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The correlation between asthma control and health status: the GOAL study

E.D. Bateman*, J. Bousquet#, M.L. Keech¶, W.W. Busse+, T.J.H. Clark§ and S.E. Pedersenƒ on behalf of the GOAL Investigators Group

ABSTRACT: The present study examined the association between guideline-derived asthma control and health-related quality of life, assessed using the Asthma Quality of Life Questionnaire (AQLQ), in patients with uncontrolled asthma whose treatment was directed towards achieving the highest possible level of control.

The present randomised, double-blind, parallel-group study compared the efficacy of fluticasone propionate (FP) and salmeterol/fluticasone propionate combination (SFC) in achieving two composite, guideline-derived measures of control: total control (TC) and well-controlled (WC) asthma. Not achieving these levels was classed as not well-controlled (NWC). Doses were augmented until patients achieved TC or reached the maximum dose. This dose was maintained for the remainder of the study. AQLQ was assessed at baseline and at each clinic visit.

AQLQ scores improved throughout the study, reaching near-maximal levels in patients achieving TC and WC, and 52-week mean scores in the three control groups were statistically significantly different. Clinically meaningful improvements (mean change from baseline) were: TC group (SFC 1.9, FP 1.8), WC (SFC 1.5, FP 1.5) and NWC (SFC 1.0, FP 0.9).

In conclusion, the treatment aimed at controlling asthma improves the health-related quality of life to levels approaching normal. The difference in Asthma Quality of Life Questionnaire scores between total control and well-controlled confirms that patients distinguish even between these high levels of control.

KEYWORDS: Asthma, control, fluticasone propionate, health status, quality of life, salmeterol

Guidelines for the management of asthma issued by the Global Initiative for Asthma (GINA)/National Institutes of Health (NIH) state that the therapeutic aim should be to achieve overall asthma control in order to minimise the impact of asthma on the individual patient [1, 2]. However, it is also increasingly recognised that asthma patients have low expectations of their therapy, leading to an acceptance of a lower level of asthma control than might be achievable [3, 4].

Assessment of health-related quality of life (HRQoL) alongside conventional clinical monitoring is increasingly proposed as a means of aligning patient expectations with the clinician's therapeutic goals [5]. However, a number of studies [6–8] have demonstrated poor correlation between conventional clinical indices and the outcomes of the Asthma Quality of Life Questionnaire (AQLQ). Conversely, studies that have used more comprehensive measures of overall asthma control have found that achieving asthma control translates into significant improvements in AQLQ score [9, 10]. Additionally, a study by KATZ *et al.* [11] found that perceived control of asthma was strongly associated with improvements in both asthma-specific and generic health status outcomes.

Based on retrospective analyses of the results of efficacy trials in asthma, the present authors have previously suggested that in contrast to conventional end-points of clinical trials, such as forced expiratory volume in one second (FEV_1), the use of a composite measure incorporating a range of clinically relevant end-points provides a more complete view of the overall level of asthma control for the individual patient [12] and is likely to correlate with patient perception of control or freedom from disease [13]. The Gaining Optimal Asthma controL (GOAL) study was designed to prospectively investigate whether, and in what proportion of patients, asthma control evaluated according to a rigorous composite measure derived from the GINA/NIH guidelines can be achieved. A further aim of the GOAL study was to compare the efficacy of individualised increasing doses of the two recommended controller therapies, fluticasone propionate (FP) alone or in

AFFILIATIONS
*University of Cape Town, Cape Town, South Africa.
#Arnaud de Villeneuve Hospital, Montpellier, France.
¶GlaxoSmithKline R&D, Greenford, and
§Imperial College, London, UK.
+University of Wisconsin Medical School, Madison, WI, USA.
ƒUniversity of Southern Denmark, Kolding Hospital, Kolding, Denmark.

