components at the individual patient level, it values cost components per average patient. Therefore, top down microcosting is more feasible than bottom up microcosting. The disadvantage of the

approach is that it fails to trace costs directly to specific patients who incur that cost. This thesis provided study design advice on the selection of costing methods per individual cost component to optimise data quality. Chapter 2 quantified the total cost differences resulting from bottom up and top down microcosting and concluded that top down microcosting was a fairly accurate alternative to bottom up microcosting. It was further concluded that the restriction of bottom up microcosting to those cost components which have a relatively large impact on the total costs may especially result in accurate cost estimates. For example, in healthcare services with a relatively long length of stay, it is recommendable to use bottom up microcosting for the cost component 'inpatient stay' and top down microcosting for the remaining cost components. Similarly, bottom up microcosting may be confined to the cost component 'labour' in healthcare services which are labour intensive.

Microcosting versus gross costing

The gross costing methodology identifies one (or few) cost component and is therefore more feasible compared with microcosting. However, the main drawback of gross costing is its inaccuracy, because it fails to trace costs directly to specific cost components. Chapter 2 explored the accuracy of gross costing and confirmed that gross costing may be weak alternative to microcosting.

Indirect cost components

For the cost assessment of indirect cost components (overheads and capital), the microcosting methodology is not applicable, because it is often not possible to identify a strong relationship between these cost components and the healthcare service under consideration. Although the allocation of indirect costs based on their relative value (weighted service allocation) is generally considered to provide the most accurate indirect cost estimates, the method is time consuming. Chapter 3 suggested that the allocation of indirect costs by means of initial treatment duration (hourly rate allocation) and the allocation by means of inpatient days (inpatient day allocation) produce estimates that are not significantly different from 'weighted service allocation'. 'Hourly rate allocation' may be a strong alternative to weighted service allocation for healthcare services with a relatively short inpatient stay. The use of 'inpatient day allocation' would likely most closely reflect the indirect cost estimates obtained by the weighted service method.

Microcosting to determining reference unit prices

Reference unit prices are predetermined estimates of what it is expected to cost or what it should cost to produce one unit of a healthcare service. Reference unit prices for healthcare services which significantly contribute to total treatment option costs encourage comparability between treatment options. This thesis has determined reference unit prices for inpatient hospital days, outpatient visits and daycare treatments in the field of oncology and haematology (chapter 4), intensive care unit days (chapter 5), general practitioner and physiotherapist visits (chapter 11). In chapter 4, the standardised application of top down microcosting resulted in cost estimates which are equally reliable in terms of generalisability compared with gross costing, because it was possible to include a large sample of healthcare providers (n=30). For inpatient hospital days, outpatient visits and daycare treatments, the cost estimates of university hospitals were significantly higher that those at general hospitals. For intensive care unit days, the cost estimates for patients requiring mechanical ventilation, blood products and renal replacement therapy were significantly higher than those of the total population. As these differences reflect daily practice, they support the establishment of generalisable unit costs. The results may be used as Dutch reference unit prices in economic evaluations.

Microcosting to comparing cost estimates

The standardised application of a costing methodology ensures consistency because all healthcare services under consideration adhere to the same costing methodology. It was confirmed that the standardised application of top down microcosting was sufficiently accurate and consistent for the cost comparison of alternative healthcare services (chapters 4-11). Nevertheless, the consistency of the top down microcosting methodology was restricted by the availability and quality of data. This thesis recommended on the preferred data source per individual cost component. Hospital information systems are generally the favoured data source, but are often not able to provide information on the resource use of the cost component 'labour'. Instead, annual accounts and expert opinion are recommended to derive 'labour' minutes.

