FDG-PET-CT for staging of high-risk breast cancer patients reduces the number of further examinations: A pilot study

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^{18}FDG-PET-CT in the follow-up of non-small cell lung cancer patients after radical radiotherapy with or without chemotherapy: An economic evaluation

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ABSTRACT

Background: The optimal follow-up strategy of non-small cell lung cancer (NSCLC) patients after curative intent therapy is still not established. In a recent prospective study with 100 patients, we showed that a FDG-PET-CT 3 months after radiotherapy (RT) could identify progression amenable for curative treatment in 2% (95% confidence interval (CI): 1–7%) of patients, who were all asymptomatic. Here, we report on the economic evaluation of this study.

Patients and methods: A decision-analytic Markov model was developed in which the long-term cost-effectiveness of 3 follow-up strategies was modelled with different imaging methods 3 months after therapy: a PET-CT scan; a chest CT scan; and conventional follow-up with a chest X-ray. A probabilistic sensitivity analysis was performed to account for uncertainty. Because the results of the prospective study indicated that the advantage seems to be confined to asymptomatic patients, we additionally examined a strategy where a PET-CT was applied only in the subgroup of asymptomatic patients. Cost-effectiveness of the different follow-up strategies was expressed in incremental cost-effectiveness ratios (ICERs), calculating the incremental costs per quality adjusted life year (QALY) gained.

Results: Both PET-CT- and CT-based follow-up were more costly but also more effective than conventional follow-up. CT-based follow-up was only slightly more effective than conventional follow-up, resulting in an incremental cost-effectiveness ratio (ICER) of

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€ 264.033 per QALY gained. For PET-CT-based follow-up, the ICER was € 69.086 per QALY gained compared to conventional follow-up. The strategy in which a PET-CT was only performed in the asymptomatic subgroup resulted in an ICER of € 42.265 per QALY gained as opposed to conventional follow-up. With this strategy, given a ceiling ratio of € 80.000, PET-CT-based follow-up had the highest probability of being cost-effective (73%).

Conclusions: This economic evaluation shows that a PET-CT scan 3 months after (chemo)radiotherapy with curative intent is a potentially cost-effective follow-up method, and is more cost-effective than CT alone. Applying a PET-CT scan only in asymptomatic patients is probably as effective and more cost-effective. It is worthwhile to perform additional research to reduce uncertainty regarding the decision concerning imaging in the follow-up of NSCLC.

1. Introduction

The most effective follow-up strategy for non-small cell lung cancer (NSCLC) patients treated with curative intent with radiotherapy (RT) with or without chemotherapy is still not established. This uncertainty is reflected in the large heterogeneity in recommendations from the different cancer societies, diverging from no imaging at all to repeated imaging with chest CT scans.[1] The added value of chest X-rays and/or chest CT has not been confirmed in any prospective study. A major reason for this lack of efficacy is the poor discriminating capacity of both imaging modalities. Here, ^{18}FDG-PET-CT could have additional benefit, which has shown to be more accurate than CT in the evaluation of response to treatment as well as in outcome prediction.[2–4] We recently reported the results of a prospective study in 100 patients treated with chemo-RT or RT alone with curative intent, which showed that indeed, an FDG-PET-CT 3 months after therapy can detect progression amenable for treatment with curative intent, and hereby, possibly lead to an increase in survival.[5] Progressive disease (PD) amenable for curative treatment, however, was only found in 2% (95% confidence interval (CI): 1–7%) of patients. The study showed that the advantage seemed to be confined to the patient group that did not have symptoms at the time that the PET-CT scan was performed. In this patient group, 5% (95% CI: 2–15%) had progression, potentially amenable for curative therapy, which were all detected with FDG-PET, not with CT alone. In contrast, none of the symptomatic patients were diagnosed with progression with curative treatment options.

While a PET-CT scan 3 months post-treatment thus seems to be potentially beneficial, at least in a subset of patients, it is also more costly. This raises the question regarding the cost-effectiveness of a PET-CT-based follow-up method compared to usual follow-up with either repeated chest X-rays or CT scans, or imaging on the basis of symptoms. In order to make an evidence-based decision regarding which follow-up strategy to prefer, the costs of each strategy are essential to take into account. Information regarding cost-effectiveness can be obtained through an economic evaluation, in which a comparative analysis is performed of alternative courses of action in terms of both their costs and consequences,[6] on the basis of the currently available evidence.

