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Obesity, Waist Circumference, Weight Change, and Risk of Incident Psoriasis: Prospective Data from the HUNT Study

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Although psoriasis has been associated with obesity, there are few prospective studies with objective measures. We prospectively examined the effect of body mass index, waist circumference, waist-hip ratio, and 10-year weight change on the risk of developing psoriasis among 33,734 people in the population-based Nord-Trøndelag Health Study (i.e., HUNT), Norway. During follow-up, 369 incident psoriasis cases occurred. Relative risk (RR) of psoriasis was estimated by Cox regression. One standard deviation higher body mass index, waist circumference, and waist-hip ratio gave RRs of 1.22 (95% confidence interval [CI] = 1.11–1.34), 1.26 (95% CI = 1.15–1.39), and 1.18 (95% CI = 1.07–1.31), respectively. Compared with normal weight participants, obese people had an RR of 1.87 (95% CI = 1.38–2.52), whereas comparing the fourth with the first quartile of waist circumference gave an RR of 1.95 (95% CI = 1.46–2.61). One standard deviation higher weight change gave an RR of 1.20 (95% CI = 1.07–1.35), and people who increased their body weight by 10 kg or more had an RR of 1.72 (95% CI = 1.15–2.58) compared with being weight stable. In conclusion, obesity and high abdominal fat mass doubles the risk of psoriasis, and long-term weight gain substantially increases psoriasis risk. Preventing weight gain and promoting maintenance of a normal body weight could reduce incidence of psoriasis.

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with an estimated prevalence of 2–4% in most European countries (Parisi et al., 2013) and 6–11% in Norway (Danielsen et al., 2013; Modalsli et al., 2016). Psoriasis may have major impact on everyday life, and there is evidence that individuals with psoriasis may die at younger ages (Abuabara et al., 2010; Gelfand et al., 2007; Stern et al., 2004). The Global Burden of Disease Study (Murray et al., 2015) reported that psoriasis made up a substantial part (0.19%) of the total global disability-adjusted life-years, and yearly costs due to treatment and loss of work are high (Feldman et al., 2014; Svedbom et al., 2016).

Obesity is a growing public health challenge, both globally (World Health Organization, 2000) and in Norway (Meyer and Tverdal, 2005; Midthjell et al., 2013). Recent studies

also support increasing psoriasis prevalence and incidence (Danielsen et al., 2013; Icen et al., 2009). A large number of observational studies have shown that people with psoriasis are more likely to be obese (Armstrong et al., 2012), but the temporal relationship is still unclear. Obesity may be a common underlying factor explaining the positive associations between psoriasis and comorbidities such as cardiovascular disease (Samarasekera et al., 2013), diabetes (Armstrong et al., 2013), and metabolic syndrome (Prey et al., 2010), or alternatively, obesity could be causally related to psoriasis onset. Two prospective studies from the United States reported a positive association between measures of adiposity, such as body mass index (BMI), waist circumference, and waist-hip ratio, and the risk of incident psoriasis in women (Kumar et al., 2013; Setty et al., 2007). Findings from a recent Norwegian study suggest that there might be a threshold around a BMI of 28 kg/m², above which psoriasis risk is increased (Danielsen et al., 2017). Moreover, self-reported weight gain since early adulthood has also been positively related to psoriasis risk (Danielsen et al., 2017; Kumar et al., 2013; Setty et al., 2007). Taken together, these previous longitudinal studies indicate that obesity and weight gain may increase psoriasis risk. However, because of sparse data on men, reliance on self-reported weight and other anthropometric measures that may be prone to bias, and heterogeneous and imprecise associations, the evidence is not conclusive.