Microcosting to determining cost differences between countries

The consistency issue faced in the standardisation of the data collection was particularly present in the studies comparing the costs of healthcare services in different countries. Therefore, it turned out to be impossible to fully exclude some methodological differences. Bearing this in mind, total costs of intensive care unit stay (chapter 6) and dental

filling procedures (chapter 7) varied widely between European countries resulting mainly from differences in labour and indirect costs. In these specific healthcare services, labour was the key cost driver and explained the increased costs at healthcare providers in the United Kingdom.

Microcosting versus reimbursement fees

Reimbursement fees were confirmed to be a weak alternative to serve as a proxy to actual costs of healthcare services. A weak positive linear relationship between top down microcosting estimates and reimbursement fees was found for dental filling procedures (chapter 7) and for diagnostic tests for the detection of coronary artery disease (chapter 8). The use of microcosting estimates instead of reimbursement fees led to different conclusions regarding the relative cost effectiveness of alternative strategies for the detection of coronary artery disease (chapter 8).

Microcosting to determining cost differences between alternative treatment options

This thesis also addressed the standardised application of the microcosting methodology to detect cost differences between treatment options (sequences of healthcare services). Initial treatment costs were generally determined to be decisive for cost differences between alternative treatment options. Although the costs of microsurgery were a manifold higher compared those of LINAC radiosurgery and gamma knife radiosurgery in benign (WHO grade I) meningioma patients, this relative cost difference decreased when one year follow up costs were considered (chapter 9). The administration of chemotherapy (oxaliplatin) was the key cost driver in the adjuvant treatment of stage III colon cancer (chapter 10), where physiotherapy visits mainly explained the cost difference between exercise therapy and 'usual care' in adolescents and young adults with the patellofemoral pain syndrome (chapter 11).

SAMENVATTING

De beslissing om bronnen voor een doeleinde aan te wenden in plaats van aan een ander doeleinde moet gestruktureerd worden afwogen, omdat bronnen – mankracht, tijd, faciliteiten, apparatuur en kennis – schaars zijn. Deze afweging wordt doorgaans gemaakt met behulp van economische evaluaties die alternatieve medische behandelingen vergelijken in termen van zowel kosten als effecten. In dit proefschrift stond de kostenkant van economische evaluaties centraal. De doelstelling was de kosten van specifieke behandelopties (opeenvolgingen van medische behandelingen), individuele medische behandelingen en individuele kostencomponenten (onderdelen van medische behandelingen) te schatten en algemene methodologische conclusies te trekken wat betreft de toepassing van de microcosting methode. Algemene methodologische conclusies werden gebaseerd op de mate waarin microcosting schattingen werkelijke kosten reflecteren (nauwkeurigheid), de mate waarin de methode toepasbaar was in de praktijk (haalbaarheid), de mate waarin verschillen tussen microcosting schattingen toe te schrijven zijn aan de medische behandeling in plaats van aan de methode (consistentie) en de mate waarin microcosting schattingen betrouwbaar zijn in andere omstandigheden dan die waarin de schatting werd gedaan (generaliseerbaarheid). De methode werd toegepast in een verscheidenheid aan medische specialismen, waaronder oncologie, hematologie, intensive care medicine, tandheelkunde, huisartsgeneeskunde, cardiologie en neurochirurgie.

Bottom up versus top down microcosting

Er bestaat nog geen consensus over de methode van voorkeur voor de kostenschatting van medische behandelingen. In economische evaluaties moeten beleidsmakers de voordelen van meer betrouwbare kosteninformatie afwegen tegen de additionele kosten en complexiteit die gerelateerd zijn aan het verzamelen van nauwkeurige en gedetailleerde gegevens. Dankzij haar nauwkeurigheid wordt bottom up microcosting over het algemeen als de gouden standaard methode beschouwd. De methode identificeert en waardeert alle relevante kostencomponenten op het individuele patiënt niveau. Dit maakt het mogelijk kosten te identificeren die direct aan een specifieke patiënt zijn toe te schrijven en inzicht te krijgen in subgroepen die een groot aandeel hebben in de totale kosten. De haalbaarheid van bottom up microcosting vormt echter een belangrijke uitdaging. De methode wordt niet op grote schaal toegepast omdat zij tijdsintensief is, in het bijzonder wanneer ziekenhuis informatie systemen afwezig of inadequaat zijn.

