## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Epidemiology of psoriasis and palmoplantar pustulosis: a nationwide study using the Japanese national claims database |
| **AUTHORS** | Kubota, Kiyoshi; Kamijima, Yukari; Sato, Tsugumichi; Ooba, Nobuhiro; Koide, Daisuke; Iizuka, Hajime; Nakagawa, Hidemi |

## VERSION 1 - REVIEW

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| **REVIEWER** | Takeo Nakayama<br>Kyoto University, Japan |
| **REVIEW RETURNED** | 16-Sep-2014 |

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| **GENERAL COMMENTS** | This manuscript is reporting the prevalence, seasonal variation of disease activity and prevalence of comorbidities in Japanese patients with psoriasis and palmoplantar pustulosis based on the national healthcare claim database. This is generally well-written and potentially worth accepting for publication.<br>Before that, there are some concerns to be addressed.<br><br>Major ones:<br>1. The rationale to examine the seasonal variation of treatment for psoriasis and PPP is not clear. Is it mainly to prove the difference in the entity of psoriasis and PPP?<br>2. Describe the method or cite the reference for the calculation of 95% CI of the difference in the sex-age standardized prevalence.<br>3. L10-L31 on the page 15, the intention of this paragraph is not clear. Considering the former part that addresses the possible under-treatment of psoriasis and PPP in the previous studies in the UK and the US, it is rather difficult to follow the latter part.<br>4. L32-L56 on the page 15, the reason that “psoriasis is a direct risk factor” is not clear. Some more explanations are necessary.<br><br>Minor one:<br><br>1. In the abstract, “PPP” at the first appearance needs to be spelled out. |

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| **REVIEWER** | Eva Hagforsen<br>University of Uppsala, Sweden |
| **REVIEW RETURNED** | 17-Dec-2014 |

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| **GENERAL COMMENTS** | The main limitation of this study is that the diagnosis codes of psoriasis and PPP are not validated. The authors have taken this in concideration and overall, all data was carefully interpreted. |

**VERSION 1 – AUTHOR RESPONSE**

Comments from Reviewer 1:
[Comment 1]
The rationale to examine the seasonal variation of treatment for psoriasis and PPP is not clear. Is it mainly to prove the difference in the entity of psoriasis and PPP?

Response:
The current study is a descriptive study and it is not intended to provide the information to prove the difference in the disease entity of psoriasis and PPP.
To clarify this contention, we changed the last sentence of INTRODUCTION to make it clear that the seasonal variation of the use of the health care service was examined for the descriptive purpose. Or, the last sentence of INTRODUCTION was altered from
"In the current study, we used the JNDB data to estimate the national prevalence and some of relevant epidemiological characteristics of psoriasis and PPP in Japanese population"
in the original to
"In the current descriptive epidemiological study, we used the JNDB data to estimate the national prevalence and some of relevant epidemiological characteristics including seasonal variation of the use of the healthcare service ,[8] of psoriasis and PPP in Japanese population."
in the revision.

When modifying the above part, we also added one paper to REFERENCE as new "reference 8" in the revision. This paper was on a descriptive study to examine seasonal variation of dermatologic office visits for several skin diseases. This new reference was added to emphasize that the seasonal variation is recognized to be one of important descriptive features of the skin diseases.

In addition, we altered the relevant sentences in DISCUSSION or the sentence beginning from the last line of page 14 in the original
"Those findings are in accordance with the proposal in the International Psoriasis Council in 2007 that PPP should be considered a separate condition from psoriasis ,[11,13]."
was altered to
"According to the proposal in the International Psoriasis Council in 2007, PPP should be considered a separate condition from psoriasis ,[12,14]. The findings in the current descriptive epidemiological study indicated some relationship between psoriasis and PPP (e.g., the proportion of patients with psoriasis in those with PPP was 8.5% and higher than 0.34%, the prevalence of psoriasis in the whole population) but the difference for several aspects between psoriasis and PPP as well in accordance with the above-mentioned proposal."
in the revision.

[Comment 2]
Describe the method or cite the reference for the calculation of 95% CI of the difference in the sex-age standardized prevalence.

