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Assessing outcome of haemophilia treatment

The role of Health-Related Quality of Life (HRQoL)

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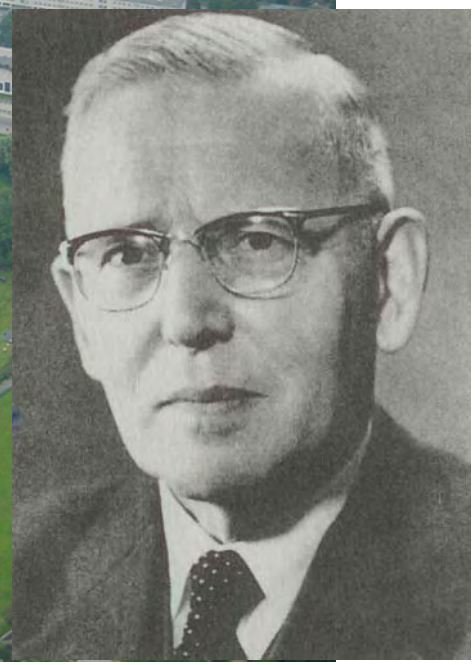

Van Creveldkliniek: 700 patients; 320 severe haemophilia

Outline

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- HRQoL instruments
- HRQoL results in different studies
- Association of HRQoL with joint damage and treatment

Why perform outcome assessment?

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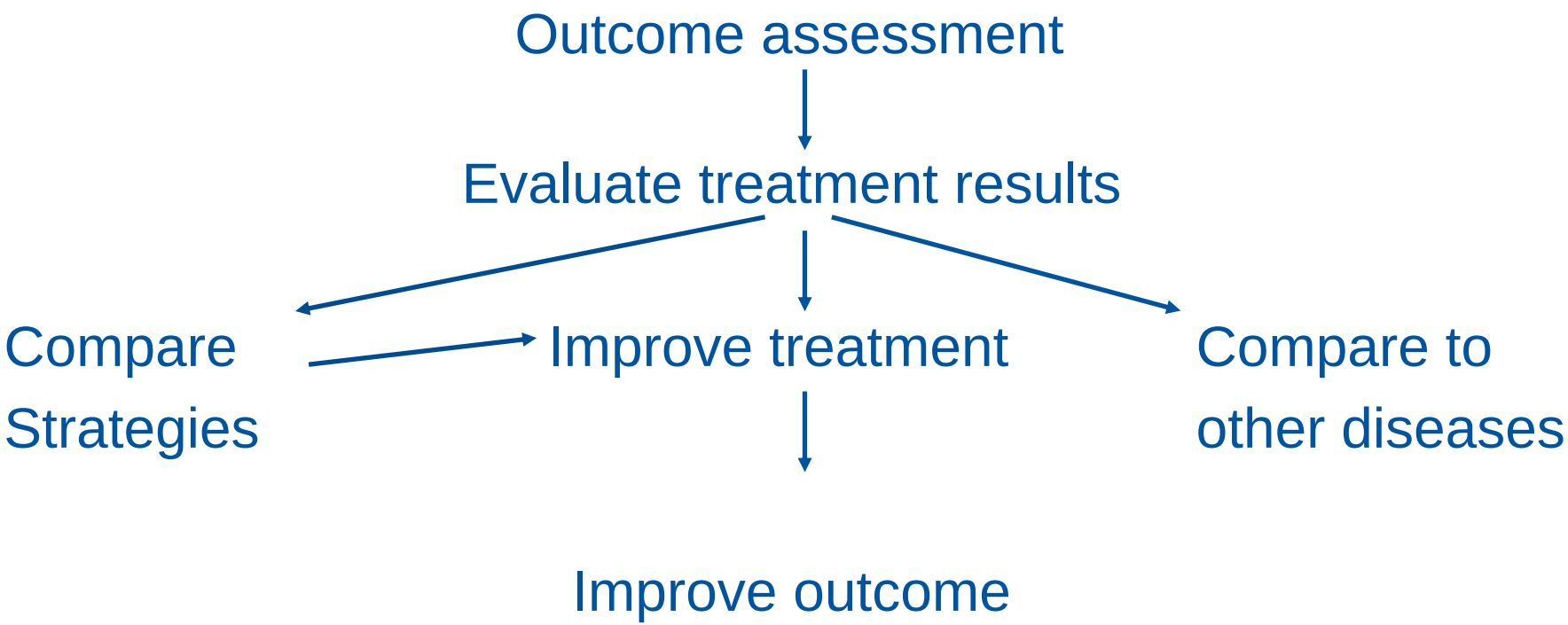
Outcome in haemophilia is highly dependent on treatment



