

## Heading to economic-based clinical guidelines

### *A long and bumpy road*

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## **Abstract**

In the 1980s clinical guidelines made their entrance in the Dutch health care arena. Several years later, in 1997, the Minister of Health proposed the incorporation of cost-effectiveness information in clinical guidelines. The reasoning behind incorporating economic considerations in clinical guidelines is it will result in treatment choices that are both consistent with clinical as well as social objectives. This study aims to provide insight in the current position of economic considerations during clinical guideline development and tries to answer the question why economic evidence is (not) included in clinical guidelines.

To get a well-informed picture, recommendations concerning (pharmaco therapeutic) interventions in the depression, Parkinson's disease and stroke guidelines were scored on the AGREE-plus efficiency questions. After the AGREE-plus efficiency scores were gathered, semi-structured interviews with clinical guideline developers were conducted. With these interviews information was gathered regarding the reasoning behind (not) including economic considerations during clinical guideline development.

The scores on the AGREE-plus efficiency questions illustrate that only limited attention is paid to economic evidence in the recommendation concerning (pharmaco therapeutic) interventions in the clinical guidelines under study. The high costs for consulting a health economist, the limited availability of high quality economic evaluations, the lack of a uniform applied development procedure and the absence of a well-defined decision-making framework were brought forward as arguments. Alongside these arguments the political arena was argued to play a key role in the journey towards economic-based guidelines. However, next to the vital role of the government, a joint deployment of all stakeholders is thought to be needed to take necessary steps toward economic-based guidelines. Effort should be put in convincing all stakeholders that economic-based guidelines, in addition to other efficiency improving measures, could lead to a more efficient and cost conscious health care system.

**Keywords:** *clinical guidelines, efficiency, economic evidence and the Netherlands*

## Introduction

The increase of health care expenditures continues. The availability of new medical technologies is for a large part accountable for this affordability problem. On the other hand new medical technologies have brought us welfare growth. The crucial question is how much we, as society, are willing to pay for welfare growth (Pomp et al. 2007). Politicians are struggling with rationing health care on economic grounds and therefore seem reluctant to give cost-effectiveness a prominent role in health care policy (Rutten et al. 2005).

What could be done to tackle the health care costs expansion? According to Pomp et al. (2007) the incorporation of cost-effectiveness in clinical guidelines could be considered as a promising policy tool. How far are we on the way to economic-based clinical guidelines? Has its additional value already been proven or do we still have a long way ahead of us?

The government is responsible for setting the right conditions to ensure the public aims of accessible, affordable and efficient health care of good quality. Within the current framework of regulated competition, the Health care insurance board (CVZ) is responsible for defining the content of the basic benefit package (Tan et al. 2008). The criteria that determine the content of the basic package are labelled as 'adequate care', which equals effective, necessary and efficient care for the patient (Raad voor de Volksgezondheid en Zorg 2007). Although these criteria correspond with the criteria as defined in the 'funnel of Dunning' (Commissie Dunning 1991), to demarcate the content of the basic benefit package, it has an important limitation. The definition of 'adequate care' is formulated on a patient level, whereas decision-making regarding reimbursements are made on a national level (Tan et al. 2008).

Due to the increasing health care expenditures, politicians struggle to find solutions to keep fulfilling the public aims today and in the future. As stated by Zuiderent-Jerak et al. (2011), the need to cut costs, in case efficiency gains can not sufficiently be reached, will result in the need to reduce the content of the basic benefit package or the increase of co-payments. These measures, as well as increasing the health insurance premium, are considered rather unpopular policy measures. A more elegant solution could be the demarcation of the content of the entitlements according to the content of clinical guidelines. The Regieraad<sup>1</sup> argued that, in case clinical guidelines will fulfil a normative role in demarcating the content of the basic benefit package, the embedding of economic considerations is inevitable (Regieraad 2011). But can this be reconciled with the primary aim of clinical guidelines?

In the Netherlands the era of clinical guidelines has its origin in the early 1980s (Zuiderent-Jerak et al. 2011). The main aim of clinical guidelines is to enhance quality of care. Clinical guidelines consist of recommendations that serve as a guidance tool for professionals to support treatment decisions. Professionals may deviate from the recommendations listed in a

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<sup>1</sup> The Regieraad is a board appointed by the ministry of Health, Wellbeing and Sport (VWS) to enhance the development and implementation of comprehensive clinical guidelines.

guideline, at least as the argumentation for the deviation is adequately documented (Regieraad 2010). The possibility to deviate from clinical guidelines is essential for providing the optimal care to each individual patient, in each unique situation.

While medical oriented decision-making represent the 'best care option', decision-making regarding entitlements represent the 'optimal care option given the budget constraints' (Regieraad 2011). The latter could therefore be considered as the best scenario to fulfil the public aims, while the 'best care option' is the most favourable scenario for the patient. Already in 1999 Mason et al. claimed that the explicit inclusion of health economic considerations would contribute to supporting clinicians in making treatment choices that are consistent with both clinical as well as social objectives (Mason et al. 1999). However history teaches us that it is quite a challenge to consistently embed economic evidence in clinical guidelines in a way both individual patients as well as society benefit.

In the Dutch progress report 'Medical technology assessment and efficiency in healthcare', from the minister of Health, Wellbeing and Sport (VWS) dd. 2<sup>nd</sup> of April 1997, it was proposed to incorporate cost-effectiveness during the development of clinical guidelines. This proposal aimed to stimulate not only effective, but also cost-effective healthcare (Rutten & Brouwer 2002). Within this context the ministry of VWS initiated a national program, to include economic considerations during clinical guideline development (Niessen et al. 2007; Regieraad 2011). During this program the ministry of VWS financed the involvement of health technology assessment (HTA) experts. This to ensure that economic information was explicitly taken into account during the clinical guideline development process. The program was in line with the governmental policy to promote effective, efficient and appropriate interventions through the use of clinical guidelines (Niessen et al. 2007).

Meanwhile, economic analysis and clinical guideline development were brought together in several other countries, like the United Kingdom, Australia, New Zealand, Canada and Sweden. It did not happen without any criticism. The critique concerned among others, as summarized by Niessen et al., some methodological issues, like the limited availability of valid high-quality cost-effectiveness data and the question, which role to attach to the economic information in priority-setting (Niessen et al. 2007). In spite of these issues, in 2003 the World Health Organization (WHO) recommended that during the development of WHO guidelines cost-effectiveness as well as resource implications should be considered (Tan-Torres Edejer 2006).

Next to the above-mentioned critique the Dutch 'guideline-support program' faced other difficulties with involving health economists during the clinical guideline development process. The main reason why it seemed difficult to contribute in a constructive manner was the absence of a well-defined framework for the incorporation of efficiency in clinical guidelines (Regieraad 2011). Two other factors referred to by the Regieraad (2011) were the artificial collaboration between the involved parties and the high costs for involving HTA experts.

Several years after the 'guidelines-support program', in 2006, the 'knowledge policy quality curative care (KKCZ) program' was initiated. This program gave the topic cost-effectiveness renewed attention. Since the start of the KKCZ program 45 clinical guidelines were developed. Despite of the fact that cost-effectiveness considerations were part of the KKCZ guideline development program, the involvement of health economists and the role of economic evaluations were both limited (Regieraad 2011). The Regieraad (2011) feared that embedding efficiency considerations in clinical guidelines did come to a halt.

But, did it indeed come to a halt? This study aims to get a clear picture of the current situation of the decision-making process of incorporating economic considerations in clinical guidelines. What are nowadays the arguments to include economic evidence in clinical guidelines, and what are the reasons not to?

To get a well-informed picture, several clinical guidelines were reviewed on the presence of economic considerations. In addition, to get an understanding of the reasoning behind (not) embedding efficiency considerations in clinical guidelines, interviews with guideline developers were conducted.

