The Relationship Between Asthma Control Questionnaire Scores and Exacerbation Risk, Resource Utilization, and Utility Values: an Analysis From the CAPTAIN Trial

CO95

Herring WL,[1] Shen Q,[2] Zhang Y,[1]* Martin A,[3] Otiker T,[3] Zhang S[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States; [2]GSK, Collegeville, Pennsylvania, United States; [3]GSK, Brentford, Middlesex, United Kingdom

*At time of study

Introduction

Despite the availability of effective treatment options, asthma control remains an unmet medical need worldwide.[1]

Poor control of asthma symptoms is associated with increased risk of exacerbations, increased levels of healthcare resource utilization (HCRU), and reduced health-related quality of life.[2–4]

Objective

The objective of this post-hoc analysis of the Phase IIIA CAPTAIN asthma study was to quantify the relationship between Asthma Control Questionnaire (ACQ) scores and exacerbation rates, HCRU, and health utility values in adults with moderate-to-severe asthma, for use in economic modeling analyses.

Methods

The CAPTAIN study

CAPTAIN was a 24- to 52-week, Phase IIIA, randomized controlled trial that investigated the efficacy and safety of the single-inhaler triple combination of fluticasone furoate, umeclidinium and vilanterol (FF/UMEC/VI) compared with FF/VI in adult patients (≥18 years) with asthma that is inadequately controlled on medium–high-dose inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA).[5]

In that parallel-group study, patients received either once-daily FF/VI (100/25 mcg or 200/25 mcg) or FF/UMEC/VI (100/31.25/25, 100/62.5/25, 200/31.25/25, or 200/62.5/25 mcg) administered via Ellipta dry powder inhaler.

ACQ-7 was measured at screening, enrollment, and randomization, and at each study visit (Weeks 4, 12 and 24, 36 and 52).

CAPTAIN study design, methods, and results have been reported in full elsewhere.[5]

Moderate and severe exacerbation rates

Negative binomial models were estimated for annualized moderate and severe exacerbation rates using time-varying ACQ-7 score, pre-study ICS dose, and severe exacerbation history as covariates; the correlation between multiple observations from the same patient was adjusted using a generalized estimating equation.

Other potential covariates considered included: treatment terms (i.e., six treatment groups, and pooled by FF 100 and 200), pre-study ICS dosage at screening (medium, high), severe asthma exacerbations in the previous year (0, ≥1), and ACQ-7 measurement visit; the final covariates were selected based on the quasi-likelihood under the independence model criterion.

HCRU outcomes

Poisson models were estimated for unscheduled HCRU rates (number of telephone calls, number of office/practice visits, number of emergency room visits, number of urgent care/outpatient visits, and rescue medication use) using time-varying ACQ-7 score as a covariate.

The correlation between multiple observations from the same patient was adjusted using a generalized estimating equation.

Utility values

For the utility analysis, Asthma Quality of Life Questionnaire (AQLQ) responses were mapped onto Asthma Quality of Life–5 Dimensions (AQL-5D) responses, to which a published time trade-off valuation was applied.[6]

The relationship between ACQ-7 score and utility values was assessed using fractional polynomial modeling (up to second order). ACQ-7 score was the independent variable with powers from the set (-2,-1,-0.5,log,0.5,1,2,3).

The best first- and second-order models were identified based on model log likelihood values; the final model was selected based on a chi-square test comparing the likelihood values of the two models.

Results

CAPTAIN study population

Patient-level data from the CAPTAIN study intention-to-treat (ITT) population, irrespective of treatment assignment, were included in the analysis (N=2436).

Demographics and baseline characteristics are reported in **Table 1**.

Table 1. Demographics and baseline characteristics of the CAPTAIN ITT population

	Total* (N=2436)
Demographics	
Age, years, mean (SD)	53.2 (13.11)
Male, n (%)	922 (38)
Body mass index, kg/m², mean (SD)	29.35 (6.64)
Baseline characteristics	
Total number of exacerbations in 12 months prior to screening, n (%) 0 1 ≥2	 364 (15) 1390 (57) 682 (28)
Pre-study ICS dose – medium dose†, n (%)	1621 (67)
ACQ-7 score‡ mean (SD) median (min-max)	*n=2383* 2.12 (0.70) 2.14 (0.14–4.71)

*ITT population, including all six treatment groups; †at screening; medium dose defined as >250 to ≤500 mcg/day fluticasone propionate (or equivalent); ‡at randomization; Note: n=patients with available data.
SD, standard deviation.