Assessment of outcome: Perspective

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- Patient
- Third Party Payer
- Society

Assessment of benefits: Perspective

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- Patient
  - number of bleeds
  - joint function, arthropathy
  - disease-specific HRQoL
- Third Party Payer
- Society

Assessment of benefits: Perspective

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- Patient
  - number of bleeds
  - joint function, arthropathy
  - disease-specific HRQoL
- Third Party Payer
  - doctor's visits
  - hospital admissions
  - surgical procedures
- Society

Assessment of benefits: Perspective

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- Patient
  - number of bleeds
  - joint function, arthropathy
  - disease-specific HRQoL
- Third Party Payer
  - doctor's visits
  - hospital admissions
  - surgical procedures
- Society
  - labourforce participation
  - disability allowances, etc
  - HRQoL, Utility→ QALY

Why is HRQoL essential?

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Health Related Quality of Life

- ‘summary parameter’
  for long-term patient relevant outcome

- translated into benefits from societal perspective
  → QALY’s

Assessment of Health Related Quality of Life

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CHILDREN

Generic

- CHQ
- KINDL
- HUI*

Specific

- Hemo-Qol (’02)
- CHoKLAT (’04)

ADULTS

Generic

- SF 36
- EQ5D (Utility)*
- HUI*

Specific

- Hemofilia-Qol (’05)
- (MedTap)
- Utility Wasserman 2005*

* Preference based

Short Form 36 (SF36)

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- physical function — **Physical summary scale (0-55)**
- bodily pain
- physical role limitations
- general health

- social function — **Mental summary scale (0-55)**
- mental role limitations
- mental health
- Vitality

Each domain: score 0 -100 (100 is optimum)

Euroqol (EQ-5D)

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- mobility — $EQ\text{-}5D_{utility}$ — (0-1) → QALY
- self-care
- usual activities
- pain/discomfort
- anxiety/depression

- Visual analogue scale (VAS) — $EQ\text{-}5D_{VAS}$ — (0-100)

Results of studies using the SF36 (1):
cross-sectional Europe (n=903, Royal et al, '02)

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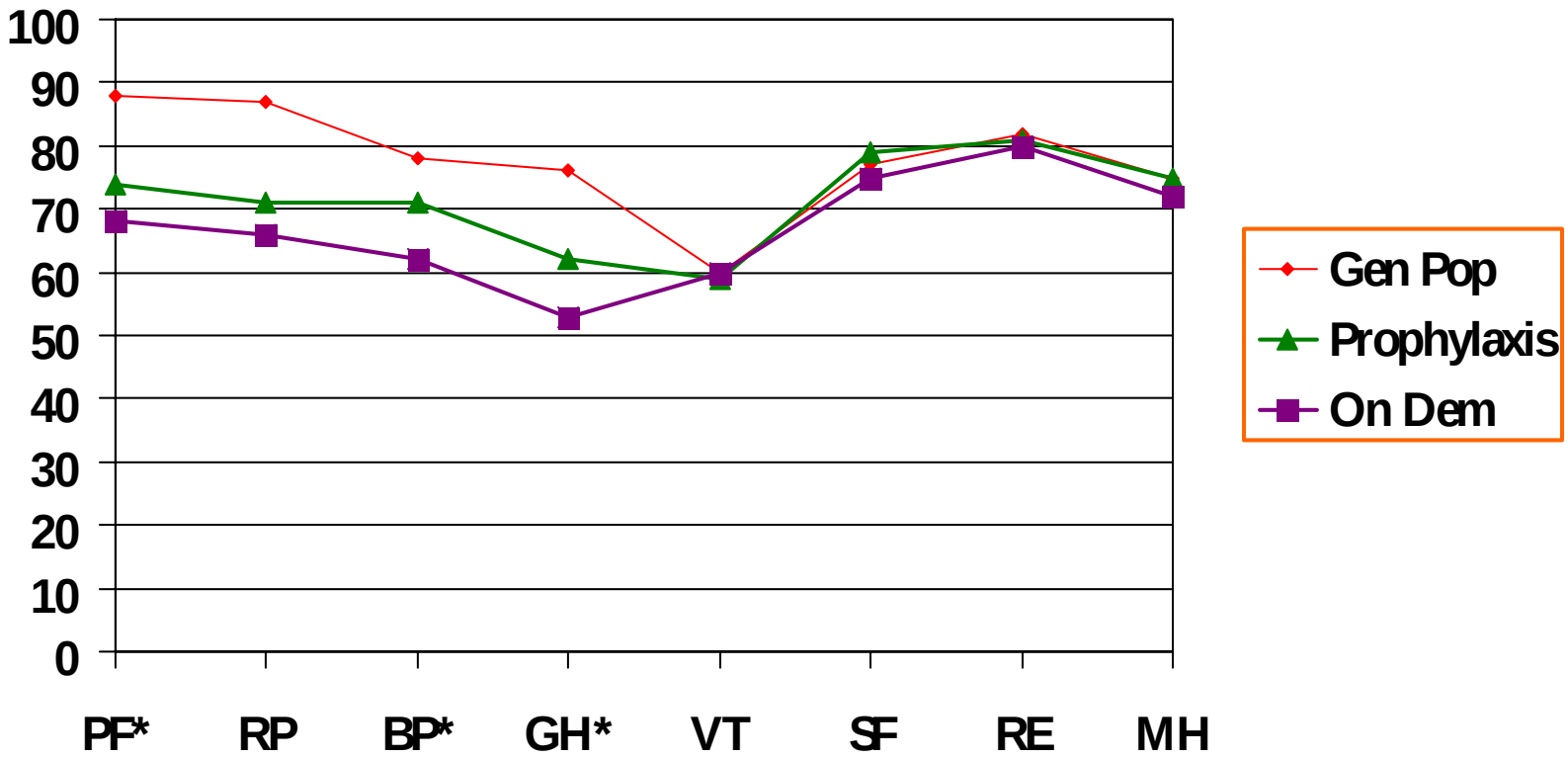

