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Quantification of the Potential Impact of Cost-effectiveness Thresholds on Dutch Drug Expenditures Using Retrospective Analysis

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ABSTRACT

Background: Other than the UK, The Netherlands has no formal threshold for cost-per-QALY values defined yet. For example, a cutoff value at €20,000 per QALY is sometimes mentioned in various discussions, however it has no formal status at all. Yet, since 2005, all new innovative do have to go through a cost-effectiveness evaluation though, with the assessment being focused on the methodology rather than on the exact cost-per-QALY outcome.

Objective: Our objective was to estimate the potential impacts on Dutch drug expenditures had a formal threshold been applied in recent years.

Methods: We analyzed national Dutch prescription data for the period 2005–2007, with respect to the costs of specific newly introduced drugs with reported positive cost-effectiveness ratios. Various threshold values were investigated.

Results: In particular, our analysis suggests that modest, though annually increasing, reductions in Dutch drug expenditures could have been

achieved in the recent period 2005–2007 if a threshold for cost-effectiveness at, for example, €20,000 per QALY been applied in The Netherlands. At thresholds of €0 and €20,000 estimated reductions in drug expenditures reflect approximately 0.25% of total Dutch drug expenditures and for thresholds of €50,000 and €80,000 this is only 0.01%.

Conclusions: Modest reductions in drug expenditures can be achieved if a formal threshold would be applied in The Netherlands. Potential reductions may be expected to increase in next years as expenditures for listed drugs increase further and new drugs become listed. Finally, we argue that for optimal and fair allocation of resources the in the health-care sector, application of a straightforward threshold is eminent and should not be postponed anymore.

Keywords: budget impact analysis, cost-effectiveness analysis, pharmacy, The Netherlands.

Introduction

Since January 2005, one of the criteria for enlisting new drugs within the Dutch Outpatient Drugs Reimbursement System (“Geneesmiddelenvergoedingssysteem” [GVS]) relates to cost-effectiveness. In the assessment process by the Dutch Foundation for Health Care Insurance (“College voor Zorgverzekeringen” [CVZ]), this criteria comes next to therapeutic value and cost consequence [1,2]. Cost-effectiveness is not considered for those drugs without added value, which are either clustered and reimbursed at maximally the cluster reference price or—in the absence of possible clustering—remain unreimbursed. However, the cost-effectiveness criteria explicitly functions as a hurdle for reimbursement for those drugs that have proven added therapeutic value and are predicted to confer extra costs to the health-care system. Examples of drugs that were considered of added therapeutic value, yet failed the cost-effectiveness criteria are ivabradine for the treatment of angina pectoris and the 4-valent human papilloma virus (HPV) vaccine for the prevention of cervical cancer. Information on such individual drugs can be found on the CVZ website, those subpages hosting the reports of the Committee Pharmaceutical Help (“Commissie Farmaceutische Hulp” [CFH]).

Internationally, The Netherlands are not unique in applying a cost-effectiveness criteria for new innovative drugs. For example, the United Kingdom’s National Institute for Health and Clinical Excellence (NICE) and similar agencies elsewhere apply similar criteria [3]. Often, to judge cost-effectiveness of a new drug, a

threshold is defined for maximum acceptable costs per quality adjusted life year (QALY). Notably, NICE applies £30,000 per QALY, whereas other countries may apply US\$50,000 or €50,000 [3,4]. Strikingly, The Netherlands lack such a formal cost-effectiveness threshold, and evaluations of the cost-effectiveness threshold are done solely on the basis of the quality of the cost-effectiveness analysis supplied by the manufacturer, rather than on the actual costs per QALY estimated for the new drug. For example, the 4-valent HPV-vaccine was denied reimbursement within the Dutch Drug Reimbursement System on the basis of criticism on the economic model underlying the cost-effectiveness estimates, regarding aspects such as the time horizon for analysis, the assumed duration of protection and face validity of the model outcomes [1]. For judging the quality of cost-effectiveness models in the framework of reimbursement decisions, Dutch guidelines for the topic have been designed.