Moderate and severe exacerbation rates

Covariates and coefficients for the negative binomial models for predicting moderate and severe exacerbation rates are presented in **Table 2**.

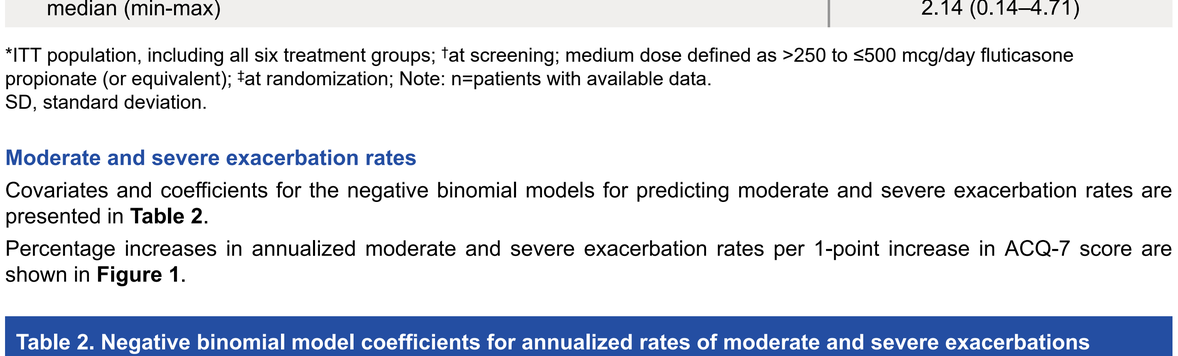
Percentage increases in annualized moderate and severe exacerbation rates per 1-point increase in ACQ-7 score are shown in **Figure 1**.

Table 2. Negative binomial model coefficients for annualized rates of moderate and severe exacerbations

Outcome	Intercept	ACQ-7 score	Pre-study ICS: Medium	Exacerbation History: Yes
Moderate exacerbation				
Coefficient point estimates	–1.32	0.30	–0.43	0.04
Lower CI	–1.61	0.17	–0.63	–0.17
Upper CI	–1.03	0.42	–0.22	0.25
Severe exacerbation				
Coefficient point estimates	–2.01	0.42	–0.22	0.55
Upper CI	–2.34	0.30	–0.44	0.30
Lower CI	–1.68	0.54	–0.01	0.81

CI, confidence interval.

Figure 1. Increase in annualized rate of moderate and severe exacerbations per 1-point increase in ACQ-7 score



HCRU outcomes

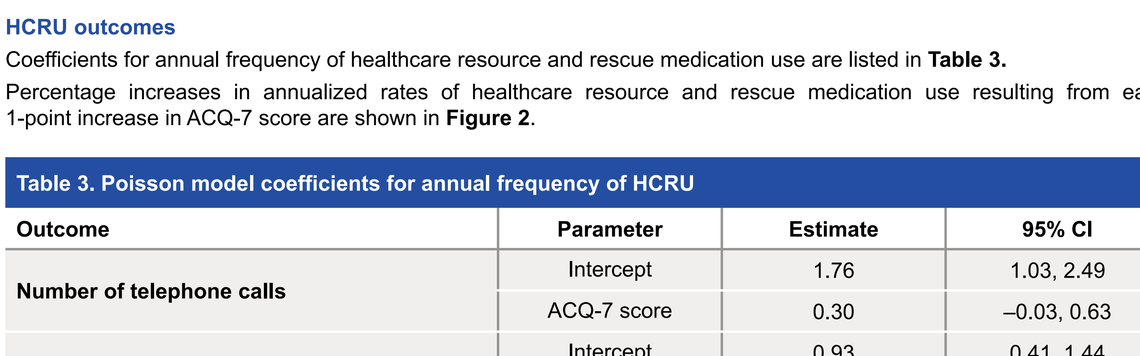
Coefficients for annual frequency of healthcare resource and rescue medication use are listed in **Table 3.**

Percentage increases in annualized rates of healthcare resource and rescue medication use resulting from each 1-point increase in ACQ-7 score are shown in **Figure 2**.