SF 36: domain of ‘Physical Function’

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10 questions, on limitations in:

- vigorous / moderate activities
- lifting/carrying groceries
- climbing stairs: > 1 flights/ 1 flight
- bending/kneeling/stooping
- walking: > 1 mile / 1 mile / 100 yards
- bathing & dressing

Results of SF36 and Euroqol (EQ5D)

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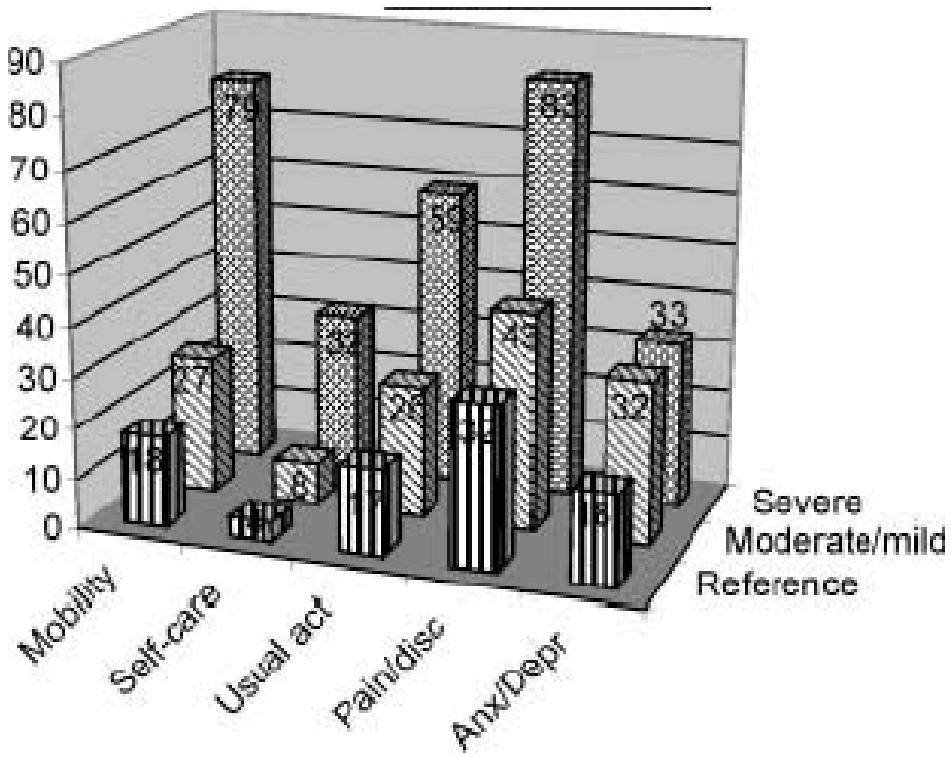
In 6 studies, 56-903 patients

SF36 ‘physical function’ scores :

- ↓ than general population
- ↓/= with HIV infection
- ↓ with ↑ bleeds on OD
- ↓ with increasing age
- ↓ with severity of disease

- ↑ with prophylaxis

Euroqol (EQ5D)



Comparing SF36 and Euroqol (EQ5D)