Table 1 – Alternative follow-up strategies.

Follow-up strategy	Imaging three months after RT	Imaging at follow-up visits after 3 months		
		No recurrence	PD, treated	PD, not treated
Usual	CXR + on basis of symptoms[a]	CXR	Chest CT	None
CT-based	Chest CT + on basis of symptoms[a]	CXR	Chest CT	None
PET-CT-based	PET-CT	CXR	Chest CT	None

Symptoms	Diagnostics
Pain	
Localised	Coventional radiography of involved region
Diffuse	Bone scintigraphy
Dyspnoea	CXR
Cough	CXR
Dysphagia	Chest CT
Malaise	CXR + screening blood sample
Neurological	CT brain
Palpable mass	CT of involved region
Fatigue	Screening blood sample

CXR: chest radiography; PD: progressive disease.
a Imaging on the basis of symptoms.

To be able to add this information to the decision-making process, we performed the current economic evaluation to evaluate the cost-effectiveness of PET-CT-based follow-up as opposed to conventional follow-up in NSCLC patients treated with curative (chemo)RT.

2. Patients and methods

Three follow-up strategies were compared with different imaging methods 3 months after therapy: the 'usual' or conventional follow-up (anamnesis, physical examination and a chest X-ray), the PET-CT-based follow-up (anamnesis, physical examination and a PET-CT scan) and the CT-based follow-up (anamnesis, physical examination and a chest CT scan). After the 3 months post-treatment time point, the follow-up was the same for the different strategies. Details regarding these follow-up policies are provided in Table 1. Because the results of the prospective study implied that the advantage of the PET-CT seems to be confined to the patient group without symptoms at the time of the PET-CT scan (55% of patients),[5] we additionally examined a strategy where a PET-CT was applied only in the asymptomatic subgroup. Within this strategy, symptomatic patients did not receive a standard PET-CT scan, but underwent imaging on the basis of the location of symptoms (conform Table 1).

2.1. Model structure

A Markov transition model was constructed with mutually exclusive health states to compare long-term costs and effects of the different follow-up strategies (Fig. 1).[7]

The model simulated the course of events in a hypothetical cohort of NSCLC patients treated with curative RT with or without chemotherapy. Health states in the model were based on the absence or presence of progression and on the treatment of progression. Patients without progression were in the health state 'no evidence of disease'. Patients with progression were subdivided according to their treatment: progression without treatment, progression with palliative treatment or progression with curative treatment. Patients in the CT-based or usual follow-up strategy, who had progression 3 months after treatment that was only detected with PET-CT and not with CT alone, were assigned the health state 'progression not detected'. The final health state was 'death'.

The start of the model was set after the first follow-up visit 3 months after radical therapy. At this time point, patients were divided between the different health states on the basis of the results of our prospective study.[5] In the model, patients moved between health states according to a set of transition probabilities. The cycle length of the model was 6 months, with a time horizon of 5 years.

2.2. Data sources

Input parameters were derived from the prospective study performed at our institute, published literature, the Dutch Health Insurance Board, and, if no other source was available, expert opinion. Details of the prospective study are published elsewhere.[5] In short, 100 patients with NSCLC, treated with curative intent with (chemo)radiation, were prospectively evaluated. All patients underwent a planned FDG-PET-CT scan 3 months after the start of radiotherapy, regardless of the presence of symptoms. Patients were judged symptomatic when any symptom was either new or had increased over time from the end of RT. Twenty-four percent (95% CI: 17–33%) of patients had progression 3 months post-treatment. No curative treatment could be offered to any of the patients who were symptomatic at the time of progression. In 2 of the 55 asymptomatic patients (4%, 95% CI: 1–12%), tumour progression, amenable for curative therapy, was found, which was detected with PET, not with CT only. The first patient was treated with re-irradiation for a locoregional recurrence, the 2nd patient was treated with adrenal resection for bilateral adrenal metastases.

