Prostate-specific antigen (PSA) screening in men without symptoms of prostate cancer

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Sections

Summary of recommendations

1 - Prostate cancer screening using prostate-specific antigen (PSA) - a BMJ Rapid Recommendation

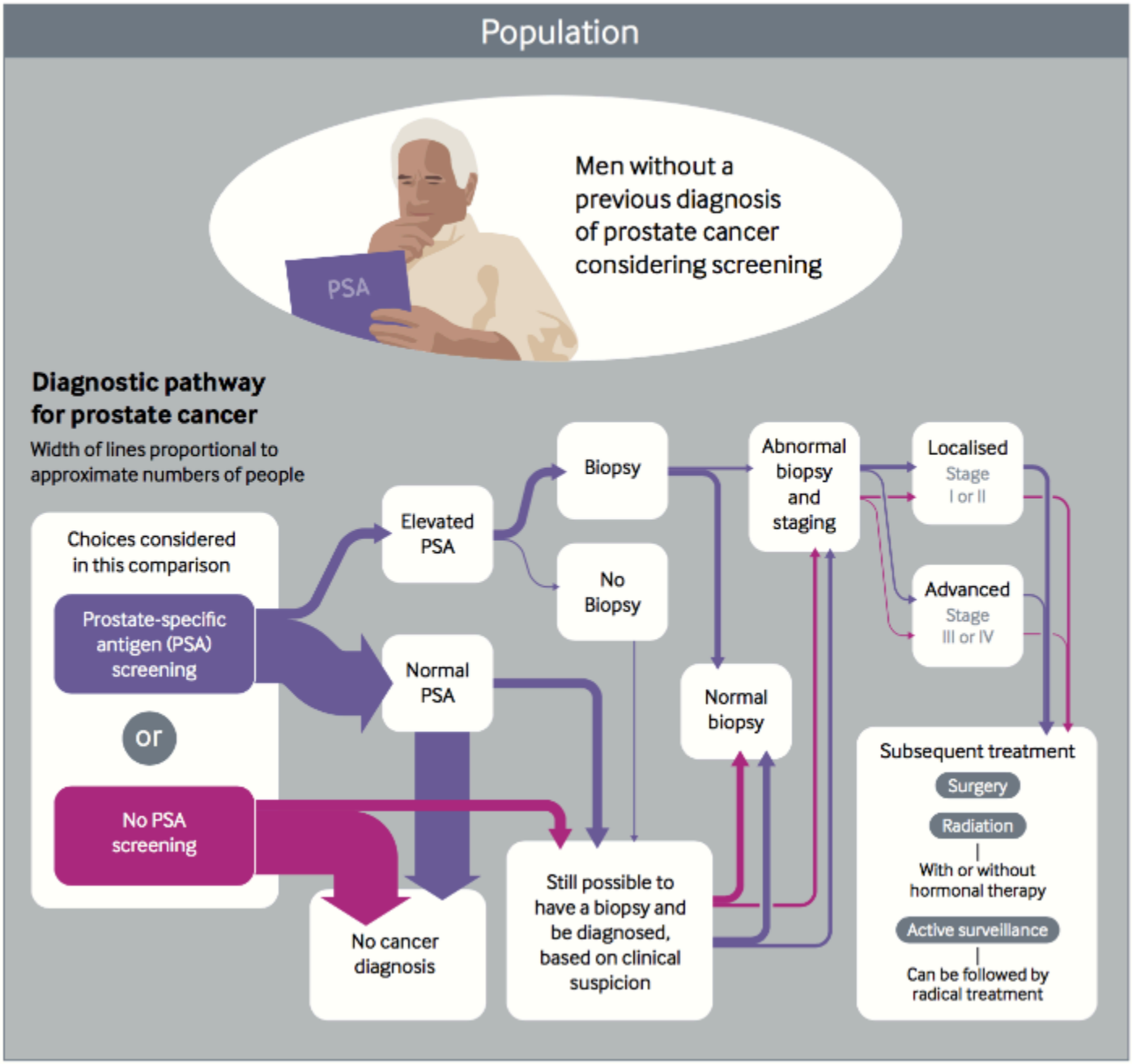
Weak Recommendation AGAINST

We suggest against systematic prostate specific antigen-based screening.

There may be a small benefit of screening on prostate cancer mortality, but there is an increased risk of complications from biopsies and cancer treatment. For patients considering screening, shared decision making is needed for men to make a decision consistent with their individual values and preferences. However, clinicians need not feel obligated to raise the issue of PSA screening with potentially eligible men. [6][7] [8]

2 - BMJ Rapid Recommendations Methods and Process

3 - Flow chart of the diagnostic pathway for prostate cancer



See corresponding BMJ Rapid Recommendation: http://www.bmj.com/content/362/bmj.k3581 *[6]*

1 - Prostate cancer screening using prostate-specific antigen (PSA) - a BMJ Rapid Recommendation

Weak Recommendation AGAINST

We suggest against systematic prostate specific antigen-based screening.

There may be a small benefit of screening on prostate cancer mortality, but there is an increased risk of complications from biopsies and cancer treatment. For patients considering screening, shared decision making is needed for men to make a decision consistent with their individual values and preferences. However, clinicians need not feel obligated to raise the issue of PSA screening with potentially eligible men. [6][7] [8]

Practical Info

The PSA test is a simple blood test. Although a raised PSA level (typically >=4 ng/ml) can be a sign of prostate cancer, it can also occur because of number of other reasons, including enlargement or inflammation of the prostate. Many men therefore may have positive PSA screening results without having cancer (i.e., false-positive results). Conversely, a substantial number of men with a normal PSA will subsequently be diagnosed with prostate cancer (i.e., false negative results).

Men with elevated PSA levels, usually by more than one measurement, typically undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer. If cancer is detected in the biopsied tissue, management options include surgery, radiation therapy, hormonal treatment, active surveillance, or watchful waiting. Diagnostic imaging studies, including ultrasound, MRI, bone scan and/or CT, are often also performed, especially in higher risk patients to assess for disease spread.

Who does this recommendation apply to?

The panel is confident the recommendation applies to all men without a previous diagnosis of prostate cancer who are considering screening.

Current evidence shows that men who present with lower urinary tract symptoms (LUTS) - including slow stream, sensation of incomplete emptying, and increased urinary frequency - are at no higher risk of prostate cancer than men without LUTS.

Key Info

Benefits and harms

Considering the whole body of evidence, at 10 years the risk of prostate-cancer mortality and all-cause mortality was similar among men who were screened and men who were not screened. PSA screening increased the detection of prostate cancer by 7 more in 1000 men screened (95% CI 1 more to 15 more), most often localized cancer (stage I or II; 7 more in 1000 men screened; 2 more to 15 more). There was no difference on the detection of advanced cancer (stage III or IV; 2 fewer in 1000 men screened; 4 fewer to 0 fewer).

Considering only studies at lower risk of bias (ERSPC trials), at 10 years there was a small benefit in prostate-cancer mortality by 1 fewer per 1000 men screened (95% CI 1 fewer to 0 fewer), but not in all-cause mortality. PSA screening increased the detection of prostate cancer by 18 more in 1000 men screened (16 more to 20 more), mostly localized cancer (14 more in 1000 men screened; 13 more to 16 more). PSA screening also slightly reduced the detection of advanced cancer by 3 fewer in 1000 men screened (4 fewer to 2 fewer).

