LEIDS UNIVERSITAIR MEDISCH CENTRUM

ACCURATE-project (nr 170885604)

Asthma Control Cost-Utility RAndomized Trial Evaluation

Goals of asthma treatment: how high should we go?

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Disclosure Dr Jaap K. Sont

Potential conflicts of interest that relate to this presentation

Dept of Medical Decision Making has received:

• 2010 Research equipment	Aerocrine Sweden
• 2015 Research grant	GSK NL
• 2014 Conference	AstraZeneca NL
• 2014 Speakers fee	Boehringer Ingelheim DE
• 2013 Research grant	Chiesi NL
• 2013 Research grant	Boehringer Ingelheim NL

International guidelines

Levels of Asthma Control
(Assess patient impairment)

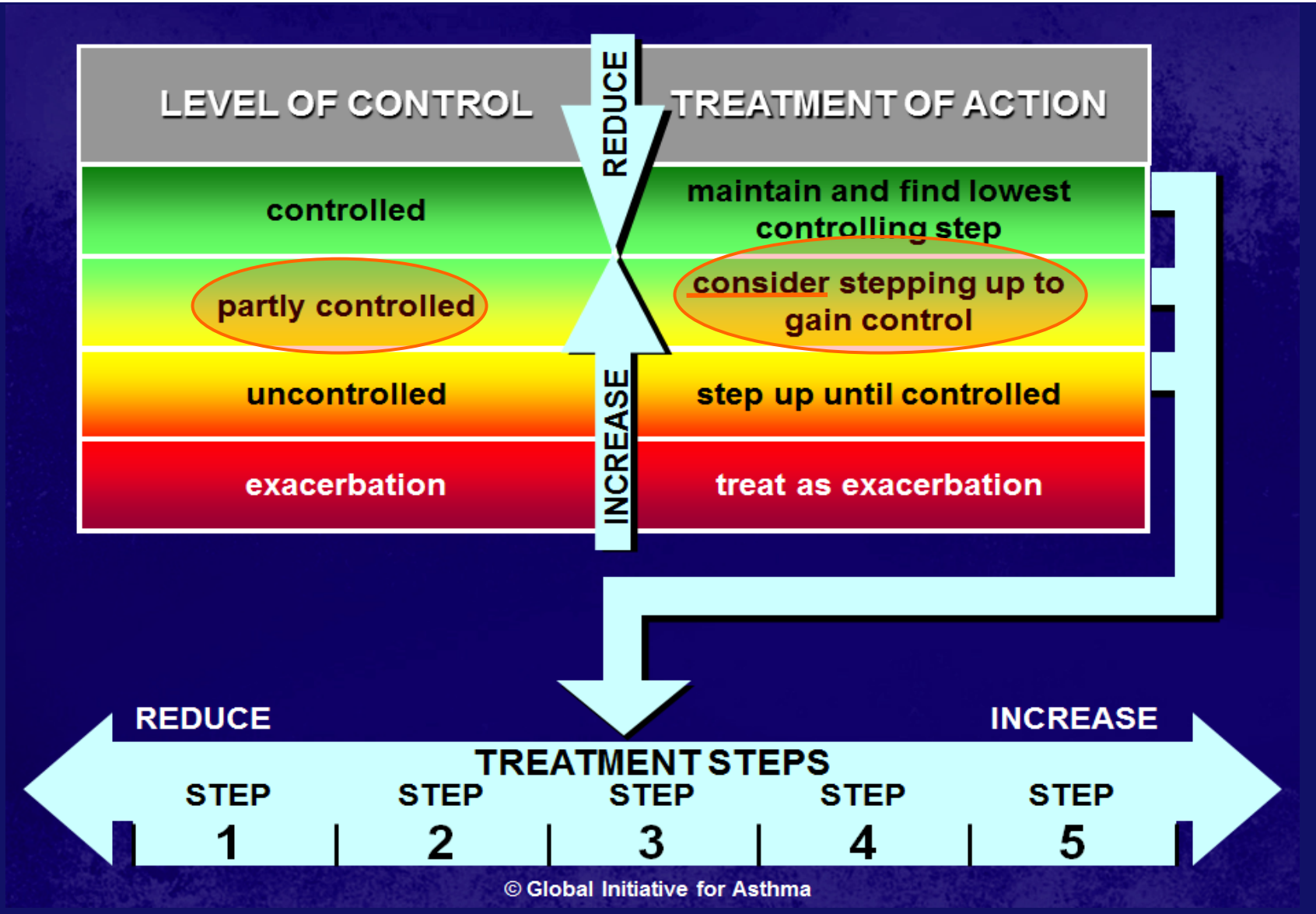
Characteristic	Controlled (All of the following)	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	Twice or less per week	More than twice per week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / "reliever" treatment	Twice or less per week	More than twice per week	
Lung function (PEF or FEV_1)	Normal	< 80% predicted or personal best (if known) on any day	

