

Epidemiological Studies on Psoriasis

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Ellen Heilmann Modalsli from the Department of Dermatology, St. Olav University Hospital, Trondheim, Norway, defended her doctoral thesis titled *Psoriasis: prevalence, osteoporosis, depressive symptoms and obesity* at the Norwegian University of Science and Technology on November 29th, 2017. Her supervisors were Marit Saunes, Bjørn Olav Åsvold and Pål Romundstad. Tamar Nijsten from the University of Rotterdam and Inger Njølstad from the Arctic University of Norway were first and second opponents. Available at: <https://www.medicaljournals.se/forum/KappenEllenHeilmannModalsli.pdf>.

Psoriasis is a chronic inflammatory skin disease. The worldwide prevalence estimate is 2–3%, but the prevalence has been reported even higher in Norway. Over the last decades, considerable progress has been made regarding the understanding of the complex pathophysiology of psoriasis, and the pipeline is full of novel drugs.

Several observational studies have reported that people with psoriasis more frequently tend to experience depressive symptoms, and have a higher risk of obesity, smoking, diabetes and other cardiovascular risk factors, compared to the general population. Osteoporotic fractures have also been reported more frequently among psoriasis patients compared to patients without psoriasis. Previous studies have hypothesized that an increased systemic inflammatory status of individuals with psoriasis may contribute to development of disease in other organs, e.g. quality of bone formation. Although there is some evidence from observational studies that several modifiable factors may play an important role in the psoriasis aetiology, causality is often challenged by residual confounding and reverse causality. Thus, more aetiological epidemiological studies are needed to strengthen causal inference.

This thesis consists of 4 study parts all based on data from the Nord-Trøndelag Health Study 2006–08 (the HUNT3 Survey). After the initial validation of the psoriasis question, we linked information from the HUNT3 Survey to clinically derived fracture data from regional hospitals, information on relevant medications from the Norwegian Prescription Database and socioeconomic data from Statistics Norway. In addition, we used genetic information provided by the K.G. Jebsen Center for Genetic Epidemiology, and publicly available summary statistics of obesity-associated genetic variants provided by a large international consortium (GIANT).

In paper I, we validated the psoriasis-question in the HUNT3 Survey. We estimated a positive predictive value of 78%, which indicated that self-reported psoriasis was valid tool for further



From left to right: Inger Njølstad (second opponent), Tamar Nijsten (first opponent), Ellen Heilmann Modalsli (doctoral candidate) and Eva Skovlund (evaluation committee chair)

studies of psoriasis in the HUNT3 Survey (1). We estimated that the validated prevalence of psoriasis was 8%. In paper II, we found no clear association between psoriasis and increased risk of fracture, reduced bone mineral density or higher prevalence of osteoporosis (2). In paper III, we found a weak association between overall psoriasis and depressive symptoms (3). The association with depressive symptoms was strengthened when psoriasis was characterized by inverse distribution, long duration or requirement of systemic anti-psoriatic treatment. In paper IV, our findings suggested that obesity is causally associated with psoriasis (4). The results have been published as part of a larger study (5).

A more accurate estimation of the global prevalence and consequences of psoriasis contributes to a better understanding of the disease from a public health perspective. Furthermore, an increased knowledge of the causes of psoriasis may help to inform decision makers about the prevention and treatment possibilities of psoriasis.

LIST OF ORIGINAL PUBLICATIONS

- I. Modalsli EH, Snekvik I, Åsvold BO, Romundstad PR, Naldi L, Saunes M. Validity of self-reported psoriasis in a general population: The HUNT study, Norway. *J Invest Dermatol* 2016; 136: 323–325. doi:

- 10.1038/JID.2015.386.
- II. Modalsli EH, Åsvold BO, Romundstad PR, Langhammer A, Hoff M, Forsmo S, et al. Psoriasis, fracture risk and bone mineral density: The HUNT Study, Norway. *Br J Dermatol* 2017; 176: 1162–1169. doi: 10.1111/bjd.15123.
- III. Modalsli EH, Åsvold BO, Snekvik I, Romundstad PR, Naldi L, Saunes M. The association between the clinical diversity of psoriasis and depressive symptoms: The HUNT Study, Norway. *J Eur Acad Dermatol Venereol* 2017; 31: 2062–2068. doi:10.1111/jdv.14449.
- IV. Modalsli EH, Vie GÅ, Brumpton BM, et al. The association between body mass index and psoriasis: A Mendelian randomization analysis of The HUNT Study, Norway. Manuscript.
- V. Budu-Aggrey A, Brumpton B, Tyrrell J, Watkins S, Modalsli EH, Celis-Morales C, et al. Evidence of a causal relationship between body mass index and psoriasis: A Mendelian randomization study. *PLoS Med* 2019;16:e1002739. doi: 10.1371/journal.pmed.1002739..