## **Method**

Three clinical guidelines were selected and reviewed, by applying the efficiency questions of the Appraisal of Guidelines for Research and Evaluation (AGREE) -plus instrument. The AGREE-instrument is developed as a tool to assess the quality of clinical guidelines. The AGREE collaboration considers the quality of a clinical guideline as high, when the potential biases of guideline development have been adequately addressed, the recommendations are both internally and externally valid and they are feasible in practice (AGREE Collaboration 2003). The AGREE-instrument consists of six quality domains with in total 23 items and two overall assessment items. These two general items concern the overall judgment of the appraiser regarding the quality of the clinical guideline and whether the appraiser would recommend the clinical guideline. Each of the six domains capture a quality aspect of clinical guidelines, namely scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability and editorial independence. The AGREE is an generic instrument and can be applied to all clinical guidelines, regardless of the disorder or step in the health care process. The instrument can be used for several purposes, for example by clinical guideline developers, to conduct an internal assessment of the thoroughness of a clinical guideline or by policy makers as a tool to inform policy decisions (AGREE Next Steps Consortium 2009).

In the basic AGREE-instrument only item 20, from the domain applicability refers to resource implications, stating: "*The potential resource implications of applying the recommendations have been considered.*" To gather more detailed information regarding the aspect of economic considerations, Zuiderent-Jerak et al. (2011) extended item 20 with four additional questions regarding costs(-effectiveness). These AGREE-plus efficiency scores provide information regarding the extent to which economic considerations are explicitly included in

clinical guidelines. The questions of the AGREE-plus questionnaire, concerning cost-effectiveness, are specified in appendix A. The questions were scored on a 4-point scale. Score 1 corresponds with 'strongly disagree' and is applicable when there is no relevant information available in the recommendation for the item. Score 4 corresponds with 'strongly agree' and is applicable when all relevant information for the item is applicable to the recommendation.

The clinical guidelines included in the current study, which were scored on the AGREE-plus efficiency questions, concern depression, Parkinson's disease (PD) and stroke. These three, rather recent guidelines are selected because the conditions are accountable for a significant share of the Dutch health care expenses. This fact makes it especially relevant for these guidelines to embed cost-effectiveness data, to make efficiency gains possible. Another reason to select these three clinical guidelines was that these were all listed in the top-25 guideline list, set by the Regieraad (see table 1).

*Table 1. Clinical guidelines under study*

Clinical guideline under study	Published in	Share of Dutch healthcare expenses in 2005*	Position in the top-25 guideline list of the Regieraad
Depression	2011	Mental health disorders: 20.8%	Depression/bipolar disorder: no. 16
Parkinson's disease	2010	Nervous system and the sense organs: 5.6%	Parkinson's disease: no. 24
Stroke	2008	Cardiovascular disorders: 8,0%	Stroke (CVA/TIA**): no. 2

\* Poos et al. 2008

\*\* CVA: cerebrovascular accident, TIA: transient ischemic attack

The clinical guidelines under study are multidisciplinary guidelines (MDG). The development and/or revision of the MDGs were all conducted with the financial support of the Dutch Organization for Health Research and Development (ZonMw). Another aspect that these guidelines have in common is that during the guideline development / revision process the evidence-based guideline development (EBRO) method was used. The depression guideline, as well as the PD guideline, were part of the before mentioned KKCZ program.

The 2009 multidisciplinary guideline for depression is already revised twice. In this paper the second revision of the multidisciplinary guideline for depression was reviewed (MDG depression 2011). The multidisciplinary guideline for stroke, reviewed in this paper, is a revision of the version published in 2000 (MDG stroke 2008). Regarding PD, the 2010 version of multidisciplinary guideline was reviewed (MDG PD 2010).

As clinical guidelines are comprehensive and often include various topics; prevention, diagnostics, interventions and rehabilitation, the focus of this study, was on the

recommendations concerning (pharmaco therapeutic) interventions. The rationale behind this choice was that, in comparison with the other topics, more cost-effectiveness data were assumed to be available. Another assumption was that cost-effective (pharmaco therapeutic) interventions could potentially contribute to sufficient efficiency gains. Regarding PD, only the recommendations regarding drug treatment for motor symptoms were scored. The reasoning behind this choice was to score a comparable number of recommendations for each clinical guideline under study.

After the AGREE-plus efficiency scores were gathered, semi-structured interviews with clinical guideline developers were conducted. During these interviews information was gathered regarding the role of economic consideration during the clinical guideline development process.

The lists of working group members of the selected clinical guidelines were reviewed. The members who had contributed to the economic component of the guideline were contacted. For the guidelines PD and depression Erik Buskens (EB), Professor Medical Technology at the University Medical Center Groningen, was contacted. For the depression guideline he advised to contact Talitha Feenstra (TF), Health economist at the epidemiology department at the University Medical Center Groningen and the National Institute for Public Health and the Environment (RIVM). Concerning the stroke guideline, it seemed that no health economist was involved. Therefore the advisor from the Central Accompaniment Organization for peer review (CBO), Margreet Pols (MP), who was involved during the clinical guideline development project, was contacted. MP currently works as senior advisor at the Association of Medical Specialists (OMS). During the interview with MP, a colleague of her, Marleen Ploegmakers (ML), advisor at OMS, was also present. Additional information regarding the respondents can be found in appendix B.

As the respondents were also involved in various other clinical guideline development projects, they were not only able to provide information about the clinical guidelines under study, but also regarding clinical guideline development more generally. The interviews were conducted according to a topic list. The topic list was constructed to get an understanding of the current situation of decision-making regarding economic considerations in clinical guidelines development. Moreover it was constructed to get insight in the arguments (not) to include economic evidence in clinical guidelines. The topic list was used as a guidance for the interviews and included the following topics: transitions in guideline development and the role of economic considerations in these transitions; attention for economic evidence in the clinical guidelines under study with reference to the AGREE-plus efficiency score; experience with other clinical guideline development projects; availability and quality of cost-effectiveness information; the content of the addendum to the 'Guideline for Guidelines' report, concerning cost-effectiveness in clinical guidelines; level of decision-making concerning economic considerations; and clinical guidelines as a policy tool. The complete topic list can be found in



appendix C. All interviews were audio-taped and transcribed to perform theory driven analyses. These interviews aimed to provide valuable insight of the story behind and beyond the explicit data (AGREE-plus scores).

## Results

### Quantitative results

Clinical guidelines consist of recommendations that describe the best care or cure interventions based on clinical evidence and or experts' opinions. An example of a recommendation from the MDG depression (2011) is: *“antidepressants are indicated for patients with a depressive disorder, especially by (moderate) severe episodes and in particular by a depressive disorder with melancholic or psychotic features”* (§ 8.2). For this study recommendations concerning (pharmaco therapeutic) interventions, were scored on the AGREE-plus efficiency questions. The results are shown in table 2. The numbers listed in the column 'recommendation' correspond with the paragraph number in the clinical guideline in which the recommendation is described.

Table 2. Scores on the efficiency questions of the AGREE-plus instrument for the recommendations under study.

<b>Multidisciplinary guideline depression (2nd revision) 2011</b>					
<b>Recommendation</b>	<b>1</b>	<b>a1</b>	<b>b1</b>	<b>c1</b>	<b>d1</b>
8.2	1	1	1	1	1
8.3	2	1	1	1	2
8.4	1	1	1	1	1
8.5	1	1	1	1	1
8.6	1	1	1	1	1
8.7	1	1	1	1	1
8.8	1	1	1	1	1
8.9	1	1	1	1	1
8.10	1	1	1	1	1
8.11	1	1	1	1	1
10.2	1	1	1	1	1
11.2	1	1	1	1	1
11.4	1	1	1	1	1
<b>Guideline diagnostics, treatment and care for patients with a stroke (2008)</b>					
<b>Recommendation</b>	<b>1</b>	<b>a1</b>	<b>b1</b>	<b>c1</b>	<b>d1</b>
1.3.1	1	1	1	1	1
1.3.2	1	1	1	1	1
1.4.1	1	1	1	1	1
1.4.2 p.45	1	1	1	1	1
1.4.2 p.47	1	1	1	1	1
1.4.3	1	1	1	1	1
1.5	1	1	1	1	1
2.1	1	1	1	1	1
2.3a	4	4	4	4	4
2.3b	4	4	4	4	4
2.3c	1	1	1	1	1
2.3d	3	3	3	3	4
2.4b	1	1	1	1	1
2.4c	1	1	1	1	1
2.4d	1	1	1	1	1

