

DIA Workshop on patient reported
outcomes
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(Draft 2)

The practicing physician's model

- How are you feeling?
- Does your asthma waken you at night?
- Can I have a listen to your chest?
- Blow into this
 - harder -- harder
- Δ any above CXR

Conventional asthma efficacy endpoints
for regulatory submission

- Lung function FEV₁ and/or PEFr
- Use of rescue medication
- Patient asthma diary – symptom score
- Frequency of, or time to, exacerbation
- Quality of life evaluation

An 'in house' model

- Night time score
 - 0 = slept through night
 - 1 = some complaint in a.m.
 - 2 = woke up once
 - 3 = woke up once +
 - 4 = awake most of night
- Day time score
 - 0 = no symptoms
 - 1 = one asthma episode
 - 2 = one + asthma episode
 - 3 = symptomatic most of day
 - 4 = can not carry out normal activities

QoL rating scales non-specific or adapted to asthma

- Standard gamble
- Rating (feeling) scale - patient utilities
- Medical Outcome Survey Short-Form-36 (SF-36)
- Sickness Impact Profile (SIP)
- Psychological and General Well Being (GWB)

QoL rating scales asthma-specific

- Asthma Quality of Life Questionnaire (AQLQ) *higher scores are better*
- Living with asthma questionnaire (LWAQ) *lower scores are better*
- Asthma Control Questionnaire (ACQ)
- Marks Asthma QoL Questionnaire
- St Georges Respiratory Questionnaire (SGRQ)

What indirect influences on QoL outcomes may exist?

Asthma/depression/QoL (Mancuso C. J Gen Intern Med 2000 15:301)

- 230 outpatients with moderate asthma in a NY tertiary referral centre
 - Mean age 41 (11) 83% female
 - 45% scored above threshold for depression

	Depressed	Non-depressed
AQLQ	3.9 (1.3)	2.8 (0.8)
SF-36 mental	48 (11)	32 (10)

Demographic and Socioeconomic influences on QoL (Apter A. J All clin Immunol 1999 103 Pt1 1:72)

- 50 outpatients with moderate/severe asthma at a University health centre
 - Mean age 46 (14) FEV1 75% normal
 - 67% of the variance of AQLQ was accounted for by
 - Ethnic group
 - Level of education
 - Employment or unemployment
 - Family income above/below \$ 20,000

Physician factors ?? (Blanc Am J Med 2003 114:581)

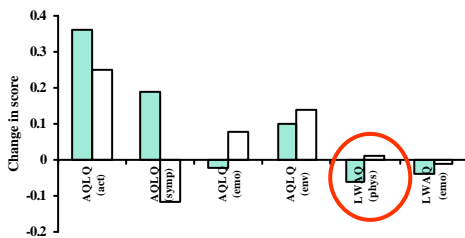
- Mail survey of 147 physicians and telephone interview with 317 of their patients

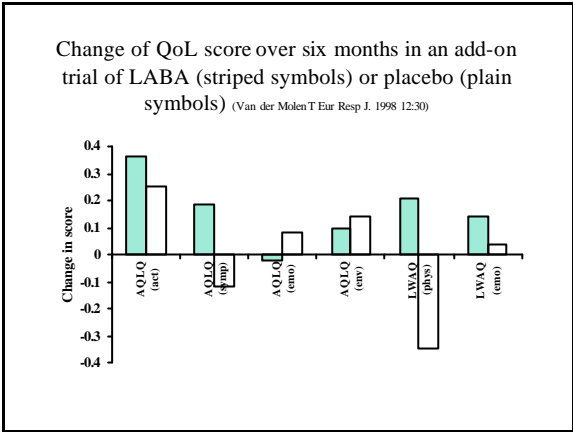
Pulmonary physician practice	HMO predominant practice
Use leukotriene antagonists & theophylline	Less use leukotriene antagonists & theophylline
	Better health status (SF-12)
No difference in QoL	

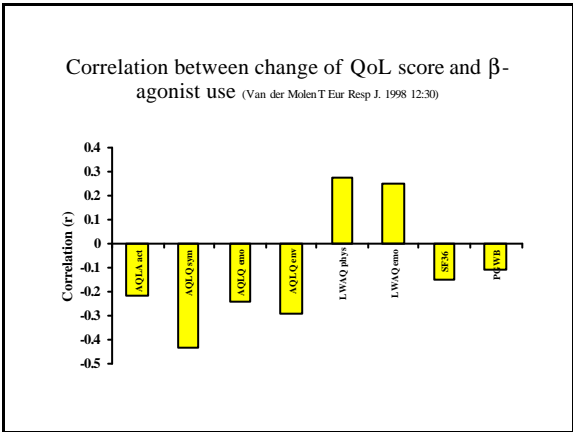
AQLQ components (scale 1-7 differences > 0.5 in component scores are clinically important)

