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ADOPTION OF NEW TECHNOLOGIES AND COSTS OF HEALTH CARE****

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ABSTRACT: New technological applications are usually expected to increase the health care costs. But they can also spawn cost savings in the long run, for example, when making time-consuming diagnostic methods more efficient and facilitating targeted therapy. This study analyses how the implementation of new technological applications in acute treatment affects the long-term cost structure of health care. The non-monetary utility is compared to cost-efficiency impacts of a new technology. A theoretical apparatus is constructed and utilized in two empirical cases: thrombolytic therapy for stroke, and Boron Neutron Capture Therapy (BNCT) on glioblastoma-type brain cancers. The empirical cases indicate how the monetary cost-efficiency of the new technologies can be related to the non-monetary patient utility.

Keywords: technology, health care, costs

JEL codes: I11, L65

1 Introduction

The health care sector has reached a major crossroads. In many Western countries the aging of the population is spurring upward pressure on health care costs. At the same time, advances in medical science bring with them new and more effective possible treatments. The discovery of previously unknown disease mechanisms and possible treatments appears to further increase the cost pressures in health care.

However, some recent technological applications are expected to spawn cost savings over the long run by, for example, making time-consuming diagnostic methods more efficient and facilitating targeted therapy. Inaccurate diagnoses or a lack of appropriate treatment easily leads to a prolonged illness and thus an increased use of resources such as personnel and medication. Examples of this are strokes and schizophrenia, the former of which is a problem of the elderly population and the latter an illness affecting one percent of the entire world's population. If more efficient ways can be found to make diagnoses and treat patients that would otherwise need long-term care, even relatively expensive methods can generate considerable cost savings.

It seems that drug approval regulation commits rarely oneself to the long term cost savings aspects. For instance, the focal regulatory in the US, Food and Drug Administration (FDA) requires evidence on safety and efficacy measures of the drug, but no evaluation of the economic impacts for a long-term cost structure. Although the cost-benefit measures of distinctive treatment methods form a conventional path of literature in health economics, the measures do not require a definition of long-run social optimum based on microeconomics. Accordingly, there is a lack of a theoretical model, which derives on the long-term social optimum and combines the context of the cost structure of the entire health care sector and the non-monetary benefits in investigation of monetary cost-efficiency of new health care technologies.

In this article we investigate how the implementation of new technological applications in acute treatment affects the long term cost structure of health care. To this end, we first construct a formal theoretical apparatus in which a new technology can be applied in acute care. This, in turn, affects to the number of patients requiring long-term care. The aim of the theoretical model is to show how the patient utility and monetary costs

obtained from the adoption of new technology in acute care can be related to those in long term care. The empirical model enables us to measure the monetary burden of marginal efficiency of a new treatment in two cases.

The first empirical case measures the monetary impacts of the introduction of a new technology for the treatment of strokes, the major cause of somatic disability and the second leading cause of death, with a global burden of 6 million ischemic strokes per year and an estimated 4.4 million individuals dying annually as a consequence thereof. The second case concerns a relatively rare disease, glioblastoma multiforme, affecting approximately 9000 patients annually. However, glioblastomas are the most severe primary brain cancer type in humans: less than 3% of the patients are alive at 5 years after diagnosis. In other words, the first case has huge impacts on the entire health care costs *per se*, whereas the second case deals with severe disease with lesser effects at macro level.

The article is organized as follows. Section 2 presents our theoretical model. First it analyzes the choice of a technology in acute care. The choice depends on the prices and effectiveness of technologies. As an end point of theoretical setting, the model presents the social optimum for a basis of empirical analysis. Section 3 measures empirically the monetary impacts of adoption of new technology in health care and relates these figures to the marginal utility of a recovering patient in the two empirical cases. The empirical cases present concrete examples on how the health care payer can utilize the model as a tool for mirroring the non-monetary benefits with the cost-efficiency of the technology adoption.

2 Model

In order to analyze the strategic decision making between the payers of health care and the service providers, we consider strategic decision-making between the payer of health care and two hospitals or hospital units called acute-care and long-term care. An acute-care hospital or unit is defined as the hospital unit giving the primary treatment for patients and the long-term

care refers to a hospital treating patients not recovering after having received acute-care1. These units can also be located in the same hospital. There are n patients in the acute-care hospital and patients can be treated using one of three treatments, treatment 0, 1, or 2. We denote the set of available technologies as $T = \{0,1,2\}$. Technology 0 refers to a minimum care technology in which all patients in the acute care are referred to the long-term hospital for care. This choice of technology is costless for the acute care hospital. The prices of technologies 1 and 2 for the acute care hospital are denoted as p_1 and p_2. It is assumed throughout the text that technology 2 is more expensive but also more effective than technology 1 and $p_1 < p_2$. Prices can measure lump-sum payments which the hospital has to pay for the use technologies or they can also measure total costs of applying technologies to a certain population of patients.

We assume that patients are identical in terms of their initial medical conditions. Patients can have low, l, or high, h, severity of disease, denoted generically as d. In what follows, we also say that a patient is mildly (ie. $d = l$) or severely (ie. $d = h$) ill. It is assumed that all patients entering the acute care hospital have a high severity of disease and are in need of treatment. The probability that a patient has low severity of disease after treatment at the acute-care hospital is given as $\tau_t = Prob(d = l \mid t)$. This probability is conditional on the chosen technology t. All patients in the high severity of illness after the acute-care will be referred to the long-term care. We assume that technology 2 is the most effective[2] health care technology and the minimum care technology is ineffective in a sense that $0 = \tau_0 < \tau_1 < \tau_2 < 1$. This means that the application of technology 2 maximizes the number of patients with only mild illness, whereas the minimum care technology either leads to death or leaves the patient with a severe illness. Although in reality a fraction of patients die after acute-care we assume that this fraction is sufficiently small to be ignored in the formal analysis.

Patients obtain utility levels u_l and u_h from being mildly or severely ill. We assume that a patient obtains no utility if her severity of disease is high, ie. $u_h = 0$, and she obtains a positive utility level in case she is only mildly ill, ie. $u_l > 0$. Therefore, a representative patient obtains expected utility $\tau_t\, u_l$ at the acute care hospital. The aggregate expected utility for patients in the acute care is then

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[1] For more standard definitions of long-term care, see Norton, E. C. (2000). "Long-Term Care." Handbook of health economics Volume 1B: 955-94..

[2] In what follows, effectiveness of a health care technology is defined in terms of probability τ_t.

$$EU(t) = n\ \tau_t\ u_l. \qquad (1)$$

We assume that both hospitals operate under the zero-profit constraint (see (Newhouse 1970; Chalkey and Malcolmson 2000)). The objective of the acute-care hospital is to maximize aggregate expected utility obtained from alternative treatments subject to the constraint that the hospital earns zero profit. The zero profit constraint for the acute care hospital can be defined as $\mu B - s - p_t = 0$, where μB is the budget share allocated to the hospital. It is assumed that any resources which the hospital obtains over and above the price of the chosen technology is spent on organizational slack, measured by the variable s. Slack can be seen as 1) pure technical inefficiency, 2) excessive profit for hospital owners, or as 3) purposeful slackness (preparedness for unexpected events).

The total cost function of the long-term care hospital is $C(q,n) = c(q)n(t)$, where $c(q)$ measures the average cost of treating one patient with treatment intensity $q > 0$ and $n(t)$ is the number of patients treated in the long-term hospital. It is assumed throughout this paper that the unit cost function $c(q)$ is a monotonically increasing and continuous function of the treatment intensity q and $c(0) = 0$.

To simplify the analysis, it is assumed that the demand for long-term care consists solely of those patients who are still severely ill after having received care at the acute-care hospital. This modeling choice creates a needed connection between treatment decisions at the acute-care hospital and the demand for and costs of the long-term care. In particular, the number of patients in the long-term care hospital can be defined as $n(t) = (1-\tau_t)n$ and depends on the health care technology chosen by the acute care unit. Consequently, the more effective is the technology chosen at the acute-care hospital the less patients the long-term care hospital will face.

The revenue of the long-term care unit is determined purely by the health care payers' budgetary decisions[3]. If the payer allocates fraction μ of the budget to the acute care hospital, the long-term care unit obtains a revenue of $(1 - \mu)B$. The payoff of the long-term care hospital can be defined as

[3] This is consistent with the way the demand for long-term care is modelled. As the hospital faces no patients paying for their care out of their own pockets, it is natural to think that all revenue the hospital earns comes from a health care authority, a payer in our case. A purely public hospital would be a good real-world example.

$$L(q,\mu,t) = (1-\mu)B - n(1-\tau_t)c(q) \qquad (2)$$

If for a given choice of treatment intensity $L(q,\mu,t) > 0$ the hospital retains a profit, and if $L(q,\mu,t) < 0$, the health care payer has to supply the long-term care hospital with more resources. However, as μ and B are chosen by the health care regulator, and the probability of recovery is a function of technology choice made by the acute-care hospital, respectively, the long term hospital can conform to the requirement of zero profits and adopt a treatment intensity q for which $L(q,\mu,t) = 0$. It is assumed that each patient obtains a (monetary-equivalent) benefit $v(q)$ from treatment intensity q at the long-term care. We assume that $v(0) = 0$ and that the benefit function $v(q)$ is increasing and continuous with treatment intensity. We further assume that treatment intensity is given and that there is a sufficiently large q_{max} such that $q \leq q_{max}$.

Decision-making occurs sequentially in three stages within the model. In the first date, Date 0, the health care payer selects a fraction μ $(1 - \mu)$ of the health care budget, B $(B > 0)$, to be allocated to the acute-care (long-term care) hospital. We define the objective function of the health care regulator more precisely in the following section.

