Compliance & Web-based treatment in IBD and IBS

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2012

Definition

- Compliance/adherence to therapy is defined as the extent to which patients take medications as prescribed by their health-care provider

Baars JE et al: APT 2009

Definition

- Patients are designated as non-compliant if they used less than 80% of the prescribed doses during reference period

Cerveny et al. IBD 2007, Lakatos et al. JCC 2009

Impact of non-compliance on outcomes

- **Increased risk of relapse**

  More than 5-fold ↑ risk of relapse in UC patients non-adherent to 5-ASA (OR 5.5, 95%CI: 2.3-13)

  Kane S et al. Am J Med 2003

- **Increased risk of developing CRC**

  10 year retrospective cohort study: 31% of UC patients who stopped or were non-compliant to 5-ASA developed CRC vs. 3% of those on long-term therapy

  Moody et al. EJGH 1996

- **Increased health-care costs**

  Costs for non-hospitalized and hospitalized IBD patients with relapse are 2-3-fold and 20-fold higher than for patients in remission

  Bassi et al. Gut 2004

Non-compliance: causes

- Non-intentional
  - forgetfulness or carelessness
  - more frequent, up to 2/3 of all non - compliance

- Intentional
  - patient´s active decision
  - less frequent, clinically more significant

Sewitch et al. AJG 2003; D´Inca et al. APT 2008

Prevalence of non-compliance in IBD

- Low rates of non - compliance of IBD patients to medication in clinical trials 5%-30%
- High rates of non-compliance in clinical practice 21-69%
- Differences in non-compliance across Europe (13% in France….46% in Germany)

Kane et al. AJG 2001, Kane et al. APT 2006
Cerveny et al. IBD 2007, Lakatos et al. JCC 2009,
Bermejo et al. JCC 2010
Robinson et al. Gastroenterology 2002

Predictive factors for non-compliance

- Patient related factors
- Disease related factors
- Medication related factors
- Doctor-patient related factors

Hawthorne et al. APT 2008*; Lakatos et al.* WJG 2009

Patient related predictive factors for non-compliance

- Male gender [OR 2.06, 95%CI: 1.17-4.88] *Kane et al. AJG 2001*
- Younger age (<40 years) [OR 1.5, 95%CI: 1.01-2.13] *D´Inca et al. APT 2008*
- Single relation status [86% vs. 52%, p<0.05] *Kane et al. AJG 2001*
- Full-time employment [OR 2.7, 95%CI: 1.1.-6.9] *Shale et al. APT 2003*
- Higher educational level [t=0.130, p=0.046] *Cerveny et al. IBD 2007*

Disease related predictive factors for non-compliance

- Shorter disease duration (<5 years):
  (OR 2.1, 95%CI: 1.30-3.39) *D´Inca et al.* APT 2008

- Quiescent disease activity (OR 2.9, 95%CI: 1.82-4.95)
  D´Inca et al. APT 2008

- More complicated disease course (higher number of previous surgeries) – better adherence (OR 1.75, 95%CI: 1.14-2.69)
  Lakatos et al. JCC 2009

Medication related predictive factors for non-compliance

- Number of medication
  (≥4 vs. <4 medications – 68% vs. 40%, OR 2.5, 95%CI: 1.4-5.7)

Kane et al. AJG 2001

- Dosing regime
  (multiple daily doses – OR 2.8, 95%CI: 0.99- 7.70)

D´Inca et al. APT 2008

- Drug formulation
  (topical vs. oral therapy – 68% vs. 40%, OR 0.25, 95%CI: 0.11-0.60)

D´Inca et al. APT 2008

- Side-effects of the medication
  (up to 1/3 of cause of intentional non-adherence)

Cerveny et al. IBD 2007

How to improve compliance: physician-patient relationship

- Important role of partnership collaboration in achieving higher rates of patient compliance to medication

- Patients with high level of concordance with their physicians had 33% better medication compliance

Kerse et al. *Ann Fam Med 2004*

- Direct correlation between patient-physician discordance and non-compliance

Sewitch et al. AJG 2003

How to improve compliance: Patients education

- Feeling of insufficient information about the disease – risk factor for non-compliance (OR 4.9, 95%CI: 1.1.-23.8)

  Bermejo et al. JCC 2010

- Written and oral education increased compliance by approximately 6-25%

  Krueger et al. Am J Pharm Assoc 2003

- Improved knowledge and patient satisfaction trend towards better compliance in patients after IBD education programme compared to those with only standard care

  Waters et al. Can J Gastroenterol 2005

How to improve compliance: Patients self-management

- 2 RCT on patient´s self-management:
  reduction in hospital visits, decrease in symptom duration, no increase in morbidity

Robinson et al. Lancet 2001; *Kennedy et al.* Gut 2004

<u>New forms of patient treatment & care</u>:

- Web-based patient education and care

Elkjaer et al. EJGH 2010;
Elkjaer et al. GUT 2011

How to improve compliance: Medication

- Dosing regimes simplification (once daily dosing vs. twice daily dosing of mesalazine)
- Avoidance of unnecessary multiple medications
- Treatment reminders (electronic reminders, pill boxes, medication placing close to daily used objects,..)

Communication is changing

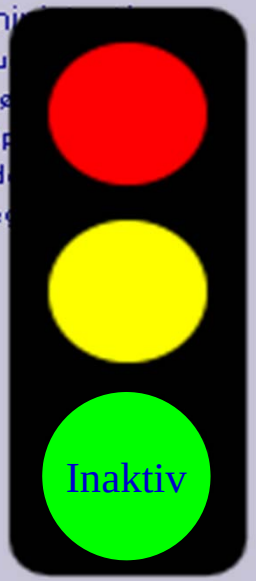
How can we best use it to help us?

