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THE SMOKING PARADOX IN THE DEVELOPMENT OF PSORIATIC ARTHRITIS AMONG PSORIASIS PATIENTS – A POPULATION-BASED STUDY

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Objectives: Smoking is strongly associated with an increased risk of psoriatic arthritis (PsA) in the general population, but not among psoriasis patients. We sought to clarify the possible methodologic mechanisms behind this paradox.

Methods: Using 1995-2015 data from The Health Improvement Network, we performed survival analysis to examine the association between smoking and incident PsA in the general population and among psoriasis patients. We clarified the paradox using mediation analysis and conducted bias sensitivity analyses to evaluate the potential impact of index event bias and quantify its magnitude from uncontrolled/unmeasured confounders.

Results: Of 6.65 million subjects without PsA at baseline, 225,213 participants had psoriasis and 7,057 developed incident PsA. Smoking was associated with an increased risk of PsA in the general population (RR, 1.27; 95% CI, 1.19-1.36), but with a decreased risk among psoriasis patients (RR 0.91; 95% CI, 0.85-0.99). Mediation analysis showed that the effect of smoking on the risk of PsA was mediated almost entirely through its effect on psoriasis. Bias sensitivity analyses indicated that even when the relation of uncontrolled confounders to either smoking or PsA was modest (both RRs = \sim 1.50), it could reverse the biased estimate of effect of smoking among psoriasis patients (RR=0.9).

Conclusions: In this large cohort representative of the UK general population, smoking was positively associated with PsA risk in the general population, but negatively associated among psoriasis patients. Conditioning on a causal intermediate variable (psoriasis) can reverse the association between smoking and PsA, explaining the smoking paradox for the risk of PsA among psoriasis patients.

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