2.3. Probabilities

All probabilities are listed in Table 2. As the cycle length was 6 months, probabilities of moving from one health state to another were calculated as 6 monthly transition probabilities.

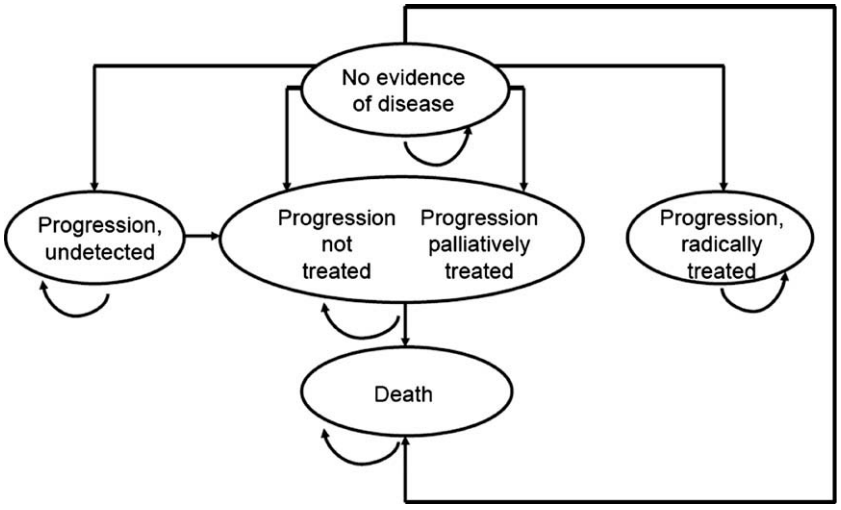

Fig. 1 – Markov model. A hypothetical cohort of patients enters the model after the follow-up visit 3 months after radical (chemo-)RT. Patients are divided over the different health states according to the results of the prospective study.

Table 2 – Inputs.

	Estimated value	SE	Distribution	Source
Transition probabilities				
First 3 months				
Strategy-independent probabilities				
PD	0.24	0.04	Beta	[5]
Symptoms with PD	0.68	0.09	Beta	[5]
Symptoms without PD	0.38	0.06	Beta	[5]
Strategy-dependent probabilities				
PET-CT				
Detection of symptomatic PD	1	Fixed		EO
Detection of asymptomatic PD	1	Fixed		EO
Treatment of asymptomatic PD	0.63	0.16	Beta	[5]
Treatment of symptomatic PD	0.81	0.095	Beta	[5]
Radical treatment of asymptomatic PD	0.4	0.2	Beta	[5]
Radical treatment of symptomatic PD	0	Fixed		[5]
CT				
Detection of symptomatic PD	1	Fixed		
Detection of asymptomatic PD	0.5	0.17	Beta	[5]
Treatment of asymptomatic PD	0.63	0.16	Beta	[5]
Treatment of symptomatic PD	0.81	0.095	Beta	[5]
Radical treatment of asymptomatic PD	0	Fixed		[5]
Radical treatment of symptomatic PD	0	Fixed		[5]
Usual				
Detection of symptomatic PD	1	Fixed		EO
Detection of asymptomatic PD	0	Fixed		EO
Treatment of asymptomatic PD	0	Fixed		[5]
Treatment of symptomatic PD	0.81	0.095	Beta	[5]
Radical treatment of asymptomatic PD	0	Fixed		[5]
Radical treatment of symptomatic PD	0	Fixed		[5]
After 3 months				
Progression				
Detection of undetected PD	0.8	Fixed		EO
PD, 1st year	0.21	0.036	Beta	[3]
PD, 2nd year	0.16	0.036	Beta	[3]
PD, 3rd year	0.23	0.036	Beta	[3]
PD, 4th year	0.12	0.036	beta	[3]
Treatment				
Radical	0.01	0.02	Dirichlet	EO
Palliative	0.56	0.02	Dirichlet	[14]
No treatment	0.43	0.02	Dirichlet	[14]
Death				
Death with PD, no treatment	0.56	0.025	Beta	[10]
Death with PD, palliative treatment	0.46	0.025	Beta	[11]
Death with PD, radical treatment				
1st year	0.33	0.019	Beta	[13,32]
2nd year	0.18	0.019	Beta	
3rd year	0.02	0.019	Beta	
Death with undetected PD	0.54	0.025	Beta	EO[a]
Utility scores				
No PD	0.68	0.1	Beta	[18]
PD, not treated	0.53	0.1	Beta	[18]
PD, palliatively treated	0.53	0.1	Beta	EO
PD, radically treated	0.68	0.1	Beta	EO
PD, undetected	0.53	0.1	Beta	[18]
Costs				
Diagnostics				
First 3 months				
PET-CT whole body	1364	Fixed		[33]