Web concept & compliance efficacy in IBD and IBS

- www.uc.constant-care.dk (published in GUT, 2011)
- www.cd.constant-care.dk (submitted to IBD)
- www.meza.contant-care.dk (starts March 2012)
- www.gravid.constant-care.dk (starts May 2012)
- www.ibs.constant-care.dk (finish April 2012)

Constant-care

- Velkommen
  - Voldsomme symptomer
  - Vurdering
  - Sikkerhed
  - Udfyldning af skemaer
- Indtastning
  - Sygdomsaktivitet (SCCAI)
  - Livskvalitet (s-IBDQ)
- Behandling
  - Behandlingsforløb
  - Behandlingsvejledning
- **Resultater**
- Om Colitis Ulcerosa
- E-learning
- Kontakt læge
- Admi…
  - Bru…
  - Spø…
    - Sp…
  - Sid…
  - Læ…



Sygdomsstatus

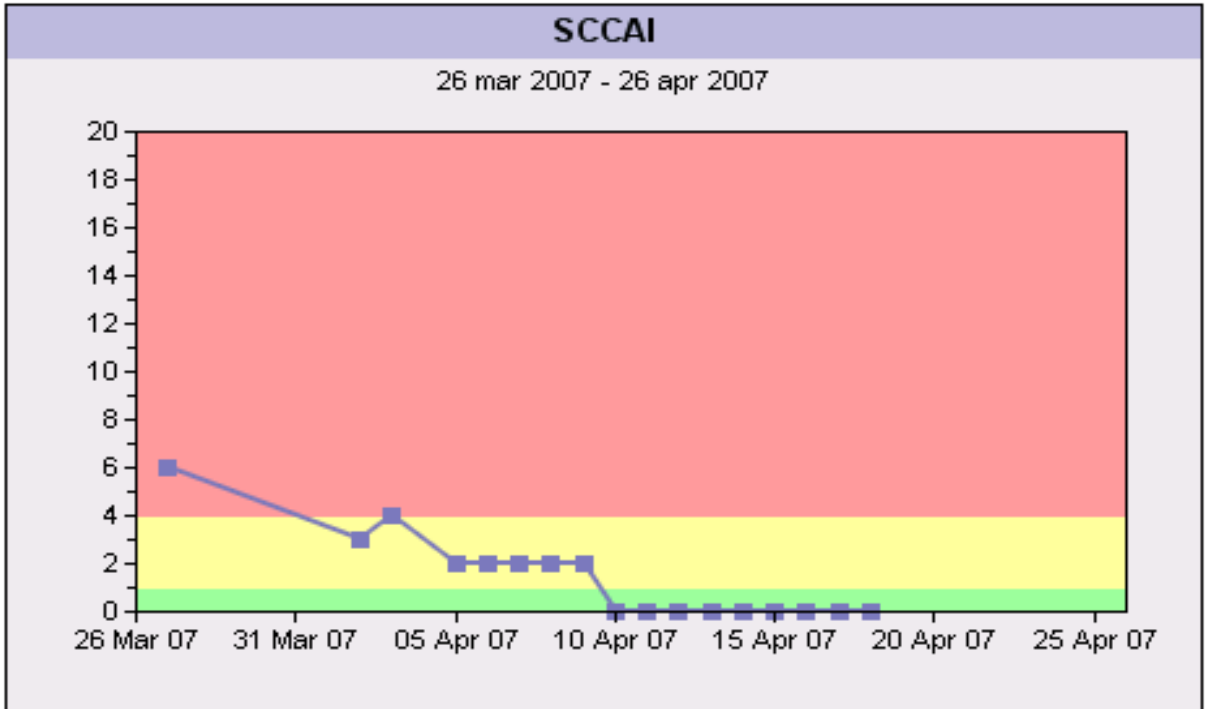
Du har et tilbagefald.
Fra den dato skal du i de næste 4 uger fortsætte med høj dosis behandling, selv om du kommer i gul eller grøn zone.

◀ Indtastning Behandling ▶

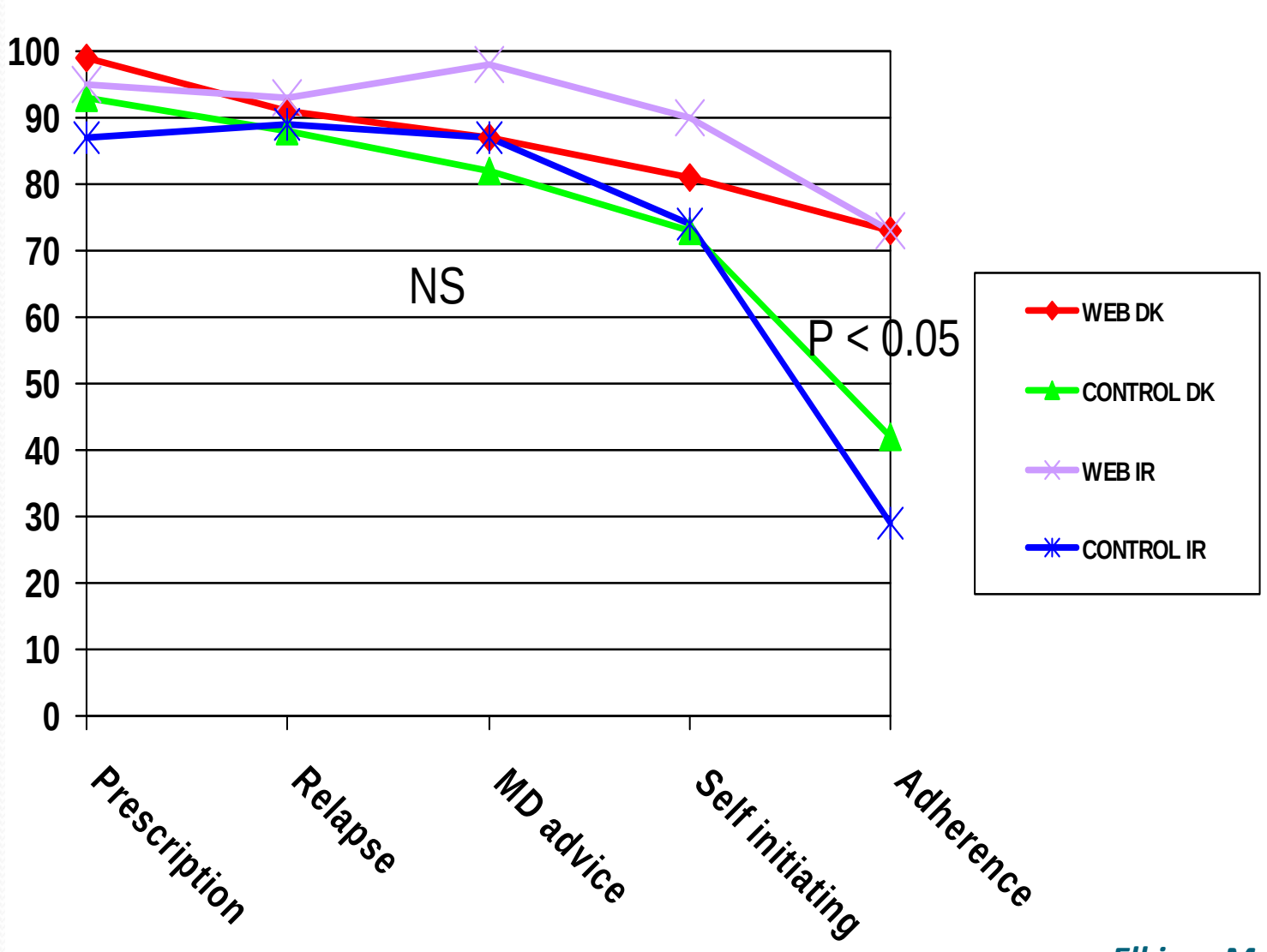
Nedenfor kan du se din sygdomsstatus målt ved symptomscore SCCAI:

