Contain guidelines checklist and the supplementaryappendix

Contents of Supplementary appendix

Abbreviations

PCa=prostate cancer

mpMRI=Multiparametric magnetic resonance imaging

TRUS= transrectal ultrasound

PB=prostate biopsy

TB=targeted biopsy

RB=ramdom biopsy

csPCa=clinically significant prostate cancer

ciPCa=clinically insignificant prostate cancer

RTE=real-time sonoelastography

CEUS=contrast-enhanced ultrasonography

TPUS= transperineal ultrasound

PRISMA=Preferred Reporting Items for Systematic Reviews and Meta-analyses

GRADE=Grading of Recommendations Assessment, Development and Evaluation

RCT=randomised controlled trial

IPB=initial prostate biopsy

PNB=previously negative biopsy

ROB=risk of bias

OR=odds ratio

DIC=Deviance Information Criterion (DIC)

NMA=network meta-analysis

SUCRA =surface under the cumulative ranking curve

MCCL=maximum cancer core length

PSA=prostate-specific antigen

DRE =digital rectal examination

na=not available

Appendix 1: Search algorithms

Scopus	
#1	“randomized controlled trial” [Title/Abstract/Keywords]
#2	“controlled clinical trial” [Title/Abstract/Keywords]
#3	“randomized” [Title/Abstract/Keywords]
#4	“randomly” [Title/Abstract/Keywords]
#5	“trial” [Title]
#6	(#1) OR (#2) OR (#3) OR (#4) OR (#5)
#7	“prostate” [Title/Abstract/Keywords]
#8	“prostate neoplasm” [Title/Abstract/Keywords]
#9	“prostate tumour” [Title/Abstract/Keywords]
#10	(#7) OR (#8) OR (#9)
#11	“biopsy” [Title/Abstract/Keywords]
#12	“prostate biopsy”[Title/Abstract/Keywords]
#13	(#11) OR (#12)
#14	“transrectal ultrasound” [Title/Abstract/Keywords] OR “transrectal ultrasonography” [Title/Abstract/Keywords]
#15	“systematic biopsy” [Title/Abstract/Keywords]
#16	“TRUS” [Title/Abstract/Keywords]
#17	“transperineal ultrasound” [Title/Abstract/Keywords] OR “transperineal ultrasonography” [Title/Abstract/Keywords]
#18	“TPUS” [Title/Abstract/Keywords]
#19	“elastography” [Title/Abstract/Keywords] OR “real-time sonoelastography” [Title/Abstract/Keywords] OR “shear-wave elastography” [Title/Abstract/Keywords] OR “magnetic resonance elastography” [Title/Abstract/Keywords]
#20	“magnetic resonance imaging” [Title/Abstract/Keywords]
#21	“MR” [Title/Abstract] OR “MRI” [Title/Abstract/Keywords]
#22	“fusion” [Title/Abstract/Keywords] OR “registration” [Title/Abstract/Keywords] OR “targeted” [Title/Abstract/Keywords] OR “target” [Title/Abstract/Keywords] OR “computer” [Title/Abstract/Keywords] OR “software” [Title/Abstract/Keywords]
#23	“contrast-enhanced ultrasound” [Title/Abstract/Keywords]
#24	“CEUS” [Title/Abstract/Keywords]
#25	“saturation biopsy” [Title/Abstract/Keywords]
#26	“mapping biopsy” [Title/Abstract/Keywords]
#27	(#14) OR (#15) OR (#16) OR (#17) (#18) OR (#19) OR (#20) OR (#21) OR (#22) OR (#23) OR (#24) OR (#25) OR (#26)
1094	

Medline	
#1	“randomized controlled trial” [Publication Type]
#2	“controlled clinical trial” [Publication Type]
#3	“randomized” [Title/Abstract]
#4	“randomly” [Title/Abstract]
#5	“trial” [Title]
#6	“Randomized Controlled Trial as Topic” [MeSH]
#7	(#1) OR (#2) OR (#3) OR (#4) OR (#5) OR (#6)
#8	“prostate” [Title/Abstract]
#9	“prostate neoplasm” [Title/Abstract]
#10	“prostate tumour” [Title/Abstract]
#11	“prostate” [Mesh]
#12	“prostatic neoplasms” [Mesh]

#13	(#8) OR (#9) OR (#10) OR (#11) OR (#12)
#14	“biopsy” [Title/Abstract]
#15	“prostate biopsy”[Title/Abstract]
#16	“biopsy” [Mesh]
#17	(#14) OR (#15) OR (#16)
#18	“transrectal ultrasound” [Title/Abstract] OR “transrectal ultrasonography” [Title/Abstract]
#19	“systematic biopsy” [Title/Abstract]
#20	“TRUS” [Title/Abstract]
#21	“transperineal ultrasound” [Title/Abstract] OR “transperineal ultrasonography” [Title/Abstract]
#22	“TPUS” [Title/Abstract]
#23	“elastography” [Title/Abstract] OR “real-time sonoelastography” [Title/Abstract] OR “shear-wave elastography” [Title/Abstract] OR “magnetic resonance elastography” [Title/Abstract]
#24	“magnetic resonance imaging” [Title/Abstract]
#25	“MR” [Title/Abstract] OR “MRI” [Title/Abstract]
#26	“fusion” [Title/Abstract] OR “registration” [Title/Abstract] OR “targeted” [Title/Abstract] OR “target” [Title/Abstract] OR “computer” [Title/Abstract] OR “software” [Title/Abstract]
#27	“contrast-enhanced ultrasound” [Title/Abstract]
#28	“CEUS” [Title/Abstract]
#29	“saturation biopsy” [Title/Abstract]
#30	“mapping biopsy” [Title/Abstract]
#31	(#18) OR (#19) OR (#20) OR (#21) OR (#22) OR (#23) OR (#24) OR (#25) OR (#26) OR (#27) OR (#28) OR (#29) OR (#30)
#32	(#7) AND (#13) AND (#17) AND (#31)
285	

Embase	
#1	‘randomized controlled trial’/exp: ti,ab,kw
#2	‘randomized controlled trial (topic)’/exp: ti,ab,kw
#3	random *: ti,ab,kw
#4	#1 OR #2 OR #3
#5	‘prostate’: ti,ab,kw
#6	‘prostate’/exp: ti,ab,kw: ti,ab,kw
#7	‘prostate neoplasm’/exp: ti,ab,kw
#8	‘prostate cancer’/exp: ti,ab,kw
#9	‘prostate carcinoma’/exp: ti,ab,kw
#10	#1 OR #2 OR #3
#11	‘biopsy’ /exp: ti,ab,kw
#12	‘prostate biopsy’ /exp: ti,ab,kw
#13	‘biopsy’ /exp: ti,ab,kw
#14	#11 OR #12 OR #13
#15	‘transrectal ultrasound’ /exp: ti,ab,kw OR ‘transrectal ultrasonography’ /exp: ti,ab,kw
#16	‘systematic biopsy’ /exp: ti,ab,kw
#17	‘TRUS’ /exp: ti,ab,kw
#18	‘transperineal ultrasound’ /exp: ti,ab,kw OR ‘transperineal ultrasonography’ /exp: ti,ab,kw
#19	‘TPUS’ /exp: ti,ab,kw
#20	‘elastography’ /exp: ti,ab,kw OR ‘real-time sonoelastography’ /exp: ti,ab,kw OR ‘shear-wave elastography’ /exp: ti,ab,kw OR ‘magnetic resonance elastography’ /exp: ti,ab,kw
#21	‘magnetic resonance imaging’ /exp: ti,ab,kw

#22	'MR' /exp: ti,ab,kw OR 'MRI' /exp: ti,ab,kw
#23	'fusion' /exp: ti,ab,kw OR 'registration' /exp: ti,ab,kw OR 'targeted' /exp: ti,ab,kw OR 'target' /exp: ti,ab,kw OR 'computer' /exp: ti,ab,kw OR 'software' /exp: ti,ab,kw
#24	'contrast-enhanced ultrasound' /exp: ti,ab,kw
#25	'CEUS' /exp: ti,ab,kw
#26	'saturation biopsy' /exp: ti,ab,kw
#27	'mapping biopsy' /exp: ti,ab,kw
#28	(#15) OR (#16) OR (#17) OR (#18) OR (#19) OR (#20) OR (#21) OR (#22) OR (#23) OR (#24) OR (#25) OR (#26) OR (#27)
#29	(#4) AND (#10) AND (#14) AND (#28)
317	

Cochrane Library Central	
#1	prostate: ti, ab, kw (Word variations have been searched)
#2	prostate neoplasm: ti, ab, kw (Word variations have been searched)
#3	prostate tumour: ti, ab, kw (Word variations have been searched)
#4	Mesh descriptor: [Prostatic Neoplasms] explode all trees
#5	(#1) OR (#2) OR (#3) OR (#4)
#6	biopsy: ti, ab, kw (Word variations have been searched)
#7	prostate biopsy: ti, ab, kw (Word variations have been searched)
#8	Mesh descriptor: [Biopsy] explode all trees
#9	(#6) OR (#7) OR (#8)
#10	(transrectal ultrasound OR transrectal ultrasonography): ti, ab, kw (Word variations have been searched)
#11	systematic biopsy: ti, ab, kw (Word variations have been searched)
#12	TRUS: ti, ab, kw (Word variations have been searched)
#13	(transperineal ultrasound OR transperineal ultrasonography): ti, ab, kw (Word variations have been searched)
#14	TPUS: ti, ab, kw (Word variations have been searched)
#15	(elastography OR Real-time sonoelastography OR shear-wave elastography OR magnetic resonance elastography): ti, ab, kw (Word variations have been searched)
#16	magnetic resonance imaging: ti, ab, kw (Word variations have been searched)
#17	(MR OR MRI): ti, ab, kw (Word variations have been searched)
#18	(fusion OR registration OR targeted OR target OR computer OR software): ti, ab, kw (Word variations have been searched)
	contrast-enhanced ultrasound: ti, ab, kw (Word variations have been searched)
#20	CEUS: ti, ab, kw (Word variations have been searched)
#21	saturation biopsy: ti, ab, kw (Word variations have been searched)
#22	mapping biopsy: ti, ab, kw (Word variations have been searched)
#23	(#10) OR (#11) OR (#12) OR (#13) OR (#14) OR (#15) OR (#16) OR (#17) OR (#18) OR (#19) OR (#20) OR (#21) OR (#22)
#32	(#5) AND (#9) AND (#23)
#33	73

International trial registers	
484	www.clinicaltrials.gov
40	www.anzctr.org.au
69	www.controlled-trials.com
17	www.umin.ac.jp/ctr/index.htm
0	www.chictr.org.cn

64	www.who.int/ictrp/zh
674	

Appendix 2: Summary of statistical analysis

The statistical analyses are presented in detail in the published protocol, which is available in the international database of prospectively registered systematic reviews, PROSPERO. Initially, we conducted a pair-wise meta-analysis by synthesizing datasets from at least two trials that compared the same interventions using a random-effects model, which assumes that different studies assessed different yet related treatment effects.[1] As all results were extracted as binary outcomes, we estimated relative treatment effects of the competing interventions by using odds ratio (OR). A OR below 1 indicated that the intervention was associated with a lower risk of the outcome (overall PCa detection rate, csPCa detection rate, ciPCa detection rate, positive core rate and adverse events rate) than the comparator while a OR above 1 indicated that the intervention was associated with a great risk of the outcome than the comparator. In network meta-analysis we assume that heterogeneity is the same for all treatment comparisons. We used the restricted maximum likelihood method to estimate heterogeneity assuming a common estimate for the heterogeneity variance across the different comparisons. We also computed the I-squared and its 95% CI that shows the percentage of variation that is not attributed to random error. The assessment of statistical heterogeneity in the entire network was based on the magnitude of the heterogeneity variance parameter estimated from the network meta-analysis models.
To incorporate indirect comparisons with direct comparisons, we conducted random-effects Bayesian network meta-analyses using Markov chain Monte Carlo methods in WinBUGS 1.4.3 (MRC Biostatistics Unit, Cambridge, UK) using methods described by Lu and Ades[2] and the statistical model suggested by Dias et al[3]. A key assumption of network meta-analysis is that of transitivity; one can learn about the relative effectiveness between two interventions indirectly. Disagreement between direct and indirect evidence challenges the transitivity assumption.[4] Model fit was evaluated using the total residual deviance, which indicated good fit if it approximated the number of data points.[5] For evaluating the global inconsistency, we present the the number of data points, Residual deviance (posterior mean) and the Deviance Information Criterion (DIC) of the NMA model. The mean posterior residual deviance should approximate the number of data points for models with good fit to the data. The DIC is a Bayesian model evaluation criterion that measures model fit adjusted with complexity of the model; smaller DIC values correspond to more preferable models. To evaluate the presence of inconsistency locally we used the loop-specific approach which evaluates the difference between direct and indirect estimates for a specific comparison in the loop (inconsistency factor).[6] We assumed a common heterogeneity estimate within each loop.[7] This “node-splitting” method excludes one direct comparison at a time and estimates the indirect treatment effect for the excluded comparison.
The relative ranking probabilities for all interventions of being at each possible rank were estimated; while the treatment hierarchy of the competing interventions was obtained by using rankograms, the surface under the cumulative ranking curve (SUCRA) and mean ranks.[8,9] SUCRA expresses as a percentage the efficacy or safety of each intervention relative to an imaginary intervention that is always the best without uncertainty[9,10] A SUCRA of 80% means that the intervention of interest achieves 80% of the effectiveness of this imaginary intervention. The larger the SUCRA value for an intervention, the more effective the intervention is. Finally, we performed subgroup and sensitivity analyses according to characteristics of the studies (bias, patients number), characteristics of the patients (mean age, mean PSA and country) and characteristics of the interventions (imaging procedure, anatomic approaches). Sensitivity analyses were also performed to verify the stability of results with alternative statistical models and priors distribution. These included: (a) frequentist network meta-analysis; (b) fixed-effect Bayesian network model; (c) worst-case scenario analysis; (d) use of vague priors in Bayesian random effect network meta-analysis.

