**Table I.** RR, attributed risk, and NNH for comorbidities associated with rosacea per 10,000 person-years

| Study | End point | Exposure | RR | 95% CI | AR per 10,000 patient-years | NNH |
|---|---|---|---|---|---|---|
| 1[1] | Thyroid cancer | Rosacea | 1.60 | 1.07-2.36 | 1.41 | 7080 |
| 1[1] | BCC | Rosacea | 1.50 | 1.35-1.67 | 16.46 | 607 |
| 2[2] | Glioma | Mild rosacea | 1.43 | 1.18-1.73 | 1.44 | 6963 |
| 2[2] | Glioma | Severe rosacea | 1.44 | 1.14-1.82 | 1.47 | 6805 |
| 2[2] | Glioma | Ocular rosacea | 1.55 | 1.14-2.11 | 1.84 | 5444 |
| 3[3] | Hepatic cancer | Rosacea | 1.42 | 1.06-1.90 | 0.46 | 21,645 |
| 3[3] | Breast cancer | Rosacea | 1.25 | 1.15-1.36 | 6.23 | 1606 |
| 3[3] | Nonmelanoma skin cancer | Rosacea | 1.36 | 1.26-1.47 | 4.32 | 2315 |

*AR*, Attributable risk; *BCC*, basal cell carcinoma; *CI*, confidence interval; *NNH*, number needed to harm; *RR*, relative risk.

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## The association between obesity and hyperhidrosis: A nationwide, cross-sectional study of 2.77 million Israeli adolescents

*To the Editor:* Hyperhidrosis is a common, stigmatizing condition that is often primary in nature. Although hyperhidrosis was linked to obesity in review articles and textbooks,[1] the evidence supporting this association is limited.[2,3] We conducted a cross-sectional study in a nationwide cohort of 2,772,468 adolescents (59.6% male) to assess the association between body mass index (BMI) and hyperhidrosis. The study was approved by the Institutional Review Board of the Israel Defense Forces Medical Corps. The study group consisted of all examinees to compulsory military service during 1967-2016. The examinees underwent a routine medical screening at a mean age of 17.3 years. The screening included the review of medical records obtained from their primary care physicians, their medical history, a physical examination, and (when indicated) referrals for further assessment as detailed elsewhere.[4] The diagnosis of hyperhidrosis was based on a documented clinical assessment made by a board-certified dermatologist. The BMI percentile groups used were the age-matched and sex-matched percentiles used by the US Centers for Disease