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	UK males	Miners '99	Trippoli '01	Pilot NL '06
Number (% severe)	1466	164 (40%)	56 (57%)	22 (68%)
Age (yrs)	35-44	43.5	38.7	20.7
SF36- PF	91.9	62.3	73.6	93.4
SF36- PCS	52.0	38.7	44.7	51.2
Utility	1.00	0.77	0.68	0.91
Correlation SF36-utility	NA	0.59	0.64	0.63

Mean values

Conclusions on SF36 and EQ5D

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- Physical domains/ components most sensitive in haemophilia
- Generic instruments:
  -able to pick up difference with general population
  -decrease HRQoL with age
  -only moderate correlation
  -able to pick up differences in haemophilia severity

Discrimination of haemophilia specific questionnaires: Hemofilia-Qol

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10 centres in Spain

121 adults, (68% severe, 30% moderate, 2% mild)

Mean age 34.9 ± 11.9 yrs

Subscale (dimension)	No. of items	Change with Nr of bleeds	Change with Chronic pain
Physical health	8	; $P = 0.000^{*}$	; $P = 0.000^{**}$
Daily activities	4	$P = 0.003^{*}$	; $P = 0.000^{**}$
→ Joint damage	3	; $P = 0.000^{*}$	; $P = 0.002^{*}$
Pain	2	$P = 0.000^{**}$	$P = 0.007^{*}$
→ Treatment satisfaction	2	$P =$ NS	$P = 0.044^{*}$
→ Treatment difficulties	4	$P =$ NS	$P = 0.073^{***}$
Emotional functioning	5	$P =$ NS	; $P = 0.000^{**}$
Mental health	3	$P =$ NS	; $P = 0.000^{**}$
Relationships and social activity	5	$P =$ NS	; $P = 0.000^{**}$
Hemofilia-QoL (total score)	36	$P = 0.004^{*}$	; $P = 0.000^{**}$

Pediatric haemophilia specific questionnaires

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Haemo- Qol

- Started from treaters' perspective
- 3 tools: age 4-7,8-12, 13-16→
  2 tools: age 4-7, 8-16 (35 Q)→
  Hemoqol Index: 4-16 yrs (8 Q)

Domains

-physical
-feeling
-view
→ -family
-friends
-others
→ -school
→ -treatment

Summary score 100-0

Correlation
Patients -0.74
Parents -0.82

CHOKLAT

- Started from patients' perspective
- One tool age 4-18
- Patient & parent form (35 Q)

Domains: not specified

Summary score 0-100

Conclusions HRQoL questionnairs in haemophilia

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GENERIC

- Physical domains/ components most sensitive in haemophilia
- Generic instruments:
  -able to pick up difference with general population
  -decrease HRQoL with age
  -only moderate correlation SF36 and EQ5D
  -able to pick up differences in haemophilia severity

DISEASE SPECIFIC

- able to pick up differences in haemophilia severity
- added domains on joint damage and treatment
- additional value??

treatment > research?

Remaining questions:

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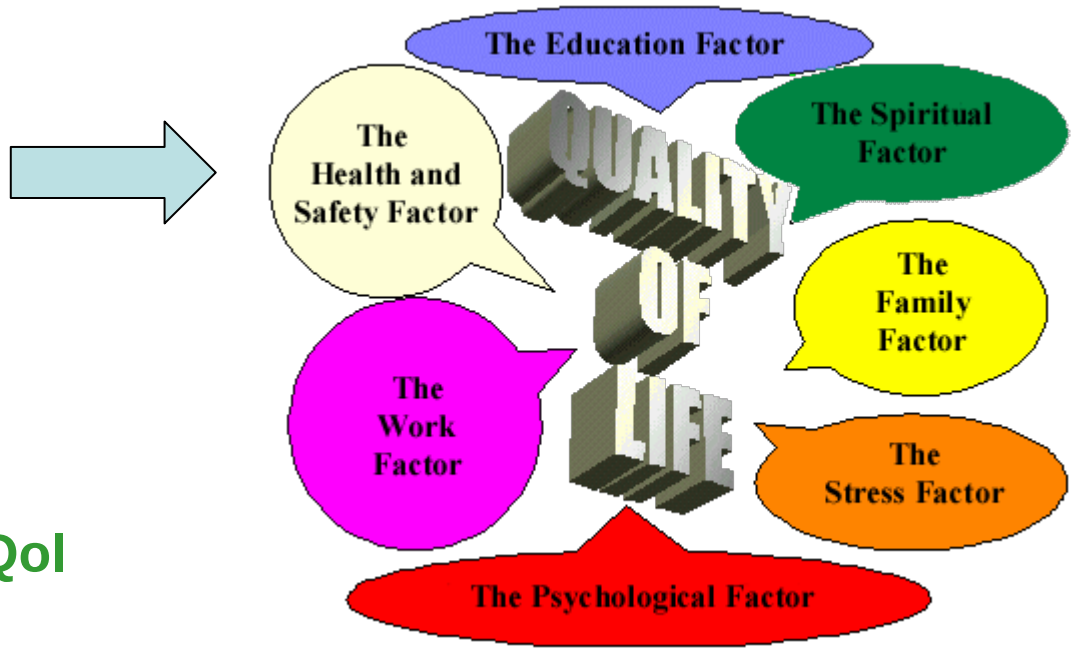
Negative effect of age: caused by age or arthropathy?

