Concept of Measurement:
RA Defining Decrements in Physical Function

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Disclosures: Consultant

Abbott
Alder
Amgen
Ampio
Antares
Anthera
AstraZeneca
BiogenIdec
BioMarin
Biotest
BMS
Cbio
CanFite
Carbyan
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Chelsea
Crescendo
Cypress
Emergent Biosolutions
Forest
Genentech
GSK
Human Genome Sciences
Idera

Incyte
Janssen
Jazz
Lexicon Genetics
Lilly
Logical Therapeutics
Medimmune
MerckSerono
Molecular Partners
Novartis
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Pfizer
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Relypsa
Rigel
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Savient
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Teikoku
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Vertex
Xencor

Responsiveness of Physician v Patient Reported Measures

Strand et al. Rheumatol 2004; 43:640-7

Responsiveness of Physician v Patient Reported Measures

Strand et al. Rheumatol 2004; 43:640-7
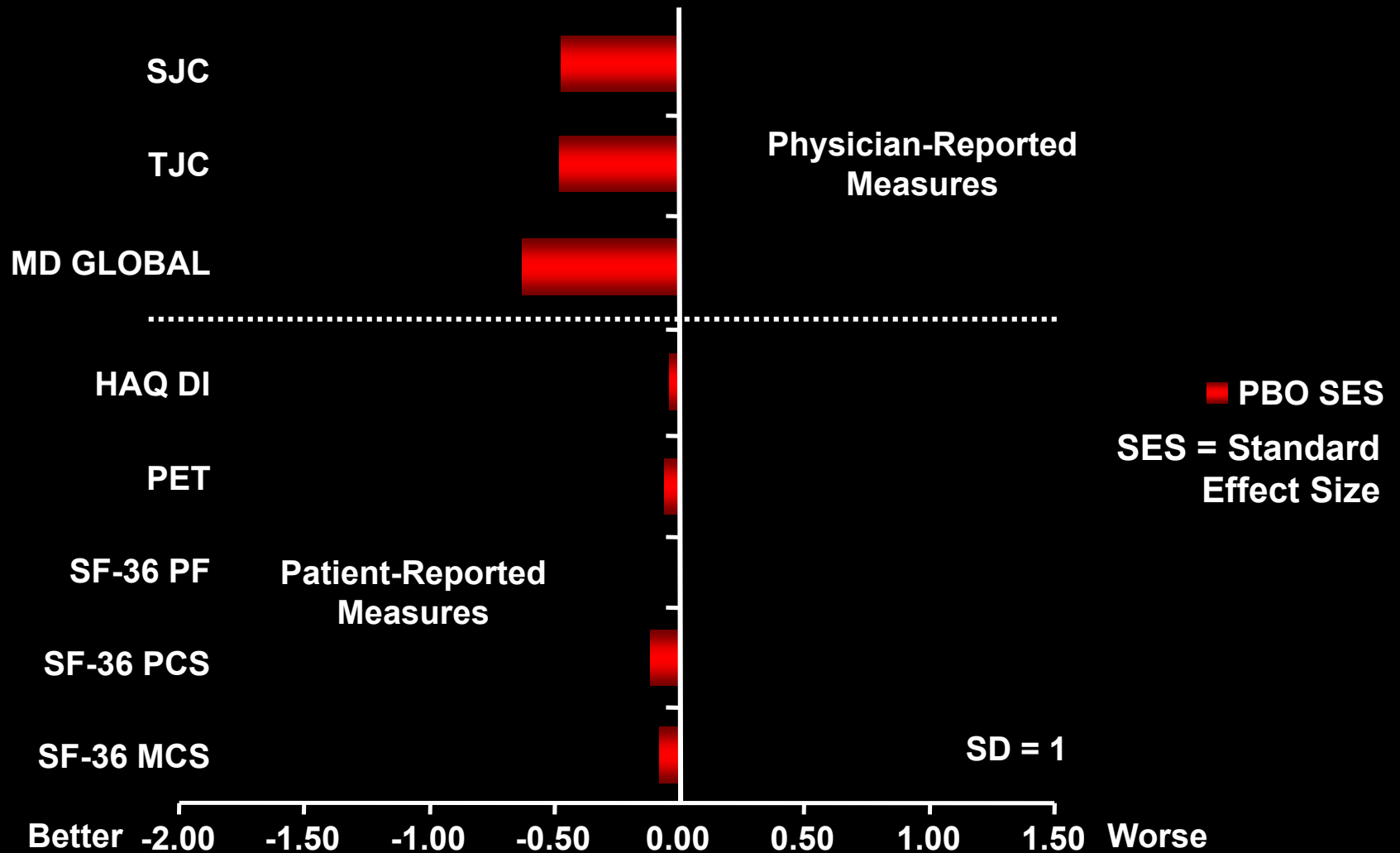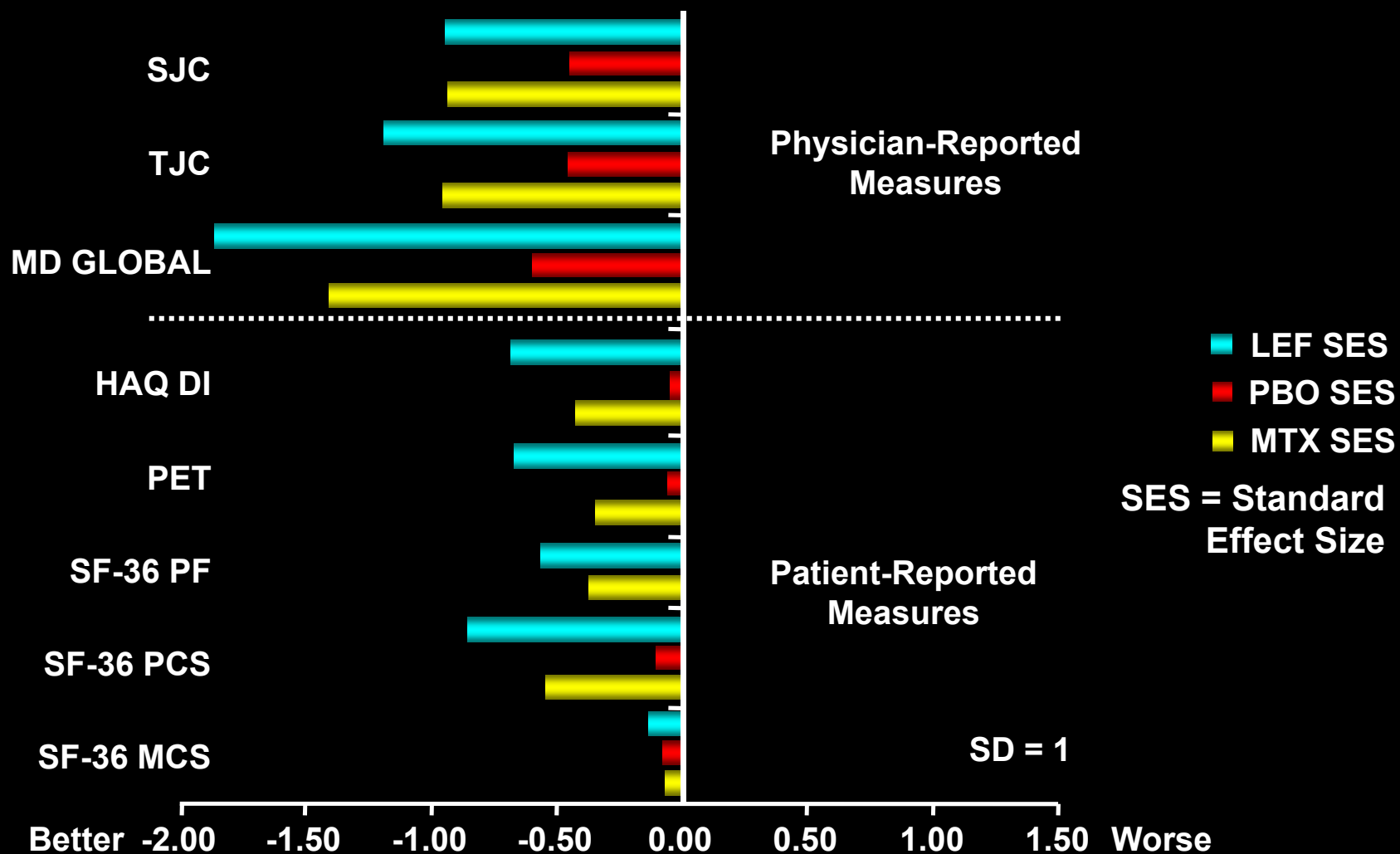
SF-36: Short Form 36 Health Survey