Ergo, if in the Dutch assessment procedure of a new innovative drug the cost-effectiveness analysis supplied by the manufacturer is considered of good quality, reimbursement will principally not be denied on the basis of cost-effectiveness, despite potentially relatively high cost-per-QALY values. Notably, two recent positive decisions on reimbursement involved cost-per-QALY performance in the range €80,000–90,000 (dasatinib for leukemia and sitagliptine for diabetes) [1], values that would be considered beyond the threshold in any country that has such a threshold formally defined. In The Netherlands, no formal threshold exists despite that some efforts to achieve a definition have been attempted. In particular, in the 1990s, a threshold of €20,000 per life-year gained has already been mentioned and has actually been applied within the framework of labeling patients with elevated cholesterol levels eligible for treatment with statins [5]. Since then, €20,000 per life-year

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gained or QALY has certainly been mentioned in discussions on rationing; however, it has never become a formal threshold for cost-effectiveness in The Netherlands. More recently the Council for Care & Public Health (“Raad voor Zorg & Volksgezondheid”) derived a threshold based on various criteria, inclusive the country’s gross domestic product (GDP) per capita [6]. In line with the World Health Organization, it was considered that two to three times GDP per capita would reflect an acceptable cost-per-QALY threshold [7]. In particular, for the Dutch situation, this would translate into a threshold for cost-effectiveness at approximately €80,000 per QALY. Again, this threshold has been discussed in decision-making forums; however, it never achieved the status of a formal cost-effectiveness threshold. Application of, for example, the threshold specified by NICE to the Dutch situation is no valid option either. Notably, cost-effectiveness thresholds differ per country. Obviously, GDPs per capita vary over countries. One further plausible reason for differing thresholds is that guidelines for the conduct of pharmacoeconomic research differ per country [8]. For example, the Dutch guidelines prescribe the use of a societal perspective; whereas, the UK favors the National Health Service’s perspective. The societal perspective allows the inclusion of a much broader spectrum of benefits and savings of the drug under consideration, which would possibly justify a lower threshold within the societal perspective.

Quantification of the Potential Effects of Thresholds

With the definition of a formal Dutch cost-effectiveness threshold still pending, an interesting question pops up regarding the financial consequences for the drug budget if since January 1, 2005 a threshold would strictly have been applied, regardless of its exact quantification. Definition and strict application of a cost-per-QALY threshold for the Dutch situation would obviously have limited the budget impacts of new drugs in recent years, as some drugs would have been denied based on the cost-per-QALY performance. Here, we examine these consequences based on estimated cost-per-QALY (or per life-year gained if per QALY was not available) figures and drug utilization during the period 2005–2007. Notably, we investigate the drug costs per year for specific drugs at three different thresholds: €20,000, €80,000 and €50,000 per QALY (or life-year gained). Both former figures have been mentioned in the Dutch decision-making context, the latter reflects their midpoint and is in accordance with some other countries’ thresholds [8]. Additionally, we investigate a theoretical threshold of €0 per QALY; i.e., no extra costs are accepted for the achieved health gains of new drugs; i.e., cost savings would be required.

For our analysis, drug utilization was taken from national figures available from the Drugs Information Project (“Geneesmiddelen Informatie Project” [GIP]), hosted by CVZ [9]. Since 2006, the GIP comprises the health-care insurance data for the whole of 16 million inhabitants of The Netherlands. Prior to 2006, the data reflect the health-care insurance administration of only 10 million persons, previously in the obligatory insurance (“Ziekenfonds”). Cost-per-QALY estimates for those drugs that were admitted to the GVS during the period 2005–2007 were taken directly from the website of CVZ [1], and—according to the Dutch procedure in this respect—reflect the manufacturer’s calculations. In particular, such estimates could be found for dorzalamid, erlotinib, fulvestrant, palivizumab, dasatinib, and sitagliptin (see Table 1). Drugs with estimated negative costs (savings) and equal or more QALYs compared with standard

