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Table 1: Summary of systematic review findings (total n=305 studies)

a. Summary of criteria within domains of inclusion, monitoring, reclassification and outcome measures

| Domains | No. of different definitions | No. of studies providing definition for this criterion |
|--|------------------------------------|---|
| Main Criteria for inclusion to deferred active treatment (DAT) | | |
| PSA cut-off | 13 | 305 |
| Gleason Sum Score | 13 | 305 |
| Clinical T-stage | 14 | 305 |
| Number of positive cores | 12 | 288 |
| Core involvement per core | 11 | 288 |
| PSA density | 9 | 288 |
| | | |
| Monitoring and follow-up characteristics during DAT | | |
| PSA testing frequency | 23 | 198 |
| DRE frequency | 26 | 160 |
| TRUS Re-biopsy frequency | 32 | 203 |
| Number of cores taken | 29 | 123 |
| mpMRI frequency | 24 | 74 |
| | | |
| Reclassification characteristics during DAT | | |
| Clinical T-stage | 13 | 92 |
| Gleason sum score | 13 | 209 |
| PSA doubling time | 5 | 88 |
| Number of positive cores | 13 | 150 |

| Core involvement per core | 8 | 128 |
|----------------------------|----|-----|
| Patient preference | 2 | 58 |
| | | |
| Types of outcomes measured | | |
| Quality of life | 6 | 81 |
| Sexual function | 3 | 75 |
| Survival outcome | 3 | 114 |
| Disease-specific outcome | 15 | 221 |

DAT = deferred active treatment; DRE = digital-rectal examination; mpMRI = multi-parametric magnetic resonance imaging; No. = number; PSA = prostatespecific antigen; TRUS = transrectal ultrasound.

b. Most common combinations of Inclusion criteria for deferred active treatment (DAT)

| PSA level | Gleason | Clinical T- | N° of | Core | PSA | N |
|-----------|---------|-------------|-------|-------|---------|----|
| | 30016 | category | cores | (%) | density | |
| ≤10 | ≤3+3 | T1c-T2c | ≤2 | NR | <0.2 | 34 |
| NR | ≤3+3 | T1c | ≤2 | <50% | <0.15 | 13 |
| ≤10 | ≤3+3 | ≤T2a | ≤3 | ≤50% | NR | 10 |
| NR | ≤3+3 | NR | NR | NR | NR | 7 |
| ≤10 | ≤3+3 | ≤T2c | ≤2 | NR | ≤0.2 | 5 |
| ≤15 | ≤7 | T1b-T2b | NR | NR | NR | 5 |
| <15 | ≤3+3 | ≤T2a | ≤2 | NR | NR | 5 |
| NR | ≤3+3 | ≤T2a | ≤2 | ≤ 20% | NR | 5 |

N = number of studies; *NR* = not recorded; *PSA* = prostate-specific antigen.

c. Most common combination of Monitoring and follow-up characteristics during DAT

| PSA frequency | DRE frequency | TRUS re-biopsy | Number of | mpMRI | Ν |
|---------------|---------------|----------------|-------------|-----------|---|
| | | frequency | cores taken | frequency | |

| 6/12 | 6/12 | 12/12 | multiple | multiple | 24 |
|-------------------------|-------------------------|----------|----------|----------|----|
| 6/12 | 6/12 | multiple | multiple | multiple | 18 |
| 3/12 for 2 yrs | 3/12 for 2 yrs | multiple | multiple | NR | 11 |
| 6/12 thereafter | 6/12 thereafter | | | | |
| 3/12 | 6/12 | multiple | multiple | NR | 9 |
| 3/12 for 2 yrs | 6/12 for 2 yrs | multiple | multiple | multiple | 6 |
| 6/12 thereafter | 12/12 | | | | |
| | thereafter | | | | |
| 3/12 1 st yr | 3/12 1 st yr | multiple | multiple | NR | 6 |
| 6/12 thereafter | 6/12 thereafter | | | | |
| 6/12 | NR | 12/12 | multiple | multiple | 6 |
| 3/12 | 3/12 | 12/12 | NR | NR | 5 |
| 3/12 1 st yr | multiple | multiple | multiple | NR | 5 |
| 6/12 thereafter | | | | | |
| 6-12/12 | 6-12/12 | multiple | multiple | multiple | 5 |

DAT = deferred active treatment; DRE = digital-rectal examination; N = number of studies; mpMRI = multi-parametric magnetic resonance imaging; NR = not recorded; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; yr = year.

| Gleason | Clinical T- | PSA | N° of | Core | Patient | Ν |
|-------------|--------------|----------|----------|-------------|------------|----|
| Score | category | doubling | positive | Involvement | preference | |
| | | time | cores | (%) | | |
| GSS > 6 | NR | NR | >2 | >50% | NR | 14 |
| Increase in | Change in T- | NR | NR | NR | NR | 11 |
| GSS | stage | | | | | |
| GSS > 6 | NR | NR | >3 | >50% | NR | 10 |
| GSS > 6 | NR | NR | >2 | >20% | NR | 7 |
| GSS >6 | NR | NR | NR | NR | NR | 7 |
| Increase in | Change in T- | NR | NR | Multiple | Yes | 6 |
| GSS | stage | | | | | |
| GSS > 6 | >T2 | <3 | >2 | NR | NR | 5 |

d. Most common for Reclassification definitions during DAT

| GSS 24+3 212C <3 >3 NR NR 4 | GSS >4+3 >T2c <3 >3 NB NB 4 |
|-----------------------------|-----------------------------|
|-----------------------------|-----------------------------|

DAT = deferred active treatment; GSS = Gleason score; N = number of studies; NR = not recorded; PSA = prostate-specific antigen.





N = number; R1 = round 1; R2 = round 2.

Table 2: Summary of characteristics of Delphi participants completing Round 1 (R1) and Round 2 (R2)

Table 3: Summary of statements and consensus status after two rounds of Delphi survey

Key:

In columns showing percentages agree/equivocal/disagree, red shaded cells = \geq 70%; yellow shaded cells = 60%-70%

In 'consensus' column:

Consensus (≥70% agree and ≤15% disagree, or vice versa). No further discussion required, not taken forward to face-to-face meeting. Near consensus (≥70% agree but ≥15% disagree, or vice versa; or ≥60% agree, and ≤20% disagree, or vice versa). Taken forward to discuss and vote in face-to-face meeting.

| | | I | Health care pr | ofessional | s (HCP) | | | | | Patients | | |
|---|---|----------------------------|-----------------------------|-------------------------|-------------------|--------------------------------|-----------|------------------------------------|-------------------------------------|------------------------------|---------------------|-------------------------------------|
| Domain | Item Number in Delphi and description | HCP % Disagree (1-3) | HCP % Equivocal (4-6) | HCP % Agree (7-9) | HCP Total N | HCP unable to score N | Consensus | Patients % Disagree (1-3) | Patients % Equivocal (4-6) | Patients % Agree (7-9) | Patients Total N | Patients unable to score N |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 1. There is no lower nor upper age limit for inclusion as long as the appropriate life expectancy criterion is fulfilled | 3.7% | 0.9% | 95.4% | 109 | 0 | 1 | NA | NA | NA | NA | NA |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 2. The appropriate life expectancy criterion for inclusion is: i. ≥10 yrs | 1.8% | 4.6% | 93.6% | 109 | 0 | 1 | NA | NA | NA | NA | NA |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 3. The appropriate life expectancy criterion for inclusion is: ii. ≥15 yrs | 18.5% | 45.4% | 36.1% | 109 | 1 | 4 | NA | NA | NA | NA | NA |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | Life expectancy in everyday practice is best evaluated by: i. Performance status (e.g. ECOG, Karnofsky) | 8.8% | 46.1% | 45.1% | 109 | 7 | 4 | NA | NA | NA | NA | NA |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 5. Life expectancy in everyday practice is best evaluated by: ii. Co-morbidity index measure (e.g. Charlson) | 5.1% | 38.4% | 56.6% | 109 | 10 | 3 | NA | NA | NA | NA | NA |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life | Life expectancy in everyday practice is best evaluated by: iii. Health status screening (e.g. Geriatric 8 screening | 6.5% | 45.2% | 48.4% | 109 | 16 | 4 | NA | NA | NA | NA | NA |

Commented [A1]: Unify MRI – mpMRI in the table?

