man, vrouw en kind

Universitair Ziekenhuis Gent

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Active surveillance

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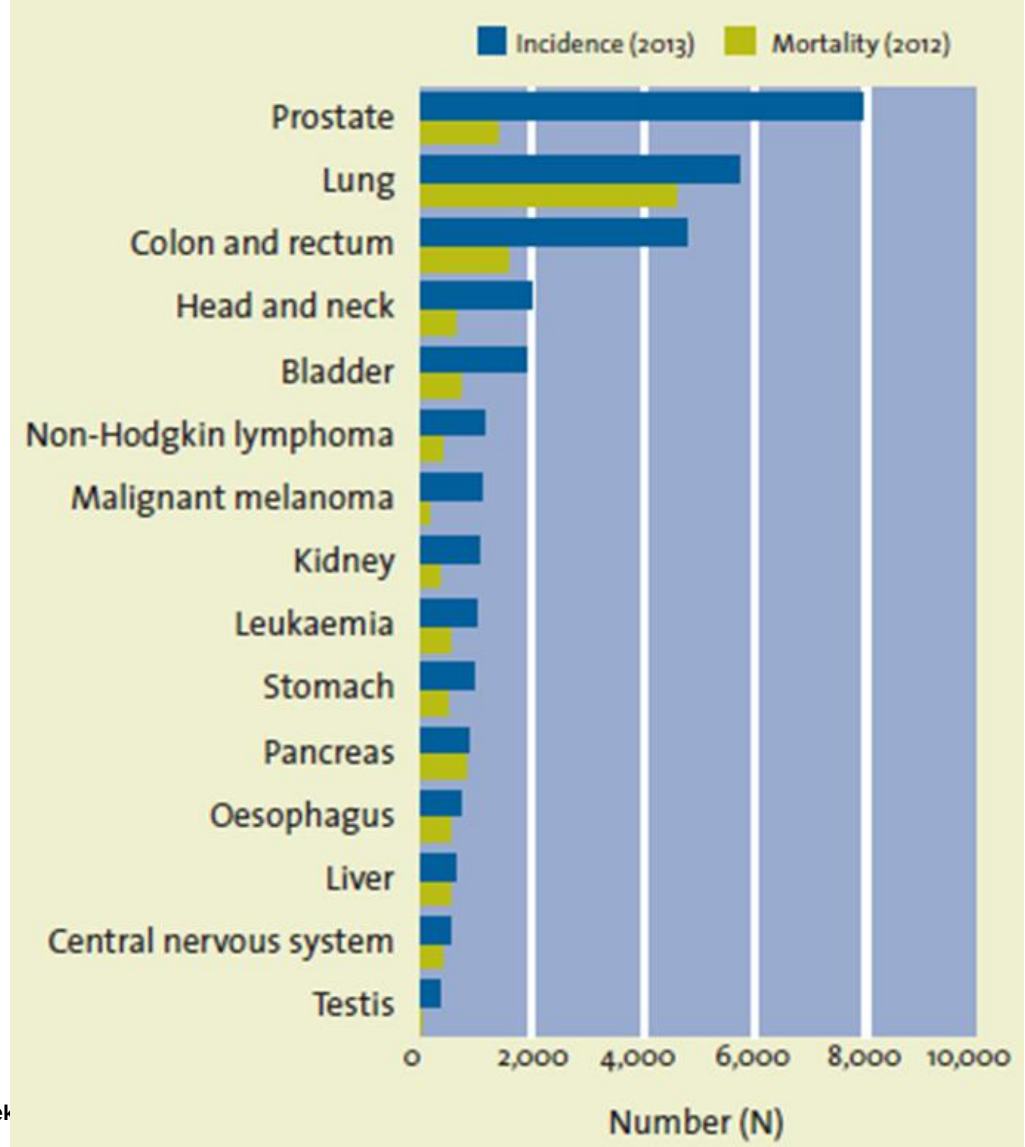
Prostaatkanker in België



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Active surveillance: quid?