Table 1 Drugs admitted to the Dutch Geneesmiddelenvergoedings-systeem during 2005–2007, their estimated cost-effectiveness (CE) in costs (€’s) per quality adjusted life year (QALY), reduced expenditures (€’s) in the Dutch drugs budget during 2005–2007 had the respective cost-per-QALY threshold been applied for denying reimbursement for those drugs with an estimated CE surpassing this threshold

	CE	€0	€20,000	€50,000	€80,000
Dorzalamid	800	1,057,400	0	0	0
Erlotinib	37,000*	12,803,700	12,803,700	0	0
Fulvestrant	46,000	4,124,700	4,124,700	0	0
Palivizumab	49,000	13,479,900	13,479,900	0	0
Dasatinib	84,000	1,745,700	1,745,700	1,745,700	1,745,700
Sitagliptin	90,000	84,000	84,000	84,000	84,000
Total		33,295,400	32,238,000	1,829,700	1,829,700

*Per life-year gained.

treatment were not taken into the analyses, as those figures would result in accepting the drug against any threshold (a recent example of such a situation poses the submitted file for dabigatran [1]).

Table 1 shows drug-specific reductions in the past Dutch expenditures within the drugs budget had respective thresholds been consistently and strictly applied. Depending on the exact threshold considered, reduced expenditures vary from €32–33 million to a modest €2 million over the 3-year period considered (approximately €0.1 to €2 per capita). Estimated reduced expenditures were considerably higher in the last year of analysis at €24,341,000 in 2007, than in the first year considered with €619,000 in 2005 (in this case evaluated at the threshold of €20,000 per QALY). Annual drug-specific figures showed that all drugs analyzed had reduced expenditures estimated in 2007. Reduced expenditures were limited to 2007 only for dasatinib and sitagliptin. For dorzalamid, erlotinib and palivizumab, part of the reduced expenditures were estimated for 2006, although consistently lower than for 2007 at 13%, 26%, and 16% of total expenditures, respectively. For fulvestrant, estimated reduced expenditures were distributed at 15% in 2005, 43% in 2006, and 42% in 2007.

With an average annual expenditure on outpatient drugs in the period 2005–2007 of €4739 million, reductions in expenditures as listed may be conceived as modest. In particular, at thresholds of €0 and €20,000 estimated reductions in drug expenditures reflect approximately 0.25% of total Dutch drug expenditures and for thresholds of €50,000 and €80,000 this is only 0.01%. These percentages were found to increase for any next year, for example, from 0.01% in 2005 to almost 0.5% in 2007 for the lowest two thresholds.

Summary and Limitations

Our analysis suggests that modest, though annually increasing, reductions in Dutch drug expenditures could have been achieved in the recent period 2005–2007 had a formal threshold for cost-effectiveness been applied in The Netherlands. During this period, manufacturers of new innovative drugs had to file an adequate cost-effectiveness analysis to have these respective drugs eligible for reimbursement. In this respect “adequate” meant that the analysis had to be performed according to the guidelines for pharmacoeconomic research [10] and “common sense” rules regarding transparency and levels of being evidence-based. Adequacy of the pharmacoeconomic model is decisive for reimbursement rather than the exact cost-effectiveness outcome.

As no formal threshold for cost-effectiveness is available in The Netherlands, it currently remains unknown against which cost-per-QALY to weigh individual drugs' cost-effectiveness outcomes. Regarding a formal threshold, €20,000 per QALY is mostly mentioned in this respect. For example, for new vaccination programs, the Health Council explicitly mentions this figure [11].

In particular, we found that drug expenditures could have been reduced with up to approximately €30 million during the period 2005–2007. At €20,000 per QALY, Dutch drug expenditures would have been reduced by 0.5% in 2007. Such percentages may be expected to even increase further in next years as expenditures on these listed drugs may increase further and new drugs with cost-effectiveness ratios above respective thresholds may additionally be covered.