**Table I.** Characteristics of study participants

| Characteristic | BMI percentile* | | | | Total |
|---|---|---|---|---|---|
| | <5th | 5th-84th | 85th-94th | ≥95th | |
| Male | | | | | |
| Participants, n | 129,676 | 1,298,072 | 140,285 | 84,624 | 1,652,657 |
| Hyperhidrosis cases, n (%) | 2003 (1.5) | 21,534 (1.7) | 3302 (2.4) | 2454 (2.9) | 29,293 (1.8) |
| Age, y, mean ± SD | 17.5 ± 0.5 | 17.4 ± 0.4 | 17.3 ± 0.4 | 17.3 ± 0.4 | 17.4 ± 0.5 |
| Height, cm, mean ± SD | 173.1 ± 7.1 | 173.5 ± 6.8 | 174.0 ± 6.9 | 174.1 ± 7.2 | 173.7 ± 6.9 |
| BMI, kg/m$^2$, mean ± SD | 17.1 ± 0.7 | 21.1 ± 1.8 | 26.5 ± 1.0 | 31.8 ± 3.1 | 21.8 ± 1.8 |
| 12 years of schooling, % | 77 | 81 | 84 | 85 | 83 |
| Low residential SES,† % | 30 | 29 | 29 | 32 | 30 |
| Born in Israel, % | 82 | 82 | 84 | 85 | 83 |
| Country of origin,‡ % | | | | | |
| Israel | 11 | 11 | 14 | 16 | 13 |
| Former USSR | 12 | 14 | 16 | 17 | 14 |
| Asia | 29 | 23 | 19 | 18 | 22 |
| Africa | 21 | 24 | 22 | 22 | 23 |
| Europe | 22 | 27 | 28 | 26 | 26 |
| Ethiopia | 5 | 1 | 1 | 1 | 2 |
| Female | | | | | |
| Participants, n | 49,687 | 924,799 | 108,706 | 36,619 | 1,119,811 |
| Hyperhidrosis cases, n (%) | 536 (1.1) | 10,663 (1.2) | 1474 (1.4) | 573 (1.6) | 13,246 (1.2) |
| Age, y, mean ± SD | 17.4 ± 0.5 | 17.3 ± 0.4 | 17.3 ± 0.4 | 17.3 ± 0.4 | 17.3 ± 0.4 |
| Height, cm, mean ± SD | 161.1 ± 6.5 | 162.1 ± 6.5 | 161.8 ± 6.2 | 162.3 ± 6.4 | 162.1 ± 6.4 |
| BMI, kg/m$^2$, mean ± SD | 16.6 ± 0.6 | 21.0 ± 2.0 | 27.0 ± 1.2 | 33.0 ± 3.0 | 21.8 ± 1.8 |
| 12 years of schooling, % | 93 | 94 | 94 | 94 | 94 |
| Low residential SES,† % | 21 | 21 | 22 | 24 | 21 |
| Born in Israel, % | 84 | 85 | 86 | 87 | 86 |
| Country of origin,‡ % | | | | | |
| Israel | 10 | 10 | 11 | 14 | 11 |
| Former USSR | 15 | 15 | 15 | 17 | 15 |
| Asia | 19 | 21 | 21 | 19 | 22 |
| Africa | 21 | 22 | 24 | 22 | 22 |
| Europe | 30 | 31 | 29 | 27 | 29 |
| Ethiopia | 5 | 1 | 1 | 1 | 1 |

*BMI*, Body mass index; *SES*, socioeconomic status; *SD*, standard deviation; *USSR*, Union of Soviet Socialist Republics.
*BMI percentile categories according to the US Centers for Disease Control and Prevention BMI percentiles for age and sex that were validated for Israeli adolescents.[5] The categories represent persons who are underweight (<5th percentile), normal weight (5th-84th percentile), overweight (85th-94th percentile), and obese (≥95th percentile).
†SES was based on data obtained from the Israeli Ministry of the Interior.
‡Country of origin was considered the father's or paternal grandfather's country of birth, categorized into 5 geographic areas as specified.

Control and Prevention.[5] Table I shows the characteristics of participants; 42,539 individuals (68.9% of which were male) had hyperhidrosis, an overall prevalence of 1.5%.

There was a gradual increase in the prevalence of hyperhidrosis from underweight to obese in both male (1.5% to 2.9%) and female (1.1% to 1.6%) participants. In logistic regression analyses, the adjusted odds ratios (aORs) for hyperhidrosis was 1.25 (95% confidence interval [CI] 1.20-1.30) in overweight male participants, 1.4 (95% CI 1.34-1.46) in obese male participants, 1.1 (95% CI 1.04-1.17) in overweight female participants, and 1.2 (95% CI 1.07-1.27) in obese female participants compared with those of normal weight (Table II).

Each BMI unit was associated with an aOR for hyperhidrosis of 3.2% (1.029-1.035) for males and 1.5% (1.010-1.019) for females. Findings were confirmed in an analysis limited to participants with unimpaired health (Table II). When the obese group was subdivided according to severity, the aORs for hyperhidrosis were increased in those with class II obesity (≥120% to <140% of the 95th percentile or BMI ≥35 kg/m$^2$, whichever was lower); the aOR among male participants was 1.5 (95% CI 1.3-1.6) and among female participants was 1.4 (95% CI 1.2-1.7).