<b>Multidisciplinary guideline Parkinson's disease (2010)</b>					
<b>Recommendation</b>	<b>1</b>	<b>a1</b>	<b>b1</b>	<b>c1</b>	<b>d1</b>
4.1.1	2	1	1	1	2
4.1.2	1	1	1	1	1
4.1.3	2	1	1	1	2
4.1.4	1	1	1	1	1
4.1.5	1	1	1	1	1
4.1.6	1	1	1	1	1
4.1.7	1	1	1	1	1
4.1.8	1	1	1	1	1
4.1.9	1	1	1	1	1
4.2.1	2	1	1	1	2
4.2.2	1	1	1	1	1
4.2.3	1	1	1	1	1
4.2.4	2	1	1	1	2
4.2.5	1	1	1	1	1
4.2.6	1	1	1	1	1
4.2.7	1	1	1	1	1
4.2.8	1	1	1	1	1
4.2.9	1	1	1	1	1
4.2.10	2	1	1	1	1

### Depression

The AGREE-plus efficiency scores show that in the MDG depression (2011) hardly any reference is made to cost-effectiveness in the recommendations concerning (pharmaco-therapeutic) interventions.

Only the scores on the recommendation in paragraph 8.3 deviate from 1 (strongly disagree). The recommendation concerns the preferred pharmaco therapeutic interventions regarding first and second line ambulant treated patients. In this recommendation reference is made to price (only in first line treatment) and reimbursement.

In the introduction of the MDG depression (2011) it is mentioned that due to the limited data regarding economic aspects of depression, and as no consensus was reached regarding the to be used outcome measures, no costs-effectiveness information was included in the 2005 version of the depression guideline. For the clinical guideline revision three types of economic evaluations were performed; costs-of-disease, efficiency and budget-impact studies. In the 2009 revision these results were added in an appendix named 'Health economic aspects of the multidisciplinary care'. Health economist TF contributed to the development of this appendix. During the interview with TF she was asked why the working group decided not to integrate cost-effectiveness information in the recommendations, but had put it an appendix. TF answered<sup>2</sup>:

*“They didn’t want it ... The attitude within the group, concerning cost-effectiveness analyses and economic evaluations in general, was quite variable. There were people who were enthusiastic about it and there were people who ... did not see the use of it. ... They maybe thought, that it was difficult enough to get all people in line concerning the effectiveness, ... to get consensus ... and then this was yet a bridge to far ...”*

<sup>2</sup> To improve the legibility of citations these were, where needed, adjusted to written language.

Because the health economic aspects are separated from the rest, it gives the impression that efficiency was just a topic on the to-do list, but was not considered as a core part of the guideline development process. TF expressed it as follows:

*"I think it was ... something ... that was part of the program prerequisites, thus they put it in."*

According to TF the cost-effectiveness information should more or less be considered as supportive. The cost-effectiveness results were used as a confirmation of what they already wanted to promote; the stepped-care method. It was considered as an additional argument, but it was certainly not a primary argument.

### Stroke

The AGREE-plus scores on efficiency show that for the MDG stroke (2008) some reference is made to cost-effectiveness in the recommendations concerning (pharmaco therapeutic) interventions. The scores of three of the reviewed recommendations deviate from 1 (strongly disagree). In paragraph 2.3a, concerning the recommendation that for patients who experienced a cerebral infarction, TIA or retinal ischemia of more than 70%, a carotid endarterectomy should be considered, reference is made to cost-effectiveness. It is mentioned that the results of an economic evaluation of the National Health Service (NHS) showed that a carotid endarterectomy at 50-70% is cost-effective with an incremental cost-effectiveness ratio (ICER) of \$4,462 per quality adjusted life year (QALY) (Patel 1999 in MDG stroke 2008). In paragraph 2.3b it is recommended that in principle no carotid endarterectomy should be done in case of an asymptomatic carotid stenosis. However for men under the age of 75 years, and an asymptomatic stenosis of more than 70%, a carotid endarterectomy could be considered if the surgery risk of a debilitating stroke or death is less than 3%. The results of a study by Cronenwett (1997 in MDG stroke 2008) showed that carotid endarterectomy is cost-effective with an ICER of \$8,000 per QALY. Also in paragraph 2.3d, recommending that for asymptomatic patients there is no indication for carotid artery stenting (CAS), neither for carotid endarterectomy, reference is made to cost-effectiveness. It is mentioned that the results of a cost-effectiveness study of the NHS showed that CAS is not cost-effective on the long run (Kilaru 2003 in MDG stroke 2008), although hospital costs would be less (Gray 2002 in MDG stroke 2008).

Besides these three recommendations, where the AGREE-plus scores were above 1, in paragraph 1.3.2, the recommendation concerning the start of intravenous thrombolysis as the preferred treatment within the first three hours after a stroke, reference is made to the feasibility of the intervention and the required resources (presence of a neuro-intervention team should be available 24 hours a day).

Finally in one of the recommendation that were reviewed regarding the treatment of patients who experienced a TIA or cerebral infarct with a statin, paragraph 2.4b, they refer to the

clinical guideline cardiovascular risk management. According to some respondents this guideline is an example of a clinical guideline where cost-effectiveness was well incorporated. Although no health economist was involved during the revision process of the MDS stroke, in the suggestions for future research it is mentioned that a budget-impact analysis should be performed. MP however commented that she thought this was not included in the project plan of the next revision.

### Parkinson

The AGREE-plus scores on efficiency show that for the MDG PD (2010) some reference is made to cost-effectiveness in the recommendations under study. Similar to the MDG depression a separate sub-group gathered the economic evidence. It is also mentioned in the MDG PD (2010) that the recommendations are based on the evidence from the literature and take among others also costs into account. Regarding this last aspect it is added that costs of medication could play a prominent role, but may not be leading in decision-making. In four of the reviewed recommendations reference is made to costs. In paragraph 4.1.3 it is recommended that mono-amino-oxidase-B (MAO-B) inhibitors could be prescribed as first choice treatment for PD patients with mild disabilities in the uncomplicated phase. It is mentioned that the costs of the treatment with rasagilini are higher than the treatment with selegiline (MDG PD 2010). In the recommendation regarding the prescription of levodopa with controlled release in the complicated phase, paragraph 4.2.1, it is mentioned that levodopa with controlled release are more expensive than levodopa with normal release (MDG PD 2010). Also in paragraph 4.2.4, where is recommended to prescribed catechol-O-methyl transferase (COMT) -inhibitors as first choice treatment as adjuvant treatment for late phase PD patients with predictable response fluctuations, reference is made to costs. It is mentioned that the stalevo (combination of entacapon and levodopa/carbidopa) could be considered as a treatment option, but this treatment comes with higher costs. However the number of pills to be taken is less (MDG PD 2010). Finally in paragraph 4.2.10 where it is recommended that under certain conditions intraduodenal infusion of levodopa/carbidopa could be considered for patients in an advanced stage of PD, attention is paid to costs. It is mentioned that physicians should weigh the very high costs of intraduodenal levodopa against the possible treatment alternatives and the effects it has for the individual patient. Besides referring to costs in the recommendations and describing the results of the costs-of-disease study, a sub-group chaired by Erik Buskens, performed a budget-impact analyses to estimate the implications of the implementation of the new intervention policy, as described in the MDG PD (2010). TF, who was also part of the sub-group, commented on the findings of the budget-impact analysis:

*“For example by Parkinson they also had very high expectations of the deployment of PD nurses and then it appears that whether it is efficient, and whether costs can be saved, very much depend on the amount of time the PD nurse spends on her consultations. If this is much longer than the medical specialist who she replaces, then this shouldn't necessarily be*

*cheaper ... this was an eye-opener at that time ..."*

### **Qualitative results**

#### Enhancing transparency

The data gathered with the AGREE-plus instrument, provided an impression of the explicit role of cost considerations. The information gathered during interviews with working group member provided information regarding the implicit role of economic evidence.

