

HEALTH TECHNOLOGY ASSESSMENT DECISIONS OVER THE LAST DECADE IN THE UNITED KINGDOM AND THE NETHERLANDS – A FOCUS ON NON-SMALL-CELL LUNG CANCER

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BACKGROUND & OBJECTIVES

Lung cancer is still the leading cause of cancer mortality, with about 80% of patients having non-small-cell lung cancer (NSCLC).^{1,2} Over the last decade new treatments emerged in NSCLC focusing more on specific mutations like epidermal growth factor receptor (EGFR), Anaplastic lymphoma kinase (ALK), and Programmed Death- (Ligand) 1 (PD-(L)1).^{2,3} Instead of monotherapy for patients with NSCLC started with chemotherapy like docetaxel as the standard, patient treatment became more individualized with sequential lines of treatment when treatment resistance develops.

The objective of this review was to evaluate economic evaluations for NSCLC in the UK and the Netherlands appraised over the last decade to identify common modeling approaches and analyse reimbursement trends of the National Institute for Health and Care Excellence (NICE) and the Dutch Health Care Institute (Zorginstituut Nederland, ZIN).

METHODS

A search for NSCLC treatments was conducted in the databases of NICE in the UK and ZIN in the Netherlands between: January 2008 - December 2018.⁴⁻⁶ The search term used concerned 'Non-small-cell lung cancer' both in English and Dutch. In addition to the database searches, the treatment guidelines for NSCLC were consulted in both countries as well the European.^{2,7,8} Exclusion criteria concerned: 'treatments for small cell lung cancer' and 'treatments outside the scope of 2008-2018'.

Data from each economic evaluation was extracted and evaluated by drug class, indication, decision, economic- and budget impact outcomes. Where more than one publication described a single appraisal, the data, analysis and outcomes of the latest appraisal were evaluated. Lacking data in the latest evaluation were supplemented with available data from previous specified treatment appraisal documents.

RESULTS

A total of 29 HTA submissions were appraised for 15 unique NSCLC treatments between 2008-2018 in the UK and the Netherlands. Three state models were applied in 41,4% of all submissions and only 3 evaluations (10,3%) used a 4-state Markov model. All models in the UK were performed from the NHS (National Health Service) and PSS (Personal Social Services) perspective, whereas the Dutch models were required to take a societal perspective into account.

The majority of collected health-related quality of life data, of which the standardized EQ-5D questionnaire was used most often used. The EORTC QLQ-C30 and EORTC QLQ-LC13 questionnaires were often used within the cluster of TKIs (tyrosine kinase inhibitors).⁹⁻¹¹

Table 1: Overview of economic evaluations for treatment of non-small-cell lung cancer appraised between January 2008 and December 2018 in the UK and the Netherlands.

