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Running Title: Psychometric Properties of EQ-5D-5L in Asthma

A Systematic Review to Identify the Scores and Psychometric Properties of the EQ-5D-5L in Asthma

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Abstract

Introduction: The EQ-5D is the most popular generic preference-based instrument used for asthma patients. This study aims to explore the psychometric properties of the EQ-5D-5L instrument in patients with asthma and identify the EQ-5D-5L scores in these patients.

Method: PubMed, Scopus, Web of Science, Google Scholar and CEA Registry were searched with English language from 2009 until April 2020. Retrieved studies were checked against the inclusion criteria. Reference lists of the included papers were also reviewed. The quality of included articles was evaluated using Mitton checklist and the data were extracted by a reviewer and were checked by a second reviewer. Meta-analysis was done to calculate the overall scores based on type of asthma control.

Results: A total of 17 articles were included. The EQ-5D-5L scores ranged from 0.45 to 0.93 and the VAS scores ranged from 35.67 to 83.80. The EQ-5D-5L is higher in well-controlled (0.88, 95% CI: 0.81- 0.96, $P = 0.0001$) than partly controlled (0.80, 95% CI: 0.74- 0.85, $P = 0.001$) and poorly controlled asthma (0.72, 95% CI: 0.67- 0.77, $P = 0.01$). Validity in two studies was weak and, in other studies, it was moderate to strong. Responsiveness of the EQ-5D-5L, that was shown in a study, was less than other generic instruments, and reliability was adequate in only study that had been reported. Ceiling effects were between 8.30% to 35%.

Conclusion: Higher score of the EQ-5D-5L was consistent with well-controlled asthma patients and those with lower severity of asthma. The assessment of psychometric properties of the EQ-5D-5L needs further observations.

Keywords Health-related Quality of Life; Psychometric Properties; EQ-5D-5L; Asthma

Introduction

Health Related Quality of Life (HRQoL) is an important outcome for assessing and comparing the effects of health care interventions. HRQoL is a broad term that usually includes five dimensions longevity, disorders, functional status, perception, and social opportunities(1-3) HRQoL is measured by a wide range of instruments including EQ-5D(4), SF-6D(5), SF-12(6) and HUI(7).

HRQoL along with the time period a person lives in that status made the quality adjusted life years (QALYs) measure (8). For example if an intervention a) adds two years of life to a patient; and b) the quality of life during this two years is one (100 percent), then this intervention has increased two QALYs ($2 \times 1 = 2$ QALYs); and if another intervention adds 5 years of life with quality of 0.8, then the intervention has produced four QALYs ($5 \times 0.8 = 4$ QALYs). QALYs is one of the most widely used generic measures to compare the effectiveness and cost effectiveness of healthcare interventions(9). QALYs is usually used in economic evaluations and cost-utility analyses (CUA) of healthcare interventions as the main outcome. QALYs is also the main outcome for priority setting in many health technology assessment institutions such as the National Institutes of Health and Clinical Excellence (NICE) in the United Kingdom(4) and is increasingly used in the United States(10).

EuroQol five-dimensions (EQ-5D) is the most commonly used instrument for measuring HRQoL and QALYs, and it can be used in two versions: three-level EuroQol five-dimensions

(EQ-5D-3L)(11) and five-level EuroQol five-dimensions (EQ-5D-5L) (12). Previous studies have shown that the EQ-5D-5L is superior to the EQ-5D-3L in terms of ease of sensitivity, ceiling effects, differentiation, validity, and reliability(13, 14). The EQ-5D-5L evaluates and describes general health conditions in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Each dimension has 5 levels, ranging from the absence of a problem (level 1) to very severe problems (level 5). A total of 3125 possible health status is obtained by this method (5^5). In addition, the questionnaire includes a Likert scale called the Visual Analogue Scale (VAS). This health self-report scale ranges the respondents on a vertical axis from zero "the worst imaginable condition" to 100 "the best imaginable health condition"(15, 16).

Concerns about the performance and relevance of public preference-based tools have, in some cases, led to the development of a number of specific preference-based tools. However, the evidence for performance of such tools differs from that of general preferences-based tools. For example, Mulhern et al. (17) compared the specific with general tools in epilepsy and found that the specific tools were generally more sensitive than EQ-5D-3L; although both methods had strengths and limitations. For example the EQ-5D questionnaire can be used in a wide range of diseases and therefore makes it possible to compare the health-related quality of life between different diseases and communities(13).