Validated, widely used generic measure of HRQOL

- 8 Domains:
  - Scored 0 (severe impairment) – 100 (no impairment); age, sex adjusted rates from 0 – 30 "raw" scores

- 2 Summary Scores
  - Physical Component: PCS
    - Measures how decrements in physical function affect day to day activities
    - Impact of physical impairment / disability on HRQOL
  - Mental Component: MCS
    - Impact of mental affect, symptoms of pain on HRQOL
  - Normative based scoring (Mean: 50, SD: 10)

Scoring Domains of SF-36

| Domains	Items	Focus
Physical functioning [PFI]	3a-3j	limitations of physical function
Role physical [ROLP]	4a-4d	difficulty performing usual activities due to physical limitations
Bodily pain [BP]	7, 8	amount of discomfort and its interference with activities
General health [GHP]	1, 11a-d	perception of overall personal health
Vitality [VIT]	9a, 9e, 9g, 9i	pep and energy
Social functioning [SF]	6, 10a	social contacts and activities
Role emotional [ROLP]	5a-5c	difficulty performing usual activities due to emotional limitations
Mental health [MHI]	9b, 9c, 9d, 9f, 9h	depression and anxiety

Physical Function [PF] Domain of SF-36

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

- **3a: Vigorous activities,** such as running, lifting heavy objects, participating in strenuous sports

- **3b: Moderate activities,** such s moving a table, pushing a vacuum cleaner, bowling or playing golf

- **3c:** Lifting or carrying groceries

- **3d:** Climbing **several** flights of stairs

- **3e:** Climbing **one** flight of stairs

- **3f:** Bending, kneeling or stooping

- **3g:** Walking **more than a mile**

- **3h:** Walking **several blocks**

- **3i:** Walking **one block**

- **3j:** Bathing or dressing yourself

Differences in Physical Activities Queried in HAQ-DI and SF-36

- Self care ADLs: HAQ, SF-36 only asks about dressing, grooming

- SF-36: Reaching overhead

- SF-36: Instrumental activities:

  - Lifting, carrying groceries

  - Bending, kneeling or stooping

  - Climbing 1 flight of stairs

  - Walking 1 or several blocks

- SF-36: Discretionary activities:

  - Walking >1 mile

  - Climbing several sets of stairs

  - Moderate activities

  - Vigorous activities
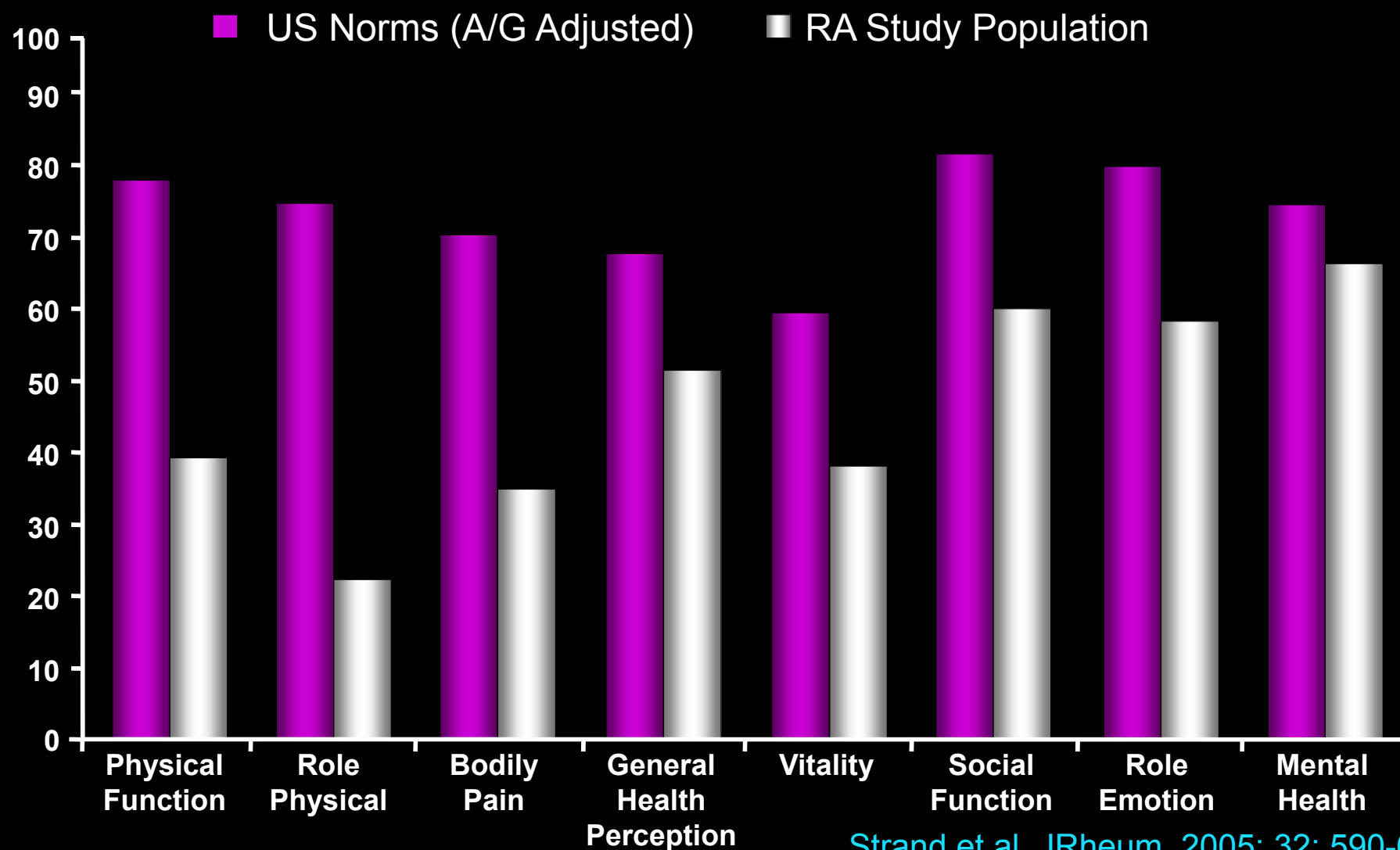
SF-36: 2 Component Model to Derive PCS, MCS
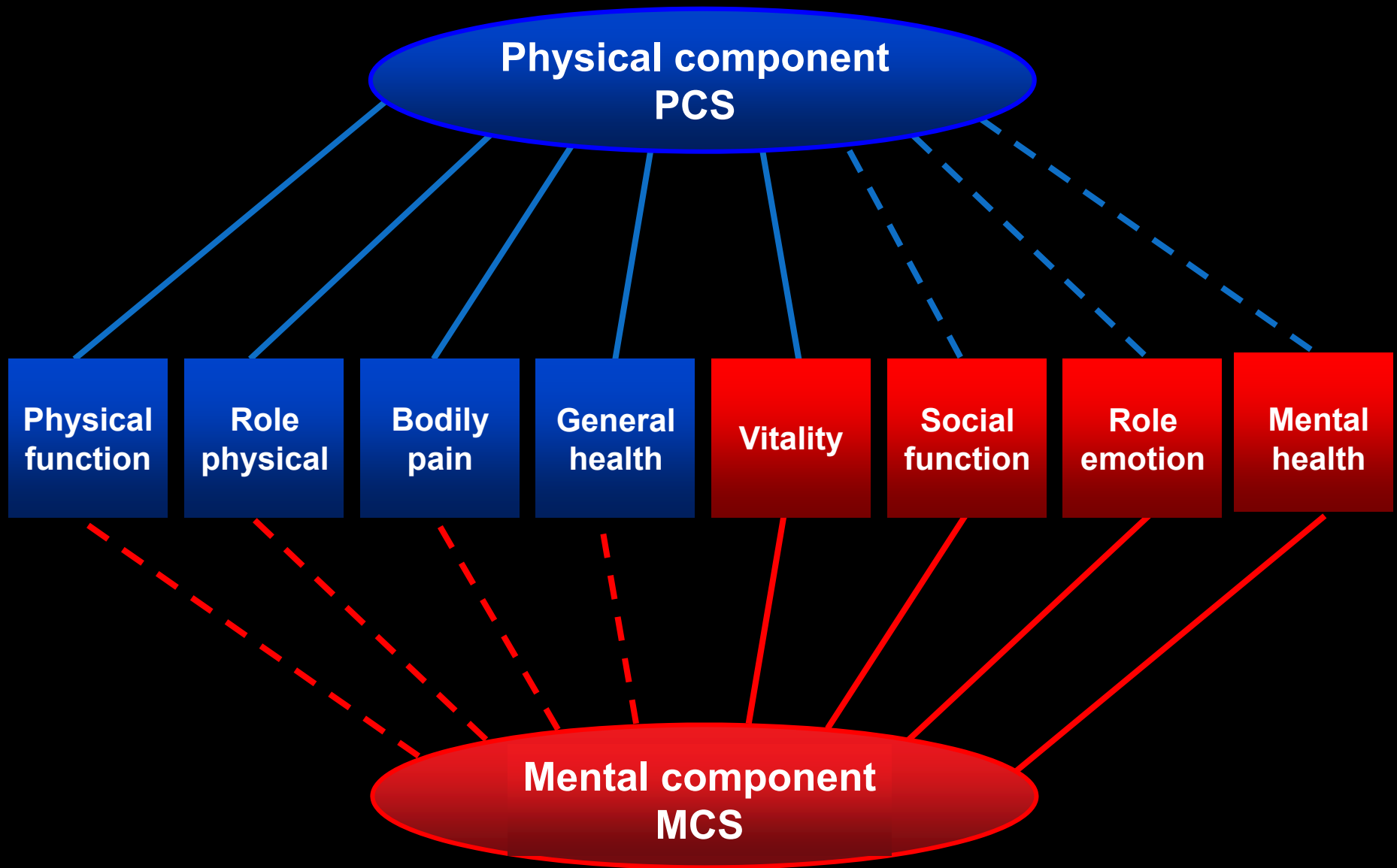
Scoring PCS and MCS

