Supplementary Materials

These supplementary materials were for the article entitled

“**The Prognostic value of Plasma Cell-free DNA Concentration in the Prostate Cancer: A Systematic Review and Meta-Analysis.**”

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Figure Legends

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Figure S3: The Sensitivity(S3A) , Specificity(S3B) and SROC curves(S3C) for cfDNA in diagnosis of prostate cancer.

Figure S4: Diagnosis of total concentration in the Pooled DOR,NLR and PLR for PCA.

Figure S5: The pooled results of biochemical recurrence free survival in the patients with PCA.

Figure S6: The comparison of other variables with the concentration of cfDNA in PCA

Figure S7: The prognosis value of the combination of PSA and cfDNA for the patients with PCA in Wyatt's and Vandekerkhov's article； S7A: PSA for PFS in Wyatt's article; S7B: CfDNA for PFS in Wyatt's article;S7C: PSA+cfDNA for PFS in Wyatt's article; S7D: PSA for OS in Vandekerkhov's article; S7E: CfDNA for OS in Vandekerkhov's article; S7F: PSA+cfDNA for OS in Vandekerkhov's article; S7G: Time-dependent ROC of them for predicting PFS in Wyatt's article; S7H: Time-dependent ROC of them for predicting OS in Vandekerkhov's article.

Table S8: The pros and cons of different cfDNA quantification methods.

Table S1:Research strategies

Databases	Total citations	Full text
PubMed	**911**	**124**
Cochrane Library	**12**	**3**
Web of science	**56**	**8**
Embase	**58**	**5**
PMC	**9**	**1**
Otherdatabase source	**63**	**6**
Total(database)	**1109**	**147**

For the meta-analysis, the authors searched PubMed, Web of Science, Medline, PMC,EMBASE and the Cochrane Library to retrieve all eligible articles from the date of database inception to June 30, 2020. The search heading terms and keywords included “prostate cancer”; “cf DNA” ,“diagnosis” and “prognosis”. Additional articles were identified by manually reviewing the references of included articles. No languages restrictions were applied. Others details could see the following .

Explicit search strategy:

steps	Strategy
Diagnosis OR prognosis	Search **((((((((((Diagnoses) OR (Diagnoses and Examinations)) OR (Examinations and Diagnoses)) OR correlation) OR relation) OR correlationship) OR prognosis) OR diagnosis) OR Prognostic Factors) OR Factor, Prognostic) OR Factors, Prognostic) OR Prognostic Factor) OR prognoses**
cfDNA	Search **((((((((((((((((((((((((((((Cell Free Nucleic Acids) OR Nucleic Acids, Cell-Free) OR Circulating Cell-Free Nucleic Acids) OR Circulating Cell Free Nucleic Acids) OR Circulating Nucleic Acids) OR Acids, Circulating Nucleic) OR Nucleic Acids, Circulating) OR Cell-Free Nucleic Acid) OR Cell Free Nucleic Acid) OR Nucleic Acid, Cell-Free) OR Cell-Free DNA) OR Cell Free DNA) OR DNA, Cell-Free) OR cfDNA) OR cirDNA) OR Cell-Free Deoxyribonucleic Acid) OR Acid, Cell-Free Deoxyribonucleic) OR Cell Free Deoxyribonucleic Acid) OR Deoxyribonucleic Acid, Cell-Free) OR Circulating DNA) OR DNA, Circulating) OR Cell-Free RNA) OR Cell Free RNA) OR RNA, Cell-Free) OR cfRNA) OR cirRNA) OR Cell-Free Ribonucleic Acid) OR Acid, Cell-Free Ribonucleic) OR Cell Free Ribonucleic Acid) OR Ribonucleic Acid, Cell-Free) OR Circulating RNA) OR RNA, Circulating**

prostate cancer	Search **((((((((((((((Prostate Neoplasms) OR Neoplasms, Prostate) OR Neoplasm, Prostate) OR Prostate Neoplasm) OR Neoplasms, Prostatic) OR Neoplasm, Prostatic) OR Prostatic Neoplasm) OR Prostate Cancer) OR Cancer, Prostate) OR Cancers, Prostate) OR Prostate Cancers) OR Cancer of the Prostate) OR Prostatic Cancer) OR Cancer, Prostatic) OR Cancers, Prostatic) OR Prostatic Cancers) OR Cancer of Prostate**
Ultimate	total

