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ORIGINAL ARTICLE

The cost effectiveness of ^{123}I-FP-CIT SPECT imaging in patients with an uncertain clinical diagnosis of parkinsonism

Koen Van Laere · Ludwig Everaert · Lieven Annemans · Michel Gonce · Wim Vandenberghe · Thierry Vander Borght

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Abstract
Purpose ^{123}I-*N*-ω-fluoropropyl-2-β-carboxymethoxy-3β-(4-iodophenyl)nortropane (^{123}I-FP-CIT) Single-photon emission computed tomography (SPECT) has been suggested to be a useful diagnostic adjunct in patients with clinically uncertain parkinsonism. We developed a pharmaco-economic (PE) model, evaluating the cost effectiveness of adding ^{123}I-FP-CIT SPECT to the diagnostic workup. As the model was developed before application of the diagnostic technique in real practice, a predictive validity assessment was performed based on data from a large nationwide patient registry in these patients.
Methods A PE model, using a Markov state transition model, was created, based on literature-derived and clinical expert panel data. Effects were expressed as adequately treated years (ATY). Key input data were compared to the real-life patterns in a nationwide multi-centre clinical setting, based on a complete national registry of 1,701 consecutive patients. The change in initial diagnosis and alteration of management of the patient after SPECT were registered.
Results In the PE model, it was calculated that management would change in 48.5% of patients by SPECT and that, over a 5-year period, 1.2 ATYs could be gained at a yearly additional cost of €72. From the studied 1,701 patients, nigrostriatal degeneration was observed in 59.8%, the initial diagnosis was changed in 51.5%, management was altered in 49%, and cost effectiveness was increased to €358 per ATY.
Conclusion Good correspondence between assumed and observed changes in patient management was found, indicating that ^{123}I-FP-CIT SPECT is influential in diagnosis and management of patients with uncertain clinical diagnosis of parkinsonism. This can be achieved at a marginal added cost to the health insurance and leads to a significant gain in ATY.

Keywords ^{123}I-FP-CIT · Dopamine transporter · Clinical impact · Pharmaco-economic modelling

K. Van Laere (✉)
Division of Nuclear Medicine,
University Hospital Leuven Gasthuisberg,
E901, Herestraat 49,
3000 Leuven, Belgium
e-mail: koen.vanlaere@uzleuven.be

L. Everaert
Medical and Pharmaceutical Information,
Zemst, Belgium

L. Annemans
Department of Public Health, Ghent University,
Ghent, Belgium

M. Gonce
Department of Neurology, CHU Citadelle,
Liège, Belgium

W. Vandenberghe
Department of Neurology, University Hospital Leuven,
Leuven, Belgium

T. Vander Borght
Division of Nuclear Medicine, Mont-Godinne Medical Center,
Université Catholique de Louvain,
Yvoir, Belgium

Introduction

The clinical impact of single-photon emission computed tomography (SPECT) imaging of the dopamine transporter (DAT) in early diagnosis of neurodegenerative parkinsonism (NDP) has been documented in several studies. Most of them were conducted in a single-centre specialist setting and have dealt with the differentiation between essential tremor (ET) and NDP. Booij et al. [1] in 33 consecutive patients and Lokkegaard et al. [2] in 90 consecutive patients initially pointed out the high positive predictive value and objectivity of DAT SPECT using ^{123}I-FP-CIT (^{123}I-*N*-ω-fluoropropyl-2-β-carboxymethoxy-3β-(4-iodophenyl)nortropane or ioflupane) or ^{123}I-β-CIT (2-β-carbomethoxy-3β-(4-iodophenyl)tropane) to confirm or exclude NDP in inconclusive cases. This clinical value in differentiating NDP from other causes was also assessed in larger monocentric studies by Eerola et al. using ^{123}I-β-CIT in 185 patients [3] and by Hesse et al. for predicting treatment response in combination with D2 receptor SPECT imaging in 312 patients [4]. The diagnostic sensitivity and specificity for qualitative analysis of ^{123}I-FP-CIT SPECT to accurately differentiate NDP and essential tremor is estimated at 95% and 93%, respectively [5]. As for change in management, an industry-sponsored multi-centre trial in 118 patients demonstrated that DAT SPECT imaging increased confidence in diagnosis and led to changes in clinical management in 72% of patients [6]. In contrast, a more moderate impact on clinical management in 28% of patients was suggested by Lokkegaard et al. [2]. Despite these data, DAT SPECT imaging has not yet found general acceptance in neurological practice as a valid diagnostic tool to rule in or out NDP [7].

