

# **Risk of skin cancer in people with vitiligo: a systematic review and meta-analysis**

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Dear Editor,

Vitiligo is a chronic disorder causing skin depigmentation with around 1% global prevalence, affecting people of all ages, skin types and genders.<sup>1</sup> Due to the absence of melanin in lesional skin there is a theoretical concern that there might be a higher risk of skin cancer in people with vitiligo. However, some studies have shown that the genetic and autoimmune profiles of vitiligo patients may confer a degree of protection against the development of melanoma and non-melanoma skin cancer (NMSC).<sup>2</sup> Therefore, the aim of this systematic review was to quantify the risk of skin cancer (melanoma and NMSC) in people with vitiligo compared to those without vitiligo.

We registered the review protocol with PROSPERO on July 19<sup>th</sup> 2017 (CRD42017072493) and reported our study following MOOSE guidelines. We searched three databases (PubMed, Embase and Web of Science), from inception to July 12<sup>th</sup> 2017, for observational studies meeting the inclusion criteria (see the protocol for further details). We also searched the British Association of Dermatologists clinical guideline for vitiligo and UK E-Theses depository for any relevant studies. Two authors (LB and SL) independently performed title/abstract and full text screening, quality assessment (using Joanna Briggs Institute's (JBI) critical appraisal tool) and data extraction. Disagreements were resolved by discussion with another author (SR). Random effects meta-analysis was used to combine the results.

A total of 2,177 studies were identified, of which 12 full text articles were assessed for eligibility. Of these, five studies were eligible to be included in the review. We searched the references of the five studies and also their Google Scholar citations, and identified one extra study. Of the six studies included in the review, four were included in the meta-analysis. Details of the search strategy and the PRISMA flow diagram are available on request to the corresponding author.

All but one study were hospital-based.<sup>3-8</sup> Four studies were cross-sectional,<sup>3-6</sup> of which three compared people with vitiligo to people without vitiligo and one compared vitiligo skin to non-vitiligo skin on the same group of patients (Table 1).<sup>6</sup> The remaining two studies were cohort<sup>7</sup> and case-control<sup>8</sup> studies. The number of people with vitiligo in the included studies ranged from 19 to 10,040. Only one study was deemed to be of high quality,<sup>8</sup> scoring 7 out of 10 using the JBI tool. The main reason for poor quality was lack of comparability between people with and without vitiligo. One study adjusted for phototherapy.<sup>4</sup> The meta-analyses for NMSC and melanoma combined results from three studies each<sup>3-5,8</sup> which included a total of 11,447 and 11,366 people with vitiligo, respectively. The two studies excluded from the meta-analysis found no events of skin cancer in either vitiligo nor non-vitiligo groups (366 patients excluded).<sup>6,7</sup> Compared to people without vitiligo, people with vitiligo had a significantly lower risk of NMSC; the crude odds ratio was 0.29 (95% confidence intervals (95%CI) 0.14-0.58, I-squared 75.9%). The same pattern occurred for melanoma but the crude odds ratio was not statistically significant; 0.52 (95%CI 0.15-1.78, I-squared 85.3%). Forest plots available on request to the corresponding author.

This review supports the current view that vitiligo may be protective of skin cancer. This could be due to the genetic and autoimmune profile of vitiligo, or the fact that patients with vitiligo are more careful regarding sun protection than those without vitiligo. This is the first review in this clinical area which has searched the literature comprehensively and synthesised data in a systematic way. However, our review is limited by the small number of included studies and high heterogeneity due to methodological and clinical differences between the included studies. Furthermore, the lack of studies has prohibited subgroup analysis and assessment of publication bias.

The main methodological limitation of the included studies was lack of adequate comparison with the controls. Furthermore, most of the studies either had an inappropriate study design or were hospital-based, limiting the internal and external validity of the results. Finally, it is important to acknowledge studies that assessed the

association between melanoma and vitiligo may have biased results because vitiligo occurring during melanoma or treatment of melanoma is very difficult to differentiate from vitiligo itself. Future research implications include the need for a population-based longitudinal study with appropriate comparisons.. Once more appropriate research has been conducted in this field, clinicians may be able to reassure people with vitiligo that they are not at increased risk of skin cancer.

## References

- 1 Zhang Y, Cai Y, Shi M, *et al.* The prevalence of vitiligo: A meta-analysis. *PLOS ONE* 2016; **11**:e0163806.
- 2 Rodrigues M. Skin Cancer Risk (Nonmelanoma Skin Cancers/Melanoma) in Vitiligo Patients. *Dermatol Clin* 2017; **35**:129–34.
- 3 Sharquie KE, Noaimi AA, Burhan ZT. The Frequency of Skin Tumors and Infections in Patients with Autoimmune Diseases. *J Cosmet Dermatol Sci Appl* 2016; **06**:140.
- 4 Paradisi A, Tabolli S, Didona B, *et al.* Markedly reduced incidence of melanoma and nonmelanoma skin cancer in a nonconcurrent cohort of 10,040 patients with vitiligo. *J Am Acad Dermatol* 2014; **71**:1110–6.
- 5 Teulings H e., Overkamp M, Ceylan E, *et al.* Decreased risk of melanoma and nonmelanoma skin cancer in patients with vitiligo: a survey among 1307 patients and their partners. *Br J Dermatol* 2012; **168**:162–71.
6. Schallreuter KU, Tobin DJ, Panske A. Decreased Photodamage and Low Incidence of Non-Melanoma Skin Cancer in 136 Sun-Exposed Caucasian Patients with Vitiligo. *Dermatology* 2002; **204**:194–201.
7. Harrist TJ, Pathak MA, Mosher DB, Fitzpatrick TB. Chronic cutaneous effects of long-term psoralen and ultraviolet radiation therapy in patients with vitiligo. *Natl Cancer Inst Monogr* 1984; **66**:191–6.
8. Beral V, Evans S, Shaw H, Milton G. Cutaneous factors related to the risk of malignant melanoma. *Br J Dermatol* 1983; **109**:165–72.