In the second date, Date 1, the acute care hospital makes a decision between the available technologies 0, 1 and 2 and pays the associated costs. The choice of the acute-care hospital is constrained by the budget share allocated to the hospital.

In the last date, Date 2, the long-term hospital selects the level of treatment intensity, given the number of severely ill patients and the budget share chosen by the health care regulator. After receiving care at the long-term hospital all patients will recover (ie. patients have $d = l$).

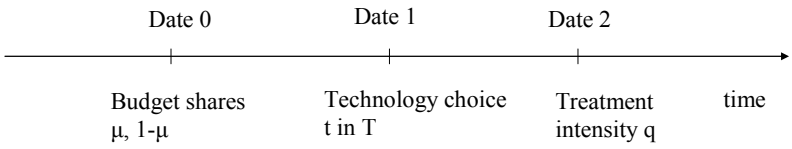

Figure 1. Sequence of decisions

Since decision-making occurs sequentially in the model and decisions in later dates depend on choices made in early dates, we apply the principle of the backward induction: we solve the model in a backward fashion by first considering decisions made at the long-term hospital.

2.1 Treatment intensity in the long-term care

The long-term hospital selects treatment intensity $q(\mu,t)$, which yields the hospital zero monetary payoff $L(q(\mu,t), \mu, t) = 0$. The zero profit condition can be solved with respect to unit cost as $c(q(\mu,t)) = \frac{(1-\mu)B}{(1-\tau_t)n}$. Since, by assumption, the unit cost function is monotonically increasing it has an inverse function $c^{-1}(z)$ for each positive average cost z. Hence the hospital will provide the level of treatment intensity $q(\mu,t) = c^{-1}(\frac{(1-\mu)B}{(1-\tau_t)n})$ and the associated total cost is given as $c(q(\mu,t))(1-\tau_t)n$. The treatment intensity in the long-term hospital decreases if the number of severely ill patients from the acute care hospital, $n(t)$, increases and if the budget share allocated to the acute care hospital, μ, grows. These results can be confirmed by taking partial derivatives of the zero-profit treatment intensity with respect to $n(t)$ and μ. As an example, let us consider the case in which the cost function is linear and $c(q) = cq$. This yields an optimal treatment intensity $q(\mu,t) = \frac{(1-\mu)B}{(1-\tau_t)nc}$, verifying the comparative static results of this example.

For a zero-profit hospital operating under the fixed budget it is reasonable that a hospital decreases its treatment intensity as the number of its patients increase. As the number of referred patients increase, the hospital faces a higher cost but since a

hospital's revenue is fixed, it has to reduce its total cost by decreasing per patient treatment intensity accordingly.

2.2 Selection of technology at the acute-care

The acute hospital's selection of technology is determined by the budget share μ chosen by the health care payer. If the payer selects a budget share which satisfies the condition $p_1 \geq \mu B \geq 0$, the acute-care has no other choice but to use the minimum care technology and refer all its patients to the long-term care. The hospital uses all its resources on excessive organizational slack and $s = \mu B$. The efficacy of the treatment decision is at its minimum and the used technology is $\tau_0 = 0$. In case the payer provides the acute care hospital more resources and $p_2 \geq \mu B \geq p_1$, feasible technologies for the acute-care hospital are technology 1 and the minimum care technology. Because $0 = \tau_0 u_l < \tau_1 u_l$, the acute-term hospital maximizes its utility by choosing technology 1 and spends any additional resources on organizational slack $s = \mu B - p_1$.

If the budget share of the acute-care hospital satisfies $\mu B \geq p_2$ any one of three technologies is feasible for the hospital. The assumption $1 > \tau_2 > \tau_1 > \tau_0 = 0$ implies that $n \tau_2 u_l > n \tau_1 u_l > n \tau_0 u_l = 0$ and the hospital ends up using the most effective and the most expensive technology, i.e. technology 2. In this case the organizational slack is given as $s = \mu B - p_2$.

2.3 The health care payer: Slackness and allocating the given budget

In order to see which technology and the level of treatment intensity the health care payer is willing to implement, we then analyze the payer's decision concerning the allocation of budget shares for the acute and long-term care at Date 0. We consider three kinds of payers with different objective functions. The first two payers are similar to each other as they both aim at minimizing the total cost of health care; the difference between the payers lies in their emphasis on different components of health care costs. The first type of payer aims at minimizing the total cost of health care, *CI*, defined as

$$CI = p_t + c(q)(1-\tau_t)n + s \qquad (3)$$

The cost-minimization problem turns out to be easy to solve because of zero-profit constraints. The zero-profit condition for the acute-care hospital implies that $\mu B = s + p_t$. Moreover, as the long-term hospital also operates under the zero-profit condition and selects a treatment intensity which satisfies $(1-\mu)B = c(q)(1-\tau_t)n$, the total cost to the health care payer for any budget allocation is $\mu B + (1-\mu)B = B$. This suggests that the cost-minimizing payer is indifferent between different allocations of the health care budget between the acute-care and long-term care units.

The second type of payer places a different weight on organizational slack than on other components of health care costs. A slack averse or slack inclined health care payer regards organizational slack as unproductive and attempts to root it out, or it puts special emphasis on slackness. Accordingly, the health care payer can attach more or less weight to organizational slack than to other components of health care costs. This idea can be formalized as a slackness-weighted cost index, *SCI*:

$$SCI = p_t + c(q)(1-\tau_t)n + \alpha s, \qquad (4)$$

where $\alpha \geq 0$ is the weight the health care payer puts on organizational slack. A slack-averse health care payer selects a weight $\alpha > 1$ and a slack-inclined payer a weight of $\alpha < 1$.

Technology choice, treatment intensity and organizational slack are endogenous and depend on the payer's choice of the budget share. If the chosen budget share satisfies $p_1 > \mu B$, then the acute care hospital uses the minimum care technology and all patients are referred to the long-term hospital, which obtains the fraction $(1-\mu)$ of the health care budget. This is used to cover the costs of long-term care. Organizational slack in the acute care hospital is given as $s = \mu B$. In such a case, the slackness-weighted cost index of health care obtains the value $SCI_0 = \alpha\mu B + (1-\mu)B = B - \mu B(1-\alpha)$. In case the budget share of the acute-care hospital exceeds the price of technology 1, that it $p_1 \leq \mu B$ holds true, the acute care hospital utilizes technology 1 and spends the rest of the resources on organizational slack; it sets $s = \mu B - p_1$. The budget share of the long-term care equals the total cost of producing long-term care. On this basis the slackness-weighted cost-index is given as $SCI_1 = p_1 + (1-\mu)B + \alpha(\mu B - p_1) = B + p_1(1-\alpha) - \mu B(1-\alpha)$. Finally,

if $p_2 \leq \mu B$, the acute-care hospital selects technology 2 with the associated cost and the organizational slack given as $s = \mu B - p_2$. Total cost of health care is now given as $SCI_2 = B + p_2(1- \alpha) - \mu B(1- \alpha)$.

If the health care payer is slack-averse, it consequently aims to implement solutions for which organizational slack is as small as possible. This leaves the payer with three allocations to compare, namely budget allocations for which the acute-care hospital share μ obtains one of the values 0, p_1/B, or p_2/B. In each such point, the total cost of health care is B implying that the payer is indifferent for such points as well as between these points randomly.

The third type of payer treats different components of health care similarly, but it takes benefits of health care into account. We further assume that the payer's goal is to maximize the difference between the health benefits and total costs of health care, to be called net benefit of health care. As the organizational slack is a real cost-item for the payer it is included in the total cost of health care. The health utility from the acute care is given by the aggregate expected utility $EU(t) = n\ \tau_t\ u_l$ and the total benefit of the long-term care can be defined as $v(q)(1-\tau_t)n$. Let us consider a payer who selects budget shares of the acute-care and long-term care hospital by maximizing the net benefit of health care

$$NB = n\tau_t u_l + v(q)(1-\tau_t)n - (p_t + c(q)(1-\tau_t)n + s) \qquad (5)$$

and shows no special preference for organizational slackness. By the zero-profit conditions it always holds true that $p_t + s = \mu B$ and $c(q)(1-\tau_t)n = (1- \mu)B$ and the total cost for the payer is B no matter how the budget shares are allocated between the acute-care and the long-term care. Any differences that might arise between different allocations of the budget must come from differences in health benefits. In case the payer selects a budget share satisfying $0 \leq \mu B \leq p_1$, all patients are treated in the long-term care and the health care benefit is given as $nv(q(\mu,0))$, where $q(\mu,0) = c^{-1}(\frac{(1-\mu)B}{n})$, and the net benefit is given as $nv(q(\mu,0)) - B$. On the other hand, if the budget share of the acute-care satisfies $p_1 \leq \mu B \leq p_2$, then the net health benefit is

$n[\tau_1 u_l + (1-\tau_1)v(q(\mu,1))] - B$, where $q(\mu,1) = c^{-1}(\frac{(1-\mu)B}{(1-\tau_1)n})$. Finally if $p_2 \leq \mu B$, then the net benefit for the payer is $n[\tau_2 u_l + (1-\tau_2)v(q(\mu,2))] - B$, where $q(\mu,2) = c^{-1}(\frac{(1-\mu)B}{(1-\tau_2)n})$.

Clearly, as the total cost of health care is always the same, the health care payer implements a technology and treatment intensity for which the per patient health benefit $\tau_t u_l + (1-\tau_t)v(q(\mu,t))$ is as high as possible. On the basis of the analysis we reach the following conclusion.

