Hvordan bliver et PRO til et brugbart PROM?

Monitorering er nødvendigt i forskning og anbefales i klinisk praksis

Robin Christensen

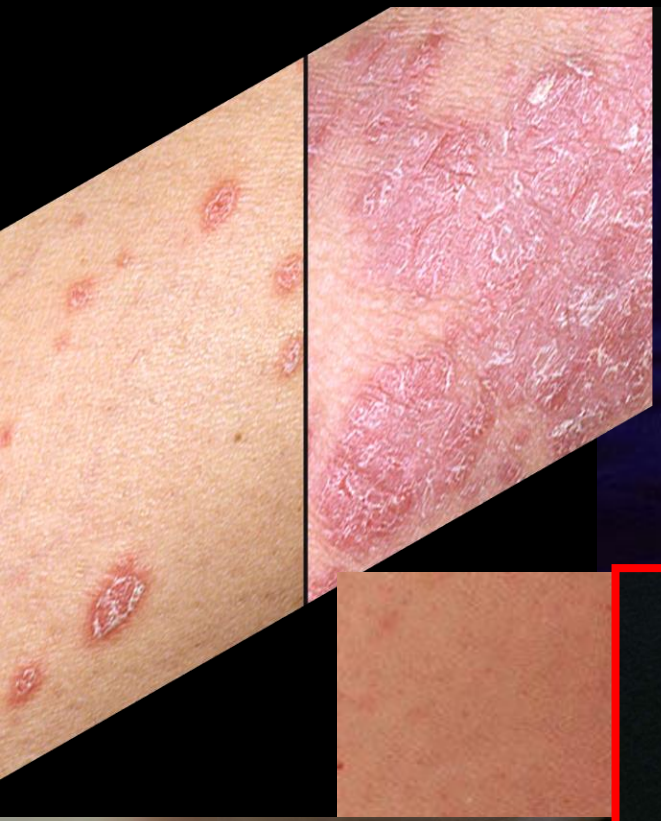
Cand. Scient., Phd. (Biostatistik)

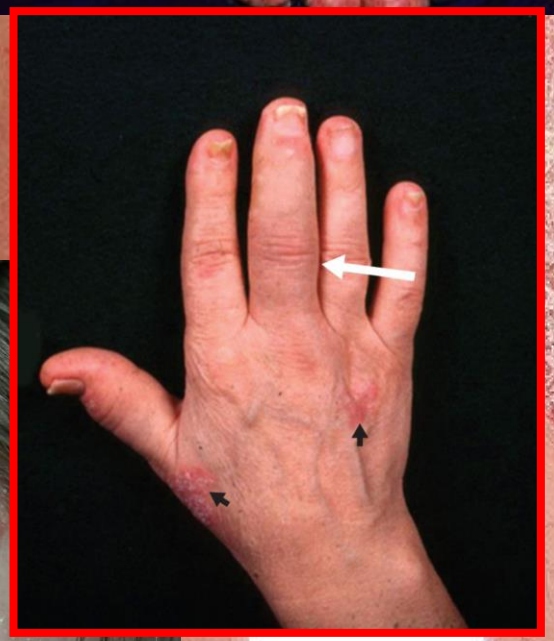
Professor i Biostatistik og Klinisk epidemiologi

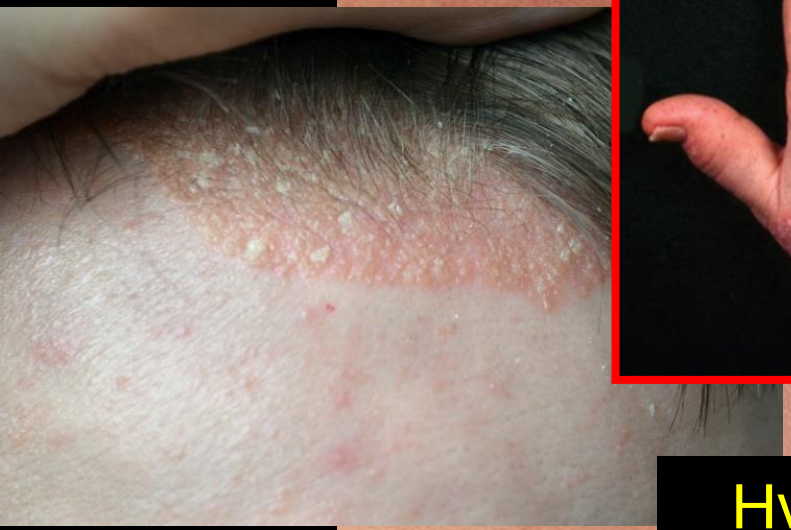
Musculoskeletal Statistics Unit,
The Parker Institute
Bispebjerg og Frederiksberg Hospital

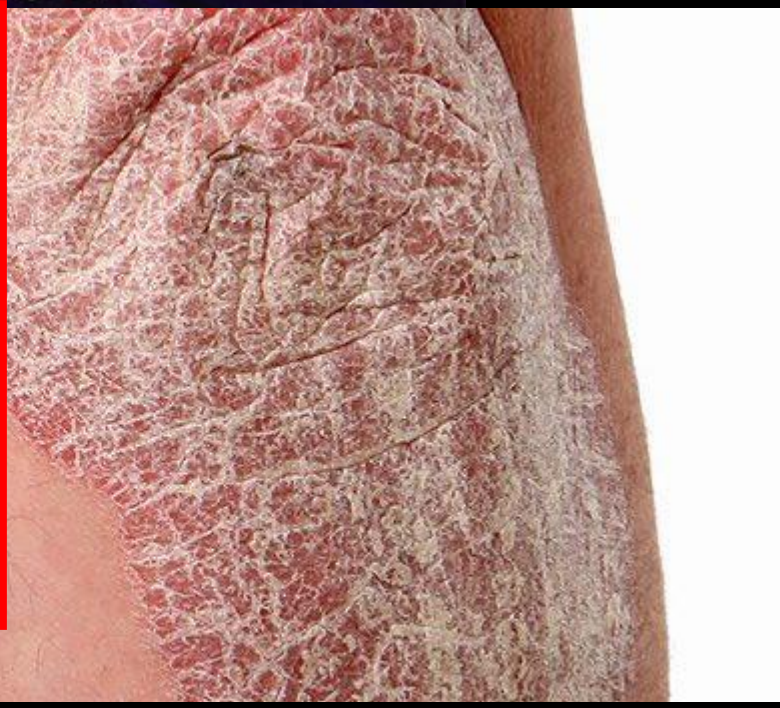
Region of Southern Denmark
OUH
Odense University Hospital

Hvad er problemet med psoriasis…..









Hvem er sværest påvirket af sin sygdom?

Hvad er et "randomiseret studie"?