(*continued on next page*)

Table 2 (continued)

	Estimated value	SE	Distribution	Source
Chest CT	206	Fixed		[33]
CXR	39	Fixed		[33]
Follow-up visit	59	Fixed		[33]
After 3 months[b]				
Follow-up, No PD[c]				[33]
1st year	196	Fixed		[33]
2nd year	98			
3rd+ year	49			
Follow-up, PD				
Treated[d]	529	Fixed		[33]
Untreated[e]	118	Fixed		[33]
Treatment				
Probability of 2nd line chemotherapy	0.47			[14]
Probability of palliative RT	0.18	0.018	Beta	[34]
Unit costs				
Radical[f]	5746	Fixed		[5,33]
Palliative chemotherapy				
1st line[g]				
No. of cycles	4			[11]
Costs/cycle	1302			[33]
Side effects	349			[16]
Total costs	5557	Fixed		
2nd line[h]				
Mean treatment time (days)	125			[33]
Costs/treatment	9100			[33]
Side effects	120			[16]
Total costs	9220	Fixed		
Palliative RT	1017	Fixed		[33]
Dying				
Dying of cancer, terminal care[i]	11,602	800	Gamma	[17]
Dying of other causes	15,448	800	Gamma	[17]

EO: expert opinion; CXR: chest X-ray; RT: radiotherapy; DHIB: Dutch Health Insurance Board.
a Calculated from the probability of dying with a recurrence without treatment and with palliative treatment.
b Costs per 6 monthly cycle.
c Based on follow-up visit with CXR, 4 times in 1st year, 2 times in 2nd year and once a year thereafter.
d Based on follow-up visit with chest-CT, 4 times/year.
e Based on follow-up visit without imaging, 4 times/year.
f Based on type of radical treatment in prospective study, being adrenal resection and radical radiotherapy.
g Docetaxel, 3-weekly cycles.
h Erlotinib.
i The costs of dying from cancer described in Kommer et al. were discounted by the costs of palliative treatment calculated in the current study.

The median age of patients assumed to enter the model was 62 years, based on the patient characteristics of the prospective study.[5] The extra mortality risk for surviving lung cancer patients as opposed to the general population was 1.4.[8,9] Age-specific mortality rates were used for 5-year age groups (Central Bureau for Statistics, 2007). The probability of progression after 3 months was calculated on the basis of a prospective study of Mac Manus and colleagues (1-, 2-, 3- and 4-year progression free survival rates of 62%, 44%, 26% and 20%, respectively).[3] Patients with progression that was not treated were assumed to have a 1-year overall survival (OS) of 19%[10]; patients who were palliatively treated for progression were assumed to have a 1-year OS of 30%.[11] The 1-year OS for patients who were treated with curative intent was assumed to be 45%, based on published results with re-irradiation and adrenal resection.[12,13] Percentages of patients receiving 2nd and 3rd line chemotherapy were based on a retrospective chart review of 417 patients with advanced NSCLC.[14]

2.4. Costs

An overview of the costs associated with the follow-up procedures, treatment and terminal care is outlined in Table 2. All costs are reported in Euros and converted to the year 2008. Future costs and effects were discounted to their present value by a rate of 4% and 1.5%, respectively.[15] Costs of diagnostic procedures and treatment were derived from the Dutch Health Insurance Board, adjusted to the 2007 price level (Central Bureau for Statistics 2007). The costs for first line chemotherapy were based on 4 cycles of docetaxel 75 mg/m^2. Costs

Table 3 – Cost-effectiveness of different follow-up strategies.