Gleason score: GSS as above?

| expectancy | tool) | | | | | | | | | | | |
|---|---|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | Life expectancy in everyday practice is best evaluated by: iv. Combination of performance status, co-morbidity index and health status screening | 0.0% | 4.9% | 95.1% | 109 | 7 | 1 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 8. Low-risk disease: i. is an automatic inclusion criterion regardless of other disease factors | 50.0% | 8.3% | 41.7% | 108 | 0 | 3 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | Low-risk disease: ii. is excluded if the extent of disease is high, based on biopsy core volume, length or number or proportion of core positivity | 28.7% | 8.3% | 63.0% | 108 | 0 | 3 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 10. Low-risk disease: iii. is excluded if the extent and/or stage of disease is high based on mpMRI | 14.8% | 21.3% | 63.9% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 11. Low-risk disease: iv. is excluded if mpMRI suggests biologically-aggressive disease | 17.8% | 21.5% | 60.7% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 12. Gleason 3+4=7 (ISUP grade 2): i. is an automatic exclusion criterion | 69.4% | 18.5% | 12.0% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | Gleason 3+4=7 (ISUP grade 2): ii. can be included only if favourable characteristics are present, including PSA (<10), clinical stage (≤cT2a) and biopsy characteristics (low core positivity) | 7.4% | 15.7% | 76.9% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 14. Gleason 4+3=7 (ISUP grade 3): i. is an automatic exclusion criterion. | 5.6% | 7.4% | 87.0% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 15. Gleason 4+3=7 (ISUP grade 3): ii. can be included only if favourable characteristics are present, including PSA (<10), clinical stage (≤cT2a) and biopsy characteristics (low core positivity) | 72.2% | 12.0% | 15.7% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 16. PSA :i. >10ng/ml is an automatic exclusion criterion, regardless of other disease characteristics | 78.7% | 13.9% | 7.4% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| Patient eligibility, inclusion and exclusion | PSA:ii. >20ng/ml is an automatic exclusion criterion, regardless of other | 19.4% | 12.0% | 68.5% | 108 | 0 | 2 | NA | NA | NA | NA | NA |

| criteria. 2. Risk classification | disease characteristics | | | | | | | | | | | |
|---|---|-------|-------|--------|-----|---|---|----|----|----|----|----|
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 18. PSA density: i. is an important inclusion criterion | 18.1% | 22.9% | 59.0% | 108 | 3 | 3 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | PSA density: ii. for inclusion should be ≤ 0.15ng/ml per g | 16.3% | 32.7% | 51.0% | 108 | 4 | 3 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 20. PSA density: iii. for inclusion should be ≤ 0.20ng/ml per g | 32.4% | 56.9% | 10.8% | 108 | 6 | 4 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 21. Clinical stage: i. ≥T2b is an automatic exclusion criterion, regardless of other disease characteristics | 38.0% | 36.1% | 25.9% | 108 | 0 | 4 | NA | NA | NA | NA | NA |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 22. Clinical stage: ii. ≥T2c is an automatic exclusion criterion, regardless of other disease characteristics | 17.6% | 8.3% | 74.1% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 23. Targeted biopsies should be reported separately from systematic biopsies | 0.0% | 0.0% | 100.0% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 24. The extent of disease should be reported in: i. length (mm) | 0.9% | 2.8% | 96.3% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 25. The extent of disease should be reported in: ii. % tumour volume (as a proportion of total volume of core) | 5.6% | 7.4% | 87.0% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 26. ISUP grade (Gleason score) should be reported for each positive core | 4.7% | 1.9% | 93.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 27. Percentage of Gleason pattern 4 carcinoma should be provided for each biopsy site with Gleason score 7 carcinoma | 1.9% | 1.9% | 96.3% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 28. Intraductal and cribriform histology are exclusion criteria | 1.0% | 10.5% | 88.6% | 108 | 3 | 1 | NA | NA | NA | NA | NA |
| Patient eligibility, inclusion and exclusion | 29. When systematic biopsies are performed, the extent of disease based | 2.8% | 6.5% | 90.7% | 108 | 0 | 1 | NA | NA | NA | NA | NA |

| criteria. 3. Pathology characteristics | on histological characteristics (e.g. core length, core volume, core positivity, etc.) is an important inclusion/exclusion criterion | | | | | | | | | | | |
|---|--|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 30. Extent of disease on histology is important even for Gleason 3+3=6//SUP Grade 1 disease because it may lead to patients being excluded | 14.2% | 9.4% | 76.4% | 108 | 2 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 31. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: i. Core positivity >20% | 89.3% | 7.8% | 2.9% | 108 | 5 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 32. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: ii. Core positivity >33% | 71.8% | 23.3% | 4.9% | 108 | 5 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 33. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: iii. Core positivity ≥50% | 58.3% | 11.7% | 30.1% | 108 | 5 | 3 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 34. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: iv. Positive cores >2 | 81.6% | 10.7% | 7.8% | 108 | 5 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 35. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: v. Positive cores >3 | 73.8% | 11.7% | 14.6% | 108 | 5 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 36. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: vi. Core length | 93.1% | 3.9% | 2.9% | 108 | 6 | 1 | NA | NA | NA | NA | NA |

| | >3mm | | | | | | | | | | | |
|---|--|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 37. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease is: vii. Core length >5mm | 87.3% | 7.8% | 4.9% | 108 | 6 | 1 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 38. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: i. Core positivity >20% | 52.0% | 24.5% | 23.5% | 108 | 6 | 3 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 39. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: ii. Core positivity >33% | 42.7% | 30.1% | 27.2% | 108 | 5 | 4 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 40. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: iii. Core positivity ≥50% | 26.2% | 8.7% | 65.0% | 108 | 5 | 3 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 41. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: iv. Positive cores >2 | 25.2% | 24.3% | 50.5% | 108 | 5 | 3 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 42. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: v. Positive cores >3 | 29.1% | 15.5% | 55.3% | 108 | 5 | 3 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 43. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: vi. Core length | 51.5% | 23.3% | 25.2% | 108 | 5 | 3 | NA | NA | NA | NA | NA |

| | >3mm | | | | | | | | | | | |
|---|---|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 44. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: vii. Core length >5mm | 36.9% | 28.2% | 35.0% | 108 | 5 | 4 | NA | NA | NA | NA | NA |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 45. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: viii. Any disease extent (because Gleason 3+4=7/ISUP Grade 2 is an automatic exclusion) | 78.6% | 8.7% | 12.6% | 108 | 5 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 46. If a patient has had upfront mpMRI followed by systematic and targeted biopsies, there is no need for confirmatory biopsies | 17.8% | 7.5% | 74.8% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 47. If targeted biopsies based upon mpMRI images are performed, the number of positive cores is not an indicator of extent of disease nor tumour volume | 5.7% | 22.6% | 71.7% | 108 | 2 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 48. The number of positive sextants based on systematic and/or targeted biopsies should be taken into account as an indicator of tumour volume | 0.9% | 11.1% | 88.0% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 49. The volume of the dominant lesion seen on mpMRI (PI-RADS V2 ≥3) should be taken into account as an indicator of tumour volume | 2.8% | 12.1% | 85.0% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 50. For inclusion, prostate biopsies should be performed by: i. mpNRI- guided targeted biopsies (including in- bore, cognitive guidance or mpNRI fusion) without systematic biopsies | 86.9% | 9.3% | 3.7% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 51. For inclusion, prostate biopsies should be performed by: ii. mpMRI- guided targeted biopsies (including in- bore, cognitive guidance or mpMRI fusion) with systematic biopsies | 2.8% | 3.7% | 93.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 52. For inclusion, prostate biopsies should be performed by: iii. Transperineal template biopsies instead of mpMRI-guided biopsies | 71.0% | 23.4% | 5.6% | 108 | 1 | 1 | NA | NA | NA | NA | NA |

| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 53. For inclusion, prostate biopsies should be performed by: iv. TRUS- guided systematic biopsies only | 79.4% | 15.9% | 4.7% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
|---|--|--------|-------|-------|-----|---|---|----|----|----|----|----|
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 54. Tumour volume (for ≤T2 disease) based purely on mpMRI characteristics is an important inclusion/exclusion criterion | 32.4% | 25.0% | 42.6% | 108 | 0 | 4 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 55. Disease aggressiveness (for ≤T2 disease) (e.g. low ADC value) based purely on mpMRI characteristics is an important inclusion/exclusion criterion | 51.9% | 33.0% | 15.1% | 108 | 2 | 3 | NA | NA | NA | NA | NA |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 56. For inclusion, all patients need an mpMRI at some point | 11.1% | 5.6% | 83.3% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 57. During active surveillance in the first 2 yrs, men should have their PSA checked: i. Every 3 mo | 37.4% | 20.6% | 42.1% | 108 | 1 | 4 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 58. During active surveillance in the first 2 yrs, men should have their PSA checked: ii. Every 6 mo | 13.1% | 6.5% | 80.4% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 59. During active surveillance in the first 2 yrs, men should have their PSA checked: iii. Not checked at all | 100.0% | 0.0% | 0.0% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 60. During active surveillance after the first 2 yrs, men should have their PSA checked: i. Every 3 mo | 86.0% | 8.4% | 5.6% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 61. During active surveillance after the first 2 yrs, men should have their PSA checked: ii. Every 6 mo | 2.8% | 4.7% | 92.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 62. During active surveillance after the first 2 yrs, men should have their PSA checked: iii. Not checked at all | 100.0% | 0.0% | 0.0% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 63. During active surveillance, men should have a digital rectal examination (DRE): | 9.3% | 6.5% | 84.1% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 64. During active surveillance, men should have a digital rectal examination (DRE): i. Every 3 mo | 94.4% | 5.6% | 0.0% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 65. During active surveillance, men should have a digital rectal examination (DRE): ii. Every 6 mo | 61.7% | 12.1% | 26.2% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 66. During active surveillance, men should have a digital rectal examination (DRE): iii. Every 12 mo | 16.8% | 14.0% | 69.2% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and | 67. During active surveillance, men should have a digital rectal examination | 84.1% | 7.5% | 8.4% | 108 | 1 | 1 | | | | | |