If obesity is associated with an increased risk of psoriasis, it is important to know whether there is a specific, incremental weight gain required to trigger incident disease. Such knowledge could have important implications for public health and may provide a means to prevent psoriasis onset in

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Abbreviations: BMI, body mass index; CI, confidence interval; HUNT, Nord-Trøndelag Health Study; RR, relative risk; SD, standard deviation

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individuals with genetic predisposition (World Health Organization, 2016). In a large, longitudinal study with objective measures of various indicators of adiposity, we prospectively examined if overweight and obesity defined by BMI were associated with the subsequent risk of incident psoriasis. We also examined if other measures of adiposity and body fat distribution, including waist circumference and waist-hip ratio, were associated with psoriasis risk. Finally, we assessed if long-term changes in body weight and BMI were associated with subsequent psoriasis risk and if this association depended on the initial body mass.

RESULTS

A total of 33,734 individuals were included: 18,499 (55%) women and 15,235 (45%) men. Of these, 369 individuals developed psoriasis during the follow-up period: 185 women and 184 men. The mean age was 47.0 years, with a standard deviation (SD) of 13.3. Baseline characteristics of the study population stratified by BMI categories are shown in more detail in Table 1. We found no evidence of violation of the proportional hazards assumption for any of the analyses presented below.

Table 2 shows that the risk of incident psoriasis was positively associated with all body composition measures. A one-SD (3.81 kg/m²) increase in BMI was associated with an adjusted relative risk (RR) of 1.22 (95% confidence interval [CI] = 1.11–1.34). The adjusted associations for one-SD increase in waist circumference (11.14 cm) and waist-hip ratio (0.08) were of largely the same magnitude, with RRs of 1.26 (95% CI = 1.15–1.39) and 1.18 (95% CI = 1.07–1.31). Analyses of categorized factors showed that obese people had nearly twice the risk of psoriasis (RR = 1.87; 95% CI = 1.38–2.52) compared with normal weight people. Comparing extreme categories (fourth and first quartiles) of waist circumference gave an RR of the same magnitude as for BMI, whereas for waist-hip ratio the association was somewhat weaker. Additional adjustment for physical activity and alcohol consumption did not change the results. Sensitivity analyses excluding individuals with onset of psoriasis within the first year after the second Nord-Trøndelag Health Study (HUNT2) did not substantially change the results described (data not shown). Although there was no evidence of statistical interaction by sex (all *P*-values > 0.09), stratified analyses gave associations that were somewhat stronger for men than for women (see Supplementary Table S1 online). Attributable fractions calculated from the estimated associations suggest that 23.6% of psoriasis cases in the study population can be attributed to either overweight (population attributable fraction = 14.9%) or obesity (population attributable fraction = 8.7%).

For the subset of participants with information regarding 10-year weight change from the HUNT1 to HUNT2 studies, we found an RR of 1.20 (95% CI = 1.07–1.35) for every SD (5.96 kg) increase in weight change (Table 2). Compared with those with nearly unchanged weight (–2.0 to 1.9 kg), people who increased their weight by 5.0–9.9 kg had an RR of 1.33 (95% CI = 0.90–1.95), whereas those who increased by 10.0 kg or more had an RR of 1.72 (95% CI = 1.15–2.58). We repeated the analyses of weight change stratifying on the initial BMI category (data not tabulated). Persons who were

Table 1. Characteristics according to categories of body mass index (BMI) at baseline (HUNT2)

Characteristics	BMI, kg/m ²		
	18.5–24.9 (n = 13,904)	25–29.9 (n = 15,010)	≥30 (n = 4,820)
Sex			
Women, n (%)	8,675 (62.4)	6,968 (46.4)	2,856 (59.3)
Men, n (%)	5,229 (37.6)	8,042 (53.6)	1,964 (40.8)
Age, mean (SD), years	43.6 (13.0)	48.5 (12.9)	50.0 (13.1)
BMI, mean (SD), kg/m ²	22.8 (1.5)	27.1 (1.4)	32.9 (2.9)
Waist circumference, mean (SD), cm	77.3 (7.9)	88.2 (7.7)	99.6 (9.2)
Hip circumference, mean (SD), cm	96.2 (4.9)	103.4 (4.6)	113.0 (7.2)
Waist-hip ratio, mean (SD)	0.80 (0.07)	0.85 (0.07)	0.88 (0.08)
Smoking status			
Never, n (%)	6,463 (46.5)	6,782 (45.2)	2,257 (46.8)
Former, n (%)	3,146 (22.6)	4,746 (31.6)	1,604 (33.2)
Current, n (%)	4,295 (30.9)	3,482 (23.2)	959 (19.9)
Education			
<10 years, n (%)	3,461 (24.9)	4,931 (32.9)	2,048 (42.5)
10–12 years, n (%)	6,748 (48.5)	6,877 (45.8)	2,057 (42.7)
≥13 years, n (%)	3,695 (26.6)	3,202 (21.3)	715 (14.8)