Our study has limitations. First, data regarding primary or secondary hyperhydrosis and focal or diffuse disease were unavailable. However, an

**Table II.** OR for the association between body mass index and hyperhidrosis

| | Body mass index percentile | | | | |
|---|---|---|---|---|---|
| **Model** | **<5th** | **5th-84th** | **85th-94th** | **≥95th** | **Continuous** |
| Males | | | | | |
| 29,293 cases out of 1,652,657 participants (unadjusted model) | | | | | |
| OR | 0.93 | 1 | 1.43 | 1.77 | 1.050 |
| 95% CI | 0.89-0.97 | | 1.38-1.48 | 1.72-1.83 | 1.047-1.053 |
| *P* | .002 | | $6.8 \times 10^{-79}$ | $6.8 \times 10^{-154}$ | $4.0 \times 10^{-10}$ |
| 28,974 cases out of 1,620,880 participants (multivariable model)* | | | | | |
| OR | 0.93 | 1 | 1.25 | 1.39 | 1.032† |
| 95% CI | 0.89-0.97 | | 1.20-1.30 | 1.34-1.46 | 1.029-1.035 |
| *P* | .003 | | $3.3 \times 10^{-31}$ | $1.9 \times 10^{-51}$ | $1.4 \times 10^{-99}$ |
| 22,327 cases out of 1,169,673 participants with otherwise unimpaired health (multivariable model)‡ | | | | | |
| OR | 1.04 | 1 | 1.27 | 1.48 | 1.036 |
| 95% CI | 0.98-1.10 | | 1.22-1.33 | 1.40-1.56 | 1.032-1.040 |
| *P* | .20 | | $1.2 \times 10^{-27}$ | $3.0 \times 10^{-48}$ | $3.5 \times 10^{-79}$ |
| Females§ | | | | | |
| 13,246 cases out of 1,119,811 participants (unadjusted model) | | | | | |
| OR | 0.94 | 1 | 1.18 | 1.36 | 1.022 |
| 95% CI | 0.86-1.02 | | 1.12-1.25 | 1.25-1.48 | 1.018-1.027 |
| *P* | .09 | | $4.4 \times 10^{-9}$ | $7.9 \times 10^{-13}$ | $5.7 \times 10^{-21}$ |
| 13,041 cases out of 1,085,610 participants (multivariable model)* | | | | | |
| OR | 0.90 | 1 | 1.102 | 1.16 | 1.015† |
| 95% CI | 0.82-0.98 | | 1.04-1.17 | 1.07-1.27 | 1.010-1.019 |
| *P* | .013 | | $6.8 \times 10^{-4}$ | $1.9 \times 10^{-51}$ | $4.0 \times 10^{-10}$ |
| 9824 cases out of 784,564 participants with otherwise unimpaired health (multivariable model)‡ | | | | | |
| OR | 0.99 | 1 | 1.13 | 1.16 | 1.018 |
| 95% CI | 0.87-1.12 | | 1.07-1.20 | 1.03-1.29 | 1.016-1.019 |
| *P* | .81 | | $1.5 \times 10^{-4}$ | .011 | $2.7 \times 10^{-6}$ |

*CI*, Confidence interval; *OR*, odds ratio.

*Birth year, country of origin, socioeconomic status, and education were included in the multivariable model (all were associated with $P < .05$).

†When the cohort was stratified by recent calendrical decades (1990-1999, 2000-2009, 2010-2016), the significance of the OR persisted among men (1.032 [95% CI 1.025-1.040], 1.033 [95% CI 1.028-1.038], 1.037 [95% CI 1.032-1.042], respectively) and women (1.014 [95% CI 1.000-1.021], 1.016 [95% CI 1.008-1.024], 1.023 [95% CI 1.015-1.031], respectively).

‡Unimpaired health was defined as no history of chronic illness (including cancer or major surgery) and without any routine drug prescription. Results were adjusted for multivariable model.