Fra: 26-03-2007 Til: 26-04-2007 Skift periode

Label



Web patients have better compliance in UC

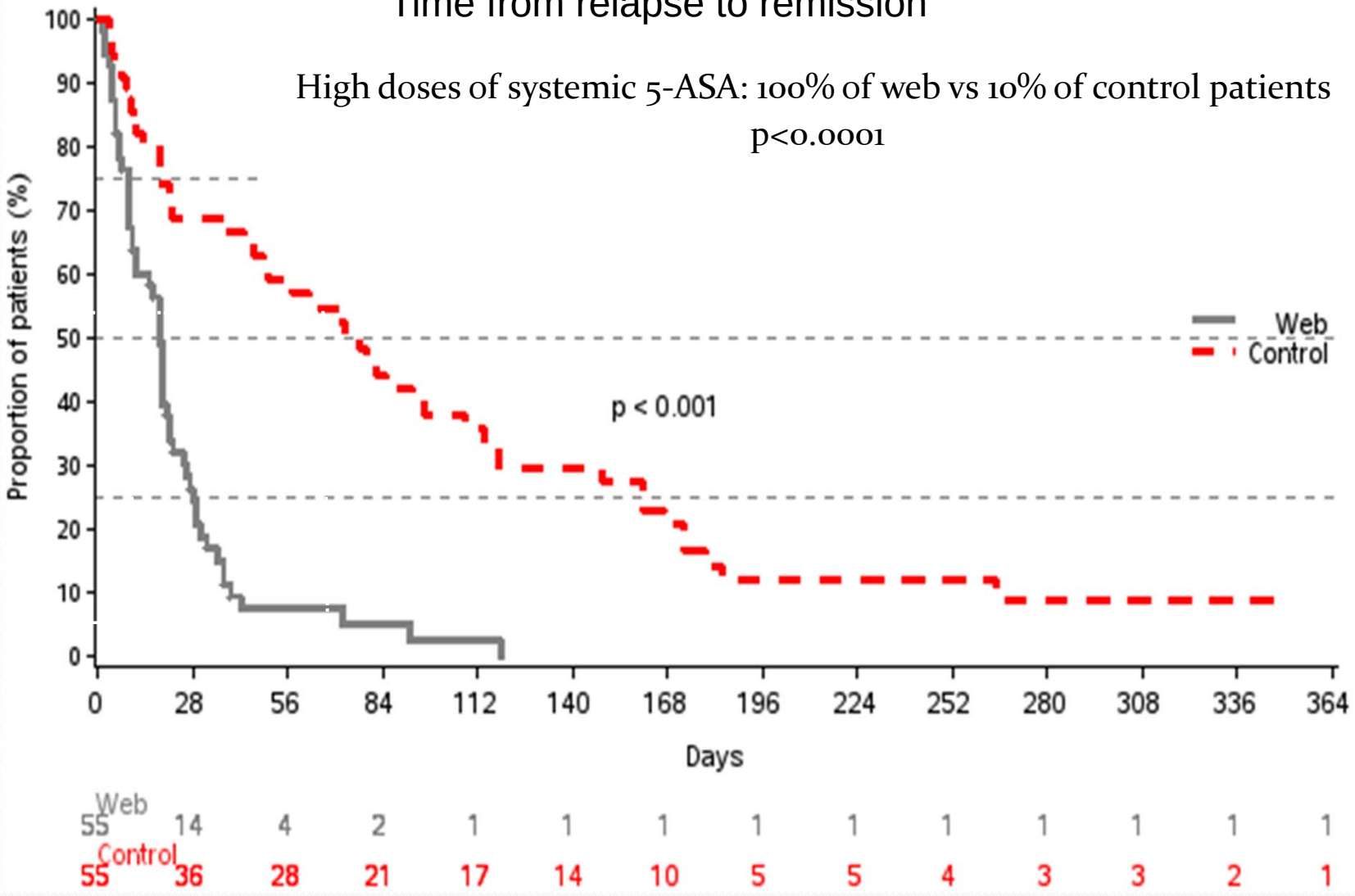


Elkjaer M et al. GUT 2010

Web patients have shorter relapses due to better compliance

Time from relapse to remission

High doses of systemic 5-ASA: 100% of web vs 10% of control patients
p<0.0001



Elkjaer M et al, GUT 2010

www.cd.constant-care.dk

Pilot study

- 27 CD patients aged 18-66
- IFX maintenance therapy Q4W-Q12W interval
- 3 visits: baseline, 6 and 12 months

Patient Education Center (PEC)

- 1 hour education regarding CD
- 1 hour practical training on www.cd.constant-care.dk

Questionnaires:

- Web-related questionnaires (weekly since 4th week after each infusion) (HBI, s-IBDQ)

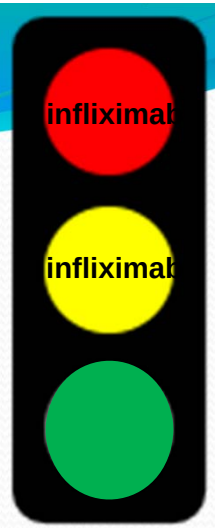
  Infusion related questionnaires (HBI, s-IBDQ)