Abbreviations: HUNT, Nord-Trøndelag Health Study; SD, standard deviation.

classified as normal weight at HUNT1 had RRs of 2.19 (95% CI = 1.22–3.94) and 2.83 (95% CI = 1.54–5.22) associated with a weight gain of 5.0–9.9 kg and 10.0 kg or greater, respectively. Conversely, among initially overweight/obese people, a weight reduction of 2.0 kg or more was associated with an RR of 0.52 (95% CI = 0.22–1.21).

Table 3 shows the risk for psoriasis in joint categories of BMI from HUNT1 and HUNT2. Compared with those who were normal weight at both surveys, persons who were stably overweight had an RR of 1.53 (95% CI = 1.07–2.19), and those who were obese at both surveys had an RR of 2.16 (95% CI = 1.29–3.62), whereas changing from normal weight to overweight was associated with an RR of 1.57 (95% CI = 1.14–2.17).

DISCUSSION

Statement of principal findings

In this large prospective study with up to 13 years of follow-up, we found that overweight and obesity were positively associated with risk of psoriasis. People classified as obese at baseline had a nearly 2-fold higher risk of psoriasis compared with those who were normal weight. Additional measures of adiposity and fat distribution, such as waist circumference and waist-hip ratio, were also positively associated with risk of psoriasis. Moreover, a weight gain of 10 kg or more during the preceding 10 years was associated with a substantially increased risk of psoriasis compared with being weight stable, particularly among those who were initially normal weight. There was suggestive evidence that a weight decrease was associated with reduced risk of psoriasis, but low statistical precision calls for cautious interpretation of these results. From a public health perspective, nearly a quarter of psoriasis cases could be attributed to overweight or obesity if the estimated associations reflect causal relations.

Table 2. Relative risk of incident psoriasis associated with body mass index, waist circumference, waist-hip ratio, and weight change

Variables	Number of Person-Years	Incident Psoriasis Cases	Rate ¹	Crude RR (95% CI)	Adjusted RR ² (95% CI)
Body mass index, kg/m ²					
18.5–24.9	154,838	122	7.9	1.00 (Reference)	1.00 (Reference)
25.0–29.9	166,586	178	10.7	1.36 (1.08–1.71)	1.45 (1.15–1.84)
≥30.0	53,327	69	12.9	1.64 (1.22–2.20)	1.87 (1.38–2.52)
Body mass index, per SD (3.81 kg/m ²)	374,750	369	9.8	1.17 (1.07–1.29)	1.22 (1.11–1.34)
Body mass index, per kg/m ²	374,750	369	9.8	1.04 (1.01–1.07)	1.05 (1.03–1.08)
Waist circumference (quartiles) ³					
First	108,860	82	7.5	1.00 (Reference)	1.00 (Reference)
Second	84,565	80	9.5	1.25 (0.92–1.71)	1.33 (0.98–1.81)
Third	87,086	88	10.1	1.34 (0.99–1.81)	1.48 (1.09–2.00)
Fourth	91,477	117	12.8	1.68 (1.26–2.23)	1.95 (1.46–2.61)
Waist circumference, per SD (11.14 cm)	383,953	367	9.9	1.21 (1.10–1.33)	1.26 (1.15–1.39)
Waist circumference, per cm	383,953	367	9.9	1.02 (1.01–1.03)	1.02 (1.01–1.03)
Waist-hip ratio (quartiles) ⁴					
First	94,793	80	8.4	1.00 (Reference)	1.00 (Reference)
Second	92,330	91	9.9	1.17 (0.87–1.58)	1.19 (0.88–1.61)
Third	93,151	85	9.1	1.08 (0.80–1.47)	1.13 (0.83–1.54)
Fourth	91,713	111	12.1	1.43 (1.07–1.91)	1.53 (1.14–2.07)
Waist-hip ratio, per SD (0.08)	371,987	367	9.9	1.15 (1.05–1.27)	1.18 (1.07–1.31)
Waist-hip ratio, per 0.1 unit	371,987	367	9.9	1.25 (1.10–1.43)	1.35 (1.12–1.61)
Weight change from HUNT1 to HUNT2, kg					
<–2.0	18,864	10	5.3	0.68 (0.34–1.38)	0.66 (0.32–1.33)
–2.0 to 1.9	47,843	37	7.7	1.00 (Reference)	1.00 (Reference)
2.0–4.9	62,939	51	8.1	1.05 (0.69–1.60)	1.05 (0.69–1.61)
5.0–9.9	91,232	92	10.0	1.31 (0.89–1.91)	1.33 (0.90–1.95)
≥10.0	58,295	77	13.2	1.71 (1.15–2.52)	1.72 (1.15–2.58)
Weight change, per SD (5.96 kg)	279,172	267	9.6	1.21 (1.08–1.36)	1.20 (1.07–1.35)
Weight change, per kg	279,172	267	9.6	1.03 (1.01–1.05)	1.03 (1.01–1.05)