Bayesian network meta-analysis code (with data) for categorical outcome

```
# Binomial likelihood, logit link
# Random effects model for multi-arm trials
model{              # *** PROGRAM STARTS
for(i in 1:ns){     # LOOP THROUGH STUDIES
w[i,1] <- 0         # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0     # treatment effect is zero for control arm
```

```
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
#Deviance contribution
dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])) + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k]))) }
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]]) for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions (with multi-arm trial correction)
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment for multi-arm RCTs
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
   }
}
totresdev <- sum(resdev[]) # Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
# vague priors for treatment effects
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }
sd ~ dunif(0,5)    # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
# Provide estimates of treatment effects T[k] on the natural (probability) scale
# Given a Mean Effect, meanA, for 'standard' treatment A,
# with precision (1/variance) precA
A ~ dnorm(meanA,precA)
for (k in 1:nt) { logit(T[k]) <- A + d[k] }
# Extra code for all odds ratios and log odds ratios, ranking, and absolute effects, and relative effects
# on alternative scales: Numbers Needed to Treat, Risk Difference, Relative Risks
# pairwise ORs and LORs for all possible pair-wise comparisons, if nt>2
for (c in 1:(nt-1))            {
for (k in (c+1):nt)      {
or[c,k] <- exp(d[k] - d[c]) lor[c,k] <- (d[k]-d[c])
                                                                    }
                                                                }
# ranking on relative scale
for (k in 1:nt) {
rk[k] <- nt+1-rank(d[],k) # assumes events are “good”
# rk[k] <- rank(d[],k) # assumes events are “bad”
best[k] <- equals(rk[k],1) #calculate probability that treat k is best
}

# Inits Random Effects (Informative)
#chain 1
```

list(d=c(NA,1.5,2,1,1,1.5,0,.5,1.5,0,1.5), var=1.5, mu=c(0,1,.5,.5,1,1.5,.5,.5,.5,.5,.5,1.5,1,1,2,.5,2,.5,1,1.5,2,1,1,1))
#chain 2
list(d=c(NA,1,1.5,0,1.5,0,0,0,1,.5,1), var=1.5, mu=c(1.5,1,0,2,.5,.5,0,1.5,1,0,1.5,2,0,2,1,1,.5,1,1,1.5,.5,1.5,1,1))
#chain 3
list(d=c(NA,.5,1,1.5,1,.5,.5,1,1.5,1.5,2), var=1.5, mu=c(1,.5,1,0,1.5,1.5,0,.5,.5,1,1,.5,1.5,0,.5,.5,0,2,1.5,1.5,1,.5,1.5,1))

WinBUGs Data Table and List Statement

Study ID	Study Name	t[,1]	r[,1]	n[,1]	t[,2]	r[,2]	n[,2]	na[]
1	Baco 2016	1	48	89	5	51	86	2
2	Arsov 2015	5	41	104	6	39	106	2
3	Tonttila 2016	1	34	60	10	34	53	2
4	Panebianco 2015	4	215	570	10	440	570	2
5	Koh 2015	2	21	26	7	18	26	2
6	Guo 2015	1	53	166	3	61	173	2
7	Zhang 2014	1	76	218	7	81	213	2
8	Irani 2013	1	71	169	4	81	166	2
9	Brock 2012	1	69	175	2	91	178	2
10	Byung 2011	1	4	41	10	13	44	2
11	Chae 2009	1	22	100	3	29	100	2
12	Rochester 2009	1	63	122	4	50	122	2
13	Takenaka 2008	1	53	100	3	47	100	2
14	Hara 2008	1	58	120	3	53	126	2
15	Eggert 2008	1	61	162	2	76	189	2
16	Naughton 2000	1	33	122	8	32	122	2
17	Kim 2004	1	21	122	8	17	118	2
18	Emiliozzi 2004	3	55	107	11	41	107	2
19	Paul 2005	1	40	100	8	32	100	2
20	Taverna 2016	4	26	100	10	24	100	2
21	Rosette 2009	1	49	128	8	45	132	2
22	Lecuona 2010	8	54	151	9	58	152	2
23	Covarrubias 2011	1	23	75	4	36	75	2
24	Porpiglia 2016	1	31	105	5	54	107	2

"t" is treatment arm, with each treatment-type assigned a number. The TRUS(10-12) BP arm is assigned the number 1. "r" is the number of events in the treatment or control arm. "n" is the total number of **patients** in the particular treatment or control arm.

Appendix 3: Description of included studies

Table1. Study characteristic

Authors	Major inclusion criteria	Major exclusion criteria	Definition of csPCa
Baco et al (2016)	(1) Age <75 yr; (2) Total PSA increase to 4–20ng/mL and/or abnormal DRE; (3) no previous prostate biopsy; (4) signed informed consent.	(1) Previous prostate biopsy or MRI of the prostate; (2) contraindication to MRI; (3) no signed informed consent.	Clinically insignificant cancer was defined as MCCL <5mm for Gleason 6 cancer
Arsov et al (2015)	(1) Patients had at least one negative BP; (2) persistent serum PSA levels >4 ng/mL	(1) Known PCa; (2) contraindication to MRI or biopsy; (3) prior MRI-guided biopsy	Gleason score > 7
Tonttila et al (2016)	(1) Age between 40 and 72 yr; (2) Total PSA <20 ng/mL or free-to-total PSA ratio 0.15 and PSA <10 ng/mL in repeated measurements; (3) no evidence of PSA increase by noncancer- ous factors, such as catheterization, bladder stones, or urinary tract infection including bacterial prostatitis; (4) signed informed consent.	(1) Known contraindication for MRI examination; (2) previous prostate biopsy or prostate surgery; (3) abnormal DRE by referring doctors	Gleason score >3 + 3, more than two positive cores, or MCCL >3 mm
Panebianco et al (2015)	(1) Total PSA level >4 ng/mL; (2) PSA density >0.15; (3) PSA velocity >0.75 ng/mL/y; (4) Free/total PSA ratio <0.10 when PSA level was between 4 and 10 ng/mL.	Patients who previously underwent a prostate biopsy	Gleason score > 7
Koh et al (2015)	(1) PSA level of 2.5 to 4.0 ng/mL and DRE or TRUS results; (2) serum PSA level >4.0 ng/mL regardless of DRE or TRUS results.	(1) Patients with a history of transurethral resection of the prostate; chemotherapy or radiotherapy for prostate cancer; prostatitis or upper urinary tract infection; (2) ingredients in SonoVue; (3) left- to-right shunt, severe pulmonary hypertension, uncontrolled systemic hypertension or adult respiratory distress syndrome.	NA
Guo et al (2015)	(1) Total PSA > 4.0 ng/mL for at least twice; (2) abnormal DRE.	(1) Age >80 yr; (2) unable to communicate effectively; (3) with a previous history of PCa or repeated biopsy; (4) with symptoms of urinary tract infection, acute urinary retention; (5) coagulation disorders.	NA
Zhang et al (2014)	(1) Total PSA level >10 ng/mL (b) abnormal PSA density, Free/total PSA ratio when total PSA level was between 4 and 10 ng/mL; (3) abnormal DRE.	NA	NA
Irani et al (2013)	(1) PSA level of 3 to 20 ng/mL and no nodule on DRE (T1c or possible T2a stage) undergoing a first TRUS PB	Previous 5-reductase inhibitor use or androgen deprivation therapy.	NA

Brock et al (2012)	NA	(1) Men who underwent previous prostate biopsies, had prior surgical or antiandrogen therapy; (2) men were diagnosed with prostatitis within 4 weeks before biopsy.	NA
Byung et al (2011)	(1) Men between 37 and 92 yr with an abnormal DRE or high PSA levels.	No patients had undergone any treatments for PCa before biopsy.	NA
Chae et al (2009)	NA	NA	NA
Rochester et al (2009)	(1) Normal DRE and PSA <20 ng/mL but over the age-specific threshold with no previous biopsy were included.	NA	NA
Takenaka et al (2008)	(1) PSA over 4ng/mL and/or abnormal findings by DRE or TRUS	All men had not previously undergone PB.	NA
Hara et al (2008)	(1) PSA level of 4.0 to 20.0 ng/mL; (2) no previous prostate biopsy, no history of prostate cancer; (3) no clinical evidence of acute or chronic prostatitis.	NA	NA
Eggert et al (2008)	The indication for biopsy was abnormal DRE in 25% or suspicious PSA elevation in 75%.		NA
Naughton et al (2000)	(1) PSA level of 2.5 to 20 ng/mL; (2) DRE findings were suspicious for prostate cancer.	Men with clinical prostatitis within 1 month of biopsy or active urinary tract infection, or who did not complete the self-administered questionnaire	NA
Kim et al (2004)	(1) PSA level of 4.0 to 20.0 ng/mL; (2) no previous prostate biopsy; (3) no history of prostate cancer; (4) no clinical evidence of acute or chronic prostatitis.	NA	NA
Emiliozzi et al (2004)	Total PSA >4 ng/mL.	Presence of acute urinary retention, with an indwelling catheter, with recent (within 3 months) acute prostatitis or previous prostate biopsy.	NA
Paul et al (2005)	(1) PSA was between 2.5 ng/ml. and 20 ng/ml; (2) DRE findings were suspicious for prostate cancer.	NA	NA
Taverna et al (2016)	(1) Asymptomatic patients with a negative DRE and a first previous negative biopsy (at least performed 6 months before); (2) PSA higher than>4 ng/ml; (3) None of the patients had previously undergone prostatic adenomectomy.	Presence of acute infection and MRI discomfort, patient having undergone treatment with finasteride or dutasteride, clinical prostatitis within 3 months before biopsy and active urinary tract infection.	Gleason score > 7
Rosette et al (2009)	(1) age dependent increased serum PSA (1.25 ng/ml or greater at ages less than 50 years, 1.75 or greater at ages 50 to less than 60 years, 2.25 or greater at ages 60 to less than 70 years and 3.25 or greater at ages 70 years or greater); (2) positive DRE; (3) suspicious TRUS.	Men with signs of prostatitis, urinary tract infection or acute urinary retention within the previous month and patients on PSA altering medicine (5-reductase inhibitors) within the previous 6 months.	NA

Lecuona et al (2010)	Total PSA level > 2.5 ng/mL.	Previous prostate biopsy or surgery, previous diagnosis of prostate cancer, a history of urinary retention, previous histological evidence of prostatitis and confirmed urinary tract infection	NA
Covarrubias et al (2011)	(1) age 45 to 75 years, 2) abnormal digital rectal examination and/or prostate specific antigen 4 to 20 ng/ml, and 3) no previous biopsy.	(1) previous PCa diagnosis; (2) PSA greater than 20 ng/ml; (3) clinical stage T3 or T4 and 4) previous 5-reductase inhibitor use (finasteride or dutasteride) or androgen deprivation therapy.	Clinically insignificant cancer was defined as maximum cancer core length (MCCL) <5mm for Gleason 6 cancer
Porpiglia et al (2016)	Biopsy-naive patients with suspected PCa (total PSA ≤15 ng/ml and negative DRE findings).	NA	NA

Table 2. Treatment characteristic

Authors	**Imaging machine**	**Score used in MRI**	**Threshold for TB**	**route**	**Navigation system**
Baco et al (2016)	1.5-T Avanto scanner (Siemens, Erlangen) without an endorectal coil.	PIRADS	MRI/TRUS: PIRADS 3–5; TRUS (10-12): Palpable and/or TRUS suspicious lesion.	TR/TR	MRI/TRUS: Accuvix-V10 ultrasound machine with an end-firing three-dimensional transrectal transducer (Medison, Seoul, Korea) for TB; TRUS: BK-Medical model 1846 ultrasound unit and a biplanar 5–10-MHz side-firing transducer (model 8531; BK-Medical, Herlev, Denmark).
Arsov et al (2015)	3-T (Magnetom Trio; Siemens, Erlangen,) with a six-channel phased-array body coil.	5-point Likert scale for each MRI sequence	5-point Likert scale for each MRI sequence: Intraprostatic lesion with a total score ≥10 (up to April 2012) or a PSsum ≥10 (after April 2012)	TR/TR	MRI-In bore: a needle guide fixed to a portable biopsy device (DynaTRIM; Invivo, Gainesville, FL, USA) using an MRI-compatible and 18G fully automatic biopsy gun (Invivo); MRI/TRUS: Urostation device (Koelis, La Tronche, France) for TB and 18G fully automatic biopsy gun (Bard Medical, Karlsruhe, Germany) for RB.
Tonttila et al (2016)	3-T MRI scanner (Magnetom Skyra; Siemens AG, Munich, Germany) with body and spine matrix surface coils.	16-region standardized prostate MRI reporting scheme	Probably cancer (abnormal focus seen on T2-weighted and DWI with abnormal finding on the ADC map) and highly suspicious of cancer (abnormal focus seen on T2-weighted and DWI with abnormal finding on the ADC map and increased enhancement with or without washout).	TR/TR	MRI-Cognitive: a diagrammatic report was used for TRUS-guided targeting; TRUS: TRUS-guided RB using 18G needles (BK Medical 2101 Falcon device with 8808 side-fire probe; BK Medical, Herlev, Denmark).

Panebianco et al (2015)	3-T magnet (Discovery MR750, GE Healthcare, Milwaukee, and MAGNETOM Verio Siemens Medical Solutions) with a phased-array coil and an endorectal coil.	PI-RADS	In patients with 2 or more dubious foci of PCa with different PI-RADS scores, the zone assumed to be the index lesion to which to direct the biopsy was the one with the higher PI-RADS score. In patients with 2 or more foci suggestive of PCa with the same PI-RADS score, the area reported to be the index lesion was the one with the lower apparent diffusion coefficient (ADC) values.	TR/TR	NA
Koh et al (2015)	CEUS: Cadence contrast pulse sequencing technology (Siemens Medical Solutions) was used with SonoVue (Bracco, Milan, Italy) as a contrast agent; ELA: eSie Touch Elasticity Imaging (Siemens Medical Solutions) technology.	NA	CEUS: rapid contrast enhancement or increased contrast enhancement relative to the surrounding parenchyma and asymmetric appearance of intraprostatic vessels compared with the contralateral lobe of the prostate on same image. RTE: NA	TR/TR	US imaging and biopsy of the prostate were performed using a 4- to 9-MHz transrectal probe (Acuson S2000 or S3000, Siemens Medical Solutions, Mountain View, CA, USA) and an 18-gauge biopsy gun.
Guo et al (2015)	NA	NA	NA	TR/TP	TPUS: real-time ultrasound guidance (EUB-6500; Hitachi Medical Systems Japan), using a transrectal biplanar transducer. TRUS: transrectal end-fire transducer for TRBx
Zhang et al (2014)	CEUS: Cadence contrast pulse sequencing technology (Siemens Medical Solutions) with SonoVue (Bracco, Milan, Italy) as a contrast agent.	NA	CEUS: rapid contrast enhancement or increased contrast enhancement relative to the surrounding parenchyma and asymmetric appearance of intraprostatic vessels compared with the contralateral lobe of the prostate on same image. TRUS:NA	TR/TR	TRUS: TRUS-guided RB using 18G needles (BK Medical 2101 Falcon device with 8808 side-fire probe; BK Medical, Herlev, Denmark).
Irani et al (2013)	NA	NA	NA	TR/TR	An ultrasound device with a 7.5 MHz biplane probe and an 18-gauge biopsy gun was used to obtain the prostatic tissue
Brock et al (2012)	ELA: NA	NA	ELA: Areas of reduced elasticity in each sector, displayed as blue lesions using RTE, were regarded as suspicious for cancer (fig.	TR	TRUS: ultrasound examination using an EUB-7500HV (Hitachi Medical, Tokyo, Japan) transrectal end fire probe (V53W 7.5 MHz).
Byung et al (2011)	MRI-cognitive: 3-T unit (Intera Achieva, Philips Healthcare)	NA	A target biopsy was performed if one or more of these MR images were positive for a cancer. On T2-weighted imaging, a cancer was defined as a hypointense region relative to the adjacent parenchyma. On apparent diffusion coefficient (ADC) map images obtained from DWI (b values of 0 and 1000 s/mm2), a cancer was defined as a region with a low ADC value relative to the adjacent parenchyma. On DCE-MRI, a cancer was defined as a region with early wash-in and wash-out of contrast	TR/TR	TRUS: transrectal ultrasound (IU22, Philips Healthcare).