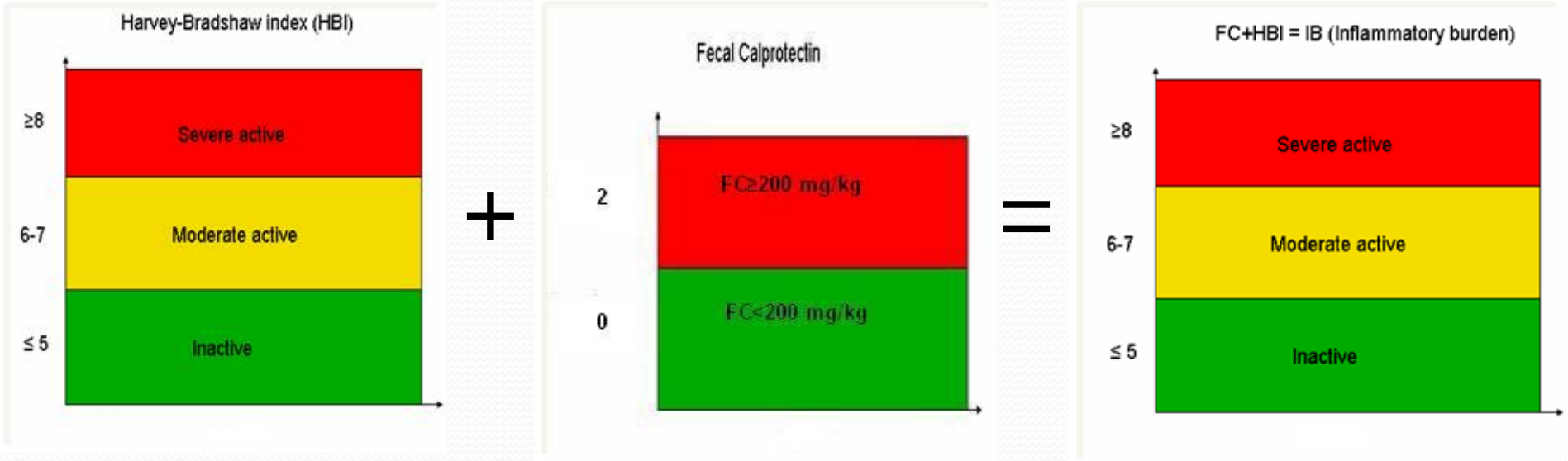
Fecal calprotectin (FC) measurement by Rapid scane test