Bij top down microcosting worden alle relevante kostencomponenten weliswaar op het individuele patiënt niveau geidentificeerd, maar gewaardeerd per gemiddelde patiënt. Daarom is top down microcosting beter haalbaar dan bottom up microcosting. Het nadeel van de methode is de onmogelijkheid kosten direct aan specifieke patiënten toe te wijzen. Dit proefschrift heeft advies gegeven over de aan te bevelen kostenmethode per individuele kostencomponent. Hoofdstuk 2 heeft de kostenverschillen die voortkomen uit bottom up en top down microcosting gekwantificeerd en geconcludeerd dat top down microcosting een redelijk nauwkeurig alternatief is voor bottom up microcosting. Kosten konden met name nauwkeurig worden geschat wanneer de bottom up microcosting uitsluitend werd toegepast voor kostencomponenten die een relatief groot aandeel in de totale kosten hadden. Zo is het in medische behandelingen met een relatief lange opnameduur aan te bevelen bottom up microcosting toe te passen voor het kostencomponent 'klinische opnames' en top down microcosting voor de overige kostencomponenten. De toepassing van bottom up microcosting zou beperkt kunnen worden tot het kostencomponent 'arbeid' in relatief arbeidsintensieve medische behandelingen.

Microcosting versus gross costing

De gross costing methode identificeert slechts één (of enkele) kostencomponent en is daarom beter haalbaar dan microcosting. De methode is echter zeer onnauwkeurig omdat kosten niet toe te wijzen zijn aan specifieke kostencomponenten. Hoofdstuk 2 heeft bevestigd dat de methode een zwak alternatief voor microcosting is.

Indirecte kostencomponenten

De microcosting methode kan niet worden toegepast op indirecte kostencomponenten (overhead en kapitaal), omdat vaak een sterke samenhang tussen de indirecte kostencomponenten en de medische behandeling ontbreekt. Hoewel de toewijzing van indirecte kosten op basis van hun relatieve waarde (weighted service allocation) verondersteld wordt tot de meest accurate kostenschatting te leiden, is de methode erg tijdsintensief. Hoofdstuk 3 suggereerde dat de toewijzing van indirecte kosten op basis van de initiële behandelduur (hourly rate allocation) en op basis van klinische verpleegdagen (inpatient day allocation) indirecte kostenschattingen geven die niet significant verschillen van die van 'weighted service allocation'. 'Hourly rate allocation' kan een sterk alternatief zijn voor medische behandelingen met een relatieve korte opnameduur. Het gebruik van 'inpatient day allocation' benadert de indirecte kostenschatting op basis van 'weighted service allocation' waarschijnlijk het meest.

Microcosting voor het vaststellen van referentie prijzen

Referentie prijzen zijn van te voren vastgelegde schattingen van de verwachte of gewenste kosten om één eenheid van een medische behandeling te produceren. Referentie prijzen voor medische behandelingen die een significante bijdrage leveren aan de kosten van een behandeloptie moedigen de vergelijkbaarheid tussen behandelopties aan. Dit proefschrift heeft referentie prijzen vastgesteld voor klinische verpleegdagen, poliklinische bezoeken en dagbehandelingen op het terrein van oncologie en hematologie (hoofdstuk 4), intensive care dagen (hoofdstuk 5), huisartsen bezoeken en fysiotherapie (hoofdstuk 11). In hoofdstuk 4 resulteerde de gestandaardiseerde toepassing van top down microcosting in kostenschattingen die in termen van generaliseerbaarheid even betrouwbaar zijn als gross costing, omdat het mogelijk was een groot aantal zorgaanbieders te includeren (n=30). De kostenschattingen voor klinische verpleegdagen, poliklinische bezoeken en dagbehandelingen waren significant hoger in academische dan in perifere ziekenhuizen. Voor intensive care dagen waren de kostenschattingen hoger in patiënten die mechanische beademing, bloedprodukten en nierfunctievervangende therapie nodig hadden. Omdat deze verschillen de dagelijkse praktijk reflecteren, versterken zij de generaliseerbaarheid van eenheidskosten. De resultaten kunnen als Nederlandse referentie prijzen worden gebruikt in economische evaluaties.