On the one hand, our quantification of potential reductions in drug budgets in relation to thresholds might be considered an underestimate as all cost-per-QALY outcomes were derived from manufacturers' files. Obviously, such manufacturers' analyses might be biased toward favorable cost-effectiveness ratios [12]. If cost-effectiveness analysis for new innovative drugs would be required to be performed by independent parties not being sponsored by the pharmaceutical industries, such as universities and national institutes, one may expect generally worse cost-effectiveness ratios to be estimated. These higher ratios would result in higher likelihoods for such drugs to surpass the threshold. Also, as noted our data reflect an underestimation for the year 2005 as the GIP database didn't yet comprise the whole Dutch population in that specific year.

On the other hand, our estimated reductions in the drugs budget might represent overestimations as other drugs might have been used as alternatives if the respective drugs had not been reimbursed. For example, the use of docetaxel and pemetrexed might have been higher had less erlotinib been used in recent years. Yet, as in other cases, no alternative would have been available (palivizumab for respiratory syncytial virus) or alternatives would be generically available and relatively cheap, we would expect the overestimation to be limited.

Had indeed a threshold been applied during the period 2005–2007, denial of some individual drugs would certainly have been at the expense of QALY losses. Notably at €20,000 per QALY, crudely evaluating on the numbers in Table 1 and neglecting potential savings of drug use, maximally 733 QALYs would have been lost had erlotinib, fulvestrant, palivizumab, dasatinib, and sitagliptin not been used during the period considered. Stated otherwise, minimally costs of €44,000 would have been saved for each QALY lost. Obviously, these potential savings could have been spent on other health-care interventions with cost-effectiveness ratios under or closer to €20,000 per QALY. We do realize that this spending could be hypothetical only, if the approach to financing health care would rather be from a more restrictive than from a strict budgetary perspective.

We do note that despite the absence of a formal cost-effectiveness threshold and the primarily qualitative assessment of manufacturer's cost-effectiveness analyses, the exact level of the cost-effectiveness ratio might have contributed to individual reimbursement decisions of specific drugs. It certainly could influence the state of mind, and generally higher ratios tend to discourage and lower to encourage reimbursement decision [13]. This might in particular have been tempting for those innovative outpatient drugs exhibiting relatively high cost-effectiveness ratios concomitantly with high budget impacts. In practice, this has, however, not yet led to the denial of reimbursement for an innovative outpatient drug with a methodologically adequate cost-effectiveness analysis.

Toward a Formal Threshold in The Netherlands?

Will we see a formal cost-effectiveness threshold to be adopted in The Netherlands? Next to the obvious argument that definition of such a threshold would enhance transparency of decision-making, some further considerations are warranted in this respect. A recent report analyses the pros and cons of a formal threshold and the complexities how to assess or define it [14]. One major aspect to account for is that formal thresholds will influence price setting of new drugs, which can both be in upward and downward direction depending on the exact relations between such a threshold, international pricing of the product and national pricing of its comparator(s). Obviously and within the existing restrictions, manufacturers would price their innovative products so as to be below, however, not far below, any defined cost-effectiveness threshold. Furthermore, it is pointed out that strict application of cost-effectiveness thresholds would not be in line with a primarily budgetary-oriented financing of health care [14].

Despite the above, we would argue that for optimal and fair allocation of resources in the health-care sector, application of a straightforward threshold is eminent and should not be postponed anymore. Such a threshold though, would have to be applied consistently over the whole health-care sector. With cost-effectiveness assessments now thoroughly implemented in drug assessments, however, not yet in various other sectors in health care such as surgery and diagnostics, the danger exists that reimbursement of drugs will be mostly and disproportionately affected by the application of a threshold. Obviously, this would hamper optimal allocation of resources in health care. Therefore, next to pointing to the necessity of defining a formal threshold for cost-effectiveness, we point to the relevance of consistently applying this to the whole spectrum of health-care interventions, inclusive non-drug-type interventions. Of course, next to such a threshold and the related cost-effectiveness perspective, other aspects should be noted in the decision-making concerning reimbursement of new drugs, including equity, affordability, continuity of care, characteristics of the disease and the specific intervention at stake and the international situation.

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