Among 1000 men with PSA screening, within 1 month, more presented with complications due to prostate biopsies: blood in semen (94), pain (45), fever (19), blood in urine (67), hospitalized for sepsis (1). Over their lifetime, more men presented with complications due to cancer treatment: erection not firm enough for intercourse (25), urinary incontinence (3).

Among men who had abnormal PSA levels (>=4 ng/ml), about 67% had a negative subsequent biopsy within 1 year (false positive). Among men who had normal PSA levels, about 15% could be false negative and will subsequently be diagnosed with prostate cancer, about 2% with high grade cancer.

The panel considered the available evidence for men with family history of prostate cancer, of African descent, and of lower socio-economic level. No randomized trials have reported effect of screening among these subgroups and it remains uncertain whether the

relative effect of screening is similar to that in the general population. However, these factors have each been associated with higher incidence of prostate cancer and higher risk of prostate cancer death. As a result, in men of African descent, baseline risk of prostate cancer mortality is likely also higher than the general population of men considering screening (estimated at about 7 per 1000 men dying at 10 years). However, PSA screening had a similar small effect in reducing mortality in absolute terms (1 fewer per 1000 men at 10 years, from 2 to 1 fewer). For men with family history, the baseline risk of developing prostate cancer is likely higher than the general population (estimated at about 50 per 1000 men diagnosed with any stage prostate cancer; and about 25 per 1000 are localized cancers). PSA screening probably increases their detection of any stage (29 more per 1000 men, from 26 to 31 more) as well as localized cancers (19 more per 1000, from 17 to 21 more). *[6][7]*

Quality of evidence

When considering the whole body of evidence, the GRADE quality of evidence is low for almost all of the critical outcomes, because of risk of bias as well as clinically important inconsistency accross studies.
When considering only studies at lower risk of bias (ERSPC trials), the quality of the evidnence is moderate for almoste all the the critical outcomes.
Biopsy and treatment related complications rate were based on high quality evidence (from intervention arm of CAP/ProtecT trial). However, the translation of the rates in absolute effects of screening invovled additional uncertainty due to estimating likelihoods along the diagnostic pathway.*[7]*

Preference and values

Substantial variability is expected or uncertain

The panel, including the patient partners, felt that this variability in values and preferences contributes to a weak recommendation. The recommendation against screening reflects a belief that most men would value avoiding complications from biopsies and subsequent treatment because the reduction in prostate cancer and death from screening is small and uncertain. Prostate cancer will often, though not always, remain indolent.
Men who place a high value on avoiding complications from biopsies and subsequent treatment are likely to decline screening. In contrast, men who place a higher value on even a small reduction of prostate cancer may opt for screening. Several panel members felt that higher risk patients—such as patients with family history of cancer or of African descent—may be more likely to seek screening because they may worry more about prostate cancer and want to rule out the diagnosis.
For men considering screening, shared decision making is critical to ensure that their decision is in line with their own values and preferences.

The panel was informed by a linked systematic review on the values and preferences of men considering PSA screening, which showed a large variability of men's values and preferences and highlights the need for shared decision making for men considering screening.*[8]*

Resources and other considerations

A recent cost-effectiveness study modelled in the USA context suggested that screening between the ages of 55-69 years combined with active surveillance for low-risk men could only be cost-effective at a $100,000 threshold if the screening frequency remains low (every 4 years) and active surveillance is offered to all men with low-risk prostate cancer (i.e., Gleason score of 6 or lower and stage T2a or lower). Strategies with shorter screening intervals or in which immediate treatment is offered to all men did not appear cost-effective. Although the panel focused on the patient-perspective rather than that of society, its recommendation is compatible with these findings.*[6]*

Rationale

The recommendation against PSA screening is weak because of the small and uncertain benefits of screening on prostate cancer mortality and the large variability in men's values and preferences. In practice, a weak recommendation means that shared decision making is important. Clinicians should support men considering screening to make a well informed decision in line with their own risk profile and individual values and preferences. Another implication of our weak recommendation is that clinicians do not need to raise the issue systematically with their patients. They could raise PSA screening or wait for the patient to raise the issue. Both approaches are reasonable. It depends on the patient's context and competing issues in each clinical encounter.

The panel believes that most informed men considering screening would decline it, although some would choose to undergo screening, accepting the diagnostic and therapeutic burden and harms that can result.

Clinical Question/ PICO

Population: Men of lower socio-economic level (as assessed by lower education)
Intervention: Prostate-specific antigen (PSA) screening
Comparator: No screening

Outcome Timeframe	Study results and measurements	Absolute effect estimates No screening	 PSA screening	Certainty in effect estimates (Quality of evidence)	Plain text summary
All cause mortality At 10 years 9 Critical	Relative risk 0.98 (CI 95% 0.95 - 1) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**196** per 1000	**192** per 1000 Difference: **4 fewer** per 1000 (CI 95% 10 fewer - 0 fewer)	**Moderate** Due to serious risk of bias [1]	PSA screening probably has little or no effect on all cause mortality
Prostate cancer mortality At 10 years 9 Critical	Relative risk 0.79 (CI 95% 0.69 - 0.91) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**4** per 1000	**3** per 1000 Difference: **1 fewer** per 1000 (CI 95% 1 fewer - 0 fewer)	**Moderate** Due to serious risk of bias [2]	PSA screening probably has little or no effect on prostate cancer mortality

1. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
2. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

References

[6] Tikkinen K : Prostate-specific antigen (PSA) screening for prostate cancer: a clinical practice guideline . BMJ 2018;362 k3581 Journal Website

[7] Ilic D : Prostate-Specific Antigen-Based Screening for Prostate Cancer: A Systematic Review and Meta-Analysis.. BMJ 2018;362 k3519 Journal Website

Clinical Question/ PICO

Population: Men of african descent

Intervention: Prostate-specific antigen (PSA) screening
Comparator: No screening

Outcome Timeframe	Study results and measurements	Absolute effect estimates No screening	 PSA screening	Certainty in effect estimates (Quality of evidence)	Plain text summary
Prostate cancer mortality At years 10 years 9 Critical	Relative risk 0.79 (CI 95% 0.69 - 0.91) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**7** per 1000	**6** per 1000 Difference: **1 fewer** per 1000 (CI 95% 2 fewer - 1 fewer)	**Moderate** Due to serious risk of bias [1]	PSA screening probably has little or no effect on prostate cancer mortality
Incidence of prostate cancer (any stage) At 10 years 7 Critical	Relative risk 1.57 (CI 95% 1.51 - 1.62) Based on data from 162,243 patients in 1 studies. Follow up 13 years	**51** per 1000	**80** per 1000 Difference: **29 more** per 1000 (CI 95% 26 more - 32 more)	**Moderate** Due to serious risk of bias [2]	PSA screening probably increases the detection of prostate cancer (any stage)

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References

[6] Tikkinen K : Prostate-specific antigen (PSA) screening for prostate cancer: a clinical practice guideline . BMJ 2018;362 k3581 Journal Website

[7] Ilic D : Prostate-Specific Antigen-Based Screening for Prostate Cancer: A Systematic Review and Meta-Analysis.. BMJ 2018;362 k3519 Journal Website

Clinical Question/ PICO

Population: Men with family history of prostate cancer
Intervention: Prostate-specific antigen (PSA) screening