CORRESPONDENCE
E.D. Bateman
UCT Lung Institute
P.O. Box 34560
Groote Schuur 7937
Cape Town
South Africa
Fax: 27 214066902
E-mail: ebateman@uctgsh1.uct.ac.za

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combination with the long-acting β_2-agonist salmeterol, in achieving asthma control. The primary efficacy results from the GOAL study have been published in detail elsewhere [14]. Some of the results of the AQLQ analysis have previously been presented in abstract form [15]. The present analysis of the results examines the extent to which patients distinguish between the different levels of clinical asthma control achieved during the study using this disease–specific health status measure.

METHODS

Study design

Full details of the GOAL study design and patient population have been reported elsewhere [14] and are summarised here.

GOAL was a 52-week, randomised, double-blind, multicentre, stratified, parallel-group step-up study designed to compare the level of asthma control achieved in adults and adolescents with salmeterol/fluticasone propionate combination (SFC; Seretide®/Advair®; GlaxoSmithKline, Middlesex, UK) *via* Diskus® (Accuhaler®) dry powder inhaler and FP (Flixotide®/Flovent®; GlaxoSmithKline) alone, also *via* Diskus® (Accuhaler®).

Following a 4-week run-in, eligible patients were allocated to one of the following three strata based on their dose of inhaled corticosteroid (ICS) during the previous 6 months. Stratum 1: no ICS; stratum 2: $\leqslant$500 μg beclomethasone dipropionate daily or equivalent; and stratum 3: >500–$\leqslant$1,000 μg beclomethasone dipropionate daily or equivalent. During phase I of the study, FP or SFC dose was increased in a stepwise manner every 12 weeks until guideline-derived total control (TC; see definition later) was achieved or the maximum dose of study medication was reached. Patients were then maintained at the final dose level for the remainder of the study (phase II). Thus, the duration of the dose titration phase (phase I) ranged 12–36 weeks and the follow-up phase (phase II) ranged 16–$\leqslant$40 weeks.

Rigorous composite measures derived from the treatment goals of the GINA/NIH guidelines [1, 2] were used to define asthma control: TC or well-controlled (WC; the full criteria are reported elsewhere [14]). When neither measure was achieved, the outcome was defined as not well-controlled (NWC).

Patient population

To be eligible for inclusion, patients had to be $\geqslant$12 yrs of age with a clinical history of asthma for $\geqslant$6 months. They also had to demonstrate an FEV_1 reversibility of $\geqslant$15% and $\geqslant$200 mL in response to inhalation of a short-acting β_2-agonist. Exclusion criteria included assessment as WC for $\geqslant$3 weeks of the 4-week run-in period or a smoking history of >10 pack-yrs.

AQLQ data was available from patients in 16 of the 44 countries involved in the study. Only those countries for which a validated translation in the local language was available were eligible for inclusion. All participants gave written informed consent prior to inclusion. The study was approved by the local research ethics committees.

Assessment of quality of life

The AQLQ consists of 32 questions in four domains: activity limitation, symptoms, emotional function and environmental stimuli. Responses in each domain and an overall score are graded on a 7-point scale, where 1 represents ''total impairment'' and 7 represents ''no impairment'' [16–18]. The AQLQ was administered at baseline and at clinic visits in weeks 4, 12, 24, 36, 48 and 52. Investigators administered the questionnaire at the same time during each visit: prior to revealing the results of lung function assessments but after enquiring about adverse events. AQLQ scores were presented as the mean of each domain, as well as an overall score. A within-subject change of 0.5 points on either the overall AQLQ score or any of the individual domains is considered the minimum change to be clinically meaningful [16–18].

Statistical analysis

The demographic data for the intention-to-treat (ITT) patients who completed at least one AQLQ questionnaire were summarised. WC and TC end-points from the primary analyses [14] are presented. Using the same logistic regression methods as the primary analyses, the proportion of patients achieving control cumulatively in both phases of the study was assessed.

The changes from baseline in AQLQ scores for each domain and the overall AQLQ score were plotted over the 1 yr treatment period for each stratum. A Chi-squared test was used to analyse the association of treatment with change from baseline in AQLQ score ($\geqslant$0.5 *versus* <0.5).