- *Pedersen N et al.*, submission

Concept of www.cd.constant-care.dk

Assessment of IB once a week four weeks after last IFX



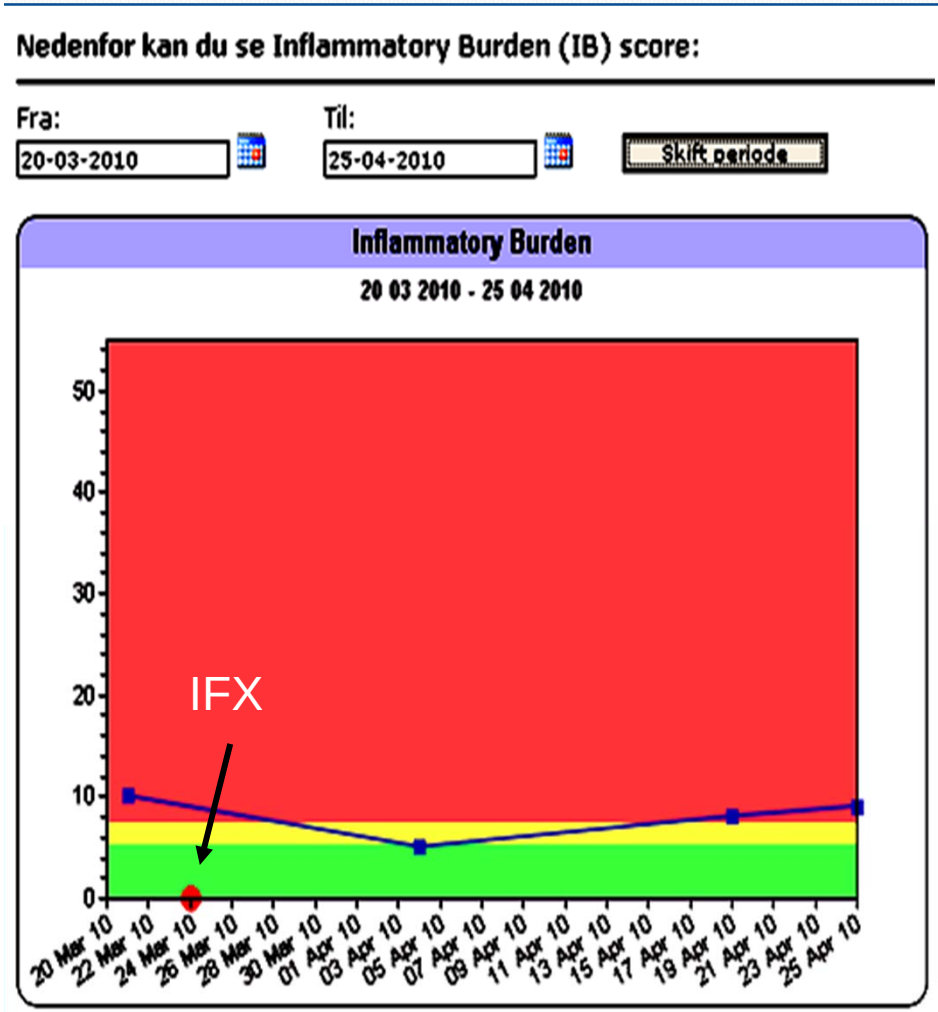


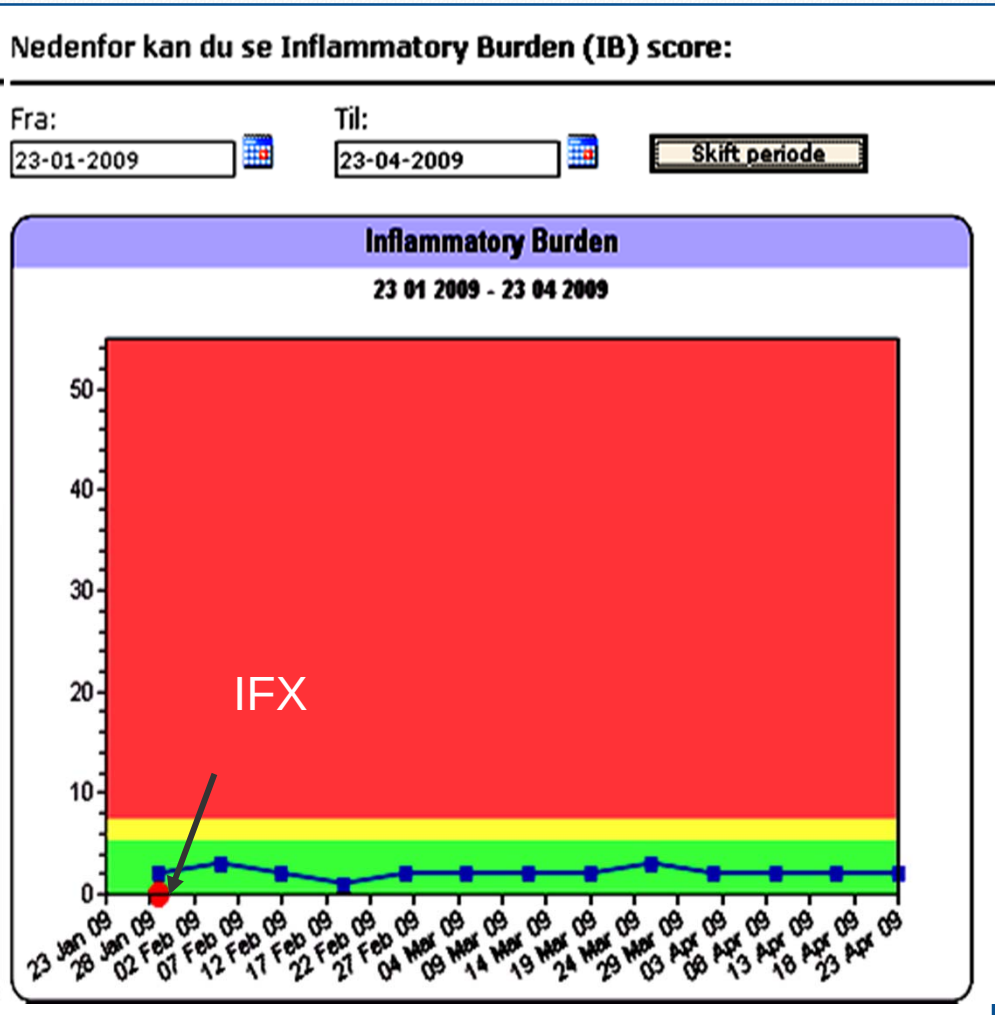
Pedersen N et al., submission

Disease status

Red area (Q4-Q12)
Contact in-patient clinic for IFX

Green area (Q12)
Contact in-patient clinic for IFX infusion





Pedersen et al. submission

Results

- **23 patients completed the study period**
- In total 121 IFX infusions given during the study period

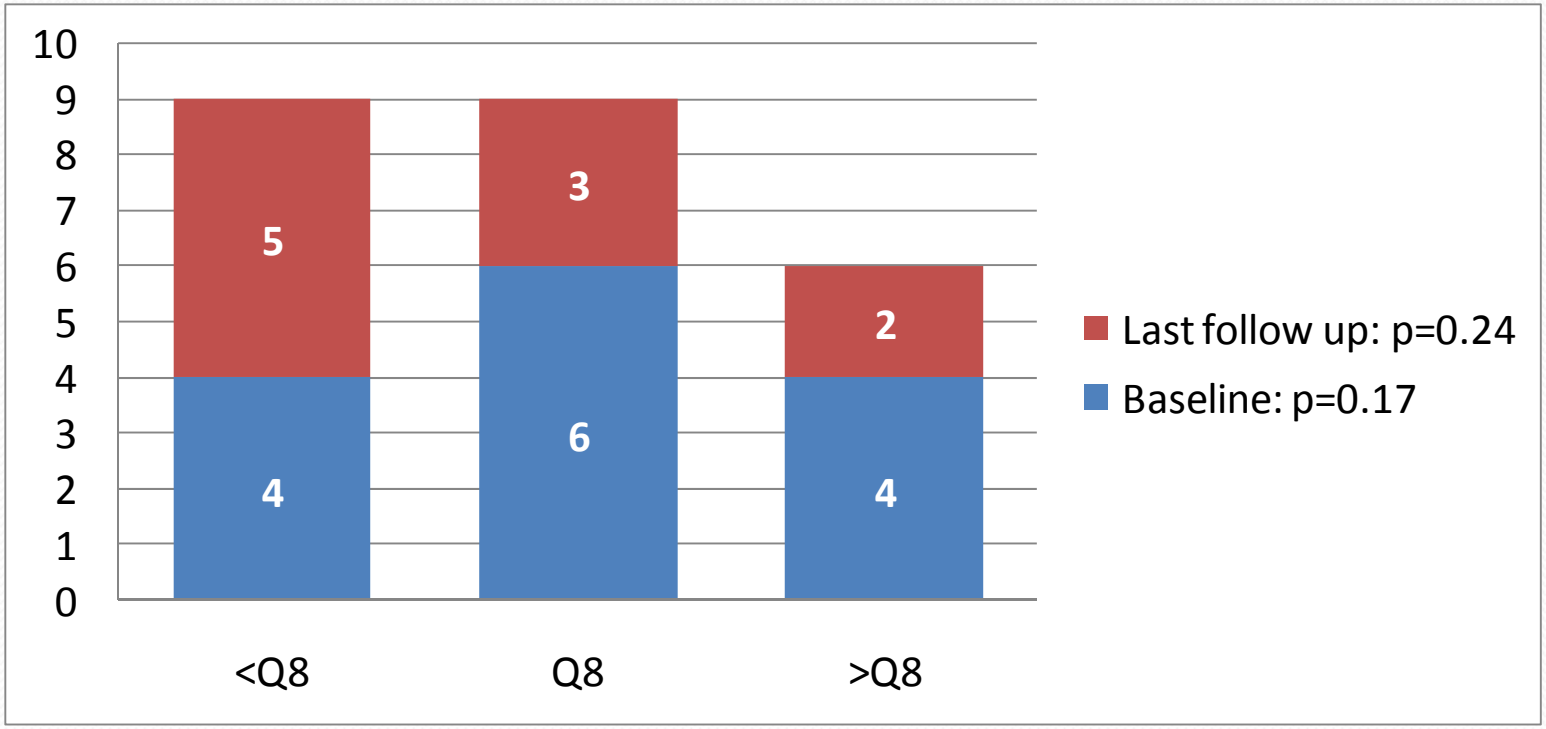
- Median interval of IFX infusions: Q9W (range 4-18)
  - 24 (20%) < 8weeks
  - 37 (31%) = 8weeks
  - 59 (49%) > 8weeks

  - Non-compliance: 16 (13%) IFX infusions were given at Q13W-Q18W (pts decision)