§There was an interaction between sex and body mass index (treated as a continuous variable) for the occurrence of hyperhidrosis (adjusted $P_{interaction} = 1.6 \times 10^{-13}$).

analysis limited to participants with unimpaired health to minimize confounding by coexisting morbidities accentuated the association. Second, our study spans 5 decades, during which the awareness and diagnostic criteria have changed. Nevertheless, the BMI-hyperhidrosis association persisted when the cohort was stratified by calendrical decades (Table II). The strengths of our study are its large power, the systematic nationwide data collection for a narrow age range, and dermatologist-based diagnosis of hyperhidrosis. These strengths might, at least partially, account for the contradictory findings on the association between obesity and hyperhidrosis.[2,3] Greater adipose tissue might increase metabolic demand and heat production, interfere with heat loss, or facilitate the secretion of sympathomimetic adipokines. However, the association might be bidirectional; the discomfort and embarrassment associated with hyperhidrosis could lead to a sedentary lifestyle and contribute to the development of obesity.

In conclusion, this study demonstrates that obesity is associated with hyperhidrosis among adolescents. Future studies are required to further investigate this association and determine whether weight reduction could play a therapeutic role in these patients.

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## Impact of dermatology consultation on the care of children with chronic graft-versus-host disease of the skin

*To the Editor:* Skin involvement is common in chronic graft-versus-host disease (cGVHD) and affects patient outcomes.[1] We sought to investigate the role of dermatologists in the management of cutaneous cGVHD by retrospectively analyzing 140 patients with cutaneous cGVHD seen during 2001-2017 at 2 pediatric tertiary care centers. In total, 57.1% (80/140) of patients in this cohort received a dermatology consultation. The mean follow-up time was 6.2 years in the group that received consultations and 5.3 years in the group that did not (no significant difference, $P = .161$).

We found that significantly more patients in the consultation group received myeloablative conditioning and had an unrelated or mismatched donor (Table I), all known risk factors for cGVHD.[2] In addition, suspicion for cutaneous cGVHD occurred significantly later after hematopoietic stem cell transplant (HSCT) in those who received dermatology consultations than in those who did not (0.9 vs 0.5 years, $P = .020$). Although not statistically significant, mortality was higher in the consultation group than in the nonconsultation group (25.0% vs 11.7%, $P = .054$). There was no significant difference in time from HSCT to death between the groups.

Among cutaneous cGVHD patients who received dermatology consultations, the median time from suspected diagnosis to consultation was 121.5 (range 0-2922) days. Most consultations (62.5%, 50/80) were to assist in diagnosis; 82.5% (66/80) of patients were treated before consultation, including 62.5% (50/80) who received systemic therapy with a mean ± standard deviation of 2.1 ± 1.1 systemic therapies. Corticosteroids was the most common systemic agent given (92.0%, 46/50), followed by tacrolimus (48.0%, 24/50) and cyclosporine (20.0%, 10/50).

Dermatology consultation changed 27.5% (22/80) of diagnoses (Table II). Alternative diagnoses included contact dermatitis, lichen nitidus, morbilliform drug eruption, and hypersensitivity reaction. Skin biopsy was performed to aid diagnosis in 20 patients, confirming cutaneous cGVHD in 17 (85.0%) patients. Management changes were recommended in 66 of 80 patients and included changes in both topical and systemic therapies. In 88.8% (71/80) of cases, the referring physician followed all the recommendations provided by the consultant.

Our data suggest that even with pediatric dermatologists available, there are barriers to dermatologic care. Although most patients were referred for diagnostic assistance, the median time from suspected diagnosis to consultation was 121.5 days, with most patients already receiving systemic treatment. Moreover, we identified a longer interval between HSCT and suspected cutaneous cGVHD and trends towards a higher mortality rate in referred patients, suggesting referred patients posed diagnostic challenges with potentially more severe disease.[3] Barriers to dermatology consultation might include diagnostic challenges, inadequate access to dermatology