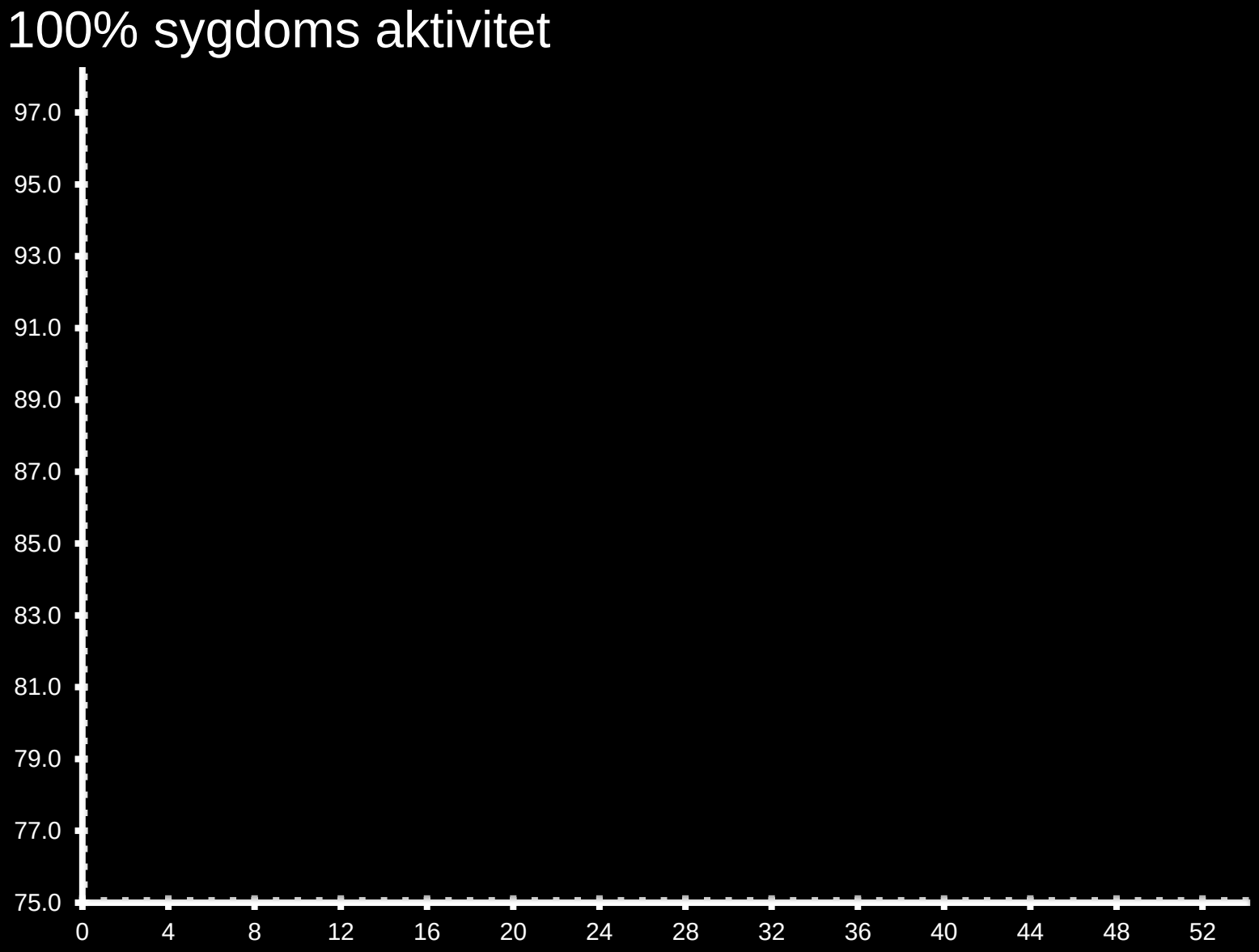
- RCT: Et randomiseret kontrolleret studie er en videnskabelig undersøgelse, der undersøger effekten af en ny behandling i forhold til standardbehandling

- Det kaldes også for et lodtrækningsforsøg….

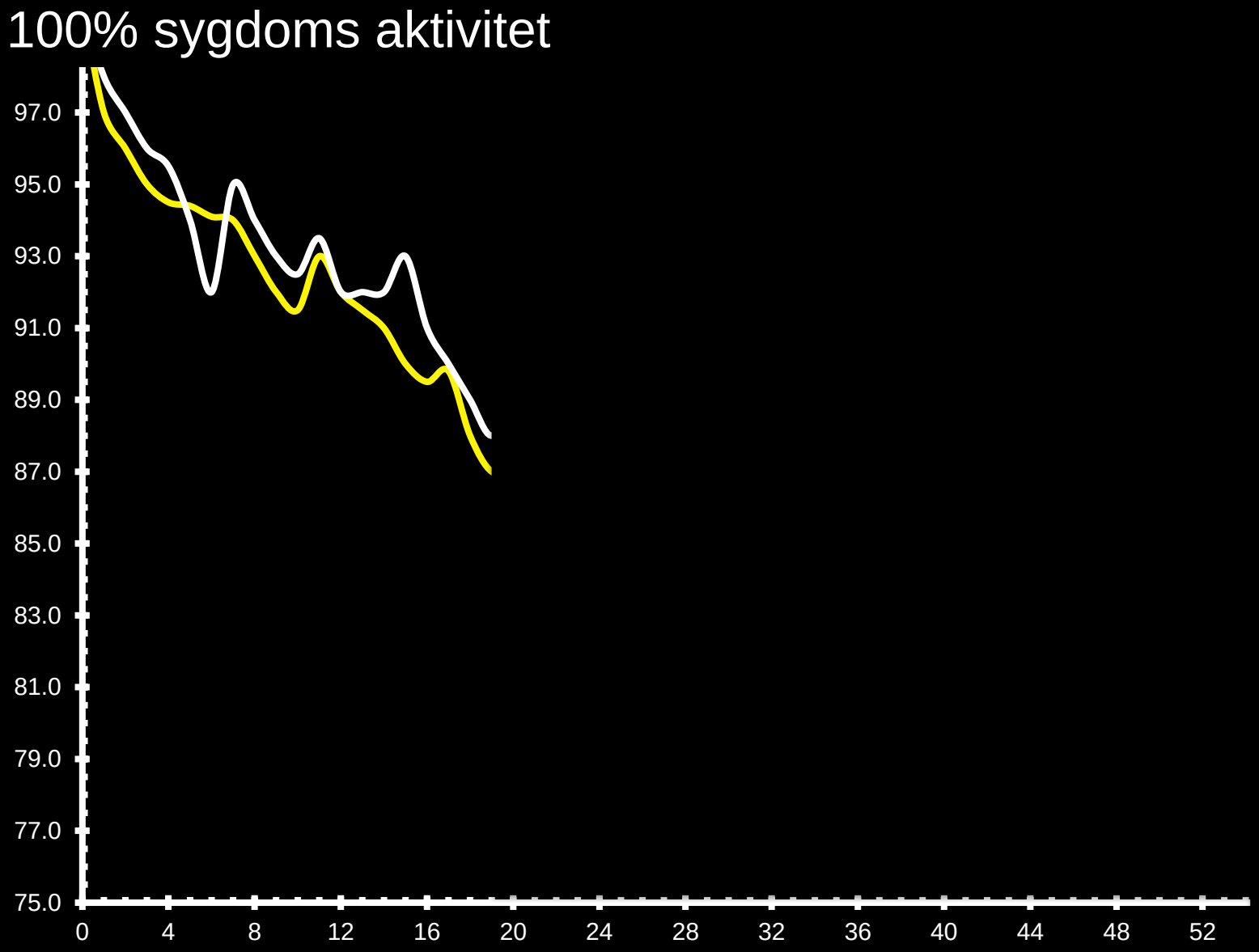
- Dvs. de deltagende patienter fordeles tilfældigt i grupper ved lodtrækning

- Resultaterne for dem, der får den nye behandling sammenlignes med dem, der opnås i en kontrolgruppe (der modtager den hidtil bedste kendte behandling).