Assessment of Future Risk (risk of exacerbations, instability, rapid decline in lung function, side effects)

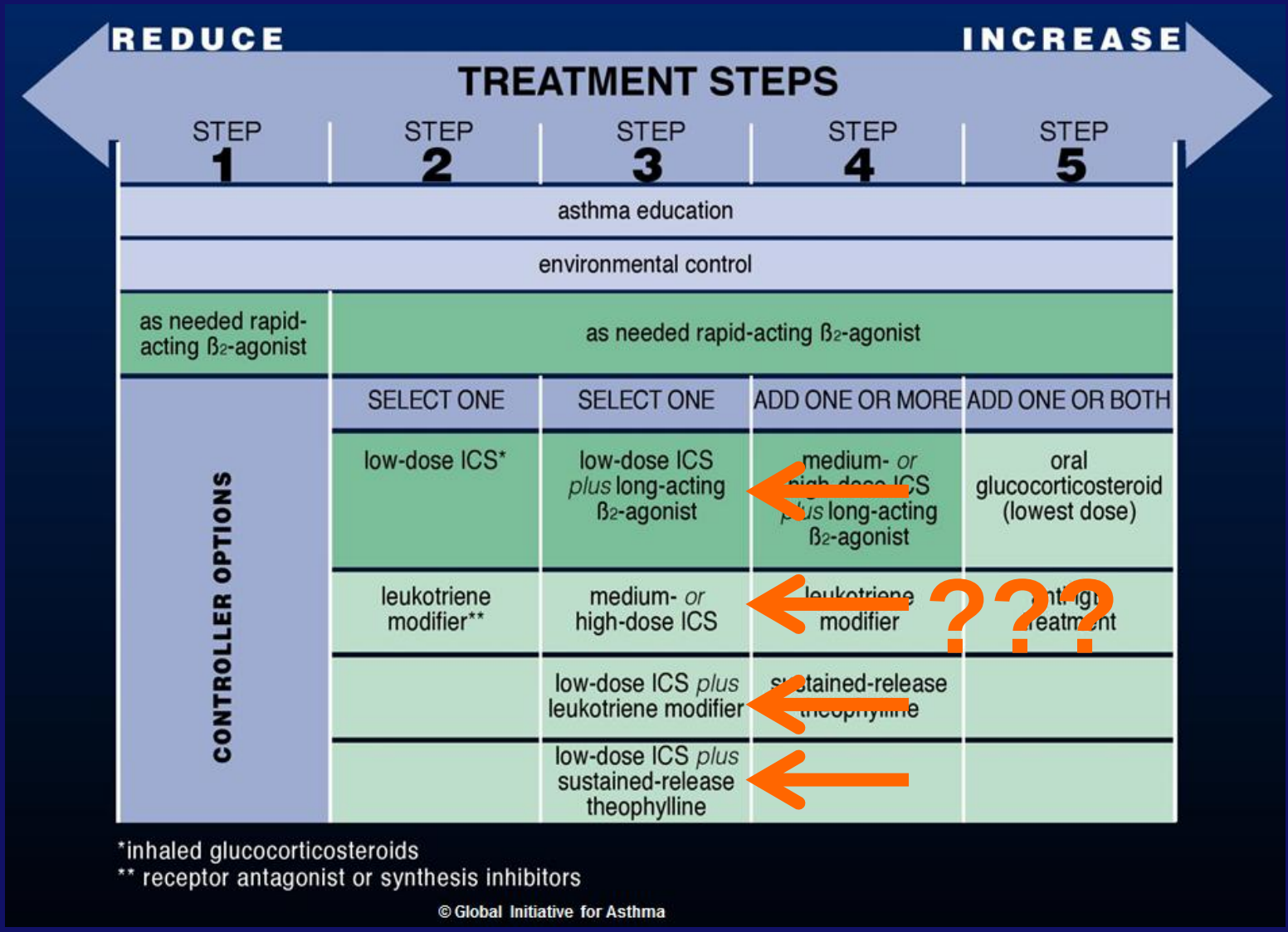
Background

- Goal Study: Controlled asthma can be achieved within 1 year [Bateman 2004]
  - 70-75% maximum daily dose ICS
  - 5-10% course of oral prednisone
- In daily practice 60-70% of patient have partly or uncontrolled asthma
- Do patients experience enough benefit of controlled compared to partly controlled asthma?