Pedersen N. et al., submission

Inflammatory Burden

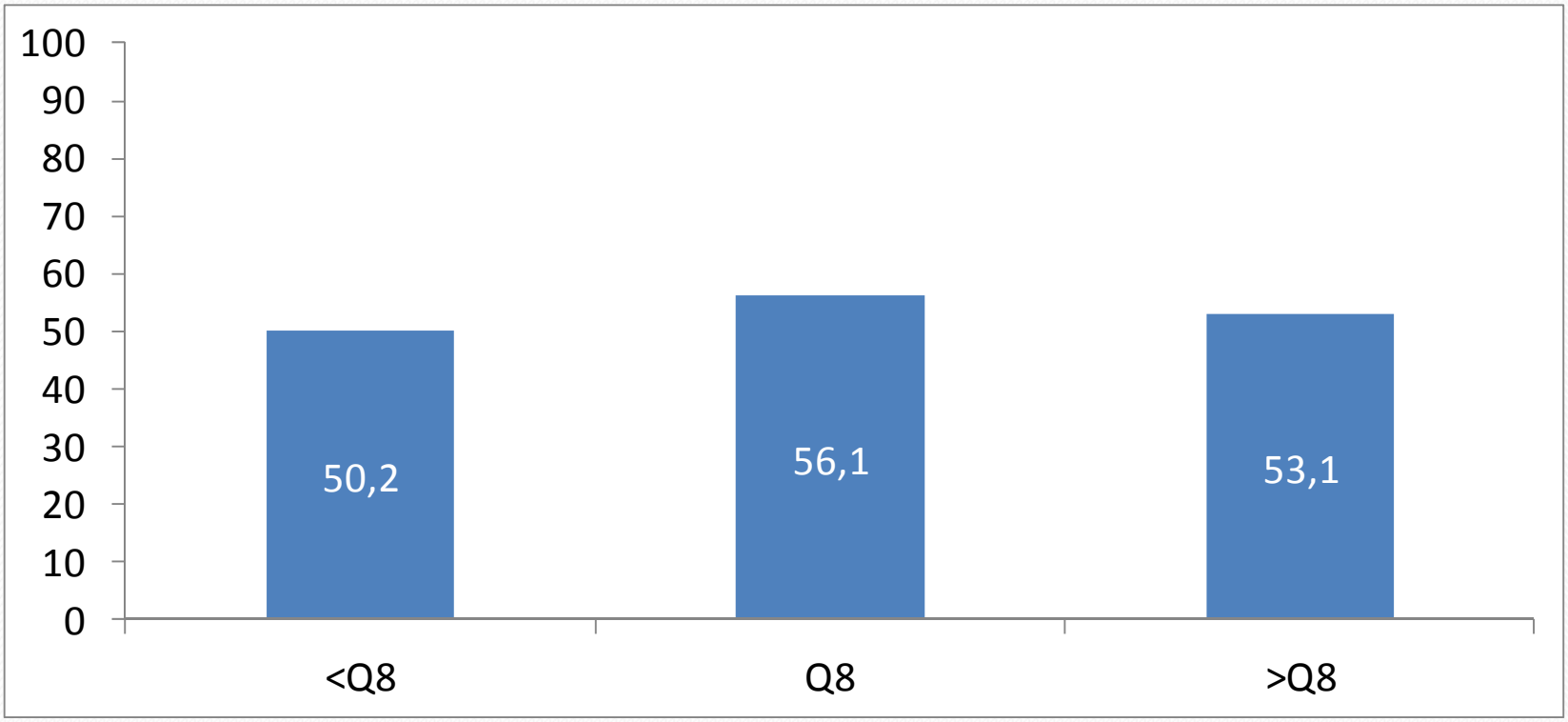
	Baseline	Last follow-up	P
Mean IB	3	4	0.09*



Wilcoxon Signed Ranks Test;; **Kruskal Wallis Test

IBDQ

	Baseline	Last follow-up	P
Mean IBDQ ±SD	55.2±10.4	55.0±12.3	0.63*



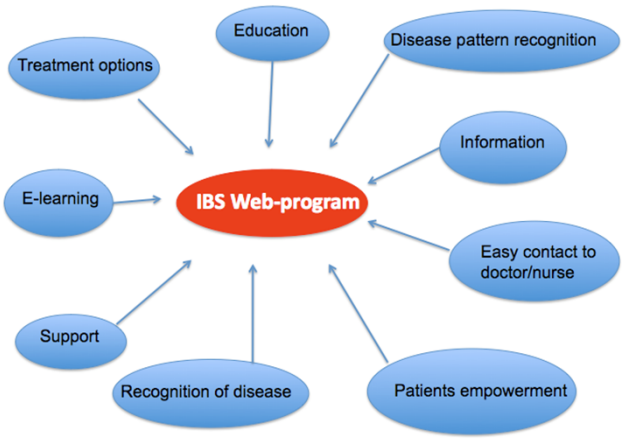
Wilcoxon Signed Ranks Test;; **Kruscal Wallis Test

www.ibs.constant-care.dk

- Randomised, controlled, web-based study, scrutinising the effect of a 6 week long treatment with FODMAP vs. Diclofor vs. Control

- Evaluation on the efficacy of a web-based treatment program for patients with IBS – does it optimize the current treatment options?

+



Can IBS patients by using the web-program:

✗ Decrease disease activity?
✗ Increase quality of life?
✗ Describe their own current phenotype by pattern recognition?
✗ Increase the effect of current treatment options?
✗ Decrease cost for themselves, the doctors and the health care system?

Could this be an easy and effective management of this difficult patient population?
Will we end up with more satisfied patients

What is "FODMAP"

(Exclusion of certain foods in the diet)

F ermentable
O ligo
D i

Examples of food to be avoided:

The evidence base is now sufficiently strong to recommend its widespread application

(Gibson et al, JGH

Dicoflor® - a probiotic

- Lactobacilli Rhamnosus GG (6 billion bacteria)
- Effective for the intestine colonization
- Resistant to the stomach juice and bile salts
- Characterised by good adherence to intestinal cells
- Immune modulator
- Its role in the treatment of IBS is still unclear

Alimentary Pharmacology & Therapeutics

A randomized double-blind placebo-controlled trial of *Lactobacillus* GG for abdominal pain disorders in children

A. GAWROŃSKA*, P. DZIECHCIARZ*, A. HORVATH† & H. SZAJEWSKA†

Constant Care

www.ibs.constant-care.dk

- Velkommen
  - Voldsomme symptomer
  - Sikkerhed
  - Vejledning
  - Udfyldning af skemaer
- Indtastning
  - IBS-SSS
  - IBS-QOL
  - Ændre medicin
  - Årsag til forværring
- Resultater
- Om colon irritable
- E-learning
- Kontakt læge
- Administration
  - Brugere
  - Læger
- Ændre Password

Eksisterende brugere:

Fuldt navn	Admin	Deaktiveret	Status	
	False	False	Grøn	Rediger
	False	False	Grøn	Rediger
	False	False	Grøn	Rediger
	False	False	Rød	Rediger
	False	False	Rød	Rediger
	False	False	Rød	Rediger
	False	False	Rød	Rediger
	False	False	Grøn	Rediger
	False	False	Gul	Rediger
	False	False	Gul	Rediger
	False	False	Rød	Rediger
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	False	False	Grøn	Rediger
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	False	False	Gul	Rediger
	False	False	Grøn	Rediger
	False	False	Gul	Rediger
	False	False	Gul	Rediger
	False	False	Data mangler	Rediger
	False	False	Gul	Rediger
	False	False	Rød	Rediger
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	True	False	Rød	Rediger
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	False	False	Data mangler	Rediger
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	False	False	Gul	Rediger
	False	False	Grøn	Rediger
	False	False	Rød	Rediger
	False	False		Rediger
	False	False	Gul	Rediger
	False	False	Rød	Rediger
	False	False	Data mangler	Rediger