- **Bij gelokaliseerd PCa**
- **ACTIEVE beslissing om niet onmiddellijk te behandelen**
- **SURVEILLANCE**
  - Indien geen progressie
  - Zoniet: curatieve therapie

- **≠Watchful waiting**
  - Palliatieve behandeling bij symptomen van PCa
  - Zowel bij lokaal als M+ PCa

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WW: SPCG-4 trial

- N=695, lokaal Pca
- RP vs WW
- Opvolging: 29j !
- ↓ meta's, PCa sterfte en algemene sterfte
- Cave: overbehandeling

	HR meta's	HR PCa sterfte	HR algemene sterfte	NTT
All	0.54 (0.42-0.70)	0.55 (0.41-0.74)	0.74 (0.62-0.87)	8.4
<65j	0.49 (0.34-0.70)	0.50 (0.34-0.75)	0.62 (0.48-0.80)	6.7
≥65j	0.59 (0.41-0.86)	0.63 (0.40-0.99)	**0.86 (0.69-1.07)**	9.9

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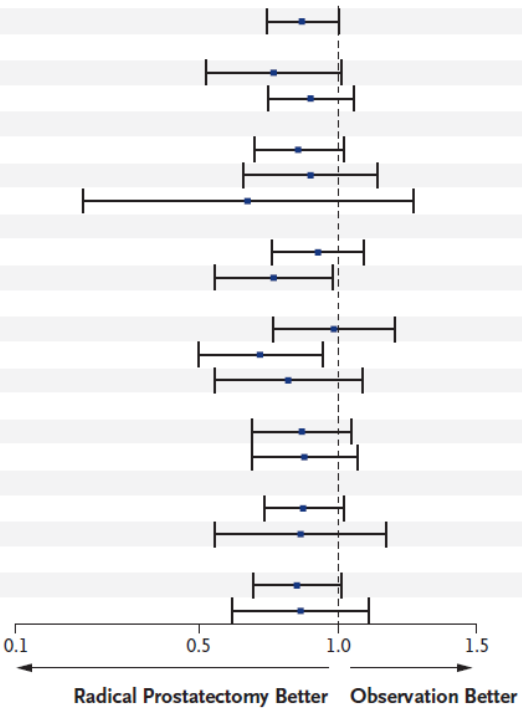
Bill-Axelson et al. NEJM 2018

WW: PIVOT trial

- N= 731, lokaal Pca
- RP vs WW
- Opvolging: 13j
- Low-risk: geen voordeel

A Death from Any Cause

Subgroup	Observation	Radical Prostatectomy	Hazard Ratio (95% CI)	P Value for Interaction
	no. of events/total no.			
Overall	245/367	223/364	0.84 (0.70–1.01)	
Age				0.56
<65 yr	78/131	58/122	0.73 (0.52–1.02)	
≥65 yr	167/236	165/242	0.88 (0.71–1.09)	
Race				0.87
White	155/220	150/232	0.82 (0.66–1.03)	
Black	75/121	64/111	0.87 (0.62–1.22)	
Other	15/26	9/21	0.64 (0.28–1.46)	
PSA				0.06
≤10 ng/ml	151/241	140/238	0.91 (0.72–1.14)	
>10 ng/ml	93/125	83/126	0.73 (0.54–0.98)	
Risk				0.08
Low	83/148	82/148	0.98 (0.72–1.33)	
Intermediate	89/120	77/129	0.68 (0.50–0.92)	
High	59/80	55/77	0.78 (0.54–1.13)	
Charlson score				0.79
0	128/220	117/224	0.84 (0.65–1.07)	
≥1	117/147	106/140	0.85 (0.65–1.10)	
Performance status				0.55
0	200/310	184/312	0.84 (0.69–1.03)	
1–4	45/57	39/52	0.83 (0.54–1.28)	
Gleason score				0.84
<7	167/261	145/254	0.82 (0.65–1.02)	
≥7	63/86	68/98	0.83 (0.59–1.17)	