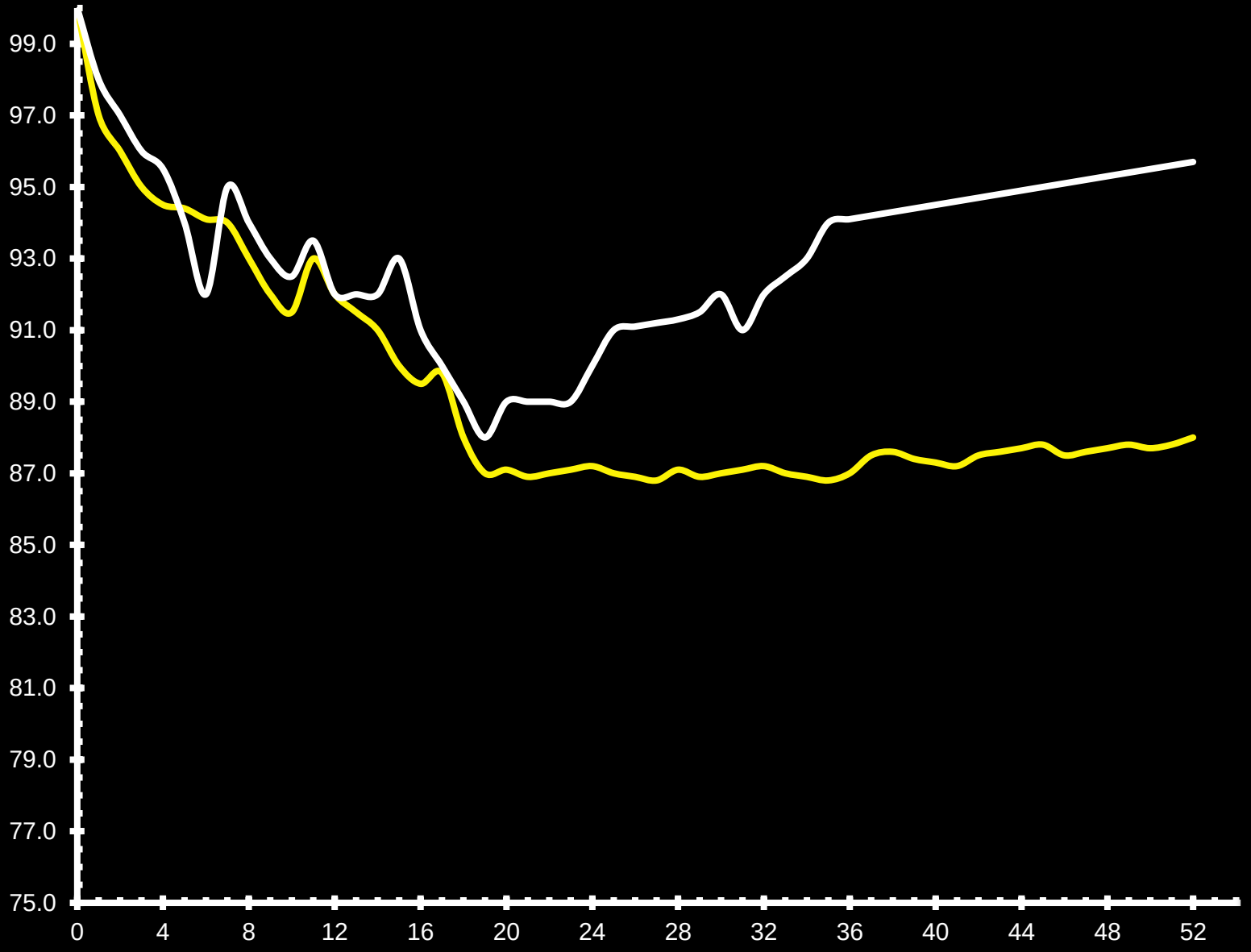
Hvordan illustreres effekten i et RCT?



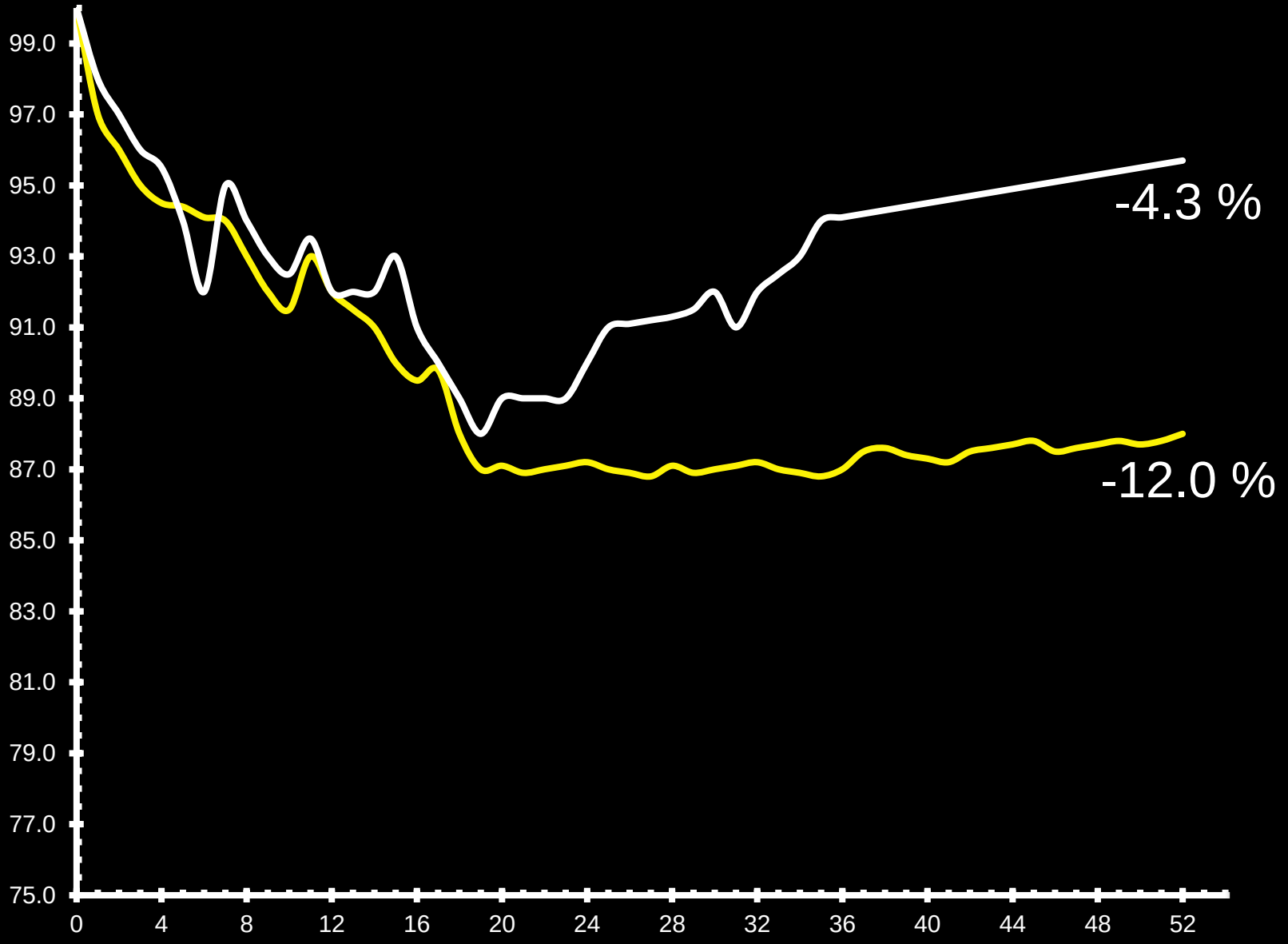
Hvordan illustreres effekten i et RCT?