IBS-SSS & IBS-QOL – traffic light

IBS-Severity score system

- Int. validated
- 5 questions
  - Pain (2)
  - Bloating
  - Stool
  - Overall influence
- Scores disease activity
  - 0-175 = inactive/mild = GREEN
  - 176-300 = moderate = YELLOW
  - 301-500 = severe = RED

IBS-Quality of life

- Int. Validated
- 34 questions
  - Dysphoria
  - Activity
  - Body image
  - Health worry
  - Avoidance
  - Social reaction
  - Impact on sex life
  - Relationship
- 0-100 % score
  - 0 % = best Qol = GREEN
  - 100% = worst Qol = RED

IBS – Severity score system = Disease activity

Constant Care

- Velkommen
  - Voldsomme symptomer
  - **Sikkerhed**
  - Vejledning
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1. Hvis du fortiden lider af mavesmerter, hvor alvorlige er de så?

Ingen smerter — Meget alvorlige

2. Angiv det antal dage du har haft mavesmerter inden for de sidste 10 dage

3. Hvis du fortiden lider af oppustet mave, hvor alvorligt er det så

Ikke oppustet — Meget alvorligt

4. Hvor tilfreds er du med dine afføringsvaner

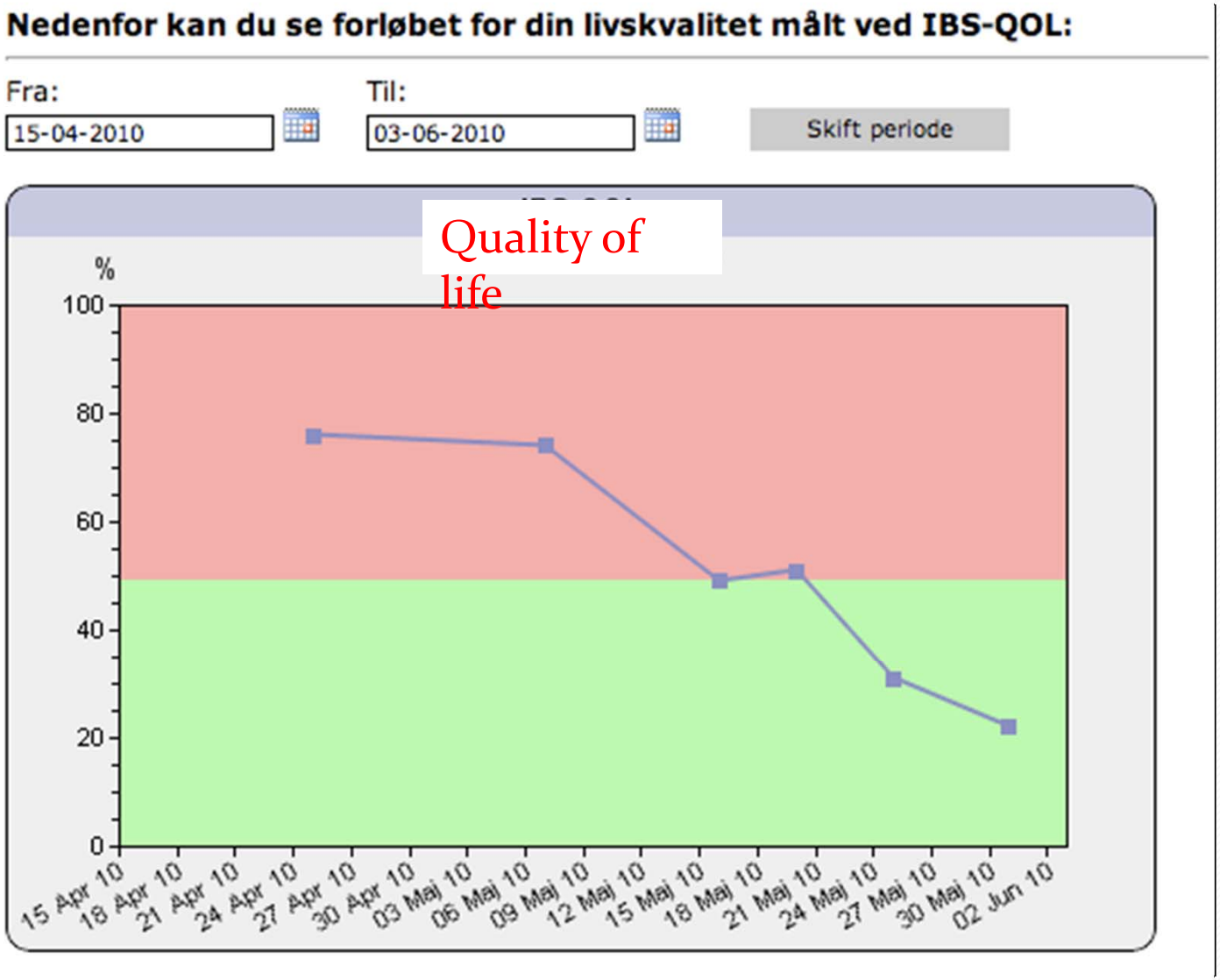
Meget tilfreds — Meget utilfreds

5. Angiv med et kryds på understående linje i hvor høj grad din irritable tyktarm påvirker eller griber ind i dit liv i al almindelighed

Slet ikke — Fuldstændig

Gem | Slet data for denne dato

Case: 38 y, female, IBS in 2009, randomized to FODMAP



Results

Patients characteristics

	FODMAP	Dicoflor	Control
Number of patients	11	15	14
Male/Female	3:8	4:11	3:11
Age: Median, range	35 (20-56)	40 (22-60)	36 (18-46)
Years since diagnosis[range]	1,45 [1-3]	2,75 [1-11]	3,6 [1-12]
IBS-A*	1 (9 %)	5 (33 %)	2 (14 %)
IBS-C**	2 (18 %)	3 (20)	3 (21 %)
IBS-D ***	7 (64 %)	5 (33 %)	8 (57 %)
Smokers [%]	23	20	14
BMI [range]	26 [19-38]	21 [18-25]	26 [19-34]

Table 1: Baseline characteristics of study sample (IBS subtypes evaluated after Bristol Stool Chart).
** IBS mixed type; ** IBS constipation predominant; ***IBS diarrheal predominant.*