Follow-up strategy	Expected costs/patient (95% CI[a])	Expected survival (months) (95% CI)	Expected QALYs (95% CI)	ICER[b]
(A) Whole group				
Conventional	€ 13.983 (€ 12.783–15.156)	24 (22–27)	1.28 (0.98–1.58)	
CT-based follow-up	€ 14.269 (€ 13.076–15.441)	24 (22–27)	1.28 (0.99–1.59)	€ 264.033
PET-CT-based follow-up	€ 15.266 (€ 14.072–16.440)	25 (22–28)	1.30 (1.00–1.61)	€ 69.086
(B) Asymptomatic patients only				
Conventional	€ 13.983 (€ 12.805–15.162)	24 (22–27)	1.28 (0.98–1.58)	
CT-based follow-up	€ 14.269 (€ 13.101–15.444)	24 (22–27)	1.28 (0.99–1.59)	€ 264.033
PET-CT-based follow-up	€ 14.768 (€ 13.584–15.952)	25 (22–28)	1.30 (1.00–1.61)	€ 42.265

QALY: quality adjusted life year.
ICER: incremental cost-effectiveness ratio.
a 95% Confidence intervals (CI) based on probabilistic analysis.
b Expressed in €/QALY gained compared to conventional follow-up.

of second line chemotherapy were based on treatment with erlotinib during 125 days. Costs associated with side effects were based on calculations from the National Institute for Clinical Excellence.[16] The costs associated with dying were based on a report of Kommer and Polder[17] in which costs associated with cancer death are described separately from costs associated with dying from other causes.

2.5. *Effects*

Global health-related quality of life (QOL) data were expressed in utility scores, varying from zero (death) to one (perfect health). The use of utility scores allows the calculation of Quality Adjusted Life Years (QALYs) and cost per QALY ratios. Utility scores were derived from a cross-sectional study performed by Trippoli and colleagues.[18] Based on this study, patients with progression had a utility score of 0.53, while patients without progression had a utility score of 0.68. Patients with progression that was curatively treated were assumed to have the same utility score as patients without progression, based on expert opinion (DDR). Furthermore, patients who were treated with palliative intent for PD were assumed to have the same utility as patients who received no treatment, on the basis of literature showing no significant difference in QOL with the administration of docetaxel 75 mg/m^2 as second line chemotherapy.[19] All utility scores are listed in Table 2.

2.6. *Cost-effectiveness analysis*

The analysis was performed from a health care perspective. The cost-effectiveness of the different follow-up strategies was compared using incremental cost-effectiveness ratios (ICERs), calculating the incremental costs per QALY gained. Whether a follow-up strategy is deemed cost-effective depends on how much the society is willing to pay for a gain in effect, which is referred to as the ceiling ratio. The Dutch Health Council advises an informal ceiling ratio of € 80.000.[20]

The input parameters of the model are inevitably associated with uncertainty. Probabilistic modelling is used to reflect this uncertainty in the parameters and to describe the effects on uncertainty over the outputs of interest.[21] Distributions to the model parameters, based on their mean value and standard error, were assigned to reflect the uncertainty in the estimation of that parameter (Table 2).[22] A probabilistic sensitivity analysis was performed using Monte Carlo simulation with 5000 random iterations from the assigned distributions. To illustrate the results of the simulation, cost-effectiveness acceptability curves (CEACs) were calculated to characterise the likelihood that a certain follow-up strategy would be deemed cost-effective at different ceiling ratios,[21,23] representing the uncertainty surrounding the cost-effectiveness for this range of thresholds.

2.7. *Expected value of perfect information*

As uncertainty exists, there is always a chance that the 'wrong' decision will be made.[21,24] In this case, society would suffer a loss as a consequence. The decision to reduce the chance of a wrong decision by performing additional research involves balancing between the costs of acquiring more information with the value associated with it. The EVPI (expected value of perfect information) is the expected value of obtaining perfect knowledge of the 'true' values of all parameters. We calculated the total EVPI by subtracting the net monetary benefit of the follow-up strategy we would choose under conditions of uncertainty, from the net monetary benefit of the optimal decision we would make if we knew the 'true' parameter values. The population EVPI was then calculated by multiplying the EVPI per patient by the number of patients who could potentially benefit from additional research. In the present study, this is the total number of patients with inoperable NSCLC treated with curative intent with (chemo)RT. We estimated that of the 1.35 million lung cancer patients per year, of whom 80% have NSCLC, 30% are amenable for curative (chemo)RT, being a total of 1.5 million patients worldwide in the next 5 years.