Adjust treatment step



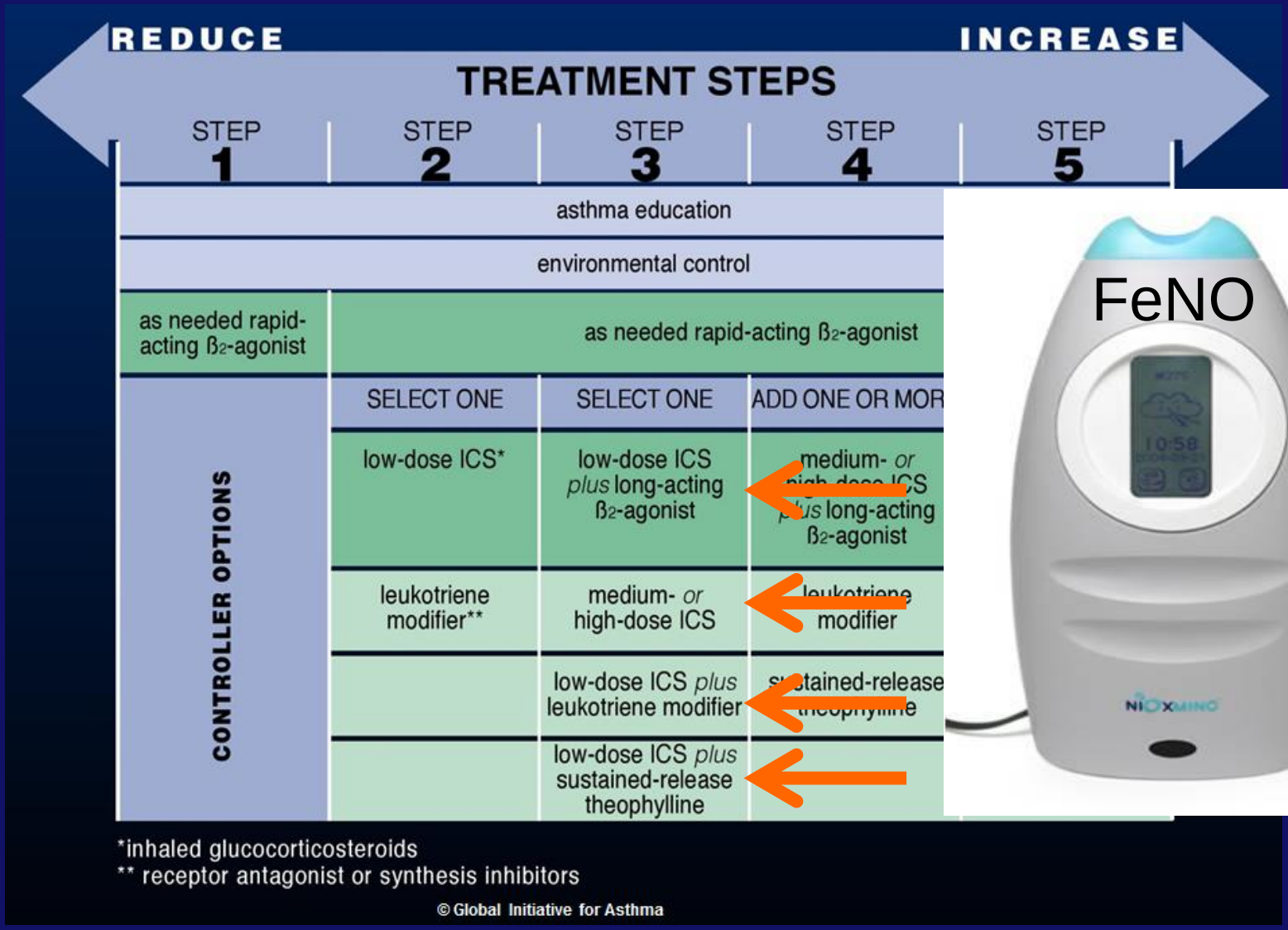
Medication choice



Fraction of exhaled Nitric Oxide (FeNO)

- Measure of airways inflammation in exhaled breath
- May lead to either lower [Smith 2005] higher [Szefler 2008] daily dose of ICS
- Does additionally guiding asthma management by FeNO lead to more tailored medication?

Medication choice



Aim

To assess the cost-effectiveness and clinical effectiveness of pursuing:

1) Partly Controlled asthma (PCa) : ACQ<1.50 *
2) Controlled asthma (Ca) : ACQ<0.75
3) FeNO-driven Controlled asthma (FCa) : ACQ<0.75 & FeNO<25