Proposition 1: *Because the hospitals operate under the zero-profit constraints,*
a) A payer interested in minimizing the total cost of health care is indifferent between different allocations of the health care budget
b) A slack-averse health care payer is indifferent between budget allocations yielding zero organizational slack, and
c) A health care payer interested in the net benefit of health care bases his decision-making on per patient health benefits only.

Let us consider when this happens in the special case of linear utility $v(q) = vq$ and cost function $c(q) = cq$. Treatment intensity at the long-term care is given as $q(\mu,t) = \frac{(1-\mu)B}{(1-\tau_t)nc}$ and per patient health benefit is $v(q(\mu,t)) = \frac{v(1-\mu)B}{(1-\tau_t)nc}$. Selecting $\mu B < p_1$ implements a technology-treatment intensity pair $(0, \frac{(1-\mu)B}{nc})$ and yield a per patient health benefit $\frac{v(1-\mu)B}{nc}$ for the payer. A budget allocation $p_1 \leq \mu B < p_2$ implements a technology-treatment intensity pair $(1, \frac{(1-\mu)B}{(1-\tau_1)nc})$, and yields the per patient health benefit $\tau_1 u_l + \frac{v(1-\mu)B}{nc}$ for the payer. Finally, a budget allocation $p_2 \leq \mu B$ will implement a pair $(2, \frac{(1-\mu)B}{(1-\tau_2)nc})$, and yields the per patient health benefit $\tau_2 u_l + \frac{v(1-\mu)B}{nc}$ for the payer. As the per patient health benefits decrease in the long term care when the budget share of the acute-care is increased, it is sufficient to

compare health benefits at points where $\mu = 0$, $\mu = \frac{p_1}{B}$, or $\mu = \frac{p_2}{B}$. Corresponding per patient health benefits are $B_0 = \frac{vB}{nc}$, $B_1 = \tau_1 ul - \frac{vp_1}{nc} + \frac{vB}{nc}$, and $B_2 = \tau_2 u_l - \frac{vp_2}{nc} + \frac{vB}{nc}$. The payer implements technology 2 if and only if $B_2 \geq B_t$, for t = 0,1,, technology 1 if $B_1 \geq B_t$ for t = 0,2 and technology 0 if $B_0 \geq B_t$, t = 1,2. Making this comparison provides results: technology 2 is implemented if $nu_l\left(\frac{c}{v}\right) \geq \max\left[\frac{p_2 - p_1}{\tau_2 - \tau_1}, \frac{p_2}{\tau_2}\right]$, technology 1 is implemented if the condition $\frac{p_1}{\tau_1} \leq nu_l\left(\frac{c}{v}\right) \leq \frac{p_2 - p_1}{\tau_2 - \tau_1}$ holds true, and technology 0 is implemented if $nu_l\left(\frac{c}{v}\right) \leq \min\left[\frac{p_1}{\tau_1}, \frac{p_2}{\tau_2}\right]$. If $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$, . Consequently the incremental cost-efficiency ratios rank in order $\frac{p_1}{\tau_1} \leq \frac{p_2}{\tau_2} \leq \frac{p_2 - p_1}{\tau_2 - \tau_1}$ and the payer implements technology 2 (and the associated treatment intensity) if the condition $nu_l\left(\frac{c}{v}\right) \geq \frac{p_2 - p_1}{\tau_2 - \tau_1}$ holds true, and technology 1 if the condition $\frac{p_1}{\tau_1} \leq nu_l\left(\frac{c}{v}\right) \leq \frac{p_2 - p_1}{\tau_2 - \tau_1}$, and technology 0 otherwise. If $\frac{p_2}{p_1} < \frac{\tau_2}{\tau_1}$, then the cost-efficiency ratios rank in order $\frac{p_2 - p_1}{\tau_2 - \tau_1} < \frac{p_2}{\tau_2} < \frac{p_1}{\tau_1}$, and the payer implements technology 2 if $nu_l\left(\frac{c}{v}\right) \geq \frac{p_2}{\tau_2}$ and technology 0 otherwise. These results can be compared with social optimum.

3 Social optimum

The above section showed that cost minimizing payers show no strict preference for any particular technology and/or treatment intensity. On the other hand, the health care payer interested in the net health benefit of health care ends up maximizing the total per patient utility from health care and does not pay any attention to the costs of health care. The fundamental reason for these results lies in the behavioral assumption that hospitals are zero-profit institutions. In general, any of the above models (in terms of

the payer type) may be associated with an equilibrium solution what is inefficient. Cost minimizing payers ignore the benefits of health care totally and a payer maximizing the net health benefit is interested in the per patient health benefits only.

We next analyze the socially optimal health care technology and the level of treatment intensity. In order to do that, we consider a social planner who maximizes the welfare function

$$W(t,q) = n\tau_t u_l + (1-\tau_t)nv(q) - p_t - (1-\tau_t)nc(q) \qquad (6)$$

The welfare function takes into account the total health benefits and total cost of health care. As the organizational slack is basically a transfer of income from the regulator to the hospital, we ignore slack from the welfare analysis.

The social planner maximizes welfare by selecting a technology from the set of available technologies and the level of treatment intensity. A socially optimal technology and treatment intensity *(t*, q*)* must satisfy the condition

$$W(t^*,q^*) \geq W(t,q) \qquad (7)$$

for all feasible treatment intensity and technology pairs $(t,q) \in T \times R_+$.

Assuming that socially optimal treatment intensity exists and is interior, it must satisfy the necessary condition for maximum

$$v'(q^*) - c'(q^*) = 0 \qquad (8)$$

Socially optimal treatment intensity equates patient level marginal benefit from the long-term care with the marginal cost. What is worth observing is that the socially optimal treatment intensity is independent of the optimal health care technology. A socially optimal health care technology *t** satisfies the condition

$$\begin{aligned} &n\tau_{t^*}u_l + n(1-\tau_{t^*})v(q^*) - p_{t^*} - n(1-\tau_{t^*})c(q^*) \geq \\ &n\tau_t u_l + n(1-\tau_t)v(q^*) - p_t - n(1-\tau_t)c(q^*) \end{aligned} \qquad (9)$$

where t is any feasible technology in the set of available technologies. The above condition can be rearranged as

$$n\left[u_1(\tau_{t^*} - \tau_t) + V(q^*)(\tau_t - \tau_{t^*})\right] \geq p_{t^*} - p_t \qquad (10)$$

where $V(q^*) = v(q^*) - c(q^*)$ is the net benefit from treating one patient in the long-term care, evaluated at the optimal treatment intensity q^*.

The first part on the left hand side of the inequality (Equation 10) denotes the net benefit offered by the optimal technology as opposed to any alternative health care technology, where the benefit is described by a change in the probability τ of having only a mild disease after an intervention with the optimal technology. The second part describes the marginal cost change induced by an optimal technology, where the cost change is described by a change in the number of severely ill patients entering long-term care after an intervention using optimal technology. The sum of these must be greater than the price of changing to optimal technology. It is to be noted that any of these can also be negative.

The above condition can be rewritten as

$$n\left[u_1 - V(q^*)\right](\tau_{t^*} - \tau_t) \geq p_{t^*} - p_t \qquad (11)$$

In the above inequality (Equation 11), the left-hand side measures the incremental total benefits between the efficient technology t^* and its alternative technology t and the right-hand side of the inequality measures the incremental cost incurred from a change from technology t^* to t. For example, if the more effective technology 2 is chosen instead of technology 1 (and the difference $\tau_2 - \tau_1 > 0$), the expected aggregate utility is increased in the acute-care, and the number of severely ill patients being referred from the acute care to the long-term care will be reduced. The reason why the net benefit $V(q^*)$ enters the above equation with a negative sign is that a more effective technology at the acute-care reduces the number of patients who would enjoy the net benefit $V(q^*)$ at the long-term care in case of a less effective technology.

The term $u_1 - V(q^*)$ denotes the total benefit a patient receives from health care. We assume for simplicity throughout the following analysis that the patient utility at the acute-care, u_1, exceeds the net benefit of long-term care, $V(q^*)$, when evaluated at the optimum, or $u_1 - V(q^*) > 0$. To simplify the notation in the following analysis, we denote the total aggregate benefit from health care as $n[u_1 - V(q^*)] = W$. In the following analysis we go further and derive the preconditions for each specific technology to be optimal technologies for society.

Conditions for technology 2 to dominate

Let us then analyze the conditions under which the socially optimal health care technology is technology 2. This occurs if technology 2 is better than technologies 1 and minimum care technology 0. As $\tau_2 - \tau_1 > 0$, $\tau_0 = 0$ and $p_0 = 0$, the formal conditions for a social planner to choose technology 2 are given as

$$W \geq \frac{p_2 - p_1}{\tau_2 - \tau_1} \tag{12}$$

denoting the comparison against technology 1, and

$$W \geq \frac{p_2}{\tau_2} \tag{13}$$

denoting the comparison against technology 0.

Condition (Equation 12) defines that technology 2 is better than technology 1 and condition (Equation 13) makes technology 2 better than the minimum care technology. Equation 12 says that the total aggregate health benefit exceeds the incremental cost-efficiency ratio between technologies 2 and 1, respectively, and the condition (14) does the same except that it compares technology 2 to technology 0.

Both conditions hold true simultaneously if the total aggregate health benefit exceeds both incremental cost-efficiency ratios, that is the condition $W = \max\left[\frac{p_2 - p_1}{\tau_2 - \tau_1}, \frac{p_2}{\tau_2}\right]$ is satisfied. Now, $\frac{p_2 - p_1}{\tau_2 - \tau_1} \geq \frac{p_2}{\tau_2}$ holds true if and only if the condition $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1} > 1$ is

satisfied. In this case a sufficient condition for the planner to prefer technology is when $W \geq \frac{p_2 - p_1}{\tau_2 - \tau_1}$. In case the condition $\frac{\tau_2}{\tau_1} \geq \frac{p_2}{p_1} > 1$ holds true, technology 2 should be chosen whenever the total health benefit exceeds the incremental cost-efficiency ratio for the minimum care technology, or $W \geq \frac{p_2}{\tau_2}$.