3. Results

3.1. *Cost-effectiveness of different follow-up strategies*

Results of the analysis regarding the cost-effectiveness of the different follow-up strategies are presented in Table 3A. With

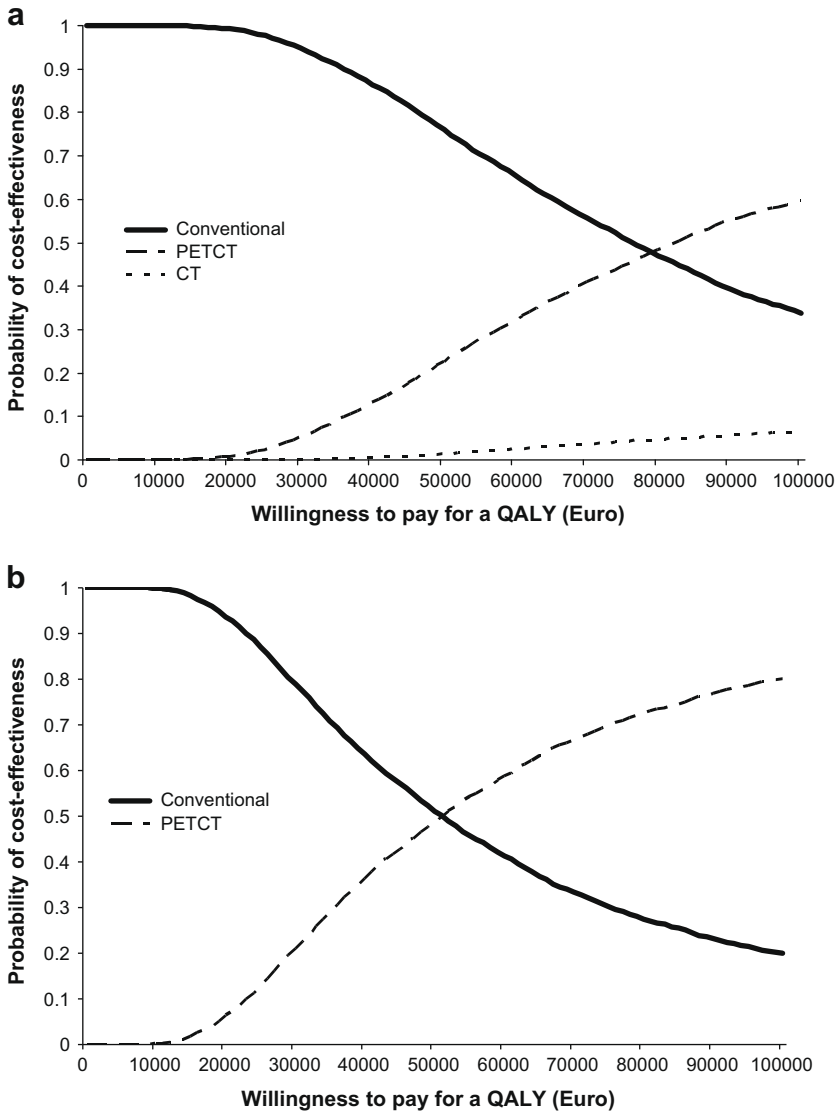

Fig. 2 – Cost-effectiveness acceptability curves (CEACs). The probability of cost-effectiveness of a certain follow-up strategy is plotted against the willingness to pay per quality adjusted life year (QALY) gained. (a) CEAC for the strategy in which a PET-CT is performed in all patients. (b) CEAC for the strategy in which a PET-CT is performed in asymptomatic patients only.

regard to PET-CT-based follow-up, the additional costs per extra curatively treated patient were € 64.096 compared to conventional follow-up. The ICER (incremental cost-effectiveness ratio) for PET-CT-based follow-up was € 69.086 per QALY gained compared to conventional follow-up. Although CT-based follow-up was less costly, it was also less effective than PET-CT-based follow-up, resulting in an ICER of € 264.033 per QALY gained.