Country	Generic name	Brand name	Submission date	Final decision	Full submission	Nr. of decisions	Model	Time horizon (Years)	Comparator	ICER	Threshold	Reimbursement decision
NL	Pemetrexed	Alimta	NA	24/07/2009	Yes	1	Markov 4-state model	3	Gemcitabine	50092	80000	Reimbursed until 2015
UK	Gefitinib	Iressa	05/08/2009	27/05/2010	Yes	2	Markov 4-state model	5	Carboplatin+ paclitaxel	20010	30000	Recommended
NL	Gefitinib	Iressa	07/08/2009	15/01/2010	Yes	1	NA	NA	NA	NA	80000	Reimbursed
UK	Afatinib	Giotrif	03/04/2013	23/04/2014	Yes	1	Partition survival 3-state model	10	Cisplatin + pemetrexed or gemcitabine	17933	20000-30000	Recommended with PAS
NL	Afatinib	Giotrif	19/08/2013	19/08/2013	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Crizotinib	Xalkori	17/02/2014	17/02/2014	No	1	NA	NA	NA	NA	80000	Reimbursed
UK	Nintedanib	Vargatef	01/08/2014	02/06/2015	Yes	1	Markov 3-state model	15	Docetaxel	68587	50000	Recommended
NL	Nintedanib	Vargatef	19/01/2015	19/01/2015	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Ramucirumab	Cyramza	19/02/2015	19/02/2015	No	1	NA	NA	NA	NA	80000	Reimbursed
UK	Ceritinib	Zykadia	12/06/2015	20/05/2016	Yes	3	Partition survival 3- state model	10	NA	62456	20000-30000	Recommended with PAS
NL	Pemetrexed	Alimta	NA	18/07/2016	Yes	2	Markov 3-state model	10	Gemcitabine	92948-116575	80000	Reimbursed until December 2020
NL	Nivolumab	Opdivo	01/09/2015	01/01/2016	Yes	3	Markov 3-state model	Company: 20 ZIN:10	Docetaxel	NA	80000	ZIN: No, unless PAS. GOV: Reimbursed+PAS
UK	Nivolumab	Opdivo	23/12/2015	20/09/2017	Yes	3		10	Docetaxel	103589	50000	Recommended with PAS
UK	Ramucirumab	Cyramza	01/01/2016	07/07/2016	Yes	1	Markov 3-state model	15	Docetaxel	194919	20000-30000	Not recommended
UK	Necitumumab	Portrazza	18/01/2016	12/08/2016	Yes	2	Markov 3-state model	15	Docetaxel	110248	50000	Not recommended
UK	Osimertinib	Tagrisso	19/02/2016	04/10/2016	Yes	2	Partition survival 3- state model	15	Gefitinib or erlotinib	41705	50000	Recommended with PAS
UK	Pembrolizumab	Keytruda	24/03/2016	02/12/2016	Yes	2	Partition survival 3- state model	20	Docetaxel	43351	50000	Recommended with PAS
NL	Osimertinib	Tagrisso	02/04/2016	02/04/2016	No	1	Markov 3-state model	20	NA	116951	80000	Reimbursed
UK	Crizotinib	Xalkori	07/07/2016	10/11/2016	Yes	1	NA	NA	Chemotherapy	NA	20000-30000	Recommended with PAS
NL	Pembrolizumab	Keytruda	11/08/2016	09/06/2017	Yes	3	Markov 3-state model	10	Docetaxel	112953	80000	ZIN: No, unless PAS. GOV: Reimbursed+PAS
NL	Necitumumab	Portrazza	05/09/2016	05/09/2016	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Alectinib	Alecensa	12/04/2017	12/04/2017	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Dabrafenib	Tafinlar	30/07/2017	30/07/2017	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Atezolizumab	Tecentriq	NA	15/05/2018	Yes	2	NA	NA	Docetaxel	NA	80000	ZIN & GOV: No, unless PAS.
UK	Atezolizumab	Tecentriq	03/08/2017	16/05/2018	Yes	3	3-State Log-logistic model	25	Docetaxel	91142	NA	Recommended with PAS
UK	Alectinib	Alecensa	26/09/2017	28/06/2018	Yes	1	Partition survival 4-state model	NA	Crizotinib	69310	20000-30000	Recommended with PAS, until 2021
NL	Ceritinib	Zykadia	30/08/2017	30/08/2017	No	1	NA	NA	NA	NA	80000	Reimbursed
NL	Osimertinib	Tagrisso	NA	07/11/2018	Yes	1	NA	NA	Gefitinib or erlotinib	NA	80000	ZIN&GOV: No, unless PAS.
UK	Osimertinib	Tagrisso	01/03/2018	-	Yes	-	NA	NA	NA	NA	NA	Expected: June 12, 2019

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RESULTS (continued)

In the UK 76.9% of all HTA appraisals received a positive recommendation for reimbursement, of which 61.5% were conditional on a patient access agreement (PAS). In the Netherlands 25% initially received a negative recommendation for reimbursement by ZIN, however after negotiations with the Dutch government 93.7% of all submissions received reimbursement. The average duration for full HTA appraisals until final decision was significantly shorter for the Netherlands in comparison to the UK: 198 versus 313 days.

During this 10 years period the budget impact regulations changed as in 2015 the Netherlands implemented an annual budget impact cap of €2.5 million per year, and the UK implemented in 2017 a cap of £20 million in any of the first 3 years.¹²⁻¹⁷ When exceeded, negotiations for PAS agreements are mandatory for reimbursement in both countries. In the UK this is regardless of the incremental cost-effectiveness ratio (ICER), whereas in the Netherlands the lock procedure for expensive medicines will be started. Both procedures can lead to a longer appraisal process.