Long-term effects of different treatment strategies on HRQoL?



→ **study association of arthropathy with HRQol**

Association of arthropathy with HRQoL: Methods

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Methods:

- 96 patients (88% severe, 12% moderate)
- Pettersson scores & SF 36 completed within 2.5 yrs

Outcome parameters:

- Pettersson score , 6 joints, 0-78 points
- score for ‘physical function’ of SF36 , 0-100 points ‘PF’
- Physical component score of SF36, 0-55 points ‘PCS’

Multivariate regression analysis:

Association of Pettersson score with SF36 *independent of age*

Association of arthropathy with HRQoL: Patients

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mean age 28.6 years (range 13-54)

- Pettersson score to SF 36: mean 0.4 yrs (sd 1.1)
- median Pettersson score 13 (24% zero score)

patients divided according to Pettersson scores

- 0-4 points
- 5-27 points
- 28-78 points

Association of arthropathy with HRQoL: outcome according to Pettersson scores

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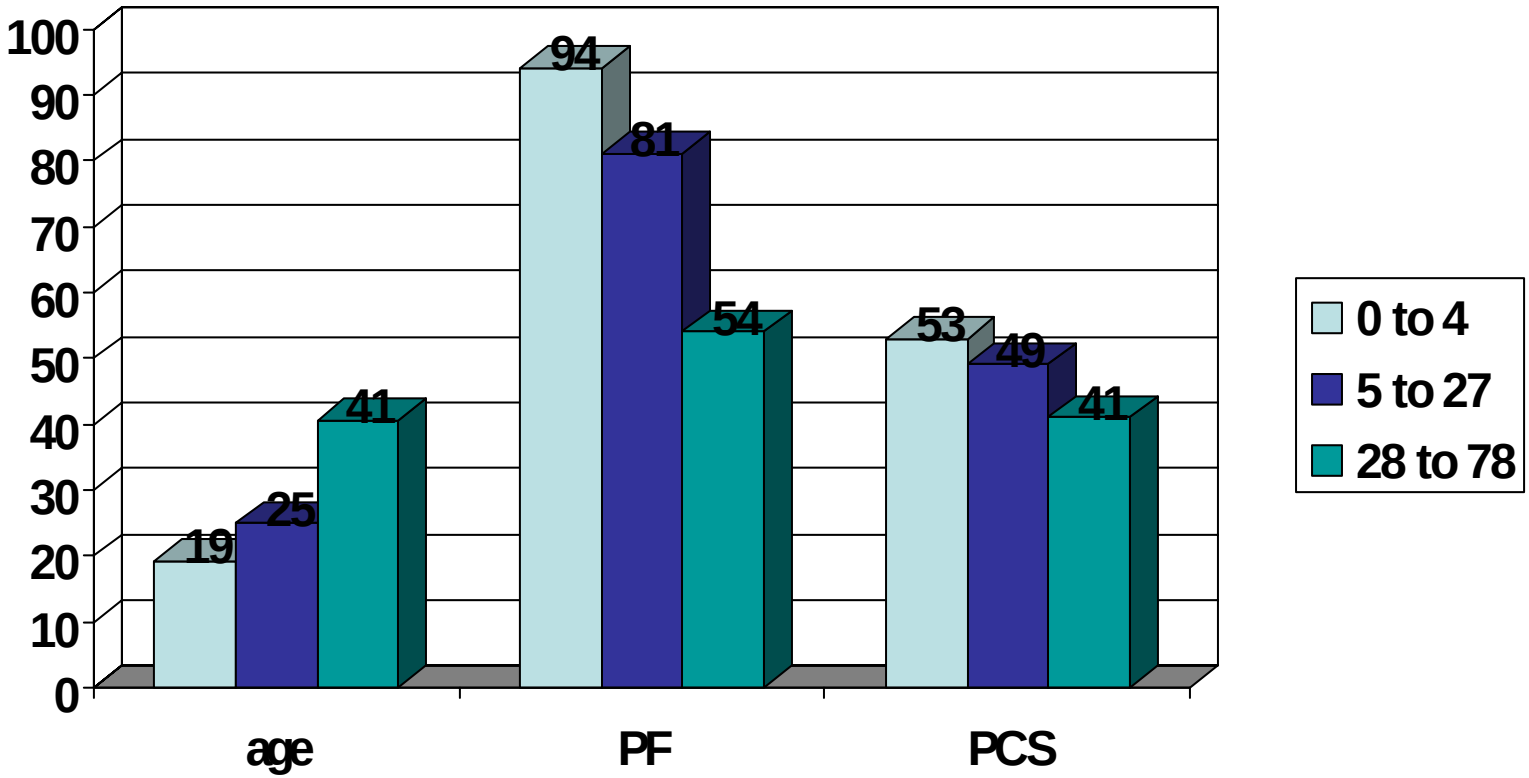