Wilt et al. NEJM 2017

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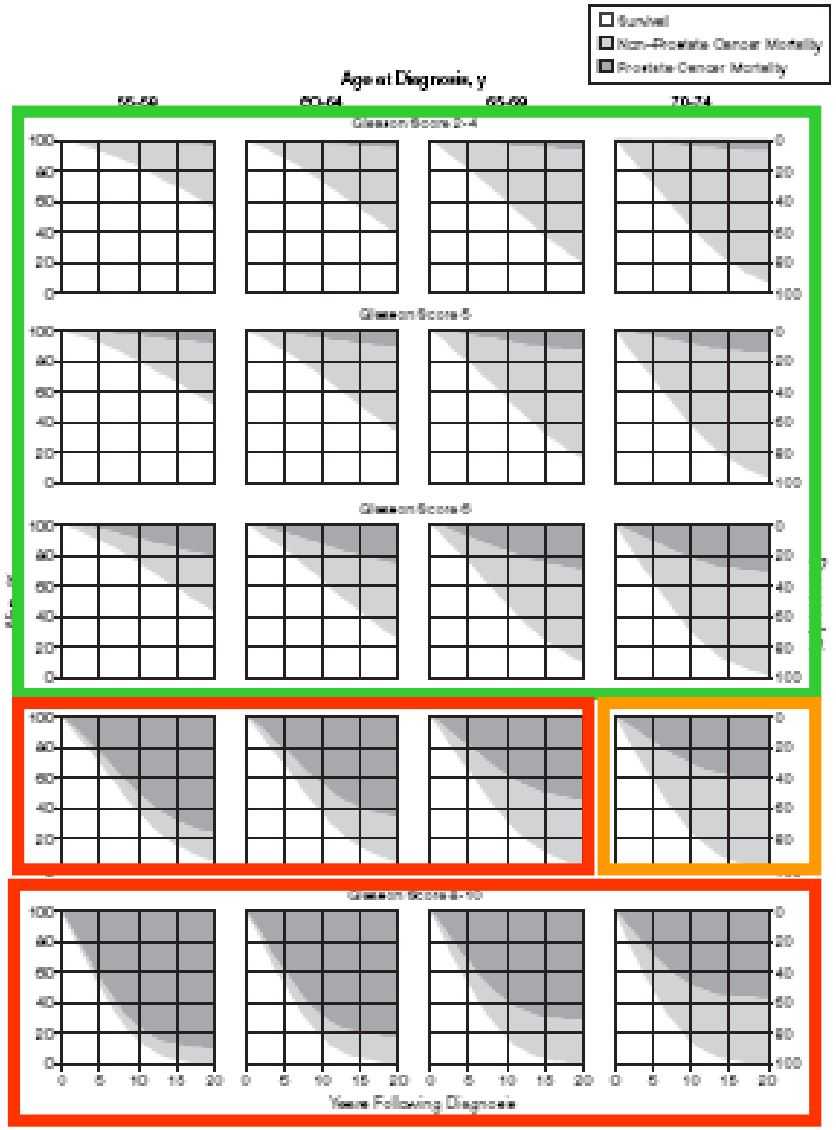
Active surveillance: rationale

- **Albertsen tables**
  - Lage sterfte
    - Gleason ≤6
    - Gleason 7 (oudere leeftijd)
  - Hoge sterfte
    - Gleason 8-10
    - Gleason 7 (jongere leeftijd)
- **Bijwerkingen curatieve therapie (RP +/- RT +/- ADT)**



JAMA 2005; 293: 2095-101.

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Active surveillance: voor wie?

Institution	Lead investigator	Clinical stage	PSA	Gleason	PSA density	No of +ve cores	% of single core
Royal Marsden	Parker	T1–T2	≤15	≤3+4	–	≤50% of total cores	–
University of Toronto-Sunnybrook	Klotz	T1c/T2a	≤10	≤6	–	–	–
UCSF	Carroll	T1–T2	≤10	≤6	–	≤1/3 of total cores	≤50
Princess Margaret Cancer Centre	Finelli	≤T2a	≤10	≤6	–	≤3	≤50
MSK	Eastham	T1–T2a	≤10	≤6	–	≤3	≤50
PRIAS	Schroder	T1c/T2	≤10	≤6	<0.20	≤2	–
University of Miami	Soloway	≤T2	≤10	≤6	–	≤2	≤20
Johns Hopkins Medical Institute	Carter	T1c	–	≤3, no pattern GS 4 or 5	≤0.15	≤2	≤50

- **Low stage, low grade, low PSA and low volume disease**

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Komisarenko et al. Trans Androl Urol 2018

Active surveillance: opvolging?