The question of acceptance in neurological practice is related to availability, added diagnostic performance and also cost effectiveness (CE). Although it is clear that possible economic advantages can be gained by avoiding unnecessary drug treatments in both neurodegenerative and other forms, so far, only a few authors have addressed the CE issue of imaging in movement disorders. Dodel et al. [8] found that although SPECT increased cost, it improved adequate early treatment when used after doubtful positive clinical examination. The above-cited single-centre and university-based studies may be confounded by some bias inherent to the referral pattern to a specialist movement disorder setting with well-equipped and experienced brain imaging centres [9], so that they may not be extendable to the common practice. Therefore, a real-life assessment of DAT SPECT imaging in a general clinical setting is warranted to support the analysis of its CE, based on the observed prevalence of true parkinsonism in the population with uncertain clinical diagnosis and the resulting management change.

The aim of the current study was twofold. Firstly, we present a pharmaco-economic model for evaluating the CE of using DAT SPECT in the differentiation of ET versus NDP, based on literature and expert panel data and applying assumptions related to the true prevalence of NDP among patients with uncertain clinical diagnosis and the medical management change resulting from the test outcome. Secondly, we have analysed actual real-life diagnostic and treatment patterns in these patients, based on a large (n=1,701) multicentre (n=57) patient registry. This was possible by analysing data that were collected on request of the Belgian National Institute for Health Insurance in support of their revision of the ^{123}I-FP-CIT (DaTSCAN, GE Healthcare, Brussels) reimbursement modalities. From these data, the pharmaco-economic model was re-evaluated based on the observed prevalence of NDP and its predictive validity and robustness with regards to management outcome were tested.

Materials and methods

Pharmaco-economic model

Research design and assumptions

We developed a pharmaco-economic model specifically for the Belgian situation and on the basis of which the National Institute for Health Insurance granted reimbursement to ^{123}I-FP-CIT in 2003. The cost perspective studied was that of the Belgian health care payers. The target population was patients with difficult clinical differential diagnosis between NDP and essential tremor. "Difficult" is interpreted as unable to make using the commonly available diagnositic procedures without ^{123}I-FP-CIT imaging. Effectiveness was expressed as time on appropriate therapy or 'adequately treated years' (ATY). In the CE analysis, only direct medical costs were assumed (ambulatory and in-hospital), via resource use times unit cost. The comparator was 'not performing the scan' and hence relying solely on clinical diagnosis.

A Markov or state transition model was used [10, 11]. While most decision trees include a simple notion of time (i.e. events on the left side of the tree occur after those on the right), there are no shortcuts in a standard tree structure for representing events that recur over time. A state transition model is designed to do this and are used to simulate both short-term processes (e.g. development of a disease) and long-term processes (e.g. an individual's lifespan). In the used Markov model, ten cycles of 6 months were applied. Input was derived from literature data for diagnostic and epidemiological variables and from a Delphi panel consisting of 13 Belgian neurologists and nuclear medicine specialists. The Delphi panel was a postal two-round design, firstly tested in a number of international and

national experts. The time horizon of the analysis used was 5 years. In the modelling study, it was assumed, based on expert opinion, that during the first 2 years, treatment (wrong or correct) was maintained, unless adverse events have occurred leading to treatment cessation or the patient died. Only as from 2 years after treatment start, treatment options were considered revisable, every 6 months.

We did not further split NDP into sub-entities, since ^{123}I-FP-CIT SPECT has no established role on its own in distinguishing Parkinson's disease from other neurodegenerative forms of parkinsonism (multiple system atrophy, progressive supranuclear palsy etc.) [12]. In addition, although non-NDP can include several conditions, we limited the model to ET as the main reference condition [5].

Analytical model

Figure 1 shows a simplified representation of the analytical model that was used for the CE calculation, based on the sequence of tests, outcome, treatment selection and result plus consequences. Eight Markov states were considered. Seven states were based on the combination of the true state of a patient and the applied therapy: NDP with first-line NDP therapy (e.g. levodopa, dopamine agonists), ET with first-line NDP therapy (i.e. inappropriate therapy), NDP with second-line NDP therapy (e.g. selegiline, anti-cholinergics, amantadine), ET with second-line NDP therapy (inappropriate therapy), ET with ET therapy (e.g. beta-blockade), NDP with ET therapy (inappropriate therapy), no therapy (inappropriate) or death.

Model data inputs

The incidence of NDP in Belgium was estimated at about 2,100–2,500 cases per year on a total population of 10.5 million [13], and the prevalence was taken as 0.18%. Using estimates of proportion of early cases that are clinically uncertain at 26% [8], the proportion of new patients eligible for scanning at 90%, the proportion of ET and NDP patients managed by movement disorder specialists at 90% and the proportion of specialists with access to ^{123}I-FP-CIT SPECT at 85% (the latter three values as estimated by the Delphi panel), this resulted in estimates of 320 new patients per year and a pool of 3,380 existing patients (calculated from prevalence × population × proportion early cases × early case proportion × proportion managed by movement disorder specialists) with uncertain parkinsonism at the beginning of the inclusion period. Since the existing pool also likely includes patients with more advanced stages of the disease, the proportion of 26% clinically uncertain cases may be an overestimation, and the size of this calculated pool needs to be interpreted as an upper-limit estimation.

