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Adolescent BMI at Northern Israel: From Trends, to Associated Variables and Comorbidities, and to Medical Signatures

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Abstract: The increasing prevalence of abnormal body mass index (BMI), mainly obesity, is becoming a significant public health problem. This cross-sectional study aimed to provide a comprehensive view of secular trends of BMI, and the associated socio-demographic variables and comorbidities among adolescents with abnormal BMI. Individuals of the study population were born mainly between 1970 and 1993, and were examined at 16 to 19 years of age during the years 1987 to 2010, at 1 conscription center in the northern district of Israel.

The study population included 113,694 adolescents. Univariate and multivariable logistic regression models were used to investigate the associations between BMI categories, socio-demographic variables, and medical conditions.

A downward trend in the prevalence of normal BMI among both male and female adolescents was obtained, while trends of overweight and obesity (in both genders) and underweight (only among females) rose. Socio-demographic variables such as religion, education, family-related parameters, residential environment, country of birth, and origin were all associated with different risks for abnormal BMI. Obesity was associated with higher risk for hyperlipidemia, endocrine disorders (only in males), knee disorders, and hypertension type I + II (in both genders). Overweight was associated with knee disorders (only in females). Underweight, exclusively in males, was associated with increased risk for endocrine disorders, proteinuria, and cardiac disorders. Hierarchical clustering analysis revealed the intricate relations between gender, BMI, and medical signatures. It brought to light novel clusters of diseases that were abundant among populations having above-normal BMI or underweight males. Furthermore, above-normal BMI was associated with a lower rate of cardiac anomalies and scoliosis/kyphosis, whereas being underweight was associated with a lower risk for hypertension and flat foot.

This study provides a reliable and in-depth view of secular trends in height, weight, and BMI of male and female adolescents. It supports previous associations between abnormal BMI and demographic variables and comorbidities, while uncovering novel associations, mainly regarding medical signatures of each gender–BMI group. This might lead to better monitoring, early detection, prevention, and treatment of various conditions associated to abnormal BMI categories and gender groups.

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Abbreviations: ADHD = attention deficit hyperactivity disorder, ANOVA = analysis of variance, BMI = body mass index, BP = blood pressure, CI = confidence interval, FCC = Functional Classification Code, FUSSR = former Union of Soviet Socialist Republics, HMO = Health Maintenance Organization, ICD = International Classification of Diseases, IDF = Israel Defense Forces, OR = odds ratio, SD = standard deviation, SE = standard error, SES = socio-economic status.

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YM and YC conceived the conception and design of this study, as well as have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. YM, YC, and RF were involved in acquisition/collection and assembly of data. YC, YM, and DD were involved in critical revision for important intellectual content. RF, YC, YM, RR, and DF performed the statistical analysis. YM, YC, RF, GW, and DD provided administrative, technical, or logistic support. All authors were involved in analysis and interpretation of the data, drafting of the article, and final approval of the article. In addition, all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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INTRODUCTION

Obesity in the young population is a worldwide epidemic,[1] threatening the long-term health and wellbeing of children and adolescents,[2] and warranting further evaluation and treatment.[3,4] Children[5–8] and adolescents[9] with obesity have a greater likelihood of becoming adults with obesity. Over the past 30 years, the prevalence of overweight or obesity among American children and adolescents has increased dramatically, as evidenced by diverse studies, such as the National Health and Nutrition Examination Survey (NHANES),[10,11] Bogalusa[12] and others.[13] If past obesity trends continue unimpeded, a dramatic negative effect on US population life expectancy is forecasted.[14] Data on the prevalence and long-time trends of obesity among adolescents worldwide are scant.[15] Although current trends in obesity prevalence among US adolescents are under debate, there is wide agreement that the prevalence of obesity is too high,[16] and greater than that in European countries.[17] High and increasing prevalence of overweight and/or obesity among adolescents has also been found across European countries such as Italy,[18] Scotland,[19] Sweden,[20] Portugal,[21] Spain,[22] and

