

Systematic Review and Meta-Analysis of Community and Choice-Based Health State Utility Values for Lung Cancer

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Supplementary Methods

Search Query

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('lung cancer'/de OR 'lung carcinoma'/de OR (((lung OR pulmonar*) NEAR/6 (cancer* OR carcino* OR neoplas*))) :ab,ti) AND ('quality of life'/exp/mj OR 'quality of life assessment'/de/mj OR 'cost utility analysis'/de OR 'cost benefit analysis'/de OR 'quality adjusted life year'/exp OR 'vignette'/de OR 'visual analog scale'/de OR ((qualit* NEAR/3 life NEAR/6 (assess* OR measure*)) OR (utilit* NEAR/3 (cost OR Health OR value* OR scale*)) OR utilities OR qaly OR (cost NEAR/3 benefit*) OR eq-5d OR eq5d OR euroqol OR euro-qol OR hui OR ((sf or short-form) NEXT/1 (6 OR 12 OR 20 OR 36 OR thirtysix OR thirty-six OR twenty OR twelve OR six)) OR sf6* OR sf12* OR sf36* OR sf36* OR ((qualit*) NEAR/3 adjusted NEAR/3 (life-year* OR life-duration* OR life-expect* OR lifeyear*)) OR qaly* OR qald* OR qale* OR qtime* OR (qualit* NEAR/3 (well-being OR wellbeing)) OR qwb OR aqol OR 15d OR vignette* OR direct-elicitation* OR time-trade-off* OR time-tradeoff* OR tto OR standard-gamble* OR best-worst-scale* OR 'visual analog* scale' OR vas OR eortc-qlq-c30 OR fact-l OR hye OR hyes OR (health* NEAR/3 year* NEAR/3 equivalent*) OR (preference* NEAR/3 (state* OR score* OR value* OR valuat* OR weight)) OR hsuv OR hsuvs):ab,ti) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim)

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(exp "Lung Neoplasms"/ OR (((lung OR pulmonar*) ADJ6 (cancer* OR carcino* OR neoplas*))) :ab,ti,kf.) AND ("Quality of Life"/ OR "Cost-Benefit Analysis"/ OR "Quality-Adjusted Life Years"/ OR "Visual Analog Scale"/ OR ((qualit* ADJ3 life ADJ6 (assess* OR measure*)) OR (utilit* ADJ3 (cost OR Health OR value* OR scale*)) OR utilities OR qaly OR (cost ADJ3 benefit*) OR eq-5d OR eq5d OR euroqol OR euro-qol OR hui OR ((sf or short-form) ADJ (6 OR 12 OR 20 OR 36 OR thirtysix OR thirty-six OR twenty OR twelve OR six)) OR sf6* OR sf12* OR sf36* OR sf36* OR ((qualit*) ADJ3 adjusted ADJ3 (life-year* OR life-duration* OR life-expect* OR lifeyear*)) OR qaly* OR qald* OR qale* OR qtime* OR (qualit* ADJ3 (well-being OR wellbeing)) OR qwb OR aqol OR 15d OR vignette* OR direct-elicitation* OR time-trade-off* OR time-tradeoff* OR tto OR standard-gamble* OR best-worst-scale* OR "visual analog* scale" OR vas OR eortc-qlq-c30 OR fact-l OR hye OR hyes OR (health* ADJ3 year* ADJ3 equivalent*) OR (preference* ADJ3 (state* OR score* OR value* OR valuat* OR weight)) OR hsuv OR hsuvs).ab,ti,kf.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt.

Cochrane CENTRAL

(((((lung OR pulmonar*) NEAR/6 (cancer* OR carcino* OR neoplas*))) :ab,ti) AND (((qualit* NEAR/3 life NEAR/6 (assess* OR measure*)) OR (utilit* NEAR/3 (cost OR Health OR value* OR scale*)) OR utilities OR qaly OR (cost NEAR/3 benefit*) OR eq NEXT/1 5d OR eq5d OR euroqol OR euro NEXT/1 qol OR hui OR ((sf or short NEXT/1 form) NEXT/1 (6 OR 12 OR 20 OR 36 OR thirtysix OR thirty NEXT/1 six OR twenty OR twelve OR six)) OR sf6* OR sf12* OR sf36* OR sf36* OR ((qualit*) NEAR/3 adjusted NEAR/3 (life NEXT/1 year* OR life NEXT/1 duration* OR life NEXT/1 expect* OR lifeyear*)) OR qaly* OR qald* OR qale* OR

qtime* OR (qualit* NEAR/3 (well NEXT/1 being OR wellbeing)) OR qwb OR aqol OR 15d OR vignette* OR direct NEXT/1 elicitation* OR time NEXT/1 trade NEXT/1 off* OR time NEXT/1 tradeoff* OR tto OR standard NEXT/1 gamble* OR best NEXT/1 worst NEXT/1 scale* OR 'visual analog* scale' OR vas OR eortc NEXT/1 qlq NEXT/1 c30 OR fact NEXT/1 l OR hye OR hyes OR (health* NEAR/3 year* NEAR/3 equivalent*) OR (preference* NEAR/3 (state* OR score* OR value* OR valuat* OR weight)) OR hsuv OR hsuvs):ab,ti)

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TS=((((lung OR pulmonar*) NEAR/5 (cancer* OR carcino* OR neoplas*)))) AND (((qualit* NEAR/2 life NEAR/5 (assess* OR measure*)) OR (utilit* NEAR/2 (cost OR Health OR value* OR scale*)) OR (cost NEAR/2 benefit*) OR ((qualit*) NEAR/2 adjusted NEAR/2 ("life-year*" OR "life-duration*" OR "life-expect*" OR lifeyear*)) OR vignette* OR "direct-elicitation*" OR "time-trade-off*" OR "time-tradeoff*" OR "standard-gamble*" OR "best-worst-scale*" OR "visual analog* scale" OR (health* NEAR/2 year* NEAR/2 equivalent*) OR (preference* NEAR/2 (state* OR score* OR value* OR valuat* OR weight))))) AND DT=(article)

Google scholar

"lung|pulmonary cancer|carcinoma|neoplasms" "quality*life assessment|measurement|"cost|Health utility"|utilities|"quality adjusted life|lifeyear|lifeyears"

The School of Health and Related Research Health Utility Database (SchARRHUD)

Lung cancer

Inclusion criteria for title/abstract screening

1a. Title/abstract reports the study includes specifically lung cancer patients

OR

1b. Title/abstract reports that results were stratified by cancer type **AND** (these cancer types include lung cancer **OR** keywords include “lung cancer”)

AND one of the following

2a. Title/abstract reports health state utility values (HSUVs) (on a 0-1 scale) were measured or reported as an outcome

OR

2b. Title/abstract reports health-related quality of life (HRQoL) was measured **AND** the instrument used was reported **AND** the instrument used is suitable for the elicitation of HSUVs:

- EQ-5D (EuroQol five dimensions)
- SF-6D (Short-Form-6D) **OR** SF-12 **OR** SF-36
- HUI (Health utility Index; version 1,2 or 3)
- QWB (Quality of Well-Being)
- AQoL (Assessment of Quality of Life)
- 15D
- Vignettes
- Direct elicitation

OR

2c. Title/abstract reports HRQoL was measured (not including pain, nausea, or other symptoms) **AND** the use of a “valuation method” suitable for the elicitation of HSUVs was mentioned:

- Time trade-off (TTO)
- Standard gamble (SG)
- Best Worst Scale (BWS)
- Visual analogue scale (VAS)

OR

2d. Title/abstract reports the study type is a cost-utility analysis (thus using quality-adjusted life years (QALYs) and not only life years (LYs))

OR

2e. Title/abstract reports the study type is a quality adjusted-survival study (sometimes referred to as Q-TWiST)

OR

2f. Title/abstract reports HSUVs were mapped from an instrument not mentioned under item 2b (for example from a disease-specific measure, such as the EORTC-QLQ-C30), onto a utility scale (0-1)