The changes from baseline in overall AQLQ scores at week 52 were categorised into $\leqslant$0, >0–<0.5, $\geqslant$0.5–<1, $\geqslant$1–<1.5 and $\geqslant$1.5. These values are summarised by treatment groups for each strata and overall. This was additionally split by control status in phase I and at the end of phase II (52 weeks).

An ANOVA model was fitted to AQLQ scores at 52 weeks, with the sole predictor variable being control status at the end of phase II (52 weeks). The p-values for all pair-wise differences in control status were calculated. To adjust for all the multiple comparisons, the Bonferroni correction method was used, which increases the p-value to account for the increased risk of incorrectly rejecting the null hypothesis. Unlike predictor variables traditionally used in ANOVA models, control status is not randomised and was not measured at any time before the AQLQ measurement.

The absolute AQLQ scores at 52 weeks were categorised and a two-sided Fisher's Exact test was used to analyse the association of treatment with AQLQ score (<6 *versus* $\geqslant$6).

RESULTS

Patient demographics

The total ITT population for the GOAL study comprised 3,416 patients. The baseline demographics, clinical characteristics and primary efficacy results of the overall GOAL population, including AQLQ scores achieved in each stratum, have been described elsewhere [14]. A total of 1,994 patients (SFC n=1,001; FP n=993) in the ITT population completed the AQLQ at least once during the study. The demographics of the AQLQ population were comparable to those of the overall study population (table 1).

TABLE 1 Baseline characteristics of patients who completed the Asthma Quality of Life Questionnaire (AQLQ)

Characteristics	Stratum 1		Stratum 2		Stratum 3	
	SFC	FP	SFC	FP	SFC	FP
Patients n# (ITT population)	291 (548)	290 (550)	351 (585)	343 (578)	359 (576)	360 (579)
Age yrs (ITT population)	37.3±14.8 (36.1)	37.0±14.6 (36.4)	40.8±16.1 (40.4)	41.0±16.3 (40.3)	42.4±16.0 (44.1)	41.3±15.9 (42.7)
Female % (ITT population)	59 (57)	54 (57)	57 (58)	58 (60)	58 (57)	61 (59)
AQLQ score						
Overall score	4.4±1.01	4.5±1.00	4.7±1.07	4.5±1.03	4.5±1.05	4.5±1.05
Activity limitation domain	4.6±1.07	4.6±1.05	4.7±1.10	4.5±1.08	4.5±1.11	4.5±1.13
Symptom domain	4.2±1.10	4.4±1.07	4.6±1.11	4.5±1.10	4.5±1.09	4.5±1.09
Emotional function domain	4.4±1.36	4.6±1.42	4.8±1.47	4.6±1.37	4.6±1.44	4.7±1.45
Environmental stimuli domain	4.4±1.32	4.4±1.35	4.6±1.40	4.4± 1.38	4.4±1.41	4.4±1.45

Data are presented as mean±SD, unless otherwise stated. SFC: salmeterol/fluticasone propionate combination; FP: fluticasone propionate; ITT: intention to treat #: completing at least one AQLQ questionnaire at any time during the study.

Improvements in quality of life

A significantly higher number of patients treated with SFC compared with FP in each stratum achieved either WC or TC status in each phase of the study ($p \leqslant 0.039$) including at study end (52 weeks; table 2) [14]. At 52 weeks, the majority of patients achieved clinically meaningful improvements in HRQoL from baseline, as demonstrated by a change in AQLQ score of $\geqslant 0.5$ (80% with SFC and 75% with FP; $p<0.01$). A total of 16 and 18% of patients achieved improvements $\geqslant 0.5$–<1.0 with SFC and FP, respectively; with 19 and 17% achieving improvements of $\geqslant 1.0$–<1.5, and 45 and 39% achieving improvements $\geqslant 1.5$. A nonclinically meaningful improvement (>0–<0.5) was achieved by 12 and 14% of SFC and FP patients, whilst 8 and 11% achieved no change or deterioration in quality of life indicated by a negative change in AQLQ score. However, the proportions of patients experiencing these different levels of change in AQLQ were similar in the three individual strata (stratum 1–3; table 3).

