aggressively with beta-blockers, aspirin, and hypo-
lipidaemic agents (usually a statin). If coronary
arterial spasm seems a likely aetiological agent in
such a patient, I also prescribe a vasodilator, i.e. a
calcium channel blocker, an ACE inhibitor, or an
angiotensin receptor blocker. These patients represent
a very interesting subset of individuals with myocar-
dial infarction. I am convinced that they will continue
to be the subject of clinical investigation in the future
in an effort to understand the pathophysiological
process that results in their transient episode of
coronary arterial obstruction.

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Economics of coronary stenting and GPIIb/IIIa blockade

See page 1476 for the article to which this Editorial
refers

Multiple studies have shown that the use of GPIIb/
IIIa blockade can reduce cardiovascular events in the
setting of percutaneous coronary intervention[1–3].
The EPISTENT trial was particularly interesting and
timely[4]. In EPISTENT, 2399 patients undergoing
coronary revascularization were randomized to three
arms: stent plus placebo, stent plus abciximab, and
PTCA plus abciximab. The primary end-point
was the composite at 30 days of death, myo-
cardial infarction, or coronary ischaemia requiring
urgent revascularization. At 30 days and 6 months,
major adverse cardiac event-free survival was highest
in the stent plus abciximab group. Abciximab
resulted largely in a decrease in acute myocardial
infarction within 1 month while stents decreased
additional revascularization at 6 months. In diabetics,
abciximab reduced revascularization rates as well.

In the current issue, Zwart-van Rijkom and van
Hout extend the results of the EPISTENT trial to
include an economic analysis[5]. EPISTENT was con-
ducted in the United States and Canada, but the
economic study presented in this issue was based on
Dutch unit costs, priced in 1998 Euros. Costs at
6 months were highest in the stent plus abciximab
group and lowest in the PTCA plus abciximab group.
Cost effectiveness was evaluated as the incremental
cost per event averted by adding abciximab to stent
plus placebo and as the incremental cost per event
averted by adding a stent to PTCA plus abciximab.
The cost per event averted of abciximab was Euros
14 198 and of a stent Euros 2167 and of a stent Euros
8040. Due to uncertainty in the cost and efficacy
measures, abciximab may be cost
saving in diabetics. Studying the subgroup with
diabetes shows that the cost-effectiveness of therapy
can be much greater in higher risk subgroups and that
therapy can then be targeted to such subgroups[6].

The study by Zwart-van Rijkom and van Hout
is limited by the design of the EPISTENT study, as
the investigators well recognize. The use of clinical data
from one geographical area for use in another geo-
ographical area for an economic study assumes that
the patterns of care are similar. Often in economic
studies there are either no local or insufficient local
data to conduct the economic study, such that data
from other countries are all that is available. Where
there is a local data subset, this subset should be
compared to the non-local data for the patterns of
clinical variables and outcomes. If local data vary significantly from non-local data, then an economic analysis based on non-local data may be seriously limited. In the present study, there was no arm receiving PTCA plus placebo. This would have been a nice addition analytically, but difficult practically and perhaps ethically. If a PTCA plus placebo group were available, then the incremental cost-effectiveness of stent to PTCA in the absence of abciximab and of abciximab to placebo in the absence of stenting would have been available. It is possible that in these situations cost per event averted would have been lower than those observed. The costs per event averted which are presented here would remain relevant as the cost-effectiveness of the second therapy (stent or abciximab) after the first therapy (stent or abciximab) had been given. However, the economics of GPIIb/IIIa blockade to PTCA have been studied in several clinical trials[7-9], as have the economics of coronary stenting in the absence of GPIIb/IIIa blockade[10]. The clinical benefits of GPIIb/IIIa blockade and coronary stenting have been achieved, at most, by a modest increase in cost[7-10].

The biggest limitation of Zwart-van Rijkom and van Hout’s paper is that a more formal cost-utility analysis could not be performed. In such an analysis, the cost-effectiveness ratio is expressed as the incremental cost per quality adjusted life years (QALYs) gained[11]. QALYs are calculated as survival multiplied by the utility of that survival, discounted in future years. Utility is a term from economic theory that describes the preference for one health state over another. Utility may be measured by using rating scales such as the EuroQol[12] or more direct measures of patient preference such as the time trade-off[13] or standard gamble[14]. Such measurements were not made in EPISTENT, having just become popular in clinical trials quite recently.