			material relative to the adjacent parenchyma. The cancer was localized at one or more segments that were divided by imaginary lines according to 10- or 12-core systematic biopsy: right and left; base, midgland, and apex; medial and lateral segments.		
Chae et al (2009)	NA	NA	NA	TP/TR	TPUS: transrectal ultrasound Logiq5pro (General Electrics, Milwaukee, USA) with a 10 MHz biplane probe and and 18-gauge biopsy gun.
Rochester et al (2009)	NA	NA	NA	TR	Biopsies were performed using a B-K Medical 7.5-MHz probe (B-K Medical, White Waltham, UK) and an 18-gauge Angiotech (Taunton, Somerset, UK) Uro II biopsy needle.
Takenaka et al (2008)	NA	NA	NA	TP/TR	TP biopsy was guided by TRUS (SSD-2000; Aloka, Tokyo, Japan), a TR linear probe (UST-672-5/7.5, 7.5MHz; Aloka) with an attachment for needle guidance was used for this procedure; TR: using the same ultrasonographic guidance. A TR radial probe (UST-670P-5, 5MHz, Aloka) with a needle-guidance attachment was used for this procedure. We
Hara et al (2008)	NA	NA	NA	TP/TR	The transperineal and transrectal approaches were both performed with TRUS guid- ance (SSD-2000, Aloka, Tokyo, Japan). For the transperineal approach, a 5 to 7.5-MHz linear probe (UST-672-5/7.5, Aloka) was used, and a 5.0-MHz convex probe (UST-670P-5, Aloka) was used for the transrectal approach. With either approach, an 18-gauge Tru-Cut needle with a cutting length of 22 mm was used.
Eggert et al (2008)	NA	NA	ELA: Areas of reduced elasticity in each sector, displayed as blue lesions using RTE, were regarded as suspicious for cancer (fig.	TR/TR	TRUS: Voluson 730 ultrasound system (GE Medical).
Naughton et al (2000)	NA	NA	NA	TR/TR	TRUS: automatic spring loaded 18 gauge needle under transrectal ultrasound guidance using a 7 MHz. transrectal transducer.
Kim et al (2004)	NA	NA	NA	TR/TR	NA

Emiliozzi et al (2004)	NA	NA	NA	TR/TP	TPUS: 23 mm Biopty (Bard, Covington, Georgia)
Paul et al (2005)	NA	NA	NA	TR/TR	TRUS: ATL HDI 1000 multiplanar 5–9 MHz probe and the Topnotch automatic 18-gauge biopsy gun (Microvasive, Boston Scientific).
Taverna et al (2016)	1.5-T using an endorectal coil or at 3-T with or without an endorectal coil.	PI-RADS 2	NA	TR	An ESAOTE MyLab 75 with a 7.5-MHz endfire probe and an 18-gauge biopsy needle
Rosette et al (2009)	NA	NA	NA	TR	An ultrasound device with a 7.5 MHz biplane probe equipped with dual 10R convex heads was used. Biopsies were taken without anesthesia with a spring loaded, 18 gauge * 21 cm TruPath™ biopsy device
Lecuona et al (2010)	NONE	NA	NA	TR	Toshiba diagnostic ultrasound machine with a 6-MHz transrectal probe
Covarrubias et al (2011)	NA	NA	NA	TR/TR	NA
Porpiglia et al (2016)	1.5-T scanner using a 32-channel phase array coil or four-channel phase array coil combined with an endorectal coil.	PI-RADS	MRI/TRUS: PIRADS 3–5	mixed	MRI/TRUS: TB was performed using the BioJet fusion system (D&K Technolo- gies, Barum, Germany). TRUS: Hawk Ultrasound scanner 2102 EXL with a biplanar transducer (B-K Medical, Herlev, Denmark). 18-gauge biopsy gun with a specimen size of 18–22 mm (Bard Medical, Covington, GA, USA).

Table 3. Results of individual studies

Authors	**Methodology recruitment**	**Overall PCa detection rate**				**Clinically significant PCa detection rate**				**Clinically insignificant PCa detection rate**				**Positive core rate**			
		r1	**n1**	**r2**	**n2**	**r1**	**n1**	**r2**	**n2**	**r1**	**n1**	**r2**	**n2**	**r1**	**n1**	**r2**	**n2**
Baco et al (2016)	TRUS(10-12) vs MRI/TRUS	48	89	51	86	44	89	33	86	4	89	18	86	-	-	-	-
Arsov et al (2015)	MRI/TRUS vs MRI-in bore	41	104	39	106	33	104	31	106	8	104	8	106	112	1248	98	560
Tonttila et al (2016)	TRUS(10-12) vs MRI-cognitive	34	60	34	53	27	60	29	53	7	60	5	53	-	-	-	-
Panebianco et al (2015)	MRI-cognitive vs TRUS(>12)	440	570	215	570	-	-	-	-	-	-	-	-	-	-	-	-

Koh et al (2015)	RTE vs CEUS	21	26	18	26	-	-	-	-	-	-	-	-	28	171	71	624
Guo et al (2015)	TRUS(10-12) vs TPUS	53	166	61	173	33	166	43	173	18	166	18	173	221	1768	266	1913
Zhang et al (2014)	TRUS(10-12) vs CEUS	76	218	81	213	-	-	-	-	-	-	-	-	301	2616	369	2025
Irani et al (2013)	TRUS(10-12) vs TRUS(>12)	71	169	81	166	-	-	-	-	-	-	-	-	286	1000	260	1125
Brock et al (2012)	TRUS(10-12) vs RTE	69	175	91	178	32	175	35	178	37	175	56	178	29	794	111	612
Byung et al (2011)	TRUS(10-12) vs MRI-cognitive	4	41	13	44	-	-	-	-	-	-	-	-	11	432	52	527
Chae et al (2009)	TRUS(10-12) vs TPUS	22	100	29	100	-	-	-	-	-	-	-	-	-	-	-	-
Rochester et al (2009)	TRUS(10-12) vs TRUS(>12)	63	122	50	122	51	122	48	122	25	122	19	122	-	-	-	-
Takenaka et al (2008)	TRUS(10-12) vs TPUS	53	100	47	100	-	-	-	-	-	-	-	-	178	1000	154	1054
Hara et al (2008)	TRUS(10-12) vs TPUS	58	120	53	126	-	-	-	-	-	-	-	-	208	1440	207	1512
Eggert et al (2008)	TRUS(10-12) vs RTE	61	162	76	189	21	162	28	189	40	162	48	189	-	-	-	-
Naughton et al (2000)	TRUS(10-12) vs TRUS(<10)	33	122	32	122	-	-	-	-	-	-	-	-	-	-	-	-
Kim et al (2004)	TRUS(10-12) vs TRUS(<10)	21	122	17	118	-	-	-	-	-	-	-	-	-	-	-	-
Emiliozzi et al (2004)	TPUS vs TRUS(<10)	55	107	41	107	-	-	-	-	-	-	-	-	-	-	-	-
Paul et al (2005)	TRUS(10-12) vs TRUS(<10)	40	100	32	100	-	-	-	-	-	-	-	-	-	-	-	-
Taverna et al (2016)	TRUS(>12) vs MRI-cognitive	26	100	24	100	12	100	15	100	14	100	9	100	-	-	-	-
Rosette et al (2009)	TRUS(10-12) vs TRUS(<10)	49	128	45	132	-	-	-	-	-	-	-	-	-	-	-	-
Lecuona et al (2010)	TRUS(Vienna nomogram) vs TRUS(<10)	58	152	54	151	-	-	-	-	-	-	-	-	-	-	-	-
Covarrubias et al (2011)	TRUS(10-12) vs TRUS(>12)	23	75	36	75	20	75	27	75	3	75	9	75	328	1350	232	900
Porpiglia et al (2016)	TRUS(10-12) vs MRI/TRUS	31	105	54	107	19	105	47	107	12	105	7	107	-	-	-	-

“t” is treatment arm, with each treatment-type assigned a number. The TRUS(10-12) PB arm is assigned the number 1. “r” the number of events in the treatment or control arm. “n” is the total number of patients in the particular treatment or control arm

Table 4. Adverse events of individual studies

Authors	Methodology recruitment	Intervention	Control
Baco et al (2016)	MRI/TRUS vs. TRUS(10-12)	None	None
Arsov et al (2015)	MRI in-bore vs. MRI/TRUS	2 (1.9%) suffered from febrile prostatitis requiring hospitalization and intravenous antibiotic therapy	1 (1.0%) suffered from febrile prostatitis requiring hospitalization and intravenous antibiotic therapy
Tonttila et al (2016)	MRI-Cognitive vs. TRUS	One patient collapsed after the biopsy procedure and experienced a minor head injury.	
Panebianco et al (2015)	MRI-Cognitive vs. TRUS(10-12)	None	None
Koh et al (2015)	CEUS vs. RTE	None	None
Guo et al (2015)	TPUS(10-12) vs. TRUS(10-12)	Minor complication: mild hematuria (19.8%), low fever (1.2%), mild rectal bleeding (0%), mild pain (35.3%); Major complications: vasovagal event (0.6%).	Minor complication: mild hematuria (23.0%), low fever (4.3%), mild rectal bleeding (8.7%), mild pain (13.0%); Major complications: high fever (1.2%), sepsis (0.6%), severe rectal bleeding (1.2%), vasovagal event (0.6%).
Zhang et al (2014)	CEUS vs. TRUS(10-12)	None	None
Irani et al (2013)	TRUS(>12) vs. TRUS(10-12)	Grade I: 7 Faintness during PB (4), Continuous hematuria (1), Fever < 38.5°C (2); Grade II: Prostatitis (1); Grade IIIa: Clotting+urinary retention (1), Urinary retention (1);	Grade I: Persistent urinary burning (1), Fever < 38.5 °C (3), continuous anal pain (1), continuous blood in stools (2); Grade II: Prostatitis (1); Grade IIIa: Prostatitis urinary retention (2); Grade IV: Cerebral hemorrhage at day 5 (1)"
Brock et al (2012)	RTE vs. TRUS(10-12)	None	None
Byung et al (2011)	MRI-Cognitive vs. TRUS(10-12)	None	None
Chae et al (2009)	TPUS(10-12) vs. TRUS(10-12)	Gross hematuria 13 (13%), Rectal bleeding 5 (5%), Hematospermia 1 (1%), Sepsis 1 (1%)	Gross hematuria 11 (11%), Rectal bleeding 4 (4%), Hematospermia 2 (2%), Sepsis 1 (1%)
Rochester et al (2009)	TRUS(>12) vs. TRUS(10-12)	None	None
Takenaka et al (2008)	TPUS(10-12) vs. TRUS(10-12)	Macrohematuria 11, Fever > 38.51°C 1, Urinary retention 2, Hematospermia 2, Vasovagal episode 1, Post-dural puncture headache 2	Macrohematuria 12, Fever > 38.51°C 2, Urinary retention 3, Rectal bleeding 1, Vasovagal episode 2
Hara et al (2008)	TPUS(10-12) vs. TRUS(10-12)	Major Complications: Urinary retention 2 (1.6%); Minor complication:Hematuria > 1 day 13 (10.3%); Hematospermia 2 (1.6%); Vasovagal event1 (0.8%); Postdural punctureheadache 5 (4.0%)	Major Complications: Fever > 38.5°C 2 (1.7); Urinary retention 3 (2.5%); Minor complication: Hematuria >1 day 11 (9.2%); Vasovagal event 2 (1.7%);
Eggert et al (2008)	RTE vs. TRUS(10-12)	None	None
Naughton et al (2000)	TRUS(<10) vs. TRUS(10-12)	Hematuria 52 (50%); Hematochezia 18 (17%); Hematospermia75 (73%); Fever > 38.5 °C 6 (6%)	Hematuria 48(55%); Hematochezia18(17%); Hematospermia75 (73%); Fever >38.5°C 6 (6%)
Kim et al (2004)	TRUS(<10) vs. TRUS(10-12)	None	None
Emiliozzi et al (2004)	TPUS(<10) vs. TPUS(10-12)	Mild and transient (1 to 7 days) initial hematuria 46 (43%), Recurrent hemospermia	Mild and transient (1 to 7 days) initial hematuria 48 (45%), Recurrent

		up to 3 months in duration 79 (74%)	hemospermia up to 3 months in duration 85 (79%)
Paul et al (2005)	TRUS(<10) vs. TRUS(10-12)	None	None
Taverna et al (2016)	MRI- Cognitive vs. TRUS(>12)	None	None
Rosette et al (2009)	TRUS(<10) vs. TRUS(10-12)	None	None
Lecuona et al (2010)	TRUS(Vienna nomogram) vs. TRUS(<10)	Minor complications were reported, with self-limiting macroscopic haematuria being the most common. Other complications included haematospermia, haematochezia, dysuria, painful ejaculation and fever 16 (59.3%)	Minor complications were reported, with self-limiting macroscopic haematuria being the most common. Other complications included haematospermia, haematochezia, dysuria, painful ejaculation and fever 14 (37.8%)
Covarrubias et al (2011)	TRUS(>12) vs. TRUS(10-12)	Grade I: 25; Grade II: 1; Grade IIIa: 1	Grade I:26; Grade II: 1; Grade IIIa:1
Porpiglia et al (2016)	MRI/TRUS vs. TRUS(10-12)	None	None

Clavien Grade I—deviation from the normal postoperative course requiring symptomatic treatment. Grade II—requiring pharmacological treatment other than symptomatic. Grade III—requiring intervention (catheterization) with patient not under general anesthesia. Grade IV—life threatening complication.