In addition, there was a significant association between treatment and the proportion of patients with week-52 AQLQ scores of $\geqslant 6$ *versus* <6. More patients in the SFC group achieved an AQLQ score $\geqslant 6$ (minimal or no impairment) compared with those receiving FP ($p<0.001$). Across all strata, the proportions were 61 *versus* 52% for SFC *versus* FP, respectively (fig. 1). For individual strata, the proportions achieving an AQLQ score $\geqslant 6$ were 63 *versus* 62% (NS; stratum 1), 64 *versus* 53% ($p<0.005$; stratum 2) and 57 *versus* 45% ($p<0.005$; stratum 3) for SFC *versus* FP, respectively.

Relationship between level of asthma control and quality of life

Mean values for the final score were significantly higher in patients achieving TC than in those with WC asthma ($p<0.001$), and between those with WC and NWC asthma ($p<0.001$, table 4). The proportions achieving clinically meaningful improvements of $\geqslant 0.5$ unit change were higher in

TABLE 2 Summary of efficacy results from the Gaining Optimal Asthma controL (GOAL) study

	Stratum 1			Stratum 2			Stratum 3		
	SFC	FP	p-value	SFC	FP	p-value	SFC	FP	p-value
ITT patients n	548	550		585	578		576	579	
Patients# achieving WC status (phase I)	383 (71)	356 (65)	0.039	400 (69)	302 (52)	<0.001	288 (51)	188 (33)	<0.001
Patients# achieving TC status (phase I)	225 (42)	169 (31)	⩽0.001	189 (32)	114 (20)	<0.001	106 (19)	43 (8)	<0.001
Patients#, ¶ achieving WC status (phase I + end of phase II)	418 (78)	380 (70)	0.003	436 (75)	344 (60)	<0.001	350 (62)	264 (47)	<0.001
Patients#, ¶ achieving TC status (phase I + end of phase II)	270 (50)	217 (40)	<0.001	257 (44)	163 (28)	<0.001	163 (29)	88 (16)	<0.001

Data are presented as n (%), unless otherwise stated. SFC: salmeterol/fluticasone propionate combination; FP: fluticasone propionate; ITT: intention to treat; WC: well-controlled; TC: total control. #: all subjects, excluding those with missing baseline forced expiratory volume in one second. ¶: cumulative number of patients.

TABLE 3 Degree of change from baseline in overall Asthma Quality of Life Questionnaire (AQLQ) scores at 52 weeks in patients receiving salmeterol/fluticasone propionate combination (SFC) or fluticasone propionate (FP), presented by individual strata and overall

Change in AQLQ score	Stratum 1		Stratum 2		Stratum 3		Overall	
	SFC	FP	SFC	FP	SFC	FP	SFC	FP
Subjects n	218	216	301	280	291	277	810	773
≥1.5	122 (56)	106 (49)	120 (40)	109 (39)	121 (42)	89 (32)	363 (45)	304 (39)
≥1.0–<1.5	35 (16)	38 (18)	67 (22)	50 (18)	52 (18)	47 (17)	154 (19)	135 (17)
≥0.5–<1.0	24 (11)	36 (17)	58 (19)	40 (14)	51 (18)	63 (23)	133 (16)	139 (18)
>0–<0.5	25 (11)	20 (9)	37 (12)	44 (16)	34 (12)	46 (17)	96 (12)	110 (14)
≤0	12 (6)	16 (7)	19 (6)	37 (13)	33 (11)	32 (12)	64 (8)	85 (11)

Data are presented as n (%), unless otherwise stated.

patients with TC (SFC 89% and FP 85%) and WC status (SFC 85% and FP 84%) compared with those NWC (SFC 67% and FP 65%; fig. 2). Even in patients with NWC status, a large proportion achieved improvements in total AQLQ scores ≥1.0 (SFC 50% and FP 47%), with 31% in each treatment group achieving changes in AQLQ score ≥1.5 (fig. 2).