The clinical data needed for input in the model, which were available from literature data or the Delphi panel, are summarized in Table 1. Additionally, the panel estimated the incidence of dyskinesia, psychosis or orthostatic hypotension with treatment for parkinsonism to 10% per year.

The input cost data for both diagnosis and treatment regimens and adverse effects as used in the CE calculation were derived from the Delphi panel and are given in Table 2. Note that current diagnosis also costs money because of a mixture of current techniques (levodopa challenge, CT, MRI, electromyography etc.). Furthermore, 'no treatment' costs are incorporated, related to the follow-up visits of the patient. From the input data and the PE model, the projected therapeutic impact of ^{123}I-FP-CIT SPECT is given in Table 3. This table shows that a change in therapy would be predicted in 48.5% of the cases, mainly due to the change of patients with ET who receive appropriate ET therapy.

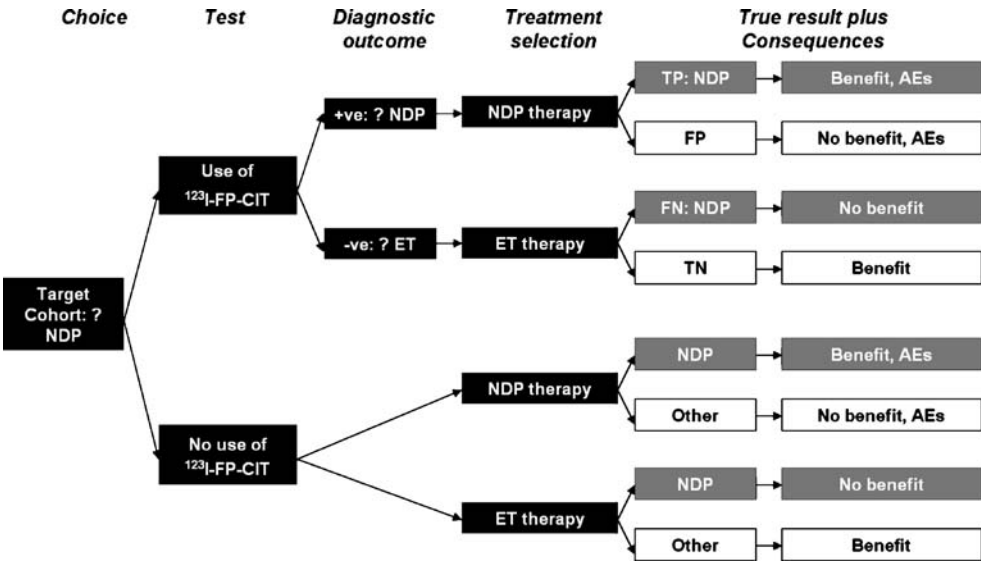


Fig. 1 Decision tree model for the pharmaco-economic modelling study. *NDP* Neurodegenerative parkinsonism, *ET* essential tremor, *TP* true positive, *TN* true negative, *FP* false positive, *FN* false negative

Table 1 Diagnostic and treatment characteristics

	Value (%)	Source
Diagnostic characteristics		
Probability true Parkinson's disease among presumed NDP (autopsy)	76	[19, 20]
Probability of physician's diagnosis of parkinsonism at start	74	[9]
If later it appeared to be NO NDP, the probability clinician was confident at diagnosis	49	[21]
Among clinically uncertain, % no NDP	47.1	Bayes theorem
Among clinically uncertain, % NDP	52.9	Bayes theorem
Clinical diagnostic sensitivity after 5 years follow-up	96.0	[9]
Clinical diagnostic specificity after 5 years follow-up	82.0	[9]
Treatment decisions		
Among clinically uncertain receive PD treatment	70.8	Delphi expert panel
Among clinically uncertain receive no treatment at all	21.3	Delphi expert panel
Among clinically uncertain receive treatment for ET	7.9	Delphi expert panel
Follow-up patterns		
Non-response after 6 months	18.7	Delphi expert panel
Leading to follow-up diagnostic tests 6 months	18.7	Delphi expert panel
Non-response after 2-5 years	16.7	Delphi expert panel
Leading to follow-up diagnostic tests after 2-5 years	16.7	Delphi expert panel
Stop treatment NDP due to adverse events at 6 months	3.0	[22]
Stop treatment ET due to adverse events at 6 months	3.0	Delphi expert panel
6-month mortality in parkinsonism	5.1	[23]

Patient registry data

A simple registry data sheet was used as proposed by an Advisory Board consisting of eight university and non-university nuclear medicine physicians with specific background in neuroimaging and neurologists specialized in movement disorders to gather imaging and patient data. The data registry form included the following fields: date of the examination, indication for the DAT SPECT scan and result of the SPECT examination.