Exclusion criteria for title/abstract screening:

- Animal studies
- Conference abstracts
- Editorials/commentaries/letters
- Reviews (systematic reviews/meta-analyses/overview articles)
- Study protocol
- Expert opinion (expert opinion was used without any instrument and/or valuation method)
- Guidelines
- Non-English or Dutch language
- Mesothelioma studies
- HRQoL not measured
- Studies with HRQoL measured as endpoint, but used instrument or valuation not mentioned in title/abstract **OR** used instrument or valuation mentioned, but other than listed under 2b and 2c.
- HRQoL values were mapped from one instrument to another **AND** HSUVs are not mentioned in title or abstract
- Economic evaluation without original HSUVs (for example, cost-effectiveness analysis not using quality adjusted life years (QALYs) but only life years (LYs), **OR** cost-utility analysis with non-original HSUVs)
- Non lung cancer specific HSUVs (non-lung cancer specific study **AND** no stratification by cancer type)
- Non-original data (previously published HSUVs reported)

Inclusion criteria for full text screening

Reports original, lung cancer specific mean or median HSUVs, including a measure of variance (e.g., sample size + variance, standard deviation, standard error, interquartile range), elicited using one of the following methods:

- EQ-5D (EuroQol Five Dimensions Questionnaire)
- SF-6D (Short-Form-6D)
- HUI (Health Utility Index; 1,2 or 3)
- QWB (Quality of Well-Being)
- AQoL (Assessment of Quality of Life)
- 15D
- Vignettes
- Direct elicitation
- Mapping of HRQOL measures from another instrument (e.g. FACT-L); HSUVs are reported in the manuscript. If utilities were mapped from an instrument listed above, include only the original HSUVs.

Exclusion criteria for full text screening:

- Animal studies
- Conference abstracts
- Editorials/commentaries/letters
- Reviews (systematic reviews/meta-analyses/overview articles)
- Study protocol
- Expert opinion (expert opinion was used without any instrument and/or valuation method)
- Guidelines
- Non-English or Dutch language
- Mesothelioma studies
- HRQoL not measured
- Economic evaluation without original HSUVs (for example, cost-effectiveness analysis not using quality adjusted life years (QALYs) but only life years (LYs), **OR** cost-utility analysis with non-original HSUVs)
- No HSUV (no numerical mean or median HSUVs reported).
- Non lung cancer specific HSUVs (non-lung cancer specific study **AND** no stratification by cancer type)
- Non-original data (previously published HSUVs reported **OR** another study used the same underlying data to derive HSUVs with higher-quality methodology, e.g. matching tariff)
- No measure of variance reported with HUVs (and no data to estimate variance)
- Full text not available

Supplementary Tables and Figures

Supplementary Table 1: Critical appraisal of studies reporting mean or median health state utility values for lung cancer

Source	Relevance			Validity			
	Respondents ^a	Valuation Population ^b	Valuation method ^c	Sample size ^d	HRQoL response ^e	Handling missing data ^f	Loss to follow-up ^g
Kimman 2015 ¹	+	+	+	624	624	NR	NAP
Yabroff 2007 ²	+	-	-	439	NR	NR	NAP
Lee 2011 ³	+	-	+	241	220	-	NAP
Grutters 2010 ⁴	+	+	+	374	245	-	NAP
Trippoli 2001 ⁵	+	NR	NR	95	92	-	NAP
Iyer 2013 ⁶	+	NR	NR	837	832	-	NAP
Jang 2010 ⁷	+	+	+	172	172	NR	NAP
Chouaid 1998 ⁸	+	-	-	10	10	NR	NAP
Blackhall 2014 ⁹	+	NR	NR	347	313	-	NAP
Rauma 2015 ¹⁰	+	+	-	276	230	-	NAP
Geerse 2017 ¹¹	+	NR	NR	223	191	-	NAP
Schuette 2012 ¹²	+	+	+	542	231	-	NAP
Khan 2014 (a) ¹³	+	+	+	670	670	NR	NAP
Khan 2014 (b) ¹³	+	+	+	130	130	NR	NAP
Lamers 2007 ¹⁴	+	+	-	210	131	-	NR
van den Hout 2006 ¹⁵	+	+	+	297	297	+	NAP
Verduyn 2012 ¹⁶	+	+	-	261	251	-	NAP
Burfeind 2010 ¹⁷	+	-	-	113	113	-	+
Huang 2017 (1) ¹⁸	+	+	±	NR	NR	-	NR
Chouaid 2013 ¹⁹	+	+	+	319	255	-	NAP
Matter-Walstra 2014 ²⁰	+	+	+	154	154	-	NAP

	Relevance			Validity			
Source	Respondents ^a	Valuation Population ^b	Valuation method ^c	Sample size ^d	HRQoL response ^e	Handling missing data ^f	Loss to follow-up ^g
Manser 2006 ²¹	+	+	+	116	91	-	+
Papatheofanis 2000 ²²	+	-	-	134	23	-	NAP
Khan 2016 ²³	+	+	+	100	97	NR	NAP
Naik 2017 ²⁴	+	+	+	NR	149	-	NAP
Shih 2006 ²⁵	+	+	+	NR	51	-	NAP
Kennedy 1995 ²⁶	-	-	+	9	9	NR	NAP
Ilonen 2007 ²⁷	+	+	NR	98	31	-	NAP
Pickard 2007 ²⁸	+	+	+	50	50	NR	NAP
Ko 2003 ²⁹	+	-	-	54	54	NR	NAP
Thongprasert 2015 ³⁰	+	+	+	150	150	NR	NAP
Galetta 2015 ³¹	+	NR	NR	118	118	+	NAP
Tramontano 2015 ³²	+	+	+	5015	2396	-	+
Bendixen 2019 ³³	+	+	+	201	201	+	NAP
Erbaycu 2018 ³⁴	+	+	+	266	266	-	NAP
Huang 2017 (2) ³⁵	+	+	±	NR	NR	-	NR
Insinga 2018 ³⁶	+	+	+	NR	NR	-	NR
Insinga 2019 ³⁷	+	+	+	NR	NR	-	NR
Kim 2018 ³⁸	-	+	+	515	515	-	NAP
Limwattananon 2018 ³⁹	+	+	+	135	135	NR	NAP
Maximiano 2018 ⁴⁰	+	+	+	760	495	-	+
Mendoza 2018 ⁴¹	+	+	+	664	664	-	NAP
Meregaglia 2019 ⁴²	+	+	+	96	96	-	+

Source	Relevance			Validity			
	Respondents ^a	Valuation Population ^b	Valuation method ^c	Sample size ^d	HRQoL response ^e	Handling missing data ^f	Loss to follow-up ^g
O'Kane 2019 ⁴³	+	+	+	519	519	NR	NAP
Reck 2018 (1) ⁴⁴	+	NR	NR	582	419	-	NAP
Reck 2018 (2) ⁴⁵	+	NR	NR	272	186	-	NAP
Rendas-Baum 2019 ⁴⁶	+	+	+	43	43	NR	NAP
Su 2019 ⁴⁷	+	+	+	104	104	-	NAP
Wood 2019 ⁴⁸	+	NR	NR	1030	1030	NR	NAP
Goodwin 1988 ⁴⁹	-	-	-	21	21	NR	NAP
Cykert 2000 ⁵⁰	-	-	+	64	64	NR	NAP
Sullivan 2011 ⁵¹	+	+	+	114	114	-	NAP

Table legend:

Abbreviations: NR = not reported; NAP = not applicable; HRQoL = health-related quality of life; HSUV = health state utility value.

Studies with low relevance (i.e., that score a “-” sign or “NR” for any of the relevance criteria) were not included for subsequent analyses because they are not societal and choice-based. These rows are shaded grey.

Superscript Arabic numerals refer to the list of references at the end of this appendix.

^a What was the respondent type?

Plus sign indicates patients

Minus sign indicates all others

^b What population was used to value HRQoL (scores or vignettes) to HSUVs?