Comparator: No screening

Outcome Timeframe	Study results and measurements	Absolute effect estimates No screening	 PSA screening	Certainty in effect estimates (Quality of evidence)	Plain text summary
Incidence of prostate cancer (any stage)	Relative risk 1.57 (CI 95% 1.51 - 1.62) Based on data from 162,243 patients in 1 studies. Follow up 13 years	**50** per 1000	**79** per 1000 Difference: **29 more** per 1000 (CI 95% 26 more - 31 more)	**Moderate** Due to serious risk of bias [1]	PSA screening probably increases the detection of prostate cancer (any stage)
Incidence of localized prostate cancer (stage I & II) At 10 years 7 Critical	Relative risk 1.75 (CI 95% 1.68 - 1.82) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**25** per 1000	**44** per 1000 Difference: **19 more** per 1000 (CI 95% 17 more - 21 more)	**Moderate** Due to serious risk of bias [2]	PSA screening probably increases the detection of localized prostate cancer (stage I & II)

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References

[6] Tikkinen K : Prostate-specific antigen (PSA) screening for prostate cancer: a clinical practice guideline . BMJ 2018;362 k3581 Journal Website

[7] Ilic D : Prostate-Specific Antigen-Based Screening for Prostate Cancer: A Systematic Review and Meta-Analysis.. BMJ 2018;362 k3519 Journal Website

Clinical Question/ PICO

Population: *Men without symptoms of prostate cancer (evidence from ERSPC trial)
Intervention: Prostate-specific antigen (PSA) screening
Comparator: No screening

Summary

PSA screening probably has little or no effect on death:

- All-cause mortality (0 fewer per 1000 men (95% CI 3 fewer to 3 more))
- Prostate cancer mortality (1 fewer per 1000 (1 to 0 fewer))
- Prostate cancer mortality is similar at longer periods of up to 18 years of follow-up (1 to 2 fewer per 1000 men)

PSA screening probably increases diagnosis of prostate cancer:

- Detection of any prostate cancer (18 more per 1000 men (16 to 20 more))
- Detection of localised cancer (14 more per 1000 (13 to 16 more))
- But it probably results in a small decrease in detection advanced prostate cancer (3 fewer per 1000 (4 to 2 fewer)).

Among a hypothetical population of 1000 men, about 94 more will present with blood in the semen with PSA screening, 67 more with blood in the urine, 45 more with pain, 19 more with fever, and 1 more hospitalised for sepsis, due to a prostate biopsy. About three more will present with urinary incontinence (any pad use) and 25 more will have an erection not firm enough for intercourse due to treatment for prostate cancer diagnosed through PSA screening.*[7]*

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** No screening	PSA screening	**Certainty in effect estimates** (Quality of evidence)	**Plain text summary**
All cause mortality At 10 years 9 Critical	Relative risk 1 (CI 95% 0.98 - 1.02) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**129** per 1000	**129** per 1000 Difference: **0 fewer** per 1000 (CI 95% 3 fewer - 3 more)	**Moderate** Due to serious risk of bias [1]	PSA screening probably has little or no effect on all cause mortality
Prostate cancer mortality At years 10 years 9 Critical	Relative risk 0.79 (CI 95% 0.69 - 0.91) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**3** per 1000	**2** per 1000 Difference: **1 fewer** per 1000 (CI 95% 1 fewer - 0 fewer)	**Moderate** Due to serious risk of bias [2]	PSA screening probably has little or no effect on prostate cancer mortality
Incidence of prostate cancer (any stage) At 10 years 7 Critical	Relative risk 1.57 (CI 95% 1.51 - 1.62) Based on data from 162,243 patients in 1 studies. Follow up 13 years	**32** per 1000	**50** per 1000 Difference: **18 more** per 1000 (CI 95% 16 more - 20 more)	**Moderate** Due to serious risk of bias [3]	PSA screening probably increases the detection of prostate cancer (any stage)
Incidence of localized prostate cancer	Relative risk 1.75 (CI 95% 1.68 - 1.82) Based on data from 162,243 patients in 1	**19** per 1000	**33** per 1000	**Moderate** Due to serious risk of bias [4]	PSA screening probably increases the detection of localized cancer (stage I & II)

(stage I & II) At 10 years 7 Critical	studies. (Randomized controlled) Follow up 13 years	Difference: **14 more** per 1000 (CI 95% 13 more - 16 more)		
Incidence of advanced prostate cancer (stage III & IV) At 10 years 8 Critical	Relative risk 0.75 (CI 95% 0.69 - 0.82) Based on data from 162,243 patients in 1 studies. (Randomized controlled) Follow up 13 years	**13** per 1000 **10** per 1000 Difference: **3 fewer** per 1000 (CI 95% 4 fewer - 2 fewer)	**Moderate** Due to serious risk of bias [5]	PSA screening probably has little effect on the detection of advanced cancer (stage III & IV)
Quality of life 8 Critical	Measured by: SF-6D Scale: 0-1 High better Based on data from: 1,088 patients in 1 studies. (Randomized controlled)	**0.76** points (Mean) **0.75** points (Mean) Difference: **MD 0.01 lower** (CI 95% 0.01 lower - 0.02 higher)	**Low** Based on risk of bias and indirectness. Data from surveys on a subsample of patient invited from sample of the Finnish ERSPC trial [6]	PSA screening may have little or no effect on quality of life
Complication rates per biopsy [7] at 1 month 6 Important	Based on data from 1,147 patients in 1 studies.	Most common complications were: Blood in semen (93%), blood in urine (66%), pain (44%), shivers (19%) and fever (18%); 1.4% (95%CI 0.8 to 2.4%) of men were admitted to the hospital (mostly for sepsis).	**High** Based on high quality and representative cohort study; intervention arm of CAP/ProtecT trial	Complication rates per biopsy (regardless of whether diagnosed through screening or not)
Biopsy-related complications [8] at 1 month 6 Important		Among a 1000 men, between those screened vs. not screened, there were about 94 more presenting with blood is semen, 67 more with blood in urine, 45 more with pain, 19 more with fever, and 1 more hospitalized for sepsis, due to prostate biopsies.	**Low** Because of additional uncertainty due to estimating likelihood along the diagnostic pathway	Absolute differences in biopsy-related complications between those getting screened vs. not screened
Complications rates per prostate cancer treatment modality 8 Critical	Based on data from 1,643 patients in 1 studies.	At 6 years, rates of any pad use (urinary incontinence) for active monitoring, surgery and radiation groups were 8%, 17% and 4%; rates of erections not firm enough for intercourse were 70%, 83% and 73%, respectively.	**High** High quality prospective cohort studies of 3-armed RCT	Complication rates per treatment modality for prostate cancer (regardless of whether diagnosed through screening or not)