Israel[23–25] (and the list continues to grow). Other studies have indicated that in some countries, the prevalence rates of obesity and overweight have reached a plateau, but a very high one.[26,27]

An elevated body mass index (BMI) in childhood or adolescence has been associated with diverse socio-demographic characteristics, such as gender, ethnicity, socioeconomic status (SES), education, and geographical parameters, as well as family functioning and weight-related attributes and behaviors,[23,24,28–32] with an increased risk of diverse psychological and physical diseases (or even death) in concurrent or later life.[25,30,33–43] Previous studies of Israeli adolescents[25,37,44–48] established the higher risks of prehypertension, hypertension, diabetes, hyperlipidemia, joint conditions of the lower extremities (hip, ankle, and knee disorders), and coronary heart disease among overweight and obese recruits, whereas underweight was associated with bronchial and lung conditions (including asthma), scoliosis, intestinal conditions, and emotional disorders. Morbidity and mortality rates from diseases attributable to obesity are expected to rise in the near future.[11,42,49–51]

Less attention has been focused on being underweight. The prevalence of underweight BMI among children and adolescents in the United States is declining, especially among: children, females, and mainly until 2006.[52] Whereas in Italy the prevalence of thinness among adolescents has declined (although it increases with age in females),[18] in Israel it is steadily increasing.[23,25] Underweight is also associated with functional limitations, though these are less likely to affect an individual's general health.[30] Underweight adolescents may also suffer from negative body image and/or psychiatric disorders, which lead to disturbed eating behavior[53,54] and/or neuroendocrine dysfunction.

Despite the abundance of research on diverse weight-related associations among adolescents, there is a need for further studies in such pediatric population over a long period. Such studies should look systematically, comprehensively, and in depth at all BMI categories, and analyze possible associations with a wide range of familial and socio-demographic variables, as well as medical conditions. Here, we analyzed trends in weight, height, and BMI categories, the associated socio-demographic variables, and coexisting comorbidities among Israeli adolescents, who were mainly born between the years 1970 and 1993 and were examined by the Israel Defense Forces (IDF) medical committee at 1 conscription center in northern Israel.

METHODS

Study Population

Adolescents in Israel are obliged to service by law. The National Military Service Act requires all 17-year-old Israelis to present themselves to a local recruitment center (see Supplemental Content 1, http://links.lww.com/MD/A755, which describes the law and the populations that are exempt from service). At the end of the medical process, a medical profile and appropriate Functional Classification Codes (FCCs) are assigned for each recruit (see Supplemental Content 2, http://links.lww.com/MD/A755, which describes in detail the medical process resulting in data acquisition and its recording to the computerized database).

Only the northern recruitment center of Israel was chosen due to its stringent assessment and the reliability of the medical data.[55,56] All subjects who had an electronic record in the computerized medical database, from its establishment in 1987 until 2010 (24 years), were included in the initial study population. The study population consisted of conscripts who were born mainly between 1970 and 1993. To ensure a uniform medical baseline, we focused on conscripts who completed the medical profiling process at the age of 16 to 19 years, and had valid height and weight measures. To analyze trends (over years of birth) of the medical parameters, a minimum cutoff of 1,000 conscripts per gender per year was determined.

Definitions

BMI categories were defined according to gender-related percentiles for 17-year-old BMI on growth charts of the Israeli Ministry of Health, similarly to the approach of the US Centers for Disease Control and Prevention.[57] As opposed to the International Obesity Task Force definitions,[58,59] these also include the underweight group, which is of high interest in this study. The actual definitions were as follows: obesity—above the 95th percentile (>28.2 and $>29.6\,kg/m^2$ for males and females, respectively); overweight—the 85th to 95th percentiles (25.0–28.2 and $25.2–29.6\,kg/m^2$, respectively); and underweight—below the 5th percentile (<17.6 and $<17.2\,kg/m^2$, respectively). The median age (and interquartile range; mean $\pm$ standard deviation [SD]) of males and females was 17.36 (17.08–17.91; 17.57 ± 0.74) and 17.24 (17.02–17.64; 17.39 ± 0.62), respectively (see Supplemental Content 3, http://links.lww.com/MD/A755, which demonstrates the age and BMI distributions of the study population).