Table 5. Patient characterstic

Authors	Methodology recruitment	Mean age, yr (range)	Mean PSA , ng/mL (range)	Mean prostate volume, mL (range)	Positive DRE n (%)	Positive MRI, n (%)
Baco et al (2016)	MRI/TRUS vs. TRUS(10-12)	64 (58–69); 65 (59–69)	6.9 (5.2–9.2); 7.6 (5.9–10.4)	45 (33–60); 40 (29–52)	20 (23.2); 29 (32.6)	na
Arsov et al (2015)	MRI in-bore vs. MRI/TRUS	66 (60–71); 68 (63–71)	10.0 (7.8–14.9); 10.8 (7.4–15.5)	54 (40–77); 60 (42–82)	na	na
Tonttila et al (2016)	MRI-Cognitive vs. TRUS	63 (60–66); 62 (56–67)	6.1 (4.2–9.9); 6.2 (4.0-10.7)	27.8 (23.5–36.6); 31.8 (26.1–44.3)	11 (21); 23 (38)	7 (13); 10 (17)
Panebianco et al (2015)	MRI-Cognitive vs. TRUS(10-12)	64 (51–82)	> 4.4	na	na	na
Koh et al (2015)	CEUS vs. RTE	62 (50-74); 63 (52-74)	11.7 (4.4-19); 8.9 (2.6-15.2)	42.3 (17.2-67.4); 42.4 (16.8-68)	na	na
Guo et al (2015)	TPUS(10-12) vs. TRUS(10-12)	67 (60-74); 66 (60-75)	8.8 (3.6–56.0); 10.5 (6.2–69.0)	47.2(12.9–97.7); 45.9(20.0–98.0)	20 (11.6); 19 (11.5)	40 (23.1); 30 (20.1)
Zhang et al (2014)	CEUS vs. TRUS(10-12)	71 (62-80); 65 (56-74)	22.5 (4.1-150); 23.3 (4.6-147)	49 (27.4-70.6); 48.2 (25.1-71.3)	119 (55.9); 125 (57.3)	80 (37.6); 83 (38.1)
Irani et al (2013)	TRUS(>12) vs. TRUS(10-12)	63; 63	6.6; 7.5	46.8; 48.3	na	na
Brock et al (2012)	RTE vs. TRUS(10-12)	64 (38–81); 65 (39–88)	8.7 (0.7–48); 13.6 (1–50)	50.3 (12–202); 51 (10–190)	na	na
Byung et al (2011)	MRI-Cognitive vs. TRUS(10-12)	63 (40–82); 61 (37–92)	6.1 (4.0–9.7); 5.6 (2.9–9.9)	37 (17–94); 38 (15–87)	8 (18); 6 (15)	na
Chae et al (2009)	TPUS(10-12) vs. TRUS(10-12)	64 (55-74); 67 (58-76)	23.1(3.6-126.7); 13.8 (3.9-34.19)	38.9(19.43-58.37); 43.3(20.48-66.12)	na	na

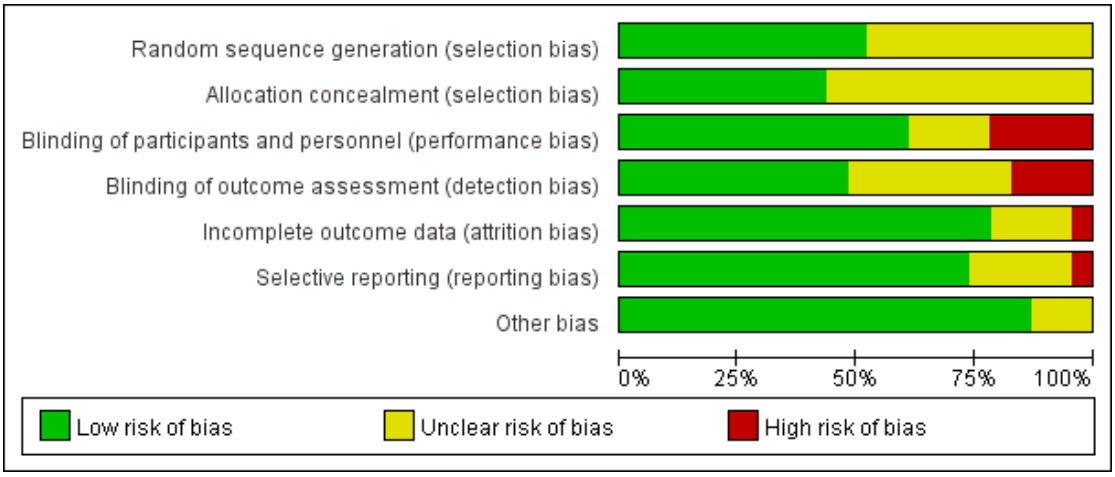
Rochester et al (2009)	TRUS(>12) vs. TRUS(10-12)	66 (59-73); 68 (58-77)	6.5 (1.4–18.5); 6.7 (2.3–24.5)	37 (10–165); 37 (10–101)	na	na
Takenaka et al (2008)	TPUS(10-12) vs. TRUS(10-12)	71 (64-79); 72 (65-80)	17.1 (4.1-47.2); 19.6 (3.5-62.8)	34.5 (17.9-53.4); 37.2 (19.7-54.7)	16 (16); 28 (28)	28 (28); 22 (22)
Hara et al (2008)	TPUS(10-12) vs. TRUS(10-12)	71 (64-78); 72 (64-79)	8.34 (4.9-11.78); 8.48 (4.58-12.38)	33.2 (18-48.4); 36 (18.9-53.1)	14 (11); 22 (18)	23 (18.3); 22 (18)
Eggert et al (2008)	RTE vs. TRUS(10-12)	65 (39-82); 66 (43-82)	13.2 (0.4-123); 12.5 (2.8-97)	49.3 (10-129); 48.4 (16-147)	na	na
Naughton et al (2000)	TRUS(<10) vs. TRUS(10-12)	66 (58-74); 65 (58-72)	5.6 (2-9.2); 6.1 (1.9-10.3)	41 (20-62); 43 (20-66)	na	na
Kim et al (2004)	TRUS(<10) vs. TRUS(10-12)	64 (57-71); 62 (52-72)	7.5 (4.09-10.93); 8.2 (4.05-12.35)	45.0 (25.4-64.5); 45.8 (27.6-64.1)	na	na
Emiliozzi et al (2004)	TPUS(<10) vs. TPUS(10-12)	68; 67	8; 8.2	na	31 (25); 26 (21)	35 (33); 29 (27)
Paul et al (2005)	TRUS(<10) vs. TRUS(10-12)	64; 64	5.9; 5.6	50; 50	na	na
Taverna et al (2016)	MRI- Cognitive vs. TRUS(>12)	65 (46-84); 63 (48-78)	12.6 (1.3-23.9); 13.1 (2.3-23.8)	na	na	na
Rosette et al (2009)	TRUS(<10) vs. TRUS(10-12)	62 (55-70); 64 (56-71)	5.6 (0.9–65.1); 6.7 (1.3–43.6)	51 (18–196); 60 (15–205)	45 (34.1); 38 (29.7)	na
Lecuona et al (2010)	TRUS(Vienna nomogram) vs. TRUS(<10)	65 (45–82); 63 (40–81)	9.4 (2.2–46); 9.2 (2.6–48)	47.4 (11–220); 51.5 (10–194)	25 (16.8); 36 (23.8)	na
Covarrubias et al (2011)	TRUS(>12) vs. TRUS(10-12)	65 (50–79); 64 (41–80)	8.4 (0.8–18); 8.9 (3.2–19.8)	54 (14–147); 53 (16–219)	10 (13); 12 (16)	na
Porpiglia et al (2016)	MRI/TRUS vs. TRUS(10-12)	64 (58–70); 66 (60–70)	5.9 (4.8–7.5); 6.7 (5.5–8.5)	46 (35–72); 46 (35–65.0)	na	na

Appendix 4: Risk of bias assessments

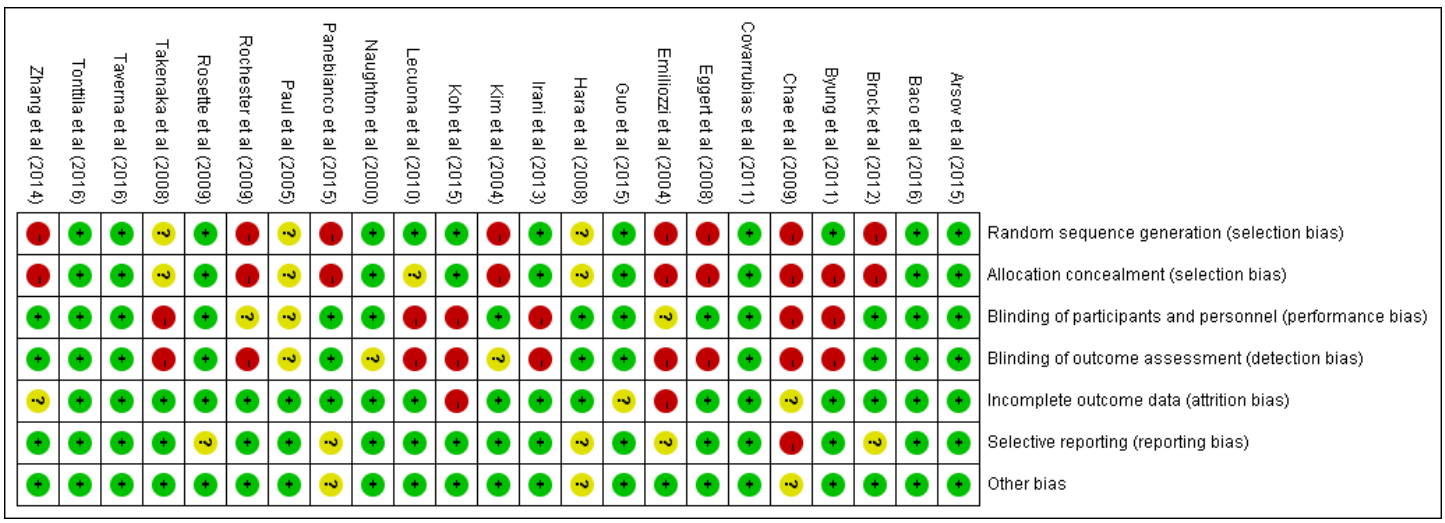
We used an updated "Risk of bias" tool from the Cochrane Collaboration recommends. This tool addresses seven specific bias domains including methods for generating the random sequence, allocation concealment, blinding of participants and investigators, blinding of outcome assessment, incompleteness of outcome data and selective outcome reporting. Each item is adjudicated within each study and the results are represented in a risk of bias table. We considered allocation concealment adequate if the investigators responsible for patient selection were unable to suspect before allocation which treatment was next. We considered blinding of patients adequate if interventions were described as indistinguishable, or if double-dummy technique was used. We considered blinding of therapists adequate if it was explicitly mentioned in the text that therapists were blinded. We considered statistical analyses to be adequate if all randomised patients were included in the analysis according to the intention-to-treat principle. We considered incomplete outcome data if it excluded at least one of the randomly assigned patients from the analysis.

Publication bias and selective might affect interventions and comparisons in different ways depending on the clinical context in the network meta-analysis. Using methodology from ecology, attempts have been made to associate the possibility of selection bias with asymmetry measures of the network. Funnel plot asymmetry can be caused by the association between sample size, heterogeneity, and the probability of publication. Sponsorships bias may reflect subtle or less subtle differences in the study designs or the conduct of a trial that only supports the preferred strategy.

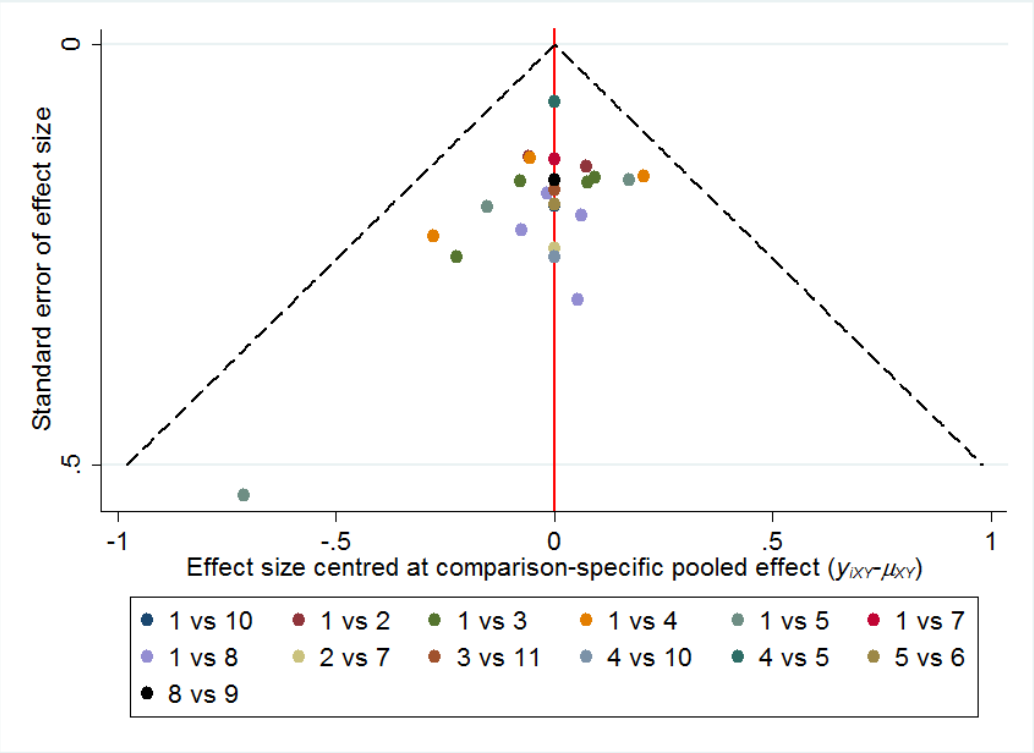
(A) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



(B)Study-level risk of bias

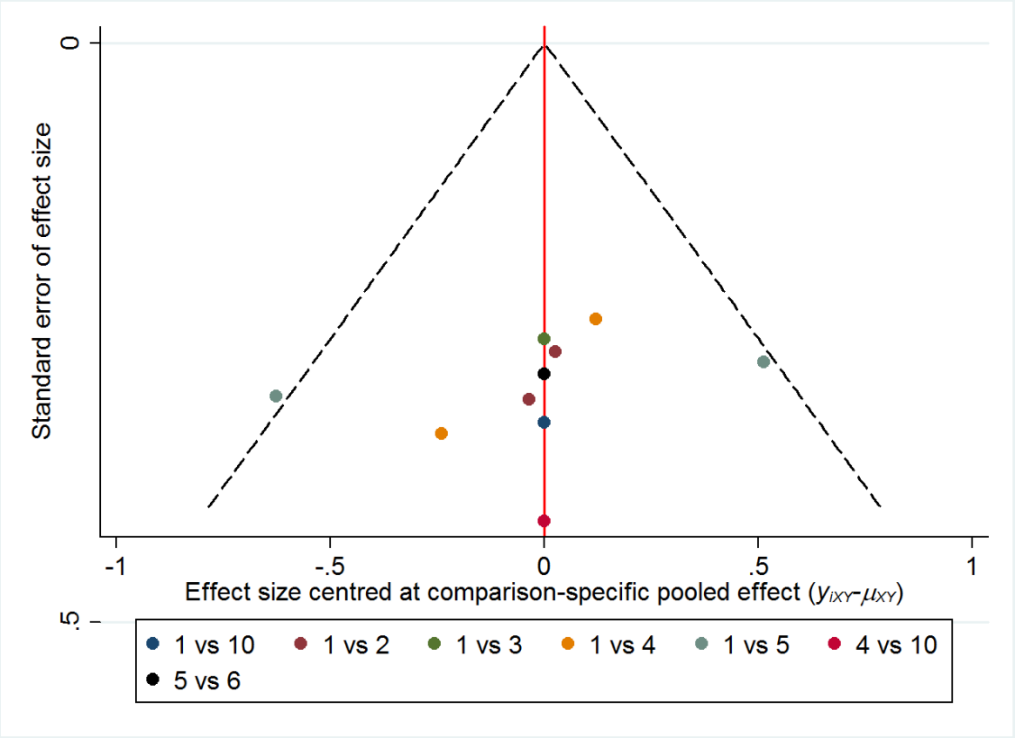


(C) Publication bias assessed via funnel plots assessed for overall PCa detection rate