Institutional origin	Eligibility criteria	Intervention criteria	Follow-up regimen
RM	GS ≤7 (3+4, if ≥65 years old), PSA levels <15 ng/mL, cT1c–T2a, ≤50% of any cores involved	GS >3+4; >50% of any cores involved; PSAV >1 ng/mL/year	PSA q3 months for 1st year, q4 months for 2nd year, then q6 months Confirmatory biopsy within 18–24 months, then q2 years
UT (Sunnybrook)	GS ≤6, PSA ≤10 ng/mL, cT1c, <3 cores positive, <50% of any cores involved (or if >70 years, GS ≤3+4, PSA <15 ng/mL)	PSA-DT <3 years (until 2008); GS >6; stage >cT2a	PSA q3 months for 2 years, then q6 months Confirmatory biopsy within 6–12 months, then q3–4 years until 80 years
UCSF	GS ≤6, PSA <10 ng/mL, cT1c–T2a, <33% of total cores	GS >6; PSAV >0.75 ng/mL/year	PSA q3 months; TRUS q6–12 months; biopsies repeated q12–24 months
PM	GS ≤6, PSA <10 ng/mL, cT1–T2a, ≤3 cores positive, <50% of any cores involved	GS >6, PSA >10 ng/mL, >3 cores positive	PSA q6–12 months; DRE q6–12 months; confirmatory biopsy before being considered on AS (within 12–18 months), re-biopsy q1–3 years until age 80; ± MRI q1–3 years
MSK	GS ≤6, PSA <10 ng/mL, cT1–T2a, ≤3 cores positive	Not standardized	PSA q6 months; confirmatory biopsy before being considered on AS, 3rd biopsy within 18 months and then, q1–3 years; ± MRI q1–3 years
PRIAS	GS ≤6, PSA ≤10 ng/mL, cT1c–T2a, PSAD <0.2 ng/mL/g, ≤2 cores involved	GS >6, >T2, PSA-DT <3 years, >2 cores involved	PSA q3 months for 2 years, then q6 months; biopsies repeated at 1, 4 and 7 years (or yearly if PSA-DT <10 years)
UM	GS ≤6, PSA ≤10 ng/mL, cT1c–T2a, ≤20% of any cores involved, ≤2 cores involved	GS >6, >2 cores involved, >20% of any cores involved	PSA q3–4 months for 2 years, then q6 months; confirmatory biopsy within 9–12 months (starting after 2000) and annually thereafter
JH	GS ≤6, PSA <10 ng/mL, cT1c, ≤50% of any cores and ≤3 cores involved, PSAD <0.15 ng/mL/g	GS >6, >2 cores involved, >50% of any core involved	PSA and free to total PSA ratio q6 months; biopsies repeated annually

- **Geen uniformiteit**
  - Intensiever <2j
  - PSA, confirmatiebiopsies, (MRI)

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Komisarenko et al. Trans Androl Urol 2018

Active surveillance: hoe?

- **≈ PRIAS protocol**
- **Jaar 1:**
  - 3- maandelijks PSA en DRE
  - Confirmatiebiopsie na 1j
- **Nadien:**
  - 6 maandelijkse PSA en DRE
  - Confirmatiebiospie elke 3 jaar
- **Biopsies: complicaties**
  - Alternatief?

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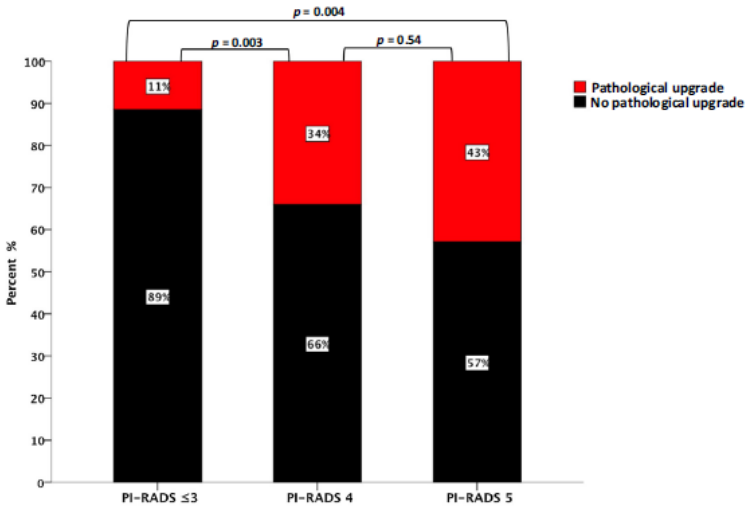
MRI ipv confirmatiebiopsie?

- **accuraatheid MRI mbt pathologsiche progressie:**
  - Tegenstrijdige resultaten
- **Meest courante grade progression: Gleason 3+3 -> Gleason 3+4**
  - MRI minder gevoelig voor Gleason 3+4
- **Wel MRI**
  - @ baseline: Pirads 4-5 -> predictor voor upgrading
  - @ follow-up: guide voor biopsie
  - MRI-TRUS fusion biopsies in ROI



Hsiang et al. Eur Urol focus 2019

Active surveillance: stopcriteria?