Profile of improvements in AQLQ: all strata

The largest improvement in overall score and in the scores for each domain was observed during the first 4 weeks of the treatment period. However, scores continued to improve throughout the study period, with highest values for each treatment being observed at 52 weeks (fig. 3). Mean AQLQ scores in each of the four domains improved by a similar magnitude in strata 2 and 3. In stratum 1, the greatest improvement was seen for symptoms. No clinically meaningful differences between domains were noted with either treatment.

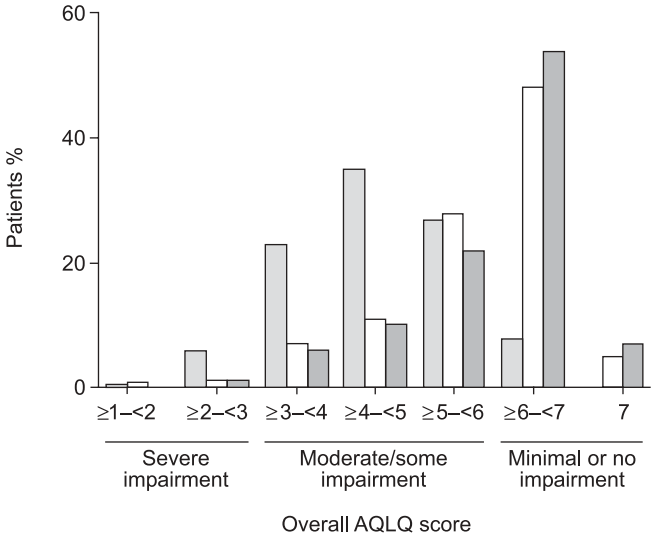

FIGURE 1. Association of achieving mean overall Asthma Quality of Life Questionnaire (AQLQ) score of ≥6 *versus* <6 at week 52 with salmeterol/fluticasone propionate combination (SFC) and fluticasone propionate (FC) in patients who completed the AQLQ at baseline and week 52 (n=1,583; p<0.001). ■: baseline; □: FP; ■: SFC.

DISCUSSION

The GOAL study is the first prospective study to evaluate the concept of achieving complete clinical control, defined in GOAL as TC, based on the goals of treatment described in international treatment guidelines [1, 2].

The AQLQ is a disease-specific, self-administered quality-of-life tool that is available in 36 languages and has been shown to be valid, reliable and reproducible for evaluating the impact of treatment regimens on the quality of life of asthma patients [16–18]. The unique design of the GOAL study permits evaluation of the relationship between asthma control and health status as measured using this AQLQ questionnaire. TC is associated with achievement of near maximal levels of HRQoL. The final values for the AQLQ for patients achieving lesser levels of clinical control (*i.e.* WC and NWC status) were lower but still statistically significant, and exceeded the minimal clinically significant difference in a large majority of patients. Furthermore, there was a statistically significant difference in mean total AQLQ score at 52 weeks between TC and WC patients, confirming that patients (assessed using this instrument) distinguish even between these high levels of control in spite of the probable ''ceiling'' effect as large proportions of subjects in both categories scored the maximum score of 7.

The difference between patients designated controlled and NWC by the definitions used in the present study has recently been used by JUNIPER *et al.* [19] to define cut-points for the Asthma Control Questionnaire (ACQ) for distinguishing ''well-controlled'' and ''not well-controlled'' asthma. Although in their analysis the definition of TC was not used, but grouped under well controlled, a cut-point of 1.5 was associated with a probability of having well-controlled asthma of only 66%. A score of 0.75 (the ACQ score is inverse to the level of control) increased the likelihood of control to 85%, suggesting that the highest levels of control can be distinguished by control measures.