Complications of subsequent prostate cancer treatment 8 Critical		Among a 1000 men, between those screened vs. not screened, there were about 3 more presenting urinary incontinence (any pad use), and 25 more with an erection not firm enough for intercourse, due to subsequent treatment for prostate cancer.	**Low** Because of additional uncertainty due to estimating likelihood along the diagnostic pathway	Absolute differences in treatment-related complications between those getting screened vs. not screened
False positive screening results Within 1 year 6 Important	Based on data from 61,000 patients in 1 studies. [9]	False positive rates were 66.5%, 66.0% and 63.0% in first, second and third round of screening, respectively.	**High** Based on high quality prospective cohort from 5 arms of the ERSPC trial.	Among men presenting a PSA >=4 ng/ml at screening, about 67 % will have a negative subsequent biopsy.
False negative screening results 5 Important	Based on data from 2,950 patients in 1 studies. [10]	Among men with PSA <=4 (age 62 to 91 years), 15.2% were diagnosed with prostate cancer during (7 years of follow-up), 2.3% developed a cancer Gleason score >= 7	**Low** Prospective observational cohort; possible verification bias (only 2950 of 3568 men with PSA >= 4 ng/ml had end-of-study biopsy)	Among men presenting with PSA <=4 ng/ml at screening, about 15% could be false negative and will subsequently be diagnosed with prostate cancer, about 2% with high grade cancer.
Anxiety about having cancer [11] 5 Important		We found no evidence comparing PSA screening with non-screening. A large cohort study in Sweden (n=4.3 millions) showed an increase risk of suicide (RR 2.6 95%CI 2.1-3.0) and cardiovascular events 1.3 (RR 1.3, 95%CI 1.3-1.3) during the first year after diagnosis. Another cohort study in the US (n=343'000) showed no increased risk of suicide during the first year since the wide-spread use of PSA (after 1993), but an increase risk of cardio-vascular death during the first month after diagnosis (aRR=1.55, 95% CI 1.3-1.8).	**Very Low** Risk of residual confounding in observational data	It is uncertain wether screening results in changes in anxiety about have a cancer. But a diagnosis of prostate cancer might increase immediate risks of suicide and cardiovascular death.

Practical issues	No screening	Prostate-specific antigen (PSA) screening	Both
 Medication routine		May have to stop blood thinners before prostate biopsy procedure	

 Tests and visits	Blood sample taken at GP/family physician Elevated results can lead to further diagnostics/additional tests Prostate biopsy is normally done in outpatient clinic/hospital
 Procedure and device	PSA testing is done with a regular blood sample Prostate biopsy is usually taken through rectum guided by ultrasound. Takes about 5-10 minutes. Antibiotics and local anaesthesia/ sedation given before procedure
 Recovery and adaptation	Allow for some recovery time dependent on adverse effects after prostate biopsy
 Coordination of care	Need for someone to drive you home after prostate biopsy procedure if sedation is given
 Adverse effects, interactions and antidote	Some drugs (finasteride, dutasteride) can lower PSA levels. Prostate biopsy often leads to soreness, blood in semen, urine and stool for days to weeks.
 Physical well-being	Prostate biopsy procedure can be uncomfortable
 Emotional well-being	Waiting for PSA and prostate biopsy results can be stressful

 Costs and access	Cost depends on health policy and health insurance; PSA tests are usually not expensive, prostate biopsy can sometimes be expensive
 Food and drinks	No dietary restrictions related to PSA testing or prostate biopsy
 Exercise and activities	Avoid vigorous exercise (e.g. cycling) in the 2 days prior to PSA testing as this may result in false positive elevation. No restrictions related to PSA testing. Avoid vigorous exercise or physical activities after prostate biopsy
 Social life and relationships	Avoid ejaculation in the 2 days prior to PSA testing as this may result in false positive elevation. Blood in semen and pain in pelvic area can impact sexual life after prostate biopsy
 Work and education	Time off work for PSA testing and prostate biopsy procedure
 Travel and driving	Should not drive directly after prostate biopsy procedure if sedation is given

1. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
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blinding of participants and personnel, resulting in potential for performance bias ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
4. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
5. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
6. **Risk of bias: Serious .** Based on cross-sectional analysis of random sample , Self-reported measure of health-related QoL. ; **Inconsistency: No serious . Indirectness: Serious .** Patients without prostate cancer were excluded from the screening arm. HrQoL of patients screened with no diagnosis of prostate cancer may differ. ; **Imprecision: No serious . Publication bias: No serious .**
7. Biopsy-related complications in 35 days (e.g. infections, bleeding, clot formation, urinary and sexual dysfunction, readmissions)
8. Biopsy-related complications in 35 days (e.g. infections, bleeding, clot formation, urinary and sexual dysfunction, readmissions)
9. Systematic review **Supporting references:** [5],
10. Systematic review **Supporting references:** [4],
11. Anxiety and uncertainty related to concerns about having prostate cancer with the need form more diagnostic procedure

References

[6] Tikkinen K : Prostate-specific antigen (PSA) screening for prostate cancer: a clinical practice guideline . BMJ 2018;362 k3581 Journal Website

[7] Ilic D : Prostate-Specific Antigen-Based Screening for Prostate Cancer: A Systematic Review and Meta-Analysis.. BMJ 2018;362 k3519 Journal Website

Clinical Question/ PICO

Population: *Men without symptoms of prostate cancer (whole body of evidence)
Intervention: Prostate-specific antigen (PSA) screening
Comparator: No screening

Summary

PSA screening may increase the detection of prostate cancer (7 more per 1000 men (95% confidence interval 1 to 15 more) at 10 years), particularly of localised cancer (7 more per 1000 men (2 to 15 more)). But the data show no difference in prostate cancer mortality. Overall confidence in these estimates across these outcomes was low because of risk of bias as well as the inconsistency of findings across studies.*[7]*

Among a hypothetical population of 1000 men, about 94 more will present with blood in the semen with PSA screening, 67 more with blood in the urine, 45 more with pain, 19 more with fever, and 1 more hospitalised for sepsis, due to a prostate biopsy. About three more will present with urinary incontinence (any pad use) and 25 more will have an erection not firm enough for intercourse due to treatment for prostate cancer diagnosed through PSA screening.*[7]*

Outcome	Study results and	Absolute effect estimates	Certainty in	Plain text summary

Timeframe	measurements	No screening	PSA screening	effect estimates (Quality of evidence)	
All cause mortality At 10 years 9 Critical	Relative risk 0.99 (CI 95% 0.98 - 1.01) Based on data from 675,232 patients in 4 studies. (Randomized controlled) Follow up 10 to 20 years	**129** per 1000	**128** per 1000 Difference: **1 fewer** per 1000 (CI 95% 3 fewer - 1 more)	**Moderate** Due to serious risk of bias [1]	PSA screening probably has little or no effect on all cause mortality
Prostate cancer mortality At 10 years 9 Critical	Relative risk 0.96 (CI 95% 0.85 - 1.08) Based on data from 721,718 patients in 5 studies. (Randomized controlled) Follow up 10 to 20 years	**3** per 1000	**3** per 1000 Difference: **0 fewer** per 1000 (CI 95% 0 fewer - 0 fewer)	**Low** Due to serious risk of bias and inconsistency [2]	PSA screening may have little or no difference on prostate cancer mortality
Incidence of cancer (any stage) At 10 years 7 Critical	Relative risk 1.23 (CI 95% 1.03 - 1.48) Based on data from 675,232 patients in 4 studies. Follow up 10 to 20 years	**32** per 1000	**39** per 1000 Difference: **7 more** per 1000 (CI 95% 1 more - 15 more)	**Low** Due to serious risk of bias and to serious inconsistency (resulting in large imprecision) [3]	PSA screening may increase the detection of prostate cancer (any stage)
Incidence of localized prostate cancer (stage I & II) At 10 years 7 Critical	Relative risk 1.39 (CI 95% 1.09 - 1.79) Based on data from 647,751 patients in 3 studies. (Randomized controlled) Follow up 10 to 20 years	**19** per 1000	**26** per 1000 Difference: **7 more** per 1000 (CI 95% 2 more - 15 more)	**Low** Due to serious risk of bias and to serious inconsistency (resulting in large imprecision) [4]	PSA screening may increase the detection of localized cancer (stage I & II)
Incidence of advanced prostate cancer (stage III & IV) At 10 years 8 Critical	Relative risk 0.85 (CI 95% 0.72 - 0.99) Based on data from 647,751 patients in 3 studies. (Randomized controlled) Follow up 10 to 20 years	**13** per 1000	**11** per 1000 Difference: **2 fewer** per 1000 (CI 95% 4 fewer - 0 fewer)	**Low** Due to serious risk of bias and inconsistency [5]	PSA screening may slightly decrease the detection of advanced cancer (stage III & IV).
Quality of life 8 Critical	Measured by: SF-6D Scale: 0-1 High better Based on data from: 1,088 patients in 1	**0.76** (Mean)	**0.75** (Mean)	**Low** Based on risk of bias and indirectness. Data	PSA screening may have little or no effect on quality of life