Fig. 2a shows cost-effectiveness acceptability curves for the 3 follow-up strategies. The figure shows that there is considerable uncertainty regarding which follow-up strategy is deemed cost-effective around the informal threshold of the Dutch Health Council. Given this ceiling ratio of € 80.000,[20] PET-CT-based follow-up and conventional follow-up had a similar probability of being cost-effective (48% and 47%, respectively), while the probability of CT-based follow-up being cost-effective was only 5% (Fig. 2a).

3.2. *Cost-effectiveness of a follow-up strategy with a PET-CT in the asymptomatic subgroup*

The same analysis was performed, but a PET-CT scan was now only performed in patients who were asymptomatic 3 months after treatment (55% of patients) (Table 3B). Symptomatic patients received imaging on the basis of the location of symptoms. The usual follow-up strategy and CT-based follow-up strategy remained the same. Performing PET-CT-based follow-up only in the asymptomatic subgroup had no influence on the effects, but reduced the costs per patient from € 15.265 to € 14.767. Hence, this strategy resulted in a lower ICER of € 42.265 per QALY gained as opposed to conventional follow-up. With this strategy, PET-CT-based follow-up had the highest probability of being cost-effective (73%) compared to conventional follow-up (27%) at a ceiling ratio of € 80.000 Fig. 2b).

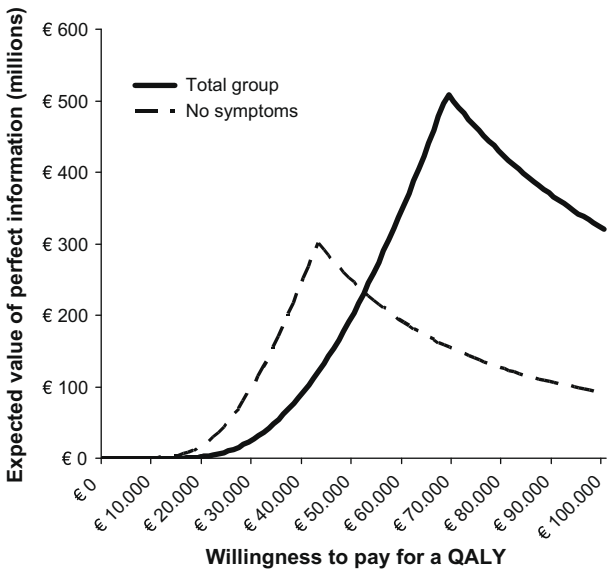

Fig. 3 – Expected value of perfect information (EVPI). The expected value of perfect information at different ceiling ratios. Total group: EVPI for the strategy in which a PET-CT is performed in all patients. No symptoms: EVPI for the strategy in which a PET-CT is performed in asymptomatic patients only.

3.3. *Expected value of perfect information*

In the current analysis, the uncertainty surrounding the decision whether or not to implement PET-CT-based follow-up resulted in an EVPI of € 282 per person, given a ceiling ratio of € 80.000. Implementing PET-CT-based follow-up affects all patients with locally advanced NSCLC, treated with curative (chemo)RT, involving a total of 1.5 million patients worldwide in the next 5 years. This makes the population EVPI $(1.5 * 10^6) * 290 =$ € 423 million, meaning that perfect information on this topic is worth € 423 million.

The EVPI for the implementation of PET-CT-based follow-up only in the subgroup of asymptomatic patients was € 83 per person, given a ceiling ratio of € 80.000. The population EVPI for this strategy was € 125 million. The population EVPI for different ceiling ratios, both for the total group and for the asymptomatic subgroup, is presented in Fig. 3.

4. Discussion

Until now, no imaging procedure has become standard in the follow-up of NSCLC, mainly because of the fact that progression or recurrence is mostly detected at a stage that no curative treatment is possible, and hence, no survival benefit can be expected.[25] Our recent prospective study on a single ^{18}FDG-PET scan 3 months post-therapy confirmed the hypothesis that this imaging modality, in contrast to CT alone, is able to detect progression amenable for curative treatment in a small percentage of patients. The question remained, however, whether this potential benefit for the individual patient outweighs the increased costs.[26]

The current economic evaluation shows that performing a PET-CT scan 3 months after curative (chemo-)RT is a potentially cost-effective follow-up method, and is more cost-effective than CT alone. Performing a PET-CT scan only in the subgroup of asymptomatic patients is probably as effective and more cost-effective.