- AGG_PHYS = (PF_Z * .42402) + (RP_Z * .35119) + (BP_Z * .31754) + (GH_Z * .24954) + (VT_Z * .02877) + (SF_Z * -.00753) + (RE_Z * -.19206) + (MH_Z * -.22069);

- AGG_MENT = (PF_Z * -.22999) + (RP_Z * -.12329) + (BP_Z * -.09731) + (GH_Z * -.01571) + (VT_Z * .23534) + (SF_Z * .26876) + (RE_Z * .43407) + (MH_Z * .48581);

- NEXT, CREATE THE FINAL NORM BASED PHYSICAL AND MENTAL COMPONENT SCORES:
  - PCS = 50 + (AGG_PHYS * 10);
  - MCS = 50 + (AGG_MENT * 10).

- THUS IF PCS and/or MCS scores are statistically significant, we choose to look across individual domains without p value corrections

Rheumatoid Arthritis

Baseline Decrements

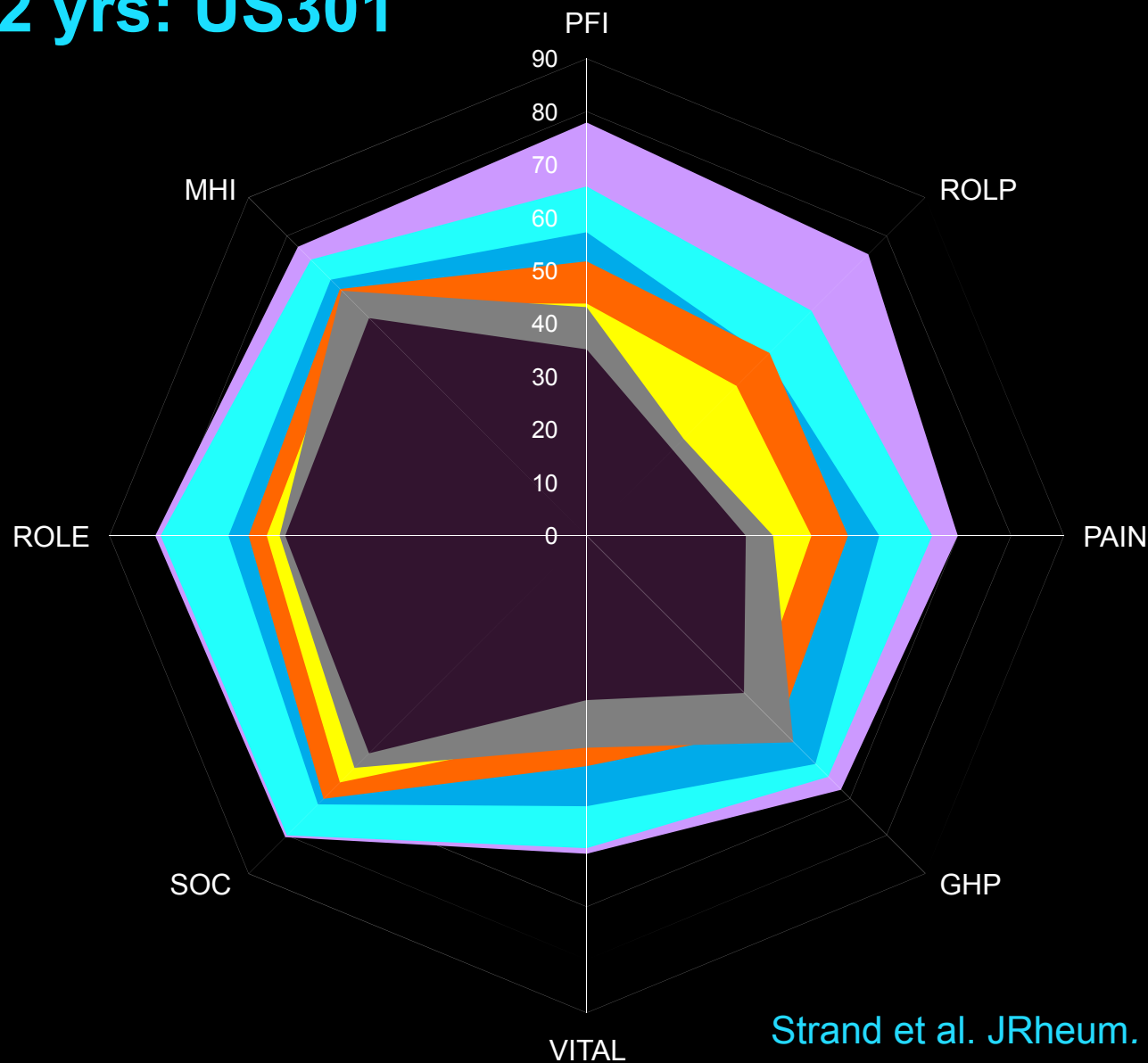## and

Treatment Associated

Improvements

Baseline SF-36 Scores in US301 Population vs US Norms