	studies. (Randomized controlled)	Difference: **MD 0.01 lower** (CI 95% 0.01 lower - 0.02 higher)	from surveys on a subsample of patient invited from sample of the Finnish ERSPC trial [6]	
Complication rates per biopsy [7] 6 Important	Based on data from 1,147 patients in 1 studies.	Most common complications were: Blood in semen (93%), blood in urine (66%), pain (44%), shivers (19%) and fever (18%); 1.4% (95%CI 0.8 to 2.4%) of men were admitted to the hospital (mostly for sepsis)	**High** Based on high quality and representative cohort study; intervention arm of CAP/ProtecT trial	Complication rates per biopsy (regardless of whether diagnosed through screening or not)
Biopsy-related complications [8] 6 Important	Based on data from 1,147 patients in 1 studies.	Among a 1000 men, between those screened vs. not screened, there were about 94 more presenting with blood is semen, 67 more with blood in urine, 45 more with pain, 19 more with fever, and 1 more hospitalized for sepsis, due to prostate biopsies.	**Low** Because of additional uncertainty due to estimating likelihood along the diagnostic pathway	Absolute differences in biopsy-related complications between those getting screened vs. not screened
Complications rates per prostate cancer treatment modality 8 Critical	Based on data from 1,643 patients in 1 studies.	At 6 years, rates of any pad use (urinary incontinence) for active monitoring, surgery and radiation groups were 8%, 17% and 4%; rates of erections not firm enough for intercourse were 70%, 83% and 73%, respectively.	**High** High quality prospective cohort studies of 3-armed RCT	Complication rates per treatment modality for prostate cancer (regardless of whether diagnosed through screening or not)
Complications of subsequent prostate cancer treatment 8 Critical		Among a 1000 men, between those screened vs. not screened, there were about 3 more presenting urinary incontinence, and 25 more with an erection not firm enough for intercourse, due to subsequent treatment for prostate cancer.	**Low** Because of additional uncertainty due to estimating likelihood along the diagnostic pathway	Absolute differences in treatment-related complications between those getting screened vs. not screened
False positive screening results Within 1 year 6 Important	Based on data from 61,000 patients in 1 studies. [9]	False positive rates were 66.5%, 66.0% and 63.0% in first, second and third round of screening, respectively.	**High** Based on high quality prospective cohort from from 5 arms of the ERSPC trials	Among men presenting a PSA >=4 ng/ml at screening, about 67 % will have a negative subsequent biopsy.

False negative screening results 5 Important	Based on data from 2,950 patients in 1 studies. [10]	Among men with PSA <=4 (age 62 to 91 years), 15.2% were diagnosed with prostate cancer during (7 years of follow-up), 2.3% developed a cancer Gleason score >= 7	**Low** Prospective observational cohort; possible verification bias (only 2950 of 3568 men with PSA >= 4 ng/ml had end-of-study biopsy)	Among men presenting with PSA <=4 ng/ml at screening, about 15% could be false negative and will subsequently be diagnosed with prostate cancer, about 2% with high grade cancer.
Anxiety about having cancer [11] 5 Important	[12]	We found no evidence comparing PSA screening with non-screening. A large cohort study in Sweden (n=4.3 millions) showed an increase risk of suicide (RR 2.6 95%CI 2.1-3.0) and cardiovascular events 1.3 (RR 1.3, 95%CI 1.3-1.3) during the first year after diagnosis. Another cohort study in the US (n=343'000) showed no increased risk of suicide during the first year since the wide-spread use of PSA (after 1993), but an increase risk of cardio-vascular death during the first month after diagnosis (aRR=1.55, 95% CI 1.3-1.8).	**Very Low** Risk of residual confounding in observational data	It is uncertain wether screening results in changes in anxiety about have a cancer. But a diagnosis of prostate cancer might increase immediate risks of suicide and cardiovascular death.

Practical issues	No screening	Prostate-specific antigen (PSA) screening	Both
 Medication routine		May have to stop blood thinners before prostate biopsy procedure	
 Tests and visits		Blood sample taken at GP/family physician Elevated results can lead to further diagnostics/additional tests Prostate biopsy is normally done in outpatient clinic/hospital	
 Procedure and device		PSA testing is done with a regular blood sample Prostate biopsy is usually taken through rectum guided by ultrasound. Takes about 5-10 minutes. Antibiotics and local anaesthesia/ sedation given before procedure	

 Recovery and adaptation	Allow for some recovery time dependent on adverse effects after prostate biopsy
 Coordination of care	Need for someone to drive you home after prostate biopsy procedure if sedation is given
 Adverse effects, interactions and antidote	Some drugs (finasteride, dutasteride) can lower PSA levels. Prostate biopsy often leads to soreness, blood in semen, urine and stool for days to weeks.
 Physical well-being	Prostate biopsy procedure can be uncomfortable
 Emotional well-being	Waiting for PSA and prostate biopsy results can be stressful
 Costs and access	Cost depends on health policy and health insurance; PSA tests are usually not expensive, prostate biopsy can sometimes be expensive
 Food and drinks	No dietary restrictions related to PSA testing or prostate biopsy
 Exercise and activities	Avoid vigorous exercise (e.g. cycling) in the 2 days prior to PSA testing as this may result in false positive elevation.