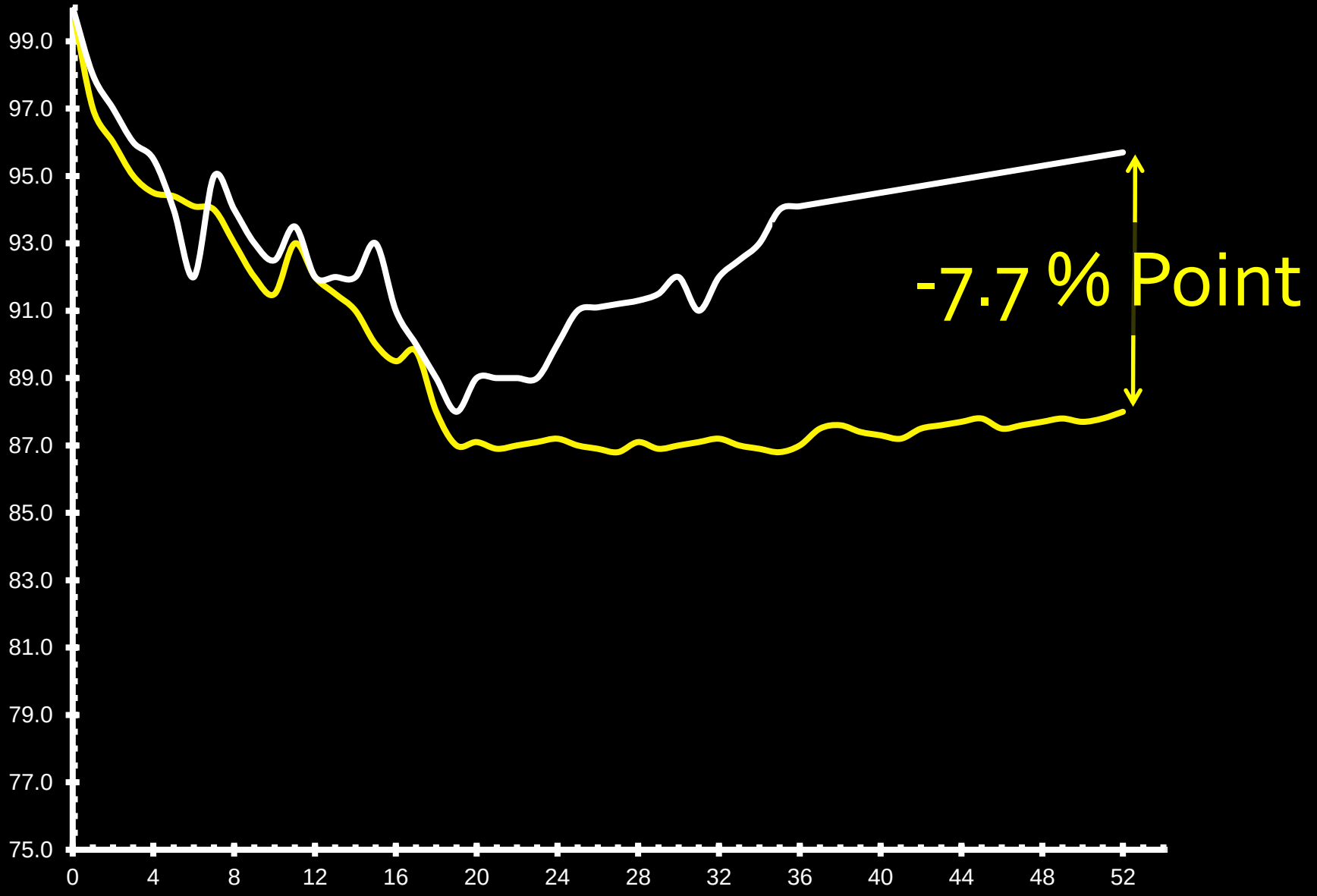
Hvordan illustreres effekten i et RCT?



Hvordan estimeres effekten i et RCT?



Hvordan estimeres effekten i et RCT?



Hvordan afprøves nye behandlinger?

- Patient-gruppe — Diagnose: Psoriasis + Overvægt
- Intervention — Vejledning af diætist + Cambridge Weight Plan
- Comparator (Kontrol gruppe) — Opfordring til Vægttab….
- Outcome (Effekt mål) — Ændring i kropsvægt & Ændring i PASI score

Jensen P, et al.
JAMA
Dermatology, 2013

STUDY

ONLINE FIRST

Effect of Weight Loss on the Severity of Psoriasis

A Randomized Clinical Study

Peter Jensen, MD, PhD; Claus Zachariae, MD, DMSc; Robin Christensen, MSc, PhD; Nina R. W. Geiker, MSc; Bente K. Schaadt, MD, PhD; Steen Stender, MD, DMSc; Peter R. Hansen, MD, DMSc; Arne Astrup, MD, DMSc; Lone Skov, MD, DMSc

Importance: Psoriasis is associated with adiposity and weight gain increases the severity of psoriasis and the risk of incident psoriasis. Therefore, we aimed to measure the effect of weight reduction on the severity of psoriasis in obese patients with psoriasis.

Objective: To assess the effect of weight reduction on the severity of psoriasis in overweight patients.

Design: Sixty obese patients with psoriasis from our dermatology outpatient clinic were enrolled in a prospective randomized clinical trial in which they were allocated to a control group or an intervention group.

Setting: University hospital outpatient dermatology clinic.

Participants: We included 60 of 69 eligible overweight patients with psoriasis (body mass index [calculated as weight in kilograms divided by height in meters squared], 27-40; aged 25-71 years).

Interventions: The intervention group received a low-energy diet (LED) (800-1000 kcal/d) for 8 weeks to induce weight loss, followed by 8 weeks of reintroduction of normal food intake, reaching 1200 kcal/d. The control group was instructed to continue eating ordinary healthy foods.