Plus sign indicates the general population.

Minus sign indicates all others (e.g., patients, caregivers, experts).

For mapping studies, consider the valuation method of the instrument to which HRQoL scores were mapped (observed data).

^c What method was used to value HRQoL scores to HSUVs?

Plus sign indicates a choice-based method (i.e. time trade-off or standard gamble).

Plus/minus sign indicates that multiple methods were used according to the country of origin of respondents; at least one of these methods was choice-based.

Minus sign indicates visual analogue scale or other non-choice based methods.

For mapping studies, consider the valuation method of the instrument to which HRQoL scores were mapped (observed data).

^d How many persons met the inclusion criteria, and, if applicable, signed informed consent and/or were randomized?

In case of multiple disease sites: only for the lung cancer stratum

In case of multiple analyses, only for the HRQoL analysis

In the case of a time series, only the baseline N for this item

^e How many participants were included in the HRQoL analysis?

In case of multiple disease sites: only for the lung cancer stratum

In case of multiple disease sites: only for the lung cancer stratum

In the case of a time series, only consider the baseline N

^f What was the method of handling missing HRQoL data?

Plus sign indicates that missing HRQoL data were mentioned and quantified in the study, and missing data were imputed; or it was explicitly stated that there were no missing data (and completeness of data was not an eligibility criterion).

Minus sign indicates that missing HRQoL data were mentioned in the study, and cases with missing data were dismissed (complete case analysis).

^g Was loss to follow-up reported?

Plus sign indicates that loss to follow-up was reported for each time-point.

Plus/minus sign indicates that loss to follow-up was reported, but not for each time-point.

Minus sign indicates that cases that were lost to follow-up were excluded.

Not applicable to non-longitudinal studies (In case of multiple HRQoL measurements in the same individuals only; if results for multiple time points were based on cross-sectional samples of different patients, do not consider loss to follow-up; also, if study design was longitudinal but numerical HSUVs are only reported for a single time-point, consider the study non-longitudinal).

Supplementary Table 2a: Scope of studies reporting community and choice-based health state utility values for lung cancer

Source	QoL response ^a	Inclusion years ^b	Lung cancer type ^c	Stage ^d	Treatment ^e	Percent male ^f	Age, mean years (range) ^g	Time of measurement, mean (range) ^h
Kimman 2015 ¹	624	2012-2013	All	All	NR	37 *	51.8 (18-100) *	27 d (<12 w) *
Grutters 2010 ⁴	245	2004-2007	NSCLC	All	Any	67	68 (40-90)	2.59 y (0.82-4.76 y)
Jang 2010 ⁷	172	NR-NR	NSCLC	All	Any	46.5	66 (32-65) §	NR
Schuette 2012 ¹²	231	2007-2009	NSCLC	III-IV	Post-first line	69.7	66.3 (39-86)	NR
Khan 2014 (a) ¹³	670	NR-NR	NSCLC	IIIB-IV	Erlotinib or placebo	NR	77 §	(<12m)
Khan 2014 (b) ¹³	130	NR-NR	NSCLC	IIIA-IIIB	Radiotherapy or chemoradiotherapy	NR	62 §	NR
van den Hout 2006 ¹⁵	297	1999-2002	NSCLC	III-IV	Radiotherapy	80 §	69 (48-85) §**	1m (0-88 m) §**
Chouaid 2013 ¹⁹	255	2010-2011	NSCLC	IIIB-IV	Any	61.2	64.8 (32.9-99.6)	NR
Matter-Walstra 2014 ²⁰	154	2011-2012	All	Advanced	Post-first line chemotherapy	59 *	62.1 (40-77)	NR
Manser 2006 ²¹	91	NR-NR	All	All	Any	68.5	67	NR
Khan 2016 ²³	97	2014-2015	NSCLC	All	Any	44	69 (39-86) §	NR
Naik 2017 ²⁴	149	2012-2014	All	All	Any	47 *	59 (18-100) §*	22 m §*
Shih 2006 ²⁵	51	NR-NR	All	All	Any	47 §	51 §*	101 d
Pickard 2007 ²⁸	50	NR-NR	All	Advanced	Chemotherapy	41	62	NR
Thongprasert 2015 ³⁰	150	NR-NR	All	III-IV	Chemotherapy or radiotherapy	52	60.9	NR
Tramontano 2015 ³²	2396	2003-2005	All	All	Any	52	NR	NR
Bendixen 2019 ³³	201	2008-2014	NSCLC	I	Surgery	50 **	66 § **	NR
Erbaycu 2018 ³⁴	266	2010-2013	All	IIIB-IV	Chemotherapy and/or radiotherapy	93.2	61.35 (35-86)	NR
Insinga 2018 ³⁶	NR	NR-NR	NSCLC	IV	Pembrolizumab and/or chemotherapy	NR	63	NR

Source	QoL response ^a	Inclusion years ^b	Lung cancer type ^c	Stage ^d	Treatment ^e	Percent male ^f	Age, mean years (range) ^g	Time of measurement, mean (range) ^h
Insinga 2019 ³⁷	NR	NR-NR	NSCLC	IV	Pembrolizumab and/or chemotherapy	NR	65	NR
Limwattananon 2018 ³⁹	135	2017-2017	NSCLC	Advanced	Chemotherapy or erlotinib	NR	NR	NR
Maximiano 2018 ⁴⁰	495	2011-2012	NSCLC	All	Any	79	63.3 (33-86)	8.1 m (0-84 m)
Mendoza 2018 ⁴¹	664	NR-NR	NSCLC	Advanced	NR	70	60.8	NR
Meregaglia 2019 ⁴²	96	2011-2014	NSCLC	III-IV	Any	68.7	61.1 (36-85)	NR
O'Kane 2019 ⁴³	519	2014-2016	All	All	Any	45	64 (29-96)	11 m (0-200 m)
Rendas-Baum 2019 ⁴⁶	43	2008-2012	All	All	NR	46.5	67.4	NR
Su 2019 ⁴⁷	104	2017-2017	All	All	Any	56 *	63.67 *	2 y *
Sullivan 2011 ⁵¹	114	2000-2003	All	All	NR	48 *	69.6	NR

Table legend:

Abbreviations: d = days; w = weeks; m = months; y = years; NR = not reported; NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer.

Superscript Arabic numerals refer to the list of references at the end of this appendix.

§ Median was reported instead of mean

* Baseline characteristics included also non-lung cancer patients

** Baseline characteristics were stratified by study arm, data from the (first) intervention group is reported here

^a How many participants were included in the health-related quality of life (HRQoL) analysis?

In case of multiple disease sites: only for the lung cancer stratum

In case of multiple disease sites: only for the lung cancer stratum

In the case of a time series, only consider the baseline N

^b Between which years were participants recruited, or from which years were data sampled?

^c What lung cancer type was included?

^d What is the stage of diagnosis of included patients?

^e Did patients receive treatment at the time of measurement of health state utility values (HSUVs)? If so, which treatments?

^f What percentage of included participants was male at baseline?

^g What is the mean age of included participants at baseline?

^h What was the mean time since diagnosis?