Asthma is a common chronic inflammatory disease of the airways with features such as variable and recurrent symptoms, reversible airflow obstruction, and bronchospasm that directly affect the HRQoL. It is currently estimated that 235 million people worldwide suffer from the disease(18), and according to the urban life model predicted, by 2025, the world's population of asthma patients will increase to 100 million. Asthma has many economic and social effects in terms of the use of health care resources, absence from work and school as well as the loss of youth production(19). The aim of the present study is to provide a catalog of the EQ-5D-5L scores obtained for asthmatic patients derived from the previous studies and explore the psychometric properties of the EQ-5D-5L questionnaire in patients with asthma.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used as a basis for the overall study approach (20).

Search Strategy

PubMed, Scopus, Web of Science, Google Scholar and CEA Registry were searched from 2009 to April 2020 using Mesh terms and keywords. The search strategy followed the combination of these terms: (Asthma OR “Bronchial Asthma” OR (Asthma AND Bronchial)) AND ((EQ5D) OR (EQ-5D) OR (Euroqol) OR (EuroQol-5D) OR (EuroQol-5D-5L) OR (EQ5D5L) OR (EQ-5D-5L) OR (EQ5D-5L) OR (EQ-5D5L)).

In order to screen the articles, all citations were imported to the EndNote 8. After removing the duplicates, titles, abstracts and, where necessary, full texts of the retrieved papers were screened by a reviewer and were double-checked by a second reviewer. The reference lists of the included studies were also manually checked to identify any further relevant studies.

Inclusion and Exclusion Criteria

Inclusion criteria were English papers that evaluated the health-related quality of life in adult asthmatic patients by EQ-5D-5L questionnaire. Exclusion criteria were studies that involved any type of respiratory diseases other than asthma, not adult patients, use of three-level EQ-5D questionnaire, and use of other measures to identify HRQoL.

Quality Appraisal, Data Extraction

The quality of included articles was assessed by the Mitton checklist(22). This checklist is composed of 5 questions of research literature, method, population and sample, data collection and analysis of results. Each item is assessed by a score from 0 to 3. Based on the checklist, each study is divided into two levels: low quality (<10) and high quality (10-15). A structured data extraction form was used to extract the data. Data was extracted by a reviewer and was double-checked by a second reviewer (SA, MSH). If there was any disagreement between the two reviewers, a third reviewer (AAS) joined them to resolve any disagreements. The EQ-5D5L values that were not in the 0 to 1 range were removed from the study. In studies that reported standard deviation, the SDs were included in the relevant charts. The properties of the questionnaire, including validity, reliability, ceiling effect and dimensional considerations, were reported in a separate table. The extracted data were compared and analyzed using narrative methods and tables. Subgroup analysis was performed when it was necessary or helpful.

Data Analysis

The evidence of the psychometric properties (content validity, construct validity, reliability and responsiveness) of the EQ-5D-5L, which had been previously reported in the studies of patients with asthma, was presented in this study. Construct validity is usually considered by two forms of convergent validity and discriminant validity. Convergent validity is the degree that two measures are correlated to each other as theoretically expected and discriminant validity refers to the degree that measures are not related to each other as theoretically expected (23). Content validity is confirmed when an instrument can measure the significant aspects of concepts that instrument purports to measure (24). Reliability is the extent to which a measure yields the similar value each time it is administered(25).

In addition, a meta-analysis was performed to estimate the overall EQ-5D-5L values according to subgroups of patients based on asthma control. Since the number of studies was small and there was a potential heterogeneity, we only conducted sub-group analyses for the EQ-5D-5L values of “well-controlled”, “partly controlled”, and “poorly controlled” using random effect model and overall utility value with 95% confidence interval.

Results

A total of 1850 articles were retrieved from PubMed, Scopus, Web of Science, CEA Registry and Google Scholar. Then, duplicate articles were removed. Screening the titles and abstracts was performed based on inclusion and exclusion criteria. For example, studies that involved any type of respiratory diseases other than asthma, or used three-level EQ-5D or other questionnaires except EQ-5D-5L were removed. 114 papers were remained and their full text were checked. 58 of these articles were excluded because they used the 3-level questionnaire, 2 articles used the EQ-5D-Y instrument, 10 articles did not report the type of EQ-5D questionnaire and 27 articles did not study adult asthmatic patients; therefore a total of 17 articles were included and were critically appraised by the Mitton Checklist. All of the included articles gained enough score (above 10).