■ US Norms (A/G Adjusted)   ▢ RA Study Population

Physical Function · Role Physical · Bodily Pain · General Health Perception · Vitality · Social Function · Role Emotion · Mental Health

Strand et al. JRheum. 2005; 32: 590-601

Baseline and Mean Change Scores in SF-36

1 & 2 yrs: US301

Strand et al. JRheum. 2005; 32: 590-601

Legend: A/G Norms, BL-MTX, BL-LEF, MTX 1yr, MTX 2yr, LEF 1yr, LEF 2yr

Axes: PFI, ROLP, PAIN, GHP, VITAL, SOC, ROLE, MHI

Scale: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90

COMET: ETN+MTX vs MTX at 1 year

PF
p < .001

90
80
70
60
50
40
30
20
10
0

RP

MH

p < .02
RE

BP
p < .001

SF

GH

p values for
ETN+MTX
improvement

p < .02 VT
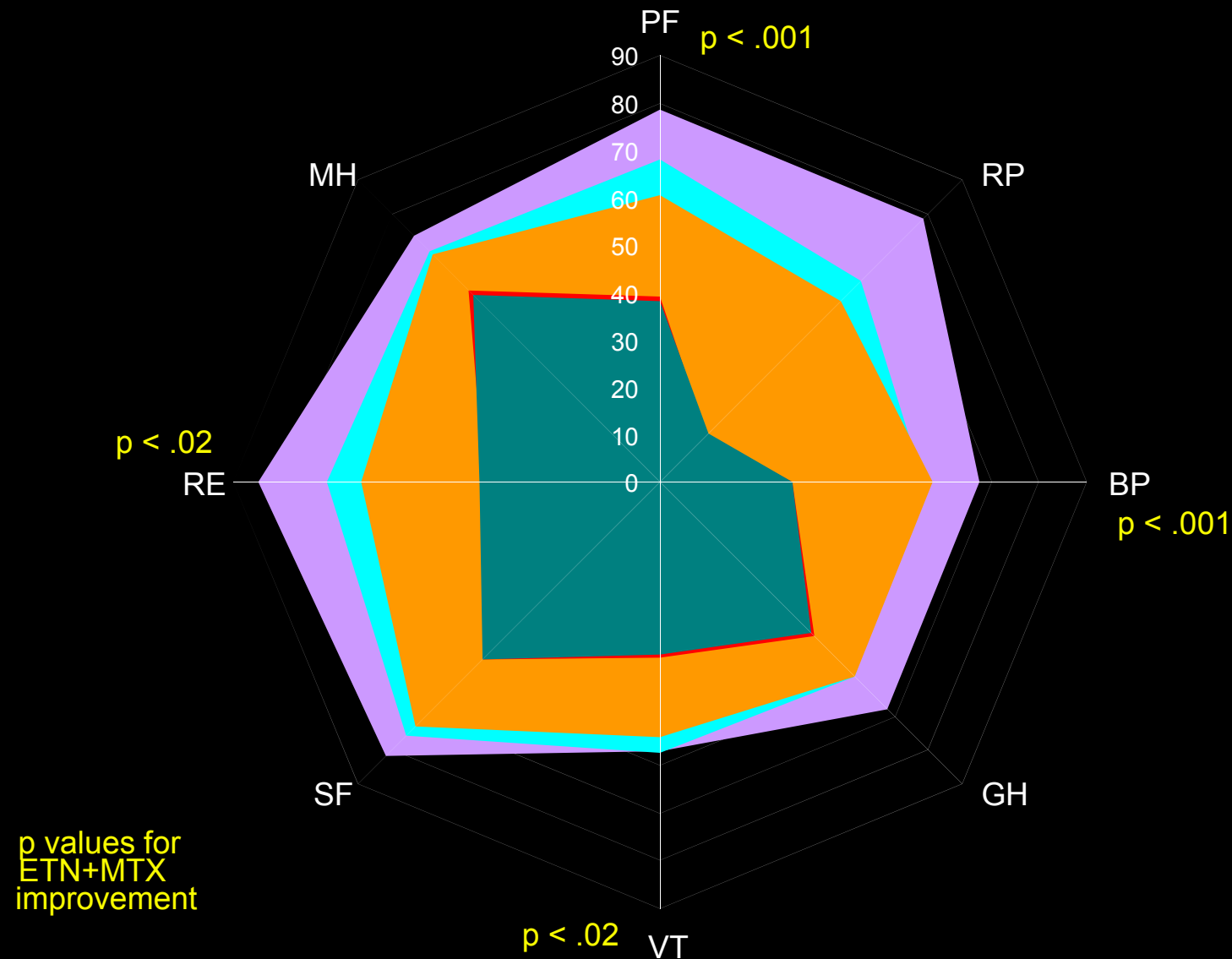
Strand et al: ARD 2012: 71:1143–50