Mean values

Effects of age in general population: physical function

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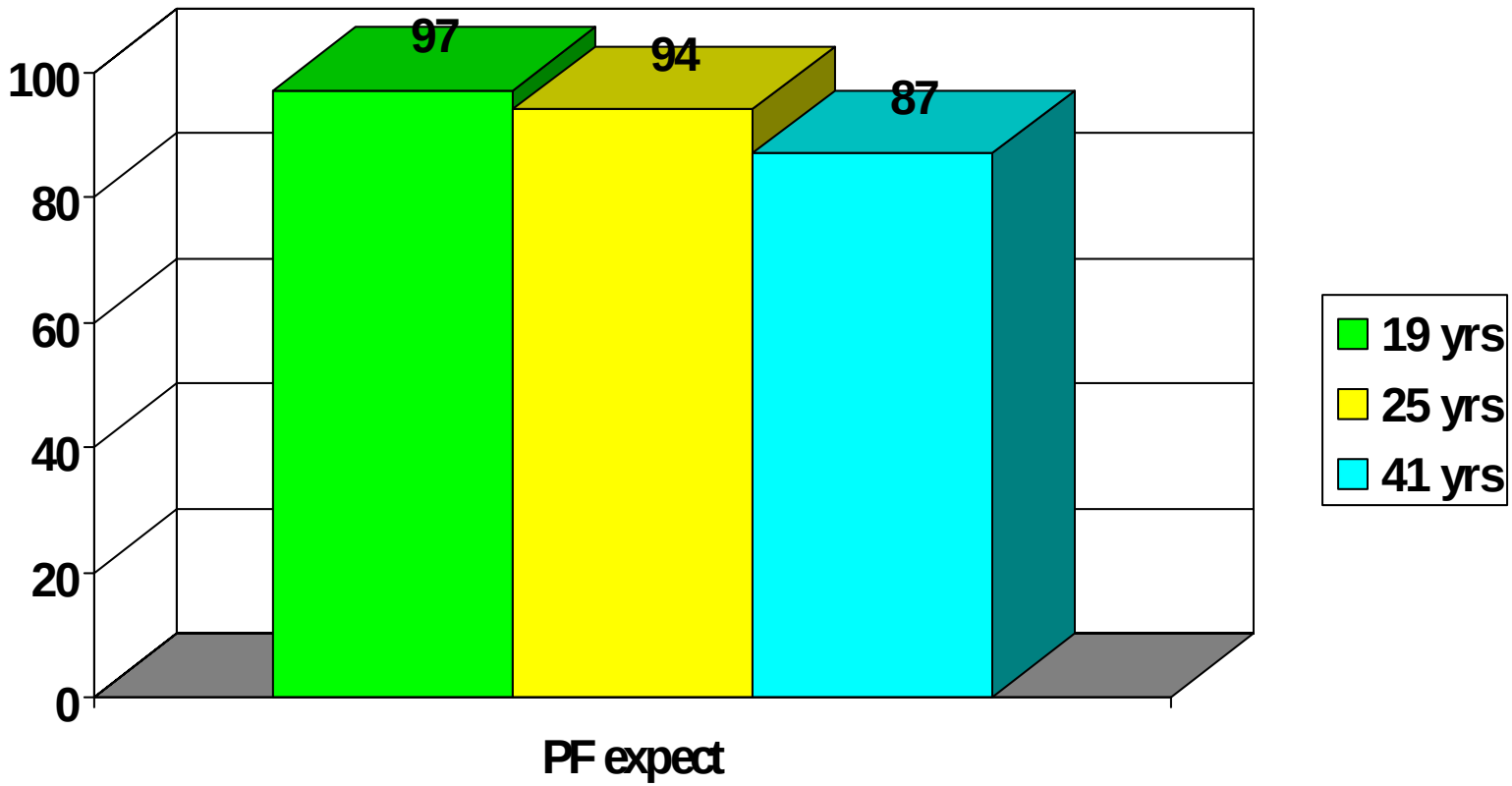