 Social life and relationships	Avoid ejaculation in the 2 days prior to PSA testing as this may result in false positive elevation. Blood in semen and pain in pelvic area can impact sexual life after prostate biopsy
 Work and education	Time off work for PSA testing and prostate biopsy procedure
 Travel and driving	Should not drive directly after prostate biopsy procedure if sedation is given

1. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious .** Lower border of CI compatible with a relevant, yet small clinical risk reduction. ; **Publication bias: No serious .**
2. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: Serious .** I^2: 53%; ERSPC trial shows significant reduction while all other trials show no significant different. ; **Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
3. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: Serious .** The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies. ; **Indirectness: No serious . Imprecision: No serious .** We did not downgrade for imprecision, because it resulted from inconsistency ; **Publication bias: No serious .**
4. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias. Some contamination. ; **Inconsistency: Serious .** The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies. ; **Indirectness: No serious . Imprecision: No serious .** We did not downgrade for imprecision, because it resulted from inconsistency ; **Publication bias: No serious .**
5. **Risk of bias: Serious .** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias. Some contamination. ; **Inconsistency: Serious .** The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies. ; **Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**
6. **Risk of bias: Serious .** Based on cross-sectional analysis of random sample , Self-reported measure of health-related QoL. ; **Inconsistency: No serious . Indirectness: Serious .** Patients without prostate cancer were excluded from the screening arm. HrQoL of patients screened with no diagnosis of prostate cancer may differ. ; **Imprecision: No serious . Publication bias: No serious .**
7. Complication rates per biopsy in 35 days (e.g. infections, bleeding, clot formation, urinary and sexual dysfunction, readmissions)
8. Biopsy-related complications in 35 days (e.g. infections, bleeding, clot formation, urinary and sexual dysfunction, readmissions)
9. Systematic review **Supporting references:** [5],

10. Systematic review **Supporting references:** [4],
11. Anxiety and uncertainty related to concerns about having prostate cancer with the need form more diagnostic procedure
12. Primary study **Supporting references:** [2], [1],

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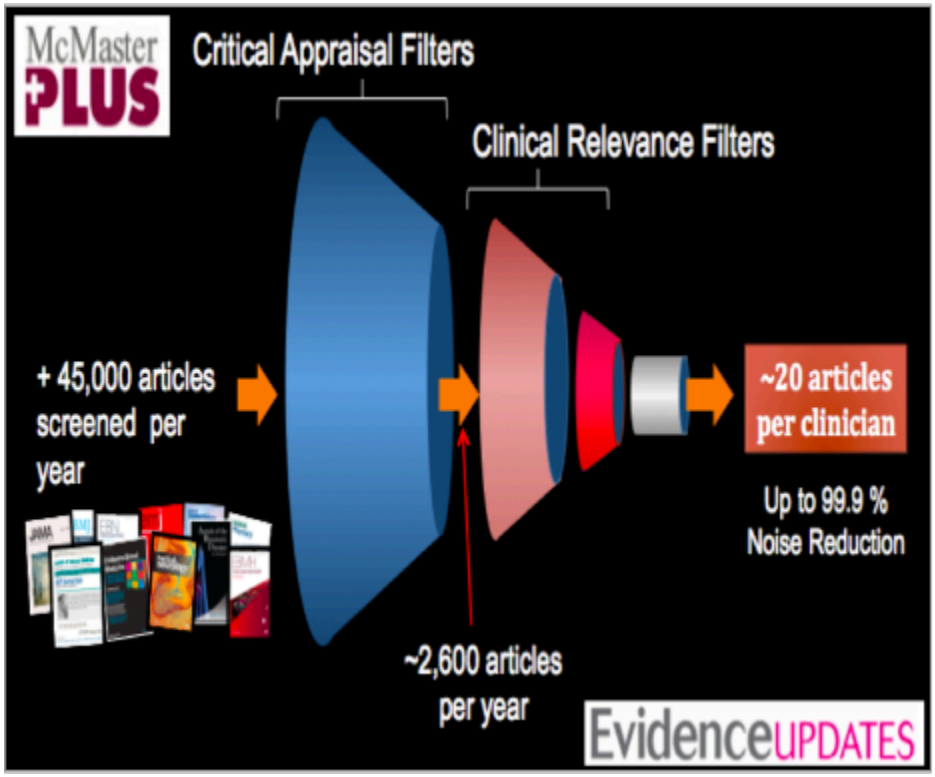
2 - BMJ Rapid Recommendations Methods and Process

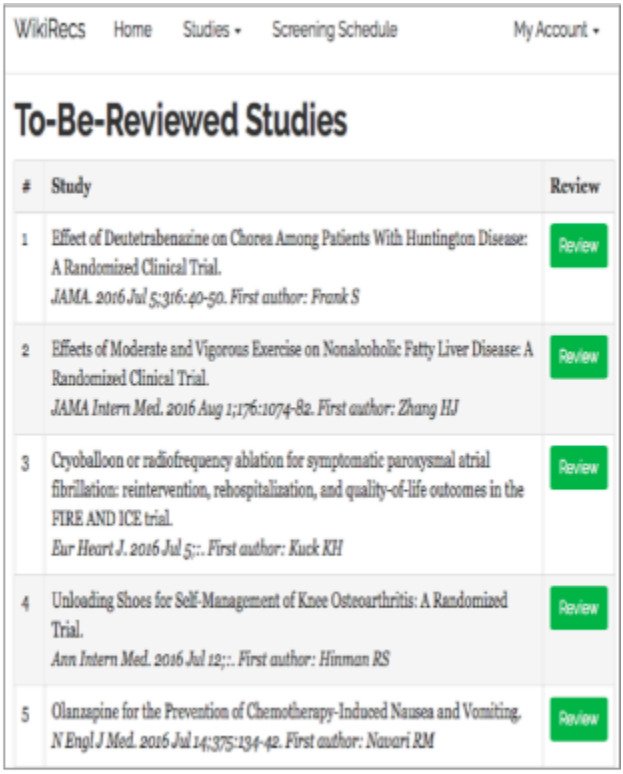
About BMJ Rapid Recommendations

Translating research to clinical practice is challenging. Trustworthy clinical practice recommendations are one useful knowledge translation strategy. Organisations creating systematic reviews and guidelines often struggle to deliver timely and trustworthy recommendations in response to potentially practice-changing evidence. *BMJ* Rapid Recommendations aims to create trustworthy clinical practice recommendations based on the highest quality evidence in record time. The project is supported by an international network of systematic review and guideline methodologists, people with lived experience of the diseases or conditions, clinical specialists, and front-line clinicians. This overview is one of a package that includes recommendations and one or more systematic reviews published by the *BMJ* group and in MAGICapp (http://www.magicapp.org). The goal is to translate evidence into recommendations for clinical practice in a timely and transparent way, minimizing bias and centred around the experience of patients. *BMJ* Rapid Recommendations will consider both new and old evidence that might alter established clinical practice.

Process overview

1. On a daily basis, we monitor the literature for practice-changing evidence:
2. Formal monitoring through McMaster Premium LiteratUre Service (PLUS)
3. Informal monitoring the literature by *BMJ* Rapid Recommendations expert groups, including clinician specialists and patients





1. The *RapidRecs* executive team and editors at *The BMJ* choose which clinical questions to pursue among the identified potentially-practice changing evidence, based on relevance to a wide audience, widespread interest, and likelihood to change practice.
2. We incorporate the evidence into the existing body of evidence and broader context of clinical practice via:
3. A rapid and high-quality systematic review and meta-analysis on the benefits and harms with a focus on the outcomes that matter to patients
4. Parallel rapid recommendations that meet the standards for trustworthy guidelines[1] by an international panel of people with relevant lived experience, front-line clinicians, clinical content experts, and methodologists.
5. The systematic review and the recommendation panel will apply standards for trustworthy guidelines.[1,2] They use the GRADE approach, which has developed a transparent process to rate the quality (or certainty) of evidence and grade the strength of recommendations.[3,4]
6. Further research may be conducted including:
   - A systematic review of observational studies to identify baseline risk estimates that most closely represent the population at the heart of the clinical question, a key component when calculating the estimates of absolute effects of the intervention.
   - A systematic review on the preferences and values of patients on the topic.