Table S2: Assessment of study quality

Detailed Newcastle-Ottawa Scale of each included case- control study

ID		Selection				Comparability		Exposure			
Cations	**References**	**Case definition**	**Representative of case**	**Control selection**	**Control definition**	**Main factor**	**Associated factor**	**Exposure ascertainment**	**Same method of ascertainment**	**Non-response rate**	**Total score**
(18)	**Boddy,et al (2005)**	*	*	*	*	*		*	*		**7**
(20)	**Altimari,et al (2008)**	*	*	*	*	*		*	*		**7**
(22)	**Cherepanova,et al (2008)**	*	*	*	*	*			*		**6**
(25)	**Goodall,et al (2017)**	*	*	*		*	*	*		*	**7**
(14)	**Hendriks.et al (2018)**	*	*	*	*	*	*	*	*	*	**9**
(27)	**Reis,et al (2015)**	*	*	*		*		*	*	*	**7**
(28)	**Jung.et al (2004)**	*	*	*	*	*	*	*	*		**8**
(30)	**Wroclawski.et al (2013)**	*	*	*	*	*	*	*	*		**8**
(31)	**Mehra.et al (2006)**	*	*	*	*	*			*		**6**
(32)	**Papadopoulou,et al (2006)**	*	*	*	*	*			*		**6**

Detailed Newcastle-Ottawa Scale of each included cohort study

ID		Selection				Comparability		Outcome			
Cations	**References**	**representativeso f exposed cohort**	**Selection of non-exposed cohort**	**Ascertainment of exposure**	**Demonstration that outcome of interest was not present at start of study**	**Adjust for the most important risk factors**	**Adjust for other risk factors**	**Assessment of outcome**	**Follow-up length> 10 years**	**Adequacy of follow-up rate**	**Total score**
(19)	**Allen , et al (2004)**	*	*	*	*	*		*			**6**
(21)	**Belic,et al (2018)**	*	*	*	*	*	*	*			**7**
(23)	**Chun,et al (2006)**	*	*	*	*	*	*	*			**7**
(24)	**Ellinger.et al (2008)**	*	*	*	*	*	*	*			**7**
(26)	**Gordian,et al (2010)**	*	*	*	*	*	*	*			**7**
(29)	**Kienel,et al (2015)**	*	*	*	*	*	*	*			**7**
(33)	**Ponti.et al (2018)**	*	*	*	*	*	*	*			**7**
(34)	**Schutz,et al (2015)**	*	*	*	*	*	*	*			**7**
(35)	**Schwarzenbach,et al (2009)**	*		*	*	*	*	*			**6**
(36)	**Torquato, et al (2019)**	*	*	*	*	*	*	*			**7**
(17)	**Vandekerkhov, et al (2018)**	*	*	*	*	*		*			**6**
(16)	**Wyatt,et al (2016)**	*	*	*	*	*	*	*			**7**
(37)	**Annala,et al (2018)**	*	*	*	*	*	*	*			**7**

Figure S3:The Sensitivity , Specificity and SROC curves for cfDNA in diagnosis of prostate cancer.