The indication for the DAT SPECT scan was to remove the uncertainty related to the diagnosis by differentiating NDP from ET. Additional possible differential diagnoses were allowed (neuroleptic parkinsonism, psychogenic parkinsonism or others), although this supplementary information was not used in the current analysis.

The result of the SPECT examinations were 'loss of dopaminergic activity,' 'no loss' or 'non-conclusive.' No intermediate possibilities were allowed, nor was possible regional abnormality further specified. A case was deemed 'non-conclusive' when no final conclusion could be reached after performance of the DAT SPECT: If the

Table 2 Costs of diagnosis, treatment and adverse events (in €)

	Value (€)	Source
Costs of diagnosis and treatment		
Current diagnosis	216	Delphi expert panel
^{123}I-FP-CIT SPECT	900	GE Healthcare
1 year PD drug treatment first line	1,625	Delphi expert panel
1 year PD drug treatment second line	1,819	Delphi expert panel
1 year PD specialist visits	170	Delphi expert panel
Follow-up diagnosis 6 months	86	Delphi expert panel
follow-up diagnosis over 2–5 years	162	Delphi expert panel
No treatment 6 months	131	Delphi expert panel
ET drug treatment 6 months	230	Delphi expert panel
Costs of treating adverse events		
Dyskinesia	1,584	Delphi expert panel
Psychosis	2,172	Delphi expert panel
Orthostatic hypotension	1,115	Delphi expert panel

Table 3 Projected therapeutic impact of ^{123}I-FP-CIT SPECT from the Markov state model

	Without ^{123}I-FP-CIT SPECT (%)	With ^{123}I-FP-CIT SPECT (%)	No change in therapy (%)
NDP+appropriate APT	42.5	57.0	42.5
ET receiving APT	28.3	2.8	2.8
ET receiving ET treatment	3.2	37.2	3.2
NDP not receiving appropriate APT	4.7	3.0	3.0
Total			51.5[a]

APT Anti-parkinson therapy

[a] The introduction of ^{123}I-FP-CIT SPECT changes therefore the therapy in 48.5% of the patients.