Conditions for technology 1 to dominate

Let us next consider the situation in which technology 1 is socially optimal. Since $\tau_1 - \tau_0 = \tau_1 > 0$ and $\tau_2 - \tau_1 > 0$, the conditions for technology 1 to dominate over other health care technologies is that technology 1 is better than technology 0 and technology 2. Formally, this occurs when conditions

$$W \geq \frac{p_1}{\tau_1} \tag{14}$$

and

$$\frac{p_1 - p_2}{\tau_1 - \tau_2} = \frac{p_2 - p_1}{\tau_2 - \tau_1} \geq W \tag{15}$$

are both satisfied. Technology 1 is optimal for society if and only if the total health benefit satisfies the condition $\frac{p_1}{\tau_1} \leq W \leq \frac{p_2 - p_1}{\tau_2 - \tau_1}$. If $\frac{p_2 - p_1}{\tau_2 - \tau_1}$ is smaller than $\frac{p_1}{\tau_1}$, the above conditions can not be satisfied and technology 1 can not be socially optimal. This happens if the condition $\frac{\tau_2}{\tau_1} > \frac{p_2}{p_1} > 1$ holds true.

Conditions for technology 0 to dominate

Since $\tau_t > 0$ for $t = 1,2$, the social planner wants to select the minimum care technology at the acute-care if and only if

$$W \leq \frac{p_t}{\tau_t} \tag{16}$$

for $t = 1,2$. The above two conditions hold simultaneously when the condition $W \leq \min\left[\frac{p_1}{\tau_1}, \frac{p_2}{\tau_2}\right]$ holds true. Now $\frac{p_2}{\tau_2} \geq \frac{p_1}{\tau_1}$ if and only if $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$.

Choosing the technology

The relationship between the ratios $\frac{p_2}{p_1}$ and $\frac{\tau_2}{\tau_1}$ plays an important role in ranking the incremental cost-effectiveness ratios (ICER) for technologies. The condition $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$ is crucial in ranking the cost-effectiveness ratios between different technologies. Let us denote the cost-effectiveness ratio for two technologies, t and s, as $ICER_{ts} = \frac{p_t - p_s}{\tau_t - \tau_s}$. Under the condition $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$ it holds true that $ICER_{10} \leq ICER_{20} \leq ICER_{21}$, and if the condition does not hold true and $\frac{p_2}{p_1} < \frac{\tau_2}{\tau_1}$ then $ICER_{21} < ICER_{20} < ICER_{10.}$

The following conclusions ensue:

1. If the relative price increase of switching from technology 1 to technology 2 is greater than the relative increase in probability of low severity, i.e. the condition $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$ holds true, then the incremental cost-effectiveness ratios can be ranked as $\frac{p_2 - p_1}{\tau_2 - \tau_1} \geq \frac{p_2}{\tau_2} \geq \frac{p_1}{\tau_1}$. In this case, technology 2 is socially optimal if the total aggregate health benefit $n[u_l - V(q^*)]$ exceeds the highest incremental cost-effectiveness ratio $\frac{p_2 - p_1}{\tau_2 - \tau_1}$, technology 1 is socially optimal if $\frac{p_2 - p_1}{\tau_2 - \tau_1} > n[u_l - V(q^*)] > \frac{p_1}{\tau_1}$, and the minimum care technology is socially optimal in case $\frac{p_1}{\tau_1} \geq n[u_l - V(q^*)]$.

2. If the relative increase in probability of health offered by technology 2 is equal to, or higher than, the relative price increase albeit technology 2 is more expensive than technology 1, i.e. $\frac{\tau_2}{\tau_1} > \frac{p_2}{p_1} > 1$, then technology 1 is never socially optimal. In such a case, technology 2 is preferred by the social planner if

$$n[u_l - V(q^*)] \geq \frac{p_2}{\tau_2} \Leftrightarrow \tau_2 n[u_l - V(q^*)] \geq p_2, \qquad (17)$$

i.e. the total benefit offered by technology 2 is considered greater than its price. Technology 0, minimum care technology, is optimal otherwise. The following proposition summarizes the above discussion.

Proposition 2: *If* $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$ *then technology 2 dominates under the condition* $n[u_l - V(q^*)] \geq \frac{p_2 - p_1}{\tau_2 - \tau_1}$, *technology 1 dominates under the condition* $\frac{p_1}{\tau_1} \leq n[u_l - V(q^*)] < \frac{p_2 - p_1}{\tau_2 - \tau_1}$, *and technology 0 dominates otherwise. If* $\frac{\tau_2}{\tau_1} > \frac{p_2}{\tau_1} > 1$, *then technology 2 dominates under the condition* $n[u_l - V(q^*)] \geq \frac{p_2}{\tau_2}$ *and the minimum care technology, dominates otherwise.*

4 Empirical Cases

4.1 Construction of an empirical model

We can modify the outcome of Proposition 2, as $V(q) = v(q) - c(q)$. Thus, the inequalities can be rewritten as follows:

if $\frac{p_2}{p_1} \geq \frac{\tau_2}{\tau_1}$, then technology 2 is socially optimal when

$$u(a^l) - v(q) \geq \frac{p_2 - p_1}{n(\tau_2 - \tau_1)} - c(q), \tag{18a}$$

technology 1 is optimal if

$$\frac{p_2 - p_1}{n(\tau_2 - \tau_1)} > u(a^l) - v(q) \geq \frac{p_2}{n\tau_2} - c(q), \tag{18b}$$

and the minimum care technology is socially optimal whenever

$$\frac{p_1}{\tau_1 n} - c(q) \geq n[u(a^l) - v(q)]. \tag{18c}$$

Similarly, if $\frac{\tau_2}{\tau_1} > \frac{p_2}{p_1} > 1$, technology 2 is socially optimal whenever

$$u(a^I) - v(q) \geq \frac{p_2}{\tau_2 n} - c(q), \qquad (19)$$

and the minimum care technology 0 is socially optimal otherwise.

Primarily, the criteria above distinguish between the benefit of active acute phase treatment as compared to the existing technology. Secondarily, they offer economic criteria for choosing between the different technologies; this is discussed in detail in the last section Conclusions and Discussion.

The right side of the inequalities 18-19 denote the economical impact of active acute treatment, with the value zero being the watershed point: a value below zero means that the introduction of a new technology offers savings for the health care payer and, consequently, values below zero strongly encourage the health care payer to intensify acute care using a new technology.

A positive value on the right side of the inequality describes the additional total costs per healed patient associated with an intensified acute care. In such a case, the left side of the inequality becomes crucial: how much does the health care payer attach value to non-monetary benefits associated with an intensified acute care? This will be discussed further in the last section.

4.2 Empirical cases

We have tested our model on two real-life cases, one representing the introduction of a new technology for the treatment of stroke, the major cause of somatic disability and the second leading cause of death, with a global burden of 6 million ischemic strokes per year and an estimated 4.4 million individuals dying annually as a consequence thereof (Murray and Lopez 1997; Wardlaw, Zoppo et al. 2003).

The second case concerns a relatively rare disease, *glioblastoma multiforme*, affecting approximately 9000 patients annually. However, glioblastomas are the most severe

primary brain cancer type in humans: less than 3% of the patients are alive at 5 years after diagnosis (Ohgaki and Kleihues 2005). Thus, there is an urgent need for more efficient therapy. In the second case, we examine the introduction of a new treatment modality, Boron Neutron Capture Therapy (BNCT), for the management of patients suffering from this serious disease.

4.2.1 Stroke

Stroke is the most common type of cerebrovascular disease. It requires several days of acute treatment followed by a long rehabilitation period, which has led to an increase in treatment costs. Patients suffering from stroke require an average of about 2.5 years of treatment, which in the Helsinki region corresponds to a cost of approximately 100,000 euros per patient (Kaste, Fogelholm et al. 1998; City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c). In total, cerebrovascular diseases induced treatment costs of EUR 440 million in Finland in 1999, and the aging of the population is estimated to cause a doubling of acute treatment by the year 2030 (Fogelholm, Rissanen et al. 2001; Statistics Finland 2005).

The Department of neurology at the Helsinki University Central Hospital (HUCH) has started to treat stroke patients with ultra-acute thrombolysis, in which the critical blood clot is removed by dissolving it. Thrombolysis is part of an efficient and costly treatment chain consisting of prompt patient screening, fast computer-aided neuro-imaging and diagnostics, timely thrombolytic therapy, and a consecutive treatment based on special expertise in a separate stroke unit. The thrombolysis must at present be initiated within 3 hours after the first signs of a stroke. Alteplase, a glycoprotein produced utilizing recombinant DNA technology, serves as the thrombolytic agent, and the costs of the product alone exceed thousand euros per dose.

In our model, the Acute care unit is represented by the Neuro-Emergency Unit (NEU) at HUCH, and the Long-term hospital by the supporting hospitals to which HUCH refers the patient no longer in need of acute and most advanced treatment.

Technology 0 represents a situation where the patient is directly admitted to a supporting hospital, i.e. no specific treatment is available. This is still a reality for

patients who have not been self-supporting before onset of stroke, such as elderly disabled people, who are directed primarily to the supporting hospitals. No further intensive interventions are implemented, and thus the patients do not incur costs on the acute care hospital (representing low and high technology, technology 1 and 2, respectively); all costs are carried by the supporting hospitals.