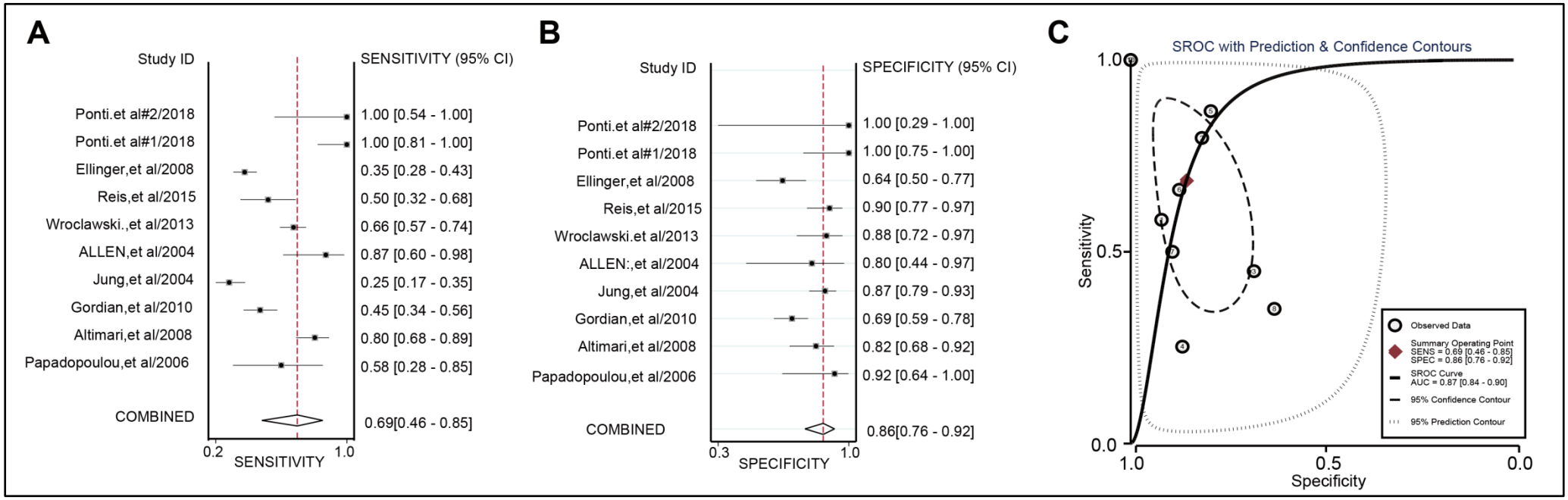


Figure S4:Diagnosis of total concentration in the Pooled DOR,NLR and PLR for PCA.