It is of relevance to be aware of the discrepancy between economic considerations that are explicitly mentioned in clinical guidelines and all that is kept invisible. The fact that economic evidence is not explicitly described in a clinical guideline does not per definition mean that costs are not considered at all or that the recommendations are not in line with the available economic evidence (Tan et al. 2008; Zuiderent-Jerak et al. 2011).

According to the Regieraad (2011) it would be recommendable to promote the incorporation of explicit consideration to improve the transparency, however there are many reasons why this is still not reality today.

#### Governmental motivating power

To realize transparency, as propagated by the Regieraad (2011), the government seems to play an important role. According to TF, the (changing) role of economic considerations in clinical guidelines is much dependent on initiated programs and financing. TF commented that:

*"... nothing structural ... is arranged about how it <referring to incorporating economic evidence> should be done or that it should be done. This makes it so dependent on initiatives and the associated financing."*

According to TF this can be illustrated by the fact that the pilot program, initiated by the ministry of VWS, induced a wave of attention for cost-effectiveness. After this program, the attention faded for a while until the KKCZ program triggered a new wave of attention. EB referred as follows to the direct and indirect effects of the KKCZ program:

*"... a benefit of the KKCZ program is that it works like a kind of stone in the pond. The waves are still lapping."*

TF mentioned that in the clinical guidelines, which were not part of one of these two programs, there was hardly any attention for cost-effectiveness. This illustrates the important motivating role of the government. A decade ago Rutten & Brouwer (2002) already argued that, due to the difficult choices that should be made in the future regarding which health care should be collectively financed, and the control function on this matter should be centralized. Such a central body was established in the form of the Regieraad. EB mentioned that the members of the Regieraad had sat around the table with all relevant parties, like the CVZ, the Dutch healthcare authority (NZa) and the Authority for consumers and markets (NMa) to

discuss how efficiency should become part of health care policy. Although all parties agreed that standardization was essential, it never resulted in a uniform procedure. This responsibility is transferred to the quality institute (part of CVZ) that is currently in development.

EB noted that the institute has expressed the intention to promote efficiency in clinical guidelines. However, the development of the institute has proven to be a long-lasting process, which is dependent on political circumstances. According to EB the previous government did not decide on the responsibilities and the legal anchoring of the institute, so the current government has to make these decisions. After these decisions are made, it will still take some time before the institute is up and running. So we have to wait and see whether the institute is capable to meet its intention to promote efficiency in clinical guidelines.

#### Watch, learn and adopt

Regarding the quality institute, the National Institute of Health and Clinical Excellence (NICE) is often referred to as a pursuable example. Not only the procedures applied by NICE, but also their products could serve as a template for Dutch clinical guidelines. Using existing clinical guidelines as starting point can save a lot of time and effort. According to TF this makes sense, as:

*“... in England they put a lot of time and attention in it. Not only in the cost-effectiveness part, but also in the rest of the guideline.”*

This is already applied in practice. A good example is the PD guideline. Before developing the multidisciplinary guideline for PD, existing PD guidelines were scored with the AGREE-instrument. Based on the AGREE-scores the NICE guideline, ‘Parkinson’s disease: diagnosis, and management in primary and secondary care (2006)’, was used as a starting point and adapted and up-dated where thought necessary (MDG PD 2010).

But also specifically for economic evidence English guidelines are referred to. So did TF mention that they had looked very closely at the English irritable bowel syndrome guideline to decide which economic evaluations they would perform for the Dutch clinical guideline. This illustrates that reference is made to foreign guidelines during the development process and that in case useful information is available, this is used for deciding for which and how economic evidence will be incorporated in the Dutch clinical guideline.

Although foreign clinical guideline can be used as an example, the most essential starting position should be the formulation of the right starting questions. Zuiderent-Jerak et al. (2011) argued that CVZ could play a role in determining these starting questions and in assuring efficiency is included during the development or revision process of a clinical guideline.

#### Urge for high quality cost-effectiveness information

The Regieraad considers the lack of economic considerations as a serious shortcoming and claimed that a more systematic approach, like the procedure applied by NICE, is recommendable (Regieraad 2011).

ML noted that although the general opinion is that, in case relevant cost-effectiveness information is available, it should be incorporated in the clinical guideline. Nevertheless, it was not structural taken into account in the clinical guideline development procedures she was involved in. ML argued that this was because the chance you find relevant cost-effectiveness studies applicable to the starting questions, is very limited. According to TF not only the availability, but also the quality of available economic evaluations is an issue. She noted:

*“The quality varies a lot. Sometimes there are a few good studies, and sometime there is just nothing.”*

That there were issues regarding the quality of economic evaluations was already recognized several years ago. Niessen et al. (2007) stated that there were methodological constrains like the short time horizons used and the lack of adequate quality of life measures used. Due to these limitations the quality of the available cost-effectiveness data varied, which made the quality level not always acceptable for clinical guideline development groups. Niessen et al. (2007: 73) therefore favoured that *“there should be a standardized data collection and use of outcome measures both on costs and health effects, and there should be a standardized approach in the model-based analysis to guarantee comparability across guidelines.”* The next step could be a grading system, like that is applied for clinical evidence, so the quality of the available economic data becomes transparent.

#### Need for a standardized development procedure

Although standardization of economic evaluations and a grading system for economic evidence are not yet generally applied, there are tools, like the manual for guideline development and the ‘toolbox in the Dutch healthcare’ (HARING), available for developing clinical guidelines. The report ‘Guidelines for Guidelines’ provides a uniform basis regarding the approach, content and design of clinical guidelines and aims to let guideline developers pursue the same objective and methodology (Regieraad 2011). Nevertheless it seems that this guideline, and the other available tools, is not applied in a uniform manner, as illustrated by the comment of EB:

*“The NHG (Dutch college of general practitioner) has its own program ... if they say, we don’t look at efficiency, than they don’t. Because they have there own responsibility and that does not extend to the fact that everybody says it is an inextricable component.”*

Although it is not yet an inextricable component, EB argued that in the ideal situation efficiency it would be inextricable linked to clinical guidelines. He advocates that in the future it will be “yes, unless...”. That economic evidence is incorporated in the clinical guideline, unless there are fair arguments to decide not to.

The current lack of a uniform applied approach makes the developmental process susceptible

for the influence of separate members of a guideline development group. EB illustrated this by noting the influence of the chairman of the MDG PD (2010) regarding including economic evidence:

*“That was especially owed to the progressiveness and openness of the chairman of the guideline Parkinson ... He was a visionary and modern medical specialist, who thought that this aspect, taken social responsibility for what should and shouldn't and why, should be part of it ... As chairman of the working group noting its importance, being conscious, and thus stand behind such an approach, that it should be integrated.”*

This citation illustrates that a few working group members could, in absence of applying a uniform development procedure, play a dominant role and have significant influence on the content of a clinical guideline. This is confirmed by Rutten et al. (2005) who argued that it is essential that the chairman of the development group supports the integration of economic evidence in clinical guidelines.

#### Position of health economists

What is the position and influence of the health economist(s) in the working group? EB commented that this varies a lot between clinical guideline development groups. He noted that for some clinical guidelines the medical specialist prevailed and that health economists were not considered as equal partners. According to EB, the development group of the Parkinson guideline could, due to the influence of the chairman, be considered as an exception. During this development process health economists were considered as serious and equivalent partners.

The position of health economists is made evident by the answer of TF on the questions whether she expected to be contacted for a revision of the depression guideline:

*“If we do nothing, I don't really think they would. No. Then you should yourself actively approach the group ... And then maybe. It would then also very much depend on the financing.”*

If health economists are involved in a clinical guideline development project, this is often at the final stage of the project. As the publication of the guideline will not wait on the economic evaluations results, this results in high time pressure, as much work has to be done in a short time period. If time is not an issue for guideline development groups, the costs and potential resistance to involve a health economist could play a role.