Technology 1 consists of prompt diagnosis, supportive acute treatment and early onset of intensive rehabilitation, all performed at HUCH and generating cost. Due to a more efficient treatment at the acute phase, the survival of stroke patients is higher and thus the patient stream to hospitals in long term care might increase. However, the patients usually require less assistance owing to the payoffs of early rehabilitation and a shorter total treatment time, leading to lower total costs for the sub-acute and long term care.

The introduction of **technology 2** has required additional investments by HUCH, as the whole treatment chain had to be set up. The strict 3 hour time window requires an efficient acute care system:

1. Short response times to emergency calls from patients, and an efficient on-site diagnosis capability
2. Sophisticated imaging techniques and advanced laboratory services available within minutes from arrival of patient
3. The staff has to be specially trained and certified for performing thrombolysis
4. There has to be resources available for high-intensive monitoring of patients that have received the therapy.

Variable costs include expenses incurred from running the functions above, as well as costs from the thrombolytic drug.

However, with the introduction of thrombolytic therapy at NEU, the neurological wards at HUCH and the long-term hospitals have benefited of significant savings due to a diminished stream of severely ill patients. A part of the patients are virtually cured at an early stage with less support and rehabilitating interventions needed, and the total treatment time becomes shorter.

In 2002, about 8 percent of the stroke patients coming to the HYKS neurological clinic received thrombolysis, and by the end of 2003 the number had doubled. About 60 percent of the patients receiving thrombolysis recovered. The total cost savings with respect to the recovered patients have been estimated to approximately 84,000 euros per patient (Kaste, Fogelholm et al. 1998; Lindsberg, Roine et al. 2000; City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c); the savings represent over 80 percent of the non-recovering patients' total treatment costs. The main part of the savings comes from the costs after the first year (Kaste, Fogelholm et al. 1998), where health care personnel expenses constitute the most significant share of the costs.

Defining the parameters for ischemic stroke

For our model we can define the following parameters:

The **regulator** is the Hospital District of Helsinki and Uusimaa, HUS.
The **acute care hospital** is represented by the Department of neurology at HUCH and regional hospitals, all serving under HUS. The acute phase is here defined to include direct costs incurring from intensive treatment up to one year after the initial stroke incident.
The **long-term care** is provided by the regional hospitals of Helsinki and Uusimaa, all serving under HUS. The bulk of long-term care is given after the first year from the initial stroke incident.
The **number of patients** is 2000 per annum (Lindsberg, Roine et al. 2000).
Technology 0, t_0, consists of supportive care given at the regional hospitals. This is a baseline treatment and does not incur additional costs; thus $\mathbf{p_0} = 0$
Technology 1, t_1, is offered initially by the Stroke unit at HUCH and continued up to 1 year after the stroke incident. It includes specialized acute-phase care after a stroke as well as intensive rehabilitation both in HUCH and in the regional hospitals. The price increase when introducing technology 1 is derived from the diagnosis-related group (DRG) price for treating one uncomplicated stroke at our teaching university hospital; $\mathbf{p_1}$ = 4 060€ / patient * 2000 patients = 8.12 M€ (Department of Neurology Hospital District of Helsinki and Uusimaa HUS 2005). The DRG price includes both intensified acute treatment as well as basic car; however, as an intensified acute treatment leads to a higher survival rate an thus increases total treatment given, we assume that the DRG price reflects sufficiently well the true total additional costs induced by technology 1.

Technology 2, t_2, is a series of events, beginning at the site of the stroke and ending either after a decision of not giving thrombolytic therapy, or at the Stroke unit after thrombolysis. The additional costs induced by the introduction of thrombolytic therapy are counteracted by the savings resulting from reduced disability during the first year (Fagan, Morgenstern et al. 1998). Thus, the price for treating one stroke with alteplase equals the price of treating a patient with technology 1; consequently, the total price for technology 2 is: p_2 = (4 060 € / patient * 1 900 patients) + (4 060 € / patient * 100 patients) = 8.12 M€ (Department of Neurology Hospital District of Helsinki and Uusimaa HUS 2005).

Severity of illness at referral to the acute hospital is defined as severe ischemic stroke with clear signs of unilateral loss of motory functions.

The health care budget B is set by a regional political council with representatives from all communities in Helsinki and Uusimaa that refer patients to HUS. We approximate the total budget for stroke treatment in the Helsinki and Uusimaa region to be 80 million € annually (Kaste, Fogelholm et al. 1998; Lindsberg, Roine et al. 2000; City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c).

The share of budget allocation to acute care **μ** is set by HUS. Typically, the acute and long term sectors have separate budgets, why HUS was established in order to facilitate a controlled budget allocation between acute and long-term care. In our example, the initial costs of introducing technologies 1 and 2 were fully born by the acute care hospital, but without a change in the budget allocation μ. This will be discussed further in chapter five.

The obtained **utility $u(a^h)$** and **$u(a^l)$** are defined as the end-points of **high** and **low severity of disease after acute treatment**, respectively. In this paper, we use the modified Rankin scale as a criteria for independence: a score of 0 – 2 is approximately equivalent to independence, and it corresponds to a score of >18 on the Barthel Index (Wade 1995). Consequently, a modified Rankin score of 0 - 2 demonstrates low severity of disease, and high severity is defined as a score of **>** 2. The obtained utility is evaluated at one year after the stroke as a function of the end-point and the probability τ_t of achieving that end-point.

In the **acute care phase** we can conclude that:
The utility in a high severity of disease $u(a^h) = 0$, when the Rankin score > 2; with a score of 0 - 2 the patient experiences a utility from the treatment, and $u(a^l) > 0$.

Slackness S is usually perceived as an unwanted way of allocating resources, and thus S is preferably minimized. The assumption holds also with all units in HUS.

The number of stroke patients is 2000 annually; n=2000.

The **probability of having a low severity of disease,** *i.e.* having a modified Rankin of 0 to 2 after receiving treatment at the acute care hospital is 0 for technology 0 ($\tau_0 = 0$), 0.22 for technology 1 ($\tau_1 = 0.22$) and 0.23 for technology 2 ($\tau_2 = \tau_1 +$ [proportion of eligible patients for thrombolytic therapy x risk reduction] = 0.22+[0.05 x 0.14] = 0.227) (Stroke Unit Trialists' Collaboration 2002; Wardlaw, Zoppo et al. 2003).

We utilized two parallel methods for counting **the average cost c(q) of treating one Finnish stroke patient with basic technology (p_0)**. The costs have originally been calculated with an extrapolation to year 1991 (Kaste, Fogelholm et al. 1998). In our first calculation we used the same assumptions as in the article, *i.e.* a discount rate of 5% and an increase of productivity by 1.5%. This yielded an average cost of 86 548 for year 2004. In our second calculation we related the unitary costs of healthcare and social services needed in the treatment of stroke patients that were used as a basis for the calculations in year 1987 to the corresponding costs in 2004 (Kaste, Fogelholm et al. 1998; City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c). The second calculation yielded a costs of 75 682 euros per patient. The average of these two calculations yields as c(q) 81 115 euros per stroke patient treated with technology zero.

By plugging in the values into proposition 1, we see that the three zero-slack allocations (s=0) get the values $\{\mathbf{0}, \frac{p_1}{B} = \frac{8.12m€}{80m€} = \mathbf{0.1015}, \frac{p_2}{B} = \frac{8.12m€}{80m€} = \mathbf{0.1015}\}$, indicating that, for an optimal treatment intensity, μ should get a value of 0 or 0.1015. As technology two incurs no additional costs as compared to technology one, the health care payer is initially indifferent between technologies one and two.

Proposition 2 makes a distinction between whether $\frac{p_2}{p_1}$ is smaller than $\frac{\tau_2}{\tau_1}$ or not.

Consequently, as $1.032 = \frac{0.227}{0.22} = \frac{\tau_2}{\tau_1} > \frac{p_2}{p_1} = \frac{8120000€}{8120000€} = 1.00$, technology 2 should be optimal if

$$n\left[u\left(a^l\right) - V(q)\right] \geq \frac{p_2}{\tau_2}. \quad (20)$$

By plugging the numbers into the equation above

$$u\left(a^l\right) - V(q) \geq 17\,885\ € / \text{patient}, \quad (21)$$

or

$$u\left(a^l\right) - v(q^*) \geq -\ 63\,330\ € / \text{patient} \quad (22)$$

we can see that technology 2 should be chosen if the added value of a successful acute treatment as compared to optimal long term treatment is appreciated to be an equivalent of -63 330 € or more. The negative number denotes that technology 2 offers a direct economic advantage, and thus the choice between technologies is evident. However, in table 1 we can see that if technology 2 would require an initial investment of 1.2 m€, the sign turns positive and the treatment would induce an extra cost of 4 599 € per additional recovered patient. This is visualized in Figure 2 where the cost-efficiency frontier for technology 2 breaks the zero level and gains positive values on the y-axis.