Association of arthropathy with HRQoL: outcome according to Pettersson scores

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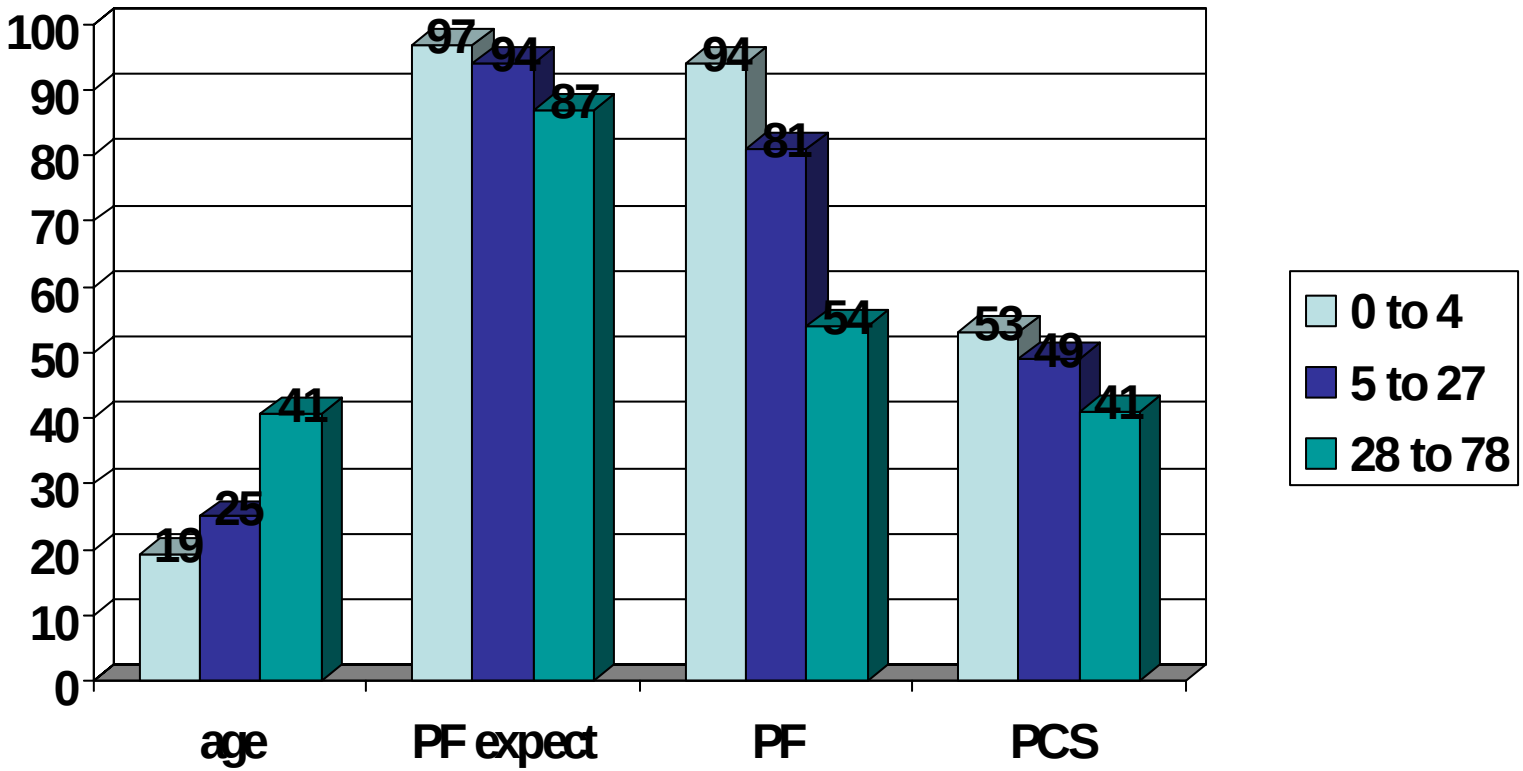

Association of arthropathy with HRQoL: age adjusted analysis

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- Effect on Physical Function (PF):
  - 4.4 points/ 10 points increase in Pettersson score
  (CI: -7.8 to -1.1, p=0.01)
- Effect on Physical Summary Score (PCS):
  -1.4 points/ 10 points increase in Pettersson score
  (CI: -3.0 to +0.2, p=0.07)
- NOT on other domains of SF36