The detailed definitions and examples of the medical conditions used in this study have been described in detail elsewhere[56,60] (see also Supplemental Content 4, http://links.lww.com/MD/A755, which describes the criteria for the diagnosis of each medical condition). Briefly, 26 medical conditions, representing approximately 90% of all FCCs commonly assigned to Israeli adolescents,[56] were analyzed in relation to BMI groups. Most of these conditions were also previously described as being associated with BMI in other studies, mostly in separate, but not group analyses (see ''Introduction'' and ''Discussion'' sections). Nevertheless, the selection of medical conditions was not limited to previously studied ones, but to those with a possibly sound hypothesis (at the epidemiological, cellular, or molecular level). We wished to investigate whether such established associations also exist in our study population, whether novel associations might be uncovered, and how such associations are related to each other.

Statistical Methods

Characteristics, such as weight, height, and BMI, were evaluated by prevalence rates (proportions), means $\pm$ SD/errors, and medians with interquartile ranges, for males and females. Univariate analyses included chi-squared tests to compare categorical variables between BMI categories. Continuous variables were compared using 1-way analysis of variance (ANOVA) or Kruskal–Wallis test. Stratification by variables was also conducted in light of criteria of the Israeli National Bureau of Statistics. Trends over the years of mean height, weight, and BMI were assessed by Spearman correlation, and further confirmed by linear models. Temporal trends of BMI categories prevalence rates were examined by linear-by-linear association tests. The choice of a parametric or nonparametric test depended on the distribution of a continuous variable. A P value below 0.05 was considered statistically significant.

Multivariable logistic regression models were run to investigate the associations between BMI categories and each of the medical conditions tested in the study. For each medical condition (outcome), a separate model was run. Each model was performed in 2 blocks. Block 1 included BMI categories (underweight, overweight, and obesity using normal BMI as reference group), considered as main effects in this study, which were forced into the models using the ''enter'' method. In block 2, a further adjustment was performed for potential clinical and socio-demographic characteristics, which were associated with BMI (Table 1), using ''LR forward stepwise'' method. Candidate variables for entrance to the model were country of birth (reference group: born in Israel), country of origin (Israeli origin), year of birth (1986–1990), religion (Jewish), level of education (12 years), intelligence score (median score), residential environment (urban), family size (2–3 children), and blood pressure (BP) index (normal BP). Only those variables for which most of the population had a valid value were tested. Therefore, SES (the 10 SES categories, based on the Israeli Central Bureau of Statistics' classification, were grouped into low, medium, and high SES as described previously)[23] was omitted, but education, residential environment, and family size, which may be viewed as mediator variables related to SES, were included. To deal with characteristics that included more than 2 categories, dummy variables were created for all categories except the reference group and were added to the model as covariates. For example, 2 BP-related dummy variables were created: prehypertension and hypertension I + II, and were added to the model, where the ''normal BP'' was the reference group. The criterion for entrance into the model was a univariate probability value of $P < 0.05$, and $P > 0.10$ for removal from the model. All analyses were performed separately for males and females. Calibration of the model was assessed with a Hosmer–Lemeshow goodness-of-fit statistic.[61] Odds ratios (OR) and 95% confidence intervals (95% CIs) were calculated.

The discriminatory power of the models was examined using C statistics, whereas C value ranges from 0.5 (indicating that the model's predictions are not better than chance) to 1.0 (the model always assigns higher probabilities to correct cases than to incorrect ones). C values of 0.7 to 0.8 are considered to show acceptable discrimination, values of 0.8 to 0.9 to indicate excellent discrimination, and values of $\geq$0.9 to show outstanding discrimination.[61] A 2-sided P value below 0.05 was considered statistically significant. All analyses were performed separately for males and females, using the SPSS version 20.0 statistical package (SPSS, Inc., Chicago, IL).