While a cost-utility analysis was not possible, an analysis using cost per life year saved was possible. However, there was little difference in survival, and the ratio would have been unstable. Furthermore, by preventing events patients may feel better, such that an analysis based on cost per life year gained would not include the benefit of stents or abciximab on health-related quality of life. Survival measured at 6 months may also not include the full benefit of abciximab or stenting on survival if the study were carried out longer. In the end, for therapy to be efficacious it must affect survival, utility, or both. Proving efficacy of therapy by effects on survival or utility may be quite challenging, leading to analyses based on more readily available data, such as that presented here.

There are two problems with cost-effectiveness analyses based on cost per event averted. The first is that it is difficult to determine at what threshold of cost per event averted that therapy is warranted. The second problem is more subtle, in that events have costs attached to them, such that costs are reflected in both the numerator and denominator of the cost effectiveness ratio.

As people read economic analyses, the question immediately arises as to how such analyses can help in clinical decision making. Efforts to use cost-effectiveness ratios as a primary tool for policymaking purposes have not been particularly successful[15]. Also, cost-effectiveness analyses have varied methodologically, making comparisons difficult. In an effort to standardize cost-effectiveness analyses, the United States Public Health Service has adopted a set of standard recommendations for cost-utility analyses[16]. While difficult to apply to actual studies, those performed according to these guidelines will allow cost-utility ratios to be compared across multiple studies across multiple disciplines.

In the study by Zwart-van Rijkom and van Hout, we must take a more limited view of the economic analysis. In higher risk groups, such as diabetics, there may be cost savings of adding abciximab to stents, which, combined with the better outcome with stents, is a situation in which abciximab dominates placebo. In this case, the decision to use abciximab is easy. In lower risk groups, the decision making can be difficult and we are left with some degree of uncertainty as to the cost effectiveness of expensive therapy. One thing has become certain, as expensive medical procedures and pharmacological therapy have expanded, society has increasingly come to demand that therapy provide benefit to an extent that it is worth the money spent, and that data are provided showing that this is the case.

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Measuring cardiac power output — the acid test

See page 1496 for the article to which this Editorial refers

The heart is a pump, and as such consumes energy and produces work. These functions may be quantified by measuring myocardial oxygen consumption ($\text{MVO}_2$) and cardiac power output, respectively. Accurate measurement of these requires invasive techniques that may not always be appropriate or indeed ethical, but both can be estimated by non-invasive means. $\text{MVO}_2$ is closely mirrored by the double product of systolic blood pressure and heart rate\(^2\), which are relatively simple to measure during a routine treadmill test. Cardiac power output also takes into account the stroke volume, so that the equation is similar to that used in electrical theory:

$$W = V \times I$$

That is:

Power output (Watts) = Pressure (Volts) \times \text{Current (Amperes)}

or:

CPO = mean arterial pressure \times \text{cardiac output (Qt)}

Both Qt and mean arterial pressure are more difficult to measure non-invasively than systolic blood pressure or heart rate. The study by Williams et al.\(^2\) in this issue explains how\(^3\), and puts this elegant theoretical idea to the acid test — does the measurement of cardiac power output predict outcome in patients with heart failure more accurately than the current gold standard\(^3\), peak achieved whole body oxygen uptake ($\text{PVO}_2$)?

$\text{PVO}_2$ itself is dependent on factors other than cardiac output, such as peripheral $\text{O}_2$ extraction, but $\text{PVO}_2$ and Qt mirror each other closely\(^4\). Both lung function\(^5-7\) and peripheral skeletal function\(^8\) are known to be altered in patients with heart failure, and hence may influence $\text{O}_2$ extraction. Furthermore, the consideration of invasive haemodynamic data in addition to the measurement of $\text{PVO}_2$ enhances its discriminatory power\(^9,10\). The cardiac power output should reflect defects in cardiac performance alone, and hence be more specific than whole body $\text{PVO}_2$.

The results of this study\(^2\) would appear to bear this out, in that power output was the only independent predictor of mortality in this group of patients. The next question then is whether it is worth the