Conclusions

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- Effect of age on HRQoL is caused by both age and haemophilic arthropathy

- age-adjusted association of Pettersson scores
  - with domain of physical function (PF)
  - with physical summary score (PCS)
  - NOT with other domains of SF36

Future research:

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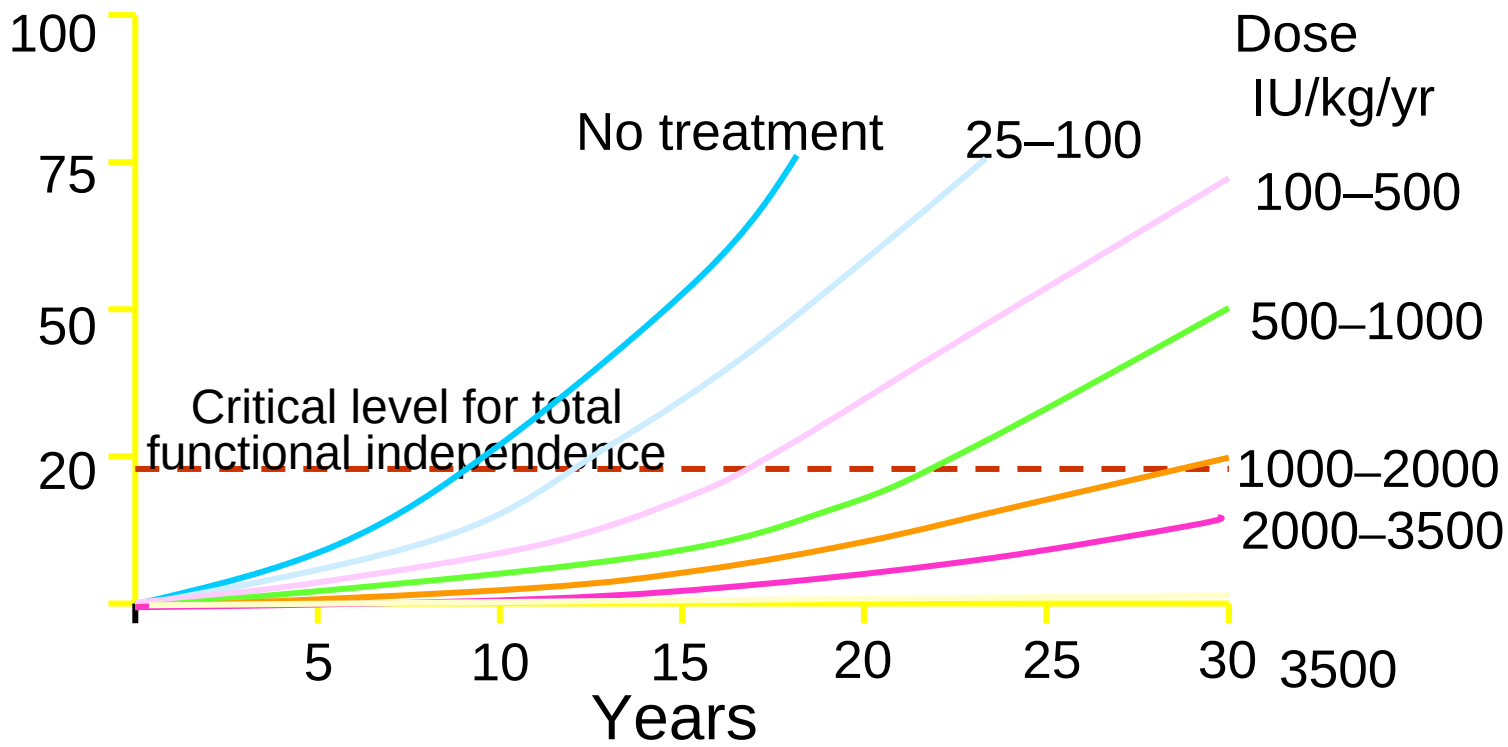
- Use of HRQoL (and Utilities) as outcome for comparison of long-term results between treatment strategies
- Look for ‘point of no return’ : threshold effect of joint damage on HRQoL?



Two studies

Severe haemophilia

NL-SW

Age 12-35

No inhibitors

Assessment

- joint structure
- joint function
- HRQoL
- physical activity

Moderate haemophilia

NL-SW-DK

All ages

No inhibitors

Assessment

joint structure	by PT
joint function	questionn
HRQoL	questionn
physical activity	questionn