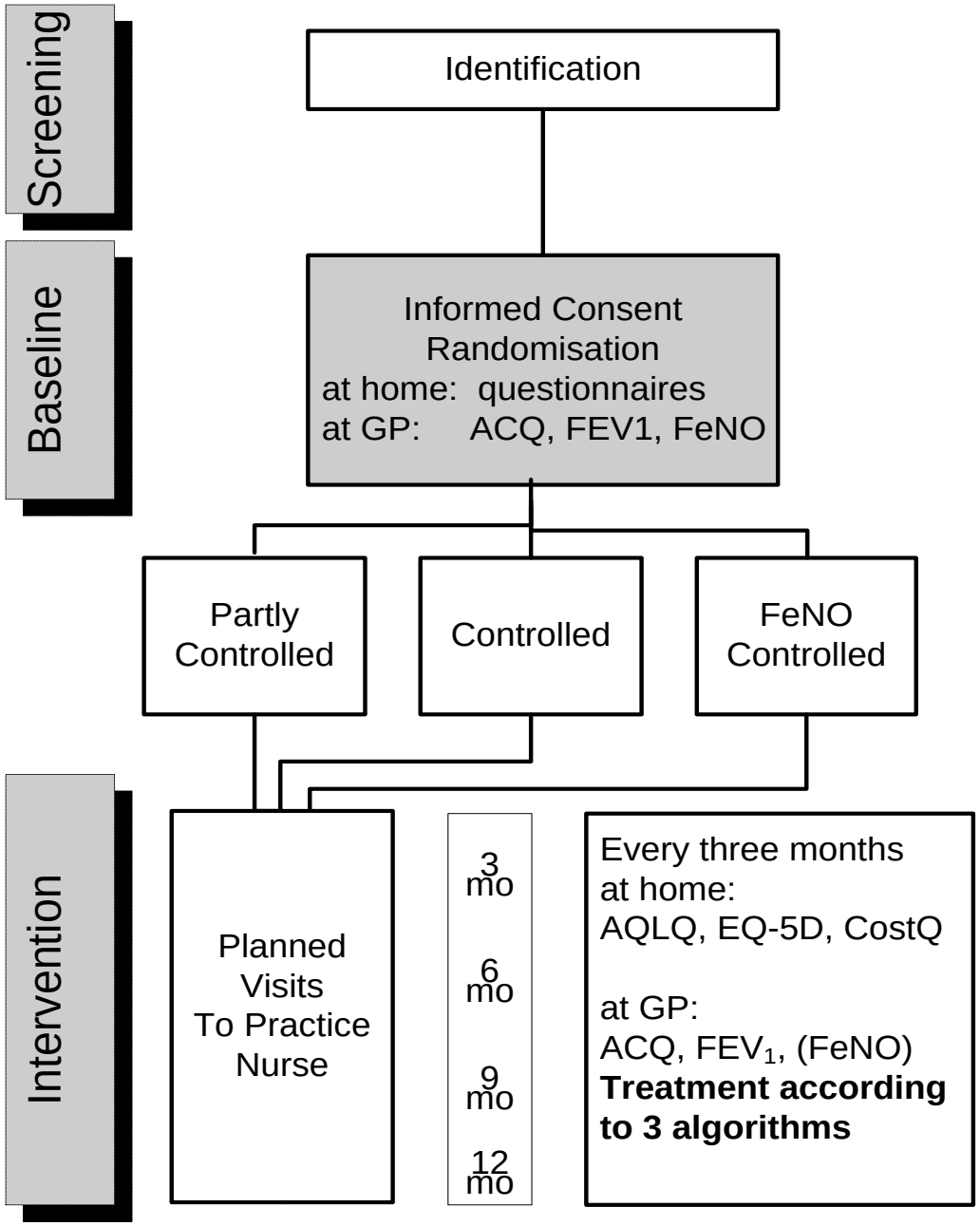
*ACQ: Asthma Control Questionnaire

Subjects

- Asthma patients 18-50 yr
- Treated in primary care
- No significant comorbidity
- Rural and urban practices

Design

Pragmatic Cluster-Randomised Trial



Algorithms

		Current level of asthma control		
Strategy		**Uncontrolled** (ACQ>1.5)	**Partly controlled** (0.75>ACQ>1.5)	**Controlled** (ACQ<0.75)
Partly Controlled (PCa)		step-up: treatment choice open	no change	step-down: treatment choice open
Controlled (Ca)		step-up: treatment choice open	step-up: treatment choice open	• 3 mo: no change • > 3 mo: step-down
FeNO-drive Controlled (FCa)				
FeNO result	Low FeNO (<25ppb)	- 3mo: step-up: LABA >6 mo: revise asthma diagnosis	• 3 mo: no change/ change within current step to LABA • > 6 mo: step-down ICS	step-down open
	Intermediate FeNO (25-50ppb)	step-up: treatment choice open	step-up: treatment choice open	no change
	High FeNO (>50ppb)	step-up: 2 x ICS	step-up: 1 × ICS	step-up/change within current step to ICS