■Age/Gender Norms   ■ETN+MTX - 52 Weeks   ■MTX - 52 Weeks   ■MTX - BL   ■ETN+MTX - BL

RAPID 1 RCT: CZP 200 vs 400 mg at Week 52
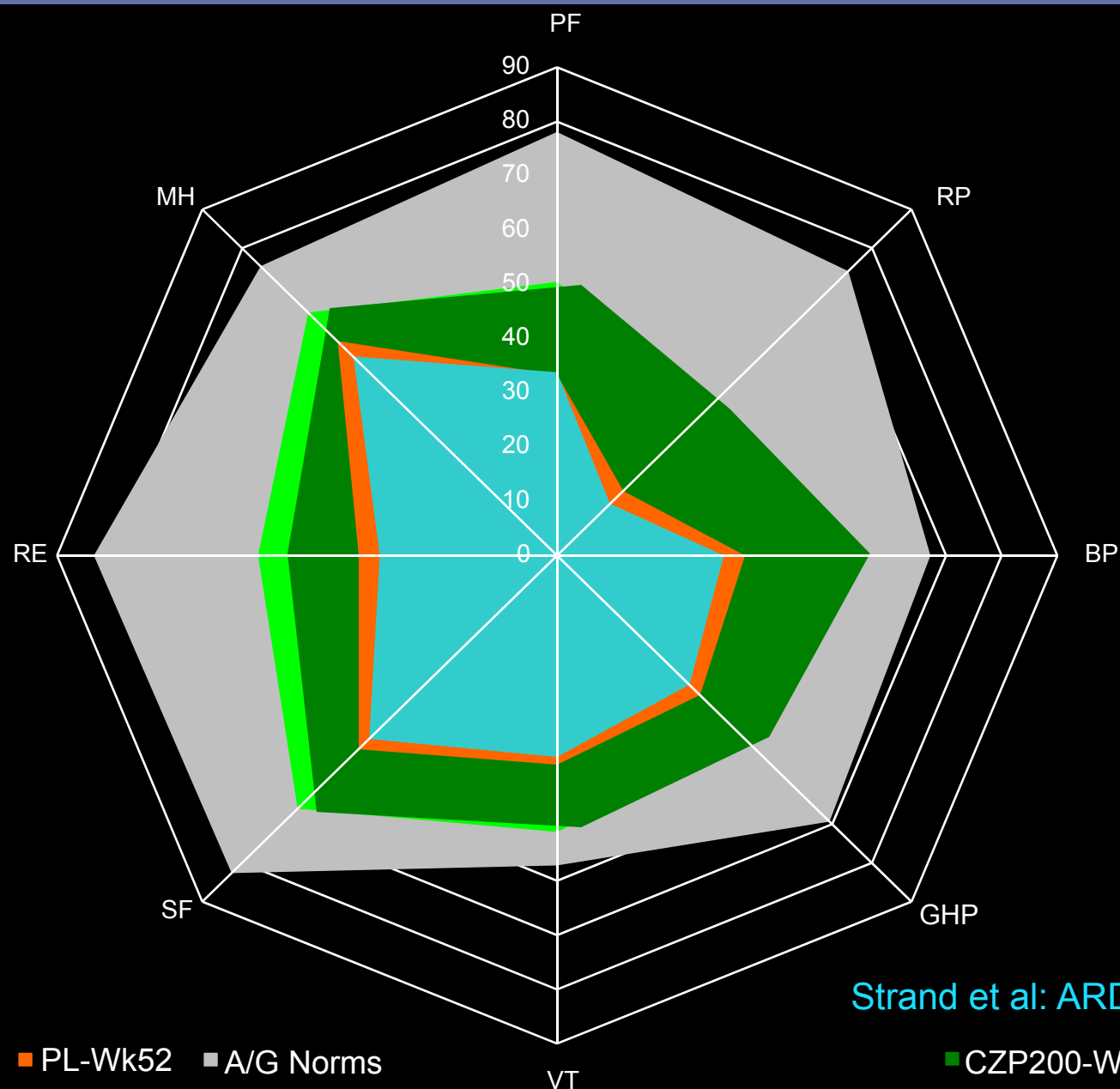
Strand et al: ARD 2011.70:996–1002

■ Baseline ■ PL-Wk52 ■ A/G Norms ■ CZP200-Wk52 ■ CZP400-Wk52

Value of Assessing HRQOL

- Baseline decrements in HR-QOL in RA, compared with age-gender matched normative values are most evident in:
    - PF: Physical function
    - RP: Role physical
    - BP: Bodily pain
    - VT: Fatigue, pep and energy and
    - RE: Role emotional domains − regardless of ds duration

- A sensitive instrument to demonstrate treatment-associated changes in RA across populations with different disease durations, treatment failures and 'damage'

Differences between SF-36 and HAQ

- Query different physical activities
  − instrumental and discretionary

- Reflects impact of early and later disease

  - Unlike HAQ, SF-36 does not have ceiling effects, eg 'irreversible' impairment

  - Largest treatment associated improvements evident in those domains with the most decrements at baseline

- As a generic instrument offers:

  - Comparison with age and gender matched norms
    − another important "goal" for treatment

  - Comparisons with other disease states and co-morbidities

Value of Assessing HRQOL

- "Patients with RA have significantly impaired HRQoL, especially in terms of physical functioning, pain, and vitality, but also in terms of their emotional state, and patients report that these facets of the disease are more important than traditional clinical measures from their perspective.