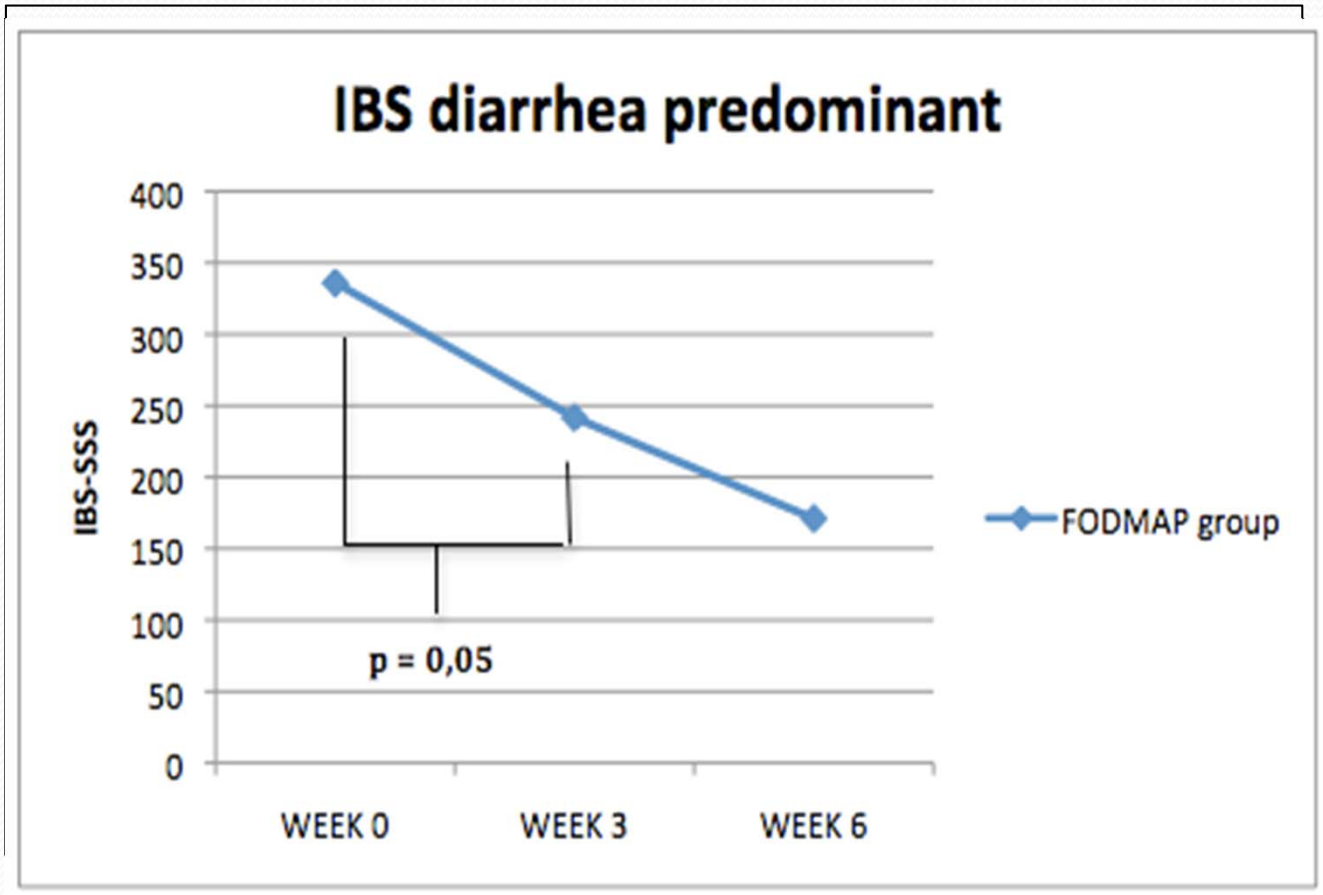
Drop outs

Six patients dropped out. Three in the FODMAP group (one were diagnosed with CD, one had a cerebral insult and one dropped out due to lack of effect of the diet). Two in the Dicoflor group (one caused by lack of compliance, one due to side effect in form of severe constipation). One dropped out in the control group due to a severe life event.

Results: The web-program

- 3 incidences were the web-program was dysfunctional due to programming errors
- No cases of patients who did not have access to the Internet at their home or work.
- The age range was 18-60 years and there were not reported any user-oriented problems in any age group.
- Completing the questionnaires once a week was a problem for 6/40 (15 %).
- There were a higher number of consultations in the FODMAP group (47 %).

Results: Disease activity (IBS-SSS)

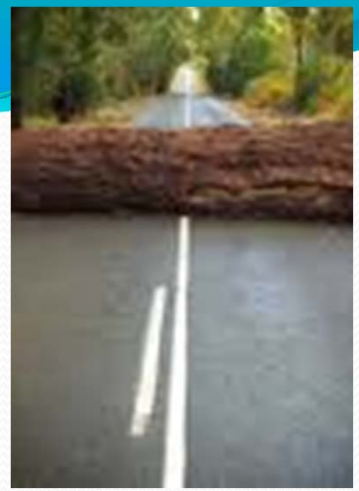


Not significant reduction but positive trend observed

Conclusion

- The web-program is well functioning and is easy for the patients to use
- Disease activity was significantly reduced during the 6 weeks in those following the low FODMAP diet who had IBS-D subtype
- No effect on Quality of life
- Further evaluation on the web-program is in progress and will reveal if there is any effect on disease cause and whether it provides any possible economical benefits for the health care system

What are the barriers?



- Undocumented efficiency of current treatment options
- Lack of experience with E-health
- Lack of patient/doctor contact
- The barriers of implementation of new technology
- Limited access to the internet
- World perspective

Conclusion

- Preliminary results indicate that the web-program could be a beneficial, cost-effective and efficient way of handling IBS
- Pattern Recognition seems to be feasible for the patients to depict
- Whether we can confirm the efficacy of the low FODMAP diet and Dicoflor® in this study design is still uncertain
- www.ibs.constant-care.dk is an efficient way to evaluate treatment impact
- E-health has yet to show impact on IBS
  - Disease course
  - Outcome
  - Cost effectiveness

Larger randomised controlled trials

- Should we take action now and change the management of IBS?

Take home messages

- Non-compliance to therapy in IBD is very common and has been reported in 40% of patients
- The cause of medication non-compliance is multi-factorial and may vary between the countries
- Poor compliance may result in higher relapse rate, disabling disease and increased risk for CRC [UC]

Take home messages

- The health care providers should understand the different patient types and identify the risk factors of non-compliance
- Improvement of medication compliance in patients with IBD is important challenge for physicians

Remarks

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“It’s time to tango”
From paternalism to partnership