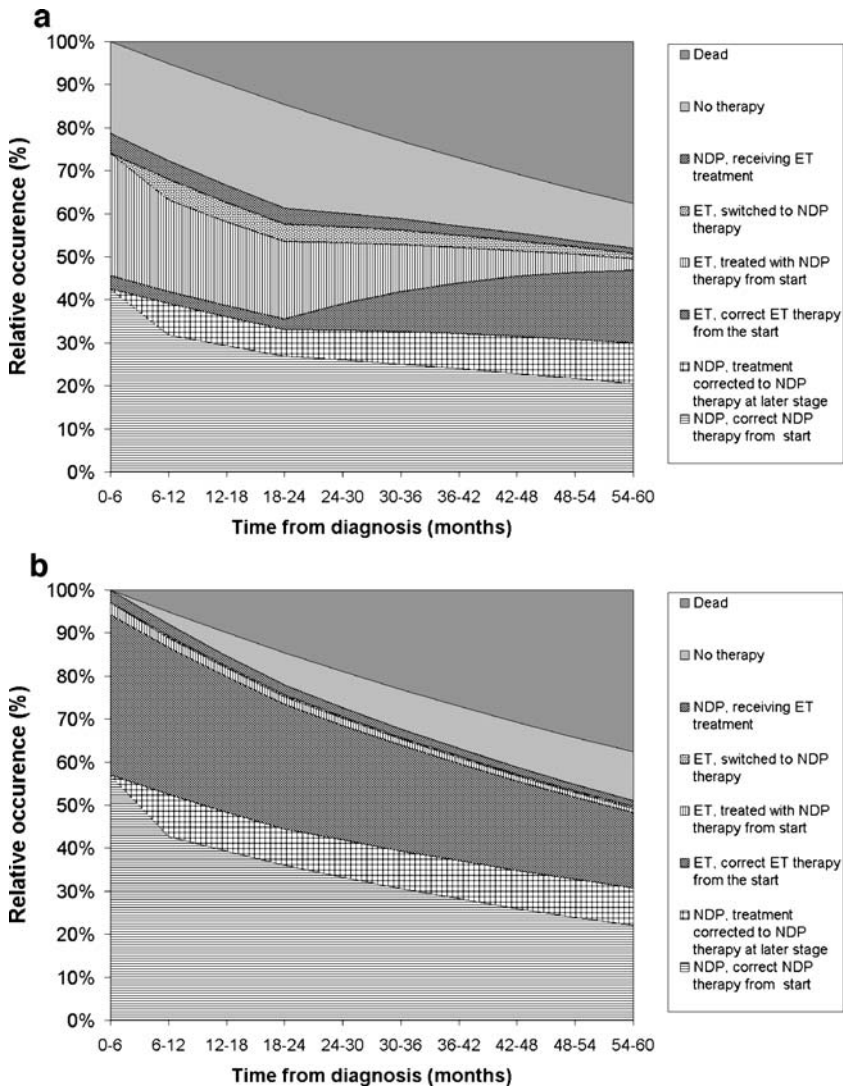


Fig. 2 Calculated decision-tree evolution of the Markov states for the patients with clinically uncertain parkinsonism **a** without ^{123}I-FP-CIT SPECT and **b** with ^{123}I-FP-CIT SPECT. *NPD* Neurodegenerative parkinsonism, *ET* essential tremor

patient had moved excessively, a borderline result was obtained, and image quality was judged insufficient or if the patient did not return for imaging after the injection of the tracer.

Additional neurological clinical information that was requested concerned a change in the initial diagnosis (yes/no) or alteration of treatment (yes/no), where applicable. Three to 12 months after scanning, this information was available for the nuclear medicine specialist completing the registry. No additional longer follow-up data were retrieved retrospectively. The category 'non-applicable' was available for those cases where no tentative diagnosis had been established yet (de novo patients) or when the neurologist did not communicate that information to the nuclear medicine specialist.

The form was dated and signed by the responsible nuclear medicine physician. Therefore, the responsibility for the content of the registry was left entirely at the professional judgement of the local nuclear medicine specialist and neurologist. Demographic data of the patient (initials, gender, age) were not registered.

Equipment used for the SPECT examination included single, dual- and triple-headed cameras of all major instrumentation manufacturers. Dual-headed cameras made up more than 80% of the total type of gamma camera use.

Statistical data analysis

In the analysis of the registry data, equal weights for all referrals were assumed. No sub-analysis for university versus non-university clinics or technical aspects (camera type, reconstruction parameters etc.) was performed. Exploratory descriptive statistics were used, calculated using Statistica (v7.1, Tulsa, USA).

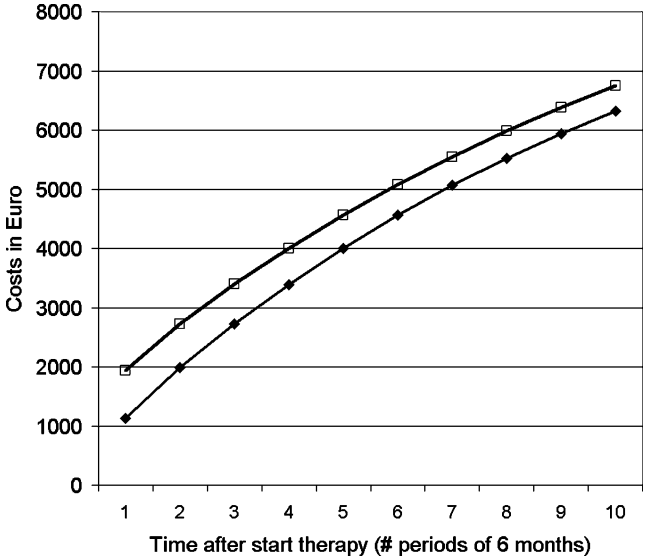


Fig. 3 Calculated cumulative discounted costs for 5 years treatment of uncertain parkinsonism without (*full diamonds*) and with (*open squares*) inclusion of ^{123}I-FP-CIT SPECT in the diagnostic workup. Each *period* on the *x*-axis represents 6 months

Results

Cost effectiveness based on the PE model

Base case

Figure 2 shows the projected evolution of the different Markov states over the five year time period. Figure 3 shows the evolution of total cumulative costs over the projected time period for both scenarios with and without the use of DAT SPECT. It can be seen that after 5 years, despite the initial investment of €900 for the inclusion of DAT SPECT at the starting point, the increase in total costs is limited to €429 per patient. At the calculated 53% true prevalence of NDP, the mean ATY in the current scheme was 1.78, while it was 3.08 for scheme 2 including imaging, leading to a difference of 1.30 additional ATY per patient.