Main Outcomes and Measures: Psoriasis Area and Severity Index (PASI) after 16 weeks, with Dermatology Life Quality Index (DLQI) as a secondary end point.

Results: The median PASI for all patients was 5.4 (interquartile range, 3.8-7.6) at baseline. At week 16, the mean body weight loss was 15.4 kg (95% CI, 12.3-18.5 kg; $P<.001$) greater in the intervention group than in the control group. The corresponding mean differences in PASI and DLQI, also in favor of the LED group, were −2.0 (95% CI, 4.1 to −0.1; $P=.06$) and −2.0 (95% CI, −3.6 to −0.3; $P=.02$), respectively.

Conclusions and Relevance: Treatment with an LED showed a trend in favor of clinically important PASI improvement and a significant reduction in DLQI in overweight patients with psoriasis.

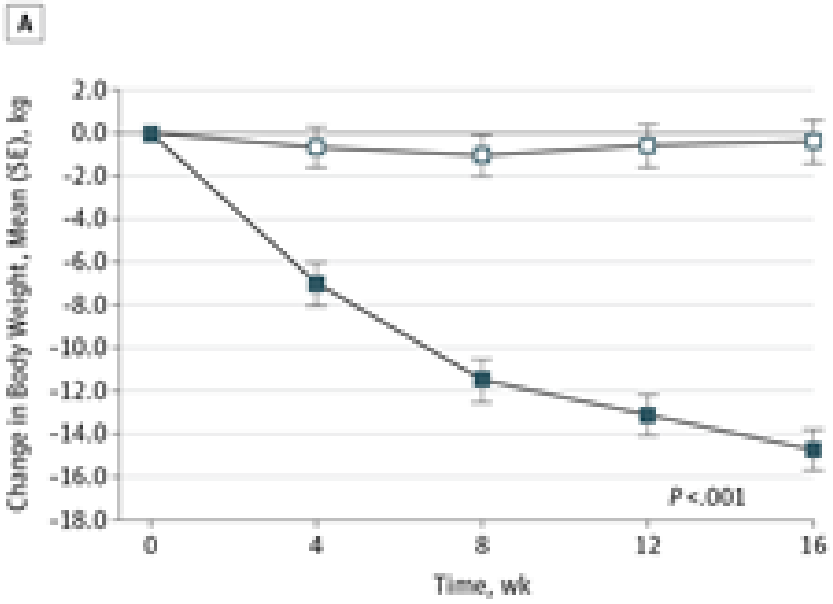
Trial Registration: clinicaltrials.gov Identifier: NCT01137188

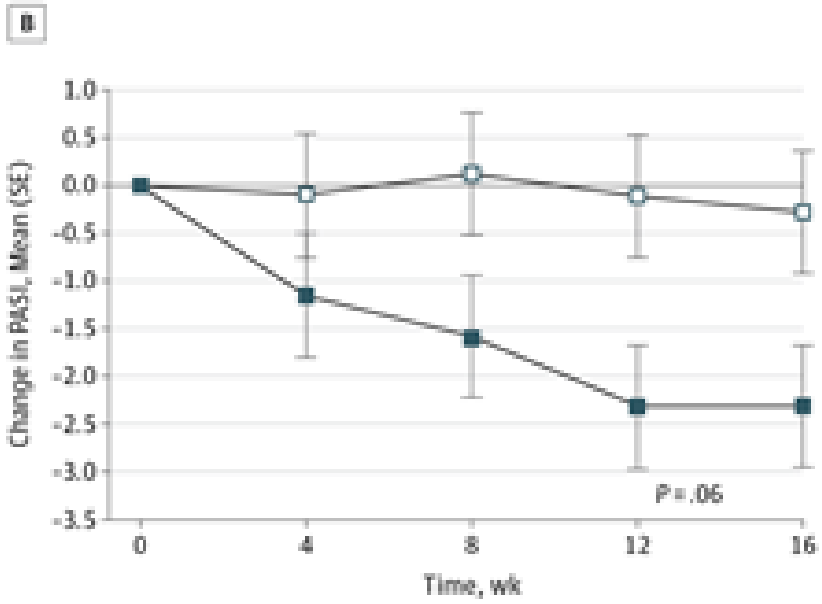
JAMA Dermatol.
Published online May 29, 2013.
doi:10.1001/jamadermatol.2013.722

PSORIASIS IS A CHRONIC INflammatory skin disease with a prevalence of about 2% in Northern Europe and North

mechanisms may exacerbate psoriatic lesions in overweight patients with psoriasis.[18] At present, the role of weight loss as a treatment for psoriasis in obese pa-

Jensen P, et al.
JAMA Dermatology, 2013





Hvad er en PASI Score?

- *P*soriasis *A*ctivity and *S*everity *I*ndex (PASI) bruges af hudlæger til at følge patienter med psoriasis over tid og til at evaluere effekten af behandlinger.

- PASI benyttes i RCT'er til at vurdere effekten af behandlinger; det kræver et trænet øje for at kunne bruge den med godt resultat.

- Vurderer hvor stort et område der er dækket, samt hvor slemt området er angrebet og derefter kombinere tallene.

- Kroppen = i fire områder; hvert af disse bedømmes individuelt og til slut lægges tallene sammen til en total score.

- Hver kropsdel vægter med en bestemt procentdel i beregningen…

RCT: Hvem ved hvad der bør måles?

Lægen?
Patienten?

Eller en kombination af begge…. (?)

About OMERACT

- 'Outcome Measures in Rheumatology' is an independent initiative of international health professionals interested in outcome measures in rheumatology
- 20+ years: has served a critical role in the development and validation of clinical and radiographic outcome measures in rheumatoid arthritis, osteoarthritis, psoriatic arthritis, fibromyalgia, and other rheumatic diseases
- Collaboration between Patients, Doctors and Methodologists
- Conferences every two years (May 2020!), and employs various other means to stimulate the development of consensus in outcome measurements

About OMERACT

- 'Outcome Measures in Rheumatology' is an independent initiative of international health professionals interested in outcome measures in rheumatology
- 20+ years: has served a critical role in the development and validation of clinical and radiographic outcome measures in rheumatoid arthritis, osteoarthritis, psoriatic arthritis, fibromyalgia, and other rheumatic diseases
- Collaboration between Patients, Doctors and Methodologists!