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- **Geen uniformiteit, exc. Grade progression**
  - PSA kinetiek (snelheid, dubbelingstijd)
  - Toename van volume

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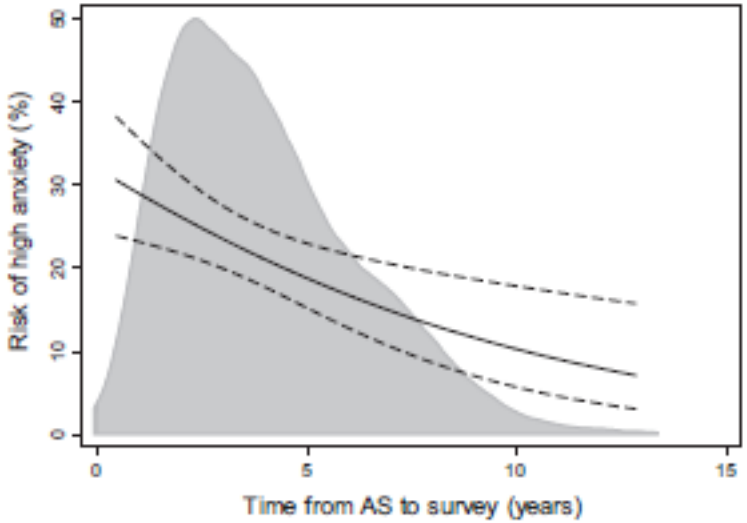
Komisarenko et al. Trans Androl Urol 2018

Active surveillance: Angst?

- **Stop obv angst**
  - UT: 6%
  - Prias: 5%
- **Angst en depressie**
  - 30% @ baseline
  - Nadien gestage daling
  - ≈ na RP of RT
  - Informeren bij beslissingskeuze!

Reason for Intervention/ Treatment	No. of Patients	% of Patients: Treated Patients (n = 267)	% of Patients: Total Cohort (N = 993)
Short PSA doubling time	116	43.5	11.7
Grade progression	94	35	9.5
Patient preference	16	6	1.6
Stage progression	8	3	0.8
Biopsy volume progression	6	2	0.6
Ureteral obstruction	3	1	0.3
Ultrasound lesion volume increase > 2x	1	0.4	0.1
Other	3	0.8	0.3
Not reported	21	7.9	2
Total	267	100	27



Klotz et al. JCO 2015
Venderbos et al. Psychooncology 2015
Marzouk et al. J Urol 2018

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Active surveillance: resultaten longitudinale studies

Institution	N	Median follow-up (months)	Biochemical recurrence	Treatment-free survival	PCa mortality	Overall survival
RM	471	68	15% at 60 months	70% at 60 months	2% at 96 months	9% at 96 months
Sunnybrook	993	102	53% at 60 months	70% at 60 months	5% at 180 months	68% at 120 months
UCSF	321	43	<1% at 36 months	67% at 60 months	NA	NA
PM	1,122	56	NA	27% at 56 months	<0.02% at 56 months	3.2% at 56 months
MSK	238	22	NA	NA	NA	NA
PRIAS	2,494	18	NA	77 at 24 months	NA	87% at 48 months
UM	230	31	NA	85.7% at 60 months	NA	NA
JH	1,298	60	9.4% recurrence at 24 months	59% at 60 months	0.1% at 180 months	69% at 180 months

- **Geen behandeling @ 5j: 14.3-73% (ca. 50%)**
- **PCa sterfte: ≤ 5%**
  - Curatie blijft mogelijk

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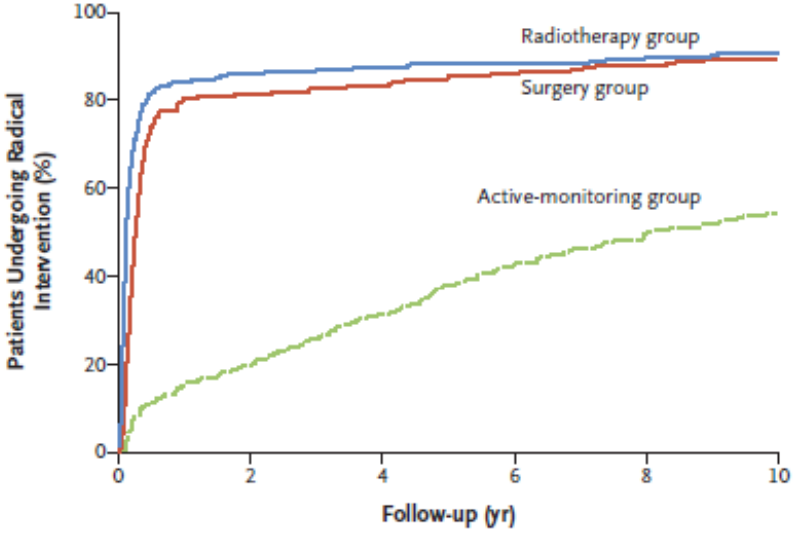
Komisarenko et al. Trans Androl Urol 2018