Abbreviations: CI, Confidence interval; HUNT, Nord-Trøndelag Health Study; RR, relative risk, SD, standard deviation.

¹Incidence of psoriasis per 10,000 person-years.

²Adjusted for age (continuous), sex, education (<10 years, 10–12 years, ≥13 years) and smoking (never, former, current).

³Waist circumference quartiles for men: first, ≤86 cm; second, 87–90 cm; third, 91–96 cm; fourth, ≥97 cm; for women: first, ≤73 cm; second, 74–79 cm; third, 80–86 cm; fourth, ≥87 cm.

⁴Waist hip ratio quartiles for men: first, ≤0.86; second, 0.86–0.89; third, 0.89–0.92; fourth, ≥0.92; for women: first, ≤0.75; second, 0.75–0.79; third, 0.79–0.82; fourth, ≥0.82.

Comparison with other studies

Most previous studies on the association between obesity and psoriasis have been cross-sectional studies or retrospective case-control studies (Armstrong et al., 2012; Gui et al., 2017; Kwa and Silverberg, 2017). Thus, the direction of the association has been difficult to disentangle. We prospectively examined the association between obesity and psoriasis in a sample of people without psoriasis who were followed up for incident psoriasis for approximately 10 years; this gave us the opportunity to determine the direction of the association between obesity and psoriasis. Our findings of almost doubled risk of incident psoriasis in obese participants compared with normal weight participants are in agreement with two former studies (Kumar et al., 2013; Setty et al., 2007). A previous study from Norway found inconsistent evidence for a relationship between BMI and risk of psoriasis; a conventional classification of BMI gave weak and imprecise associations, whereas the results suggested that there might be a threshold around 28 kg/m² at which the risk of psoriasis increases (Danielsen et al., 2017). A recent cohort study from Korea showed

weak positive associations between obesity and incident psoriasis (Kim et al., 2017), and a nested case-control study from the United Kingdom General Practice Research Database (Huerta et al., 2007) found a 30% increased risk of developing psoriasis in obese individuals. However, it could be speculated that a sample obtained from a general practitioner database differs from the general population when it comes to health status and morbidity, and that such selection could have influenced the estimated association between obesity and psoriasis.

BMI is a commonly used measure of body composition, but evidence suggests that measures reflecting abdominal adiposity, such as waist circumference and waist-hip ratio, are better indicators of metabolic abnormalities and cardiovascular disease risk (World Health Organization, 2011). There are two previous studies restricted to women that have investigated waist circumference and waist-hip ratio with regard to risk of psoriasis (Kumar et al., 2013; Setty et al., 2007). These studies found the risk to be highest in the uppermost categories and are in accordance with the results of this population-based study.