The majority of included studies were conducted in the UK, France and the USA. The majority of these studies were cross-sectional ($n = 12$, 80%), followed by cohort ($n = 1$, 6.6%), qualitative interview ($n = 1$, 6.6%) and RCT ($n = 1$, 6.6%). Patient age ranged from 16 to +65 years. The studies included patients with mild to severe asthma. The study sample size ranged from 19 patients to 7820 patients. (Table 1)

The EQ-5D-5L ranged from 0.45 to 0.93. The highest value was observed in UK in patients with well-controlled asthma (well-controlled patient) and the lowest quality was reported in England in patients with severe asthma. The VAS scores were in the range of 35.67 and 83.8. The highest quality of life observed by VAS scores were in Italy and the lowest one was reported from the UK. One study reported the value of each EQ-5D-5L dimension separately, the highest value was related to self-care dimension and the lowest value was related to pain-discomfort and anxiety-depression; and EQ-5D-L scores of women were worse than men in all dimensions. (Table 2)

The lowest EQ-5D-5L scores that were measured by EQ-5D-5L instrument was related to patients with severe asthma and the highest value was related to patients whose asthma were well controlled. (Figure 1)

The lowest EQ-5D-5L scores that were measured by VAS was related to the patients with severe asthma and the highest value was related to patients whose asthma was well controlled. (Figure 2)

Five studies reported the validity of EQ-5D-5L instrument for measuring HRQoL of asthmatic patients (Table 3). Three of them did not report a high validity (28-30). While one study reported that the instrument had a good construct validity, distribution, and reliability(31); and one study reported a moderate to strong convergent validity (32); other studies found low validity for patients with severe asthma(33), low acceptability and content validity(34), and lower sensitivity and validity compared to instruments such as SF-6D, HUI3, 15 D, QWB and AQoL –8 D(30). Three studies (31, 33, 34) showed a ceiling effect about 8.30%, 26.5% and 35%. In two studies no floor effect was observed(31, 33), and another study did not report it(34).

Seven studies examined different dimensions of the questionnaire (Table 3). Whalley et al. (29) reported that the EQ-5D-5L dimensions were partially or generally irrelevant to determine the quality of life of patients with asthma, because either of these dimensions were not related to the patients disease experience or these concepts were not properly expressed. In this study, it was shown that the dimensions of mobility and self-care were two irrelevant dimensions for most patients. Moreover, the two dimensions of pain and anxiety were more relevant in asthma than pain and depression, but because they were combined, it makes it difficult for patients to respond. Two studies reported that some of the important concepts in the dimensions of this questionnaire have not been considered, which limits the use of this questionnaire for asthmatic patients(29, 35). These

include asthma triggers, asthma symptoms, sleep and other anxiety or depression symptoms(29), and medication side effects, relationship/social life, sleep deprivation, family relationship, and work limitation(35). Richardson et al. (30)reported that in general, this questionnaire was more sensitive in the pain dimension and less sensitive in psychosocial dimension compared to other Multi-Attribute Utility Instruments (MAUIs). Whalley et al.(29) considered the usual activity dimension to be the most relevant dimension compared to other dimensions to assess the quality of patients with asthma. Hernandez et al.(31) showed that patients reported higher health problems compared to other dimensions for usual activities, pain/discomfort, and anxiety/depression. Younger women, on the other hand, reported higher mobility. Johnson et al.(36)reported that in patient with mild and moderate exacerbation, the most report was pain/discomfort dimension, and Lucas et al. (37)showed that the most reported problems for patients with severe asthma were related to mobility, self-care, and usual activities. Bittner et al.(34) pain/discomfort was selected by patients more than other dimensions.

Whalley et al. (29)showed that the EQ-5D-5L questionnaire has limitations in measuring the quality of life of patients, especially patients with mild asthma, and using this questionnaire in health technology assessment decision models can lead to undervalue of the benefits of effective interventions. Crossman-Barnes et al. (32)recommend using this questionnaire for use in asthma-related economic assessment studies.

Subgroup analyses

Based on type of asthma control, subgroup analyses showed that the pooled score of the EQ-5D-5L was higher in well-controlled (0.88, 95% CI: 0.81– 0.96, $P = 0.0001$) than partly controlled (0.80, 95% CI: 0.74– 0.85, $P = 0.001$) and poorly controlled asthma (0.72, 95% CI: 0.67– 0.77, $P = 0.01$) (Figure 4).