Active surveillance: resultaten ProtecT-trial

- RCT: AS (n=545) vs RP (n=553) vs RT (545)
- Gelokaliseerd Pca
- 10j opvolging
- Behandeling in AS-groep: 54.8%



Hamdy et al. NEJM 2016

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Active surveillance: resultaten ProtecT-trial

Variable	Active Monitoring (N=545)	Surgery (N=553)	Radiotherapy (N=545)	P Value*
Prostate-cancer mortality				
Total person-yr in follow-up	5393	5422	5339	
No. of deaths due to prostate cancer†	8	5	4	
Prostate-cancer–specific survival — % (95% CI)†				
At 5 yr	99.4 (98.3–99.8)	100	100	
At 10 yr	98.8 (97.4–99.5)	99.0 (97.2–99.6)	99.6 (98.4–99.9)	
Prostate-cancer deaths per 1000 person-yr (95% CI)†	1.5 (0.7–3.0)	0.9 (0.4–2.2)	0.7 (0.3–2.0)	0.48
Incidence of clinical progression‡				
Person-yr of follow-up free of clinical progression	4893	5174	5138	
No. of men with clinical progression	112	46	46	
Clinical progression per 1000 person-yr (95% CI)	22.9 (19.0–27.5)	8.9 (6.7–11.9)	9.0 (6.7–12.0)	<0.001
Incidence of metastatic disease				
Person-yr of follow-up free of metastatic disease	5268	5377	5286	
No. of men with metastatic disease	33	13	16	
Metastatic disease per 1000 person-yr (95% CI)	6.3 (4.5–8.8)	2.4 (1.4–4.2)	3.0 (1.9–4.9)	0.004
All-cause mortality				
Total person-yr in follow-up	5393	5422	5339	
No. of deaths due to any cause	59	55	55	
All-cause deaths per 1000 person-yr (95% CI)	10.9 (8.5–14.1)	10.1 (7.8–13.2)	10.3 (7.9–13.4)	0.87