Microcosting voor het vergelijken van kosten schattingen

De gestandaardiseerde toepassing van een kosten methode zorgt voor consistentie omdat alle alternatieve medische behandelingen volgens dezelfde methode worden vastgesteld. De gestandaardiseerde toepassing van top down microcosting bleek voldoende nauwkeurige en consistente kosten te geven voor de vergelijking van alternatieve medische behandelingen (hoofdstuk 4-11). De consistentie van top down microcosting werd wel beperkt door de beschikbaarheid en kwaliteit van gegevens. Dit proefschrift heeft aanbevelingen gedaan voor de gegevensbron van voorkeur per individuele kostencomponent. Ziekenhuis informatie systemen zijn over het algemeen de gegevensbron van voorkeur, maar vaak niet in staat informatie te leveren over het zorggebruik van het kostencomponent 'arbeid'. Daarom worden jaarverslagen en 'expert opinion' aanbevolen als bron voor arbeidsminuten.

Microcosting voor het vaststellen van kostenverschillen tussen landen

Het consistentie aspect die in de standaardisatie van de gegevensverzameling naar voren kwam speelde voornamelijk een rol in de internationale kosten studies. Het bleek niet mogelijk methodologische verschillen volledig te excluderen. Dit in acht genomen

werden grote kostenverschillen tussen Europese landen gevonden in de totale kosten van intensive care dagen (hoofdstuk 6) en tandheelkundige vullingen (hoofdstuk 7). Voor deze specifieke behandelingen konden de verschillen met name worden toegeschreven aan arbeid en indirecte kosten. Arbeid was de hoofdkostenpost en verklaarde de hogere kosten van zorgaanbieders in het Verenigd Koninkrijk.

Microcosting versus vergoedingen

Vergoedingen bleken een zwak alternatief te zijn voor schattingen op basis van microcosting. Er werd een zwakke positieve lineaire relatie gevonden tussen top down microcosting en vergoedingen voor tandheelkundige vullingen (hoofdstuk 7) en diagnostische testen voor de opsporing van coronaire hartziekten (hoofdstuk 8). Het gebruik van microcosting in plaats van vergoedingen leidde tot andere conclusies wat betreft de kosteneffectiviteit van alternatieve strategieën voor de opsporing van coronaire hartziekten (hoofdstuk 8).

Microcosting voor het vaststellen van kostenverschillen tussen behandelopties

Tevens heeft dit proefschrift de gestandaardiseerde toepassing van de microcosting methode voor het opsporen van kostenverschillen tussen behandelopties (opeenvolgingen van medische behandelingen) bestudeerd. De initiële behandelkosten waren over het algemeen beslissend voor de kostenverschillen tussen alternatieve behandelopties. Hoewel de kosten voor microchirurgie een veelvoud hoger waren dan die van LINAC en gamma knife radiochirurgie in patiënten met een goedaardig (WHO graad I) meningioom, verminderde het relatieve kostenverschil wanneer follow up kosten werden meegenomen (hoofdstuk 9). De toediening van chemotherapie (oxaliplatin) was de hoofdkostenpost in de adjuvante behandeling van stadium III darmkanker (hoofdstuk 10), terwijl fysiotherapie het kostenverschil tussen oefentherapie en 'usual care' voor een groot deel verklaarde in adolescenten en jong volwassenen met het patellofemorale pijn syndroom (hoofdstuk 11).

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