Algorithms

		Current level of asthma control		
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Partly Controlled (PCa)		step-up: treatment choice open	no change	step-down: treatment choice open
Controlled (Ca)		step-up: treatment choice open	step-up: treatment choice open	• 3 mo: no change • > 3 mo: step-down
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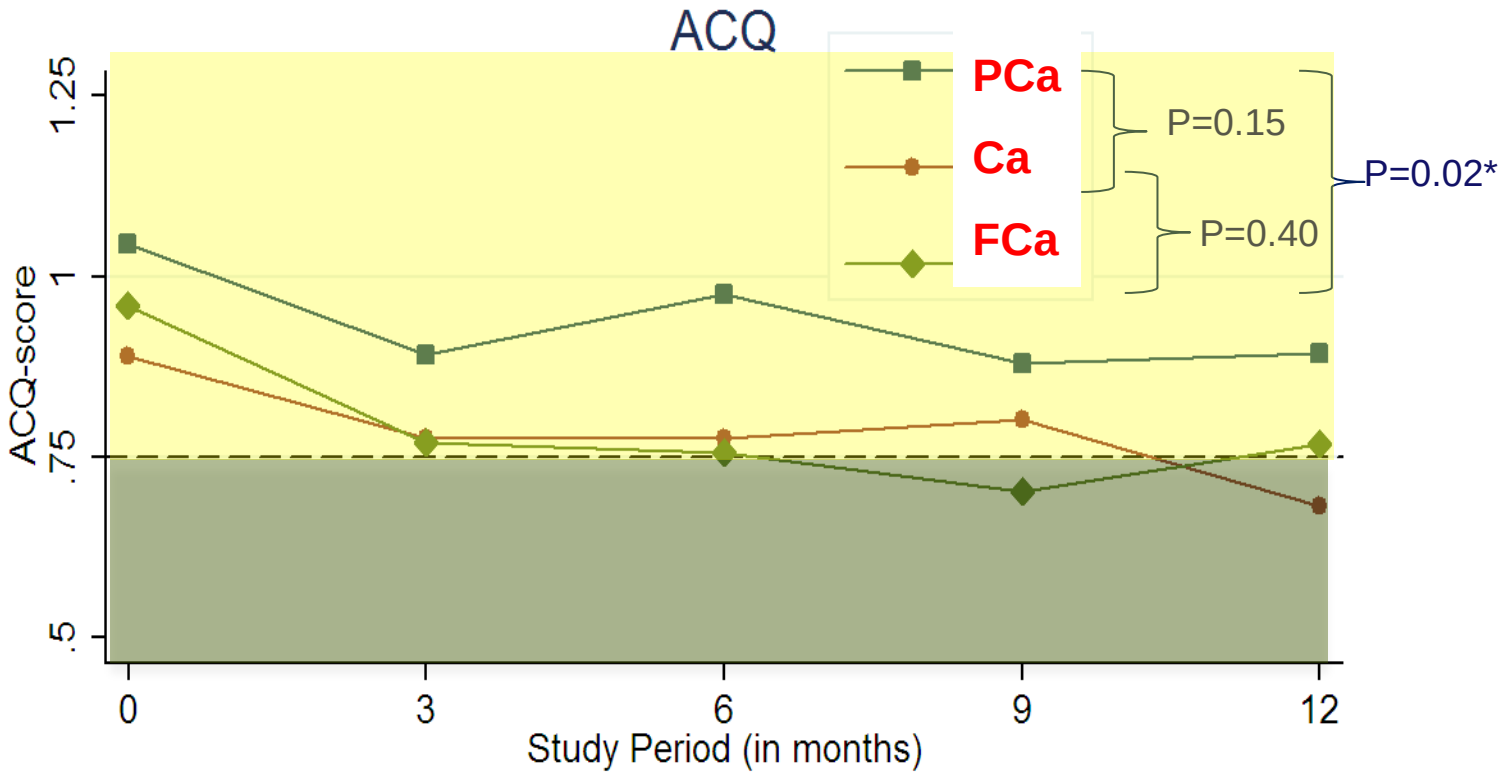
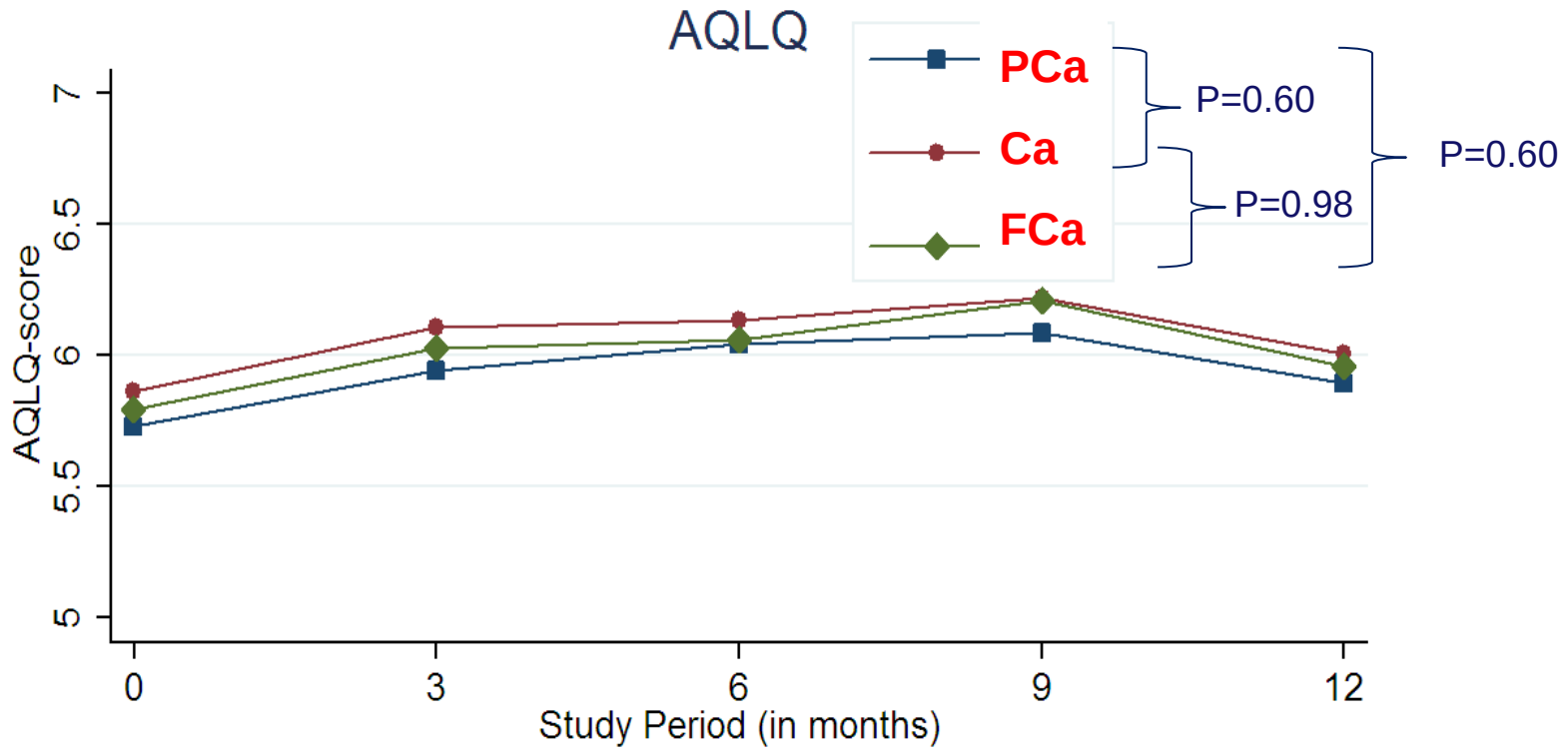
Results: baseline characteristics