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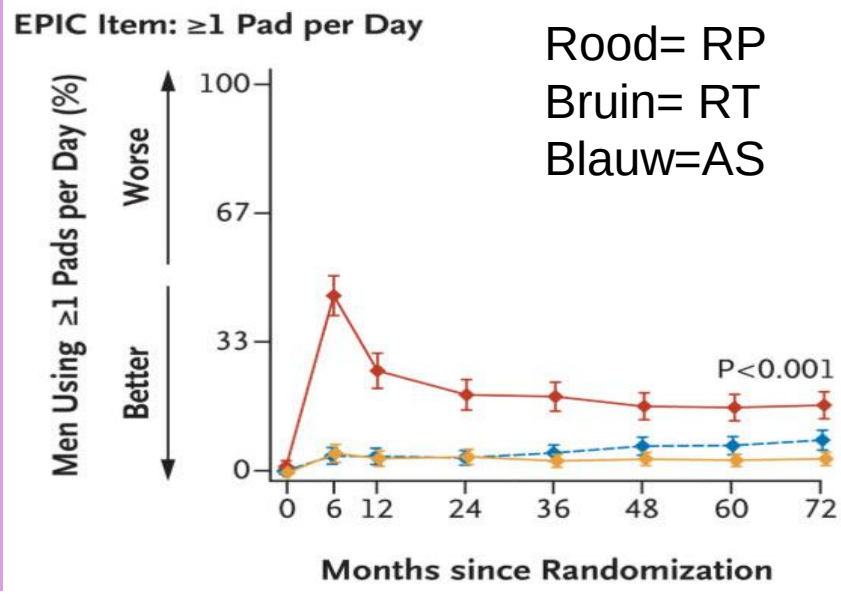
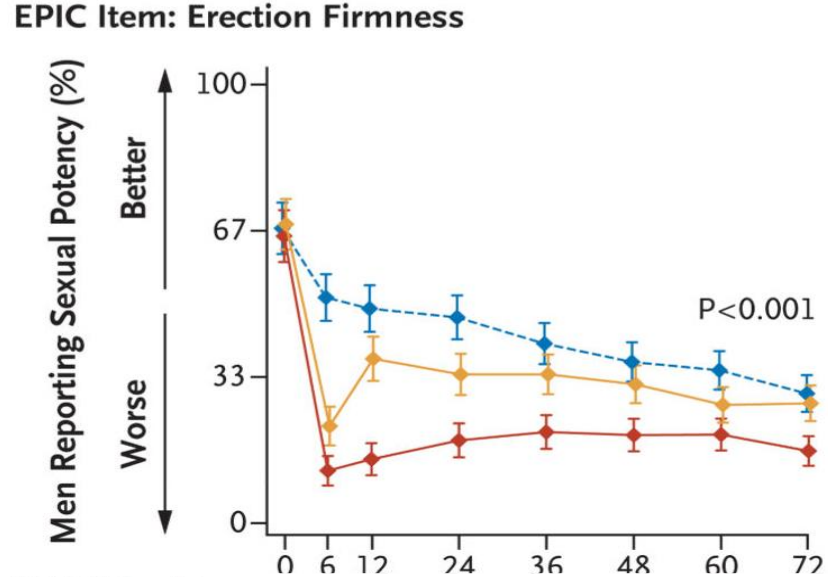
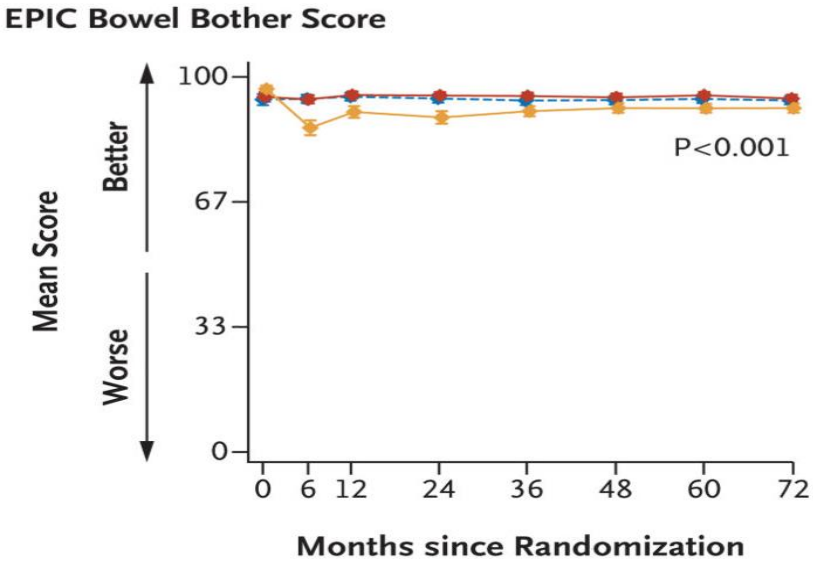
Hamdy et al. NEJM 2016

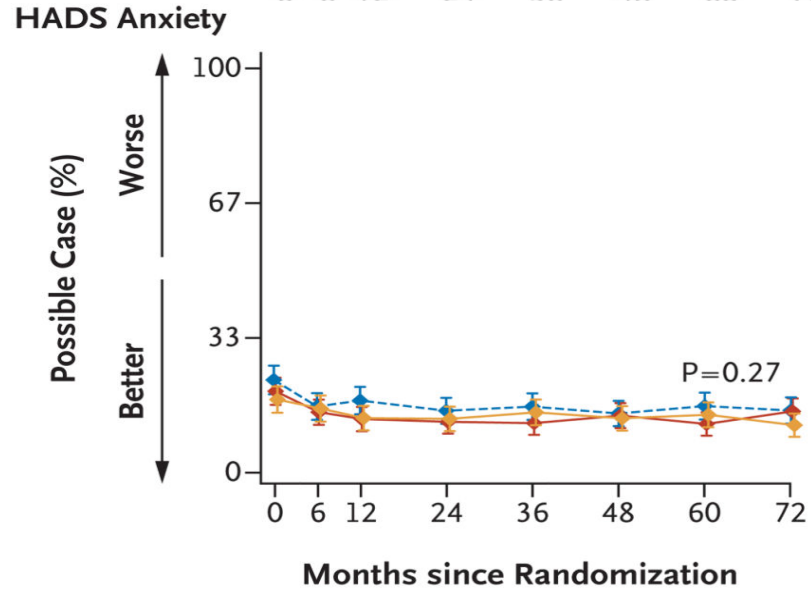
Active surveillance: resultaten ProtecT-trial (Donovan NEJM 2017)