Response:
In the original, the reference was cited as reference 9 or "Greenland S, Rothman KJ. Introduction to stratified analysis. In: Rothman KL, Greenland S, Lash T, eds. Modern Epidemiology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008: 258-82." The method is fully given in this chapter ("Introduction to stratified analysis", page 258-282) of this textbook but may require careful reading to recognize that the part gives full information on the calculation for standardized prevalence. Equation [15-4] gives how to calculate the point estimate of the difference of two standardized prevalences. Though this equation seems to give the differences of two standardized risks (incidence proportions), if one reads the following sentence given after equation [15-2] "Standardized prevalences or standardized means can be constructed using the same formulas ---", it is clear that equation [15-4]

can be also used for the prevalence. Likewise Equation [15-10] gives how to calculate the standard deviation (therefore 95% CI) of the difference of two standardized prevalences. Though this equation again seems to give the differences of two standardized rates, if one reads the following sentence given after equation [15-11] “Parallel formulas can be applied to estimate ---- standard deviations of RDw ---” together with the above-mentioned sentence given after equation [15-2], it is clear that “parallel formula” to equation [15-10] can be also used for the prevalence. However, this context may be missed unless one reads this part carefully and therefore, we altered the description beginning Line 54 of page 8 in the original
“The difference of the standardized prevalence and its 95% CI were estimated using the severity class III as a reference ,[9].”
to
“The difference of the standardized prevalence and its 95% CI were estimated using the severity class III as a reference. The standard textbook ,[10] was used to calculate the difference of the standardized prevalence and its 95% CI (equation [15-4] and “parallel formula” to equation [15-10], respectively in reference 10).”
in the revision. The above description in the revision may be viewed to be too detailed and we will eventually follow the indication by the editor.

[Comment 3]
L10-L31 on the page 15, the intention of this paragraph is not clear. Considering the former part that addresses the possible under-treatment of psoriasis and PPP in the previous studies in the UK and the US, it is rather difficult to follow the latter part..

Response:
The intention of this paragraph is to give some guide which may be useful in guessing the severity of the “severity class IV” (no treatment). We expanded the last sentence of the paragraph in the original
“In our study, patients with no treatment for psoriasis and PPP included more patients with arthropathy than those with topical therapy particularly in the department subgroup B (other specialty) where the severity class IV (no treatment) might represent more severe psoriasis or PPP than the severity class III (topical therapy only).”
to
“Likewise, about 9% of patients with psoriasis and about 16% of patients with PPP receiving no therapy for psoriasis and PPP in our study may include those who are dissatisfied with the treatment. However, some of them might receive no therapy for psoriasis and PPP simply because they had very mild disease. Interestingly, as shown in online supplementary table S5, patients with no treatment for psoriasis and PPP included more patients with arthropathy than those with topical therapy particularly in the department subgroup B (other specialty). Thus, the severity class IV (no treatment) in the department subgroup B might represent more severe psoriasis or PPP than the severity class III (topical therapy only) while in other department subgroups, the severity class IV might represent not so severe psoriasis or PPP when compared to the severity class III.”
in the revision. We hope that Reviewer finds that the intention of the paragraph is clear in the revision.

[Comment 4]
L32-L56 on the page 15, the reason that “psoriasis is a direct risk factor” is not clear. Some more explanations are necessary.

Response:
We accept that what is meant by the “direct risk” is not clear and decided to avoid the use of this term. Accordingly, we changed relevant two parts.
First, the following sentence in the original
“Psoriasis itself may be the direct risk factor for those conditions but the increased risk of those conditions may be due to the high prevalence of obesity and other known predisposing factors ,[19]”

was altered to
“The reasons why the increased risk of those conditions is increased in psoriasis have not been fully determined but the increased risk may be due to the high prevalence of obesity and other known predisposing factors ,[20].”
in the revision.

Second, the following sentences in the original
“This observation may indicate that psoriasis is a direct risk factor. However, another interpretation may be that ciclosporin is the major contributor to the high prevalence of the comorbidity because ciclosporin was used by more than half of patients with psoriasis receiving a systemic therapy while ciclosporin was used only by 10% of those with PPP receiving a systematic therapy.”
were altered to
“One possible interpretation for this observation is that ciclosporin is the major contributor to the high prevalence of the comorbidity because ciclosporin was used by more than half of patients with psoriasis receiving a systemic therapy while ciclosporin was used only by 10% of those with PPP receiving a systematic therapy.”
in the revision.

[Minor Comment]
In the abstract, “PPP” at the first appearance needs to be spelled out.

Response:
We amended the abstract and “PPP” is spelled out at the first appearance in the revision as detailed in response to the editor.

Comments from Reviewer 2:
[Comment]
The main limitation of this study is that the diagnosis codes of psoriasis and PPP are not validated. The authors have taken this in concideration and overall, all data was carefully interpreted.

Response:
We appreciate that Reviewer 2 has recognized that we have taken in consideration for the main limitation that the diagnosis codes of psoriasis and PPP are not validated. We also appreciate that Reviewer 2’s observation that all data was carefully interpreted.