- The disease-related reductions in the physical and mental/emotional aspects of HRQoL are influenced by each other."

- Pain and fatigue are both associated with impairments in physical function and significantly impact patients' HRQoL by restricting their usual activities, including social and work functions.

- RAPPPI included HRQOL: "enjoying life again, and valued activities"

Kirwan JR, Hewlett SE et al: Incorporating the patient perspective into outcome assessment in rheumatoid arthritis-- progress at OMERACT 7. J Rheum 2005; 32: 2250-6.
Carr A, Hewlett SE et al: Rheumatology outcomes: Patient's perspective J Rheum 2003: 30:880-3
Hewlett SE et al: Patients' perspectives of fatigue in RA. Arth Rheum 2005; 53:697-702S
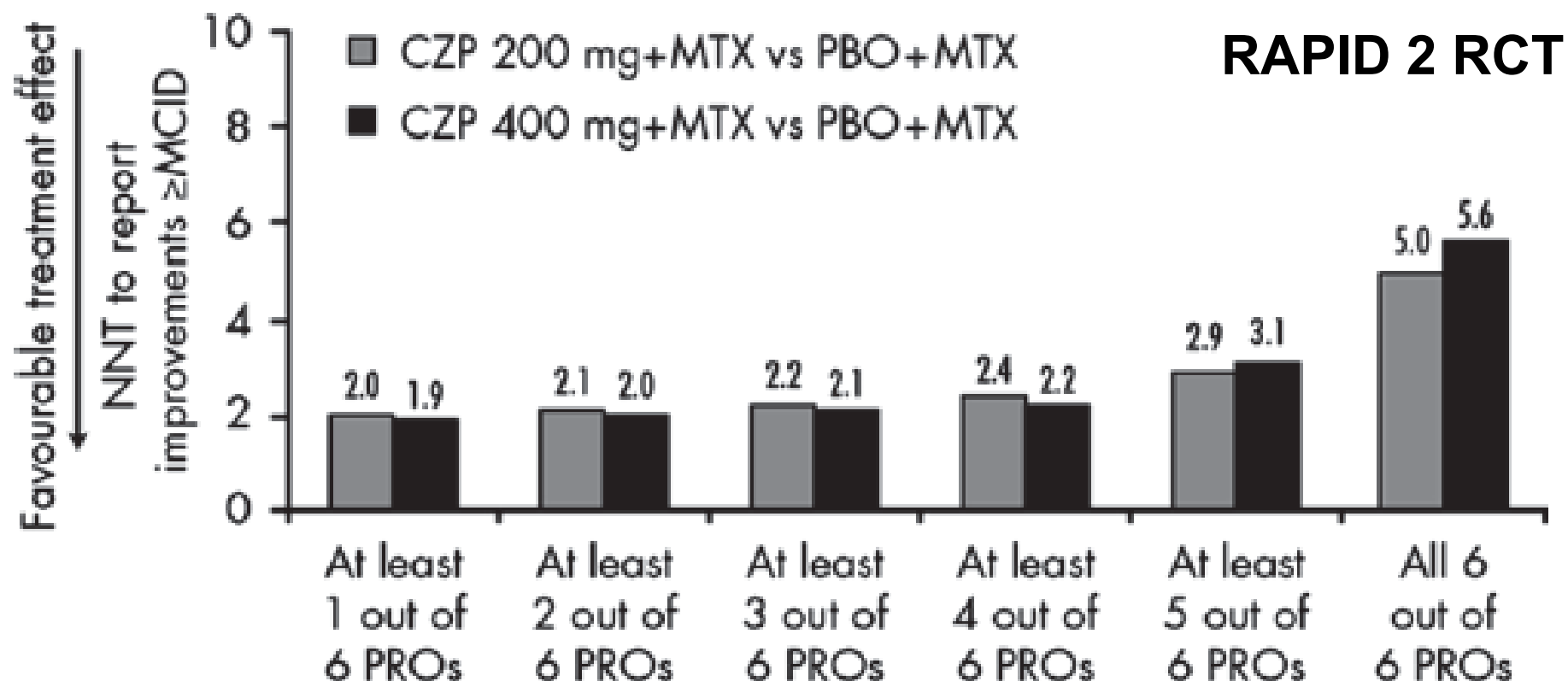Sanderson T et al: AC&R 2010: 62:640-46

% Patients Reporting Clinically Meaningful Improvements in Specific Activities

ACTIVITY	ERA		PREMIER				ABA			
	MTX or ETN		ADA+MTX		MTX		ABA+MTX		PL+MTX	
	BL	12m	BL	24m	BL	24m	BL	12m	BL	12m
Walking 1 block	65	36	46	8	44	13	72	42	61	62
Climbing 1 flight stairs	75	43	68	12	66	21	–	–	–	–
Difficulty performing at work	90	53	89	15	88	34	42	23	57	36
Time lost at work due to health			66	9	65	18	70	32	66	46
Less time feeling tired/worn out							40	14	39	31
Less interferance on social activities							37	9	15	16

Strand and Singh Drugs 2010; 70:1-25

Correlations between PROs, DAS28, CDAI/SDAI

- **PF domain**: HAQ: -0.66, BP domain: 0.63

- **RP domain**: RE domain: 0.63

- **BP domain**: Pain VAS: -0.67; Global VAS: -0.66; HAQ: -0.60; PF domain: 0.63; SF domain: 0.64

- **VT domain**: SF domain: 0.67; MH domain: 0.67; fatigue: -0.68

- VAS Pain: VAS global: 0.97; HAQ: 0.64; **BP domain: -0.67**; DAS28/SDAI/CDAI: 0.63 – 0.65