Supplementary Table 2b: Methodological characteristics of studies reporting community and choice-based health state utility values for lung cancer

Source	Instrument ^a	Valuation ^b	Country ^c	Tariff ^d	Matching tariff ^e	Mode of administration ^f	Longitudinal ^g	Mean or median ^h
Kimman 2015 ¹	EQ-5D	TTO	Cambodia; Indonesia; Laos; Malaysia; Myanmar; Philippines; Thailand; Vietnam	Thailand	±	Personal interview	No	Mean
Grutters 2010 ⁴	EQ-5D (3L)	TTO	Netherlands	United Kingdom	-	Self-administered	No	Both
Jang 2010 ⁷	EQ-5D (3L)	TTO	Canada	United States	-	NR	No	Mean
Schuette 2012 ¹²	EQ-5D (3L)	TTO	Germany; Austria	United Kingdom	-	Self-administered	No	Mean
Khan 2014 (a) ¹³	EQ-5D (3L)	TTO	United Kingdom	United Kingdom	+	NR	No	Mean
Khan 2014 (b) ¹³	EQ-5D (3L)	TTO	United Kingdom	United Kingdom	+	NR	No	Mean
van den Hout 2006 ¹⁵	EQ-5D	TTO	the Netherlands	United Kingdom	-	Self-administered	No	Mean
Chouaid 2013 ¹⁹	EQ-5D (3L)	TTO	Australia; Belgium; Canada; France; Italy; Turkey; the Netherlands; Sweden; United Kingdom	United Kingdom	±	Self-administered	No	Mean
Matter-Walstra 2014 ²⁰	EQ-5D (3L)	TTO	Germany	Germany ⁱ	+	NR	No	Mean
Manser 2006 ²¹	AQoL	TTO	Australia	Australia	+	Self-administered	Yes, individual	Median
Khan 2016 ²³	EQ-5D (3L) ^j	TTO	United Kingdom	United Kingdom	+	Self-administered	No	Mean
Naik 2017 ²⁴	EQ-5D (3L)	TTO	Canada	Canada ^k	+	Self-administered	No	Mean
Shih 2006 ²⁵	SF-6D	SG	China	United Kingdom	-	Self-administered	No	Mean
Pickard 2007 ²⁸	EQ-5D (3L)	TTO	United States	United States ^l	+	NR	No	Mean
Thongprasert 2015 ³⁰	EQ-5D	TTO	Thailand	Thailand	+	NR	No	Mean
Tramontano 2015 ³²	EQ-5D (3L) ^m	TTO	United States	United States	+	Personal interview	Yes, individual	Both
Bendixen 2019 ³³	EQ-5D (3L)	TTO	Denmark	Denmark	+	Self-administered	Yes, cross-sectional	Mean
Erbaycu 2018 ³⁴	EQ-5D	TTO	Turkey	United Kingdom	-	Self-administered	No	Mean

Source	Instrument ^a	Valuation ^b	Country ^c	Tariff ^d	Matching tariff ^e	Mode of administration ^f	Longitudinal ^g	Mean or median ^h
Insinga 2018 ³⁶	EQ-5D (3L)	TTO	NR	United States	NR	NR	Yes, individual	Mean
Insinga 2019 ³⁷	EQ-5D- (3L)	TTO	NR	United States	NR	NR	Yes, individual	Mean
Limwattananon 2018 ³⁹	EQ-5D	TTO	Thailand	Thailand	+	NR	No	Mean
Maximiano 2018 ⁴⁰	EQ-5D (3L)	TTO	Spain	Spain	+	NR	Yes, individual	Mean
Mendoza 2018 ⁴¹	EQ-5D (3L)	TTO	NR	United Kingdom	NR	NR	No	Mean
Meregaglia 2019 ⁴²	EQ-5D (5L)	TTO	Poland and Hungary	United Kingdom ⁿ	-	NR	Yes, individual	Mean
O'Kane 2019 ⁴³	EQ-5D (3L)	TTO	Canada	Canada	+	Self-administered	No	Mean
Rendas-Baum 2019 ⁴⁶	SF-6D	SG	United States	United Kingdom	-	NR	No	Mean
Su 2019 ⁴⁷	EQ-5D (5L)	TTO	China	China	+	Personal interview	No	Mean
Sullivan 2011 ⁵¹	EQ-5D	TTO	United States	United Kingdom	-	NR	No	Mean

Table legend:

Abbreviations: NR = Not reported; TTO = time trade-off; SG = standard gamble; VAS = visual analogue scale.

Superscript Arabic numerals refer to the list of references at the end of this appendix.

^a What instrument was used to elicit health state utility values (HSUVs)?

^b What method was used to value health-related quality of life (HRQOL) scores to HSUVs?

^c From what country were HRQoL respondents recruited?

^d What tariff was applied for valuation of HRQoL?

^e What tariff was used for valuation?

Plus sign indicates that the tariff was used of the same country or region as the participants were recruited from. In case participants were from multiple countries, the correct tariff was applied to each patient.

Plus/minus sign indicates the use of a single value set while participants were recruited from more than one country.

Minus sign indicates that a different tariff was used than the county of origin of respondents. Not applicable to vignette studies, mapping, or direct elicitation of patient's own health.

^f What was the mode of administration? (Self-administered; personal interview; or telephone interview)

^g Are HSUVs reported for multiple time points?

If yes, code as either "individual" (multiple time points measured in individual patients) or "cross-sectional" (multiple time-points assessed based on stratification of cross-sectional sample of different patients).

If measured at multiple time points but numerical values only reported at a single time-point, code as no.

^h Were HSUVs reported as mean or median?

ⁱ This study also applied direct rating to patients (VAS), and general population tariffs from France, the United Kingdom, and the European union to HRQoL data from the same sample of German patients. We included only the matching German tariff in the meta-analysis.

^j This study also performed crosswalking of EQ-5D-3L HSUVs to the EQ-5D-5L instrument. We included the original EQ-5D-3L values for analysis.

^k This study also applied the United Kingdom and United States general population tariffs to HRQoL data from the same sample of Canadian patients. We included only the matching Canadian tariff in the meta-analysis.

^l This study also applied the United Kingdom tariff to HRQoL data from the same group of US-based patients. We included only the US-based tariff in the meta-analysis.

^m This study also used the SF-6D instrument. We only include the EQ-5D HSUVs because that instrument is preferred by the National Institute for Clinical Excellence.

ⁿ This study applied tariffs from the United Kingdom and the Netherlands to HRQoL data from a combined sample of Polish and Hungarian patients. We included only the United Kingdom tariff in the meta-analysis because that tariff was applied more frequently across other studies, hence improving comparability of results.

Supplementary Table 2c: Stratification variables used in studies reporting community and choice-based health state utility values for lung cancer

Source	Stratification variables ^a
Kimman 2015 ¹	Overall
Grutters 2010 ⁴	Age; gender; initial treatment; stage; survival time; recurrence; adverse events
Jang 2010 ⁷	Overall; stage; recurrence status + treatment status
Schuetz 2012 ¹²	Overall
Khan 2014 (a) ¹³	Overall
Khan 2014 (b) ¹³	Overall
van den Hout 2006 ¹⁵	Treatment (radiotherapy regimen)
Chouaid 2013 ¹⁹	Overall; progression status; progression status + treatment (line)
Matter-Walstra 2014 ²⁰	Overall
Manser 2006 ²¹	Time since diagnosis + the following: overall; age; gender; employment; language; education; marital status; resectability; stage; histology; ECOG grade; comorbidities
Khan 2016 ²³	Overall
Naik 2017 ²⁴	Overall; stage
Shih 2006 ²⁵	Overall
Pickard 2007 ²⁸	Overall; by ECOG grade
Thongprasert 2015 ³⁰	Overall
Tramontano 2015 ³²	Time since diagnosis + the following: overall; gender; race/ethnicity; age; stage; histology; treatment (surgery; chemo; radiotherapy combinations); comorbidity
Bendixen 2019 ³³	Time since surgery + treatment (type of surgery)
Erbaycu 2018 ³⁴	Gender; marital status; occupation; smoking status; graduation; comorbidity; age; histology; stage
Insinga 2018 ³⁶	Time to death
Insinga 2019 ³⁷	Time to death
Limwattananon 2018 ³⁹	Treatment (systemic regimen); progression status
Maximiano 2018 ⁴⁰	Time since baseline
Mendoza 2018 ⁴¹	Overall
Meregaglia 2019 ⁴²	Time since baseline
O'Kane 2019 ⁴³	Age; gender; histology; brain metastasis status; smoking status; treatment (number of previous lines of chemotherapy treatment; radiotherapy; surgery); brain metastasis status
Rendas-Baum 2019 ⁴⁶	Overall
Su 2019 ⁴⁷	Overall
Sullivan 2011 ⁵¹	Overall

Table legend:

Superscript Arabic numerals refer to the list of references at the end of this appendix.