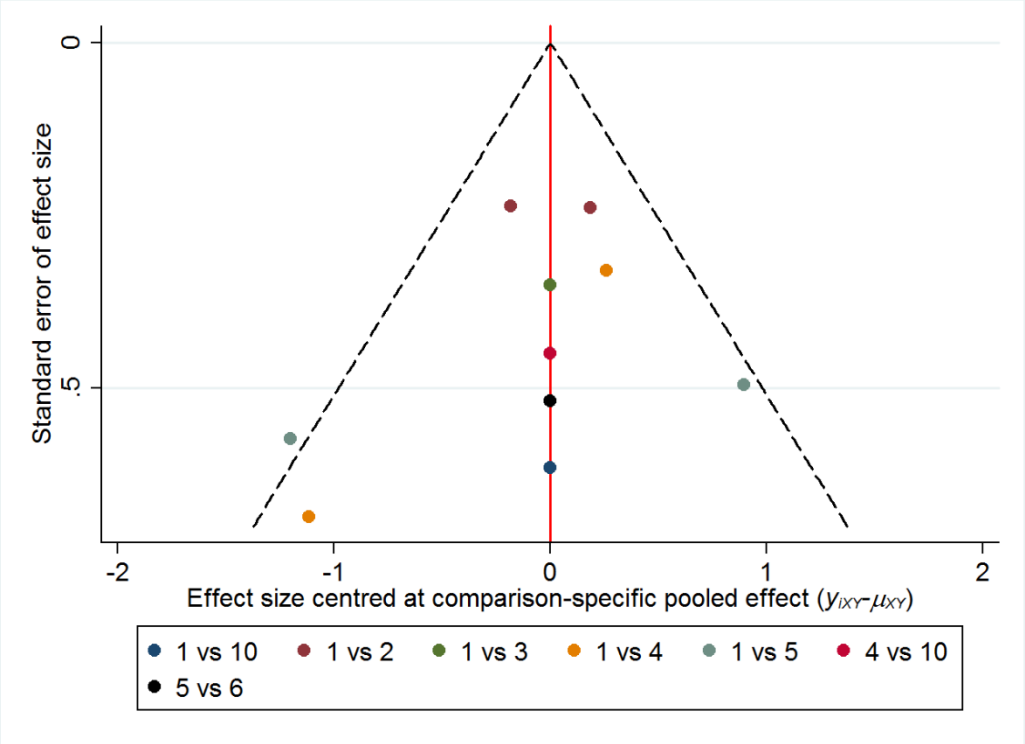
TRUS(10-12) is “1”, RTE is “2”, TPUS(10-12) is “3”, TRUS(>12) is “4”, MRI/TRUS is “5”, MRI-in bore is “6”, CEUS is “7”, TRUS(<10) is “8”, TRUS(Vienna nomogram) is “9”, MRI-cognitive is “10”, TPUS(<10) is “11”

(D) Publication bias assessed via funnel plots assessed for csPCa detection rate



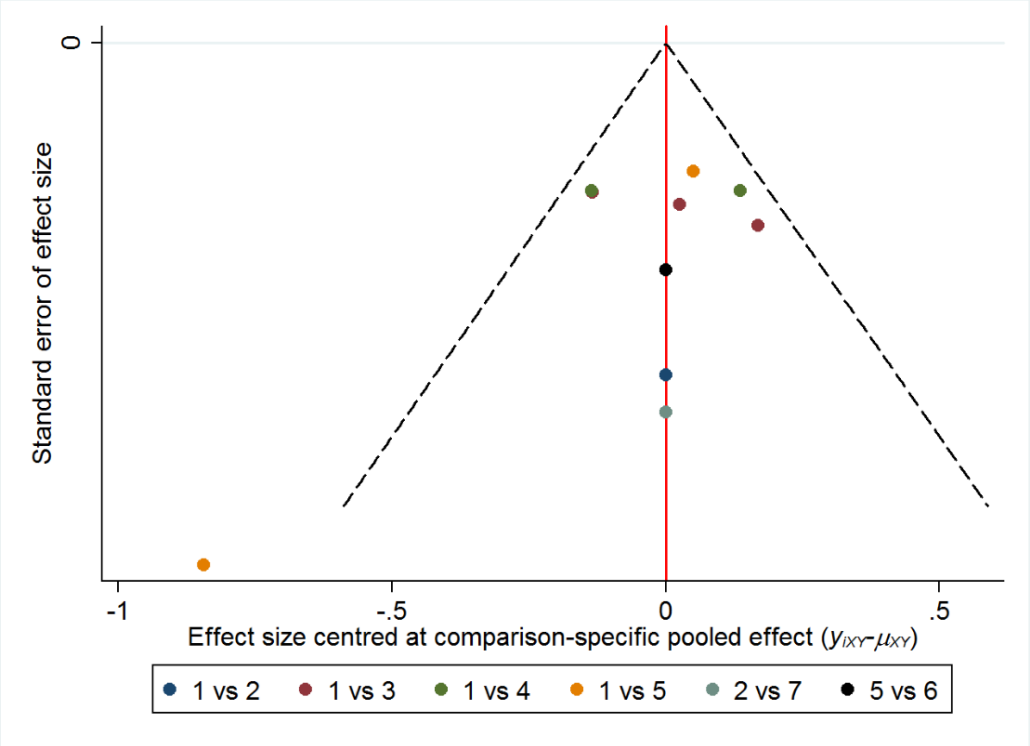
TRUS(10-12) is “1”, RTE is “2”, TPUS(10-12) is “3”, TRUS(>12) is “4”, MRI/TRUS is “5”, MRI-in bore is “6”, CEUS is “7”, TRUS(<10) is “8”, TRUS(Vienna nomogram) is “9”, MRI-cognitive is “10”, TPUS(<10) is “11”

(E) Publication bias assessed via funnel plots assessed for ciPCa detection rate



TRUS(10-12) is “1”, RTE is “2”, TPUS(10-12) is “3”, TRUS(>12) is “4”, MRI/TRUS is “5”, MRI-in bore is “6”, CEUS is “7”, TRUS(<10) is “8”, TRUS(Vienna nomogram) is “9”, MRI-cognitive is “10”, TPUS(<10) is “11”

(F) Publication bias assessed via funnel plots assessed for positive core rate



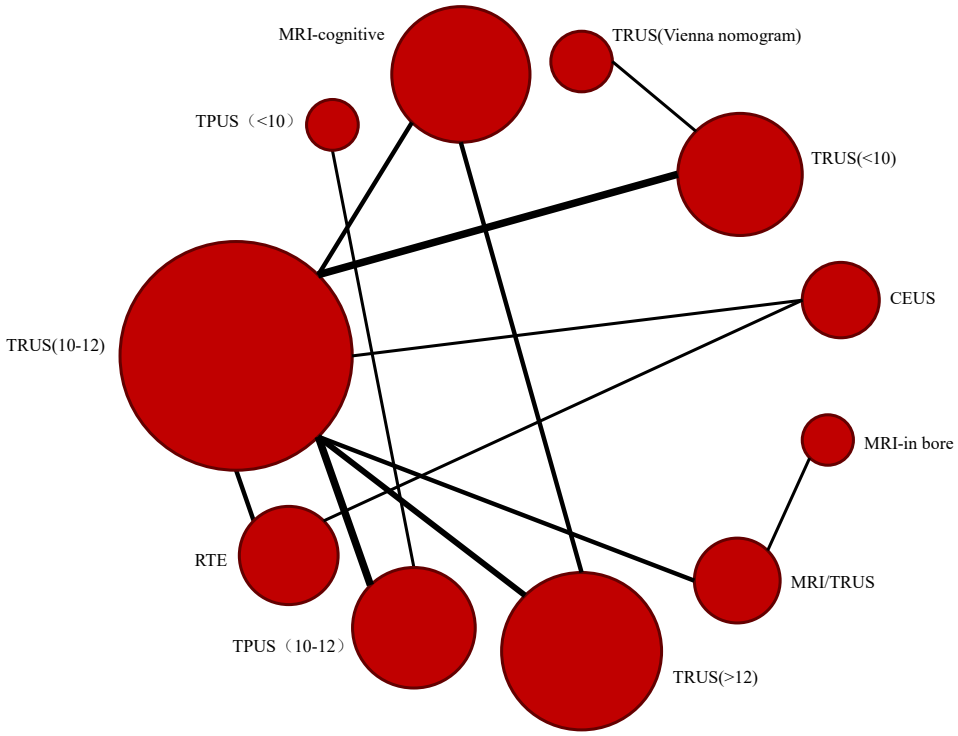
TRUS(10-12) is “1”, RTE is “2”, TPUS(10-12) is “3”, TRUS(>12) is “4”, MRI/TRUS is “5”, MRI-in bore is “6”, CEUS is “7”, TRUS(<10) is “8”, TRUS(Vienna nomogram) is “9”, MRI-cognitive is “10”, TPUS(<10) is “11”

Table1. Risk of bias and sponsorship of included studies

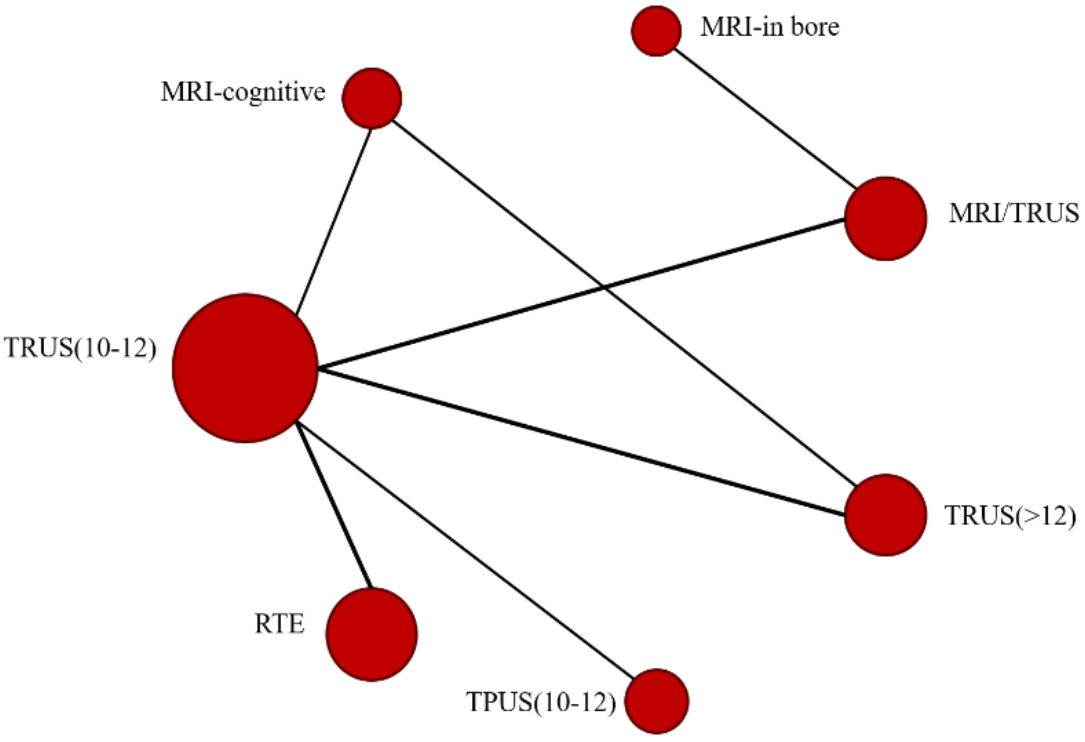
Trial name, year	Adequate sequence generation	Allocation concealment	Patient blinding	Investigator blinding	Incomplete outcome data	Selective reporting	Other bias	Industry sponsorship
Baco et al (2016)	Low	Low	Low	Low	Low	Low	Low	Low
Arsov et al (2015)	Low	Low	Low	Low	High	Low	Low	Low
Tonttila et al (2016)	Low	Low	Low	Low	High	Low	Low	Low
Panebianco et al (2015)	High	High	Low	Low	Low	Low	Unclear	Unclear
Koh et al (2015)	Low	Low	High	High	High	Low	Low	Low
Guo et al (2015)	Low	Low	Low	Low	Low	Unclear	Low	Low
Zhang et al (2014)	High	High	Low	Low	Unclear	Low	Low	Unclear
Irani et al (2013)	Low	Low	High	High	Low	Low	Low	Unclear
Brock et al (2012)	High	High	Low	Low	Low	Unclear	Low	Unclear
Byung et al (2011)	Low	High	High	High	Low	Low	Low	Unclear
Chae et al (2009)	High	High	High	High	High	High	Unclear	Low
Rochester et al (2009)	High	High	Unclear	High	High	Low	Low	Unclear
Takenaka et al (2008)	Unclear	Unclear	High	High	Low	Low	Low	Unclear
Hara et al (2008)	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Eggert et al (2008)	High	High	Low	High	Low	Low	Low	Unclear
Naughton et al (2000)	Low	Low	Low	Unclear	Low	Low	Low	Unclear
Kim et al (2004)	High	High	Low	Unclear	Low	Low	Low	Low
Emiliozzi et al (2004)	High	High	Unclear	High	High	Unclear	Low	Unclear
Paul et al (2005)	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low
Taverna et al (2016)	Low	Low	Low	Low	Low	Low	Low	Low
Rosette et al (2009)	Low	Low	Low	Low	High	Unclear	Low	Low
Lecuona et al (2010)	Low	Unclear	High	High	Low	Low	Low	Unclear
Covarrubias et al (2011)	Low	Low	Low	Low	Low	Low	Low	Unclear

Appendix 5: Network plot for each outcome

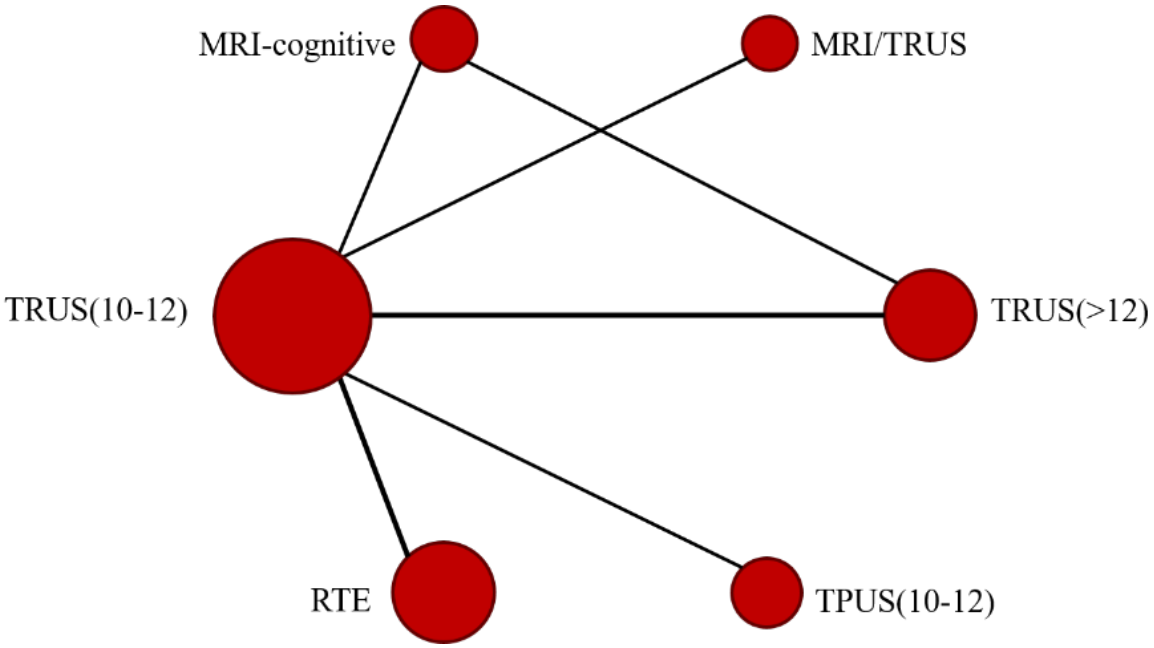
(A) Network of eligible comparisons for overall PCa detection rate