Discussion

EQ-5D is the most widely used generic instrument to measure HRQoL in different patient groups such as COVID-19(38), and cancers(14, 39). The present review confirms that EQ-5D-5L has been commonly used as a generic instrument for measuring HRQoL in patients with asthma, therefore, assessment of psychometric properties of the EQ-5D-5L and its utility values is useful for evaluating the outcomes of health interventions. This review found that the EQ-5D-5L scores of patient with asthma ranged from 0.45 to 0.93 when the EQ-5D-5L was used, and from 35.67 to 83.8 when the VAS was used. This is similar to the results of studies that used EQ-5D-3L. For example Pickard et al.(40) found that HROL ranged from 0.042 in patients with severe asthma to 0.93 in patients with good control. Hazell et al.(41) also found that the mean HRQoL of patients was 0.78 when EQ-5D-3L was used and 74.58 when the VAS was used. This wide range of HRQoL might have several reasons including severity of disease, level of disease control, and whether the HRQoL has been measured at the time of asthma crisis or when the diseases has been under control(31, 42–44). Chen et al. (42) found that HRQoL was dependent on the severity of disease and ranged from 0.73 to 0.86 when using EQ-5D-3L and from 57.4 to 73.8 when using the VAS.

Few studies have explored the validity of EQ-5D questionnaire for measuring HRQoL in asthmatic patients(40). These studies have suggested that EQ-5D can accurately measure HRQoL of patients with different severity and control level of asthma (31, 42–44). Whalley et al. (29)have reported that mobility and self-care were relatively less relevant compared to other dimensions of the EQ-5D questionnaire for assessing HRQoL in patients with asthma. Lucas et al. (37)showed that patients with severe asthma had more severe problem in mobility, self-care, and usual activity dimension. Hernandez et al.(31) also reported that young women with asthma had the most severe

problem with mobility dimension. Whalley et al. (29) reported that the most relevant dimension of EQ-5D was usual activity; and Lucas et al. (37) showed that the most relevant dimensions of EQ-5D were usual activity, mobility and self-care. Several studies have reported the presence of ceiling effect in EQ-5D-3L questionnaire, especially in patients with mild asthma; however, their reported ceiling effect has been at an acceptable level (31, 32, 45). Other studies have suggested that EQ-5D has limitation in capturing some aspects of asthma such as relationship, social life, work limitation and sleep; however, it is argued that all these aspects of the disease are indirectly reflected in EQ-5D (29, 35).

There are a wide range of specific and general instruments for measuring HRQoL in any disease including asthma. It seems that clinicians are more comfortable with using specific instruments compared with general questionnaires. This is perhaps because they assume that the specific instruments might be more valid and reliable. However, using specific instruments significantly limit the ability to compare the effect of healthcare interventions among different diseases. On the other hand, it is very important for policy makers to efficiently allocate limited healthcare resources between different healthcare programs. Health Technology Assessment is a standard technique that is very commonly used for this purpose. Generic instruments like EQ-5D is very helpful for measuring and comparing the HRQoL as a common outcome of different healthcare programs. Crossman et al. (32) have recommended the use of this questionnaire in HTA studies; although others (29) have suggested that this instrument should be used with caution and with considering its limitations especially in mild asthma.

Conclusion

This review showed that EQ-5D-5L has commonly used as a generic instrument for measuring HRQoL in patient with asthma. Using this instrument, the HRQoL of patients varied widely as expected depending on severity of disease, level of disease control, and other factors. Although the result of literature review showed that the EQ-5D-5L was relatively valid and reliable for identifying HRQoL in asthma patients, the assessment of psychometric properties of the EQ-5D-5L needs further observations.

Conflict of interest

the authors declare no conflict of interest.

Compliance with Ethical Standards

This report is part of a PhD project that was approved by the ethics committee of Tehran University of Medical Sciences, approval number: IR.TUMS.VCR.REC.1398.058

Finding

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Table 1: Description of included studies that used EQ5D5L to identify HRQL in adult patients with asthma.