7. Disseminate the rapid recommendations through:
8. Publication of the research in *BMJ* journals
9. Short summary of recommendations for clinicians published in *The BMJ*
10. Press release and/or marketing to media outlets and relevant parties such as patient groups
11. Links to *BMJ* group's *Best Practice* point of care resource
12. MAGICapp which provides recommendations and all underlying content in digitally structured multilayered formats for clinicians and others who wish to re-examine or consider national or local adaptation of the recommendations.

Who is involved?

Researchers, systematic review and guideline authors, clinicians, and patients often work in silos. Academic journals may publish work from any one or combinations of these groups of people and findings may also be published in the media. But it is rare that these groups work together to produce a comprehensive package. *BMJ-RapidRecs* circumvents organisational barriers in order to provide clinicians with guidance for potentially practice-changing evidence.

Our collaboration involves:
1. The *RapidRecs* group with a designated Executive team responsible for recruiting and coordinating the network of researchers who perform the systematic reviews and the recommendation panels.. The *RapidRecs* group is part of MAGIC (www.magicproject.org), a non for profit organization that provides MAGICapp (www.magicapp.org) an authoring and publication platform for evidence summaries, guidelines and decision aids, which are disseminated online for all devices.[5]
2. *The BMJ* helps identifiying practice-changing evidence on key clinical questions, coordinates the editorial process and publishes the package of content linking to the MAGICapp that is presented in a user-friendly way.

METHODS FOR THE RAPID RECOMMENDATIONS

The formation of these recommendations adheres to standards for trustworthy guidelines with an emphasis on patient involvement, strict management of conflicts of interests, as well as transparent and systematic processes for assessing the quality of evidence and for moving from evidence to recommendations.[1,2,6]

Guidance on how the panel is picked and how they contribute

Panel members are sought and screened through an informal process. The following panel members are important:
- At least one author of the individual systematic reviews.
- At least one patient representative with lived experience of the disease or condition. This person receives patient-oriented documents to explain the process and is allocated a linked panel member to empower their contribution.
- A full spectrum of practicing clinicians involved in the management of the clinical problem and patients it affects, including front-line clinicians with generalist experience and those with deep content clinical and research expertise in the particular topic.
- Methodological experts in health research methodology and guideline development.

Any potential conflicts of interest are managed with extreme prudence:
- No panel member can have a financial interest – as assessed by the panel chair, the *RapidRecs* executive team or *The BMJ* editors as relevant to the topic.
- No more than two panel members with an intellectual interest on the topic (typically having published statements favouring one of the interventions).

Illustrative example: For the BMJ *Rapid Recommendations on antiretroviral therapy for pregnant women living with HIV, the panel recruitment of content experts and community panel members was challenging. Content experts in this area are infectious diseases experts, many of whom have financial conflicts of interests through interactions with the pharmaceutical industry through advisory boards and participation in industry-funded trials. The group reached out to more than 17 potential panel members who were eventually excluded from participating because of conflicts – notably, all of these persons had not disclosed any relevant conflicts on related and recent publications in the topic area. Many more potential panel members were not recruited because of publicly declared conflicts. The chair and MAGIC team were able, with considerable effort and ingenuity, to recruit several excellent and unconflicted content experts.*

How the panel meets and works

The international panel communicates via teleconferences and e-mail exchange of written documents throughout the process. Minutes from teleconferences are audiorecorded, transcribed, and stored for later documentation (available for peer-reviewers on request).

Teleconferences typically occur at three timepoints, with circulated documents by e-mail in advance:
1. At the initiation of the process to provide feedback on the systematic review protocol (for example, on selection of patient-important

outcomes and appropriate prespecified analysis of results) before it is performed.
2. At the evidence summary stage with discussion, feedback and agreement on draft evidence (GRADE evidence profile) prepared by the Chair and the methods editor based on the systematic review.
3. At the recommendation formulation phase with discussion, feedback and agreement on draft recommendations and other content underlying the recommendation (e.g. GRADE SoF-table, key information, rationale, practical advice)
Following the last teleconference the final version of the recommendations is circulated by e-mail specifically requesting feedback from all panel members to document agreement before submission to The BMJ. Additional teleconferences are arranged as needed.

Illustrative example: For the BMJ Rapid Recommendations on antiretroviral therapy for pregnant women living with HIV, two large-group teleconferences were arranged. First, content experts provided crucial input to evidence assessment (e.g. subgroups to identify). For the recommendation formulation phase the panel needed two teleconferences to discuss all elements in detail, followed by more than 100 e-mails with specific issues to be sorted out. Multiple teleconferences were held to allow the scheduling flexibility required so that all could participate.

How we move from research findings to recommendations

What information is considered?
The panel considers best current evidence from available research. Beyond systematic reviews - performed in the context of the BMJ Rapid Recommendations - the panel may also include a number of other research papers to further inform the recommendations.

How is a trustworthy guideline made?
The Institute of Medicine (IOM)'s guidance on out how trustworthy guidelines should be developed and articulated key standards as outlined in the table below.[1] The standards are similar to those developed by the Guideline International Network (G-I-N).[2] These standards have been widely adopted by the international guideline community. Peer reviewers of the recommendation article are asked whether they found the guideline trustworthy (in accordance with IOM standards). The table below lays out how we hope to meet the standards for our rapid recommendations:

1. Establishing transparency **"The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible."***
• This method is available and published as a supplementary file as well as in MAGICapp where all recommendations and underlying content i available. • We ask the peer-reviewers to judge whether the guidance is trustworthy and will respond to concerns raised.
2. Managing conflicts of interest **"Prior to selection of the guideline development group, individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity....",**
• Interests of each panel member are declared prior to involvement and published with the rapid recommendations. • No one with any potential financial interests in the past three years, or forthcoming 12 months will participate - as judged by the panel chair and *The BMJ*. • No more than two panel members have declared an intellectual conflict of interest. Such conflicts include having taken a position on the issu for example by a written an editorial, commentary, or conflicts related to performing a primary research study or written a prior systematic review on the topic. • The Chair must have methods expertise, a clinical background and no financial or intellectual interests. • Funders and pharmaceutical companies have no role in these recommendations.
3. Guideline Development Group Composition **"The guideline development group should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG."**
• The RapidRecs group will aim to include representation from most or every major geographic region in the world, with specific efforts made achieve gender-balance. • We will facilitate patient and public involvement by including patient experience, via patient-representatives and systematic reviews addressing values and preferences to guide outcome choices and relative weights of each outcome, where available.

- Patient-representatives will be given priority during panel meetings and will have an explicit role in vetting the panel's judgements of values and preferences.

4. Clinical Practice Guideline–Systematic Review Intersection
"CPG developers should use systematic reviews that meet standards set by the IOM. Guideline development group and systematic review team should interact regarding the scope, approach, and output of both processes."

- Each rapid recommendation will be based on one or more high-quality SRs either developed and published in parallel with our *BMJ* Rapid Recommendations or produced by other authors and available at the time of making the recommendaiton.
- The recommendation panel and SR teams will interact, with up to three members participating in both teams to facilitate communication an continuity in the process.

5. Establishing Evidence Foundations for and Rating Strength of Recommendations
"For each recommendation: explain underlying reasoning, including a clear description of potential benefits and harms, a summary of relevant available evidence and description of the quality., explain the part played by values, opinion, theory, and clinical experience in deriving the recommendation, "provide rating of strength of recommendations."