Hierarchical Clustering

ORs, presented in Table 2, were transformed following these conditions: statistically nonsignificant ($P > 0.05$) ORs were transformed into 0; statistically significant ORs smaller than 1 were transformed into −1/OR whereas those bigger than 1 were not transformed. Hierarchical clustering of the ORs of the different medical conditions (only those comprising over 0.1% were taken into account) and gender–BMI groups was performed in Partek® Genomics Suite® software, version 6.6© 2014 (Partek Inc., St. Louis, MO) with Pearson dissimilarity and complete linkage.

Institutional Review Board Approval

The IDF Institutional Board and Helsinki Committee approved the study on the basis of preservation of participants' anonymity.

RESULTS

Study Population

The initial study population consisted of 158,255 conscripts. Inclusion criteria were completion of the medical evaluation process, as evidenced by valid medical profile; completion of the medical process at the age of 16 to 19 (inclusive) years; and available data on both weight and height measures. Thus, 29,227 subjects who had not completed their medical evaluation at all, as well as 12,049 subjects who had completed their medical evaluation, but not at 16 to 19 years of age, and 3,285 who answered the first 2 criteria but lacked readings of height and/or weight, were all excluded (see Supplemental Content 5, http://links.lww.com/MD/A755, which portrays the socio-demographic characteristics of the excluded and included populations) leaving a total of 113,694 adolescents who formed the final study population (71.85% of the initial population): 66,569 (58.6%) males and 47,125 (41.4%) females. Of these, 99.8% were born between 1970 and 1994, and more specifically, 97.4% were born between 1972 and 1993 (the period selected for the trends analysis, in light of the criteria described in the ''Methods'' section).

General Trends

For clarity, ''increase'' and ''decrease'' are used in the following to describe trends or changes in average (Figure 1) or prevalence-rated (Figure 2) height, weight, BMI (Figure 1), and BMI categories (Figure 2) in males and females.

The males' average height did not change dramatically over the period of 22 years, whereas a slight though significant decrease in females' average height was observed (Figure 1A). A significant increase in average weight was observed in both genders, being more pronounced among males (Figure 1B). Consequently, a significant increase in average BMI was obtained in both genders, mainly among males, in terms of trend size and duration (Figure 1C). The year of birth 1981 was the first year in which the average BMI of males was higher than that of females (Figure 1C). All these trends are particularly evident since early and mid-1980s among males and females, respectively. Independent analysis by separate linear models for each of these 3 variables and year of birth further support these findings (data not shown).

BMI Category Trends

A significant downward trend in the prevalence of normal BMI was observed in both male ($P < 0.0001$) and female ($P < 0.0001$) adolescents (Figure 2A). A significant upward trend in the prevalence of underweight BMI was observed among females ($P < 0.0001$), with 2 peaks: at years of birth 1975 (5.9%) and 1984 (8.5%) (Figure 2B). Significant upward trends ($P < 0.0001$) in the prevalence of overweight (Figure 2C) and obese (Figure 2D) BMI were observed in both genders. Whereas the prevalence of overweight increased gradually from the early 1980s, that of obesity increased mainly from the mid to late 1970s, in both genders. The prevalence of underweight and overweight BMI was higher among females, while that of obesity (and normal BMI) was higher among males.

Association With Socio-Demographic Parameters

The relationships between prevalence of BMI categories and familial/socio-demographic parameters were examined (Table 1).