study ID	country	study design	Study population	Age (SD), (mean $\pm$ SD)	Sample size= (women , Men)
Hernandez, G. / 2018	France	Cross-sectional	Patients with persistent asthma	18-40 (30.3 $\pm$ 6.7)	222= (136 , 86)
Yorke, J./ 2016	England	randomized controlled parallel group trial	Patients with severe asthma and a clinically significant diagnosis of anxiety and/or depression	20-70 (46.7)	44= (19, 25)
Bittner, C. / 2016	German	cross-sectional	The bakers with allergic occupational asthma and with the available baseline level of IgE (f4, f5)	47.2 $\pm$ 7.7	19
Mitchell, P. M. / 2015	Australia, Canada, UK , USA.	cross-sectional online survey		≥ 18 (18 to +65)	579 (399,180)
Hyland M. E/ 2018	UK	cross-sectional	Patients with severe asthma	≥ 16	96
Terzano, C. / 2012	Italy	cross-sectional phase and a 12-month prospective phase (follow up)	patients who had uncontrolled or partly controlled asthma	cross-sectional phase	46 (15) 1017 (674,343)
				12-month follow-up	739
Whalley, D. / 2018	UK	Qualitative interview	Patients who had a self-reported physician-diagnosis of asthma and used at least one controller asthma medication,	20 to 57	40 (25,15)
Richardson, J., a; 2014 & b; 2015	Australia, Canada, Germany, Norway, UK & US	cross-sectional online survey		≥ 18	856 (548,308)
Hernandez, G/2019	France & UK	Cross-Sectional Study online survey		18-40	279 (169,110) French: 222 (79.6) UK: 57 (20.4)
Efthymiadou, O. /2018	International patient population (47 countries)	cross-sectional online survey			24
Phaedra/ 2019	US	internet-based cross-sectional surveys		48.2 (16.7)	302= (184,118)
Crossman-Barnes/ 2019	UK	prospective observational cohort study	patients who had an asthma-related crisis event (accident and emergency attendance or hospital admission)	≥ 18	120
Lanario/ 2020	UK	cross-sectional survey	patients with severe asthma	≥ 16	96
Lucas/ 2020	France	cross-sectional survey	patients with severe asthma	42.2 $\pm$ 16.4	96= (41, 55)
Lee/ 2020	US	cross-sectional Survey		42.4	7820

Table 2: Summary of EQ-5D-5L values, VAS values by EQ5D5L dimensions.

study	different levels of medicine dose/ disease		EQ-5D-5L Index mean (SD)	VAS mean (SD)	Each dimension				
					MO	SC	UA	PD	AD
Hernandez, G. / 2018			0.83 (0.17) Women: 0.81 (0.18) Men: 0.86 (0.15)	77.3 (16.5) Women: 76.1 (18.5) Men: 79.2 (12.4)	78 Wo men : 7.25 Men : 89.5	99.1 Wo men : 98.6 Men : 100	77.5 W: 75.8 Men: 80.25	38.65 W: 30.8 M: 51.1	45.9 W: 41.9 M: 52.3
Yorke, J./ 2016	G-CBT (Group - Cognitive Behavior al Therapy)	Study beginning	0.49 (0.26)	47.2	-	-	-	-	-
		After Week 16	0.53	52.7					
	Control (usual care only)	Study beginning	0.45 (0.32)	50.0					
		After Week 16	0.47	44.5					
Bittner, C./2016			-	81.1 ± 11.9	-	-	-	-	-
Mitchell, P. M. / 2015	severity category	total	0.749	-	-	-	-	-	-
		Mild	0.844						
		Moderate	0.652						
		Sever	0.475						
Hyland M. E/ 2018	prednisol one dose ranges mg·day – 1 (CI)	0	2.01 (1.79-2.23)	65.4					
		1-9	1.69 (1.24-2.14)	70.47					
		10	2.69 (2.14-3.23)	55.77					
		>10	3.11 (2.48-3.75)	35.67					
Terzano, C. / 2012	Asthma control	cross- sectional phase	Total	0.72 (0.2)	-	-	-	-	-
			Partly controlled	0.75 (0.2)					
			Uncontrol led	0.69 (0.2)					
		12-month follow-up	Total	0.87 (0.19)					
			Controlled	0.91 (0.13)					
			Partly controlled	0.71 (0.23)					
			Uncontrol led	0.62 (0.30)					
Hernandez, G/2019	Total		French: 0.83 (0.19) UK: 0.88 (0.14)	-	-	-	-	-	-
	asthma control	Well-controlled	UK: 0.93 (0.10) French: 0.91 (0.13)	81.65 (13.80)	-	-	-	-	--
		Intermediate- controlled	UK: 0.87 (0.11) French: 0.81 (0.15)	79.18 (11.92)	-	-	-	-	-
		Not well-controlled	UK: 0.78 (0.19) French: 0.69 (0.24)	68.39 (20.23)	-	-	-	-	-
Efthymiadou, O.2018			0.76	-					
Phaedra/ 2019			-	74.2 (16.0)					
Crossman- Barnes/2019			0.635 (0.274)	45.7 (19.3)					

Lanario/ 2020			2.18	62.02 (57.31– 66.74)					
Lucas/ 2020			0.68 ± 0.26	63.3 ± 18.3					
Lee/ 2020	asthma control	Well-controlled	0.81						
		partly controlled	0.76						
		poorly controlled	0.71						

MO=MOBILITY; SC= SELF-CARE; UA= USUAL ACTIVITIES; PD= PAIN/DISCOMFORT;
AD=ANXIETY/DEPRESSION.