- Conferences every two years (May 2020!), and employs various other means to stimulate the development of consensus in outcome measurements

Multiple Endpoints in Clinical Trials

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

[January 2017]
Clinical/Medical

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 December 2016
EMA/CHMP/44762/2017
Committee for Human Medicinal Products (CHMP)

Guideline on multiplicity issues in clinical trials

About COMET

- ‘Core Outcome Measures in Effectiveness Trials’ brings together people interested in the development and application of agreed standardised sets of outcomes, known as ‘core outcome sets’ (COS).
- The minimum that should be measured and reported in all clinical trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials.
- The existence of a COS does not imply that outcomes in a particular trial should be restricted…
- Rather, the core outcomes will be collected and reported (Key Secondary!) making it easier for the results of trials to be compared, contrasted and combined as appropriate

About COMET

- 'Core Outcome Measures in Effectiveness Trials' brings together people interested in the development and application of agreed standardised sets of outcomes, known as 'core outcome sets' (COS).
- The minimum that should be measured and reported in all clinical trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials.
- The existence of a COS does not imply that outcomes in a particular trial should be restricted…
- Rather, the core outcomes will be collected and reported (Key Secondary!) making it easier for the results of trials to be compared, contrasted and combined as appropriate

PLOS | MEDICINE

GUIDELINES AND GUIDANCE

Core Outcome Set-STAndards for Development: The COS-STAD recommendations

Jamie J. Kirkham[1], Katherine Davis[1], Douglas G. Altman[2], Jane M. Blazeby[3], Mike Clarke[4], Sean Tunis[5], Paula R. Williamson[1]*

1 MRC North West Hub for Trials Methodology Research, Department of Biostatistics, University of Liverpool, Liverpool, United Kingdom, **2** Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, **3** MRC ConDuCT II Hub for Trials Methodology Research, School of Social & Community Medicine, University of Bristol, Bristol, United Kingdom, **4** Northern Ireland Hub for Trials Methodology Research, Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom, **5** Center for Medical Technology Policy, Baltimore, Maryland, United States of America

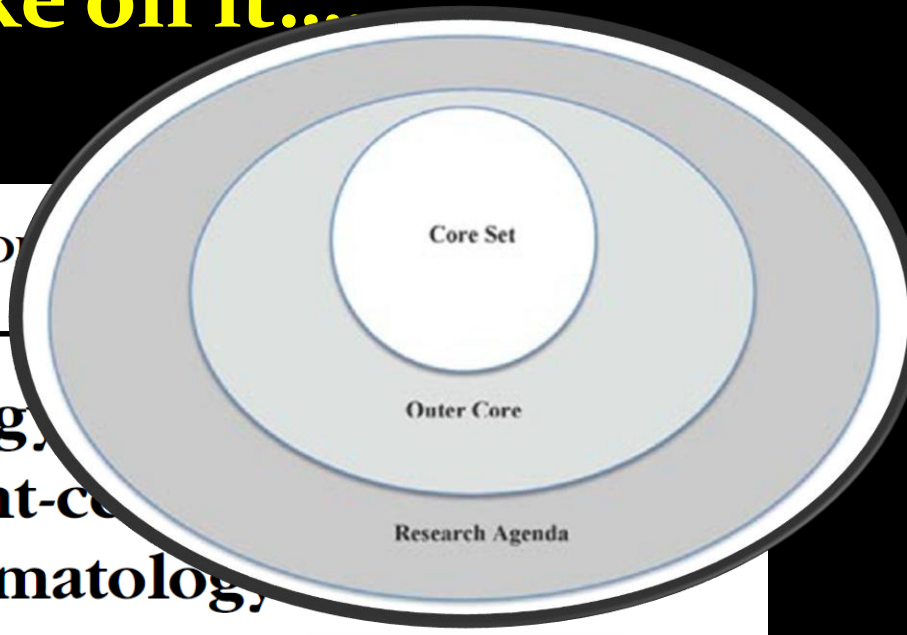
Core Outcome Set?

1: Outcome Domain(s) Set (represent the "*What*")

--- →

(represent the "*How*") 2: Outcome Measurement(s) Set

IDEOM's take on it...



FROM THE ACAD

The International Dermatolog
Group: Formation of patient-c
measures in dermatolog

Alice B. Gottlieb, MD, PhD,[a,b] Adriane A. Levin, BA,[a,c] April W. Armstrong, MD, MPH,[d] April Abernethy, MD,[e] Kristina Callis Duffin, MD, MS,[f] Reva Bhushan, MA, PhD,[g] Amit Garg, MD,[h] Joseph F. Merola, MD, MMSc,[i] Mara Maccarone,[j] and Robin Christensen, MSc, PhD[k]

Boston, Massachusetts; Denver, Colorado; Portland, Oregon; Salt Lake City, Utah; Schaumburg, Illinois; Manhasset, New York; Rome, Italy; and Copenhagen, Denmark

Core: *p* (combined) >70% (AND a lower limit of the 95% confidence interval >0.50);

p (combined) = the proportion of votes for an item/domain being important across both patients and health care providers.

J Am Acad Dermatol. 2015 Feb;72(2):345-8.

Core Domain Sets:

Psoriasis related

eular

EXTENDED REPORT

Ann Rheum Dis 2016;

International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials

Ana-Maria Orbai,[1] Maarten de Wit,[2] Philip Mease,[3] Judy A Shea,[4] Laure Gossec,[5,6] Ying Ying Leung,[7] William Tillett,[8] Musaab Elmamoun,[9] Kristina Callis Duffin,[10] Willemina Campbell,[11] Robin Christensen,[12] Laura Coates,[13] Emma Dures,[14] Lihi Eder,[15] Oliver FitzGerald,[9] Dafna Gladman,[16] Niti Goel,[17,18] Suzanne Dolwick Grieb,[19] Sarah Hewlett,[14] Pil Hoejgaard,[12] Umut Kalyoncu,[1,20] Chris Lindsay,[21] Neil McHu[illegible] Alexis Ogdie[25]

JAMA Dermatology | Original Investigation

JAMA Dermatology October 2018 Volume 154, Number 10

Identifying a Core Domain Set to Assess Psoriasis in Clinical Trials

Kristina Callis Duffin, MD, MS; Joseph F. Merola, MD, MMSc; Robin Christensen, MSc, PhD; John Latella, MS; Amit Garg, MD; Alice B. Gottlieb, MD, PhD; April W. Armstrong, MD, MPH

Core Domain Sets:

Psoriasis related

Psoriatic Arthritis (PsA)

- musculoskeletal disease activity,
- skin disease activity,
- pain,
- patient global,
- physical function,
- health-related quality of life,
- fatigue,
- systemic inflammation.

Psoriasis (Pso)

- skin manifestations,
- psoriasis and psoriatic arthritis symptoms,
- health-related quality of life,
- investigator global assessment,
- patient global assessment,
- treatment satisfaction.