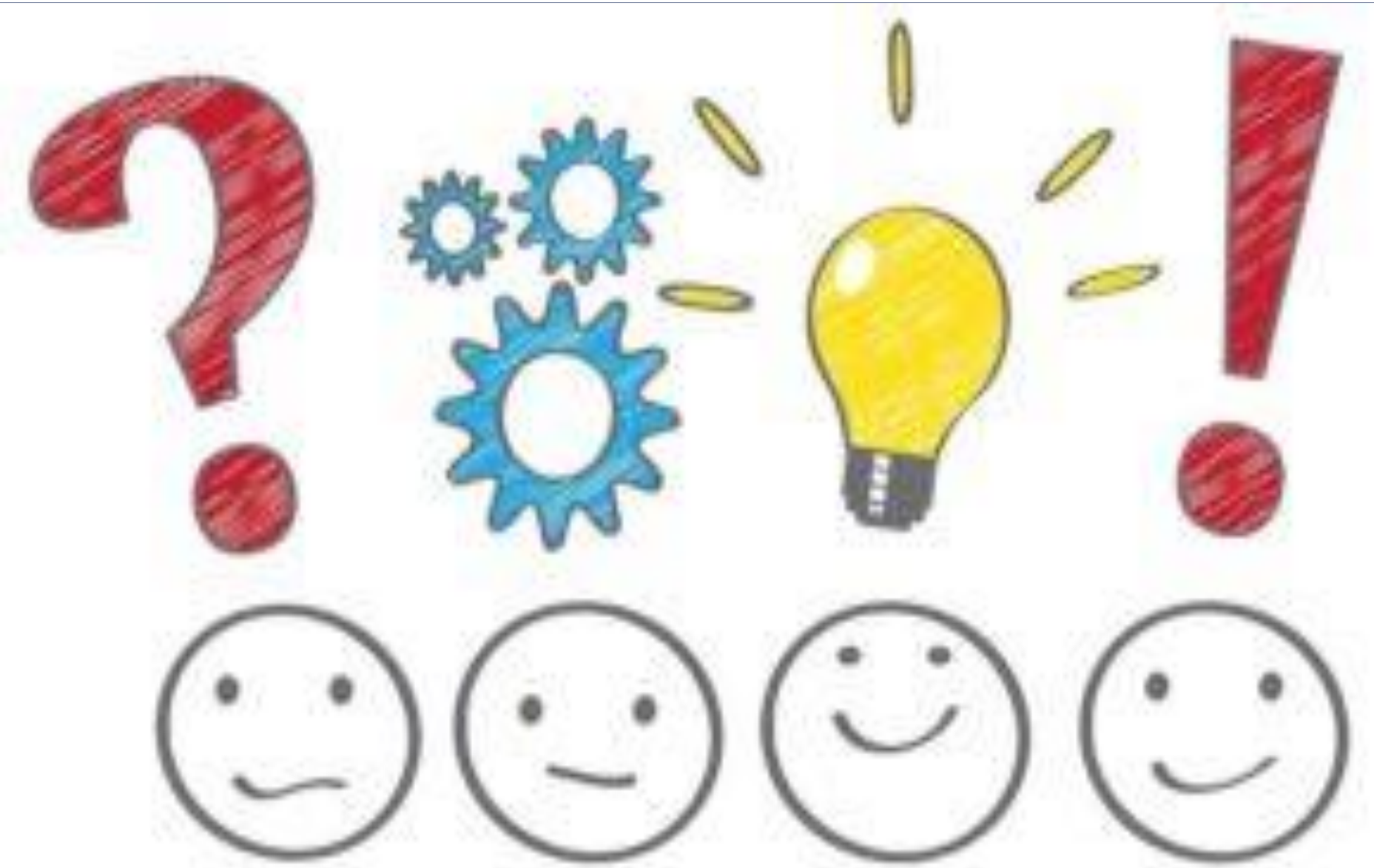
Rood= RP
Bruin= RT
Blauw=AS











conclusies

- **Behandelingsoptie voor laag-risico PCA**
- **Adequate patiëntenselectie: MRI**
- **Strikte opvolging**
- **Krachtig middel om overdiagnose en overbehandeling van PCA-screening tegen te gaan**

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