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Table 3: psychometric properties of EQ-5D5L questionnaire in measuring quality of life of asthma patients.

study	Validity, reliability, Sensitivity	Ceiling effect, floor effect	Dimensions considerations	Other consideration
Hernandez, G. / 2018			Patient reported high problems in usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD). The youngest women reported more problems in mobility (MO)	
Bittner, C./2016		Ceiling effect was Approximately 35%.	The dimension for which problems were most frequently reported was pain/discomfort (PD)	
Hyland M. E/ 2018	This measure might not be valid for assessing the quality of life in patients with severe asthma.			
Whalley, D. / 2018	The measure failed to meet basic standards for acceptability and content validity as a measure to assess the impact of asthma.		MO : the mobility dimension did not relate to patient experiences with asthma. SC : Self-care was not a relevant issue for a majority of participants, either in living with asthma day to day or during an attack. UA : The usual activity was the most important dimension. it was a relevant and central issue in patient asthma. PD : for most participants, discomfort was a more relevant concept than pain; and the combination of pain and discomfort in a single question had implications for how participants responded. AD : anxiety generally was considered to be the more relevant issue. Anxiety and depression combination in a single item was problematic. Concepts reported as missing from the EQ-5D-5L included asthma triggers, asthma symptoms, emotions other than anxiety or depression, and sleep	The EQ-5D has limitations in asthma, and especially so in mild asthma. So use of EQ-5D in health technology assessment decision models could undervalue the benefit of effective interventions
Richardson, J., 2014	the sensitivity and validity of EQ-5D-5L was less than average of other MAUI instrument sensitivity and validity investigated in this study			
Richardson, J., 2015			The EQ-5D is more sensitive to pain than the SF-6D, HUI 3, 15 D, and AQoL-8D for asthma and other disease. the EQ-5D is less sensitive to the psychosocial dimensions than the SF-6D, 15 D, and AQoL-8D for asthma and other disease It is less sensitive than the HUI 3 to senses and happiness for asthma and other disease	
Hernandez/2019	It showed good construct validity and adequate distribution and reliability.	The floor effect was null, and the ceiling effect was 26.5%. The new EQ-5D-5L questionnaire has an acceptable ceiling effect		The completion of the EQ-5D-5L by most of the Web-based survey respondents supports the feasibility of this administration form.
Efthymiadou,			The most common aspects not captured by the EQ-	

O. /2018			5D-5L are medication side effects, relationship/ social life, sleep deprivation, family relationship, and work limitation. about half of the asthmatic patients considered that the tool didn't capture all the important wellbeing aspects that added a significant burden to their HRQL So EQ-5D-5L missed important health aspects	
Phaedra/ 2019			The greatest perceived impact of mild and moderate exacerbations was pain/discomfort (PD)	
Crossman-Barnes/ 2019	It shows moderate to strong correlations for convergent validity. No statistical significance was observed for discriminative validity It is well correlated and sensitive to change for participants who have had an asthma-related crisis event.			Authors consider the AQL-5D and the EQ-5D-5L for use in economic evaluations for asthma studies
Crossman-Barnes/ 2019		Floor effects: 0.00% The new EQ-5D-5L questionnaire has an acceptable ceiling effect (8.30%)		
Lucas/ 2020			Patient with severe asthma more frequently reported problems with mobility (MO), self-care (SC) and usual activities (UA).	

