Prognostic Value of Biochemical Recurrence Following Treatment with Curative Intent for Prostate Cancer: A Systematic Review

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CONTEXT
In men with prostate cancer (PCa) treated with curative intent, controversy exists regarding the impact of biochemical recurrence (BCR) on oncological outcomes.

OBJECTIVE
To perform a systematic review of the existing literature on BCR after treatment with curative intent for nonmetastatic PCa. Objective 1 is to investigate whether oncological outcomes differ between patients with or without BCR. Objective 2 is to study which clinical factors and tumor features in patients with BCR have an independent prognostic impact on oncological outcomes.

EVIDENCE ACQUISITION
Medline, Medline In-Process, Embase, and the Cochrane Central Register of Controlled Trials were searched. For objective 1, prospective and retrospective studies comparing survival outcomes of patients with or without BCR following radical prostatectomy (RP) or radical radiotherapy (RT) were included. For objective 2, all studies with at least 100 participants and reporting on prognostic patient and tumor characteristics in patients with BCR were included. Risk-of-bias and confounding assessments were performed according to the Quality in Prognosis Studies tool. Both a narrative synthesis and a meta-analysis were undertaken.

EVIDENCE SYNTHESIS
Overall, 77 studies were included for analysis, of which 14 addressed objective 1, recruiting 20,406 patients. Objective 2 was addressed by 71 studies with 29,057, 11,301, and 4,272 patients undergoing RP, RT, and a mixed population (mix of patients undergoing RP or RT as primary treatment), respectively.
There was a low risk of bias for study participation, confounders, and statistical analysis. For most studies, attrition bias, and prognostic and outcome measurements were not clearly reported. BCR was associated with worse survival rates, mainly in patients with short prostate-specific antigen doubling time (PSA-DT) and a high final Gleason score after RP, or a short interval to biochemical failure (IBF) after RT and a high biopsy Gleason score.

CONCLUSIONS
BCR has an impact on survival, but this effect appears to be limited to a subgroup of patients with specific clinical risk factors. Short PSA-DT and a high final Gleason score after RP, and a short IBF after RT and a high biopsy Gleason score are the main factors that have a negative impact on survival. These factors may form the basis of new BCR risk stratification (European Association of Urology BCR Risk Groups), which needs to be validated formally.

PATIENT SUMMARY
This review looks at the risk of death in men who shows rising prostate-specific antigen (PSA) in the blood test performed after curative surgery or radiotherapy. For many men, rising PSA does not mean that they are at a high risk of death from prostate cancer in the longer term. Men with PSA that rises shortly after they were treated with radiotherapy or rapidly rising PSA after surgery and a high tumor grade for both treatment modalities are at the highest risk of death. These factors may form the basis of new risk stratification (European Association of Urology biochemical recurrence Risk Groups), which needs to be validated formally.