^a By what variables are utilities stratified?

Supplementary Table 3: Results of studies reporting community and choice-based health state utility values for lung cancer as well as for a control group of members of the general population.

Source ^a	Stage III-IV		All stages		Controls		Disutility
	n	mean (SD)	n	mean (SD)	n	mean (SD)	Difference cases-controls (95% CI)
Thongprasert 2015 ^{30 b}	150	0.67 (0.30)	-	-	150	0.78 (0.17)	0.11 (0.05-0.17) *
Sullivan 2011 ^{51 c}	-	-	114	0.56 (0.46)	79522	0.83 (0.42)	0.27 (0.18-0.36) *

Table legend

Abbreviations: SD= standard deviation; 95%CI = 95% confidence interval.

Superscript Arabic numerals refer to the list of references at the end of this appendix.

^a Both studies used the EQ-5D instrument, applying a time-trade-off tariff.

^b This study applied the Thai tariff to EQ-5D data from Thai persons. Controls were younger than the patient sample (mean age 44.4 years compared to 60.9 years for the patient sample).

^c This study applied the United Kingdom tariff to EQ-5D data from persons from the United States. Controls were younger than the patient sample (mean age 42.8 years compared to 69.6 years for the patient sample).

* p<.001

Supplementary Figure 1: Pooled results of studies reporting community and choice-based health state utility values for lung cancer, explicitly elicited using the EQ-5D-3L instrument, by stage

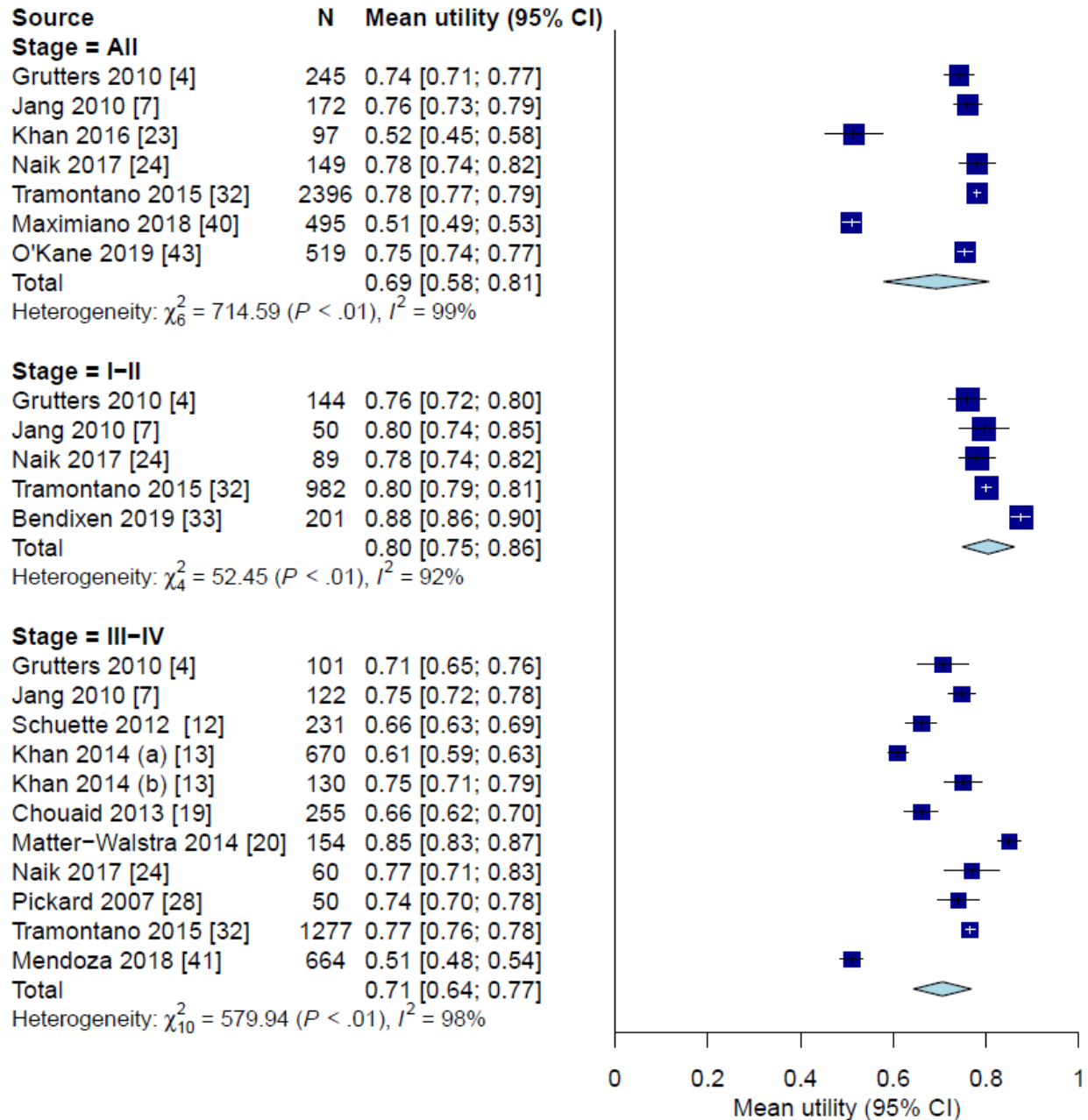


Figure legend

The size of the symbol representing the effect size in each study is relative to the weight it had in random effects meta-analysis. Not all studies included both stage I-II and stage III-IV cases. Not all studies that did include all stages stratified by stage. Arabic numerals between square brackets refer to the reference list in this appendix.

Supplementary Figure 2: Subgroup analysis of community and choice-based health state utility values for lung cancer by histology

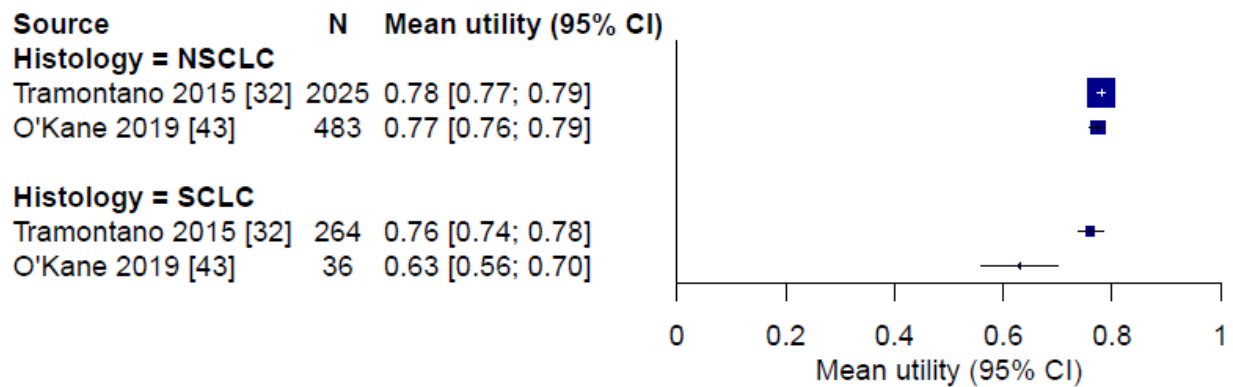


Figure legend

Arabic numerals between square brackets refer to the reference list in this appendix. Abbreviations: NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer.