Reluctance to the incorporation of economic evidence in clinical guidelines is still present. TF said she could understand when people claim that cost-effectiveness should not play a role in clinical guidelines. TF noted:

*“I can understand the reluctance. Because as you claim; a guideline is meant to describe the current status of medical practice as good as possible. What is the best care for the patient, efficiency doesn't belong there. It then just matters what is the best care and then are*



*effectiveness, side effects, and patient satisfaction relevant aspects, but what the costs are is not relevant.”*

Hakkaart-van Rooijen et al. (2010) however argued that economic information could optimize the recommendations listed in clinical guidelines and that the involvement of a HTA-expert in the guideline development group could be considered essential for the integration of economic evaluation data with clinical evidence based data. Therefore, ideally, (a) health economist(s) should be part of the clinical guideline development group from the start (among other advocated by Tan-Torres Edejer 2006). The suggestion to involve experts in cost-effectiveness analysis in the guideline development group was also recommended by the WHO and was included in the ‘Guidelines for WHO guidelines’ (Tan-Torres Edejer 2006). Despite of several attempts, it has proven to be difficult for health-economists to really contribute to the incorporation of economic evidence in clinical guidelines.

MP commented that consulting the expertise of a health economist could be included in the budget proposal, but this is not always done. The Regieraad (2011) argued that this is due to the absence of a framework for efficiency within guidelines and the high costs for consultation of health-economics. EB also argues that costs of consulting a health economist play a role, especially when economic evidence is not available:

*“... so you can't include it <referring to economic evidence> without significant extra effort in a guideline, and you have no time and you have no money, than you say: 'we don't do it.' ”*

Furthermore EB noted:

*“And if the government says: ‘we find it important’, a professional association will then say: ‘glad you find it important, but our budget is determined on developing guidelines from a medical profession, ... why should we also add an economic paragraph? We don't have the expertise ... it costs additional money...’ ”*

According to Rutten et al. (2005) the integration of economic evidence in clinical guidelines adds substantially to the costs of clinical guideline development. The average costs for conducting separate economic studies, to collect the required information for adding economic evidence to clinical guidelines, were approximately 30,000 euro per guideline. According to Rutten et al. this should be paid by the government (Rutten et al. 2005).

#### *Critically assessing the use of economic considerations in clinical guidelines*

Due to these additional costs the efficiency topic should be approached critically. Not for all recommendations, or for all clinical guidelines, it is useful to incorporate cost-effectiveness data. According to Rutten & Brouwer (2002: 2258) cost-effectiveness should be considered at least in: *“important new programs concerning public health, for all drugs with a higher effectiveness compared to existing drugs and for all other (new) technologies of which the*

*costs are high, of which the added value is considerably uncertain or, of which the chance of inefficient deployment is major.*” These criteria are comparable with those applied by NICE. That it is important to critically decide whether the inclusion of economic evidence is efficient, is illustrated by the following example put forward by ML:

*“... if you look at biologicals for reuma, there you should do it <referring to the incorporation of economic considerations>. But the last version I have seen, this was not included. A consideration had been that the development just goes to fast. ... and also the price developments and the insight in effectiveness ...”*

Although biologicals are expensive drug, due to the rapid ongoing developments, it would not be cost-effective to continually spend money on performing economic evaluations. But could it today in general be considered as a cost-effective measure? Niessen et al. (2007) argued that it is difficult to say whether this is value for money as economic evaluation studies on clinical guideline implementation have been limited (Niessen et al. 2007). EB however claimed that it is efficient.

*“You could make a serious movement towards either efficiency, or deny on reasonable grounds access to the market for a certain expensive intervention.”*

EB added that the costs of consulting an HTA-expert are easily recovered, as a clinical guideline is used on a national level for several years and is applicable for, approximately 80% of the patients. On the other hand TF believes that at present the benefits of incorporating economic evidence in clinical guidelines do not outweigh the costs. She adds that it could have a positive cost-effect ratio when it receives a role in policy making and it would make a difference when clinical guidelines will be used as a basis for the demarcation of entitlements.

MP notes that the essence of clinical guidelines today is still to provide a tool for the medical professional to choose the best care for their patient. If clinical guidelines are linked to reimbursing the ‘best care option’ this could conflict with the ‘optimal care option given the budget constraints’. There is a discrepancy between the care we wish to receive as a patient and the care we are willing to pay for from public funds. According to MP the differences between the considerations on an individual level compared to societal considerations cause ethical dilemmas.

#### Defining (in)efficiency

Who is responsible for solving these dilemmas? MP believes that the government has the responsibility to determine what is cost (in)efficient. According to TF this is mainly a joint responsibility of the government and health insurers. They should, in case economic considerations will be assigned a normative role, clearly define the classification of (in)efficiency.

Rutten & Brouwer (2002) also claimed that, to make choices in health care, efficiency considerations should be made explicit by cost-effectiveness ratios.

Defining official thresholds has however proven to be difficult. The most common mentioned threshold is about 20,000 euro per QALY. Other thresholds, as mentioned by the Council for Public Health and Health Care (RVZ) and the CVZ, range from 10,000 to 80,000 depending on the severity of the disease (Regieraad 2011). Pomp et al. (2007) argued that, due to the indistinct thresholds, various thresholds have been used by attempts to incorporate cost-effectiveness in clinical guidelines. According to Niessen et al. (2007) this indicates that individual guideline developing groups make the decisions on priorities in health care, but *“as the provision of health care is a collective societal activity, these kinds of decisions should be taken collectively through the appropriate political channels”* (Niessen et al. 2007: 73).

Niessen et al. (2007) expressed the need to involve representatives that are responsible for the financing of health care as difficult trade-offs, e.g. between efficiency and equity considerations, have to be made. This should not be something to be decided by clinical guidelines development groups. ML agrees with this as she noted that defining what is cost-effective is per definition a responsibility of the government. A well-defined threshold would provide clinical guideline development groups something to work with. Also EB agrees that the ministry of VWS should, as the voice of the nation, possibly with health insurers, set the framework. He argued that this could be done in consultation with the CVZ and the quality institute. Despite the fact that policy makers and ministers are unwilling to set a threshold, as this is a politically charged decision, according to EB they should set the framework, including potential exceptions. When the framework is set, medical professionals could take their responsibility. They would then have the autonomy to do what they think is best within a well-defined and clear framework. This does not mean that without well-defined boundaries, medical professionals can not do anything. As noted by EB, the chairman of the PD guideline gave a good example. He was prepared to take his responsibility as a physician and suggested that efficiency should be considered as a prominent part of the weighting mechanism when developing a clinical guideline.

In accordance with this, TF argued that, in the Netherlands, it is insufficiently rationed how a threshold should be defined and which factors, like the severity of the disease and different thresholds for prevention or palliative care, should play a role. A strict decision-making procedure is lacking and no-one seems to be willing to make efficiency decisions. TF describes the situation as follows:

*“... it is like a hot potato which is passed on. The physician says: ‘the government has to set boundaries, I will provide the best care within those boundaries.’ The government says: ‘we have delegated that to the insurers’ ... And the insurers then say: ‘we are not capable to make such choices, that is something the physicians should do’. And then the circle is round again.”*

### *Incorporating economic awareness in medical training*

TF mentioned that physicians are well aware of the affordability issue. The problem however is that they are the one who are sitting in front of the patient. It is hard to say that a treatment is available, but it can not be provided due to financial reasons.

MP recalled a discussion during the hernia guideline development process. In one of the recommendations in this guideline it is mentioned that a MRI-scan should only be provided in case the physician intends to perform surgery. In case the physician does not have this intention, it is not cost-effective to provide a MRI-scan as nothing will be done with the scan result. However, during the guideline development process physicians indicated that it is difficult to stick to the recommendation in the clinical guideline when a patient is sitting in front of them. If they do not give their consent for a MRI-scan to the patient, they go to a private clinic. They argued that regardless on what they decide as a physician, a MRI-scan would be provided, so why not provide it themselves? This illustrates the need for education. It would be desirable to give the social responsibility a place in the education of medical professionals. EB noted that it is remarkable that, although the responsibility for the accessibility of healthcare is part of their oath, there is no attention for it during their training.