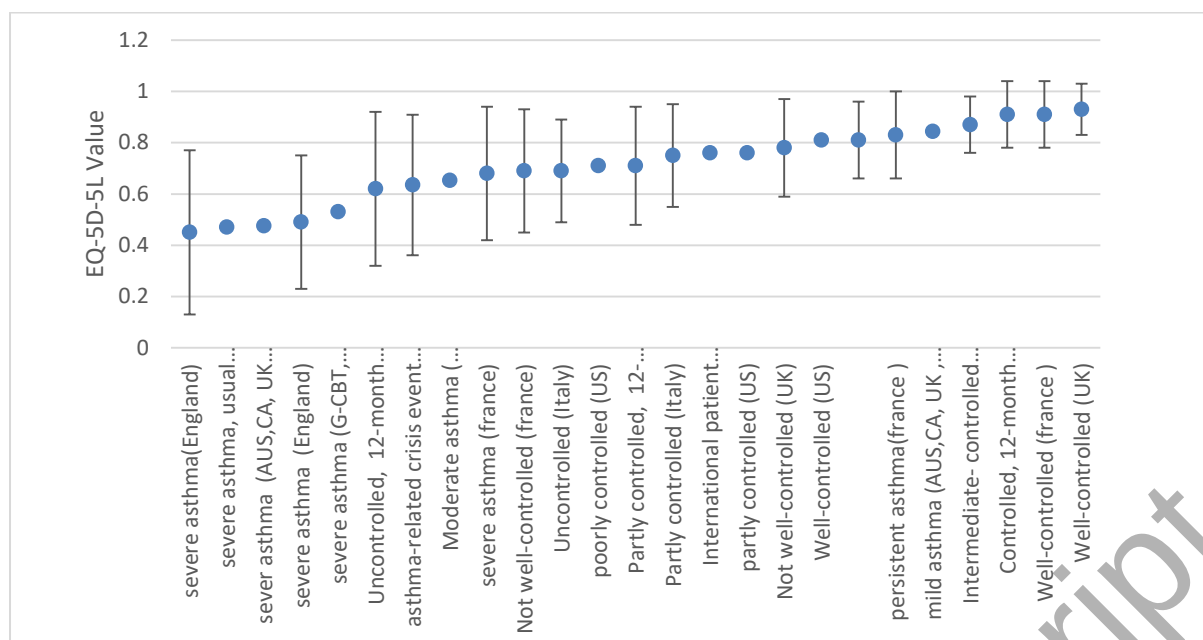


Figure 1: HRQL measured through EQ-5D-5L instruments by study population

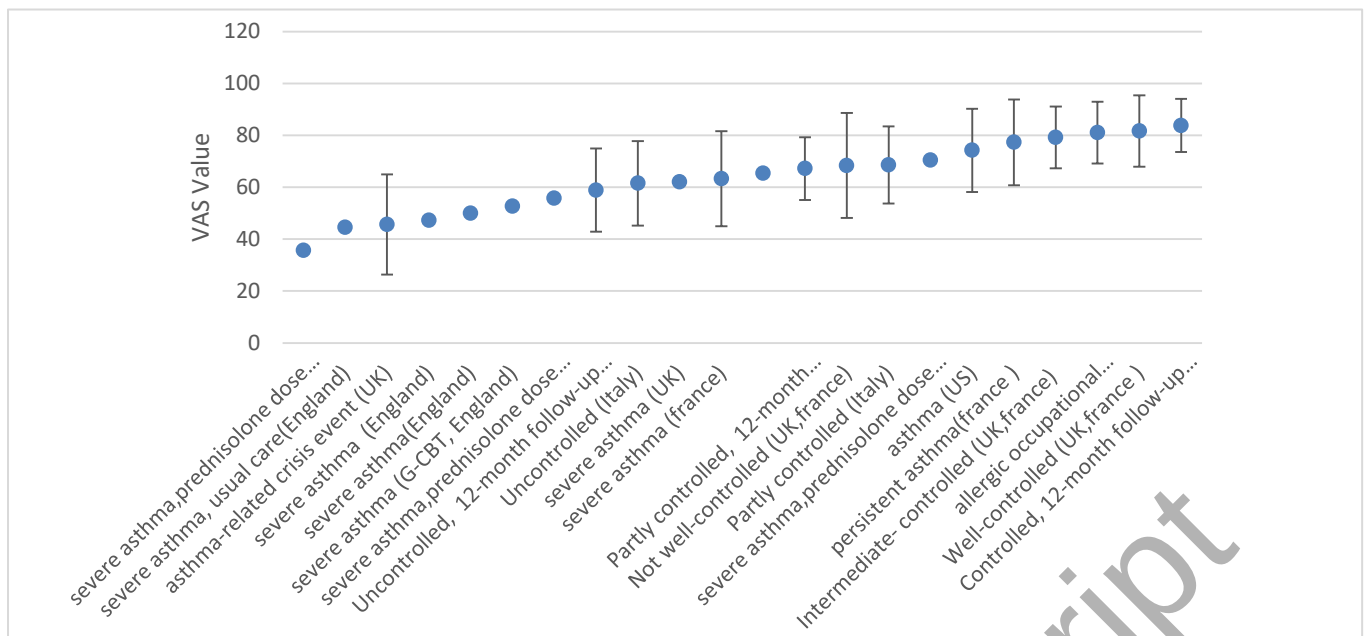