Table 3. Multivariable¹ relative risk of psoriasis according to weight categories in HUNT1 and HUNT2

BMI Category at HUNT1	BMI Category at HUNT2		
	18.5–24.9 kg/m ²	25.0–29.9 kg/m ²	≥30.0 kg/m ²
18.5–24.9 kg/m ²			
Cases/person-years	72/98,301	77/70,540	3/3,142
RR (95% CI)	1.00	1.57 (1.14–2.17)	1.31 (0.41–4.18)
25.0–29.9 kg/m ²			
Cases/person-years	6/3,925	59/59,457	27/25,135
RR (95% CI)	2.15 (0.93–4.96)	1.53 (1.07–2.19)	1.69 (1.08–2.65)
≥30.0 kg/m ²			
Cases/person-years	0/67	0/1,196	19/14,860
RR (95% CI)	NC	NC	2.16 (1.29–3.62)

Abbreviations: BMI, body mass index; CI, confidence interval; HUNT, Nord-Trøndelag Health Study; NC, not calculated; RR, relative risk.

¹Adjusted for age (continuous), sex, education (<10 years, 10–12 years, ≥13 years) and smoking (never, former, current).

We also studied weight change before baseline. Former studies have found weight gain to be a risk factor for onset of psoriasis (Danielsen et al., 2017; Kumar et al., 2013; Setty et al., 2007), which is consistent with our findings. However, whereas we used objectively measured weight 10 years before baseline, those studies relied on self-reported weight at ages 18 and 25 years. Despite low statistical power, our results also indicate that weight loss may be beneficial with regard to the risk of developing psoriasis.

Potential biological mechanisms

Our findings that adiposity is associated with psoriasis risk, with the strongest association for central obesity, suggest that fat mass plays a role in disease causation (Versini et al., 2014). This is in contrast to the more often cited mechanism where “systemic inflammation” associated with psoriasis leads to weight gain and fat redistribution. Adipose tissue, especially visceral fat, produces adipokines, which have a role in chronic inflammation. Adipokines that display pro-inflammatory activities such as leptin, visfatin, and resistin are increased in psoriasis patients, whereas the level of adiponectin, an anti-inflammatory adipokine, is decreased (Toussiro et al., 2014). Resident macrophages within adipose tissue contribute in the production of psoriasis-signature cytokines such as IL-6 and tumor necrosis factor- α , which are also thought to induce insulin resistance and may lead to altered lipid metabolism, hypertension, and enhanced risk of cardiovascular disease (Chiricozzi et al., 2016). Inflammation has also been proposed as a possible mechanism for other obesity-associated diseases, such as asthma (Ali and Ulrik, 2013) and rheumatoid arthritis (Feng et al., 2016). Other mechanisms could involve a common genetic link between psoriasis and obesity, as suggested in a recent twin study (Lonnberg et al., 2016).