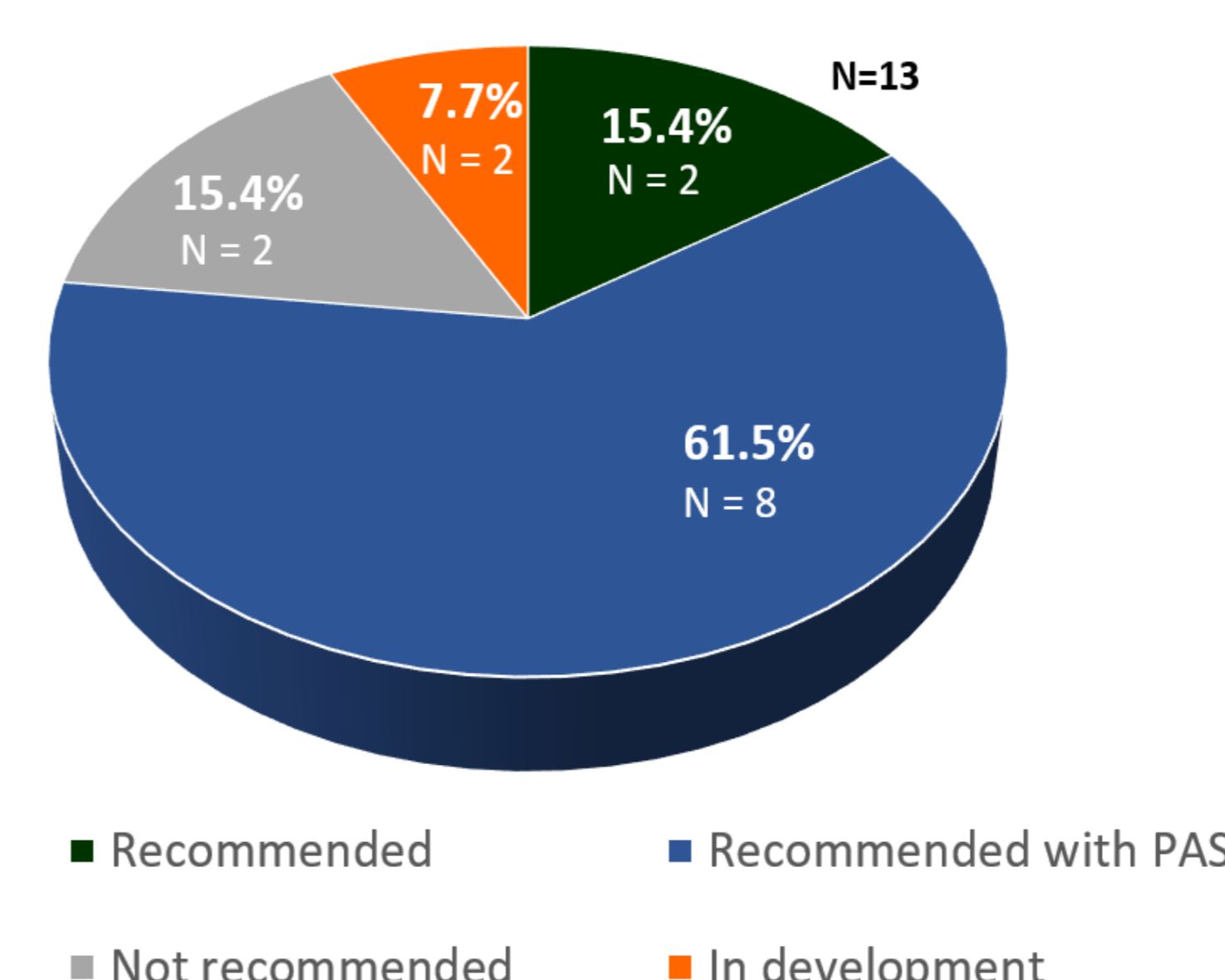


Figure 1: Distribution of final NICE decisions regarding reimbursement for HTA submissions.

PAS: Patient Access Scheme

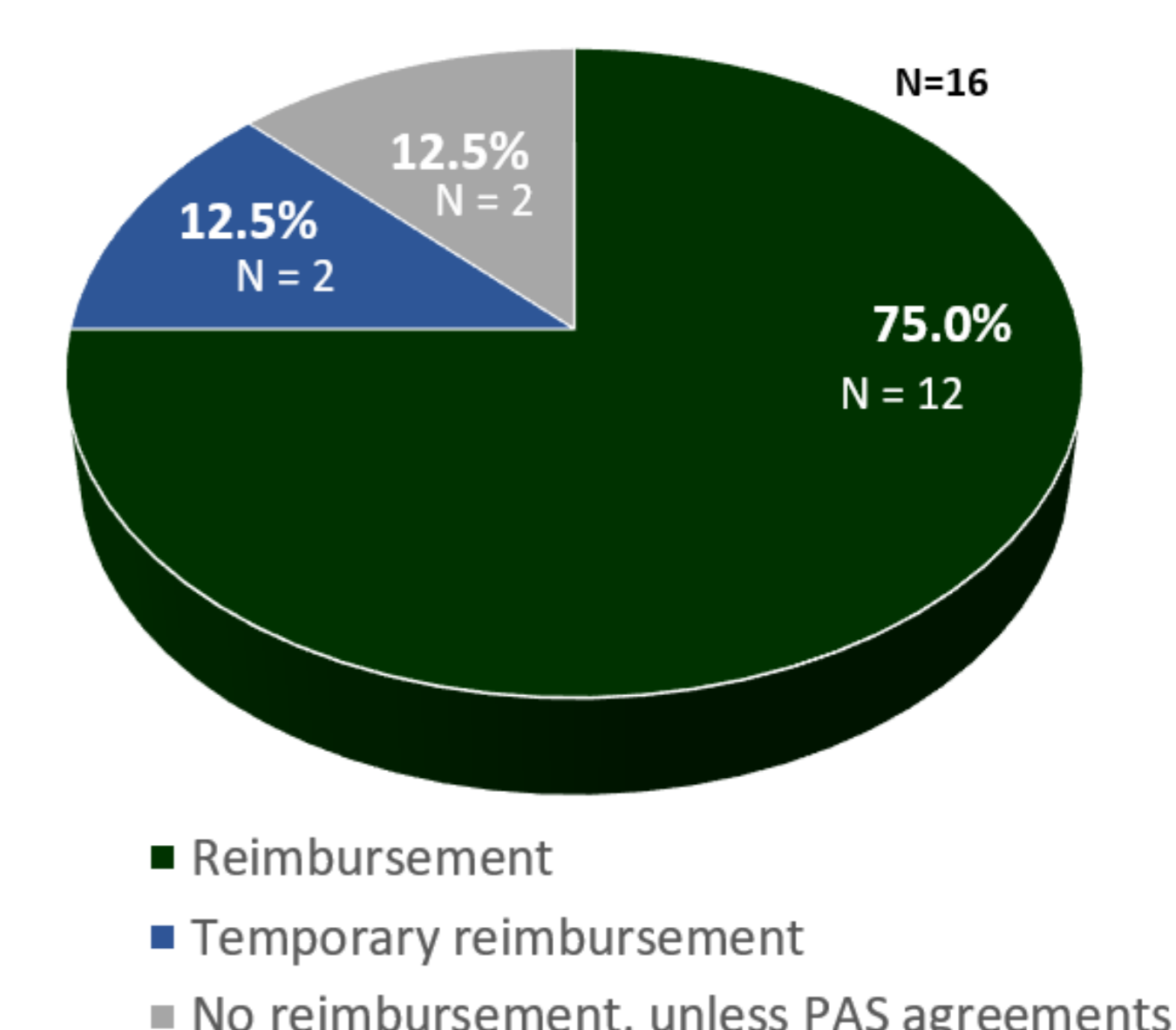


Figure 2: Distribution of final government decisions regarding reimbursement for HTA submissions or notifications.

CONCLUSION

In conclusion, both countries showed an increasing challenging reimbursement environment for NSCLC treatments and budget impact regulations have changed drastically for both countries in the period observed in this analysis. The percentage of positive recommendations for reimbursement were comparable in both countries, whereas the Netherlands showed a higher reimbursement rate after negotiations.