- VAS Global: VAS pain: 0.97; HAQ: 0.82; **BP domain: -0.66**

- HAQ: **PF domain: -0.66, BP domain: -0.60**

Strand V et al: Annals Rheum Ds 2011; 70:996–1002

Number Needed to Treat Based on % Reporting Improvements ≥ MCID in 1 – 6 PROs

RAPID 2 RCT

- □ CZP 200 mg+MTX vs PBO+MTX
- ■ CZP 400 mg+MTX vs PBO+MTX

Favourable treatment effect → NNT to report improvements ≥MCID

Category	CZP 200	CZP 400
At least 1 out of 6 PROs	2.0	1.9
At least 2 out of 6 PROs	2.1	2.0
At least 3 out of 6 PROs	2.2	2.1
At least 4 out of 6 PROs	2.4	2.2
At least 5 out of 6 PROs	2.9	3.1
All 6 out of 6 PROs	5.0	5.6

PROs: Pain VAS, Global VAS, HAQ, Fatigue, SF-36 PCS, SF-36 MCS

SF-36 Domains are Independent of Each Other

- Based on unique questions

- Reflect impact of early and later disease

- Well defined MCID values for improvement as well as deterioration

- As a generic instrument offers:

  - Comparison with age and gender matched norms
    − an important "goal" for treatment, especially now!

  - Comparisons with other disease states and co-morbidities

- Effect sizes are moderate to large indicating sensitive to change

- Well validated instrument with a wealth of data across countries and cultures; should be administered in its entirety

Value of Assessing HRQOL

- Measures of HR-QOL and physical function are not interchangeable in RA

    - Individuals perceive HRQOL differently; patients report impact of their disease on function and HR-QOL differently.

    - Assessment of HR-QOL offers multidimensional view of the impact of RA and improvements associated with effective treatment

- Unlike the HAQ, SF-36 does not show 'irreversible' impairment and remains a sensitive instrument to demonstrate treatment-associated changes in RA across populations with different disease durations, treatment failures and 'damage'

The Impact of RA on Women: Focus on Pain, Productivity and Relationships

V Strand,[1] P Emery,[2] S Fleming,[3] E Coke[4]

[1]Stanford University School of Medicine, Portola Valley, USA;
[2]University of Leeds, Leeds, UK; [3]UCB, Slough, UK;
[4]Echo Research, London, UK

"Good Days Survey": Methods

- 27,459 women were recruited via an internet survey

  – Aged 25–65 years with a formal RA diagnosis ≥6 months

- Questions: physical, emotional and social impact of RA

- Respondents

  – 1,958 women with RA completed the internet survey (30 July–31 August 2009)

  – 7 countries: UK, France, Germany, Italy, Spain, USA and Canada

- Demographics

  – Mean age: 46 years

  – 75% had RA diagnosed >1 year

  – 69% reported moderate to severe RA

Definition of a "Good Day"

Which of the following defines a good day for you?

Day free of pain

57

| 0 | 25 | 50 | 75 | 100 |
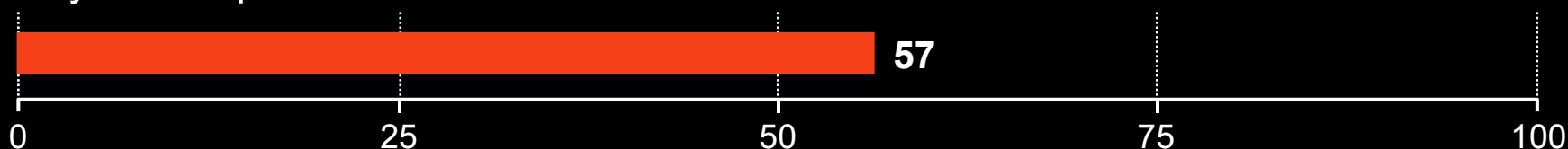
Free of fatigue, having energy

58

| 0 | 25 | 50 | 75 | 100 |
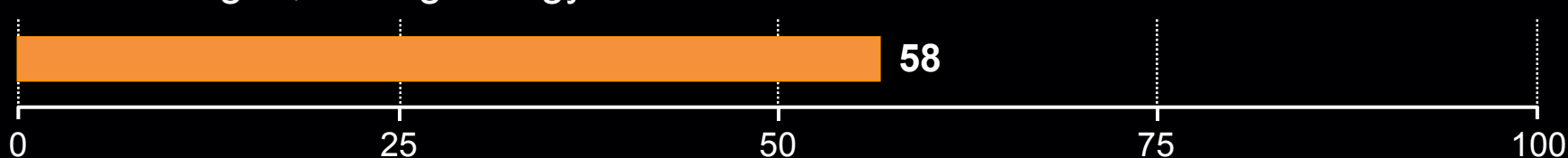
Able to do everyday things easily

29

| 0 | 25 | 50 | 75 | 100 |
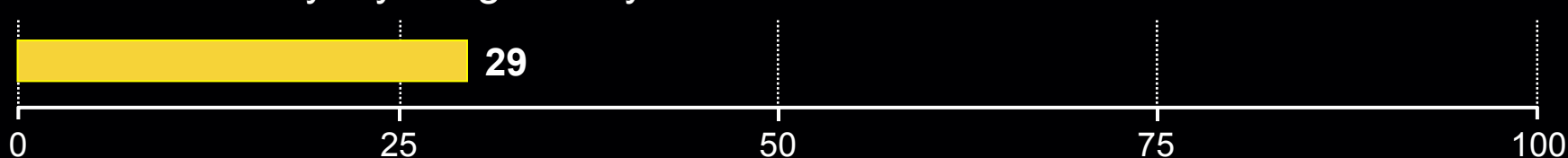
For most, being pain-free and having energy
are clear defining features of a good day