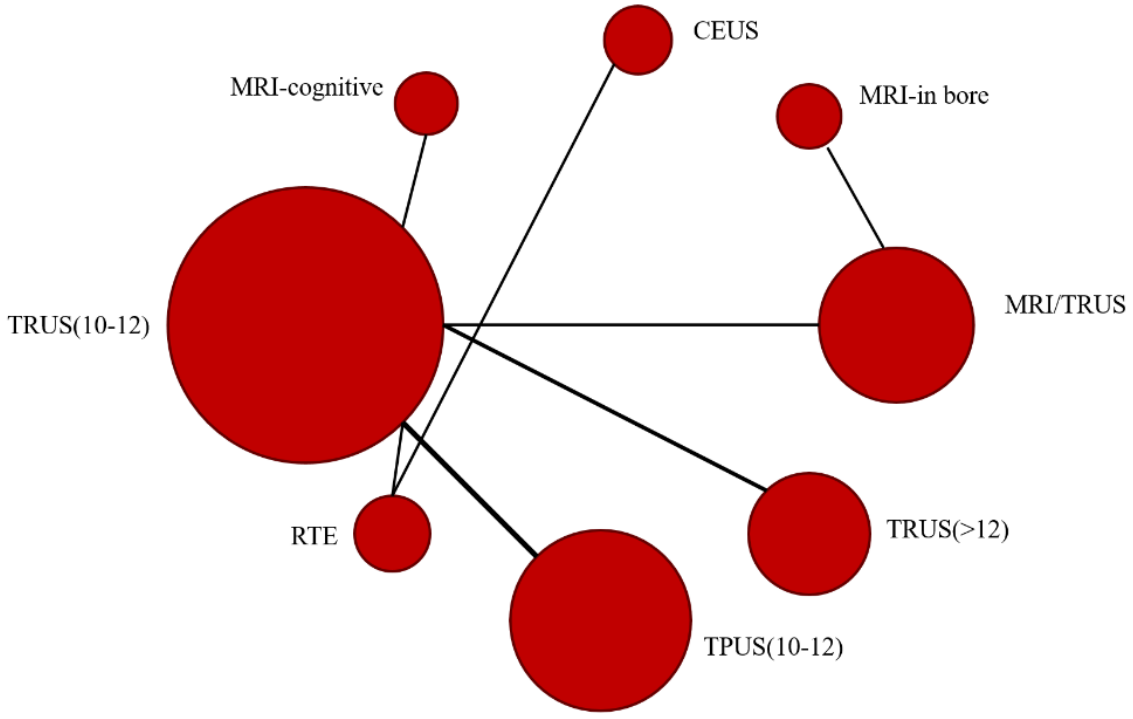
(B) Network of eligible comparisons for clinically significant PCa detection rate



(C) Network of eligible comparisons for clinically insignificant PCa detection rate



(D) Network of eligible comparisons for positive core rate



Appendix 6: Assessment of inconsistency

1. Evaluation of the global inconsistency

	Overall PCa detection rate	Clinically significant PCa detection rate	Clinically insignificant PCa detection rate	Positive core rate
Consistency				
Number of data points	48	20	20	20
Residual deviance	42.83	19.645	17.86	19.34
DIC	334.66	137.08	125.85	170.84
Inconsistency				
Number of data points	48	20	20	20
Residual deviance	43.35	18.501	19.55	19.85
DIC	334.26	136.97	125.21	170.79
Test of global inconsistency	0.27	0.76	0.83	0.53

2. Evaluation of the local inconsistency

I. Loop specific approach

(A) Evaluation of the local inconsistency of overall PCa detection rate

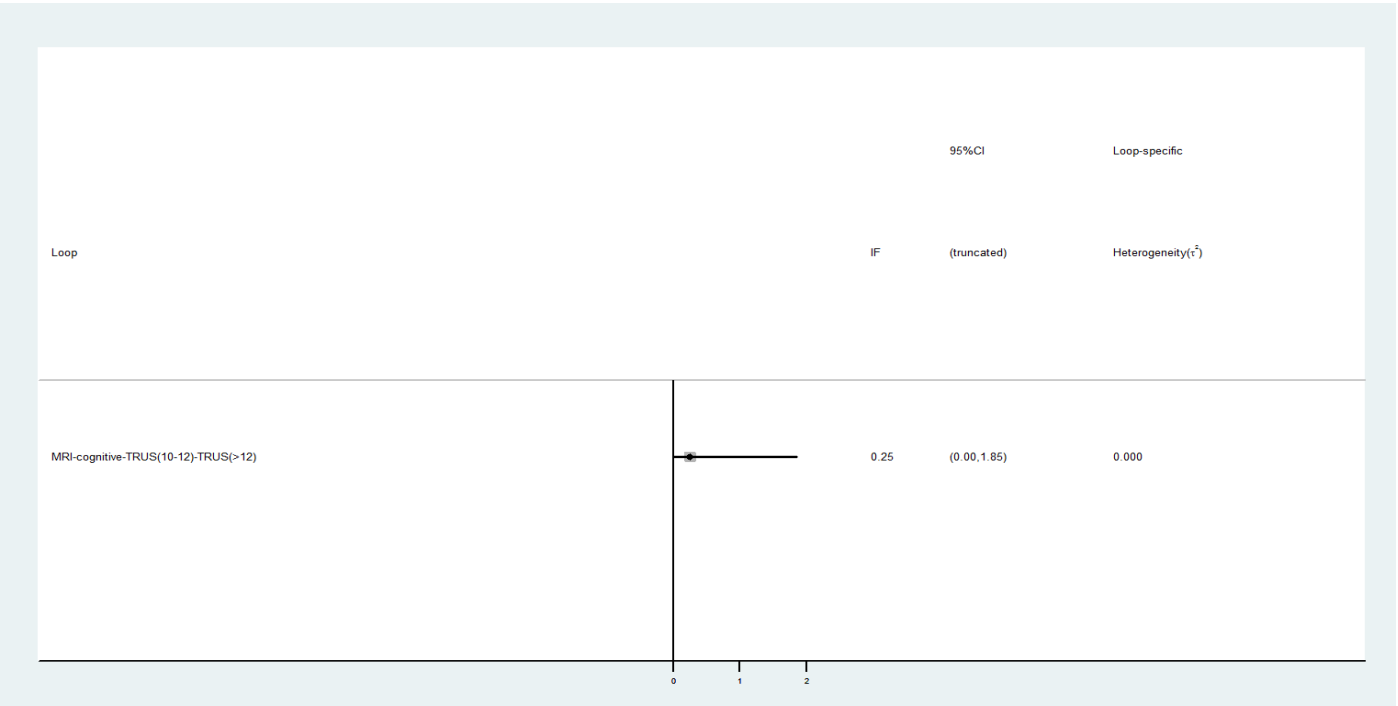
Loop	IF	z-value	P-value	95%CI	τ^2
MRI/TRUS-TRUS(10-12)-TRUS(>12)	0.400	1.047	0.295	(0.00,1.15)	0.045
TPUS(10-12)-TRUS(10-12)-TRUS(<10)	0.159	0.513	0.608	(0.00,0.76)	0.000
MRI-cognitive-TRUS(10-12)-TRUS(>12)	0.118	0.209	0.835	(0.00,1.23)	0.039
CEUS-RTE-TRUS(10-12)	0.073	0.151	0.880	(0.00,1.02)	0.000

(B) Evaluation of the local inconsistency of csPCa detection rate

Loop	IF	z-value	P-value	95%CI	τ^2
MRI-cognitive-TRUS(10-12)-TRUS(>12)	4.962	3.312	0.001	(2.03,7.90)	0.000

(C) Evaluation of the local inconsistency of ciPCa detection rate

Loop	IF	z-value	P-value	95%CI	τ^2
MRI-cognitive-TRUS(10-12)-TRUS(>12)	0.246	0.300	0.764	(0.00,1.85)	0.000



(D) Evaluation of the local inconsistency of positive core rate

Loop	IF	z-value	P-value	95%CI	τ^2
CEUS-RTE-TRUS(10-12)	0.779	2.342	0.019	(0.13,1.43)	0.000

3. Evaluation of the inconsistency by node-splitting model Tests

(A) Evaluation of the inconsistency by node-splitting model tests of overall PCa detection rate

Comparisons	Direct Effect		Indirect Effect		Overall		P-Value
	LogOR	SE	LogOR	SE	LogOR	SE	
TRUS(10-12) vs. MRI-cognitive	0.32	1.29	1.15	1.01	0.84	0.77	0.31
TRUS(10-12) vs. RTE	0.29	0.82	0.77	2.06	0.35	0.73	0.66
TRUS(10-12) vs. TRUS(>12)	0.17	0.69	-0.64	1.62	0.05	0.62	0.33
TRUS(10-12) vs. CEUS	0.13	1.16	-0.37	0.39	0.02	0.92	0.65
MRI-cognitive vs. TRUS(>12)	-0.97	0.88	-0.15	1.49	-0.79	0.75	0.31
RTE vs. CEUS	-0.67	1.7	-0.18	1.45	-0.34	1.04	0.65

(B) Evaluation of the inconsistency by node-splitting model tests of csPCa detection rate

Comparisons	Direct Effect		Indirect Effect		Overall		P-Value
	LogOR	SE	LogOR	SE	LogOR	SE	
TRUS(10-12) vs. TRUS(>12)	0.16	1.3	0.33	2.3	0.18	1.08	0.91
TRUS(10-12) vs. MRI-in bore	-0.22	1.74	-0.33	2.07	-0.30	1.32	0.94
TRUS(>12) vs. MRI-in bore	-0.56	1.62	-0.35	1.89	-0.48	1.2	0.89

(C) Evaluation of the inconsistency by node-splitting model tests of ciPCa detection rate

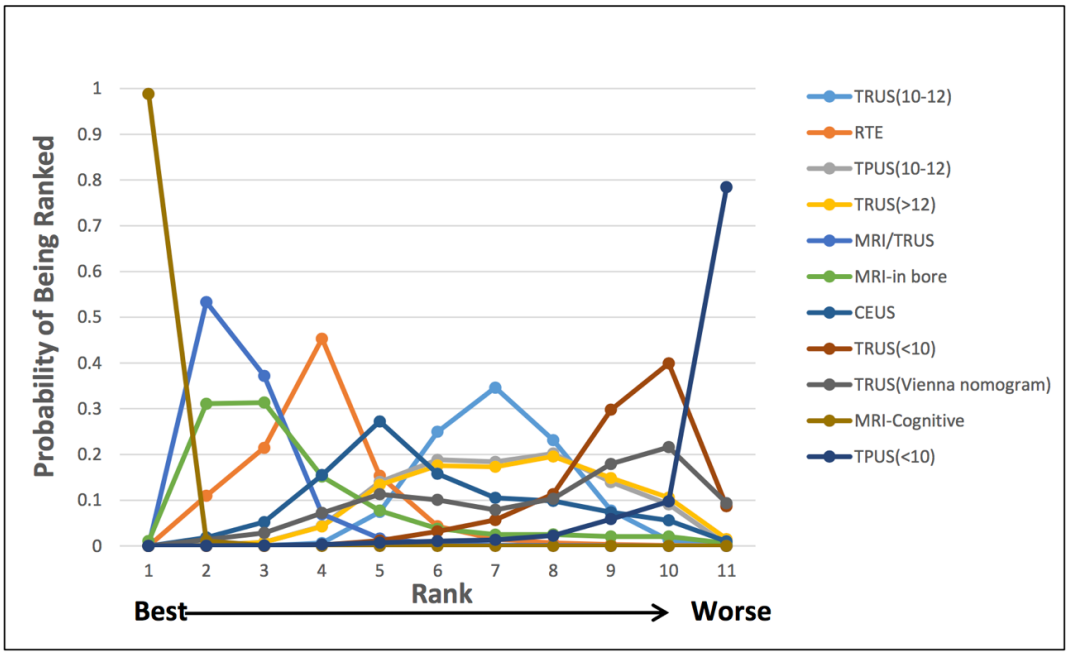
Comparisons	Direct Effect		Indirect Effect		Overall		P-Value
	LogOR	SE	LogOR	SE	LogOR	SE	
TRUS(10-12) vs. TRUS(>12)	0.16	1.31	0.15	2.46	0.18	1.05	0.96
TRUS(10-12) vs. MRI-in bore	-0.28	1.76	-0.33	2.11	-0.26	1.25	0.95
TRUS(>12) vs. MRI-in bore	-0.52	1.64	-0.48	2.02	-0.46	1.12	0.98

Appendix 7: Treatment ranking and SUCRA plot for each outcome

Treatment strategy	HAMD overall change	Patient response rate	Patient remission rate
N+A	0.9487	0.6620	0.6682
NRI	0.6906	0.6912	0.354
TCA	0.5568	0.5443	0.4066
P+A	0.5242	0.4074	0.4488
SSRI	0.5205	-	-
TCM	0.4592	0.2324	0.6027
SNRI	0.3832	0.5636	0.5825
Psychotherapy	0.3237	0.3991	0.4372
rTMS	0.3041	-	-
Control	0.2910	-	-

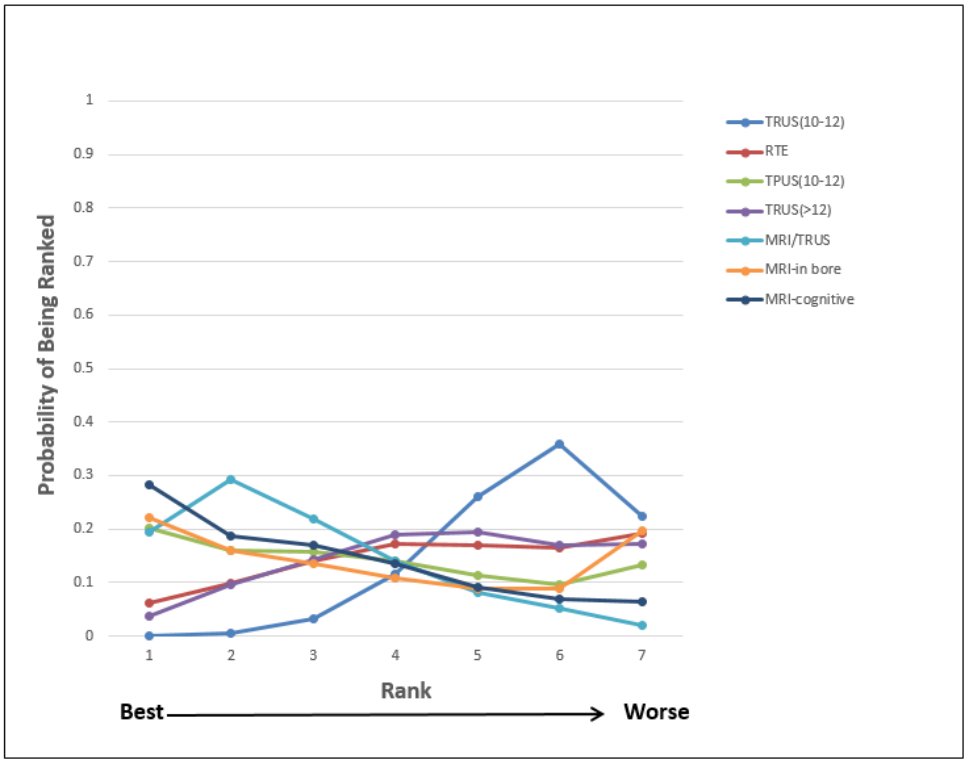
Larger SUCRAs denote better procedure.