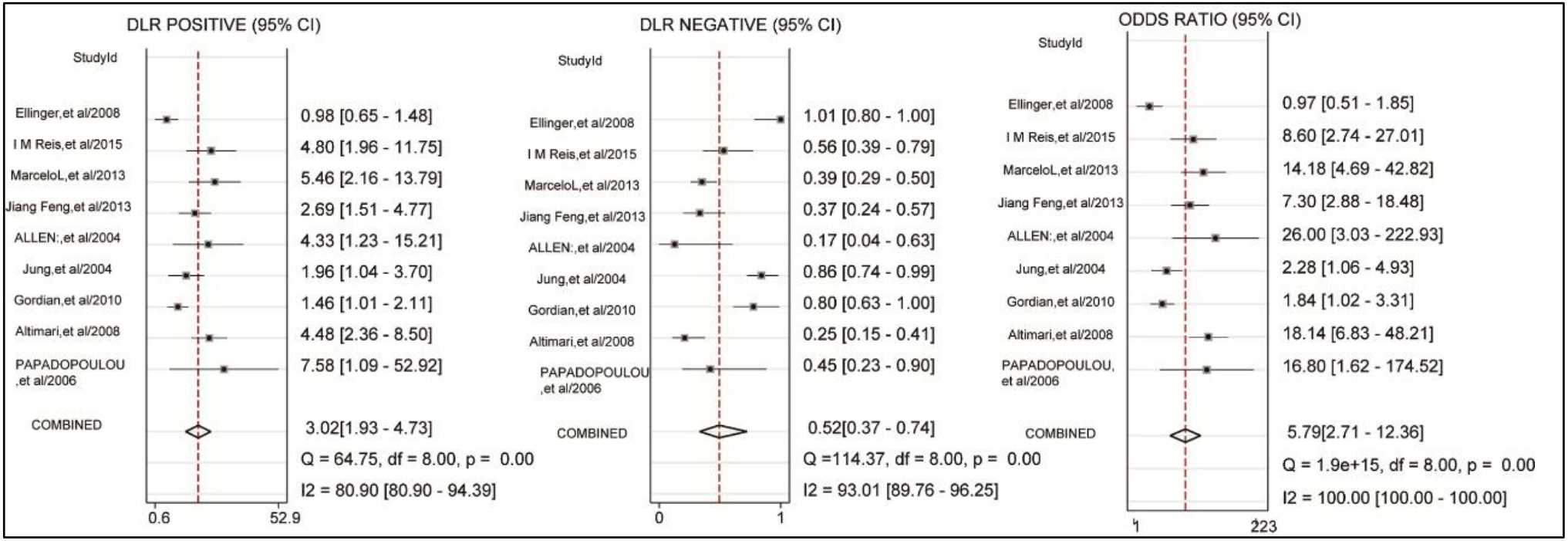


Figure S5:The pooled results of biochemical recurrence free survival in the patients with PCA

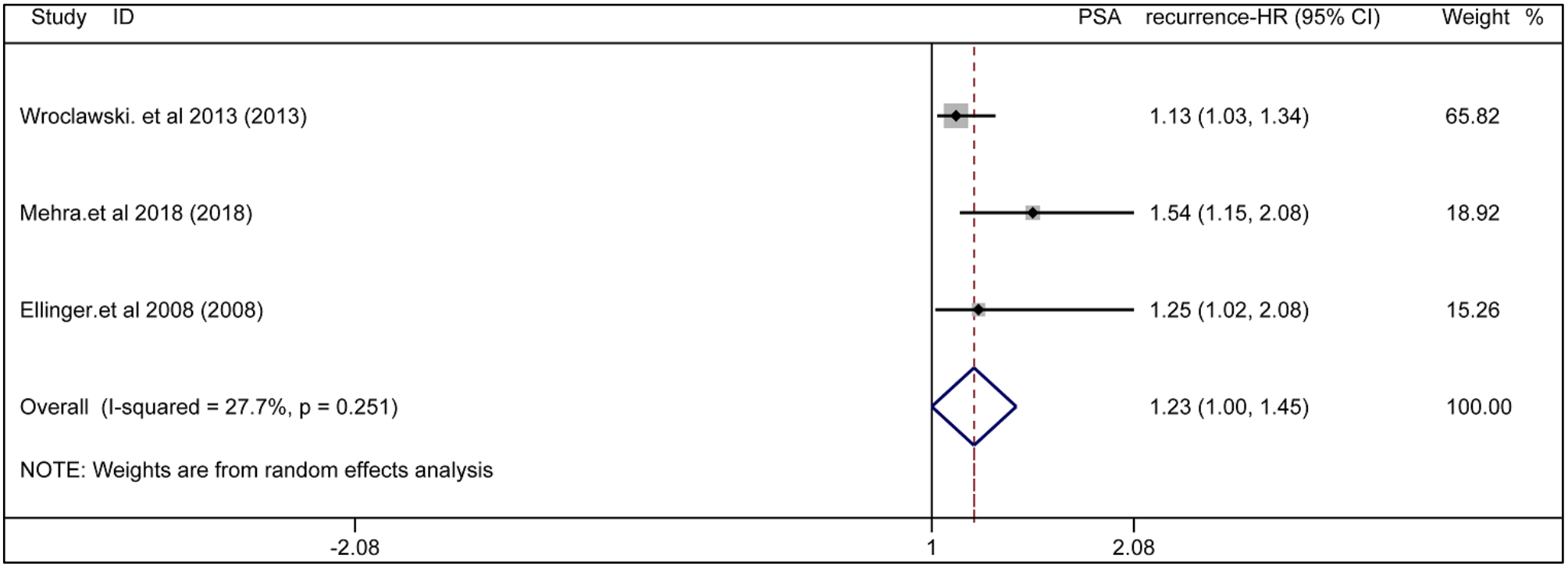


Figure S6: The comparison of other variables with the concentration of cfDNA in PCa

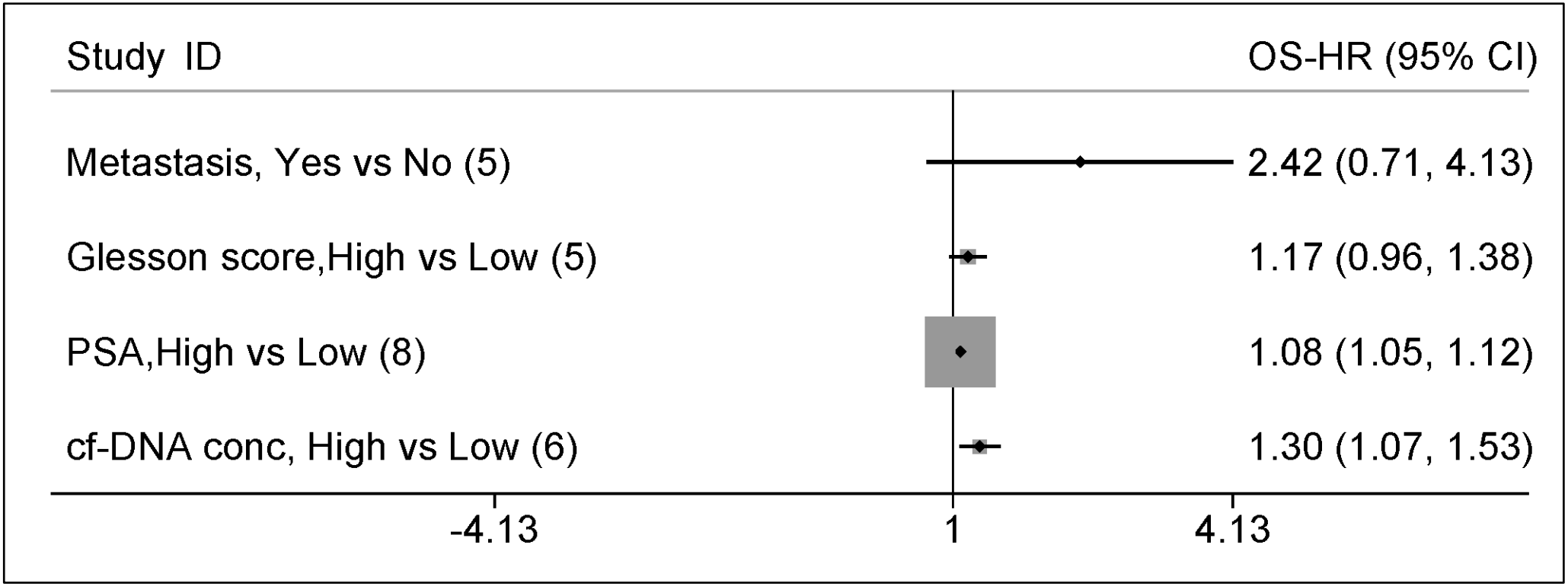
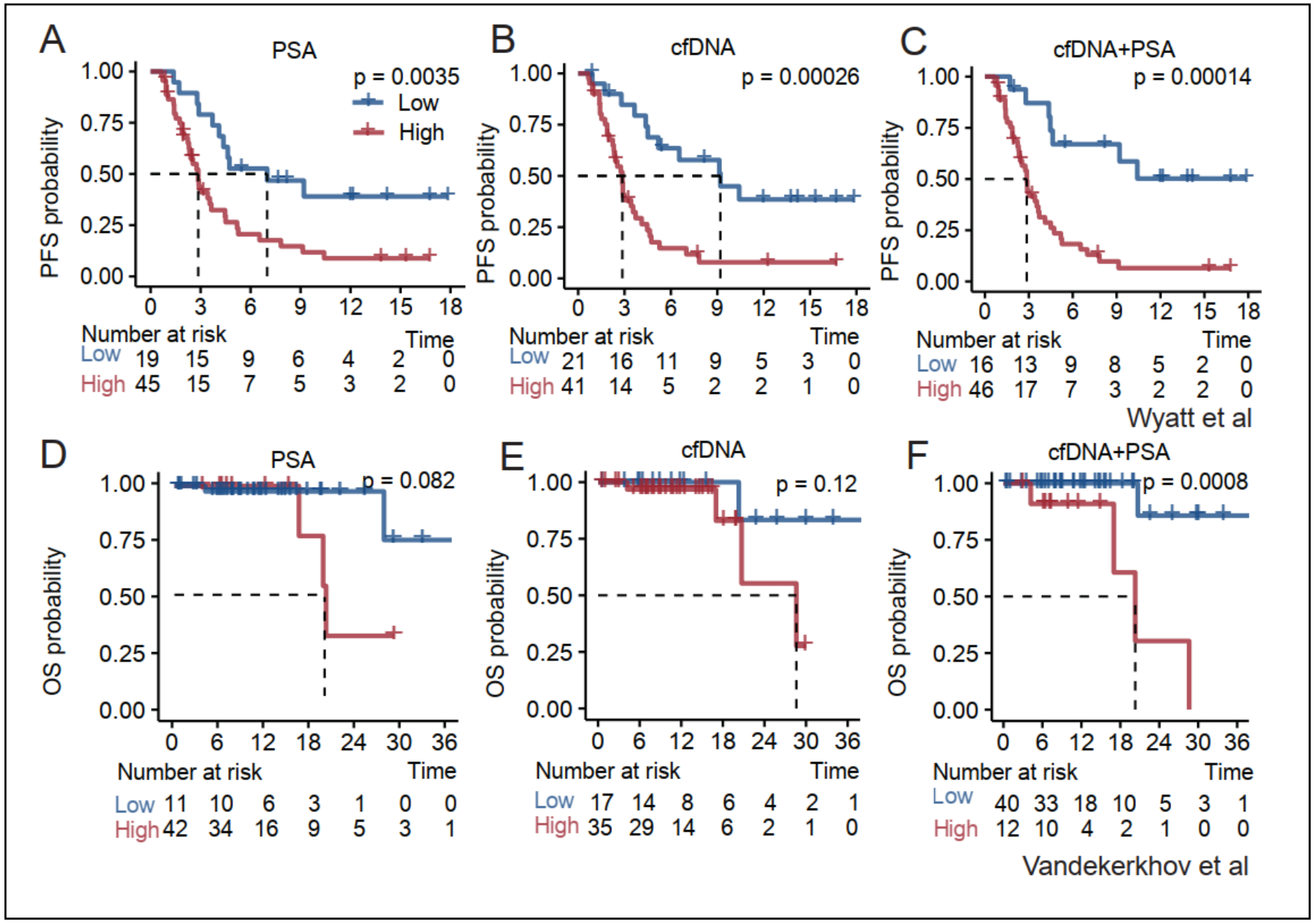


Figure S7: The prognosis value of the combination of PSA and cfDNA for the patients with PCa.



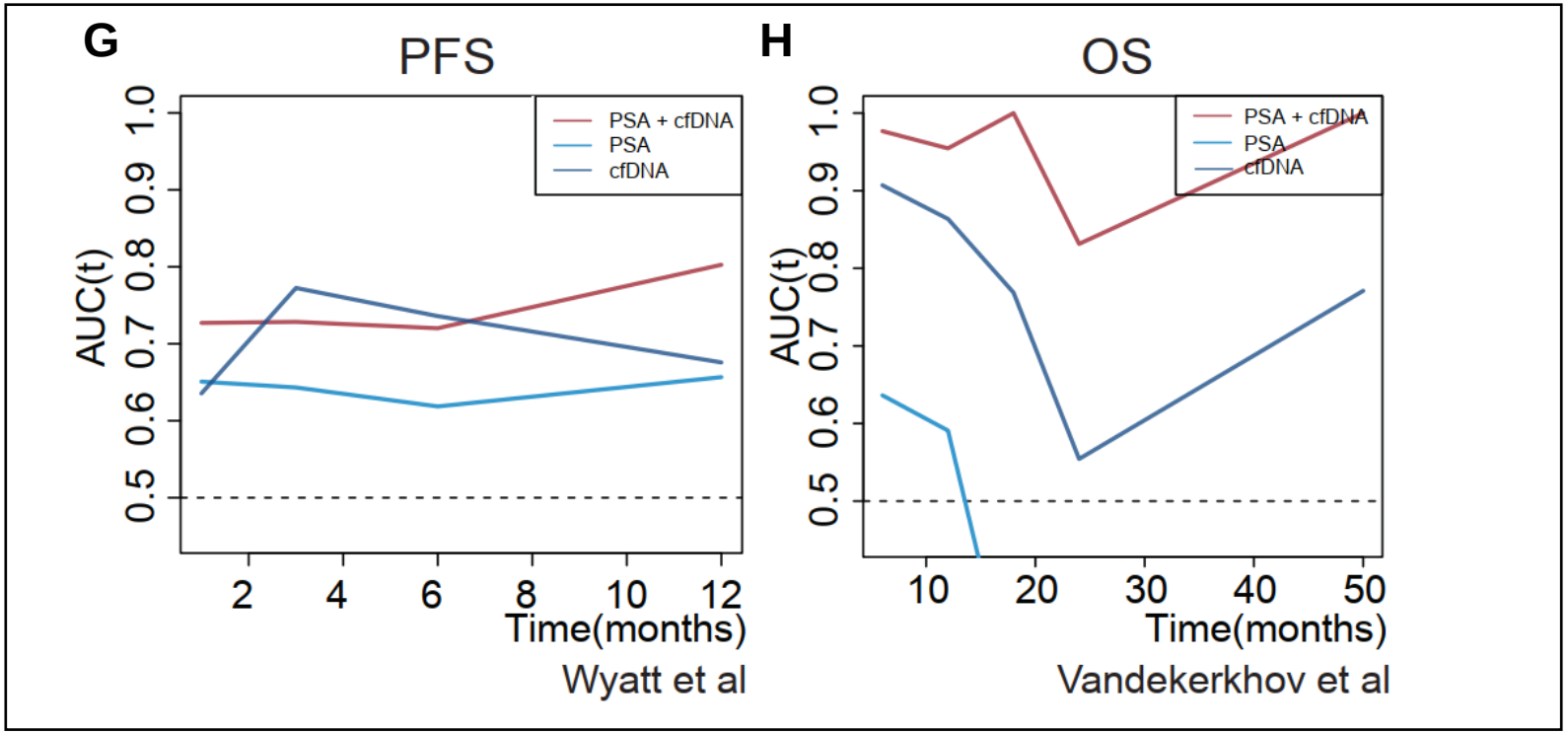

G
PFS
PSA + cfDNA
PSA
cfDNA
AUC(t)
0.5
0.6
0.7
0.8
0.9
1.0
2
4
6
8
10
12
Time(months)
Wyatt et al
H
OS
PSA + cfDNA
PSA
cfDNA
AUC(t)
0.5
0.6
0.7
0.8
0.9
1.0
10
20
30
40
50
Time(months)
Vandekerkhov et al

Table S8: The pros and cons of different cfDNA quantification methods.

Methods		Pros	Cons	citations
Spectrophotometric methods:NanoDrop		Inexpensive; Easy to perform; Be used to estimate the quality of a sample	Cannot distinguish between dsDNA, ssDNA, RNA, oligonucleotides, and free nucleotides; Have a poor predictive ability	[23],[29],[35]
Fluorometric methods	SYBRGreen I or PicoGreen	More accurate and more sensitive compared to spectrophotometry technics	More expensive; Lower accuracy	[22],[25],[30],
	Qubit	Fast, cost-effective	Lower accuracy	[14],[33]
Quantitative real-time PCR.	QPCR,digital PCR	Fast,high technical sensitivity, high precision	Expensive,The accuracy can be affected by fragmentation,	[18],[19],[20],[21],[24], [26],[27], [28], [31],[32]
Next Generation Sequencing		More sensitive; More precise	More expensive	[16],[17],[34],[36],[37]