| follow-up | (DRE): iv. Not needed | | | | | | | | | | | |
|---|--|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 68. During active surveillance, repeat biopsy should be performed: i. Every 12 mo | 79.4% | 9.3% | 11.2% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 69. During active surveillance, repeat biopsy should be performed: ii. Every 24 mo | 55.1% | 17.8% | 27.1% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | During active surveillance, repeat biopsy should be performed: iii. Every 48 mo | 77.6% | 15.0% | 7.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 71. During active surveillance, repeat biopsy should be performed: iv. At 1 yr, 4 ys and 7 yrs | 20.8% | 26.4% | 52.8% | 108 | 2 | 3 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 72. During active surveillance, repeat biopsy should be performed: v. Not routinely pre-planned unless triggered | 62.6% | 9.3% | 28.0% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 73. During active surveillance, repeat biopsy should be performed: vi. Triggered by a change in mpMRI (i.e. increase PLRADS score, lesion volume or radiological T stage) | 2.8% | 3.7% | 93.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 74. During active surveillance, repeat biopsy should be performed: vii. Triggered by PSA doubling time <3 yrs | 13.2% | 17.9% | 68.9% | 108 | 2 | 2 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 75. During active surveillance, repeat biopsy should be performed: viii. Triggered by DRE progression | 9.3% | 6.5% | 84.1% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 76. If repeat biopsies are needed, they should be performed by: i. 10-12 core TRUS-guided | 44.3% | 18.9% | 36.8% | 108 | 2 | 4 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 77. If repeat biopsies are needed, they should be performed by: ii. mpMRI- guided targeted biopsies (including in- bore, cognitive guidance or mpMRI fusion) without systematic biopsies | 70.1% | 13.1% | 16.8% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 78. If repeat biopsies are needed, they should be performed by: iii. mpMRI- guided targeted biopsies (including in- bore, cognitive guidance or mpMRI fusion) with systematic biopsies | 3.7% | 2.8% | 93.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 79. If repeat biopsies are needed, they should be performed by: iv. Transperineal template biopsies instead of mpMRI-guided biopsies | 69.8% | 23.6% | 6.6% | 108 | 2 | 2 | NA | NA | NA | NA | NA |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 80. If repeat biopsies are needed, they should be performed by: v. TRUS- guided systematic biopsies | 57.0% | 19.6% | 23.4% | 108 | 1 | 3 | NA | NA | NA | NA | NA |

| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 81. Reclassification should only apply to patients with a life expectancy of ≥10 yrs at the time of assessment | 7.6% | 7.6% | 84.8% | 108 | 3 | 1 | NA | NA | NA | NA | NA |
|--|--|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 82. Reclassification should only apply to patients with a life expectancy of ≥15 yrs at the time of assessment | 34.3% | 39.0% | 26.7% | 108 | 3 | 4 | NA | NA | NA | NA | NA |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 83. Active surveillance should only be continued in patients with life expectancy of ≥10 yrs | 9.5% | 1.9% | 88.6% | 108 | 3 | 1 | NA | NA | NA | NA | NA |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 84. Active surveillance should only be continued in patients with life expectancy of ≥15 yrs | 38.1% | 33.3% | 28.6% | 108 | 3 | 4 | NA | NA | NA | NA | NA |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 85. Patient anxiety or depression is a valid reason for triggering reclassification (including active treatment) | 6.5% | 9.3% | 84.1% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 86. Patient reluctance to undergo repeat biopsies or repeat imaging is a valid reason for triggering reclassification (including active treatment) | 17.8% | 18.7% | 63.6% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | PSA progression is sufficient to indicate reclassification in the absence of other factors. | 72.2% | 8.3% | 19.4% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 88. A rise in PSA mandates re-biopsy irrespective of other findings. | 66.7% | 14.8% | 18.5% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 89. A rise in PSA mandates re-imaging of the patient. | 19.4% | 14.8% | 65.7% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 90. A shortening of PSA doubling time: i. is sufficient to indicate reclassification in the absence of other factors | 68.2% | 16.8% | 15.0% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| 7. Reclassification (i.e. leaving active surveillance | 91. A shortening of PSA doubling time: ii. Should only indicate reclassification if | 39.6% | 25.5% | 34.9% | 108 | 2 | 4 | NA | NA | NA | NA | NA |

| for an active treatment) criteria. 2. Based on PSA | it falls below a defined threshold | | | | | | | | | | | |
|--|--|--------|--------|--------|-----|---|---|----|----|----|----|----|
| 7. Reclassification (i.e. leaving active surveillance | 92. A shortening of PSA doubling time: iii. of < 36 mo indicates reclassification | 65 7% | 20.5% | 2.00/ | 109 | 2 | | NA | NA | NA | NA | NA |
| for an active treatment) criteria. 2. Based on PSA | | 03.7 % | 50.5% | 3.0 % | 100 | 5 | 2 | | | | | |
| 7. Reclassification (i.e. leaving active surveillance | 93. A shortening of PSA doubling time: iv. of < 24 mo indicates reclassification | 17.6% | 23.8% | 28.6% | 108 | 3 | | NA | NA | NA | NA | NA |
| for an active treatment) criteria. 2. Based on PSA | | 47.076 | 23.070 | 20.078 | 100 | 5 | 4 | | | | | |
| 7. Reclassification (i.e. leaving active surveillance | 94. A shortening of PSA doubling time: v. even if minimal would indicate | 00.0% | 20.0% | 7.50/ | 100 | 0 | | NA | NA | NA | NA | NA |
| for an active treatment) criteria. 2. Based on PSA | reclassification if accompanied by other PSA-based parameter changes | 62.3% | 30.2% | 7.5% | 108 | 2 | 2 | | | | | |
| 7. Reclassification (i.e. | 95. A rise in PSA above an absolute threshold i of > 10 would indicate | | | | | _ | | NA | NA | NA | NA | NA |
| for an active treatment) criteria, 2, Based on PSA | reclassification | 67.0% | 14.2% | 18.9% | 108 | 2 | 2 | | | | | |
| 7. Reclassification (i.e. | 96. A rise in PSA above an absolute | | | | | | | NA | NA | NA | NA | NA |
| for an active treatment) criteria 2 Based on PSA | reclassification | 24.5% | 11.3% | 64.2% | 108 | 2 | 3 | | | | | |
| 7. Reclassification (i.e. | 97. A PSA velocity: i. of > 0.75/yr would | | | | | | | NA | NA | NA | NA | NA |
| for an active treatment) | Indicate reclassification | 62.7% | 36.3% | 1.0% | 108 | 6 | 2 | | | | | |
| 7. Reclassification (i.e. | 98. A PSA velocity: ii. of > 1.0/yr would | | | | | | | NA | NA | NA | NA | NA |
| for an active treatment) criteria 2 Based on PSA | indicate reclassification | 52.9% | 37.3% | 9.8% | 108 | 6 | 3 | | | | | |
| 7. Reclassification (i.e. | 99. An increase in PSA density: i. is | | | | | | | NA | NA | NA | NA | NA |
| for an active treatment) | the absence of other factors | 70.5% | 27.6% | 1.9% | 108 | 3 | 1 | | | | | |
| 7. Reclassification (i.e. | 100. An increase in PSA density: ii. | | | | | | | NA | NA | NA | NA | NA |
| leaving active surveillance | would indicate reclassification if | 42.9% | 48.6% | 8.6% | 108 | 3 | Α | | | | | |
| criteria. 2. Based on PSA | parameter changes | | | | | | | | | | | |
| 7. Reclassification (i.e. leaving active surveillance | 101. A change in PSA parameters which by itself is not sufficient, would | 0.001 | 0.00/ | 00.404 | 100 | | | NA | NA | NA | NA | NA |
| for an active treatment) | indicate reclassification if accompanied | 0.9% | 0.0% | 99.1% | 108 | 1 | 1 | | | | | |
| 7. Reclassification (i.e. | 102. A change in PSA parameters | | | | | | | NA | NA | NA | NA | NA |
| leaving active surveillance | which by itself is not sufficient, would indicate reclassification if accompanied | 10.3% | 20.6% | 69.2% | 108 | 1 | 2 | | | | | |
| criteria. 2. Based on PSA | by: ii: changes in imaging | | | | | | 2 | | | | | |
| 8. Reclassification (i.e. leaving active surveillance | 103. A higher Gleason score (or ISUP grade) on re-biopsy is required for | 15.9% | 3.7% | 80.4% | 108 | 1 | 2 | NA | NA | NA | NA | NA |
| | | | | | | | | | | | | |

| for an active treatment) criteria. 3. Based on histopathology grade | reclassification | | | | | | | | | | | |
|---|--|-------|-------|-------|-----|---|---|----|----|----|----|----|
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 104. An increase in the number of positive cores on re-biopsy: i. indicates re-classification (i.e. no threshold needed) | 65.7% | 19.4% | 14.8% | 108 | 0 | 2 | NA | NA | NA | NA | NA |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 105. An increase in the number of positive cores on re-biopsy: ii. if > 2 cores on re-biopsy indicates reclassification | 58.3% | 29.6% | 12.0% | 108 | 0 | 3 | NA | NA | NA | NA | NA |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 106. An increase in the number of positive cores on re-biopsy: iii. If > 3 cores on re-biopsy indicates reclassification | 40.7% | 21.3% | 38.0% | 108 | 0 | 4 | NA | NA | NA | NA | NA |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 107. An increase in the extent of core involvement: i. indicates re-classification (i.e. no threshold needed) | 74.1% | 19.4% | 6.5% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 108. An increase in the extent of core involvement: ii. If > 20% of a core indicates reclassification | 73.1% | 24.1% | 2.8% | 108 | 0 | 1 | NA | NA | NA | NA | NA |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 109. An increase in the extent of core involvement: iii. If > 33% of a core indicates reclassification | 57.4% | 30.6% | 12.0% | 108 | 0 | 3 | NA | NA | NA | NA | NA |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 110. An increase in the extent of core involvement: iv. If > 50% of a core indicates reclassification | 32.4% | 28.7% | 38.9% | 108 | 0 | 4 | NA | NA | NA | NA | NA |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 111. An increase in the extent of core involvement: v. Is not important for Gleason 3+3=6/ISUP Grade 1 disease | 33.3% | 17.6% | 49.1% | 108 | 0 | 4 | NA | NA | NA | NA | NA |
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 112. An increase in the clinical T- category based on DRE , as the sole criterion: i. If increase to cT2a, indicates reclassification | 78.5% | 15.9% | 5.6% | 108 | 1 | 1 | NA | NA | NA | NA | NA |

| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 113. An increase in the clinical T- category based on DRE , as the sole criterion: ii. If increase to cT2b indicates reclassification | 56.1% | 21.5% | 22.4% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
|--|---|-------|-------|-------|-----|---|---|----|-----|-----|----|----|
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 114. An increase in the clinical T- category based on DRE , as the sole criterion: iii. If increase to cT2c indicates reclassification | 31.8% | 5.6% | 62.6% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 115. Radiological evidence of disease progression is sufficient to reclassify in the absence of other factors. | 62.6% | 15.0% | 22.4% | 108 | 1 | 3 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 116. Radiological evidence of progression mandates an image- directed biopsy. | 0.9% | 4.7% | 94.4% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 117. A new focus of cancer on repeat imaging indicates re-classification: i. Always | 75.7% | 19.6% | 4.7% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 118. A new focus of cancer on repeat imaging indicates re-classification: ii. Only if accompanied by a re-biopsy | 0.9% | 4.7% | 94.4% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 119. Increase in tumour volume (for ≤T2 disease) on imaging alone (i.e. in the absence of re-biopsy, PSA, etc.) indicates re-classification. | 72.0% | 21.5% | 6.5% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 120. An increase in the PI-RADS score indicates reclassification in the absence of other features. | 73.6% | 16.0% | 10.4% | 108 | 2 | 1 | NA | NA | NA | NA | NA |
| 12. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 7. Based on patient preference | 121. Patient preference to switch to active treatment, regardless of other factors, should trigger reclassification. | 5.6% | 8.4% | 86.0% | 108 | 1 | 1 | NA | NA | NA | NA | NA |
| 13. Outcome measures. Primary outcome measures which must be measured | 122. Overall survival (i.e. how long you live, between your diagnosis and dying from any cause) is a critically important | 2.8% | 0.9% | 96.3% | 108 | 0 | 1 | 6% | 19% | 75% | 16 | 0 |

| and prioritised by all active | outcome for clinicians to measure for | | | | | | | | | | | |
|-------------------------------|--|-------|--------|--------|-----|---|---|------|-------|-------|----|----------|
| surveillance programmes | men on active surveillance | | | | | | | | | | | |
| 13. Outcome measures. | 123. Prostate cancer-specific survival | | | | | | | 6% | 19% | 75% | 16 | 0 |
| Primary outcome measures | (i.e. how long you live, between your | | | | | | | | | | | |
| which must be measured | diagnosis and dying from prostate | 1.9% | 0.0% | 98.1% | 108 | 0 | | | | | | |
| and prioritised by all active | cancer) is a critically important outcome | | | | | - | | | | | | |
| surveillance programmes | to measure for men on active | | | | | | 1 | | | | | |
| | surveillance | | | | | | | | | | | |
| 13. Outcome measures. | 124. Progression to metastatic disease | | | | | | | 6% | 0% | 94% | 16 | 0 |
| Primary outcome measures | (i.e. your cancer spreading to other | | | | | | | | | | | |
| which must be measured | organs) is a critically important outcome | 0.0% | 0.9% | 99.1% | 108 | 0 | | | | | | |
| and prioritised by all active | to measure for men on active | | | | | | 1 | | | | | |
| surveillance programmes | surveillance | | | | | | | | | | | |
| 13. Outcome measures. | 125. Local progression (i.e. your cancer | | | | | | | 0% | 0% | 100% | 16 | 0 |
| Primary outcome measures | getting bigger or more advanced locally) | 4.00/ | 10.000 | 00.00/ | 400 | | | | | | | |
| which must be measured | is a critically important outcome to | 1.9% | 10.2% | 88.0% | 108 | 0 | | | | | | |
| and prioritised by all active | measure for men on active surveillance | | | | | | 1 | | | | | |
| surveillance programmes | | | | | | | | | | | | - |
| 13. Outcome measures. | 126. Symptomatic progression (i.e. your | | | | | | | 0% | 0% | 100% | 16 | 0 |
| Primary outcome measures | cancer progressing locally to cause | | | | | | | | | | | |
| which must be measured | symptoms such as pain, bleeding in | 0.0% | 1.9% | 98.1% | 108 | 0 | | | | | | |
| and prioritised by all active | urine, difficulty in urinating, etc.) is a | | | | | - | | | | | | |
| surveillance programmes | critically important outcome to measure | | | | | | 1 | | | | | |
| 12.0.1 | for men on active surveillance | | | | | | | 001 | 001 | 0.404 | 10 | <u>^</u> |
| 13. Outcome measures. | 127. Re-classification (i.e. switching | | | | | | | 0% | 6% | 94% | 16 | 0 |
| Primary outcome measures | from active surveillance to active | | | | | | | | | | | |
| which must be measured | curative treatment e.g. surgery or | 0.0% | 3.7% | 96.3% | 108 | 0 | | | | | | |
| and prioritised by all active | radiotnerapy) is a critically important | | | | | | | | | | | |
| surveillance programmes | outcome to measure for men on active | | | | | | 1 | | | | | |
| 12 Outrans manual | 100 Unice function (i.e. machine | | | | | | | 00/ | 4.20/ | 070/ | 40 | 4 |
| 13. Outcome measures. | 128. Uninary function (i.e. problems | | | | | | | 0% | 13% | 87% | 10 | I |
| Philliary outcome measures | important outcome to measure for man | 0.00/ | 11 10/ | 06 10/ | 100 | 0 | | | | | | |
| which must be measured | important outcome to measure for men | 2.0% | 11.170 | 00.1% | 100 | U | 4 | | | | | |
| and phontised by an active | on active surveillance | | | | | | 1 | | | | | |
| 12 Outcome measures | 120 Covuel function (i.e. problems | | | | | | | 70/ | 070/ | 679/ | 16 | 1 |
| Primary outcome measures. | relating to creation libida acculation | | | | | | | 1 70 | 2170 | 07 % | 10 | 1 |
| which must be measured | eta) is a critically important outcome to | 1.0% | 12.0% | 96 10/ | 109 | 0 | | | | | | |
| and prioritised by all active | measure for men on active surveillance | 1.570 | 12.070 | 00.170 | 100 | 0 | 2 | | | | | |
| surveillance programmes | medsure for men on active surveillance | | | | | | 2 | | | | | |
| 13 Outcome measures | 130 Overall quality of life (i.e. | | | | | | | 0% | 0% | 100% | 16 | 1 |
| Primary outcome measures | satisfaction with general health and | | | | | | | 0 % | 0 76 | 100 % | 10 | 1 |
| which must be measured | well-being) is a critically important | 0.0% | 0.9% | 99.1% | 108 | 0 | | | | | | |
| and prioritised by all active | outcome to measure for men on active | 0.070 | 0.070 | 00.170 | 100 | Ŭ | 1 | | | | | |
| surveillance programmes | surveillance | | | | | | | | | | | |
| 13 Outcome measures | 131 Anxiety (due to your cancer or | | | | | | | 7% | 7% | 87% | 16 | 1 |
| Primary outcome measures | treatment) is a critically important | 0.0% | 1.9% | 98.1% | 108 | 0 | 1 | 770 | 770 | 0170 | 10 | |
| which must be measured | outcome to measure for men on active | 0.070 | 1.070 | 30.170 | 100 | Ŭ | | | | | | |
| | | | | | | | | | 1 | | | |

| and prioritised by all active | surveillance | | | | | | | | | | | |
|-------------------------------|---|-------|-------|-------|-----|----|---|----|----|-----|----|----|
| surveillance programmes | | | | | | | | | | | | |
| 13. Outcome measures. | 132. Depression (due to your cancer or | | | | | | | 7% | 7% | 87% | 16 | 1 |
| Primary outcome measures | treatment) is a critically important | | | | | | | | | | | |
| which must be measured | outcome to measure for men on active | 0.0% | 2.8% | 97.2% | 108 | 0 | | | | | | |
| and prioritised by all active | surveillance | | | | | | 1 | | | | | |
| surveillance programmes | | | | | | | | | | | | |
| Additional R2 | 9991. Biomarkers are useful in | | | | | | | NA | NA | NA | NA | NA |
| | stratifying risk of disease progression | 25.0% | 38.5% | 36.5% | 108 | 4 | 4 | | | | | |
| | for men undergoing active surveillance | | | | | | | | | | | |
| Additional R3 | 9992. Men known to carry the BRAC2 | | | | | | | NA | NA | NA | NA | NA |
| | mutation are ineligible for active | 30.9% | 30.9% | 38.1% | 108 | 11 | 4 | | | | | |
| | surveillance | | | | | | | | | | | |

BRAC2 = DNA repair associated gene; DRE = digital-rectal examination; ECOG = Eastern Cooperative Oncology Group (performance status); HCP = healthcare professional; ISUP = International Society of Urological Pathology; mpMRI = multi-parametric magnetic resonance imaging; mo = month; N = number; NA = not applicable; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; yr = year.