(A) Ranking probability of overall PCa detection rate



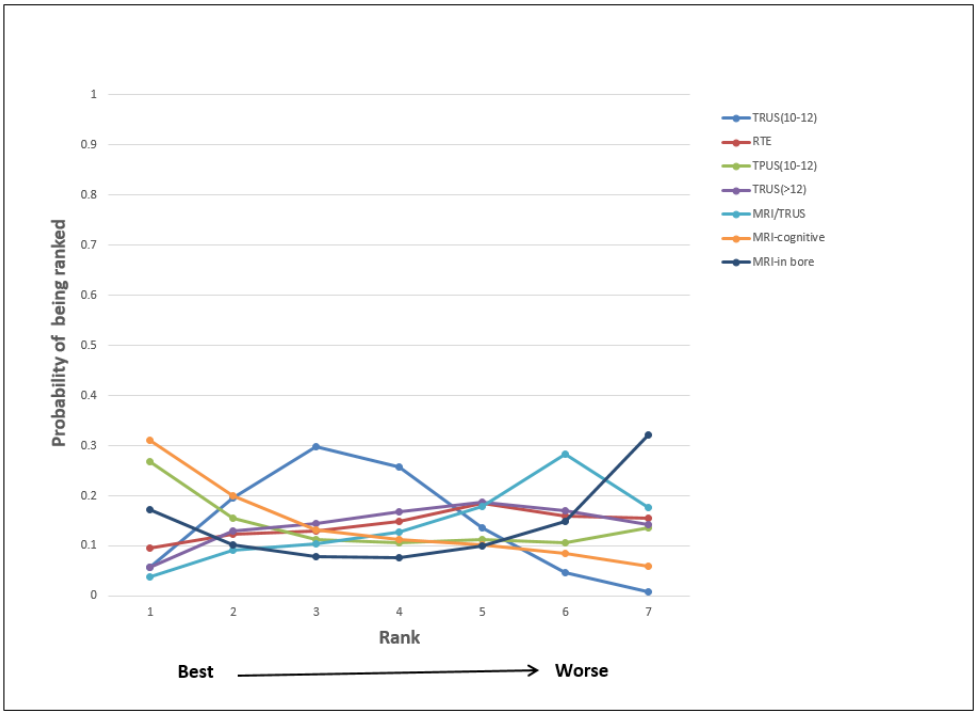
Ranking probability demonstrate the probability of a treatment to be the most effective in the network (for example, 100% if certainly the most effective, 0% if certainly the least). MRI=magnetic resonance imaging. TRUS= transrectal ultrasound. RTE=real-time sonoelastography. CEUS=contrast-enhanced ultrasonography. TPUS= transperineal ultrasound.

(B) Ranking probability of csPCa detection rate



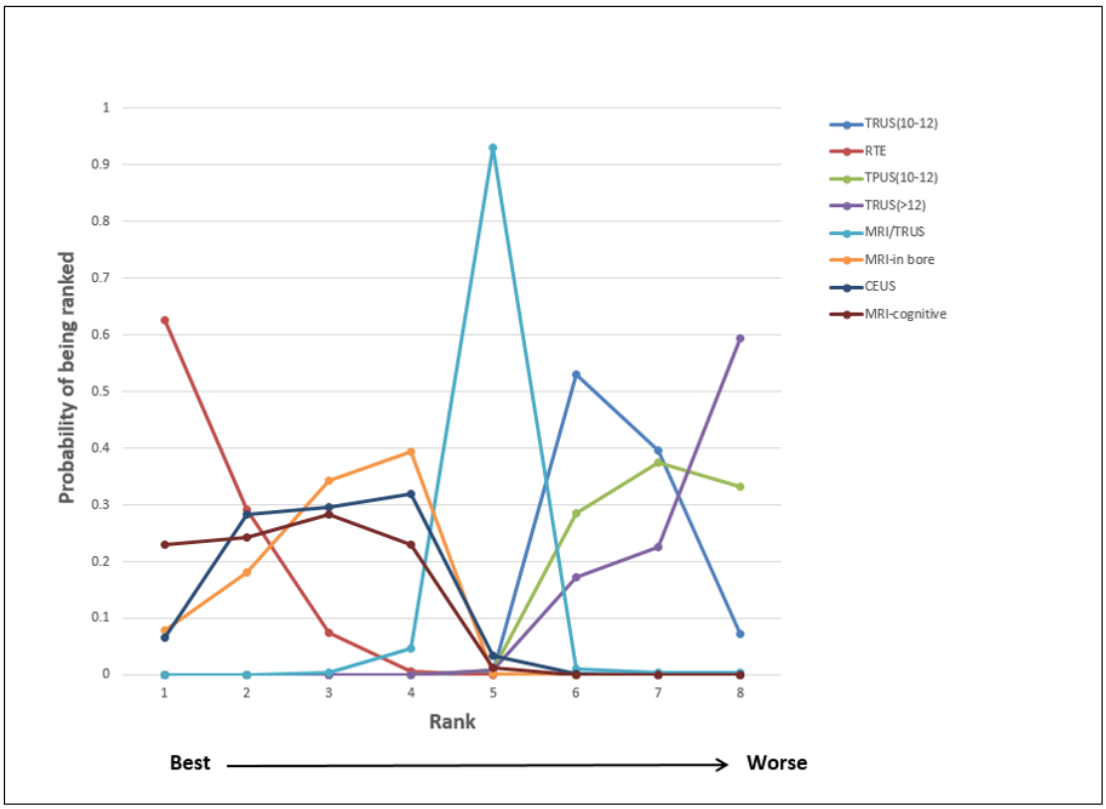
Ranking probability demonstrate the probability of a treatment to be the most effective in the network (for example, 100% if certainly the most effective, 0% if certainly the least). MRI=magnetic resonance imaging. TRUS= transrectal ultrasound. RTE=real-time sonoelastography. CEUS=contrast-enhanced ultrasonography. TPUS= transperineal ultrasound. SUCRA=surface under the cumulative ranking curve.

(C) Ranking probability of ciPCa detection rate



Ranking probability demonstrate the probability of a treatment to be the most effective in the network (for example, 100% if certainly the most effective, 0% if certainly the least). MRI=magnetic resonance imaging. TRUS= transrectal ultrasound. RTE=real-time sonoelastography. CEUS=contrast-enhanced ultrasonography. TPUS= transperineal ultrasound.

(D) Ranking probability of positive core rate



Ranking probability demonstrate the probability of a treatment to be the most effective in the network (for example, 100% if certainly the most effective, 0% if certainly the least). MRI=magnetic resonance imaging. TRUS= transrectal ultrasound. RTE=real-time sonoelastography. CEUS=contrast-enhanced ultrasonography. TPUS= transperineal ultrasound.

Appendix 8: Subgroup analysis

Name	All trials	Mean Age (95% CrI)		Mean PSA (95% CrI)		Country		Image procedure	
		< 65 years	≥ 65 years	< 10	> 10	Western countries	Other countries	With MRI	Without MRI
MRI-Cognitive	**2.66 (1.44 – 4.72)**	**2.95 (1.42 – 5.85)**	–	0.93 (0.36 – 2.43)	**1.96 (0.10 – 3.86)**	**3.30 (1.57 – 5.76)**	**4.07 (1.23 – 17.70)**	2.09 (0.78 – 5.92)	–
MRI/TRUS	1.77 (0.90 – 3.49	1.25 (0.41 – 3.81)	**2.47 (1.30 – 4.75)**	**2.45 (1.20 – 5.09)**	1.25 (0.63 – 2.46)	1.25 (0.55 – 2.84)	–	1.76 (0.73 – 4.16)	–
MRI-in bore	1.58 (0.50 – 5.04)	–	2.21 (0.89 – 5.53)	2.20 (0.79 – 6.17)	–	1.11 (0.35 – 3.48)	–	1.57 (0.36 – 6.86)	–
RTE	1.41 (0.80 – 2.53)	1.61 (0.57 – 4.50)	1.12 (0.65 – 1.92)	1.61 (0.87 – 3.00)	1.12 (0.65 – 1.92)	1.34 (0.81 – 2.22)	2.18 (0.52 – 9.59)	–	1.38 (0.96 – 2.01)
TRUS(>12)	1.06 (0.67 – 1.73)	1.31 (0.70 – 2.56)	–	1.04 (0.63 – 1.77)	1.32 (0.77 – 2.25)	0.77 (0.47 – 1.20)	**2.09 (1.00 – 4.45)**	0.78 (0.23 – 3.23)	1.14 (0.81 – 1.64)
CEUS	1.04 (0.48 – 2.18)	0.83 (0.12 – 5.56)	1.15 (0.69 – 1.92)	1.15 (0.63 – 2.07)	0.59 (0.13 – 2.56)	–	1.15 (0.69 – 1.92)	–	1.09 (0.67 – 1.73)
TPUS(10-12)	1.00 (0.63 – 1.58)	–	0.99 (0.73 – 1.35)	0.99 (0.70 – 1.41)	–	–	0.99 (0.72 – 1.35)	–	0.99 (0.73 – 1.36)
TRUS(10-12)	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
TRUS(Vienna nomogram)	0.92 (0.33–2.50)	0.86 (0.25 – 2.94)	–	1.06 (0.40 – 2.79)	–	–	0.88 (0.34 – 2.32)	–	0.91 (0.47 – 1.79)
TRUS(<10)	0.83 (0.51–1.33)	0.78 (0.41 – 1.49)	0.96 (0.50 – 1.85)	0.95 (0.47 – 1.91)	0.78 (0.53 – 1.15)	0.82 (0.47 – 1.45)	0.80 (0.37 – 1.72)	–	0.82 (0.59 – 1.15)
TPUS(<10)	0.58 (0.20–1.67)	–	0.58 (0.29 – 1.19)	0.57 (0.26 – 1.27)	–	–	–	–	0.58 (0.29 – 1.17)

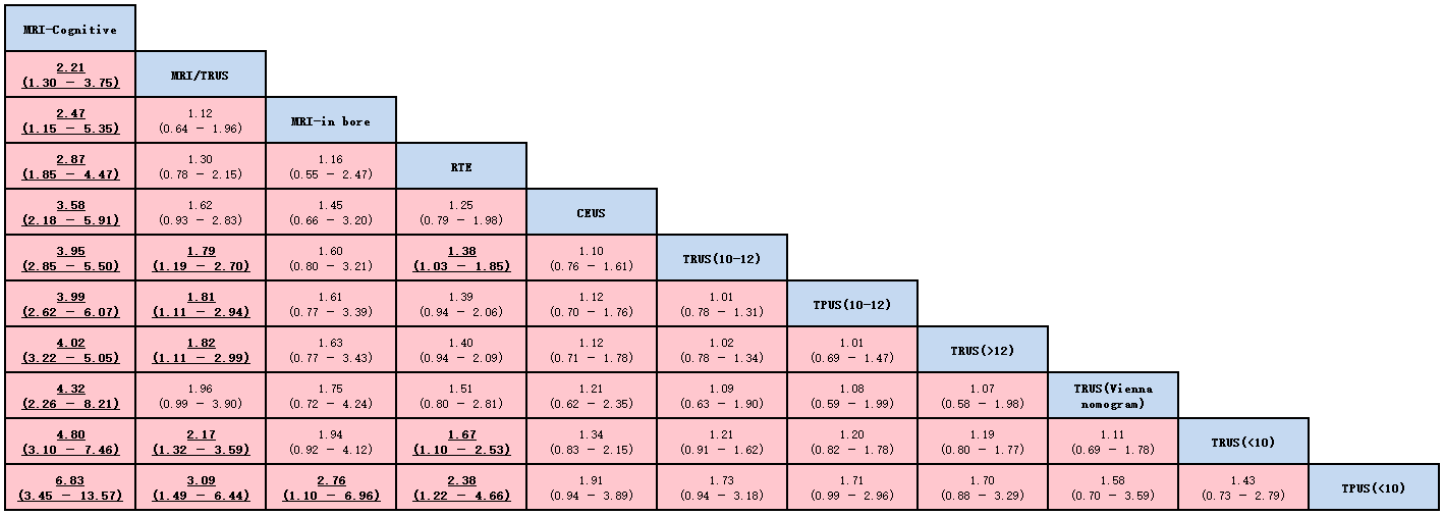
Appendix 9: Sensitivity analyses

Name	Standard analysis	SUCRA rank	Exclusion of high RoB studies for blinding	SUCRA rank	Exclusion of small studies (<100 patients)	SUCRA rank	Exclusion of positive DRE > 30%	SUCRA rank	Exclusion of TP anatomic approach.	SUCRA rank	Exclusion of PNB patient	SUCRA rank	Exclusion of prostate volume >50 mm^3	SUCRA rank
MRI-Cognitive	**2.66 (1.44 – 4.72)**	1	**2.19 (1.10 – 4.53)**	1	**2.41 (1.17 – 4.62)**	1	**2.64 (1.40 – 4.80)**	1	**2.60 (1.31 – 4.92)**	1	**3.92 (2.17 – 6.41)**	1	1.94 (0.98 – 3.96)	1
MRI/TRUS	1.77 (0.90 – 3.49)	2	1.77 (0.84 – 3.67)	2	1.76 (0.88 – 3.52)	2	1.77 (0.87 – 3.54)	2	1.25 (0.42 – 3.69)	3	**1.78 (1.02 – 3.07)**	2	**1.78 (1.09 – 2.89)**	2
MRI-in bore	1.58 (0.50 – 5.04)	3	1.58 (0.45 – 5.59)	3	1.58 (0.48 – 5.14)	3	1.58 (0.47 – 5.21)	3	1.11 (0.24 – 5.08)	4	–	–	–	–
RTE	1.41 (0.80 – 2.53)	4	1.34 (0.68 – 2.65)	4	1.34 (0.71 – 2.55)	4	1.34 (0.71 – 2.56)	4	1.34 (0.66 – 2.72)	2	1.34 (0.84 – 2.17)	3	1.21 (0.72 – 2.08)	3
TRUS(>12)	1.06 (0.67 – 1.73)	5	0.92 (0.49 – 1.79)	8	1.15 (0.47 – 2.78)	6	1.07 (0.66 – 1.78)	5	1.08 (0.64 – 1.87)	5	0.95 (0.65 – 1.41)	7	0.96 (0.63 – 1.45)	8
CEUS	1.04 (0.48 – 2.18)	6	1.14 (0.44 – 2.95)	5	1.03 (0.62 – 1.72)	5	0.69 (0.13 – 3.57)	9	0.69 (0.12 – 3.85)	8	1.15 (0.60 – 2.21)	4	1.07 (0.64 – 1.74)	4
TPUS(10-12)	1.00 (0.63 – 1.58)	7	0.95 (0.48 – 1.92)	7	1.00 (0.62 – 1.61)	7	1.00 (0.62 – 1.62)	6	–	–	0.99 (0.68 – 1.45)	6	0.99 (0.72 – 1.37)	7
TRUS(10-12)	Reference	8	Reference	6	Reference	8	Reference	7	Reference	6	Reference	5	Reference	6
TRUS(Vienna nomogram)	0.92 (0.33–2.50)	9	–	–	0.91 (0.32 – 2.63)	9	0.91 (0.30 – 2.70)	8	0.91 (0.27 – 3.03)	7	0.66 (0.37 – 2.00)	8	0.99 (0.44 – 2.16)	5
TRUS(<10)	0.83 (0.51–1.33)	10	0.82 (0.49 – 1.39)	9	0.82 (0.50 – 1.35)	10	0.81 (0.45 – 1.45)	10	0.82 (0.43 – 1.54)	9	0.78 (0.50 – 1.22)	9	0.89 (0.53 – 1.47)	9
TPUS(<10)	0.58 (0.20–1.67)	11	0.56 (0.16 – 1.92)	10	0.58 (0.20 – 1.69)	11	0.58 (0.20 – 1.72)	11	–	–	0.58 (0.25 – 1.35)	10	–	–
Residual deviance	49.49		37.74		45.60		45.81		33.57		45.04		34.16	
pD	42.83		33.611		40.33		40.11		29.83		34.18		26.23	
DIC	334.66		258.00		314.19		306.27		222.37		285.03		218.66	
#data points	48		36		44		44		32		40		32	
Heterogeneity (tau)	0.36 (moderate)		0.40 (moderate)		0.38 (moderate)		0.38 (moderate)		0.42 (moderate)		0.23 (moderate)		0.15 (moderate)	