Inherently to the design of the study, there are some limitations that need to be addressed. Firstly, the current results are surrounded by considerable uncertainty, caused by uncertainty in the input parameters of the model. One important cause is the relatively small patient population (N = 100) in the prospective study, from which the extent of the potential benefit of PET-CT was derived.[5] This economic evaluation aimed however, to base the decision regarding which follow-up strategy is to be preferred on the currently available evidence. Decisions will have to be made anyway, so it is better to support the decision with the available evidence including its uncertainties than doing something without any evidence at all.[27] Using decision-analytic modelling we were able to incorporate this uncertainty in the model by assigning distributions to the model parameters. The incorporation of uncertainty also makes results easier to interpret by decision makers, as one can calculate which strategy has the highest probability of being cost-effective at different ceiling ratios (Fig. 2). The EVPI analysis shows us to what extent reduction of uncertainty by performing additional research is worthwhile. The value of totally eliminating uncertainty of the input parameters of the model was € 435 million, for a ceiling ratio of € 80.000, implying that additional research on this subject is of great value and outweighs the associated costs.

Secondly, the threshold (also referred to as the ceiling ratio) below which a certain strategy is considered cost-effective is arbitrary and differs between countries. In the current analysis, a threshold of € 80.000 (informal ceiling ratio of the Dutch Health Council) was used. Thresholds reported in literature range from € 35.000 ($ 50.000) to € 210.000 ($ 300.000).[26,28,29] With a higher ceiling ratio, the probability that the PET-CT-based follow-up strategy is cost-effective becomes higher, while the usual follow-up strategy has the highest probability of being cost-effective at lower ceiling ratios. Hence, whether a strategy is deemed cost-effective depends on how much the society is willing and able to pay for a gain in effect.

Thirdly, the use of a model to estimate costs and effects is always associated with a simplification of reality.[27] In the current analysis, we have chosen to compare the PET-CT-based follow-up method with two follow-up strategies most commonly used according to the guidelines of the different institutions.[1] Furthermore, in the model, the difference between the three strategies was based upon different imaging only at one time point during follow-up, i.e. 3 months after curative treatment. This time point was chosen based on the prospective study which showed a possible advantage of PET over CT in detecting potentially curable progression at 3 months after treatment and because a PET scan performed at this interval has shown to be prognostic of outcome.[2,4] In none of the patients in the prospective study, additional investigations were requested to confirm the findings of the PET-CT scan. Hence, in the current economic evaluation, no costs were calculated to take into account false positive findings in the PET-CT strategy. No costs were calculated for false positive findings in the usual and CT-based follow-up strategy

either, minimising the chance of overestimating the cost-effectiveness of PET-CT. Another drawback of the limitation to one time point is that the potential gain of repeated imaging with e.g. chest CT scans cannot be derived from this study. The available literature however, does not confirm a benefit of repeated CT-scanning in the follow-up.[30] A definitive answer regarding the value of CT-based follow-up can be expected from a multicentre phase III trial which is currently ongoing in France, in which conventional follow-up with chest X-rays is compared with an intensive follow-up strategy with repeated chest CT scans in NSCLC patients after curative resection.[31]

The performed economic evaluation is aimed to guide decision making regarding which strategy to choose, and is not intended to reveal scientific truth.[22] On the basis of the currently available evidence, however, the following conclusions can be drawn: Firstly, performing a chest CT scan in the follow-up is less cost-effective than performing a PET-CT scan 3 months after treatment. Hence, if any imaging is wished to be performed for treatment evaluation, one would prefer to perform a PET-CT scan 3 months after therapy above CT alone. Secondly, irrespective of the question whether certain imaging is cost-effective, the final decision to perform the test depends on what the society can afford.[26] Finally, the results show that it is worthwhile to perform additional research to reduce the uncertainty surrounding the decision whether to implement PET-CT in the follow-up, including questions regarding the time point and frequency and what the additional financial burden is.

Conflict of interest statement

None declared.

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