

Sam Soon et al. Association of absolute amount of pattern 4 disease on prostate biopsy with oncologic outcomes in intermediate-risk prostate cancer: A systematic review

APPENDIX A. Search details

Ovid MEDLINE(R) ALL <1946 to May 04, 2023>

1	exp Prostatic Neoplasms/	147713
2	(prostat* adj2 (cancer or neoplasm* or carcinoma or tumo?r* or adenocarcinoma*)).tw,kf.	161343
3	exp Prostatectomy/ or prostatectom*.tw,kf.	47638
4	or/1-3	205957
5	"pattern 4".tw,kf.	771
6	pattern four.tw,kf.	144
7	(gleason 4 or gleason grade 4 or gp4).tw,kf.	812
8	Neoplasm Grading/ and grade 4.tw,kf.	268
9	5 or 6 or 7 or 8	1871
10	4 and	9950
11	exp animals/ not humans/	5118677
12	10 not 11	950

Embase Classic+Embase <1947 to 2023 May 05>

1	exp Prostatic Neoplasms/	298677
2	(prostat* adj2 (cancer or neoplasm* or carcinoma or tumo?r* or adenocarcinoma*)).tw.	242876
3	exp prostatectomy/ or prostatectom*.tw.	79783
4	or/1-3	347305
5	"pattern 4".tw.	1516
6	pattern four.tw.	198
7	(gleason 4 or gleason grade 4 or gp4).tw.	1628
8	gleason score/ and grade 4.tw.	579
9	or/5-8	3509
10	4 and	92293
11	conference abstract.pt.	4756973
12	10 not 11	1036

EBM Reviews - Cochrane Central Register of Controlled Trials <April 2023>

1	exp Prostatic Neoplasms/	7465
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2 (prostat* adj2 (cancer or neoplasm* or carcinoma or tumo?r* or
adenocarcinoma*)).tw,kw. 15565
3 exp Prostatectomy/ or prostatectom*.tw,kw. 5482
4 or/1-3 18758
5 "pattern 4".tw,kw. 45
6 pattern four.tw,kw. 4
7 (gleason 4 or gleason grade 4 or gp4).tw,kw. 70
8 Neoplasm Grading/ and grade 4.tw,kw. 12
9 or/5-8 125
10 4 and 984
11 conference proceeding.pt. 219918
12 10 not 11 52

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APPENDIX B: Supplementary tables

Supplementary Table 1. Summary of key relevant findings		
Study	Outcome	Summary of key relevant findings
Dean, 2019	Adverse pathology	Multivariable analysis: Max % Gleason 4 in any single core OR 1.02 (95% CI 1.00–1.05), p=0.049 Overall GP4% per 1% increase OR 1.06 (95% CI 1.03–1.10), p=0.001 GP4-TL per mm increase OR 1.33 (95% CI 1.11–1.58), p=0.002 *Note study does not specify if this is per 10% or 1% increase
	Prognostic value	On multivariable analysis, the largest increase in AUC was with GP4-TL. On decision curve analysis, GP4-TL demonstrated the strongest benefit when compared to overall % Gleason pattern 4 (relative amount of GP4 vs. GP3) and max % Gleason pattern 4
Martell, 2019	BCR	Multivariable analysis: APP4 >3.3% vs. ≤ 3.3% HR 2.3 (95% CI 1.1–4.7), p=0.031 Ln (PSA) predictive of biochemical failure HR 2.5 (95% CI 1.1–6.1), p=0.037
	ADT use for BCR	APP4 >6.6% vs. ≤ 6.6% HR 3.7 (95% CI 1.4–10.0), p=0.009 Ln (PSA) predictive of ADT-free survival HR 4.2 (95% CI 1.4–12.4), p=0.010
	Distant metastasis	APP4 >17.5% vs. ≤17.5% HR 25.7 (95% CI 4.9–135.3), p<0.001 Ln (PSA) not predictive of metastatic disease
Sato, 2020	BCR	In cohort with GP4 ≥5% but GP4-TL <0.5 mm and only 1 core of GS 7, then biochemical failure was the same as GS6
Delahunt, 2022	Prostate cancer-specific mortality	Multivariable analysis: Gleason 4+3 vs. 3+4 HR 2.68 (95% CI 1.32–5.44), p=0.006 GP4-TL, mm HR 1.01 (95% CI 1.00–1.02), p<0.0001 %GP4 continuous HR 1.02 (95 CI 1.01–1.04), p=0.0003 APP4, continuous HR 1.03 (95% CI 1.02–1.04), p<0.0001
	Distant progression	Multivariable analysis: Gleason 4+3 vs. 3+4 HR 2.38 (95% CI 1.59–3.54), p<0.0001 GP4-TL, mm HR 1.02 (95% CI 1.01–1.02), p<0.0001 %GP4 continuous HR 1.02 (95 CI 1.02–1.03), p<0.0001 APP4, continuous HR 1.03 (95% CI 1.02–1.04), p<0.0001
	All-cause mortality	Multivariable analysis: Gleason 4+3 vs. 3+4 HR 1.23 (95% CI 0.90–1.68), p≤0.19

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		GP4-TL, mm HR 1.01 (95% CI 1.00–1.02), p=0.0002 %GP4 continuous HR 1.01 (95% CI 1.00–1.01), p=0.0018 APP4, continuous HR 1.02 (95% CI 1.01–1.03), p<0.0001
	Prognostic value	According to AIC (Akaike Information Criteria) and Harrell's concordance index, the best predictor for distant progression, prostate cancer-specific mortality, all-cause mortality was APP4 when compared to Gleason 4+3 vs. 3+4, GP4-TL, and relative % GP4
Glicksman, 2022	BCR	Multivariable competing risk analysis: Higher PSA at baseline sHR 3.2, 95% CI 1.5–7.0, p=0.003 APP4 >5% sHR 5.9 95% CI 2.2–15.9, p=0.0004 after adjusting for age, T-stage and BED factors
	Distant-metastasis free survival	APP4 >20% not statistically significant sHR 1.9, (95% CI 0.9–3.8), p=0.08 Older age only significant variable in MVA
Perera, 2022	BCR	Multivariable analysis: Max % Gleason 4 in any single core per 10% increase 1.30 (95% CI 1.07–1.59), p=0.009 Overall % Gleason 4 per 10% increase HR 1.61 (95% CI 1.21–2.15), p=0.003 Total length Gleason 4 in highest core per mm HR 1.32 (95% CI 1.11–1.57), p=0.001 GP4-TL per cm HR 2.48 (95% CI 1.36–4.52), p=0.003
Sato, 2023	Adverse pathology	In multivariable analysis, only significant predictor was the highest % GP4: OR 1.61, 95% CI 1.26–2.07 GP4-TL not predictive of adverse pathology

APP4: absolute percentage pattern 4; BCR: biochemical recurrence; GP4: Gleason pattern 4; GP4-TL: total linear length of Gleason pattern 4; HR: hazards ratio; OR: odds ratio.