- The GRADE approach will provide the framework for establishing evidence foundations and rating strength of recommendations.[6] For each recommendation systematic and transparent assessments are made across the following key factors:
  - Absolute benefit and harms for all patient-important outcomes through structured evidence summaries (e.g. GRADE Summary of Findings tables)[4]
  - Quality of the evidence[7]
  - Values and preferences of patients
  - Resources and other considerations (e.g. feasibility, applicability, equity)

- Each outcome will - if data are available through systematic reviews - include an effect estimate and confidence interval, with a measure of certainty in the evidence, as presented in Summary of Findings tables. If such data are not available narrative summaries will be provided.
- A summary of the underlying reasoning and all additional information (e.g. key factors, practical advice, references) will be available online in an interactive format at www.magicapp.org. This summary will include descriptions of how theory (e.g. pathophysiology) and clinical experience played into the evidence assessment and recommendation development.
- Recommendations will be rated either weak or strong, as defined by GRADE.[8]
- If the panel members disagree regarding evidence assessment or strength of recommendations, we will follow a structured consensus proce customized to the GRADE system and report any final differences in opinion, with their rationale, in the online supplement and online at www.magicapp.org.

6. Articulation of recommendations
"Recommendations should be articulated in a standardized form detailing precisely what the recommended action is, and under what circumstances it should be performed, and so that compliance with the recommendation(s) can be evaluated."

- Each recommendation will appear at the top of the guideline infographic, published in *The BMJ*, and will be available in standardised formats MAGICapp, articulated to be actionable based on best current evidence on presentation formats of guidelines.[9]
- There will be a statement included in each summary article in *The BMJ* and in the MAGICapp that these are recommendations to provide clinicians with guidance. They do not form a mandate of action and should be contextualised in the healthcare system a clinician's works in, and with an individual patient.

7. External review
"External reviewers should comprise a full spectrum of relevant stakeholders...., authorship should be kept confidential....., all reviewer comment should be considered....a rationale for modifying or not should be recorded in writing.... a draft of the recommendation should be made available t general public for comment..."

- At least two external peer-reviewers and one patient reviewer will review the article for *The BMJ* and provide open peer review. Each will have access to all the information in the package. They will be asked for general feedback as well as to make an overall judgement on whether they view the guidelines as trustworthy.
- A *BMJ* series adviser with methodological and/or statistical expertise will review the *BMJ* Rapid Recommendations publication and the systematic reviews.
- The *RapidRecs* panel will be asked to read and respond to the peer review comments and make amendments where they judge reasonable.
- *The BMJ* and *RapidRecs* executive team may, on a case-by-case basis, choose to invite key organizations, agencies, or patient/public representatives to provide and submit public peer-review.
- There will be post-publication public review process through which people can provide comments and feedback through MAGICapp (or through *The BMJ*). The Chair will, on behalf of panel authors, aim to respond to each publicly-available peer-review within 30 days, for a period o six months after publication.

8. Updating
"The date for publication, systematic review and proposed date for future review should be documented, the literature should be monitored regularly and the recommendation should be updated when warranted by new evidence."

- The *RapidRecs* panel will, through monitoring of new research evidence for published *BMJ* Rapid Recommendations, aim to provide updates the recommendations in situations in which the evidence suggests a change in practice. These updates will be initially performed in MAGICapp and submitted to *The BMJ* for consideration of publication of a new Rapid Recommendation.

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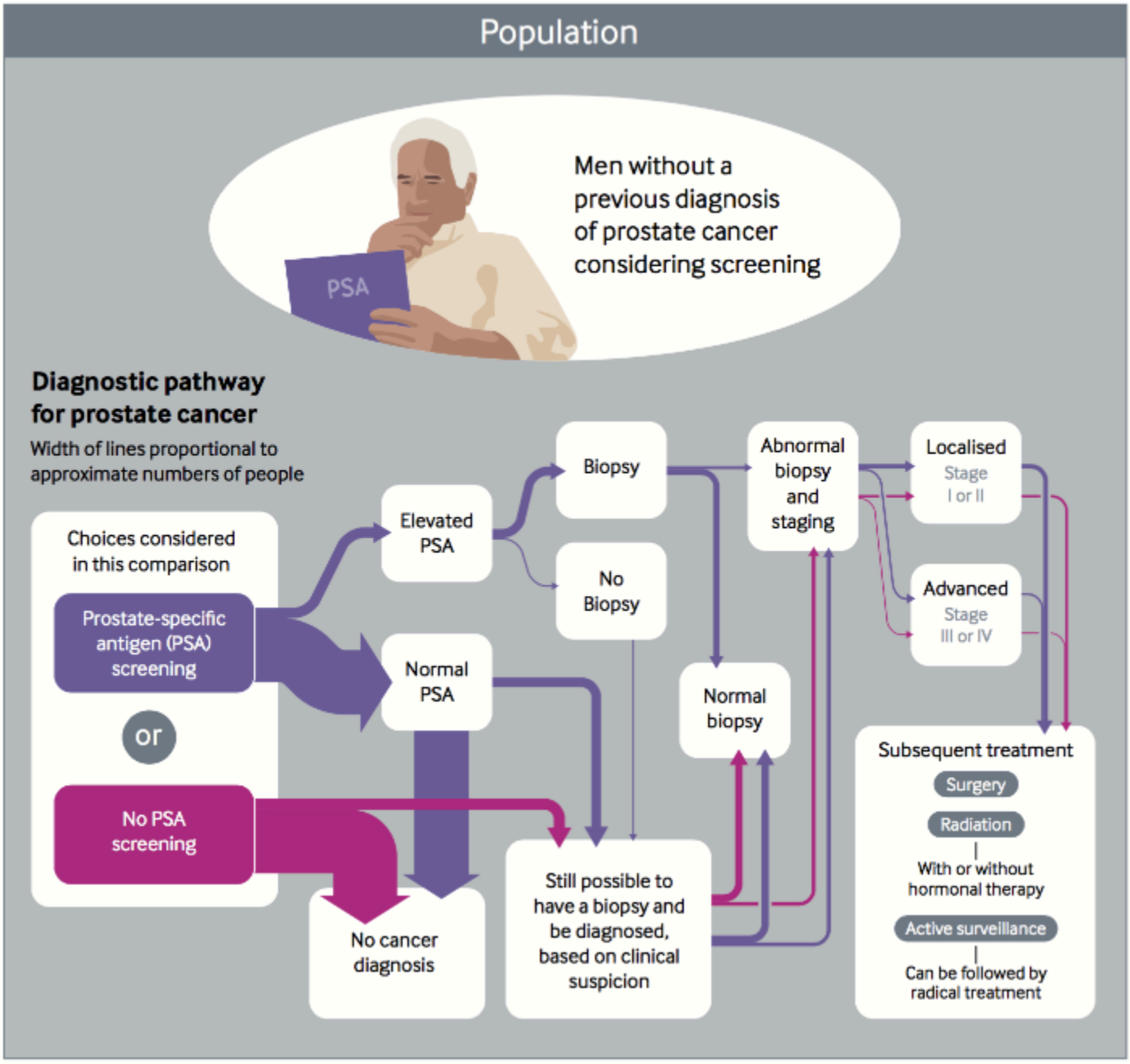
3 - Flow chart of the diagnostic pathway for prostate cancer



See corresponding BMJ Rapid Recommendation: http://www.bmj.com/content/362/bmj.k3581 *[6]*

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[9]

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