Supplementary Figure 3: Subgroup analysis of community and choice-based health state utility values for lung cancer by sex

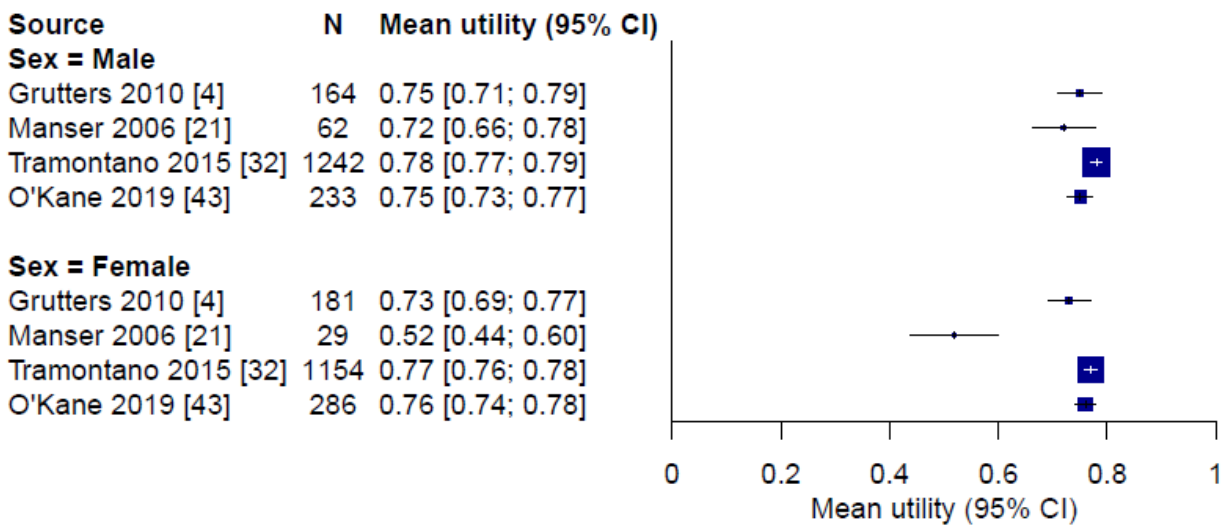


Figure legend

Arabic numerals between square brackets refer to the reference list in this appendix.

Supplementary Figure 4: Subgroup analysis of community and choice-based health state utility values for lung cancer by age

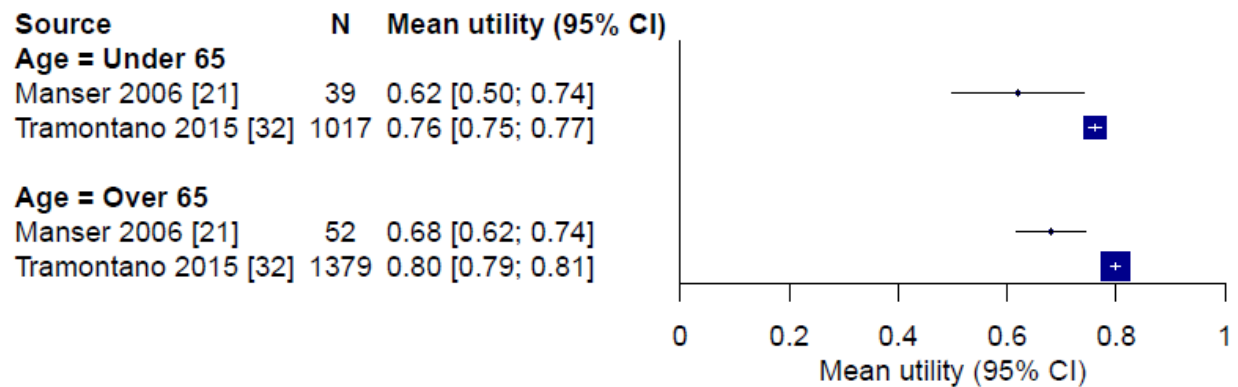


Figure legend

Please note that in Tramontano 2015, age 65 was included in the “over 65” category. In Manser 2006, age 65 was included in the “under 65” category. Arabic numerals between square brackets refer to the reference list in this appendix.

Supplementary Figure 5: Subgroup analysis of community and choice-based health state utility values for lung cancer by treatment modality

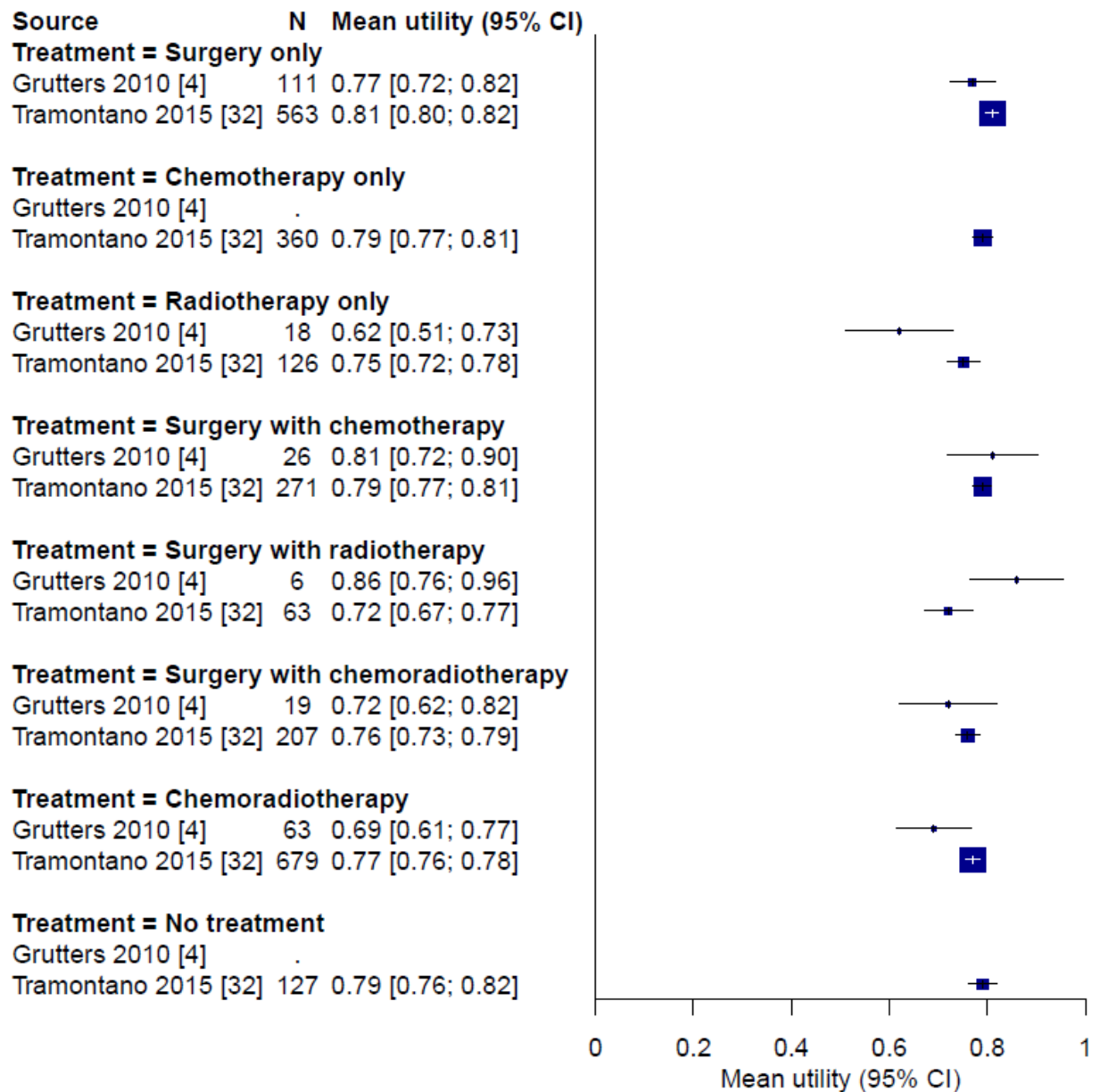


Figure legend

Manser 2006 did not report health state utility values for those receiving no treatment. In addition, Manser 2006 only included 2 patients in the stratum that received chemotherapy only. Those 2 patients had a perfect health state utility value, but no standard deviation was given. Therefore, these 2 patients were omitted from the current analysis. Arabic numerals between square brackets refer to the reference list in this appendix.