Figure 2: HRQL measured through VAS instruments by study population

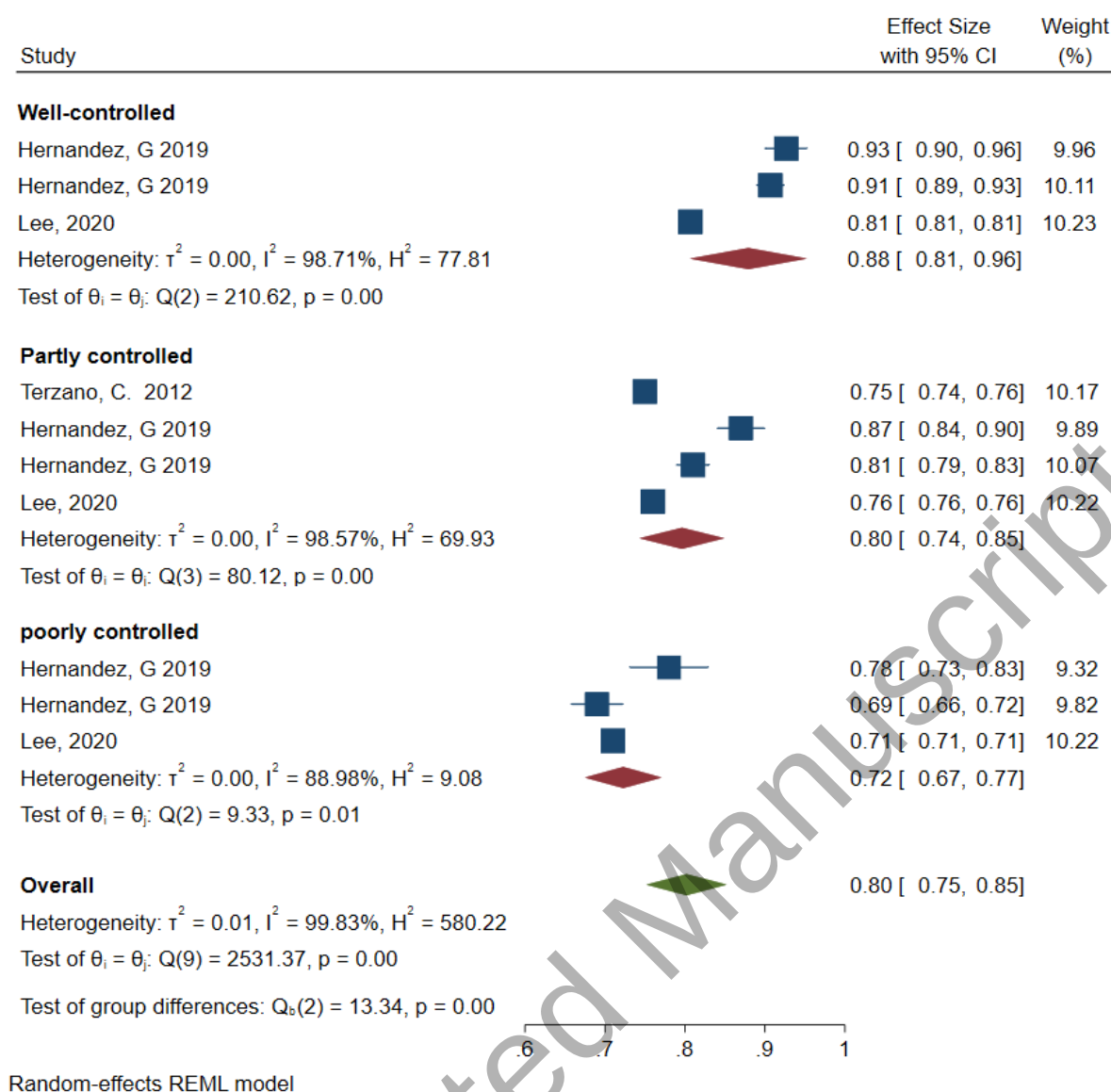


Figure 3. Subgroup analyses based on type of asthma control