### *Clinical guidelines as a policy tool*

Nevertheless as long as the threshold(s) and decision-making procedure are unclear it causes tensions, as commented by TF:

*"I think that the government, as legislator, should think carefully what the aim of guidelines is and as long as that is not clear, you keep these kinds of tensions."*

TF noted that enormous investments should be put into the guideline development process to overcome these tensions. At this moment the developmental process as well as the quality of clinical guidelines is too variable to connect them to such important decisions and to make it possible for insurers to fulfil their role as purchasers of health care. Rutten et al. (2005: 93) noted that insurers are seeking how to fulfil *"their role as prudent purchaser of cost effective care appropriately since they lack the required knowledge."* This is still applicable today. ML mentioned that health insurers still do not have enough knowledge about the quality of care.

In order to link clinical guidelines to reimbursement decision, clinical guidelines should receive another position in the health care sector. Also in this case reference is made to England. ML noted that:

*"If in England there is something mentioned in the guideline, it will also be reimbursed and in The Netherlands this is separate from each other."*

In England, since January 2002, clinical guidelines are compulsory entities. Patients are entitled to receive the care as described in the clinical guideline and medical professionals

are obliged to provide the care (Rutten & Brouwer 2002).

EB agrees that clinical guidelines could be guiding. Clinical guidelines should be considered applicable for an average patient, approximately 80% of the people. For this 80% the recommendations of the guidelines should be sufficient. For the other 20%, due to co-morbidity and exceptions, a good decision-making procedure should be in place to decide which care to provide.

However, according to MP and ML, with the current available clinical guidelines it is not feasible to use clinical guidelines to demarcate the basic benefit package. It would only be possible when guidelines described the care process from beginning to end. That is not today's practice. ML mentioned that at this moment guidelines are focused on bottlenecks, thus not reflecting the care process from A to Z. Would it be desirable to describe everything from A to Z? To also write everything down where everyone agrees on, where consensus is reached? According to the following example by MP, regarding performing a CT-scan, it could at least preclude confusion:

*"I can recall a discussion with insurers about stroke ... A CT-scan is not mentioned in the guideline and every neurologist says: 'every patient who has a stroke gets a CT-scan as the first thing you want to know is, whether it is an infarct or a bleeding. You don't put that in the guidelines, as everybody knows it.' This discussion you get, if healthcare insurers without the relevant knowledge are going to reimburse based on a guideline."*

#### Step by step, hurdle by hurdle

The combination of explicit and implicit information shows that there is still a long way to go to reach the destination of economic-based clinical guidelines. EB noted that there is a change in awareness going on, but the transition goes very slowly. The high costs for consulting a health economist, the limited availability of high quality economic evidence, the absence of a uniform applied development process and the reluctance to incorporating economic evidence in clinical guidelines could be considered as arguments why today it is still not common practice to include economic evidence in clinical guidelines. Besides these arguments the political arena plays an important role. EB described it as follows:

*"... many traffic lights are on red, at least on orange to just give efficiency a place and that could only happen if we get a brave government."*

*"It takes a lot of political courage to really initiate a trend break and to anchor the efficiency criterion in guidelines and then say this is applicable on the majority of the insured."*

However, despite of all these constraining circumstances, economic-based clinical guidelines could still be considered as a potential tool for making treatment choices that are consistent with both clinical as well as social aims (Mason et al. 1999). Confidence and patience are needed as illustrated by a comment of EB. He mentioned that in his inaugural speech he had said that he hoped that during his very last speech he could say that efficiency has acquired its appropriate place in clinical guidelines.

## Discussion

The results show that the incorporation of economic considerations in clinical guidelines did not come to a halt, but that the pace is slow. Nevertheless, the current situation is in contrast with what Rutten & Grijseels (2002) had hoped for; cost-effectiveness becoming an integral part of Dutch clinical guidelines. The AGREE-plus scores, regarding the current status of economic evidence in clinical guidelines, illustrate that there is still a long way to go to reach the destination of economic-based clinical guidelines. The information gathered by the interviews provided the reasoning behind the current situation and delineate the path that still lies ahead of us.

The scores on the AGREE-plus efficiency questions illustrate that only limited attention is paid to economic evidence during the formulation of recommendation concerning (pharmaco therapeutic) interventions. These results are in line with those of previous studies. A study by Tan et al., commissioned by the ministry of VWS, examined the availability of cost-effectiveness and budget impact data for the top-5 drug (based on their expenses in 2007) and the presence of the available cost-effectiveness data in the corresponding clinical guidelines. The general conclusion of this study was that, although efficiency data were available, the representation of these data in clinical guidelines was limited (Tan et al. 2008). Several years later another study concerning clinical guidelines, commissioned by the Regieraad, examined among others the topic of cost-effectiveness. Sixty-two clinical guidelines were analyzed according to the AGREE-plus instrument. The results of the study showed that only in one third of the clinical guidelines under consideration cost-considerations explicitly played a role (Zuiderent-Jerak et al. 2011).

During the interviews several reasons for the lack of economic considerations in clinical guidelines were put forward. The respondents addressed, among others, the absence of a uniform applied development process, the limited availability of high quality economic evidence and lack of the definition of (in)efficiency as arguments. Furthermore the importance of a well defined aim and scope of clinical guidelines became evident during the interviews. Clinical guidelines are originally developed as a tool for medical professionals to provide the best care. They are primary based on clinical effectiveness evidence and expert opinions. By adding efficiency information to clinical guidelines, medical professionals are encouraged to provide cost-effective care. This shift could cause confusion and resistance. Therefore it is of importance that the aim of clinical guidelines and its purposes are evident for all players in the field.

Besides being clear about the aim and scope of clinical guidelines, the government should put effort in standardizing the development process. Although there is a general guideline and there are tools available for developing clinical guidelines, these are not applied in a uniform matter. In this context reference is made to NICE as a pursuable example to enhance the

application of a standardized approach to develop clinical guidelines. The ministry of VWS should take the lead in uniforming clinical guideline development. A uniform procedure would limit the influence of individual working groups, which is currently a hurdle for incorporating economic evidence in clinical guidelines. The attention paid to economic considerations is now much depending on the opinion of individual working group members regarding the relevance of the topic efficiency.

The Regieraad advocates a systematic approach regarding the incorporation of economic evidence in clinical guidelines. They consider setting uniform criteria for performing economic evaluations and including the results in clinical guidelines as a necessary development (Regieraad 2011). However, this has not yet become reality. As long as it is not a prerequisite and no money is made available to conduct economic evaluations, it should not be expected that clinicians or pharmaceutical companies will initiate the conduct economic evaluations.

As it is not obligatory to perform economic evaluations, there is a lack of high-quality economic evaluations, which is another reason efficiency is not standard included in clinical guidelines. Niessen et al. already appointed this argument in 2007. They assessed the quality and use of economic evidence in clinical guidelines that were part of the 'guidelines support-program'. A checklist was composed to assess the quality of the cost(-effectiveness) information. Among others, the results showed that the quality of economic evidence, the relatively low availability of QALYs and the simplistic statistical analysis of most studies were disappointing (Niessen et al. 2007). The respondents still consider the lack of high-quality economic evidence as a limiting factor to include economic considerations in clinical guidelines. This shows that little progress has been made to enhance the availability of high-quality economic evidence, applicable for clinical recommendations.

Next to sufficient available economic evidence and the realization of a uniform applied guideline development process, the content of clinical guidelines is also subject of discussion. Some respondents claimed that, to let health insurers act as prudent purchasers of health care, it would be helpful if clinical guidelines describe the health care process from beginning to end. Although it could make them more suitable for the demarcation of entitlements, it also has its downsides. Describing the process from A to Z would cost a lot of time, effort and money. And if resources are deployed to describe the total health care process, fewer resources will be available for consulting a health economist during the development process. This raises the questions whether 'A to Z' clinical guidelines contribute to efficient health care. The argument that health insurers would benefit from A to Z information to act as prudent purchasers is of interest, but other tools, in addition to clinical guidelines, could be developed to support them fulfilling this role.