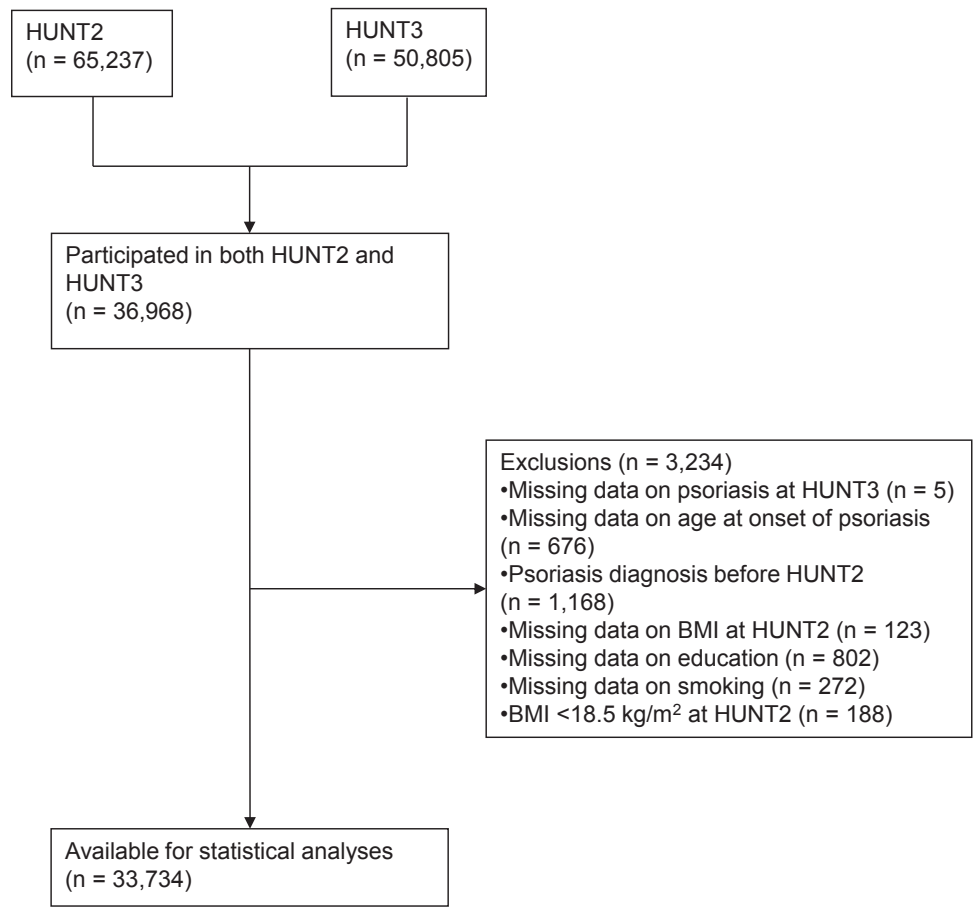
Strengths and limitations

The strengths of this study include the population-based sample, prospective design, and large number of participants

with information on objectively measured body height, weight, and waist circumference, as well as 10-year weight change. Standardized measurement methods limit possible misclassification bias. The number of new psoriasis cases provided relatively high precision in the estimated associations, particularly for the continuous body mass measures. However, for some of the less prevalent exposure categories, especially regarding weight change, the estimates were more imprecise. To our knowledge, this is the largest population-based study to date that includes several obesity-related measurements from both men and women. Two studies from the United States have included women only (Kumar et al., 2013; Setty et al., 2007) and thus were not able to examine possible sex differences in the association between adiposity and psoriasis. Whereas a former Norwegian study suggested a slightly stronger effect of BMI for women than men (Danielsen et al., 2017), our estimates suggest somewhat stronger associations in men than in women for all body mass measures. However, the results from these stratified analyses have lower precision than the overall findings and are thus more influenced by chance. A recent validation study from our research group showed that the self-report of psoriasis in the HUNT3 study had a positive predictive value of 78% and a negative predictive value of 96%, with a sensitivity of 56% and a specificity of 99% (Modalsli et al., 2016). Although several cases remain undetected in the study cohort, these figures also imply that four out of five people classified as having psoriasis in our study are true cases. However, to identify new cases of psoriasis occurring after baseline we had to rely on self-reported year of diagnosis. Few studies have validated self-reported age at onset of disease, but studies on asthma have found a high reliability of the reported age at onset (Mirabelli et al., 2014; Pattaro et al., 2007; Toren et al., 2006). However, it is conceivable that some of the psoriasis cases with reported onset just after baseline were not true incident cases, but sensitivity analysis excluding the first year of follow up did not change the results.