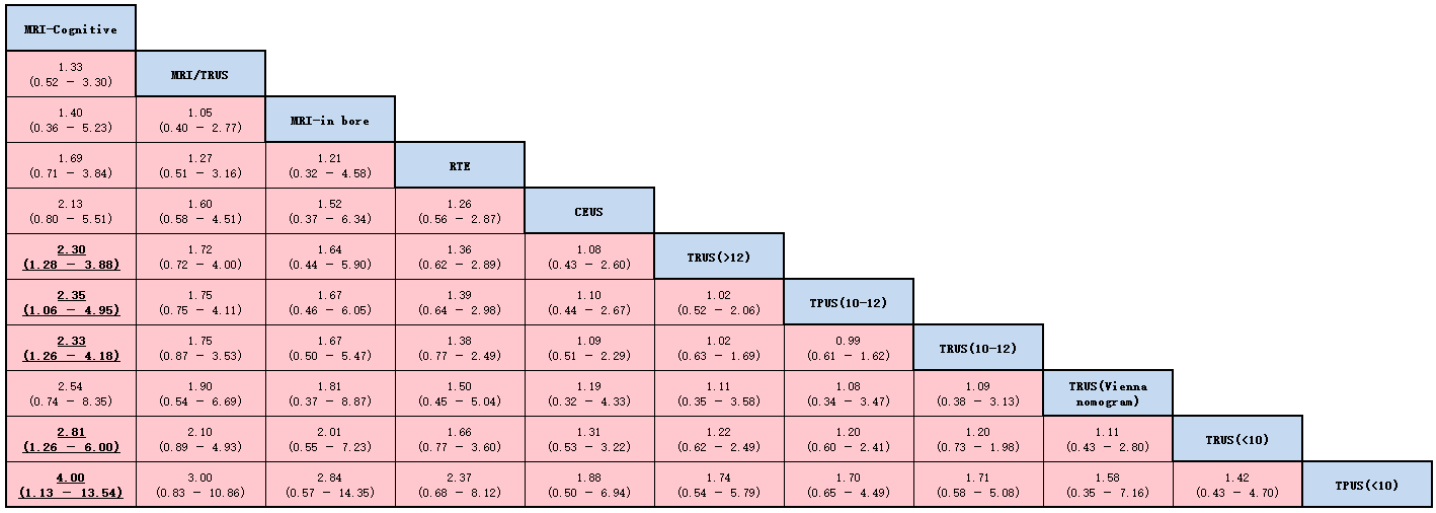
Sensitivity analyses: Frequentist network meta-analysis

Biopsy strategies	Overall PCa detection rate	csPCa detection rate	ciPCa detection rate	Positive core rate
Compared with TRUS(10-12)				
CEUS	1.08 (0.77-1.51)	-	-	1.83 (1.30-2.58)
MRI/TRUS	1.01 (0.65-1.57)	1.34 (0.73-2.44)	1.51 (0.53-4.31)	3.88 (1.84-8.17)
MRI-in bore	1.70 (0.96-2.99)	1.23 (0.44-3.47)	1.48 (0.25-8.96)	7.56 (3.17-18.04)
MRI-cognitive	1.82 (1.44-2.30)	1.27 (0.62-2.60)	0.80 (0.25-2.55)	-
RTE	1.19 (0.92-1.55)	1.11 (0.61-2.01)	1.24 (0.55-2.79)	3.69 (2.41-5.66)
TPUS(10-12)	1.03 (0.83-1.28)	1.25 (0.56-2.80)	0.96 (0.27-3.37)	0.96 (0.76-1.21)
TRUS(<10)	0.85 (0.66-1.08)	-	-	-
TRUS(>12)	0.96 (0.78-1.19)	1.08 (0.62-1.86)	1.22 (0.50-3.02)	0.93 (0.70-1.22)
TRUS(10-12)	1.00	1.00	1.00	1.00
TRUS(Vienna nomogram)	0.91 (0.55-1.49)	-	-	-
TPUS(<10)	0.83 (0.61-1.02)	-	-	-
Heterogeneity (p-value)	0.6596	0.0717	0.2158	0.0046

Sensitivity Analysis: Fixed-effect model



Sensitivity analyses: Worst-case scenario



Sensitivity analyses: Vague priors distribution

MRI-Cognitive										
1.45 (0.47 – 4.32)	MRI/TRUS									
1.79 (0.62 – 4.85)	1.23 (0.40 – 3.70)	RTE								
1.62 (0.32 – 7.94)	1.12 (0.35 – 3.61)	0.91 (0.18 – 4.58)	MRI-in bore							
2.35 (1.17 – 4.44)	1.62 (0.57 – 4.44)	1.32 (0.51 – 3.34)	1.45 (0.30 – 6.70)	TRUS(>12)						
2.51 (0.77 – 8.19)	1.73 (0.50 – 6.12)	1.41 (0.51 – 4.08)	1.55 (0.28 – 8.74)	1.07 (0.36 – 3.37)	CEUS					
2.56 (1.00 – 6.32)	1.76 (0.63 – 4.85)	1.43 (0.56 – 3.66)	1.58 (0.34 – 7.33)	1.09 (0.48 – 2.53)	1.02 (0.33 – 3.03)	TPUS(10-12)				
2.56 (1.24 – 5.18)	1.76 (0.76 – 4.07)	1.43 (0.70 – 3.00)	1.58 (0.38 – 6.65)	1.09 (0.61 – 2.01)	1.02 (0.39 – 2.58)	1.00 (0.56 – 1.79)	TRUS(10-12)			
2.80 (0.64 – 11.86)	1.92 (0.42 – 8.78)	1.56 (0.36 – 6.83)	1.72 (0.26 – 11.81)	1.19 (0.30 – 4.93)	1.11 (0.23 – 5.37)	1.09 (0.27 – 4.47)	1.09 (0.31 – 3.88)	TRUS(Vienna nomogram)		
3.12 (1.22 – 7.83)	2.15 (0.77 – 5.98)	1.74 (0.69 – 4.52)	1.93 (0.41 – 9.08)	1.33 (0.58 – 3.11)	1.24 (0.40 – 3.73)	1.22 (0.54 – 2.80)	1.22 (0.67 – 2.20)	1.12 (0.36 – 3.42)	TRUS(<10)	
4.39 (0.98 – 18.98)	3.02 (0.64 – 14.04)	2.46 (0.55 – 10.99)	2.70 (0.39 – 18.77)	1.87 (0.45 – 7.90)	1.75 (0.34 – 8.47)	1.72 (0.53 – 5.51)	1.71 (0.46 – 6.27)	1.57 (0.25 – 9.62)	1.41 (0.34 – 5.85)	TPUS(<10)

Appendix 10: Risk of bias assessments for primary outcome

Comparison	Confidence in OR for overall PCa detection rate	Nature of the evidence	Downgrading reason
MRI-Cognitive vs. MRI/TRUS	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-Cognitive vs. MRI-in bore	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-Cognitive vs. RTE	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-Cognitive vs. TRUS(>12)	Very Low	Mixed	Downgrade by three levels due to study limitations, heterogeneity and indirectness
MRI-Cognitive vs. CEUS	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-Cognitive vs. TPUS(10-12)	Moderate	Indirect	Downgrade by one level due to study indirectness
MRI-Cognitive vs. TRUS(10-12)	Moderate	Mixed	Downgrade by one level due to study indirectness
MRI-Cognitive vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-Cognitive vs. TRUS(<10)	Moderate	Indirect	Downgrade by one level due to study indirectness
MRI-Cognitive vs. TPUS(<10)	Moderate	Indirect	Downgrade by one level due to study indirectness
MRI/TRUS vs. MRI-in bore	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI/TRUS vs. RTE	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI/TRUS vs. TRUS(>12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI/TRUS vs. CEUS	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI/TRUS vs. TPUS(10-12)	Low	Indirect	Downgrade by three levels due to study limitations and indirectness
MRI/TRUS vs. TRUS(10-12)	Very Low	Indirect	Downgrade by three levels due to study imprecision and indirectness
MRI/TRUS vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI/TRUS vs. TRUS(<10)	Low	Indirect	Downgrade by three levels due to study imprecision and indirectness
MRI/TRUS vs. TPUS(<10)	Low	Indirect	Downgrade by three levels due to study imprecision and indirectness
MRI-in bore vs. RTE	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-in bore vs. TRUS(>12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-in bore vs. CEUS	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-in bore vs. TPUS(10-12)	Low	Indirect	Downgrade by three levels due to study imprecision and indirectness
MRI-in bore vs. TRUS(10-12)	Low	Indirect	Downgrade by three levels due to study imprecision and indirectness
MRI-in bore vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-in bore vs. TRUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
MRI-in bore vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness

RTE vs. TRUS(>12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
RTE vs. CEUS	Very Low	Mixed	Downgrade by three levels due to study limitations, imprecision and indirectness
RTE vs. TPUS(10-12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
RTE vs. TRUS(10-12)	Very Low	Mixed	Downgrade by three levels due to study limitations, imprecision and indirectness
RTE vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
RTE vs. TRUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
RTE vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(>12) vs. CEUS	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(>12) vs. TPUS(10-12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(>12) vs. TRUS(10-12)	Very Low	Mixed	Downgrade by three levels due to study limitations, imprecision and indirectness
TRUS(>12) vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(>12) vs. TRUS(<10)	Very Low	Indirect	Downgrade by three levels due to study limitations, imprecision and indirectness
TRUS(>12) vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
CEUS vs. TPUS(10-12)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
CEUS vs. TRUS(10-12)	Very Low	Mixed	Downgrade by three levels due to study limitations, imprecision and indirectness
CEUS vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
CEUS vs. TRUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
CEUS vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TPUS(10-12) vs. TRUS(10-12)	Very Low	Indirect	Downgrade by three levels due to study limitations, imprecision and indirectness
TPUS(10-12) vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TPUS(10-12) vs. TRUS(<10)	Very Low	Indirect	Downgrade by three levels due to study limitations, imprecision and indirectness
TPUS(10-12) vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(10-12) vs. TRUS(Vienna nomogram)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(10-12) vs. TRUS(<10)	Very Low	Indirect	Downgrade by three levels due to study limitations, imprecision and indirectness
TRUS(10-12) vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
TRUS(<10) vs. TPUS(<10)	Low	Indirect	Downgrade by two levels due to study imprecision and indirectness
Ranking of treatment	Low	-	Downgrade by two levels due to study imprecision and indirectness

Using GRADE to rate quality of evidence from a network meta-analysis involved several steps: First, we rated quality of evidence for direct comparisons; second, we rated quality of evidence for indirect estimates (starting at the lowest rating of the two pairwise direct estimates that contribute as first-order loops to the indirect estimate, which can be rated down further for imprecision or intransitivity), and then third, rating the quality of evidence for the network combining direct and indirect estimates. In this step, if direct and indirect estimates from second-order comparisons are similar, the higher of the ratings was assigned to the network meta-analysis estimates.[11]

Appendix 11: PRISMA network meta-analysis checklist of items to include when reporting a systematic review involving a network meta-analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review incorporating a network meta-analysis (or related form of meta-analysis).	**p.1**
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: **Background:** main objectives **Methods:** data sources; study eligibility criteria, participants, and interventions; study appraisal; and synthesis methods, such as network meta-analysis. **Results:** number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity. **Discussion/Conclusions:** limitations; conclusions and implications of findings. **Other:** primary source of funding; systematic review registration number with registry name.	**p.2**
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, including mention of why a network meta-analysis has been conducted._	**p.3**
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	**p.3**
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number.	**p.4**
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification)._	**p.4**
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	**p.4**
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**p.5 and appendix 1 (pp.3-6)**
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	**p.5-6**
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	**p.6-7**
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	**p.6-7 and appendix 2, 3, 4, 5, 6, 7 (pp. 5-36)**

Geometry of the network	**S1**	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	**p.8**
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	**p.8**
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.	**p.6-7 and appendix 2 (pp.7-9)**
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: • Handling of multi-arm trials; • Selection of variance structure; • Selection of prior distributions in Bayesian analyses; and • Assessment of model fit.	**p.6-7 and appendix 2 (pp.7-9)**
Assessment of Inconsistency	**S2**	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	**p.7 and appendix 2 (pp.8-9)**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	**p.7 and appendix 2 (pp.8-9)**
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: • Sensitivity or subgroup analyses; • Meta-regression analyses; • Alternative formulations of the treatment network; and • Use of alternative prior distributions for Bayesian analyses (if applicable)._	**p.7 and (pp.9)**
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	**p.7-8 and figure 1**
Presentation of network structure	**S3**	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	**Appendix 5 (pp 28)**
Summary of network geometry	**S4**	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	**p.8 and table 1**
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	**p.8, table 2 and appendix 3 (pp 10-22)**
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	**p.8 and appendix 4 (pp.23-26)**
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. Modified approaches may be needed to deal with information from larger networks.	**Appendix 3 (pp.16)**

Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.	**p.9-10, table 3, figure 2 and appendix 7 (pp.31-33)**
Exploration for inconsistency	**S5**	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, P values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.	**p.8 and appendix 6 (pp.28-31)**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	**p.10-11 and appendix 9 (pp.40) e.g. quality of evidence by GRADE methodology**
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).	**p.10-11, appendix 8(pp.34), and appendix 8 (pp.35-38)**
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	**p.11-13**
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).	**pp.13**
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	**p.13-14**
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	**p.1**

PICOS = population, intervention, comparators, outcomes, study design.

Appendix 13: References for included trials

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