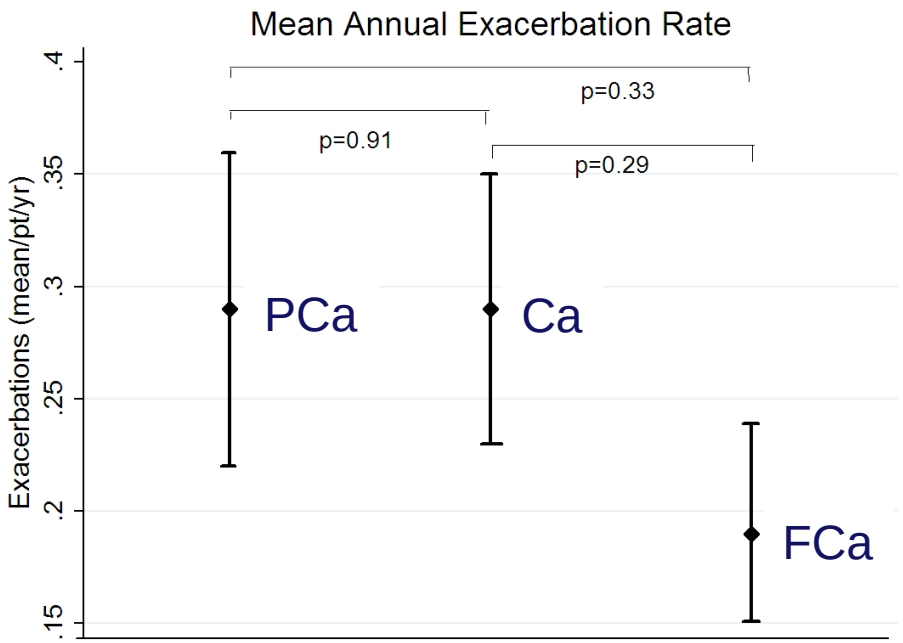
	PCa	Ca	FCa
Patients randomised (n)	232	210	192
Patients ITT (n)	219	203	189
General practices	44	43	44
Gender % F	68.4	65.8	72.3
Mean age (SD)	38.9 (9.3)	39.9 (9.8)	39.5 (9.3)
Asthma duration in years (SD)	18 (13)	16 (12)	20 (14)
FEV1 (SD) in % predicted	92.4 (17.2)	93.0 (17.0)	93.1 (17.0)
Daily ICS dose in mcg (SD)	831 (701)	825 (639)	853 (642)
LABA use %	49	52	47
Mean baseline ACQ (SD)	1.08 (0.84)	0.93 (0.80)	0.99 (0.73)