The inhabitants in the county of Nord-Trøndelag are considered representative of the Norwegian population (Langhammer et al., 2012). Studies have indicated that non-participants are older, have higher morbidity and mortality, and have lower socioeconomic status than participants (Langhammer et al., 2012). However, representativeness is not necessarily a prerequisite for validity (Rothman et al., 2013). Still, there is potential for selection bias because participants must have attended both HUNT2 and HUNT3 to be included in this study. It is conceivable that individuals with high BMI had increased morbidity and mortality between the surveys and were therefore less likely to participate at follow up, which may have underestimated the observed associations between obesity and psoriasis. Moreover, it is unclear whether obese people have a different health seeking behavior than normal weight people that could influence the likelihood of being diagnosed with psoriasis. We were able to adjust for several factors that could act as confounders, but residual confounding because of unmeasured or poorly measured factors cannot be ruled out. For instance, we did not have information on nutrition or genetic variants that could be common to obesity and psoriasis. Moreover, we used complete case strategy, whereby people with missing

Figure 1. Flow chart. Selection and exclusion procedures of participants for statistical analyses. BMI, body mass index; HUNT, Nord-Trøndelag Health Study.



information on possible confounders were excluded. This may reduce the possibility for residual confounding because of misclassification, but although few people were excluded, this could potentially increase selection bias.

CONCLUSIONS AND IMPLICATIONS

In conclusion, our study supports former findings that body weight is associated with psoriasis risk, and we found a consistent dose-response relationship across multiple obesity-related measurements. Strong associations between waist circumference and psoriasis risk could indicate that central adiposity plays an important role in disease development. We also found that the risk of psoriasis was substantially increased among people with a long-term weight gain of 10 kg or more, whereas there was suggestive evidence that weight loss could reduce psoriasis risk. These data indicate that obesity is an important, potentially modifiable risk factor in the development of psoriasis that provides an opportunity for disease prevention.

METHODS

Data source

The HUNT Study is a large population-based longitudinal study conducted within the county of Nord-Trøndelag, Norway. All residents in the county age 20 years or older have been invited to participate in the study at three different surveys. At HUNT1 (1984–1986), 86,404 persons were invited, and 77,212 (89%) chose to participate; at HUNT2 (1995–1997) 93,898 were invited, and

65,237 (70%) participated; and at HUNT3 (2006–2008) 93,860 were invited and 50,807 (54%) participated (Krokstad et al., 2013). Comprehensive questionnaires were completed to obtain information on health and lifestyle related factors, including psoriasis (HUNT3), smoking history, and educational attainment. Standardized measures of height, weight, waist circumference, and hip circumference were obtained at clinical examinations of all participants. More detailed information about participation, examinations, and questionnaires can be found at <http://www.ntnu.edu/hunt>.

Study population

For the purpose of this prospective study of adiposity and risk of psoriasis, we selected all 36,968 persons who had participated in both the HUNT2 and HUNT3 surveys (Figure 1). Of these, 3,234 persons were excluded because of either missing information on psoriasis at HUNT3; having a psoriasis diagnosis at baseline in HUNT2; or missing information on height, weight, education, and smoking at HUNT2. People with a BMI of less than 18.5 kg/m² at HUNT2 were also excluded because of few cases in this group. After these exclusions, a total of 33,734 persons who were free from psoriasis at HUNT2 were available for statistical analyses of BMI and risk of psoriasis. Because of missing data on waist circumference (n = 249) and waist-hip ratio (n = 249), the analyses of these factors were conducted on a slightly smaller sample. Additionally, we used information on objectively measured body weight on 25,148 persons who participated in all three HUNT surveys to examine if weight change from HUNT1 (1984–1986) to HUNT2 (1995–1997) was related to subsequent risk of psoriasis.

Outcome: Psoriasis diagnosis

Information on psoriasis was obtained at follow-up in HUNT3 using the question, “Do you have or have you had any of the following?” and where “Psoriasis (Yes, No)” was one of the response options. Participants with a positive response to the question were asked about the age at onset of psoriasis. We used this information to calculate follow-up time from participation in HUNT2 until onset of psoriasis between HUNT2 and HUNT3. 1,168 people with a psoriasis diagnosis before HUNT2 were excluded, and the follow-up time for people without psoriasis was calculated as the difference in age between participation in HUNT2 and HUNT3.