Sensitivity analysis

The CE model was found to be robust in several of the modelling assumptions such as rates of adverse events and withdrawals from therapy. For a prevalence between 1% and 9% of the adverse events dyskinesias, psychosis and hypotension, it was concluded that ^{123}I-FP-CIT SPECT remains in the same order of CE. The CE of DAT SPECT is not affected to a significant extent with dropout rates ranging from 0% to 6%. The underlying prevalence of the true fraction of NDP in the tested population of unknown clinical diagnosis was found to be a critical variable, as shown in Table 4. With a prevalence of 53%, an additional annual cost to the health care system of €126 would be spent per additional ATY for the strategy of including ^{123}I-FP-CIT SPECT in the patient workup. This could vary between −€303 and +€625 per ATY, in the range of 40–66%. Because of this high sensitivity of the PE model on NDP prevalence, it was concluded that objectively observed data were needed to refine this estimate and to assess the presence of a cost-saving (net cost value<0) outcome or not.

^{123}I-FP-CIT registry data

Patient characteristics

Forty-eight (39 peripheral and nine university) hospitals contributed to the registry, 38 in the Flemish part and 19 in the French part of the country. During the 16-month registration period (from May 1, 2004 until August 31, 2005), a total of 1,701 consecutive cases were scanned. The distribution of ^{123}I-FP-CIT SPECT volume (number of scans per center) is given in Fig. 4. The mean number of scans performed in a single centre was 29.8, ranging from less than 10 to more than 120.

In 1,526 subjects (89.7%), complete neurological outcome data were available (pre-scan diagnosis, change in

Table 4 Sensitivity of the CE to NDP prevalence (costs and health outcomes discounted at 5% per year)

Prevalence of NDP (%)	Strategy without ^{123}I-FP-CIT SPECT		Strategy with ^{123}I-FP-CIT SPECT		Difference		Cost per ATY gained (in €)
	Total cost (in €)	ATY (years)	Total cost (in €)	ATY (years)	Total cost (in €)	ATY (years)	
40	6053	1.568	5601	3.061	−452	1.493	−302.6
46	6134	1.666	5946	3.071	−188	1.404	−133.6
53[a]	6228	1.781	6349	3.082	+121	1.301	92.7
60[b]	6322	1.896	6751	3.094	+429	1.198	358.0
66	6403	1.995	7096	3.104	+693	1.109	624.7

ATY Adequately treated year
[a] A priori estimated prevalence
[b] Observed prevalence from the registry study

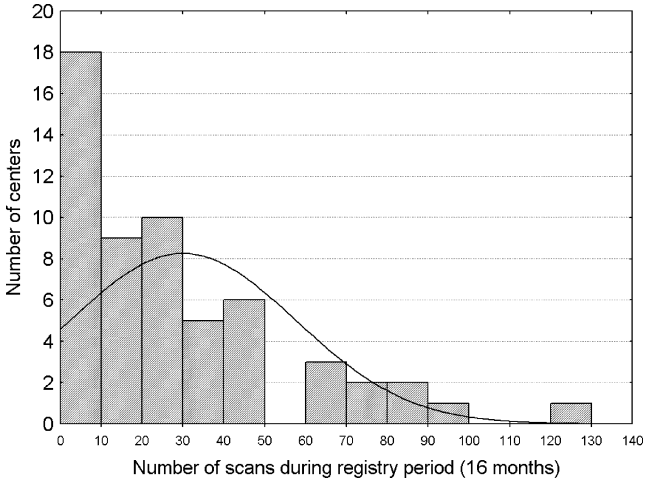


Fig. 4 Distribution histogram of the participating centres in the multi-centre registry

diagnosis and change in therapy). Of the pre-scan diagnoses, 781 subjects (51.1%) were thought to have a NDP, while 745 were tentatively diagnosed with essential tremor (48.8%).

Diagnostic outcomes

Table 5 shows the results of the SPECT scans. In 1,018 (59.8%) patients, the scan showed loss of dopaminergic activity. The scan was non-conclusive in only 40 cases (2.4%). In combination with a presumed diagnostic sensitivity and specificity for visually analysed ^{123}I-FP-CIT SPECT of 95% and 93%, respectively [5], the fraction of patients suffering from true NDP in this population was estimated by the Bayes theorem at 60.0%, as shown in Table 6.