Table 3. Poisson model coefficients for annual frequency of HCRU

Outcome	Parameter	Estimate	95% CI
Number of telephone calls	Intercept	1.76	1.03, 2.49
	ACQ-7 score	0.30	–0.03, 0.63
Number of office or practice visits	Intercept	0.93	0.41, 1.44
	ACQ-7 score	0.29	–0.09, 0.68
Number of emergency room visits	Intercept	–1.82	–3.31, –0.32
	ACQ-7 score	0.64	0.02, 1.25
Number of urgent care or outpatient visits	Intercept	–0.92	–1.77, –0.07
	ACQ-7 score	0.34	–0.05, 0.74
Number of puffs of rescue medication	Intercept	4.29	4.16, 4.42
	ACQ-7 score	0.83	0.77, 0.89

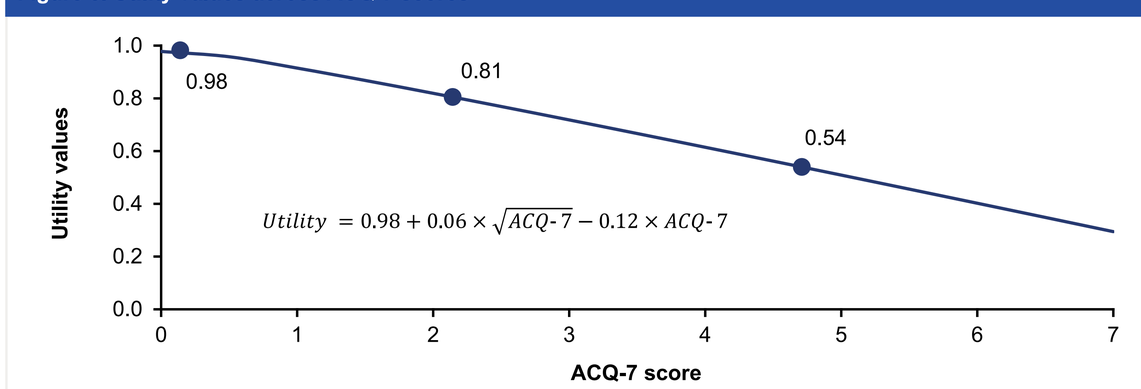
Figure 2. Increase in annualized rate of HCRU per 1-point increase in ACQ-7



Utility values

Utility values from the AQLQ/AQL-5D analysis ranged from 0.98 to 0.54 across ACQ-7 scores (0.14–4.71) observed at baseline (**Figure 3**).

Figure 3. Utility values across ACQ-7 scores



Filled circles represent utility scores at the minimum, median, and maximum baseline ACQ-7 score. Coefficient estimates (95% CIs) for intercept, square root of ACQ-7, and ACQ-7 were 0.98 (0.96, 1.00), 0.06 (0.02. 0.09), and –0.12 (–0.14, –0.10), respectively.

Conclusions

This study quantifies the relationship between poorer symptom control (measured by ACQ-7) and higher exacerbation rates, increased HCRU, and lower utility values in a moderate-to-severe asthma population.

Our results may support future economic evaluations for therapies in asthma.

Disclosures

This study was funded by GSK (GSK ID 206918, HO-17-17257) and all statistical analyses were performed by GSK. RTI Health Solutions contributed to the design and interpretation of the study under a research contract with GSK.

WLH is a full-time employee of RTI Health Solutions, an independent research organization. **YZ** was a full-time employee of RTI Health Solutions, an independent research organization, at the time the study was conducted. **AM**, **QS**, **TO**, and **SZ** are full-time employees of GSK and own stocks/shares.

Editorial support (in the form of writing assistance, including preparation of the draft poster under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Fishawack Indicia Ltd, UK, part of Fishawack Health, and was funded by GSK.

References

1. Caminati M, et al. *J Asthma Allergy* 2021;14:457–466
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available from: https://ginasthma.org/gina-reports/ (Accessed September 19, 2022)
3. Lee LK, et al. *BMJ Open Resp Res* 2020;7:e000534
4. Davis J, et al. *J Asthma* 2018;56:332–340
5. Lee LA, et al. *Lancet Respir Med* 2021;9:69–84
6. Yang Y, et al. *HEDS Discussion Paper* 2007;29804

SCAN ME

Author email address: wherring@rti.org

Poster presented at International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe, November 6–9 2022, Vienna, Austria