Supplementary Figure 6: Subgroup analysis of community and choice-based health state utility values for lung cancer by treatment line

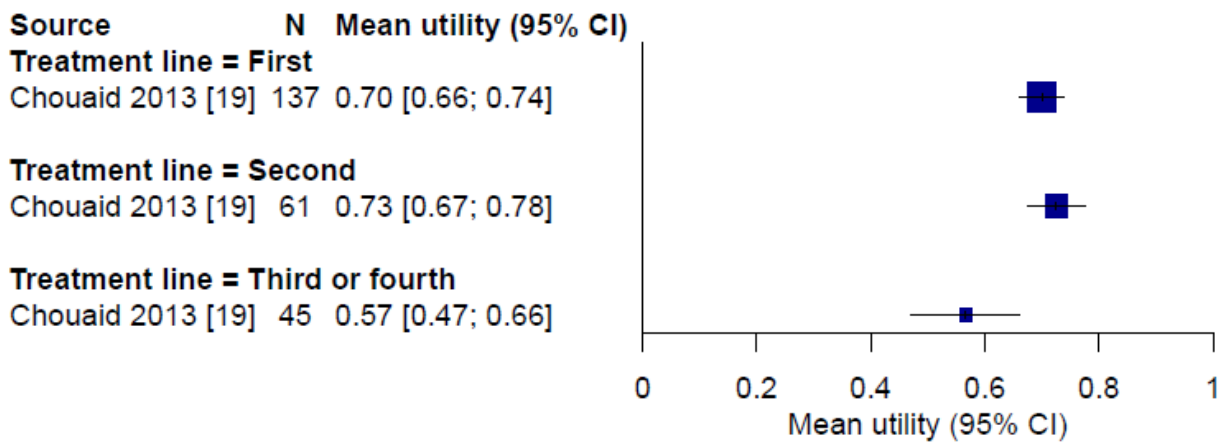


Figure legend

Arabic numerals between square brackets refer to the reference list in this appendix.

Supplementary Figure 7: Subgroup analysis of community and choice-based health state utility values for lung cancer by progression status

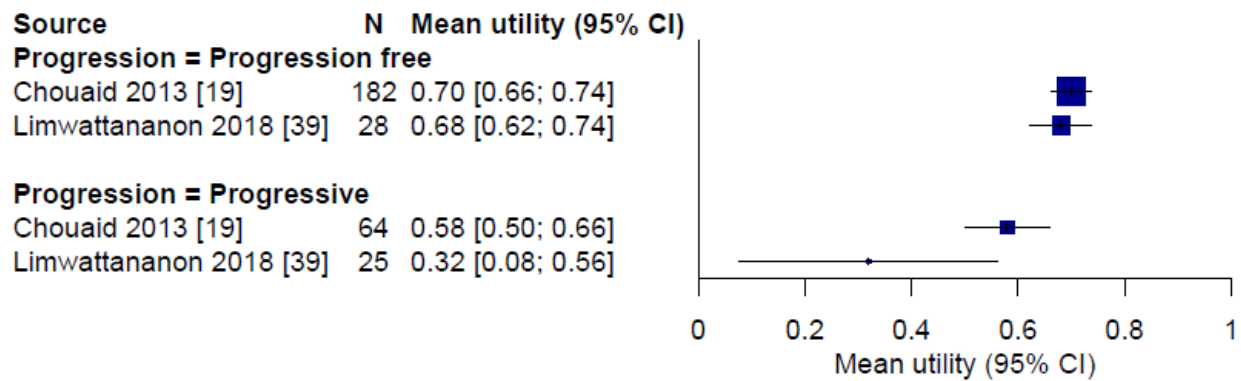


Figure legend

Both studies included metastatic non-small cell lung cancer cases and used the EQ-5D instrument. Arabic numerals between square brackets refer to the reference list in this appendix.

References

1. Kimman M, Jan S, Monaghan H, Woodward M. The relationship between economic characteristics and health-related quality of life in newly diagnosed cancer patients in Southeast Asia: results from an observational study. *Qual Life Res* 2015;24(4):937-949.
2. Yabroff KR, McNeel TS, Waldron WR, et al. Health limitations and quality of life associated with cancer and other chronic diseases by phase of care. *Med Care* 2007;45(7):629-637.
3. Lee LJ, Chung CW, Chang YY, et al. Comparison of the quality of life between patients with non-small-cell lung cancer and healthy controls. *Qual Life Res* 2011;20(3):415-423.
4. Grutters JPC, Joore MA, Wiegman EM, et al. Health-related quality of life in patients surviving non-small cell lung cancer. *Thorax* 2010;65(10):903-907.
5. Trippoli S, Vaiani M, Lucioni C, Messori A. Quality of life and utility in patients with non-small cell lung cancer. *Pharmacoeconomics* 2001;19(8):855-863.
6. Iyer S, Taylor-Stokes G, Roughley A. Symptom burden and quality of life in advanced non-small cell lung cancer patients in France and Germany. *Lung Cancer* 2013;81(2):288-293.
7. Jang RW, Isogai PK, Mittmann N, et al. Derivation of utility values from European Organization for Research and Treatment of Cancer Quality of Life-Core 30 questionnaire values in lung cancer. *J Thorac Oncol* 2010;5(12):1953-1957.
8. Chouaid C, Bassinet L, Fuhrman C, Monnet I, Housset B. Routine use of granulocyte colony-stimulating factor is not cost-effective and does not increase patient comfort in the treatment of small-cell lung cancer: An analysis using a Markov model. *J Clin Oncol* 1998;16(8):2700-2707.
9. Blackhall F, Kim DW, Besse B, et al. Patient-reported outcomes and quality of life in PROFILE 1007: A randomized trial of crizotinib compared with chemotherapy in previously treated patients with ALK-positive advanced non-small-cell lung cancer. *J Thorac Oncol* 2014;9(11):1625-1633.
10. Rauma V, Sintonen H, Räsänen JV, Salo JA, Ilonen IK. Long-term lung cancer survivors have permanently decreased quality of life after surgery. *Clin Lung Cancer* 2015;16(1):40-45.
11. Geerse OP, Hoekstra-Weebers JEHM, Stokroos MH, et al. Structural distress screening and supportive care for patients with lung cancer on systemic therapy: A randomised controlled trial. *Eur J Cancer* 2017;72:37-45.
12. Schuette W, Tesch H, Buttner H, et al. Second-line Treatment of Stage III/IV Non-Small-Cell Lung Cancer (NSCLC) with pemetrexed in routine clinical practice: Evaluation of performance status and health-related quality of life. *BMC Cancer* 2012;12:1-12.
13. Khan I, Morris S. A non-linear beta-binomial regression model for mapping EORTC QLQ- C30 to the EQ-5D-3L in lung cancer patients: A comparison with existing approaches. *Health Qual Life Outcomes* 2014;12:1-16.
14. Lamers LM, Uyl-de Groot CA, Buijt I. The use of disease-specific outcome measures in cost-utility analysis: The development of Dutch societal preference weights for the FACT-L scale. *Pharmacoeconomics* 2007;25(7):591-603.
15. van den Hout WB, Kramer GWPM, Noordijk EM, Leer JWH. Cost-utility analysis of short- versus long-course palliative radiotherapy in patients with non-small-cell lung cancer. *J Natl Cancer Inst* 2006;98(24):1786-1794.
16. Verduyn SC, Biesma B, Schramel FMNH, et al. Estimating quality adjusted progression free survival of first-line treatments for EGFR mutation positive non small cell lung cancer patients in The Netherlands. *Health Qual Life Outcomes* 2012;10:1-7.
17. Burfeind Jr WR, Jaik NP, Villamizar N, et al. A cost-minimisation analysis of lobectomy: thoracoscopic versus posterolateral thoracotomy. *Eur J Cardio-thorac Surg* 2010;37(4):827-832.