| Table 4: Summary | of characteristics | of consensus | meeting | participants |
|------------------|--------------------|--------------|---------|--------------|
| Table 4: Summary | of characteristics | of consensus | meeting | participants |

| Name | Role | Country of residence |
|-----------------------|----------------------|------------------------|
| Erik Briers | Patient | Belgium |
| Christopher Wallis | Urologist | Canada |
| Philippe Violette | Urologist | Canada |
| Jacques Irani | Chair (Urologist) | France |
| Alberto Bossi | Oncologist | France |
| Olivier Rouvière | Radiologist | France |
| Raphaele Renard-Penna | Radiologist | France |
| Nicolas Mottet | Urologist | France |
| Thomas Wiegel | Radiation Oncologist | Germany |
| Derya Tilki | Urologist | Germany |
| Michael Lardas | Urologist | Greece |
| Nikolaos Grivas | Urologist | Greece |
| Maurizio Colecchia | Pathologist | Italy |
| Giorgio Gandaglia | Urologist | Italy |
| Alberto Briganti | Urologist | Italy |
| Maria J Ribal | Urologist | Spain |
| Anders Bjartell | Urologist | Sweden |
| Christian Fankhauser | Urologist | Switzerland |
| Monique Roobol | Epidemiologist | The Netherlands |
| Arno Van Leenders | Pathologist | The Netherlands |
| Ruud Baanders | Patient | The Netherlands |
| Ivo Schoots | Radiologist | The Netherlands |
| Peter-Paul Willemse | Urologist | The Netherlands |
| Michiel Sedelaar | Urologist | The Netherlands |
| Chris Bangma | Urologist | The Netherlands |
| Theo van der Kwast | Pathologist | The Netherlands/Canada |

| Patient | United Kingdom |
|--|---|
| Radiologist | United Kingdom |
| Radiotherapist | United Kingdom |
| Urologist | United Kingdom |
| Urologist | United Kingdom |
| Urology Nurse Consultant & Research Fellow | United Kingdom |
| Uro-oncology Nurse Specialist | United Kingdom |
| Chair (Methodologist) | United Kingdom |
| Urologist | United Kingdom |
| | United Kingdom/ |
| Oncologist | Switzerland |
| Radiation oncologist | United States |
| | Patient Radiologist Radiotherapist Urologist Urologist Urology Nurse Consultant & Research Fellow Uro-oncology Nurse Specialist Chair (Methodologist) Urologist Oncologist Radiation oncologist |

| Domain | Item number from Delphi and description | % Disagree | % Equivocal (4-6) | % Aaree | Total N | Consensus Yes/No/ Not voted |
|--|--|---------------|----------------------|------------|---------|--------------------------------|
| | | (1-3) | | (7-9) | | |
| 1. Patient eligibility, inclusion and exclusion | 3. The appropriate life expectancy criterion for inclusion is: ii. ≥15 yrs | 0% | 0% | 0% | NA | Not voted |
| criteria. 1. Age and life expectancy | | | | | | |
| Patient eligibility, inclusion and exclusion | Life expectancy in everyday practice is best evaluated by: i. | 0% | 0% | 0% | NA | Not voted |
| criteria. 1. Age and life expectancy | Performance status (e.g. ECOG, Karnofsky) | | | | | |
| Patient eligibility, inclusion and exclusion | 5. Life expectancy in everyday practice is best evaluated by: ii. Co- | 0% | 0% | 0% | NA | Not voted |
| criteria. 1. Age and life expectancy | morbidity index measure (e.g. Charlson) | | | | | |
| Patient eligibility, inclusion and exclusion | Life expectancy in everyday practice is best evaluated by: iii. Health | 0% | 0% | 0% | NA | Not voted |
| criteria. 1. Age and life expectancy | status screening (e.g. Geriatric 8 screening tool) | | | | | |
| Patient eligibility, inclusion and exclusion | 8. Low-risk disease: i. is an automatic inclusion criterion regardless of | 0% | 0% | 0% | NA | Not voted |
| criteria. 2. Risk classification | other disease factors | | | | | |
| Patient eligibility, inclusion and exclusion | 9. Low-risk disease: ii. is excluded if the extent of disease is high, based | 46% | 15% | 39% | 28 | No |
| criteria. 2. Risk classification | on biopsy core volume, length or number or proportion of core positivity | | | | | |
| Patient eligibility, inclusion and exclusion | 10. Low-risk disease: iii. is excluded if the extent and/or stage of disease | 7% | 9% | 84% | 30 | Yes |
| criteria. 2. Risk classification | is high based on mpMRI | | | | | |
| Patient eligibility, inclusion and exclusion | 11. Low-risk disease: iv. is excluded if mpMRI suggests biologically- | 23% | 27% | 50% | 30 | No |
| criteria. 2. Risk classification | aggressive disease | | | | | |
| Patient eligibility, inclusion and exclusion | 12. Gleason 3+4=7 (ISUP grade 2): i. is an automatic exclusion criterion | 80% | 6% | 13% | 29 | Yes |
| criteria. 2. Risk classification | | | | | | |
| 2. Patient eligibility, inclusion and exclusion | 15. Gleason 4+3=7 (ISUP grade 3): ii. can be included only if favourable | 97% | 3% | 0% | 27 | Yes |
| criteria. 2. Risk classification | characteristics are present, including PSA (<10), clinical stage (≤cT2a) | | | | | |
| | and biopsy characteristics (low core positivity) | | | | | |
| 2. Patient eligibility, inclusion and exclusion | 17. PSA:ii. >20ng/ml is an automatic exclusion criterion, regardless of | 55% | 0% | 45% | 29 | No |
| criteria. 2. Risk classification | other disease characteristics | | 1-01 | | | |
| 2. Patient eligibility, inclusion and exclusion | PSA density: i. is an important inclusion criterion | 7% | 15% | 78% | 28 | Yes |
| criteria. 2. Risk classification | | | | | | |
| 2. Patient eligibility, inclusion and exclusion | 19. PSA density: ii. for inclusion should be ≤ 0.15 mg/ml per g | 12% | 24% | 64% | 24 | No |
| criteria. 2. Risk classification | | | | | | |
| 2. Patient eligibility, inclusion and exclusion | 20. PSA density: iii. for inclusion should be ≤ 0.20 ng/ml per g | 52% | 32% | 16% | 25 | No |
| criteria. 2. Risk classification | | 700/ | | 100/ | | |
| 2. Patient eligibility, inclusion and exclusion | 21. Clinical stage: $I \ge I 2b$ is an automatic exclusion criterion, regardless | 78% | 9% | 13% | 23 | Yes |
| criteria. 2. Risk classification | of other disease characteristics | 00/ | 00/ | 000/ | 00 | N/ |
| 2. Patient eligibility, inclusion and exclusion | 22. Clinical stage: II. ≥ I 2C is an automatic exclusion criterion, regardless | 8% | 0% | 92% | 26 | Yes |
| criteria. 2. Risk classification | of other disease characteristics | 00% | 40/ | 40/ | 00 | N/ |
| 3. Patient eligibility, inclusion and exclusion | 33. The threshold of disease extent beyond which patients are | 92% | 4% | 4% | 23 | Yes |
| criteria. 3. Pathology characteristics | automatically excluded based on systematic biopsy regardless of other | | | | | |
| | disease characteristics for Gleason 3+3=6/ISUP Grade 1 disease IS: III. | | | | | |
| 2. Defined all all life inclusion and such that | Core positivity ≥00% | C 49/ | 400/ | 4.00/ | 00 | N |
| 3. Patient eligibility, inclusion and exclusion | 30. The threshold of disease extent beyond which patients are | 04% | 10% | 18% | 28 | INO |
| chiena. 5. Pathology characteristics | disease obstactoristics for Closese 2.4-7/ISLIB Crede 2 disease in i | | | | | |
| | Core positivity >20% | | | | | |

 Table 5: Consensus Meeting: Summary of statements discussed, reviewed and voted upon, and consensus status – Consensus (Yes/No/Not voted*)

 *Some items were discussed by the consensus meeting group and decided to have been superseded by the answer to a previous question and therefore not requiring a vote.

| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 39. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: ii. Core positivity >33% | 48% | 24% | 28% | 25 | No |
|---|---|-----|-----|-----|----|-----------|
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 40. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: iii. Core positivity ≥50% | 30% | 33% | 37% | 27 | No |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 41. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: iv. Positive cores >2 | 34% | 18% | 48% | 27 | No |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 42. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: v. Positive cores >3 | 30% | 19% | 51% | 27 | No |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 43. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: vi. Core length -3mm | 64% | 24% | 12% | 25 | No |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 44. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: vii. Core length >5mm | 50% | 27% | 23% | 26 | No |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 46. If a patient has had upfront mpMRI followed by systematic and targeted biopsies, there is no need for confirmatory biopsies | 10% | 8% | 82% | 28 | Yes |
| 4. Patient eligibility, inclusion and exclusion criteria, 4. Imaging characteristics | 54. Tumour volume (for ≤T2 disease) based purely on mpMRI characteristics is an important inclusion/exclusion criterion | 68% | 0% | 32% | 25 | No |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 55. Disease aggressiveness (for ≤T2 disease) (e.g. low ADC value) based purely on mpMRI characteristics is an important inclusion/exclusion criterion | 74% | 14% | 12% | 27 | Yes |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 57. During active surveillance in the first 2 yrs, men should have their PSA checked: i. Every 3 mo | 27% | 10% | 63% | 29 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 65. During active surveillance, men should have a digital rectal examination (DRE): ii. Every 6 mo | 79% | 4% | 17% | 28 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 66. During active surveillance, men should have a digital rectal examination (DRE): iii. Every 12 mo | 10% | 17% | 72% | 29 | Yes |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 69. During active surveillance, repeat biopsy should be performed: ii. Every 24 mo | 73% | 10% | 17% | 30 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 71. During active surveillance, repeat biopsy should be performed: iv. At 1 yr, 4 yrs and 7 yrs | 22% | 30% | 48% | 27 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 72. During active surveillance, repeat biopsy should be performed: v. Not routinely pre-planned unless triggered | 59% | 6% | 35% | 29 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 74. During active surveillance, repeat biopsy should be performed: vii. Triggered by PSA doubling time <3 yrs | 18% | 19% | 64% | 28 | No |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 76. If repeat biopsies are needed, they should be performed by: i. 10-12 core TRUS-guided | 0% | 0% | 0% | NA | Not voted |

| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 77. If repeat biopsies are needed, they should be performed by: ii. mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) without systematic biopsies | 81% | 3% | 16% | 30 | No |
|---|--|-----|-----|-----|----|-----------|
| Monitoring and follow-up criteria. Monitoring and follow-up | 79. If repeat biopsies are needed, they should be performed by: iv. Transperineal template biopsies instead of mpMRI-guided biopsies | 90% | 10% | 0% | 29 | Yes |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 80. If repeat biopsies are needed, they should be performed by: v. TRUS- guided systematic biopsies | 0% | 0% | 0% | NA | Not voted |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 82. Reclassification should only apply to patients with a life expectancy of ≥15 yrs at the time of assessment | 0% | 0% | 0% | NA | Not voted |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 84. Active surveillance should only be continued in patients with life expectancy of ≥15 yrs | 0% | 0% | 0% | NA | Not voted |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 86. Patient reluctance to undergo repeat biopsies or repeat imaging is a valid reason for triggering reclassification (including active treatment) | 11% | 11% | 78% | 28 | Yes |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. Based on PSA | PSA progression is sufficient to indicate reclassification in the absence of other factors. | 84% | 3% | 13% | 31 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 88. A rise in PSA mandates re-biopsy irrespective of other findings. | 89% | 0% | 11% | 28 | Yes |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. Based on PSA | 89. A rise in PSA mandates re-imaging of the patient. | 47% | 11% | 42% | 28 | No |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | A shortening of PSA doubling time: i. is sufficient to indicate reclassification in the absence of other factors | 86% | 6% | 8% | 29 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 91. A shortening of PSA doubling time: ii. Should only indicate reclassification if it falls below a defined threshold | 38% | 16% | 46% | 26 | No |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 92. A shortening of PSA doubling time: iii. of < 36 mo indicates reclassification | 92% | 4% | 4% | 28 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 93. A shortening of PSA doubling time: iv. of < 24 mo indicates reclassification | 0% | 0% | 0% | NA | Not voted |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 94. A shortening of PSA doubling time: v. even if minimal would indicate reclassification if accompanied by other PSA-based parameter changes | 96% | 4% | 0% | 25 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 95. A rise in PSA above an absolute threshold: i. of > 10 would indicate reclassification | 86% | 7% | 7% | 29 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 96. A rise in PSA above an absolute threshold: ii. of > 20 would indicate reclassification | 34% | 11% | 55% | 27 | Not voted |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. Based on PSA | 97. A PSA velocity: i. of > 0.75/yr would indicate reclassification | 92% | 4% | 4% | 25 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 98. A PSA velocity: ii. of > 1.0/yr would indicate reclassification | 93% | 6% | 0% | 27 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 100. An increase in PSA density: ii. would indicate reclassification if accompanied by other PSA-based parameter changes | 82% | 11% | 7% | 28 | Yes |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 102. A change in PSA parameters which by itself is not sufficient, would indicate reclassification if accompanied by: ii: changes in imaging | 48% | 18% | 34% | 27 | No |
| 8. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 3. Based on histopathology grade | 103. A higher Gleason score (or ISUP grade) on re-biopsy is required for reclassification | 27% | 10% | 63% | 30 | No |

| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 104. An increase in the number of positive cores on re-biopsy: i. indicates re-classification (i.e. no threshold needed) | 89% | 0% | 11% | 27 | Yes |
|---|--|-----|-----|-----|----|-----|
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 105. An increase in the number of positive cores on re-biopsy: ii. if > 2 cores on re-biopsy indicates reclassification | 77% | 4% | 19% | 26 | No |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 106. An increase in the number of positive cores on re-biopsy: iii. If > 3 cores on re-biopsy indicates reclassification | 64% | 12% | 24% | 25 | No |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 109. An increase in the extent of core involvement: iii. If > 33% of a core indicates reclassification | 86% | 4% | 10% | 27 | Yes |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 110. An increase in the extent of core involvement: iv. If > 50% of a core indicates reclassification | 84% | 8% | 8% | 25 | Yes |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. Based on histopathology extent | 111. An increase in the extent of core involvement: v. Is not important for Gleason 3+3=6/ISUP Grade 1 disease | 20% | 8% | 72% | 25 | No |
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 113. An increase in the clinical T-category based on DRE , as the sole criterion: ii. If increase to cT2b indicates reclassification | 88% | 4% | 8% | 27 | Yes |
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 114. An increase in the clinical T-category based on DRE , as the sole criterion: iii. If increase to cT2c indicates reclassification | 42% | 26% | 32% | 24 | No |
| Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 115. Radiological evidence of disease progression is sufficient to reclassify in the absence of other factors. | 92% | 0% | 8% | 26 | Yes |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 129. Sexual function (i.e. problems relating to erection, libido, ejaculation, etc.) is a critically important outcome to measure for men on active surveillance | 3% | 7% | 90% | 30 | Yes |
| Additional R2 | 9991. Biomarkers are useful in stratifying risk of disease progression for men undergoing active surveillance | 41% | 28% | 31% | 22 | No |
| Additional R3 | 9992. Men known to carry the BRAC2 mutation are ineligible for active surveillance | 63% | 21% | 16% | 19 | No |

BRAC2 = DNA repair associated gene; DRE = digital-rectal examination; ECOG = Eastern Cooperative Oncology Group (performance status); HCP = healthcare professional; ISUP = International Society of Urological Pathology; mo = month; mpMRI = multi-parametric magnetic resonance imaging; N = number; NA = not applicable; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; yr = year.

Table 6: Final consensus statements from DETECTIVE Study

| Domain | Item Number in Delphi and description | Consensus stage (Delphi/ Meeting) | Direction of Consensus (Agree/ |
|--|--|---|--------------------------------------|
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 1. There is no lower nor upper age limit for inclusion as long as the appropriate life expectancy criterion is fulfilled | Delphi | Agree |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 2. The appropriate life expectancy criterion for inclusion is: i. ≥10 yrs | Delphi | Agree |
| 1. Patient eligibility, inclusion and exclusion criteria. 1. Age and life expectancy | 7. Life expectancy in everyday practice is best evaluated by: iv. Combination of performance status, co-morbidity index and health status screening | Delphi | Agree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 10. Low-risk disease: iii. is excluded if the extent and/or stage of disease is high based on mpMRI | Meeting | Agree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 12. Gleason 3+4=7 (ISUP grade 2): i. is an automatic exclusion criterion | Meeting | Disagree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 13. Gleason 3+4=7 (ISUP grade 2): ii. can be included only if favourable characteristics are present, including PSA (<10), clinical stage (≤cT2a) and biopsy characteristics (low core positivity) | Delphi | Agree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 14. Gleason 4+3=7 (ISUP grade 3): i. is an automatic exclusion criterion. | Delphi | Agree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 15. Gleason 4+3=7 (ISUP grade 3): ii. can be included only if favourable characteristics are present, including PSA (<10), clinical stage (≤cT2a) and biopsy characteristics (low core positivity) | Meeting | Disagree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 16. PSA :i. >10ng/ml is an automatic exclusion criterion, regardless of other disease characteristics | Delphi | Disagree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 18. PSA density: i. is an important inclusion criterion | Meeting | Agree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 21. Clinical stage: i. ≥T2b is an automatic exclusion criterion, regardless of other disease characteristics | Meeting | Disagree |
| 2. Patient eligibility, inclusion and exclusion criteria. 2. Risk classification | 22. Clinical stage: ii. ≥T2c is an automatic exclusion criterion, regardless of other disease characteristics | Meeting | Agree |
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 23. Targeted biopsies should be reported separately from systematic biopsies | Delphi | Agree |