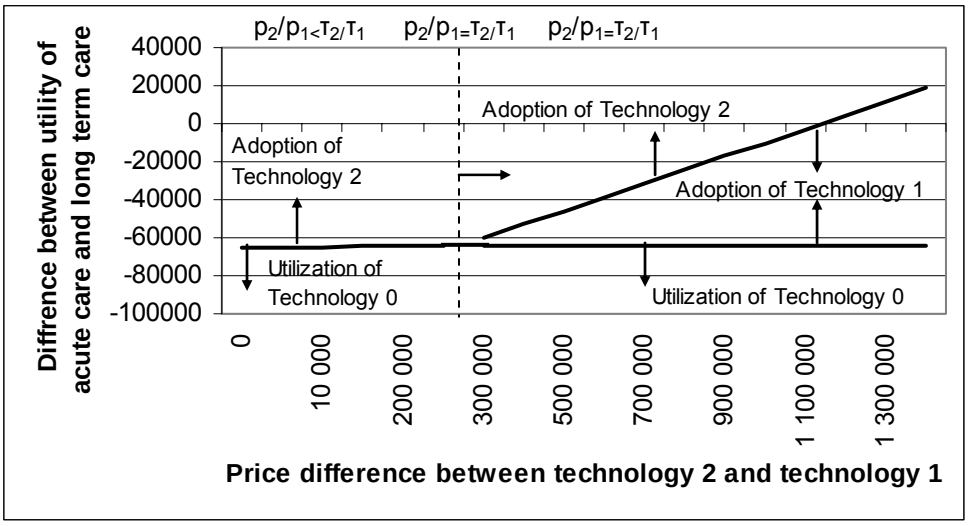

Figure 2. The Cost-Efficiency Frontiers in Acute Care Treatment of Stroke in increasing prices of thrombolytic therapy.

In the latter case, technology 2 is not economically competitive; however, it can be chosen on other grounds. Such arguments could be an interest for the technology *per se*, a vision of a development of the technology to become more competitive, or a lower risk of death or dependency. This will be discussed further in chapter five.

In should be noted, that all other things being equal, $u - v$ should logically be ≥ 0 because long-term care can never be preferable to acute care if their effect is equal; it would not be meaningful to keep the patient sick for a longer period instead of a shorter. However, a social dictator might purposely choose to promote long-tern care, even at an additional cost, *e.g.* in order to promote jobs in the sector. In this case, the dictator might choose to spend 63 330 € / patient so that the hospital can be kept running.

The share of eligible patients for thrombolysis has been a central point in economic calculations concerning thrombolytic therapy (Hankey and Warlow 1999; Lindsberg, Roine et al. 2000). Our model suggests that available data strongly support the rationale for adopting technology two irrespective of even significant changes in the achieved eligibility percentages: for eligibility percentages between 1 and 33 percent, technology two remains dominant, with only a marginal change in the achieved utility (Figure 3).

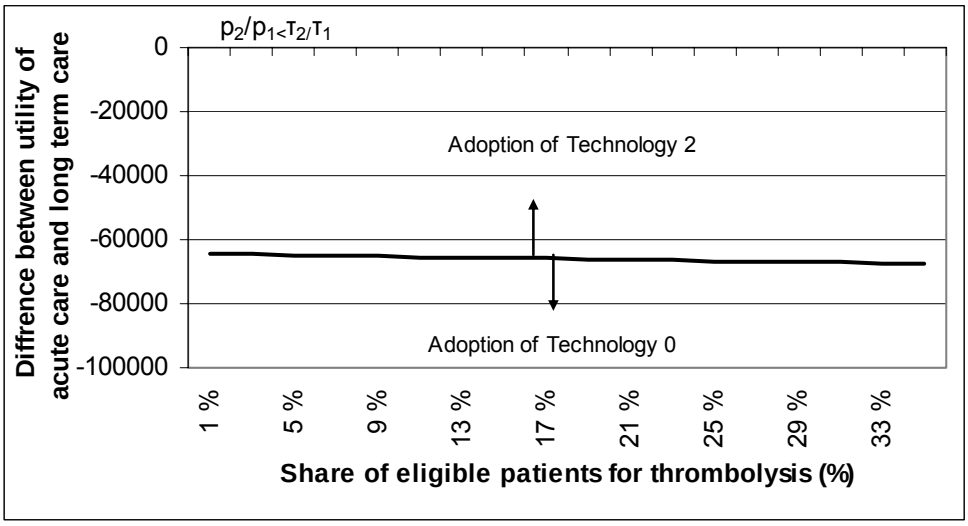

Figure3. The Cost-Efficiency Frontiers in Acute Care Treatment of Stroke with an increasing number of eligible patients for thrombolytic therapy.

Finally, technology 1 remains economically competitive up to a cost of 17 845, after which the same situation applies as with technology 2: other reasons can defend a choice of technology 1 as compared to the basic technology, τ_0, but always inducing an economical burden for the health care payer.

4.2.2 Boron Neutron Capture Therapy

Glioblastoma multiforme has eluded efficient therapy, with the most efficient available treatment offering roughly a doubling of the median survival time to approximately 40 weeks after diagnosis (Andersen 1978; Walker, Alexander et al. 1978; Walker, Green et al. 1980; Chin, Young et al. 1981; Kristiansen, Hagen et al. 1981). In an attempt to offer significant improvement to the prognosis of this deleterious disease, the Finnish Boron neutron capture therapy project was launched in 1994. In this paper we define it as **technology 2**.

Boron Neutron Capture Therapy (BNCT) is based on boron-10 atoms that are coupled to a carrier molecule with an affinity towards malignant cells. Both boron-10 and the carrier molecule are non-toxic as such. However, once inside the cancer cell, the boron-10 molecule (^{10}B) is activated by relatively inert, low-energy neutron irradiation: the ^{10}B molecule catches a neutron and disintegrates quickly to yield a highly energetic helium-4 nucleus (i.e. alpha-particle, ^{4}He) and a recoiling lithium-7 ion (^{7}Li).

The alpha particles and lithium ions from the $^{10}B(n,alpha)^{7}Li$ reaction give rise to closely spaced ionizing events with a high linear energy transfer (LET) but a very short combined path length, only 12 microns. The high LET irradiation induces injuries with little if any cellular repair, but only near to, on, or within the cells containing ^{10}B atoms; a typical glioblastoma tumour cell is within the size range 10-40 μm. The damage produced can be extremely localized, thereby sparing normal tissue components. Thus, the tumour cells are eliminated but the normal tissue is spared.

In basic treatment **(technology 0)** the patient is diagnosed and given basic life support, and a normal neurosurgical removal of the visible tumour mass is performed. In some cases the patient can be severely ill already at time of diagnosis or the location of the tumour can un-accessible, contraindicating normal treatment measures; these patients are, however, exceptions.

If the patient does not present with specific contraindications, the patient is usually offered concomitant radiation after the neurosurgical debulkment. We define **Technology 1** as consisting of 1. A neurosurgical operation with the aim of removing all malignant tissue, and 2. A full series of radiation therapy sessions, in addition to normal supportive procedures and therapy.

Technology 2 encompasses 1. A normal neurosurgical operation, followed by 2. BNCT-treatment as described above. The introduction of technology 2 has required major investments: extensive modifications of the nuclear research reactor FiR-1 in Espoo (Auterinen, Hiismäki et al. 1998), quality assurance measures thereof (Auterinen, Seren et al. 2004; Uusi-Simola, Seren et al. 2004), development of a boron measurement system (Laakso, Kulvik et al. 2001), preclinical safety testing (Kulvik, Vahatalo et al. 2004) and the complete development work from synthesis experimentation to clinical applications for the boron-carrier-complex (Kulvik, Vahatalo et al. 2003).

The patient treatments started in 1999 through a specific BNCT treatment company, and the treatments have been ongoing since (Joensuu, Kankaanranta et al. 2003; Kankaanranta 2005; Pakkala 2005).

Defining the parameters for glioblastoma treatments

The main treatment is always given in a University hospital, where the treatment costs are intercomparable. Additionally, BNCT is performed only in HUCH, why we use the interventions provided at HUCH as representing the whole country.

For our model we can define the following parameters:

The **regulator** is the (Neurosurgical department Hospital District of Helsinki and Uusimaa HUS 2005), HUS. However, as there is and will in Finland be only one BNCT treatment station in the foreseeable future, and as *glioblastomas* are rare, our implementation will cover the whole of Finland.

The **acute care hospital** is represented by the Departments of neurology, neurosurgery and Oncology at HUCH, serving under HUS. The acute phase is here defined to include direct costs that are additional to normal treatment costs for patients suffering from *glioblastoma multiforme*.

The **long-term care** is provided by HUCH and the regional hospitals of Helsinki and Uusimaa, all serving under HUS. The bulk of long-term care is given during the first year from diagnosis.

The **number of patients** is approximately 150 per annum (Ohgaki and Kleihues 2005).

Technology 0, t_0, consists of prompt diagnosis, acute care, a neurosurgical operation and supportive care given initially at HUCH and later mainly at the regional hospitals. This is a baseline treatment and does not incur additional costs; thus $\mathbf{p_0} = 0$.

Technology 1, t_1, is offered by the Department of neurology at HUCH (diagnosis and acute care), the Department of Neurosurgery at HUCH (neurosurgical debulkment and histological-pathological diagnosis of tumour), and the Department of oncology at HUCH (radiation therapy); of these, however, only the radiation therapy incurs additional cost when compared to technology 0. As the equipment is used mainly for the treatment of other, more abundant diseases, we do not accrue initial fixed costs for the introduction of technology 1; the fixed costs are sufficiently well included in the DRG price for *glioblastoma multiforme*. The price increase when introducing technology 1 is derived from the diagnosis-related group (DRG) price for treating one *glioblastoma multiforme* -patient at HUCH; $\mathbf{p_1}$ = 2420 € / patient * 150 patients = 363 000 € (Neurology 2005; Neurosurgery 2005; Oncology knowledge center Hospital

District of Helsinki and Uusimaa HUS 2005). As an intensified acute treatment leads to a longer survival time, we assume that the DRG price reflects sufficiently well the true total additional costs induced by technology 1.

Technology 2, t_2, consists of a series of events and interventions, identical with technology 1 until neurosurgical debulkment is performed. The additional costs induced by technology 2 consist of a fixed part and per patient -based running costs, less the price for giving a full series of conventional radiotherapy. As several other brain cancer treatment modalities are under continuous research, and especially as accelerator based neutron sources are under intensive development, we assume that the effective life cycle for nuclear reactor based BNCT is 10 years, after which the technology has become too obsolete to be competitive (Blue and Yanch 2003; Svensson and Moller 2003; Kononov, Kononov et al. 2004; Lee, Han et al. 2004). The first patient in Finland was treated on May 1999, and in May 2005 a total of 42 brain tumour patients have received BNC-treatment (Kankaanranta 2005). Assuming a steadily rising patient stream we somewhat optimistically assume 100 more patients to be treated during the following four years. We additionally assume that the increasing patient stream brings about savings due to a streamlining of the procedures, which compensates for the impact of inflation on costs; we keep the price for one treatment at the 1999 level, i.e. 20 000 €. Consequently, we yield a price for technology 2 totalling $\mathbf{p_2}$ = (2420 €/*patient* * 136 patients/year) + 2 000 000 €/10 years + 20 000 € / patient*14.2 patients/year = 329 120 + 200 000 + 280 000 € = 890 120 €.

Severity of illness at referral to the acute hospital is defined as glioblastoma with clear symptoms of disease and a Karnofsky score below 70; the Karnofsky score will be discussed in more detail below.

The health care budget B is in principle set regionally by respective political councils or equal. However, in the case of rare diseases with interventions centralized to university hospitals, the budget is set by the respective university hospitals. As BNCT is given solely at HUCH, the decisions are made by a political council with representatives from all communities in Helsinki and Uusimaa that refer patients to HUS. We approximate the total budget for treatment of glioblastoma multiforme in Finland to be 4.440 million € annually (Neurological department Hospital District of

Helsinki and Uusimaa HUS 2005; Neurology 2005; Neurosurgery 2005; Neurosurgical department Hospital District of Helsinki and Uusimaa HUS 2005; Oncology knowledge center Hospital District of Helsinki and Uusimaa HUS 2005; City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c) [4].

The share of budget allocation to acute care **μ** is also in brain tumour treatment set by HUS. However, in contrast to treatment of stroke, only the initial costs of introducing technology 1 were born by the acute care hospital. The establishment of the BNCT treatment station was strongly supported by the National Technology Agency of Finland and incurred therefore no costs on HUCH. Our model intends, however, to take a broad view as possible, and thus we include also the fixed costs for technology 2 into the calculations. As the funding comes from outside, μ is not changed.

The obtained **utility $u(a^h)$** and **$u(a^l)$** are defined as the end-points of **high** and **low severity of disease**, respectively. The Karnofsky Performance Scale combines the degree of disease with a person's ability to care for self (Karnofsky, Abelmann et al. 1948). It is widely used, but offers only a rather arbitrary assessment of severity of disease (Slevin, Plant et al. 1988; Murray, Nelson et al. 1995; Green 1997). However, it has been commonly used in clinical trials concerning brain tumour treatment, and we deem it adequate for the purpose of this paper. Consequently, we define a Karnofsky score of ≥ 70 (70 = Cares for self, unable to perform normal activity or to do active work) as demonstrating low severity of disease, and high severity is defined as a Karnofsky score of < 70.
The obtained utility is evaluated at one year after diagnosis as a function of the end-point and the probability τ_t of achieving that end-point.

In the **<u>acute care phase</u>** we can conclude that:
The utility in a high severity of disease $u(a^h) = 0$, when the Karnofsky score < 70; with a score of **≥** 70 the patient experiences a utility from the treatment, and $u(a^l) > 0$.

[4] This consists of initial treatment costs of (2 400 € + 7 020 € + 2420 €) =11 840 / patient (diagnosis, initial treatment, neurosurgery and radiation therapy) and a three month late stage period totalling 16 200 €, where the patient is again in need of intensified support and treatment.

Slackness S is usually perceived as an unwanted way of allocating resources, and thus S is preferably minimized. The assumption holds also with all units in HUS.

Annually 150 **patients** are diagnosed with *glioblastoma multiforme*.

The enhanced **probability of having a low severity of disease** after basic treatment**,** *i.e.* a Karnofsky score of ≥ 70 at one year after diagnosis, is 0 for technology 0 ($\tau_0 = 0$), 0.082 for technology 1 ($\tau_1 = 0.082$) (Kristiansen, Hagen et al. 1981; Laperriere, Zuraw et al. 2002)[5]. For BNCT, the developers strived for an enhancement of τ by 50%[6], yielding $\tau_2 = 0.123$ (Kallio, Kulvik et al. 1997).

We derived **the average cost c(q) of treating one Finnish glioblastoma patient with basic technology (p_0)** by combining several data sources. The DRG price 2 400 € / patient reflects costs accrued from initial diagnosis and treatment (Neurological department Hospital District of Helsinki and Uusimaa HUS 2005). The initial CT-scan has to be complemented by an MR-imaging and followed by neurosurgery, adding up to a total cost of 7 020 € (Neurosurgical department Hospital District of Helsinki and Uusimaa HUS 2005). We exclude costs related radiation therapy. With such treatment the weighted average median survival of patients is 18 weeks, with an initial improvement phase, a long phase of deterioration and concomitantly an increasing need of care with occasional visits to an acute care unit (Chin, Young et al. 1981; Laperriere, Zuraw et al. 2002). The supportive phase is about two thirds of the total survival time (Kristiansen, Hagen et al. 1981), and thus we approximate the average price of later stage treatment to 83 days * 214 €/day = 17 762 € (City of Helsinki 2005a; City of Helsinki 2005b; City of Helsinki 2005c). This yields a total average cost of c(q) = 27 182 € / patient.

By plugging in the values into proposition 1, we see that the three zero-slack allocations (s=0) get the values $\{\mathbf{0}, \frac{p_1}{B} = \frac{363\,000}{4\,440\,000} = \mathbf{0.082}, \frac{p_2}{B} = \frac{890120}{4440000} = \mathbf{0.200}\}$

---

[5] τ_1 was derived by combining 1. Performance data on glioblastoma patients after operation and radiotherapy with or without chemotherapy, yielding an average 62% of patients not capable of caring for self at one year, with 2. Risk ratio for 1-year mortality of post-operative radiotherapy versus no radiotherapy = 0.81; these correspond to the terms σ_t and δ_t in equation (2), respectively.

[6] The enhancement reflected anticipations of both a better survival for a subpopulation as well as a better quality of life as assessed by ability of caring for self.

indicating that for an optimal treatment intensity μ should get a value of 0.082 or 0.109. Proposition 2 makes a distinction between whether $\frac{p_2}{p_1}$ is smaller than $\frac{\tau_2}{\tau_1}$ or not.

Consequently, as

$$\frac{890120}{363000} = 2.452 = \frac{p_2}{p_1} > \frac{\tau_2}{\tau_1} = \frac{0.123}{0.082} = 1.500, \quad (23)$$

technology 2 should be optimal if

$$n[u(a^l) - V(q)] \geq \frac{p_2 - p_1}{\tau_2 - \tau_1}. \quad (24)$$

The right side of the inequality can be regarded as emphasizing the economic rationale of introducing a new technology, whereas the left side highlights other, non-monetary arguments in favor of an intensified acute phase treatment.

By plugging the numbers into the equation above

$$u(a^l) - V(q) \geq \text{EUR 85 710 / patient} \quad (25)$$

or

$$\Leftrightarrow u(a^l) - (v(q^*) \geq \text{EUR 58 528 / patient} \quad (26)$$

we can see that technology 2 should be chosen if the added value (or opportunity cost) of a successful acute treatment compared to optimal long-term treatment is appreciated to be an equivalent of EUR 58 528 or more. In other words, technology 2 does not offer any direct economic advantage, and thus the choice between technologies is ambiguous.

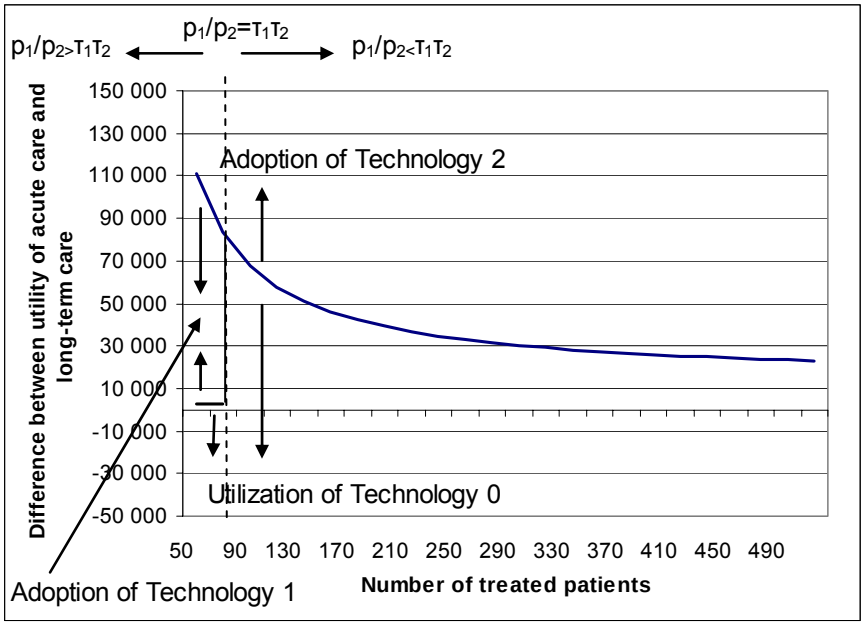

Figure 4. The costs associated with one recovered patient as a function of the probability of achieving good health with technologies 1 and 2.

This is visualized in Figure 4 where the cost-efficiency frontier for technology 2 does not break the zero level. High sunk costs (initial investment of 1.2 million euros) in development of the technology 2 can be overtaken either by enhancing the patient base and the size of units providing this kind of treatment, or by introducing a new technology with higher direct health effects. With the sunk costs that high, the cost-efficiency frontier for technology 2 breaks the zero level with recovery rates no less than 55 percent, as shown in Figure 5.

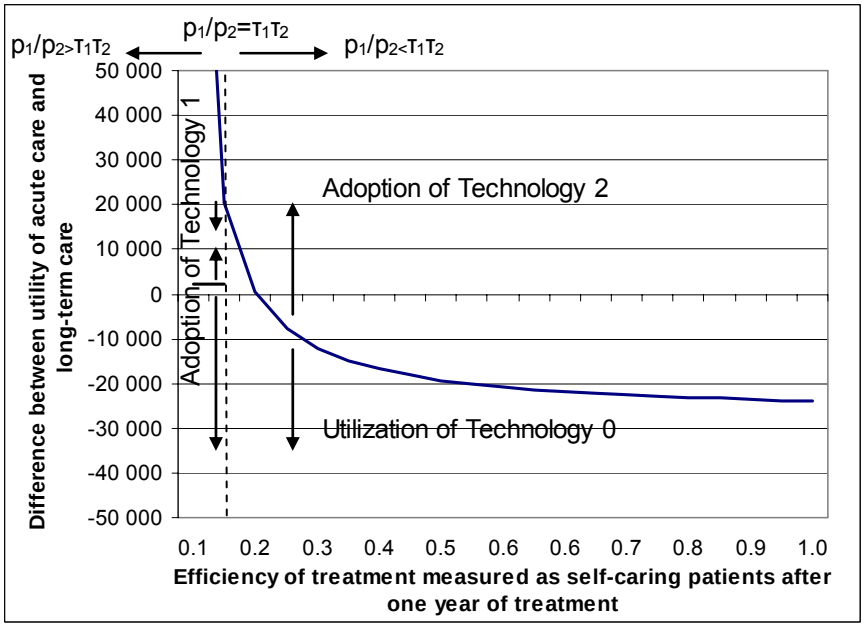

Figure 5. The costs associated with the probability of achieving good health with technologies 1 and 2.

5 Conclusions and discussion

This study analyses how the implementation of new technological applications in acute treatment affects the long-term cost structure of health care. The non-monetary utility is compared to cost-efficiency impacts of a new technology. A theoretical apparatus is constructed and utilized in two empirical cases: thrombolysis therapy for stroke, and Boron Neutron Capture Therapy (BNCT) on glioblastoma-type brain cancers. The empirical cases indicate how the monetary cost-efficiency of the new technologies can be related to the non-monetary patient utility.

The first empirical case shows, that the introduction of a new treatment technology can induce direct savings for the healthcare payer. Critical factors are the probability of the treatment being effective, the incidence of the disease, as well as the costs of acute versus long term treatment and the initial sunk costs. The introduction of the assessed technologies is clearly rational as compared to baseline technology.

In the second empirical case all critical factors are nearly opposite to the first case: it presents a rare disease with a low probability of recovery, high sunk costs as well as acute phase costs but relatively low long term treatment costs due to the harsh progression of the disease. A new technology showing low effect but high initial costs calls for a larger population base. This gives rationale for a cooperation abridging national borders.

Finally, we still discuss four issues, which can be dealt with from different perspectives than those above in our model. First, we relate the non-monetary benefits presented in the model with the monetary measures of cost-efficiency of our model. Second, the model provided an assumption on the zero-slackness in acute health care, which is questioned and discussed. Third, some perspectives on the risk profiles and pricing of new technologies especially at the early stage of development are adduced. Fourth, we discuss how the probability of the patient dying affects the cost-efficiency calculus.

1. Non-monetary benefits vs. monetary cost-efficiency. The benefits from an adoption of new technology can be purely humanitarian, or they might involve economic impacts,

typically secondary and indirect, that have not been taken into account in the conventional cost-benefit calculations. Examples of potential benefits are:
- the non-monetary value of avoiding deaths *per se*
- the non-monetary value of an early recovery, leading to a better quality of life
- a preponderance of new technology *per se*
- potential secondary benefits from supporting a novel technology (e.g. applications in other fields)
- a preference towards labor intensive solutions.

The above benefits are difficult to measure in monetary terms. The main idea of the presented analysis is, however, that the model enables the comparison between the non-monetary benefits and monetary cost-efficiency. Accordingly, the model presents the non-monetary benefits and the cost-efficiency of acute care. The model enables the direct valuation distinctive policy regimes. For instance, empirical comparison between the BNCT treatment and conventional radiation therapy resulted in the actual improvement in acute care efficiency being relatively costly after the adoption of BNCT technology.

Our model suggested that the health care payer decides to adopt the BNCT technology as the main application in acute care if the payer values a single additional self-caring patient at EUR 58 528 in monetary terms. Thus, even though our model does not provide strict answers, should the payer accept the adoption of the new technology or not, the model reflects the non-monetary benefits to the cost-efficiency of adopting the technology.

Strokes are a disorder plaguing the elderly population in particular and it is interesting that the development of effective and expensive comprehensive treatment applied at the right time has proven to generate significant savings from society's perspective. Therefore, reasoning not to adopt the new technology would be based on a disutility of patient cure.

Introducing a new technology always induces initial additional costs. However, a clinic has been allocated money mainly for running their ordinary services, and thus there is an intrinsic barrier to introducing a costly new technology. Additionally, there might be

non-intentional factors hampering the introduction of a new technology. Examples thereof are:

- system inertia (labor unions, sectoral thinking)
- aversion to primary expenditure; blurred vision
- ignorance concerning the positive effects of intensified acute care
- reluctance towards new technologies.

2. Organizational Slackness. From an operational point of view, slackness should always be minimized as long as it incurs cost savings. In health care the importance of redundancy, seemingly contradictory to operational efficiency, has drawn increasing attention because of recent crises such as acts of terrorism and threats of SARS-type pandemics. However, slackness and redundancy are not mutually contradictory; a predefined share of health care resources should be allocated to create a redundancy, and additional inefficiency regarded as inefficiency or slackness. In medical ethics, if a treatment is established and possible to supply, it is considered that the treatment has to be supplied to all patients eligible for the intervention. Thus the choice is either-or.

A typical clinic is running optimally in an economical sense: according to the given principles, it does not yield a profit or loss. However, an operating unit can reallocate resources by, for example, shutting down a ward for a certain period, and thus it possesses in reality some discretionary power. This can be regarded as a hidden slackness lowering the overall threshold for developmental changes but invisible to an external assessor.

3. Risk profiles and pricing of new technologies.

The patient is regarded as potentially eligible for thrombolytic therapy. The additional costs are incurred immediately, actually already at the decision to adopt the new technology:

- optimized transportation of a patient: must be in place before closing the treatment window
- sufficient on-site primary diagnosis capacity (= special schooling)
- specialized personnel, capable of performing thrombolysis
- high-tech equipment for precise and fast laboratory and radiology what?

4. Probability that the patient dies (for clarity, we will denote the risk of a patient dying as δ). The risk of death δ for patients annually referred to the long-term care varies with the chosen technology as follows:

Technology 0: all patients access primarily long-term care, and thus n_{t0} = 2000. It is noteworthy, that only 62% of these patients will survive their stroke (Numminen, Kotila et al. 1996). Thus, $\delta_0 = 0.38$.

Technology 1: All patients are primarily treated at a specialized stroke unit, which enhances the survival rate by 11%; consequently, approximately 69% of the patients will survive the initial phase; $\delta_1 = 0{,}31$ and n_{t1} for the long-term care equals 1377 patients (Stroke Unit Trialists' Collaboration 2002).

Technology 2: A conservative approach suggests that 5% of all ischemic stroke patients will receive thrombolytic therapy (Lindsberg, Roine et al. 2000). Of these, 17% will die (Numminen, Kotila et al. 1996; Hacke, Kaste et al. 1998; Lindsberg, Roine et al. 2000). However, one out of seven have been reported as avoiding dependency, that is, the NNT for avoiding dependency is 7 (Donnan 1998) (see also (Cornu, Amsallem et al. 2001; Donnan and Davis 2001)). In our population, 100 out of 2000 stroke patients will receive thrombolysis, with 83 patients surviving the treatment and 14 avoiding dependency; without thrombolysis, all 14 would be severely debilitated with a Rankin score above 2. Consequently, $\delta_2 = (\frac{1.9}{2} \times 0{,}31) + (\frac{0.1}{2} \times 0{,}17) = 0.303$, and n_{t2} = (0.73-0.05(1-0.17))*2000=1377 patients will be remitted to long-term treatment.

The technology-dependent risk of death could preferably be included in the model by differentiating between the probabilities of dying or remaining severely ill, respectively. Death can decrease long term treatment costs, sometimes even with a significant impact, but simultaneously the potential labour input of the patient is lost. The concept of Quality-adjusted life-year (QALY) attempts to address the issue. In doing so, QALY combines non-monetary and monetary utilities (se *e.g.* (Dranove 2003) and citations therein). Our intention with the presented model has been to keep the monetary and non-monetary utilities strictly separate, yet allowing each party to bring their expertise into the assessment process.

The presented model is built on a theoretically solid microeconomic foundation. The empirical background is from the area of healthcare, but might it be implemented also in other setups concerning decision making of introducing a new technology?

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