Information about change in diagnosis was available for 1526 patients (89.7%). Of these, pre- and post-scan diagnosis were different in 876 cases (57.4% in this subgroup or 51.5%

Table 5 SPECT, diagnostic and management results from the registry study

Results of ^{123}I-FP-CIT SPECT examination	Loss of dopaminergic activity	No loss of dopaminergic activity	Not conclusive
Number	1,018	643	40
Percent	59.8	37.8	2.4
Change in the initial diagnosis	Yes	No	Not applicable/ not answered
Number	876	683	142
Percent	51.5	40.2	8.3
Alteration of treatment	Yes	No	Not applicable/ not answered
Number	834	680	187
Percent	49.0	40.0	11.0

Table 6 Bayes theorem to calculate the estimated prevalence of NDP from the registry data

	NDP	Non-NDP	Subtotals
Positive ^{123}I-FP-CIT SPECT	0.57	0.028	0.598
Negative ^{123}I-FP-CIT SPECT or inconclusive SPECT exam	0.030	0.372	0.402
Subtotals	0.600	0.400	

of the total number of 1701 performed investigations, which is the relevant proportion from the health economics point of view). Figure 5 shows this change after subdivision into pre-scan diagnosis for the available complete datasets (N= 1,526). Amongst those patients initially assumed not to suffer from loss of dopaminergic activity, the scan pointed out that 60.3% had true NDP. In 45.4% of the patients initially assumed to have NDP, no loss of dopaminergic activity was demonstrated.

Change in management

After ^{123}I-FP-CIT SPECT, overall patient treatment was altered in 49% (834 of 1,701). This parameter could not be evaluated in 41 additional patients for whom the pre- and post-scan diagnosis was available but the change in therapy data were missing (total 11%). Management was unaltered in 40% (680 of 1,701).

For patients where full clinical and unequivocal scan data were available regarding diagnostic and management change, management change was investigated in relation to pre-scan diagnosis (Fig. 6; change in treatment expressed relative to the partial number of patients in the pre-scan groups). When considering patients with a clinical pre-scan NDP diagnosis, therapy was not altered in 25% of these, even though ^{123}I-FP-CIT SPECT showed no loss of dopaminergic activity. In the pre-scan ET group, 10% had altered management in spite of a diagnosis that was

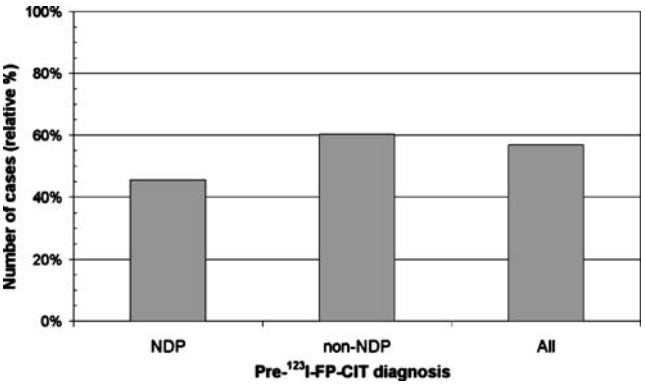


Fig. 5 Percentage of subjects with change of diagnosis following ^{123}I-FP-CIT SPECT, divided into pre-SPECT scan results. The graphs are based on a total available data N=1,526 (175 patients without information on change in diagnosis or inconclusive SPECT)

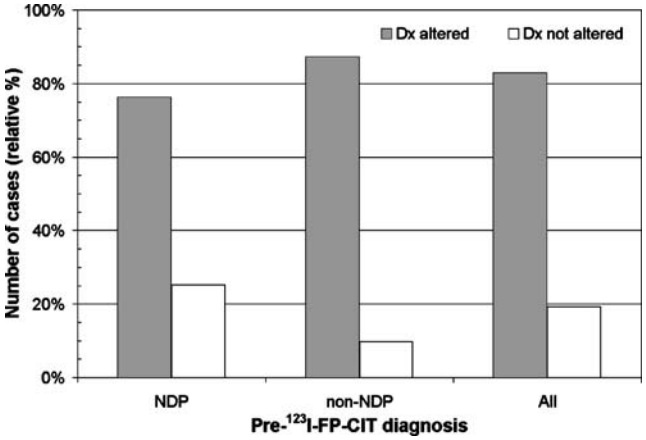


Fig. 6 Percentage of subjects with change in therapy following ^{123}I-FP-CIT SPECT, sub-divided into pre-scan diagnostic groups and relative to the total in the diagnostic sub-group

maintained. In the overall group where the final diagnosis was not altered, still 19% of patients had an alteration in management after the scan.

Adjustment of the CE study based on the true observed prevalence

Whereas it was initially estimated that the incidence of true NDP among patients with uncertain clinical diagnosis was 52.9%, the calculated true prevalence based on the registry was significantly higher (60.0%), although it still was within the range of the original input data sensitivity analysis.

Based on the observed prevalence, the incremental CE was calculated to approximately €358 per ATY instead of €92.7 (Table 4). However, the difference in ATY was still 3.1–1.9=1.2 years over the 5-year observation period, resulting in the additional cost of €429 to the health security and an incremental CE of €358 per extra ATY.