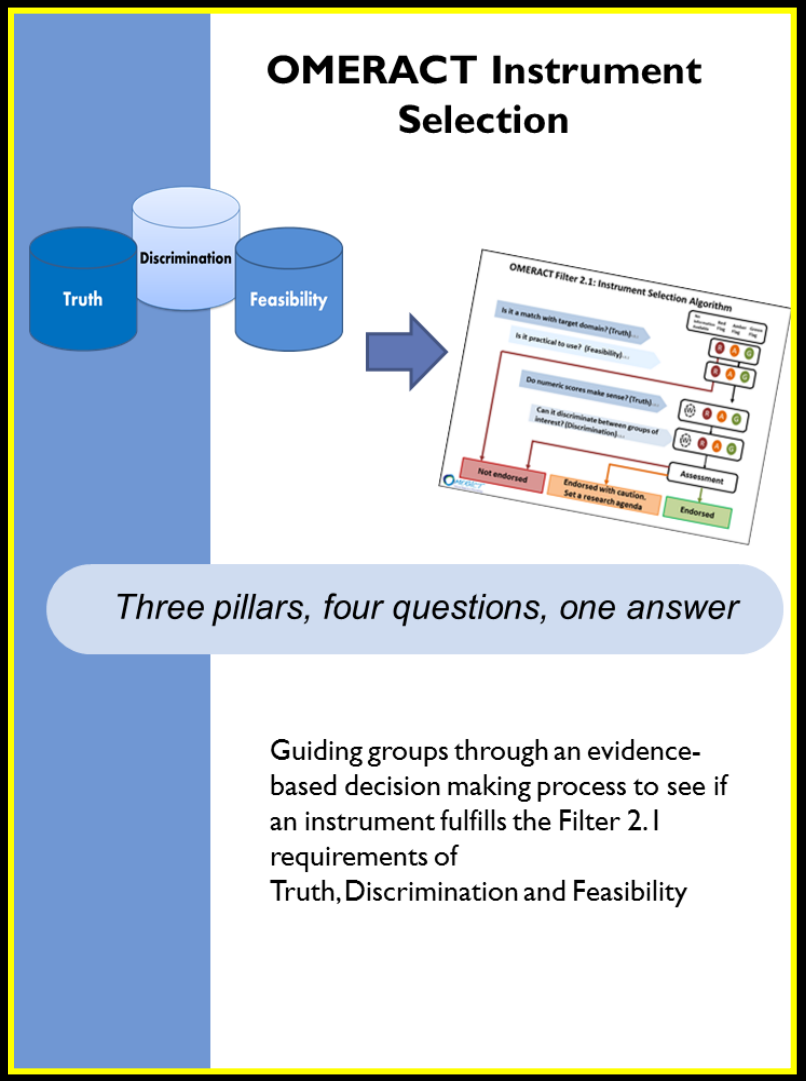
Moving from:

a PRO: *Domain* (the *what)*

to

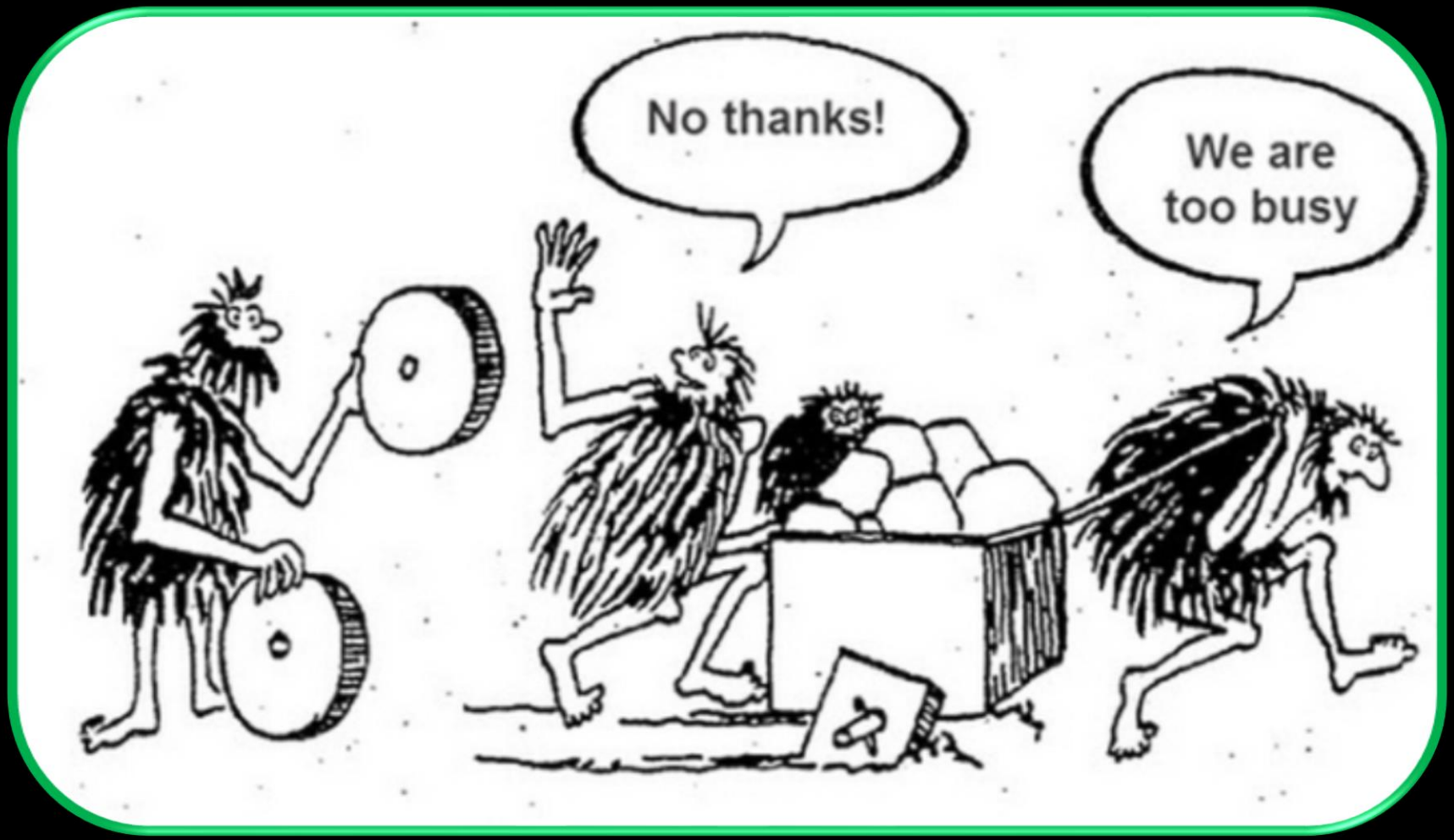
a PROM: *Measurement* (the *how)*

PRO: Patient-Reported Outcome
PROM: PRO Measure

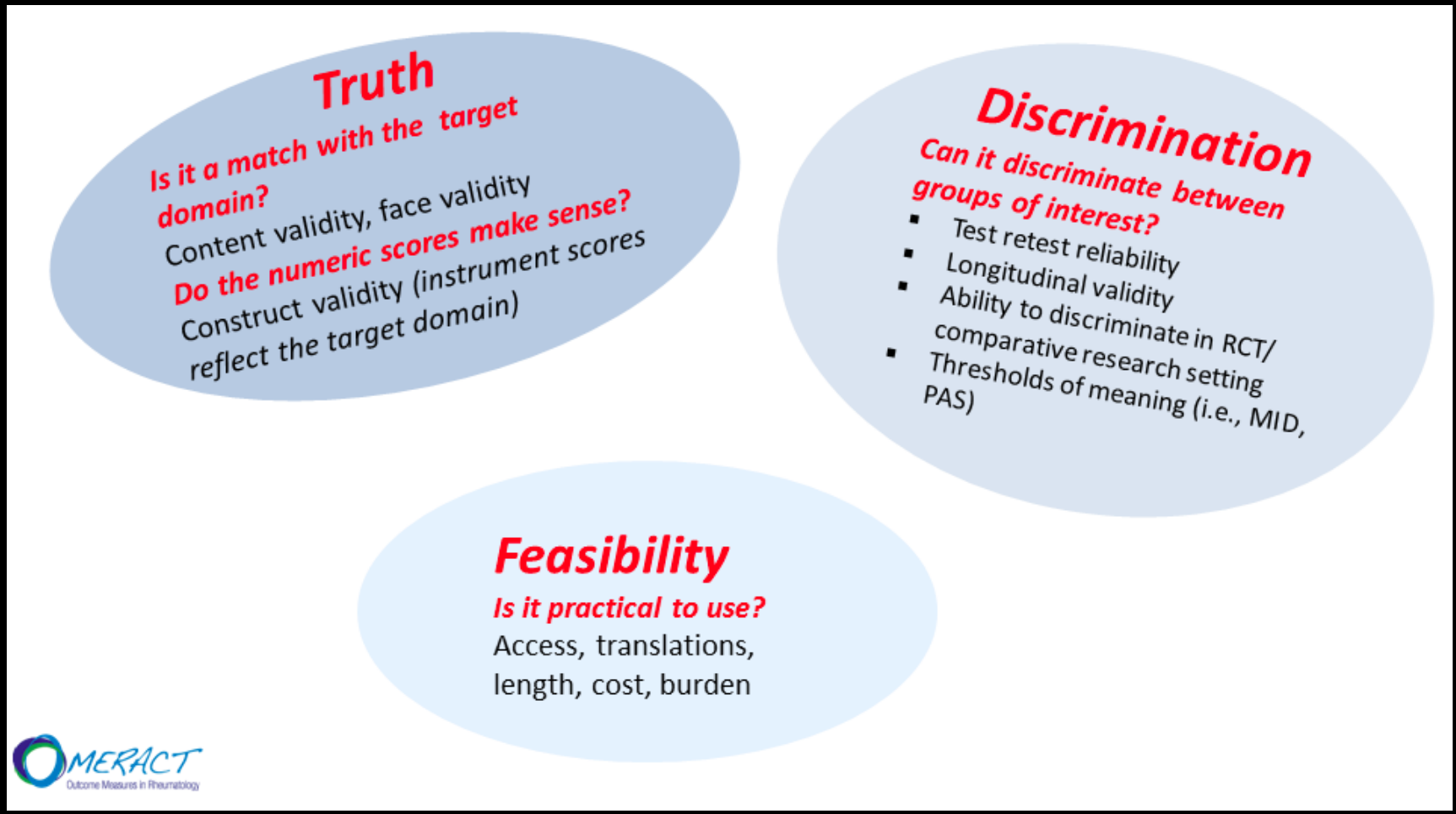


OMERACT Principles at play:

- Engagement of key stakeholders
- Great insight
- Help with buy-in from colleagues, broader community
- See opportunities for improvements, dissemination of results
- Must include patients and fellows in the steering group
- Steering group should include members from at least three continents (global group!)


No thanks!
We are too busy

An instrument to cover a specific domain:
Needs consensus based on 3 pillars…



DLQI © Finlay AY, Khan GK. 1994/Zachariae et al. 2000

Hospital/afd: Dato: Score:
Navn:
Adresse/nr: Diagnose: cpr:

Formålet med dette spørgeskema er at måle, i hvor høj grad Deres hudproblem har påvirket Deres liv **I DEN FORLØBNE UGE** (inkl. dagen i dag). Sæt venligst et mærke (✓) i den boks, der passer til Deres oplevelse.

1.	Hvor **kløende, øm, smertende** eller **sviende** har Deres hud været i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	
2.	Hvor **flov** eller **generet** har De været pga. Deres hud i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	
3.	I hvor høj grad har Deres hud generet Dem i forbindelse med **indkøb** eller **pasning af Deres hus** eller **have** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
4.	I hvor høj grad har Deres hud påvirket Deres **valg af påklædning** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
5.	I hvor høj grad har Deres hud påvirket Deres **sociale aktiviteter** eller **fritidsaktiviteter** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
6.	I hvor høj grad har Deres hud besværliggjort Deres muligheder for at dyrke **sport** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
7.	Har Deres hud forhindret Dem i at **arbejde** eller **studere** i den forløbne uge?	Ja ☐ Nej ☐	
	Hvis "NEJ", i hvor høj grad har Deres hud været et problem i forbindelse med **arbejde** eller **studier**?	Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
8.	I hvor høj grad har Deres hud skabt problemer i forholdet til Deres **partner, nære venner** eller **slægtninge** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
9.	I hvor høj grad har Deres hud skabt **seksuelle problemer** i den forløbne uge?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐
10.	I hvor høj grad i den forløbne uge har **behandlingen** af Deres hudproblem givet problemer, f.eks. ved at gøre hjemmet rodet eller snavset, eller ved at være tidskrævende?	Særdeles meget ☐ Meget ☐ En smule ☐ Slet ikke ☐	Ikke relevant ☐

Undersøg venligst om De har besvaret alle spørgsmål.

Bemærkninger til scoring:
Særdeles meget = 3
Meget = 2
En smule = 1
Slet ikke = 0
Ikke relevant = 0

PRO
SEKRETARIATET

Nyheder | Kontakt | Om os | English

SPØRGESKEMAER | AKTIVITETER | PRO-LANDSKAB

Del | Mail | Læs højt | Udskriv

- Info til patient
- Info til sundhedsfaglig
- Info til leverandører
- Jura

PRO

Her finder du generel information om, hvad PRO er, og hvad PRO-data kan bruges til, hvornår det kan benyttes, og hvordan det kan anvendes.

Kontakt

PRO-sekretariatet

Sanne Jensen:
T: 9133 4807

Trine Honnens de Lichtenberg:
T: 9133 4808

Nina Balk-Møller
T: 4046 8576

E: PROsekr@sundhedsdata.dk

"Patientrapporterede data, der omhandler patientens helbredstilstand, herunder det fysiske og mentale helbred, symptomer, helbredsrelateret livskvalitet og funktionsniveau".

Senest opdateret 29.03.2019

COS: indeholder PRO, evalueres med PROM

- Udvikling af et COS kræver global deltagelse (≥ 3 kontinenter)
- Patient involvering er *ikke bare* en mulighed – det er *et krav* !
- Systematisk review: Al tidligere litteratur gennemgås (hvad plejer man at måle?)
- Kvalitativ forskning: Listen af "ting der måles" diskuteres og evalueres (både patienter og "professionelle")
- Gentagne "surveys" (kaldet Delphi) dokumenterer hvorvidt både patienter (>70%) og "professionelle" (>70%) mener at et outcome skal måles (dvs begge grupper: >70%)
- COS: langt de fleste indeholder PRO (domæner) – derfor vigtigt at vælge validerede PROM (instrumenter)
- *DK-Psoriasis-Vision*: Mindst ét PROM bliver obligatorisk i dansk special-læge-praksis inden for et *par år*.....

Dvs: Der er tale om gruppe-arbejde….

Robin.Christensen@Regionh.DK