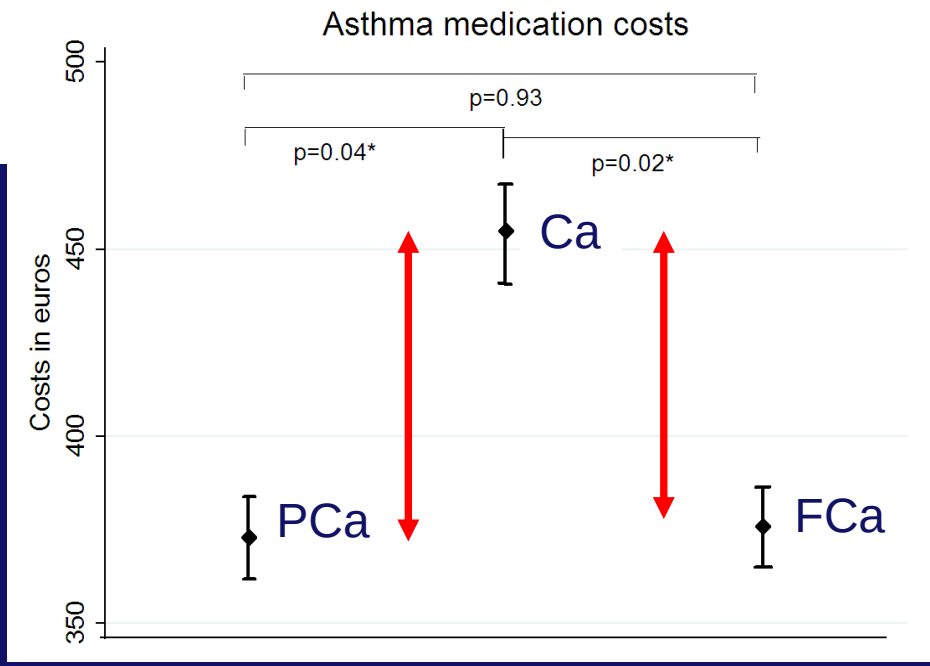
Asthma control

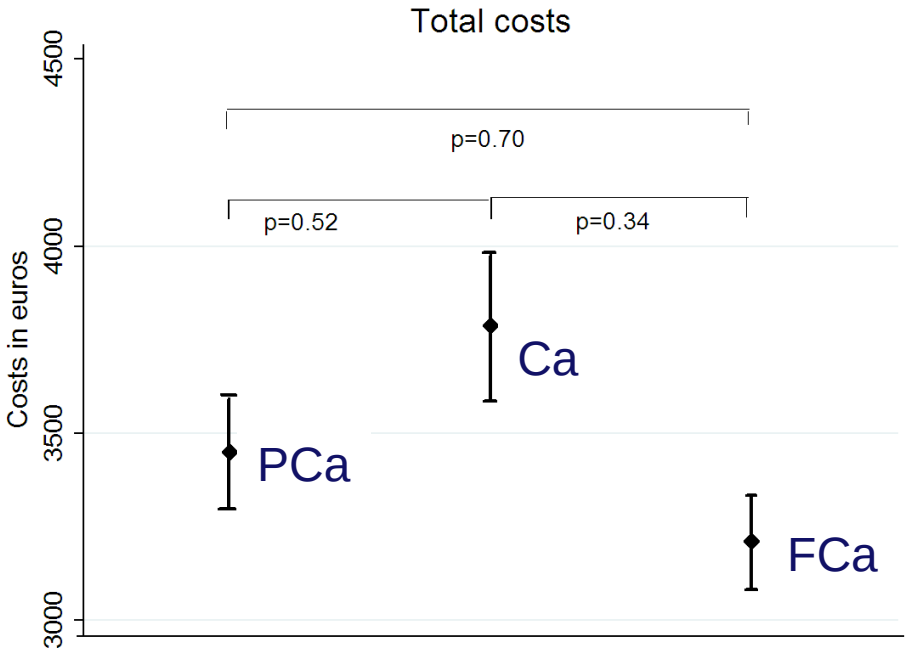


Asthma related quality of life



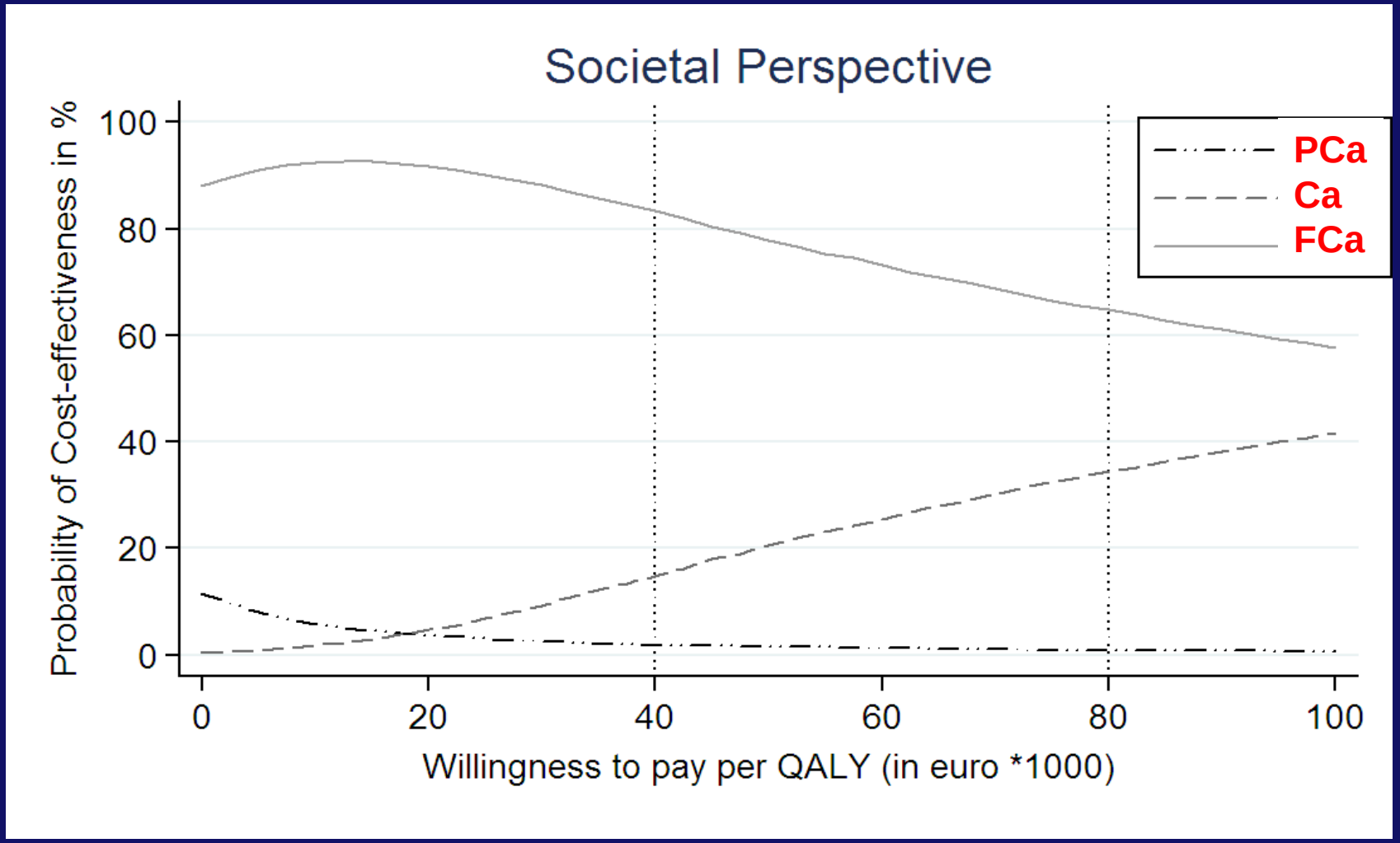






- No significant differences in Quality Adjusted Life Years (EQ-5D, p>0.36)
- FCa has highest probability of being cost-effective (80%) at a Willingness To Pay of €40.000 per QALY

Cost-Effectiveness Acceptability Curve



Conclusions

- Asthma control improved in all three treatment strategies
  - Significantly more improvement in FeNO-driven strategy compared to partly controlled strategy

- A symptom- plus FENO-driven strategy reduces asthma medication use while sustaining asthma control and quality of life in adult asthmatic patients in primary care

Implication

From a societal, patient, and clinical perspective, a symptom- and fraction of exhaled nitric oxide (FeNO)–driven treatment strategy seems to be the preferred management strategy for adult asthmatic patients in primary care

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Dank!

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Symptom- and fraction of exhaled nitric oxide–driven strategies for asthma control: A cluster-randomized trial in primary care

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Background: Aiming at partly controlled asthma (PCa) instead of controlled asthma (Ca) might decrease asthma medication use. Biomarkers, such as the fraction of exhaled nitric oxide (FENO), allow further tailoring of treatment.

Objective: We sought to assess the cost-effectiveness and clinical effectiveness of pursuing PCa, Ca, or FENO-driven controlled asthma (FCa).

Methods: In a nonblind, pragmatic, cluster-randomized trial in

The FCa strategy had the highest probability of cost-effectiveness at a willingness to pay of $50,000/quality-adjusted life year (86%; PCa, 2%; Ca, 12%). There were no differences in severe exacerbation rate.

Conclusion: A symptom- plus FENO-driven strategy reduces asthma medication use while sustaining asthma control and quality of life and is the preferred strategy for adult asthmatic patients in primary care. (J Allergy Clin Immunol 2015;135:682-8.)