A further important conclusion of the current study is that, even when the desired levels of control were not achieved, a

TABLE 4 Mean Asthma Quality of Life Questionnaire (AQLQ) scores at 52 weeks and mean change from baseline within each strata split by level of asthma control at the end of phase II

	Stratum 1		Stratum 2		Stratum 3		Overall	
	SFC	FP	SFC	FP	SFC	FP	SFC	FP
TC								
Patients n	77	57	110	50	66	37	253	144
Score at 52 weeks	6.5±0.78	6.6±0.47	6.6±0.55	6.5±0.64	6.6±0.54	6.5±0.47	6.5±0.63	6.6±0.53
Mean change	2.0±1.09	2.1±1.08	1.8±1.07	1.7±1.21	1.9±0.84	1.7±1.03	1.9±1.02	1.8±1.12
WC								
Patients n	73	67	101	88	96	90	270	245
Score at 52 weeks	6.2±0.67	6.2±0.77	6.1±0.80	6.1±0.74	6.2±0.78	6.1±0.86	6.2±0.76	6.1±0.79
Mean change	1.8±1.17	1.6±0.90	1.4±0.92	1.5±1.12	1.5±1.10	1.3±0.84	1.5±1.06	1.5±0.97
NWC								
Patients n	68	92	90	142	129	150	287	384
Score at 52 weeks	5.4±1.12	5.5±1.05	5.4±1.20	5.4±1.18	5.2±1.19	5.1±1.09	5.3±1.18	5.3±1.12
Mean change	1.2±1.25	1.1±1.13	0.9±1.08	0.9±1.09	0.9±1.02	0.8±1.04	1.0±1.10	0.9±1.09

Data are presented as mean±SD, unless otherwise stated. SFC: salmeterol/fluticasone propionate combination; FP: fluticasone propionate; TC: total control; WC: well-controlled; NWC: not well-controlled.

great majority of patients benefited from the treatment approach, with most achieving clinically significant improvements in AQLQ. Indeed, many patients not achieving TC or WC status reached high scores on the AQLQ, regardless of baseline values and treatment received. At the end of the 52-week randomised period, virtually all patients from all strata had achieved at least moderate improvements in HRQoL, as defined by an increase in AQLQ score of ⩾1.0 [16–18]. In nearly half of all patients, the improvement exceeded the threshold for a large improvement (defined by an AQLQ score

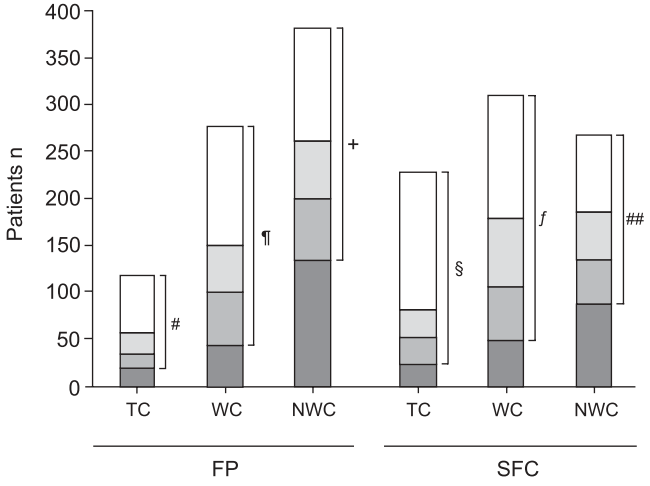

FIGURE 2. Number and proportion of patients achieving improvements in overall Asthma Quality of Life Questionnaire score at 52 weeks according to level of control and treatment group. TC: total control; WC: well-controlled; NWC: not well-controlled; FP: fluticasone propionate; SFC: salmetrol/fluticasone propionate combination. □: ⩾1.5; ▫: ⩾1.0–<1.5; ▪: ⩾0.5–<1.0; ■: <0.5. Although the proportions achieving meaningful improvement (⩾0.5) were similar with SFC and FP, a higher number of patients achieved control with SFC. #: 85%; ¶: 84%; +: 65%; §: 89%; f: 85%; ##: 67%.

increase of ⩾1.5) [16–18] and came close to reaching the maximum achievable score. The clinical implications of these findings are that when treatment is individualised and directed towards achieving TC, it offers the vast majority of asthma patients (regardless of the severity of asthma) the prospect of achieving quality-of-life scores approaching the maximum, *i.e.* with little or no impact of asthma on patients' daily lives.