| 3. Patient eligibility, inclusion and exclusion | 24. The extent of disease should be reported in: i. length (mm) | Delphi | Agree |
|--|---|---------|--------------|
| 2. Definition of the second evolution | DE The extent of discours should be repeated in ii. 0/ turns us always (as a properties | Delahi | A |
| 3. Patient eligibility, inclusion and exclusion | 25. The extent of disease should be reported in: II. % turnour volume (as a proportion | Delphi | Agree |
| criteria. 3. Pathology characteristics | of total volume of core) | | |
| 3. Patient eligibility, inclusion and exclusion | 26. ISUP grade (Gleason score) should be reported for each positive core | Delphi | Agree |
| criteria. 3. Pathology characteristics | | | |
| Patient eligibility, inclusion and exclusion | 27. Percentage of Gleason pattern 4 carcinoma should be provided for each biopsy | Delphi | Agree |
| criteria. 3. Pathology characteristics | site with Gleason score 7 carcinoma | | |
| Patient eligibility, inclusion and exclusion | 28. Intraductal and cribriform histology are exclusion criteria | Delphi | Agree |
| criteria. 3. Pathology characteristics | | | - |
| 3. Patient eligibility, inclusion and exclusion | 29. When systematic biopsies are performed, the extent of disease based on | Delphi | Agree |
| criteria, 3. Pathology characteristics | histological characteristics (e.g. core length, core volume, core positivity, etc.) is an | - 1- | J • • |
| 5, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, | important inclusion/exclusion criterion | | |
| 3. Patient eligibility, inclusion and exclusion | 30. Extent of disease on histology is important even for Gleason 3+3=6/ISUP Grade 1 | Delphi | Aaree |
| criteria, 3. Pathology characteristics | disease because it may lead to patients being excluded | - o.p | , .g. ee |
| 3 Patient eligibility inclusion and exclusion | 31 The threshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| criteria 3 Pathology characteristics | based on systematic bionsy regardless of other disease characteristics for Gleason | Dolpin | Diougroo |
| shona. o. r athology sharastensites | 3+3=6/ISUP Grade 1 disease is: i Core positivity >20% | | |
| 3 Patient eligibility inclusion and exclusion | 32 The threshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| criteria 3 Pathology characteristics | based on systematic bionsy regardless of other disease characteristics for Gleason | Dolpin | Diougroo |
| chema. o. r athology characteristics | 3+3=6/ISLIP Grade 1 disease is: ii. Core positivity >33% | | |
| 3 Patient eligibility inclusion and exclusion | 33 The threshold of disease extent beyond which patients are automatically excluded | Meeting | Disagree |
| criteria 3 Dathology characteristics | based on systematic bioney regardless of other disease characteristics for Glesson | Meeting | Disagree |
| citteria. 5. 1 attology citaracteristics | 3+3-6/151 IP Grade 1 disease is: iii Gore positivity >50% | | |
| 3 Datient eligibility inclusion and evaluation | 3+5-0/1001 Grade 1 disease action bound which nations are automatically avaluated | Dolphi | Disagroo |
| 5. Fallent engibility, inclusion and exclusion | 54. The timeshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| chiena. 5. Pathology characteristics | based on systematic biopsy regardless of other disease characteristics for Gleason | | |
| | 3+3=6/ISUP Grade 1 disease is: IV. Positive cores >2 | | |
| 3. Patient eligibility, inclusion and exclusion | 35. The threshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| criteria. 3. Pathology characteristics | based on systematic biopsy regardless of other disease characteristics for Gleason | | |
| | 3+3=6/ISUP Grade 1 disease is: v. Positive cores >3 | | |
| Patient eligibility, inclusion and exclusion | 36. The threshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| criteria. 3. Pathology characteristics | based on systematic biopsy regardless of other disease characteristics for Gleason | | |
| | 3+3=6/ISUP Grade 1 disease is: vi. Core length >3mm | | |
| Patient eligibility, inclusion and exclusion | 37. The threshold of disease extent beyond which patients are automatically excluded | Delphi | Disagree |
| criteria. 3. Pathology characteristics | based on systematic biopsy regardless of other disease characteristics for Gleason | | - |

| | 3+3=6/ISUP Grade 1 disease is: vii. Core length >5mm | | |
|---|--|---------|----------|
| 3. Patient eligibility, inclusion and exclusion criteria. 3. Pathology characteristics | 45. The threshold of disease extent beyond which patients are automatically excluded based on systematic biopsy regardless of other disease characteristics for Gleason 3+4=7/ISUP Grade 2 disease is: viii. Any disease extent (because Gleason 3+4=7/ISUP Grade 2 is an automatic exclusion) | Delphi | Disagree |
| Patient eligibility, inclusion and exclusion criteria. Imaging characteristics | 46. If a patient has had upfront mpMRI followed by systematic and targeted biopsies, there is no need for confirmatory biopsies | Meeting | Agree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 47. If targeted biopsies based upon mpMRI images are performed, the number of positive cores is not an indicator of extent of disease nor tumour volume | Delphi | Agree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 48. The number of positive sextants based on systematic and/or targeted biopsies should be taken into account as an indicator of tumour volume | Delphi | Agree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 49. The volume of the dominant lesion seen on mpMRI (PI-RADS V2 ≥3) should be taken into account as an indicator of tumour volume | Delphi | Agree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 50. For inclusion, prostate biopsies should be performed by: i. mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) without systematic biopsies | Delphi | Disagree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 51. For inclusion, prostate biopsies should be performed by: ii. mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) with systematic biopsies | Delphi | Agree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 52. For inclusion, prostate biopsies should be performed by: iii. Transperineal template biopsies instead of mpMRI-guided biopsies | Delphi | Disagree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 53. For inclusion, prostate biopsies should be performed by: iv. TRUS-guided systematic biopsies only | Delphi | Disagree |
| 4. Patient eligibility, inclusion and exclusion criteria. 4. Imaging characteristics | 55. Disease aggressiveness (for ≤T2 disease) (e.g. low ADC value) based purely on mpMRI characteristics is an important inclusion/exclusion criterion | Meeting | Disagree |
| Patient eligibility, inclusion and exclusion criteria. Imaging characteristics | 56. For inclusion, all patients need an mpMRI at some point | Delphi | Agree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 58. During active surveillance in the first 2 yrs, men should have their PSA checked: ii. Every 6 mo | Delphi | Agree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 59. During active surveillance in the first 2 yrs, men should have their PSA checked: iii. Not checked at all | Delphi | Disagree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 60. During active surveillance after the first 2 yrs, men should have their PSA checked: i. Every 3 mo | Delphi | Disagree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 61. During active surveillance after the first 2 yrs, men should have their PSA checked: ii. Every 6 mo | Delphi | Agree |

| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 62. During active surveillance after the first 2 yrs, men should have their PSA checked; iii. Not checked at all | Delphi | Disagree |
|--|--|---------|----------|
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 63. During active surveillance, men should have a digital rectal examination (DRE): | Delphi | Agree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 64. During active surveillance, men should have a digital rectal examination (DRE): i. Every 3 mo | Delphi | Disagree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 66. During active surveillance, men should have a digital rectal examination (DRE): iii. Every 12 mo | Meeting | Agree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 67. During active surveillance, men should have a digital rectal examination (DRE): iv. Not needed | Delphi | Disagree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 68. During active surveillance, repeat biopsy should be performed: i. Every 12 mo | Delphi | Disagree |
| Monitoring and follow-up criteria. 1. Monitoring and follow-up | 70. During active surveillance, repeat biopsy should be performed: iii. Every 48 mo | Delphi | Disagree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 73. During active surveillance, repeat biopsy should be performed: vi. Triggered by a change in mpMRI (i.e. increase PI-RADS score, lesion volume or radiological T stage) | Delphi | Agree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 75. During active surveillance, repeat biopsy should be performed: viii. Triggered by DRE progression | Delphi | Agree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 78. If repeat biopsies are needed, they should be performed by: iii. mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) with systematic biopsies | Delphi | Agree |
| 5. Monitoring and follow-up criteria. 1. Monitoring and follow-up | 79. If repeat biopsies are needed, they should be performed by: iv. Transperineal template biopsies instead of mpMRI-guided biopsies | Meeting | Disagree |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 81. Reclassification should only apply to patients with a life expectancy of ≥10 yrs at the time of assessment | Delphi | Agree |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 83. Active surveillance should only be continued in patients with life expectancy of ≥10 yrs | Delphi | Agree |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 85. Patient anxiety or depression is a valid reason for triggering reclassification (including active treatment) | Delphi | Agree |
| 6. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 1. Based on patient characteristics | 86. Patient reluctance to undergo repeat biopsies or repeat imaging is a valid reason for triggering reclassification (including active treatment) | Meeting | Agree |

| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 87. PSA progression is sufficient to indicate reclassification in the absence of other factors. | Meeting | Disagree |
|--|---|---------|----------|
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 88. A rise in PSA mandates re-biopsy irrespective of other findings. | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 90. A shortening of PSA doubling time: i. is sufficient to indicate reclassification in the absence of other factors | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 92. A shortening of PSA doubling time: iii. of < 36 mo indicates reclassification | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 94. A shortening of PSA doubling time: v. even if minimal would indicate reclassification if accompanied by other PSA-based parameter changes | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 95. A rise in PSA above an absolute threshold: i. of > 10 would indicate reclassification | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 97. A PSA velocity: i. of > 0.75/yr would indicate reclassification | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 98. A PSA velocity: ii. of > 1.0/yr would indicate reclassification | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 99. An increase in PSA density: i. is sufficient to indicate reclassification in the absence of other factors | Delphi | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 100. An increase in PSA density: ii. would indicate reclassification if accompanied by other PSA-based parameter changes | Meeting | Disagree |
| 7. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 2. Based on PSA | 101. A change in PSA parameters which by itself is not sufficient, would indicate reclassification if accompanied by: i. changes in histology | Delphi | Agree |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. | 104. An increase in the number of positive cores on re-biopsy: i. indicates re- classification (i.e. no threshold needed) | Meeting | Disagree |