Discussion

Including ^{123}I-FP-CIT SPECT in the diagnostic workup of patients with uncertain parkinsonism leads to additional costs to the health insurance budget, for the Belgian situation. However, the additional cost is small compared to the total indirect treatment costs even over the first period of 5 years. Furthermore, this additional cost is counterbalanced by a very significant gain in ATY on a population basis and therefore expected overall patient wellbeing.

The results of the pharmaco-economic modelling shows that the incremental cost per unit of beneficial effect is lower in this Belgian study compared to findings by Dodel et al. [8], who developed a decision tree model to predict a similar parameter, adequate treatment-month equivalents, over a 12-month time horizon in patients with suspected NDP from the German health care perspective. They demonstrated that compared to clinical examination alone without DAT SPECT, the incremental costs would be €733 per ATY-equivalent gained, compared to €358 in the current situation. In addition, in that study, sensitivity to the true NDP prevalence was high, since NDP treatment has the highest impact on indirect costs for these clinically uncertain patients, as can be seen also from Table 2. We agree therefore that the choice to include ^{123}I-FP-CIT SPECT does indeed depend on the decision maker's willingness to pay for adequate treatment.

A direct question arising from our results that were obtained in a Belgian health care setting is the possibility to extrapolate to other countries and health care organization systems. Since the examination cost of ^{123}I-β-CIT and ^{123}I-FP-CIT is considered equivalent and the statistical significance of DAT reduction in NPD is similar [14], the current CE calculations should also be applicable to ^{123}I-β-CIT. In countries with a less developed distribution system for ^{123}I, due to geographical or production density differences, ^{99m}Tc-labelled ligands such as ^{99m}Tc-TRODAT may offer an alternative. However, the possible lower cost due to on-site kit preparation possibilities needs to be weighed to the overall lower diagnostic accuracy, as has been suggested in a number of independent recent studies [15–17].

The changes in management found in this study are within the range of the observed frequencies in previous studies by Lokkegaard et al. (28%) [2] and Catafau et al. (72%) [6]. Furthermore, the differentiation accuracy according to pre-scan diagnosis is similar to the results from the latter study, although less closely for the non-NDP group: For NDP, this was 42% versus 44% in our study and for non-NDP 54% versus 68% in this study.

Overall, these studies demonstrate that in this patient population, DAT SPECT has a highly significant impact on clinical patient management. An interesting observation from the registry study was that management was not changed in 20% of patients with nonetheless changed diagnosis. Explanations for this could be remaining confidence of the neurologist in the clinical diagnosis, presumed false-positive findings on DAT SPECT or decision to refrain from drug therapy initiation upon confirmation of the absence of dopaminergic deficiency.

Although the number of included patients is very large due to the specific registry, there are also some caveats to be addressed from this study. Firstly, there is lack of full demographic data, specific disease characteristics and hard clinical endpoints. This is partially due to the fact that the DaTSCAN provider's advisory board suggested before

initiation of the study to make the registry administration as light as possible in view of the large number of participating centers. Furthermore, no follow-up of the patients was foreseen after the completion of the registry, which was several months after the scan acquisition. Nevertheless, since during a 16-month interval, the results for all patients scanned in Belgium for this specific indication were recorded systematically, we can assume that the available data are representative for the typical prevalence/incidence patterns for degenerative and non-degenerative NDP. This dataset does provide a true sample of those patients that will be eligible for DAT SPECT imaging in the future.

Secondly, there were no a priori criteria for pre- or post-scan diagnosis by the neurologist, and there were no formal a priori defined technical criteria for SPECT. SPECT evaluation was performed on site without central analysis or readout of the data. The image data could be analysed by either visual or semi-quantitative analysis, and reconstruction parameters and processing corrections for attenuation or scatter were left at the current practice of the nuclear medicine specialist. Although therefore not necessarily scientifically optimized and performed according to the highest possible imaging standards, the dataset does give a reliable indicator of current clinical practice in brain imaging as performed in Belgium. In view of the large proportion of the scans done by non-specialized/non-university centres, the overall results may even be more representative of this non-specialized setting.

In conclusion, this registry can be seen as a source of highly representative data for ^{123}I-FP-CIT SPECT. As a result of ^{123}I-FP-CIT SPECT imaging in patients with clinically uncertain parkinsonian syndrome, an initial tentative diagnosis is changed in 52% of the patients and the consecutive therapy in 49%. These figures support the value of DAT SPECT imaging also in community clinical practice. Furthermore, when the results of the registry are fed into the original pharmaco-economic model, the same percentage of changes in therapy is found, confirming the predictive validity of the model. The model can also be extended to assess the CE of other radioligands for DAT or novel clinically useful indications such as differential diagnosis of dementia with Lewy bodies versus Alzheimer's disease [18].

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