Throughout the present study, the AQLQ score values for patients treated with SFC were higher than for those treated with FP, except for the suggestion of a ceiling effect as values approached maximal levels.

Comparisons between studies of different design should be performed with care. However, the magnitude of the increase and end-of-study values in the present study were high, comparing favourably with values in the Formoterol And Corticosteroids Establishing Therapy (FACET) study [6], which was of similar duration. This is to be expected since the individualised treatment was increased in GOAL with the purpose of achieving the best possible level of control, whereas the FACET study employed only a single fixed dose of treatment and a ''step-down'' study design. The GOAL results confirm the findings of the earlier retrospective analysis by BATEMAN *et al.* [13], that guideline-derived control is associated with attainment of near-normal AQLQ scores.

The main improvements were seen during the initial dose-titrating phase of the study, particularly in the first 4 weeks of treatment. However, further improvement in AQLQ score was observed throughout the remainder of the 52-week study, beyond the point at which patients received no further dose increase in the controller treatment. The plateauing of the values towards the end of the study may reflect the absence of further dose increases and the fact that no further benefit or a ceiling effect [6] was being achieved (the limits of efficacy) as more and more patients approached maximum scores. By

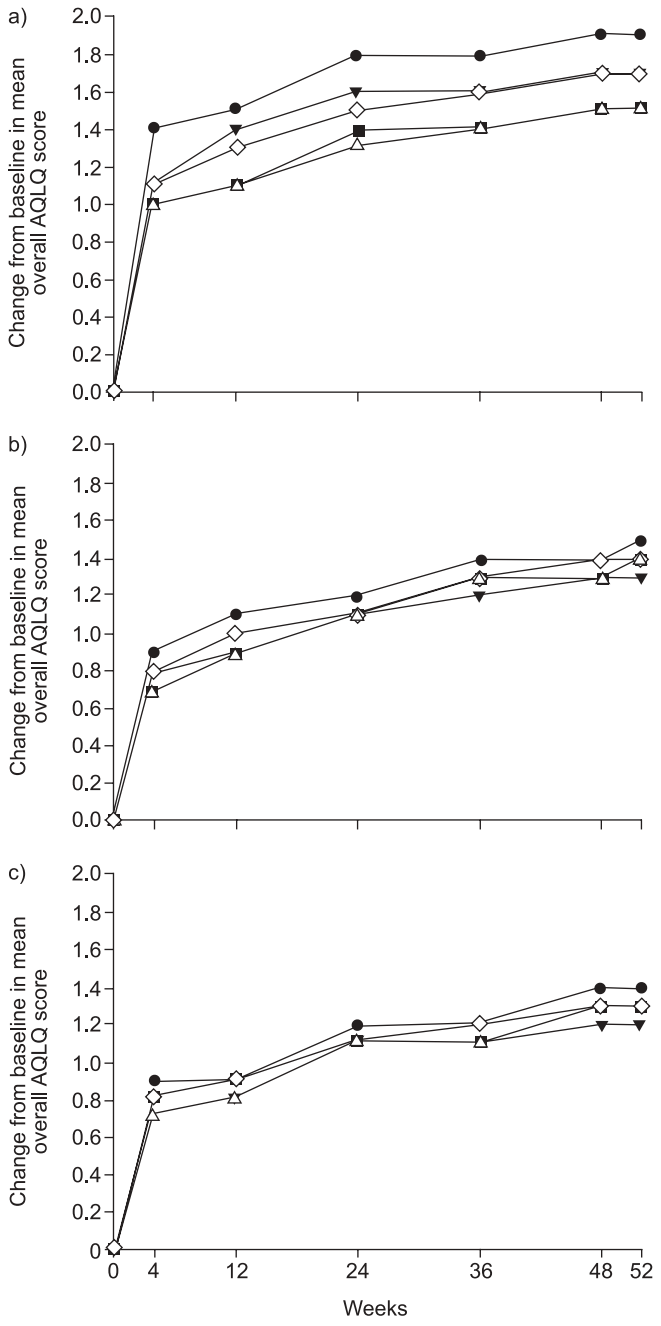

FIGURE 3. Changes from baseline in mean overall Asthma Quality of Life Questionnaire (AQLQ) scores and in the individual domain scores for patients receiving salmeterol/fluticasone propionate combination (SFC) in each of the three strata. a) Stratum 1, b) stratum 2 and c) stratum 3. The profile of improvements in mean overall AQLQ scores and for the individual domain scores for patients treated with fluticasone propionate, although numerically lower, were similar (not shown). ◇: Overall; ■: activity limitation; ●: asthma symptoms; ▼: emotional function; △: environment.

contrast, in the FACET study an initial large increase in AQLQ score was followed by a gradual decline over the remainder of the 1-yr study period, suggesting gradual loss of control [6].

In the GOAL study, all three strata showed similar improvements in each of the four AQLQ domains. The exception was the greater improvement in the symptoms domain in stratum 1. It is reasonable to assume that the greatest impact of achieving control, as per the composite measure employed in the GOAL study, might have been in the symptoms domain because the parameters within the composite measure tend to be symptom-based. However, it is important to note that, in all strata, comparable improvement occurred in all AQLQ domains, even those not represented in the composite measure. This supports the view that the composite measure of control used in the GOAL study provides a simple measure that reflects a patient-reported outcome, such as the AQLQ.