Exposures: Body mass measurements

Main exposures were BMI, waist circumference, and waist-hip ratio. All exposures were assessed using standardized methodology. Specifically, at the clinical examination, specially trained nurses or technicians recorded body height and body weight with the participants wearing light clothes and no shoes. Height was measured to the nearest centimeter and weight to the nearest half kilogram. BMI was calculated as weight divided by the squared value of height (kg/m^2) and classified into three categories; normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥ 30.0 kg/m^2) (World Health Organization, 2000). Waist and hip circumference were measured with a steel band to the nearest centimeter; waist circumference was measured at the level of the umbilicus and hip circumference at the thickest part of the hip (Holmen et al., 2003). Waist-hip ratio was calculated as waist circumference (cm) divided by hip circumference (cm). Based on the distribution of waist circumference and waist-hip ratio, we classified people into four categories using the sex-specific quartiles as cut-offs: for waist circumference the cut-offs were 86, 90, and 96 cm in men and 73, 79, and 87 cm in women; for waist-hip ratio the cut-offs were 0.86, 0.89, and 0.92 in men and 0.75, 0.79, and 0.82 in women. In the subsample of persons with information on body weight from HUNT1 we calculated the 10-year change in body weight from HUNT1 to HUNT2 by subtracting weight at HUNT1 from weight at HUNT2 and categorized people into five arbitrary groups: less than -2.0 kg, -2.0 to 1.9 kg, 2.0 to 4.9 kg, 5.0 to 9.9 kg, and 10.0 kg or greater. Finally, we calculated sex-specific SD scores (*z*-scores) for all the anthropometric measures as the observed value minus the sex-specific mean value, divided by the sex-specific SD.

Analysis

We used Cox regression to calculate hazard ratios as estimates of RR for incident psoriasis within categories of BMI, waist circumference, and waist-hip ratio measured at HUNT2, and weight change between HUNT1 and HUNT2, compared with a reference category. We also estimated RRs associated with continuous measures of the anthropometric variables, using both the original scale and sex-specific normalized values (*z*-scores). The precision of all estimates was assessed by 95% CI. We selected potential confounders based on a priori considerations of factors that are related to both psoriasis risk and body mass measures. All estimated associations were adjusted for possible confounding by age (years), sex (women, men), smoking (never smoker, former smoker, and current smoker), and education (<10 years [i.e., elementary school], 10 – 12 years [i.e., high school], and ≥ 13 years [i.e., college/university]). Other factors, such as physical activity and alcohol consumption, could also be possible confounders, although the rationale is less clear. In

additional analyses, we also adjusted for physical activity (no, low, medium, high, and unknown [$n = 1,621$]) and alcohol consumption (no, 1–4 times per week, ≥ 5 times per week, abstainer, and unknown [$n = 2,306$]).

Assuming that the estimated associations reflect causal relations between high BMI and psoriasis, we calculated the population attributable fraction (Rothman, 2012) to quantify the proportion of psoriasis that could be attributed to overweight and obesity. Because adipose tissue could be differentially distributed and have differential biological effects between men and women, we conducted analyses stratified by sex and evaluated possible statistical interaction (i.e., departure from multiplicative effect) in a likelihood ratio test of a product term of sex and the relevant anthropometric factor. To reduce the influence of imprecise reporting of age at onset of psoriasis and possible reverse causality because of existing undiagnosed disease, we also conducted sensitivity analyses excluding people who reported onset of psoriasis during the first year after HUNT2 ($n = 38$).

Departure from the proportional hazards assumption was evaluated by tests of Schoenfeld residuals and by graphical inspection of log-log plots. All analyses were conducted using Stata for Windows (Version IC 14.1, StataCorp, College Station, TX).

Ethics

Participation in the HUNT Study was voluntary and based on written informed consent. Our study was approved by the Regional Committee for Medical and Health Research Ethics (2014/1791).

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CONFLICT OF INTEREST

CHS has received departmental research funding from Abbvie, Pfizer, Novartis, GSK, Roche, Regeneron, and Janssen. The other authors state no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at <http://dx.doi.org/10.1016/j.jid.2017.07.822>.

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