18. Huang M, Lou Y, Pellissier J, et al. Cost-effectiveness of pembrolizumab versus docetaxel for the treatment of previously treated PD-L1 positive advanced NSCLC patients in the United States. *J Med Econ* 2017;20(2):140-150.
19. Chouaid C, Agulnik J, Goker E, et al. Health-related quality of life and utility in patients with advanced non-small-cell lung cancer: A prospective cross-sectional patient survey in a real-world setting. *J Thorac Oncol* 2013;8(8):997-1003.
20. Matter-Walstra K, Klingbiel D, Szucs T, Pestalozzi BC, Schwenkglenks M. Using the EuroQol EQ-5D in Swiss cancer patients, which value set should be applied? *Pharmacoeconomics* 2014;32(6):591-599.
21. Manser RL, Wright G, Byrnes G, et al. Validity of the Assessment of Quality of Life (AQoL) utility instrument in patients with operable and inoperable lung cancer. *Lung Cancer* 2006;53(2):217-229.
22. Papatheofanis FJ. Utility evaluations for Markov states of lung cancer for PET-based disease management. *Q J Nucl Med* 2000;44(2):186-190.
23. Khan I, Morris S, Pashayan N, et al. Comparing the mapping between EQ-5D-5L, EQ-5D-3L and the EORTC-QLQ-C30 in non-small cell lung cancer patients. *Health Qual Life Outcomes* 2016;14:1-15.
24. Naik H, Howell D, Su S, et al. EQ-5D Health Utility Scores: Data from a Comprehensive Canadian Cancer Centre. *Patient* 2017;10(1):105-115.
25. Shih YCT, Wang XS, Cantor SB, Cleeland CS. The association between symptom burdens and utility in Chinese cancer patients. *Qual Life Res* 2006;15(8):1427-1438.
26. Kennedy W, Reinharz D, Tessier G, et al. Cost utility of chemotherapy and best supportive care in non-small cell lung cancer. *Pharmacoeconomics* 1995;8(4):316-323.
27. Ilonen IK, Räsänen JV, Sihvo EI, et al. Pneumonectomy: Post-operative quality of life and lung function. *Lung Cancer* 2007;58(3):397-402.
28. Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes* 2007;5:1-8.
29. Ko CY, Maggard M, Livingston EH. Evaluating health utility in patients with melanoma, breast cancer, colon cancer, and lung cancer: A nationwide, population-based assessment. *J Surg Res* 2003;114(1):1-5.
30. Thongprasert S, Crawford B, Sakulbumrungsil R, et al. Willingness to pay for lung cancer treatment: Patient versus general public values. *Int J Technol Assess Health Care* 2015;31(4):264-270.
31. Galetta D, Cinieri S, Pisconti S, et al. Cisplatin/pemetrexed followed by maintenance pemetrexed versus carboplatin/paclitaxel/bevacizumab followed by maintenance bevacizumab in advanced nonsquamous lung cancer: The GOIM (Gruppo Oncologico Italia Meridionale) ERACLE phase III randomized trial. *Clin Lung Cancer* 2015;16(4):262-273.
32. Tramontano AC, Schrag DL, Malin JK, et al. Catalog and comparison of societal preferences (utilities) for lung cancer health states: results from the Cancer Care Outcomes Research and Surveillance (CanCORS) study. *Med Decis Making* 2015;35(3):371-387.
33. Bendixen M, Kronborg C, Jorgensen OD, Andersen C, Licht PB. Cost-utility analysis of minimally invasive surgery for lung cancer: a randomized controlled trial. *Eur J Cardiothorac Surg* 2019;56(4):754-761.
34. Erbaycu AE, Goksel T, Eser E, et al. The assessment of the effect of changes in lung cancer follow-up period on the quality of life using EQ-5D questionnaire and follow data (AKAYAK-1 multicenter project). *International Journal of Hematology and Oncology (UHOD)* 2018;28(1):1-10.

35. Huang M, Lou Y, Pellissier J, et al. Cost Effectiveness of Pembrolizumab vs. Standard-of-Care Chemotherapy as First-Line Treatment for Metastatic NSCLC that Expresses High Levels of PD-L1 in the United States. *Pharmacoeconomics* 2017;35(8):831-844.
36. Insinga RP, Vanness DJ, Feliciano JL, et al. Cost-effectiveness of pembrolizumab in combination with chemotherapy in the 1st line treatment of non-squamous NSCLC in the US. *J Med Econ* 2018;21(12):1191-1205.
37. Insinga RP, Vanness DJ, Feliciano JL, et al. Cost-effectiveness of pembrolizumab in combination with chemotherapy versus chemotherapy and pembrolizumab monotherapy in the first-line treatment of squamous non-small-cell lung cancer in the US. *Curr Med Res Opin* 2019;35(7):1241-1256.
38. Kim EJ, Ock M, Kim KP, et al. Disease severity-based evaluation of utility weights for lung cancer-related health states in Korea. *BMC Cancer* 2018;18(1):1-8.
39. Limwattananon C, Limwattananon S, Waleekhachonloet O, Rattanachotphanit T. Cost-effectiveness analysis of policy options on first-line treatments for advanced, non-small cell lung cancer in Thailand. *Lung Cancer* 2018;120:91-97.
40. Maximiano C, López I, Martõn C, et al. An exploratory, large-scale study of pain and quality of life outcomes in cancer patients with moderate or severe pain, and variables predicting improvement. *PLoS One* 2018;13(4):e0193233.
41. Mendoza TR, Dueck AC, Shi Q, et al. The contribution of pain in determining the health status of cancer patients with bone metastases: A secondary analysis of data from three Phase III registration trials. *Eur J Pain* 2018;22(3):565-571.
42. Meregaglia M, Borsoi L, Cairns J, Tarricone R. Mapping health-related quality of life scores from FACT-G, FAACT, and FACIT-F onto preference-based EQ-5D-5L utilities in non-small cell lung cancer cachexia. *Eur J Health Econ* 2019;20(2):181-193.
43. O'Kane GM, Su J, Tse BC, et al. The Impact of Brain Metastases and Associated Neurocognitive Aspects on Health Utility Scores in EGFR Mutated and ALK Rearranged NSCLC: A Real World Evidence Analysis. *Oncologist* 2019;24(7):e501-e509.
44. Reck M, Brahmer J, Bennett B, et al. Evaluation of health-related quality of life and symptoms in patients with advanced non-squamous non-small cell lung cancer treated with nivolumab or docetaxel in CheckMate 057. *Eur J Cancer* 2018;102:23-30.
45. Reck M, Taylor F, Penrod JR, et al. Impact of Nivolumab versus Docetaxel on Health-Related Quality of Life and Symptoms in Patients with Advanced Squamous Non-Small Cell Lung Cancer: Results from the CheckMate 017 Study. *J Thorac Oncol* 2018;13(2):194-204.
46. Rendas-Baum R, D'Alessio D, Bjorner JB. Health-related quality of life predicted subsequent health care resource utilization in patients with active cancer. *Qual Life Res* 2019;28(4):1085-1095.
47. Su M, Hua X, Wang J, et al. Health-related quality of life among cancer survivors in rural China. *Qual Life Res* 2019;28(3):695-702.
48. Wood R, Taylor-Stokes G, Smith F, Chaib C. The humanistic burden of advanced non-small cell lung cancer (NSCLC) in Europe: a real-world survey linking patient clinical factors to patient and caregiver burden. *Qual Life Res* 2019;28(7):1849-1861.
49. Goodwin PJ, Feld R, Evans WK, Pater J. Cost-effectiveness of cancer chemotherapy: an economic evaluation of a randomized trial in small-cell lung cancer. *J Clin Oncol* 1988;6(10):1537-1547.
50. Cykert S, Kissling G, Hansen CJ. Patient preferences regarding possible outcomes of lung resection: what outcomes should preoperative evaluations target? *Chest* 2000;117(6):1551-1559.
51. Sullivan PW, Slejko JF, Sculpher MJ, Ghushchyan V. Catalogue of EQ-5D scores for the United Kingdom. *Med Decis Making* 2011;31(6):800-804.