The absence of a placebo group is a potential limitation in the design of the GOAL study, with respect to HRQoL, which may restrict its validity in a wider patient population. For ethical reasons, it was not acceptable to include a placebo arm in a study of patients with uncontrolled asthma, of whom the majority in strata 2 and 3 had severe asthma. It seems improbable that spontaneous improvements could account for the high AQLQ scores at the end of the study. Other potential limitations are that no record was made of overall patient satisfaction with treatment and treatment approach, due to the current lack of validated and approved satisfaction instruments. In addition, AQLQ measurements were dependent on patient recall of the 2 weeks prior to the clinic visit.

Since improving HRQoL is a slow process and changes may be subtle, there is a risk of perceived lack of progress and under-reporting of improvements, especially if patients have low expectations of their asthma treatments to begin with [3, 4]. However, the clear, consistent and biologically plausible trends and correlations suggest that the results are reliable.

Quality-of-life instruments, such as the Asthma Quality of Life Questionnaire, reflect patients' real experiences and perceptions of living with asthma. Despite ''control'' being described as the goal of asthma treatment, current surveys confirm that the majority of patients do not achieve control and are consequently condemned to an impaired quality of life [3, 4]. The strong correlation between Asthma Quality of Life Questionnaire scores and guideline-derived asthma control seen in the Gaining Optimal Asthma controL study supports the case for attempting to achieve and maintain asthma control at a higher level than at present. It also confirms that patients are able to distinguish between and appreciate the benefits of this approach. The Gaining Optimal Asthma controL study confirms that impaired quality of life is an unnecessary hardship and can be avoided by aiming for total control (a composite measure derived from guideline goals) through individualised treatment escalated, where necessary, in accordance with accepted treatment steps. It further confirms that, with sustained dosing, gains are maintained and further improvements may occur. Since the Gaining Optimal Asthma controL study protocol made no provision for stepping down treatment in patients achieving control, further studies are required to examine whether it is possible to maintain the high levels of quality of life achieved in Gaining Optimal Asthma controL when controller treatment is reduced. Nevertheless, these results confirm that near-normal health-related quality of life can be achieved when treatment aims for total control of asthma, and that results with salmeterol/fluticasone propionate combination are superior to fluticasone propionate alone.

This should serve to increase the expectations of patients and their caregivers regarding what can be achieved for all people with asthma.

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