As said the aim and scope of clinical guidelines should be clear. So if the government aims to make clinical guidelines suitable for reimbursement decisions based on best affordable care,

this should be made evident. There should be no need to describe the health care process from A to Z, but economic evidence should be included where it is considered to have added value.

To make the incorporation of efficiency information in itself cost-effective, one should look carefully for which recommendations it would be desirable. It could, for example, be of relevance when the recommendation concerns an intervention that has a significant budget impact. Then the benefits for including economic evidence could outweigh the costs. On the other hand, it could also be the case that in advance it is already evident that an intervention is not cost-effective. For some of these cases exceptions should be formalized. As inclusion of economic considerations does not per definition enhance efficiency in healthcare, a clearly defined framework, when (not) to include cost-effectiveness, is of importance. Based on a pre-defined set of criteria it can then be decided whether cost-effectiveness should be integrated in a recommendation or not.

Another argument addressed by the respondents for the limited incorporation of economic evidence in clinical guidelines, is the lack of (a) threshold(s). To make the incorporation of economic evidence in clinical guidelines worthwhile the government, possibly with health insurers, should make a statement regarding what should be considered as in(efficient) health care. As long as this is not clear, there is a chance that clinical guideline development groups will make their own judgment on what is (in)efficient. As this is an undesirable situation, the government has to step forward and show courage to make these politically sensitive decisions.

A downside of defining thresholds is that pharmaceutical companies can easily calculate what a new (drug) intervention should cost to stay below the applicable cost-effectiveness threshold. According to EB, pharmaceutical companies already apply the informal threshold of 20,000 euro per QALY, as he thought it to be rather remarkable that pharmaceutical companies often end up around this threshold when making cost-calculations. The reasoning behind this is that, as long as the ICER stays below the 20,000 euro per QALY, the chance that a new (drug) intervention enters the market is high.

When the time has come that the government makes threshold(s) decisions, it would be wise to pay attention to the collaboration between medical professionals and HTA experts in guideline development groups. This because recommendations based on effectiveness versus efficiency, will not always coincide. When discussions between best care and best affordable care arise, health economist could easily be depicted as the evil-doer. It would provoke a lot of media attention and would damage the image of health economics. Therefore the government, health insurers and medical professionals should anticipate on the consequences of setting threshold(s) and explain to the public why the focus on efficient health care is inevitable. The government should already start with providing information to the public. This information should clearly describe the societal responsibility and why the to be made efficiency choices are crucial and should not be translated to individual patients. The



public should become aware of the reasoning behind rationing health care on economic grounds. That it is inevitable to set threshold(s) and to follow a well-defined decision-making procedure, so the government is able to keep fulfilling the public aims of accessible, affordable and efficient health care of good quality now and in the future.

Besides informing the public awareness of medical professionals regarding their social responsibility should be encouraged. This could be done by including the importance of the social responsibility of a medical professional in their education. They should understand the framework in which they (will) have to provide care (in the future). If health professionals understand the reasoning behind the efficiency considerations, they would be able to properly inform their patients. This would contribute to making patients more (cost-) conscious and aware of the rational behind certain treatment choices.

Finally, when economic-based clinical guidelines are reality, attention should be paid to their implementation. According to Grol (2000) the method of introduction of clinical guidelines is one of the important factors that determine the use of a clinical guideline. Therefore it is crucial that there is a proper implementation procedure for clinical guidelines, otherwise this tool will not have a fair chance to become a valuable method to realize cost-effective health care.

Although this study provides an illustration of the current status of economic considerations during the clinical guideline development process, the results should be interpreted with caution, as the study has some methodological constraints.

First of all the AGREE-plus efficiency questions were only scored by one appraiser. This while the AGREE collaboration recommends that each clinical guideline should at least be scored by two appraisers, to guarantee the reliability of the scores. However, as the scoring methodology is rather straightforward and the AGREE-plus scores are in line with other study results, one may assume the reliability level of the scores is acceptable.

Furthermore the scoring was limited to only three clinical guidelines of which only a selection of recommendations was scored. However, as the respondents were involved during various clinical guidelines development procedures, the information gathered during the interviews extended to clinical guideline(s) (procedures) more generally. Elaborating on the respondents, as only clinical guideline development group member were interviewed, it would be of interest to explore the opinion of policy makers concerning these study results. This would probably further clarify which (f)actors play a crucial role along the way to providing cost-effective care.

Finally, the fact that only three interviews were conducted with in total four respondents and the fact that the interviewer had little experience in conducting interviews with a topic list could be considered as constraints. Due to these methodological aspects it should be noted that the results should be interpreted as a rough representation of the current situation.

It can be concluded that the government fulfils a key role during the journey towards economic-based guidelines. They should take a clear position and execute the corresponding actions. The clinical guideline development procedure should be standardized, which will decrease the individual influence of working group members. And, as economic considerations will not by itself become an integrated part of clinical guidelines, economic considerations in clinical guidelines should be made mandatory. Furthermore the government should show courage and establish a decision-making procedure with well-defined criteria and thresholds, which should be explained to the public.

Besides the vital role of the government a joint deployment of all stakeholders is needed to take the necessary steps toward economic-based guidelines. Health insurers and medical professionals should not wait and see until the governmental has the courage to take decisions, but they should explore what is within their ability to improve efficiency in health care.

It has become clear that a long breath is needed to convince all stakeholders that economic-based guidelines could lead to a more efficient and cost conscious health care system. However, as economic-based guidelines are only one of the contributing paths, one should question which other paths could contribute to reaching the destination of a sustainable, affordable and efficient health care system. Let's hope that these study results will work as just another stone in the pond, which, together with all the other stones, will contribute to the awareness of the need for efficiency considerations in health care.

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## Abbreviations

CAS:	Carotid artery stenting
CBO:	Centraal begeleidingsorgaan voor integrale toetsing / Central Accompaniment Organization for peer review
COMT:	Catechol-O-methyl transferase
CVZ:	College voor zorgverzekeringen / Health care insurance board
EBRO:	Evidence based richtlijn ontwikkeling / guideline development
HARING:	Handleiding richtlijnontwikkeling en toolbox in de Nederlandse gezondheidszorg / Manual guideline development and toolbox in the Dutch healthcare
HTA:	Health technology assessment
ICER:	Incremental cost-effectiveness ratio
iMTA:	Institute of Medical Technology Assessment
KKCZ:	Kennisbeleid kwaliteit curatieve zorg / Knowledge policy quality curative care
MAO-B:	Mono-amino-oxidase-B
MDG:	Multidisciplinary guideline
NHG:	Nederlands huisartsen genootschap / Dutch college of general practitioner
NHS:	National Health Service
NICE:	National Institute of Health and Clinical Excellence
NMa:	Nederlandse mededingingsautoriteit / Authority for consumers and markets
NZa:	Nederlandse zorgautoriteit / Dutch healthcare authority
OMS:	Orde van medisch specialisten / Association of Medical Specialists
PD:	Parkinson's disease
RIVM:	Rijksinstituut voor Volksgezondheid en Milieu / National Institute for Public Health and the Environment
RVZ:	Raad voor de Volksgezondheid en Zorg / Council for Public Health and Health Care
VWS:	Volksgezondheid, Welzijn en Sport / Health, Wellbeing and Sport
WHO:	World Health Organization
ZonMW:	Zorgonderzoek Nederland medische wetenschappen / The Netherlands Organisation for Health Research and Development

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## Appendix A: AGREE-plus efficiency questions<sup>3</sup>

### Item AGREE

1. The potential resource implications of applying the recommendations have been considered.

Score: *strongly disagree* 1 2 3 4 *strongly agree*

2. The potential resource implications of applying the recommendations have been considered.

*Explanation based on the AGREE-instrument 'where applicable'; possibly supplemented with research comments*

<Free text field>

### Additional questions in the AGREE-plus

a.1. The cost-effectiveness question is clearly formulated.

Score: *strongly disagree* 1 2 3 4 *strongly agree*

a.2. The cost-effectiveness question is clearly formulated.

*Explanation:*

- Costs and effects are analyzed*
- The alternatives are clearly formulated*
- Other: <free text field>*

b.1. The outcome measure are adequately identified, measured and rated.