| Based on histopathology extent | | | |
|--|--|---------|----------|
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 107. An increase in the extent of core involvement: i. indicates re-classification (i.e. no threshold needed) | Delphi | Disagree |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 108. An increase in the extent of core involvement: ii. If > 20% of a core indicates reclassification | Delphi | Disagree |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 109. An increase in the extent of core involvement: iii. If > 33% of a core indicates reclassification | Meeting | Disagree |
| 9. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 4. Based on histopathology extent | 110. An increase in the extent of core involvement: iv. If > 50% of a core indicates reclassification | Meeting | Disagree |
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 112. An increase in the clinical T-category based on DRE , as the sole criterion: i. If increase to cT2a, indicates reclassification | Delphi | Disagree |
| 10. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 5. Based on clinical extent | 113. An increase in the clinical T-category based on DRE , as the sole criterion: ii. If increase to cT2b indicates reclassification | Meeting | Disagree |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 115. Radiological evidence of disease progression is sufficient to reclassify in the absence of other factors. | Meeting | Disagree |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 116. Radiological evidence of progression mandates an image-directed biopsy. | Delphi | Agree |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 117. A new focus of cancer on repeat imaging indicates re-classification: i. Always | Delphi | Disagree |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 118. A new focus of cancer on repeat imaging indicates re-classification: ii. Only if accompanied by a re-biopsy | Delphi | Agree |
| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 119. Increase in tumour volume (for ≤T2 disease) on imaging alone (i.e. in the absence of re-biopsy, PSA, etc.) indicates re-classification. | Delphi | Disagree |

| 11. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 6. Based on imaging | 120. An increase in the PI-RADS score indicates reclassification in the absence of other features. | Delphi | Disagree |
|---|--|---------|----------|
| 12. Reclassification (i.e. leaving active surveillance for an active treatment) criteria. 7. Based on patient preference | 121. Patient preference to switch to active treatment, regardless of other factors, should trigger reclassification. | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 122. Overall survival (i.e. how long you live, between your diagnosis and dying from any cause) is a critically important outcome for clinicians to measure for men on active surveillance | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 123. Prostate cancer-specific survival (i.e. how long you live, between your diagnosis and dying from prostate cancer) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 124. Progression to metastatic disease (i.e. your cancer spreading to other organs) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 125. Local progression (i.e. your cancer getting bigger or more advanced locally) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 126. Symptomatic progression (i.e. your cancer progressing locally to cause symptoms such as pain, bleeding in urine, difficulty in urinating, etc.) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 127. Re-classification (i.e. switching from active surveillance to active curative treatment e.g. surgery or radiotherapy) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| 13. Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance programmes | 128. Urinary function (i.e. problems relating to passing urine) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| 13. Outcome measures. Primary outcome | 129. Sexual function (i.e. problems relating to erection, libido, ejaculation, etc.) is a | Meeting | Agree |

| measures which must be measured and | critically important outcome to measure for men on active surveillance | | |
|--|---|--------|-------|
| prioritised by all active surveillance | | | |
| programmes | | | |
| 13. Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance | 130. Overall quality of life (i.e. satisfaction with general health and well-being) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| programmes | | | |
| 13. Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance | 131. Anxiety (due to your cancer or treatment) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| programmes | | | |
| 13. Outcome measures. Primary outcome measures which must be measured and prioritised by all active surveillance | 132. Depression (due to your cancer or treatment) is a critically important outcome to measure for men on active surveillance | Delphi | Agree |
| programmes | | | |

ADC = apparent diffusion coefficient; BRAC2 = DNA repair associated gene; DRE = digital-rectal examination; ISUP = International Society of Urological Pathology; mo = month; mpMRI = multi-parametric magnetic resonance imaging; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; yr = year.

Table 7: Recommendations based on consensus statements from DETECTIVE Study

| Recommendations |
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| Eligibility, inclusion and exclusion criteria |
| 1. For inclusion, patients must have a life expectancy ≥10 yrs but there is no lower nor upper age limit for inclusion. |
| 2. Evaluate life expectancy using a combination of performance status, co-morbidity index and health status screening. |
| 3. Patients with low-risk localised disease should be excluded if the extent and/or stage of disease is high based on mpMRI. |
| 4. Patients with Gleason 3+4=7 (ISUP grade 2) should NOT be automatically excluded, if favourable characteristics are present, including PSA (<10), clinical stage (≤cT2a) and biopsy characteristics (low core positivity). |
| 5. Patients with Gleason 4+3=7 (ISUP grade 3) should be automatically excluded. |
| 6. Patients with PSA >10ng/ml should NOT be automatically excluded; instead PSA density should be utilised. However, the thresholds for inclusion/exclusion based on PSA density remain uncertain. |
| 7. Patients with cT2b should NOT be automatically excluded. |
| 8. Patients with ≥T2c should be automatically excluded. |
| 9. Following targeted and systematic biopsies, the results of targeted biopsies should be reported separately from those of systematic biopsies. |
| 10. Following prostate biopsies, the extent of disease should be reported in length (in mm) or % tumour volume (as a proportion of total volume of core). |
| 11. Following prostate biopsies, the ISUP grade (Gleason sum score) should be reported for each positive core. |
| 12. Following prostate biopsies, percentage of Gleason pattern 4 carcinoma should be provided for each biopsy site with Gleason score 7 carcinoma. |
| 13. Patients with intraductal and cribriform histology on biopsy should be automatically excluded. |
| 14. When systematic biopsies are performed, the extent of disease based on histological characteristics (e.g. core length, core volume, core positivity, etc.) should be |

reported as it influences inclusion and exclusion criteria.

15. Patients with Gleason 3+3=6/ISUP Grade 1 disease should be excluded if they have a high extent of disease on histology. However, the definition of 'high extent' remains uncertain.

16. There is no need for confirmatory biopsies if an upfront mpMRI followed by systematic and targeted biopsies have been performed.

17. If targeted biopsies based on mpMRI images have been performed, the number of positive cores should not be used as an indicator of extent of disease nor tumour volume. Instead, the number of positive sextants based on systematic and/or targeted biopsies should be considered as an indicator of tumour volume.

18. The volume of the dominant lesion seen on mpMRI (PI-RADS V2 ≥3) should be considered as an indicator of tumour volume.

19. For inclusion, prostate biopsies should be performed by mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) with systematic biopsies.

20. Patients with ≤T2 disease should NOT be automatically excluded on the basis of disease aggressiveness (e.g. low ADC values) based purely on mpMRI characteristics.

21. Perform mpMRI at some point for inclusion.

Monitoring and follow-up criteria

22. During active surveillance, men should have their PSA checked every 6 mo.

23. During active surveillance, men should have a digital rectal examination (DRE) every 12 mo.

24. During active surveillance, repeat biopsy should be performed if there is a change in mpMRI (i.e. increase in PI-RADS score, lesion volume or radiological T stage), or by DRE Progression or PSA progression.

25. If repeat biopsies are needed, they should be performed by mpMRI-guided targeted biopsies (including in-bore, cognitive guidance or mpMRI fusion) with systematic biopsies. However, it remains unclear when mpMRI should be performed during monitoring, and whether it should be performed routinely or triggered (e.g. by PSA or DRE changes.

26. Active surveillance should only be continued in patients if their life expectancy continues to be \geq 10 yrs.

Reclassification criteria (i.e. leaving active surveillance for an active treatment)

27. Reclassification should only apply to patients with a life expectancy of ≥10 yrs at the time of assessment.

28. Consider reclassifying patients if they develop anxiety or depression due to prostate cancer.

29. Consider reclassifying patients if they are reluctant to undergo repeat biopsies or repeat imaging.

30. Patients should NOT be automatically reclassified based on PSA progression (including level of PSA, PSA kinetics or PSA density) alone in the absence of other factors. PSA progression should only lead to reclassification if accompanied by changes in histology on repeat biopsy (i.e. upgrade in Gleason sum score/ISUP Grade).

31. Patients should NOT be automatically reclassified based on histological changes showing increase in disease extent (e.g. core positivity, % involvement of core, etc.) as the sole criterion.

32. Patients should NOT be automatically reclassified based on DRE showing an increase in clinical stage to cT2a or cT2b as the sole criterion.

33. Patients should NOT be automatically reclassified based on radiological evidence of disease progression as the sole criterion. Instead, radiological evidence of progression mandates an image-directed biopsy and only reclassify patients if this confirms upgraded disease.

34. Patients should NOT be automatically reclassified based on a new focus of cancer shown on repeat imaging; instead they should only be reclassified if imagedirected biopsy confirms upgraded disease.

35. Patients should NOT be automatically reclassified based on an increase in tumour volume (for ≤T2 disease) on imaging alone (i.e. in the absence of re-biopsy, PSA, etc.); instead this mandates an image-directed biopsy and only reclassify patients if this confirms upgraded disease.

36. Patients should NOT be automatically reclassified based on an increase in the PI-RADS score as the sole criterion.

37. Consider reclassifying patients if they choose to undergo active treatment, independent of other factors.

Outcome measures which must be prioritised

38. The following outcome measures should be prioritised in all protocols of deferred active treatment:

| iverall survival | |
|----------------------------------|--|
| rostate cancer-specific survival | |
| rogression to metastatic stage | |
| ocal progression | |
| ymptomatic progression | |
| eclassification | |
| rinary function | |
| exual function | |
| Iverall quality of life (QoL) | |
| nxiety | |
| epression | |
| | |

ADC = apparent diffusion coefficient; DRE = digital-rectal examination; ISUP = International Society of Urological Pathology; mpMRI = multi-parametric magnetic resonance imaging; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen.