

# Peer Review File

Article information: <https://dx.doi.org/10.21037/lcm-21-49>

Reviewer A

Comment 1: The authors state that they searched for studies between 2011 and 2021 (Page 3/Line 76), but why cite ""Reference 33"" published in 2006? Of course, we can cite references before 2011, but clearly, this reference is used to support the key points as that main literature between 2011 and 2021. I suppose the authors have done an extra search. If so, I suggest supplementing other searches that have been done.

Reply 1: Thank you for the comment. This was by mistake. We moved this statement into introduction (page 3 line 87-89) as “Administration of vitamin D3 analogue, prescribed for 3 months has also been shown to reduce prostate volume intervening with natural history of benign hyperplasia”.

Comment 2:

Page 3/Line 83-88 and Page 4/Line 107-108: Vitamin D and prostate cancer: “... both high and low concentrations of vitamin D ... vitamin D deficiency... adequate vitamin D levels” and “the regular doses needed ...”.

What are the exact concentrations of high, low level, vitamin D deficiency, and regular doses? Please report it as authors do in the section on “Vitamin D and benign prostate hyperplasia” (Page 5/Line 125-127).

Reply 2: Thank you for the comment. We amended the statement at page 4 line 112-116 as “Moreover, vitamin D deficiency (<30 ng/ml or <25 nmol/L) has been associated with adverse pathology (dominant Gleason pattern 4, presence of any pattern 5, and pathologic stage pT3aN0M0 or higher) in men with localized prostate cancer undergoing radical prostatectomy and a higher overall and specific mortality in men diagnosed with the disease compared to men with adequate vitamin D levels”. Also, we amended the statement at page 5-6 line 136-139 to “The recommended dosage needs further evaluation; doses at 500-1,000 mg calcium and 200-500 IU vitamin D per day might not be efficient to sustain bone health during androgen deprivation treatment, whereas the effect on oncological endpoints such as PSA response might be modest”. I hope this satisfies the reviewer.

Comment 3:

Page 3/Line 90: Vitamin D and prostate cancer: “Genetic variations of the vitamin D receptors ...”.

Page 5/Line 127: Vitamin D and benign prostate hyperplasia: “Low (25-OH) vitamin D levels ...”.

Please add a brief introduction of VDR and 25-OH, so that readers can understand their relationship with vitamin D.

Reply 3: At page 5 line 118-122 “This hypothesis has also been observed in other adenocarcinomas such as the colorectal cancer and the understanding of the association between VDR and vitamin D is crucial. The binding product of the fat-soluble vitamin D and the (nuclear) VDR mediates the cellular proliferation, apoptosis and metaplastic process and interferes with the progression of carcinogenesis (20)”. We hope that a parallel example works for the scope.

Comment 4:

Page 3/Line 85: Vitamin D and prostate cancer: “..., whereas sunlight carries a protective effect”.

Page 4/Line 100-101: Vitamin D and prostate cancer: “Despite evidence that vitamin D deficiency is associated with prostate cancer risk and ultraviolet radiation decreases that risk, ...”.

The “sunlight” and “ultraviolet radiation” are the main natural source of vitamin D, but the introduction only mentions dietary intake as a means of supplementation.

Reply 4: We would be grateful if the reviewer would clarify the amendment needed. From our end, we commented on the role of sunlight as an additional information linked to the physiology of vitamin D; it was not our scope to further illustrate the role of sunlight or radiation.

Comment 5:

Page 5/Line 131-137: Vitamin D and benign prostate hyperplasia: “Zendejdel and colleagues ... in comparison to tamsulosin alone”.

This paragraph is mainly about the influence of vitamin D deficiency. However, what these three studies show is the effect of vitamin D supplementation. It is recommended that they be placed in the next paragraph.

Reply 5: Thank you for your comment. A new paragraph has been introduced, as appropriate (page 7, line 160).

Comment 6:

Page 7/Line 186-190: Vitamin D and Urinary tract infections.

Please add a brief introduction to Urinary tract infections.

Reply 6: Thank you for the comment. We added a small paragraph at page 9 line 211-213 “Urinary tract infections (UTI) are of the commonest infections in the community and healthcare setting. In general, their prevalence seems to be increasing with age (46). In children, UTIs follow second to the respiratory infections and prompt investigations is mandatory (47)”

Comment 7:

Please provide full names or a list of abbreviations for the abbreviations that appear in this article (E.g. “PSA” on Page 4/Line 105). Abbreviations that have provided full names can be used directly in the following text (E.g., “VDR” on Page 3/Line 90 and Page 4/Line122).

Reply 7: We performed necessary changes (page 5, line 133 – page 5, line 117).

Comment 8: Please unify the writing of professional vocabulary (E.g. “TaqI” on Page 3/Line 93 and “Taq-I” on Page 4/Line 123).

Reply 8: Corrected (page 5, line 124).

Comment 9: One space is needed between the number and the unit (E.g. “20ng/mL” on Page 5/Line 126).

Reply 9: Corrected (3 occasions).

Comment 10: I suggest the authors adding ""between 2011 and 2021"" in the title.

Reply 10: Amended as “A narrative review of past decade literature”.

Reviewer B

Comment 1: In the abstract, better also specify the five urological conditions.

Reply 1: We have reconstructed the abstract as per editorial suggestion. Please find in the text.

Comment 2: In the introduction, before introducing what the review aimed to do (line 62), the authors should better explain why they choose these five urological conditions instead of others.

Reply 2: The selection of the topic was matter of preference. However, we added as above: page 3, 90-92 “In this review, we are focusing on the common urological entities of prostate cancer and hyperplasia, urolithiasis, urinary tract infections and male infertility, reviewing the advancements of the past decade on the topic”

Comment 3: In the methods, line 70, the authors mentioned that they also have shared the epidemiology of prevalence of vitamin D status. However, the main text (line 80~line252) does not contain this information. Please keep the description consistent, either adding such information or deleting the description in the methods.

Reply 3: Thank you for the comment. At page 4, line 96-99, we amended the material & methods section.

Comment 4: I strongly suggest the authors draw a table to summarize the key findings of vitamin D (pathophysiology and therapeutic potential) in the mentioned five urological conditions. This would clearly save readers' time and highlight the key points.

Reply 4: A table has been produced (please find attached).

Comment 5: In the abstract, the authors need to briefly explain why there is a need for this review topic and indicate the clinical significance. I think the authors can not only described the work to be done in this study, which made the abstract not informative. Please briefly summarize the main findings from studies reviewed. Also, please have some summary comments on these findings and their clinical implications.

Reply 5: The abstract was reconstructed as per the Editorial comments as well. We hope the amendments satisfy the reviewer.

Comment 6: In the introduction part, it remains unclear why the authors performed this review. Please provide more insights on the necessity and clinical significance of this review topic.

Reply 6: We have amended the introduction (page 3 line 87-92). We hope this satisfies the reviewer.

Comment 7: In the methods part, please explain why studies published before 2011 were not searched and indicate detailed dates of the search in 2021.

Reply 7: We set our search limit within the past decade as our effort was to provide update evidence. We have amended our material & methods section accordingly explaining our methodology and scope.

Comment 8: In the part of literature review, I suggest the authors not to only repeat what the studies found. Please have comments on their methodology, because this is related to the level of clinical evidence from these studies. Also, insights on unaddressed or unanswered questions in these studies are also needed.

Reply 8: Please review the new table summarizing the role and potential benefit of vitamin D.

Comment 9: In the discussion part, please have overall comments on the potential therapeutic roles of vitamin D in common urological conditions, in relation to efficacy, safety, and level of clinical evidence. The authors need to use separate paragraph to discuss unaddressed problems in this area, and suggest possible research topics in the future. It is also necessary to suggest the clinical implications of the available findings.

Reply 9: Please note the last paragraph of discussion page 12 304-309.

Reviewer C

Comment 1: I only suggest adding the following reference on vitamin D and urolithiasis.: de Carvalho JF, Churilov LP. Safety of megadose of vitamin D in patients with nephrolithiasis. *Nutrition*. 2021 Jul-Aug;87-88:111201. doi: 10.1016/j.nut.2021.111201. Epub 2021 Feb 12. PMID: 33744642.

Reply 1: Thank you for your kind suggestion. We included the study at page 9 line 204-206.