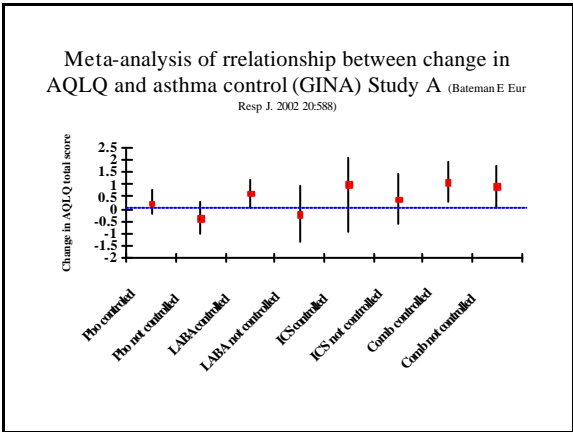
- Activity
- Emotion
- Environment
- Symptoms
- Overall

Change of QoL score over six months in an add-on trial of LABA (striped symbols) or placebo (plain symbols) (Van der Molen T Eur Resp J. 1998 12:30)









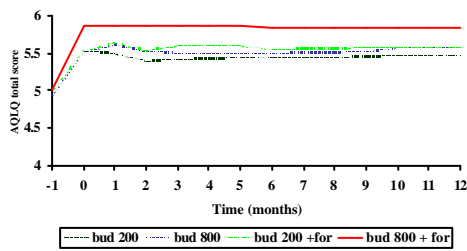
AQLQ comparison of two [active] asthma treatments

	Treatment difference (LSM)	p value
Activities	-0.24	0.0024
Emotion	-0.3	0.0009
Environment	-0.22	0.0164
Symptoms	-0.24	0.0139
Overall	-0.25	0.0025

Same study - median percentage symptom free days - comparison of two [active] asthma treatments

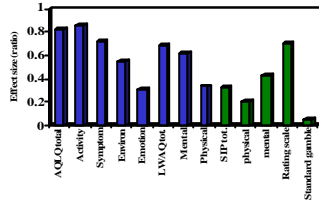
- Treatment A – 18%
- Treatment B – 30%
- p = 0.0422

Change in QoL score by time and treatment – data extrapolated (Juniper E Eur Resp J 1999 –14:1038 FACET study)



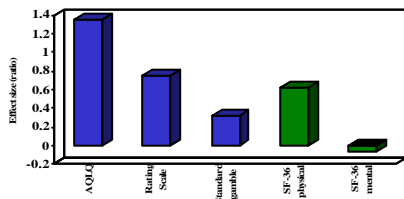
Effect size (Δ LABA/ Δ LABA + Δ SABA) of various QoL instruments (van Molken Eur Resp J 1995 8:888)

- 120 asthma patients aged 18 – 70 and with FEV₁ 50 – 70% predicted in a DB comparison of LABA vs. SABA



Responsiveness index (Δ sd Δ) of various QoL instruments (Juniper E Eur Resp J 2001 18:38)

- 40 asthma patients aged 18 – 65 with mean FEV₁ 78% predicted no pharmacological intervention – outcome stable vs. non-stable



‘Components of symptom burden’ (Juniper E Eur Resp J. 2004 23:287)

- ‘Factor analysis’ –orthogonal rotation & loading (correlation) suggests groups of related symptoms
 - Asthma specific QoL
 - Airway calibre
 - Daytime symptoms & β -agonist use
 - Night-time symptoms & β -agonist use

Possible reasons for differences between QoL and other measurements

- ‘informed administration’
- Factors extraneous to disease social/emotional
- Adaptation to a chronic illness
- Increasing activity may increase symptoms

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- Acceptability of end-points
 - Total symptom score
 - Exacerbation data
 - Steroid sparing
 - Sputum cytology
 - ‘Bronchospasm’ (COPD)
 - Methacholine/antigen challenge

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- Study duration
- Immunosuppression
- Paediatric requirements (number/age)
- Differentiation COPD/asthma
- Pre-clinical programme
- FEV₁ value of 30-85% predicted

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- Co-medication
- FEV1 or morning PEFr
- 1st or 2nd line treatment and comparator requirements

Conclusions

- It is unclear what QoL measurements actually measure (c.f. I.Q testing)
- Potentially susceptible to non-disease influences – personality, personal circumstances
- Better longer term correlation to lung function, exacerbation frequency, desirable