Score: *strongly disagree* 1 2 3 4 *strongly agree*

b.2. The outcome measure are adequately identified, measured and rated.

*Explanation – outcome measures:*

- Intermediate endpoints*
- Disease specific endpoints*
- Won life years*
- QALYs or DALYs*

c.1. All relevant costs for alternative treatments are measured.

Score: *strongly disagree* 1 2 3 4 *strongly agree*

c.2. All relevant costs for alternative treatments are measured.

*Explanation - perspective:*

- Societal perspective*
- Health care perspective (including expenses of patients)*
- Only costs within the health care budget*
- Other: <free text field>*

d.1. There is explicit attention for the financial implications for the use of medical technologies (costs and benefits)

Score: *strongly disagree* 1 2 3 4 *strongly agree*

d.2. There is explicit attention for the financial implications for the use of medical technologies (costs and benefits)

*Explanation based on the AGREE-instrument 'where applicable'; possibly supplemented with research comments*

<Free text field>

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<sup>3</sup> Translation of the questions as listed in Zuiderent-Jerak et al. 2011

## Appendix B: Respondents

Name	Talitha Feenstra	Margreet Pols	Marleen Ploegmakers	Erik Buskens
Date interview	18 January 2013	25 January 2013	25 January 2013	6 February 2013
Background	MSc. in econometrics PhD in environmental economy	MD and PhD in epidemiology	MSc. in Health technology assessment (biomedical sciences)	MD and PhD in epidemiology
Current function	Health economist at the epidemiology department at the University Medical Center Groningen and the RIVM	Senior advisor at OMS	Advisor at OMS	Professor Medical Technology at the University Medical Center Groningen
Currently guideline development process(es) involved in	None	Several guidelines concerning neurological disorders, i.a. epilepsy.	Child anesthesia	None
Previously guideline development process(es) involved in, i.a.	Depression Parkinson's disease Heart failure Outpatient pharmacy Irritable bowel syndrome	Stroke Hernia Brain injury Operative processes	Otitis externa Radiotherapy by patients with a pace-maker Several guidelines for	Cardiovascular risk management Depression Parkinson's disease Heart failure Irritable bowel syndrome

## Appendix C: Topic list semi-structured interviews

### 1. Transitie in richtlijnontwikkeling

- 1.1. Wat zijn volgens u de belangrijkste ontwikkelingen in de afgelopen 10 jaar geweest op het gebied van richtlijnontwikkeling?
- 1.2. Welke (veranderende) rol hebben economische overwegingen hierin gespeeld?
- 1.3. Hoe zou u de rol die economische overwegingen hebben in klinische richtlijnontwikkeling in Nederland beschrijven t.o.v. die in andere landen?

### 2. Richtlijn <depressie / Parkinson / beroerte>

- 2.1. Kunt u kort beschrijven hoe er bij de ontwikkeling van de richtlijn <depressie / Parkinson / beroerte> aandacht is besteed aan economische overwegingen / welke procedures zijn er gevolgd (waarom wel/geen aandacht besteed aan economische overwegingen)?
- 2.2. Was er binnen de werkgroep sprake van discussie over het opnemen van economische overwegingen in klinische richtlijnen (zoja, kunt u een voorbeeld geven van een discussiepunt?)

*Terugkoppeling van de AGREE-plus scores van de aanbevelingen m.b.t. (farmaco)therapeutische interventies in de richtlijn <depressie / Parkinson / beroerte>.*

- 2.3. Komen deze resultaten overeen met de mate waarin economische overwegingen naar uw idee een rol hebben gespeeld bij de ontwikkeling van de richtlijn (waarom wel/niet)?
- 2.4. Kunt u een voorbeeld geven van hoe bij een specifieke aanbeveling de economische overwegingen zijn meegenomen (wat waren de redenen hiervoor)?
- 2.5. Kunt u een voorbeeld geven van een specifieke aanbeveling waarbij het meenemen van economische overwegingen moeilijkheden opleverde (en waarom, welke moeilijkheden)?
- 2.6. Wat waren de redenen om economische overwegingen al dan niet expliciet te vermelden in de klinische richtlijn (kunt u hier een praktijkvoorbeeld van geven)?

### 3. Overige richtlijnen

- 3.1. Was er ten opzichte van de richtlijn <depressie / Parkinson / beroerte> bij de ontwikkeling van andere richtlijnen meer/minder aandacht voor economische overwegingen (en waarom)?
- 3.2. Is uw mening ten aanzien van het opnemen van economische overwegingen in richtlijnen in de loop van de jaren veranderd (hoe, waarom en kunt u hier een praktijkvoorbeeld van geven)?
- 3.3. Is volgens u de algemene mening (o.a. van overige betrokkenen bij richtlijnontwikkeling) in de loop der jaren veranderd (hoe, waarom en kunt u hier een praktijkvoorbeeld van geven)?

### 4. Beschikbaarheid van kosteneffectiviteit informatie

- 4.1. Kunt u een voorbeeld noemen van een aanbeveling waarvoor geen hoogwaardige kosteneffectiviteit informatie beschikbaar was, maar er toch economische overwegingen zijn meegenomen (zoja, hoe is dit verlopen)?
- 4.2. Kunt u een voorbeeld noemen van het omgekeerde: een aanbeveling waarvoor wel hoogwaardige kosteneffectiviteit informatie beschikbaar was, maar deze niet zijn opgenomen (zoja, hoe is dit verlopen)?
- 4.3. Welke eisen zou u stellen aan kosteneffectiviteit informatie alvorens deze op te kunnen nemen in klinische richtlijnen?

### 5. Richtlijn voor richtlijnen

- 5.1. Bent u bekend met het document 'gaan richtlijnen en doelmatigheid samen?' (aanvulling op de 'richtlijn voor richtlijnen')? Zoja, wat vindt u van de adviezen die hierin vermeld staan?
- 5.2. Bent u van mening dat klinische richtlijnen de juiste plek zijn om economische overwegingen aan bod te laten komen (waarom wel/niet)?



- 5.3. Heeft de toevoeging van economische overwegingen volgens u invloed op de tijdsduur van het richtlijn ontwikkelproces (zoja, hoe en wat vindt u hiervan)?
- 5.4. Heeft de toevoeging van economische overwegingen volgens u invloed op de kwaliteit van zorg (zoja, kunt u hier een praktijkvoorbeeld van geven)?
- 5.5. Wat is volgens u het effect van het opnemen van economische overwegingen in klinische richtlijnen op de efficiënte cq doelmatigheid van zorg (kunt u hier een praktijkvoorbeeld van geven)?
- 5.6. Wegen de kosten van het toevoegen van economische overwegingen volgens u op tegen de baten (hoe en waarom wel/niet)?
- 5.7. Indien u iets mocht veranderen aan de huidige 'richtlijnen voor richtlijnen' en de adviezen zoals vermeld in het document 'gaan richtlijnen en doelmatigheid samen?' wat zou dat dan zijn (en waarom)?

#### **6. Invloed van economische overwegingen op besluitvorming**

- 6.1. Op welk niveau (ministerie VWS / zorgverzekeraars / medisch professionals / patiënt) zouden economische overwegingen volgens u invloed moeten hebben op de besluitvorming (en waarom)?
- 6.2. Wordt uw mening hierover volgens u gedeeld door anderen (waarom wel/niet en door wie)?

#### **7. Klinische richtlijnen als beleidsinstrument**

- 7.1. Wat is volgens u het belangrijkste doel van klinische richtlijnen en is dit doel volgens u bereikt met de ontwikkeling van de klinische richtlijn <depressie / Parkinson / beroerte>? Wat heeft de richtlijn opgeleverd (zowel in positieve als in negatieve zin)?
- 7.2. Wat vindt u van de ontwikkeling om klinische richtlijnen te gaan gebruiken voor de afbakening van het verzekeringspakket?
- 7.3. Beschouwd u klinische richtlijnen momenteel meer als beleidsinstrument of als instrument voor klinisch handelen (waarom, kunt u dit onderbouwen met een voorbeeld en wat vindt u hiervan)?