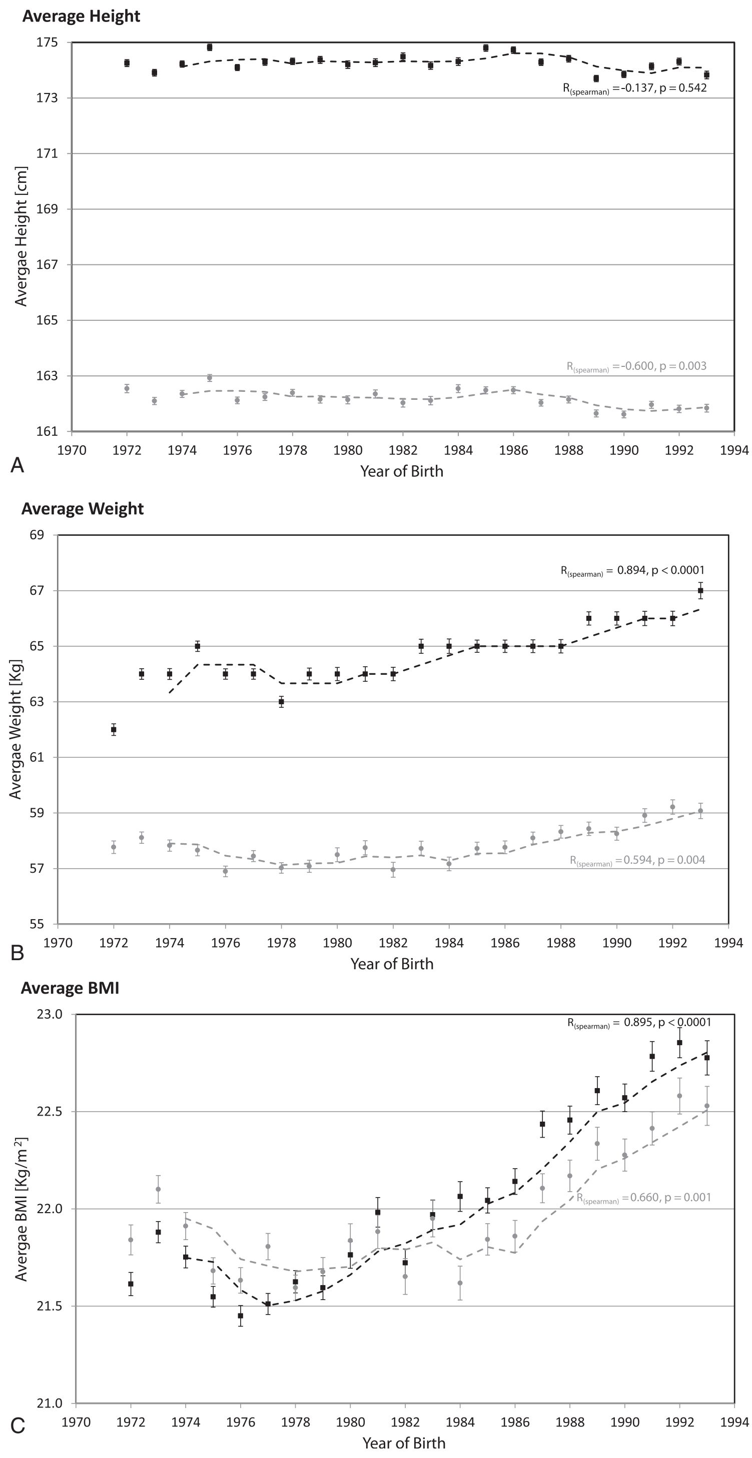

FIGURE 1. Trends of height (A), weight (B), and body mass index (C) among adolescent males (black square) and females (gray square) who were born between the years 1972 and 1993. Data are shown as mean values, I bars indicate standard errors (SE), while spearman correlation parameters (*R* and *P* value) are also indicated. A moving average trendline of 3 y period is presented.

Stratification by 5 years of birth revealed a significant increase in the average BMI in both male and female subjects (from 1976 to 1980), accompanied by trends of increasing prevalence of both obesity (both genders) and overweight (only males), and by a negative trend in the prevalence of normal BMI (both genders). The prevalence of being underweight initially rose—in males until 1976 to 1980 and in females until 1981 to 1985, and then declined. Stratification by season of birth

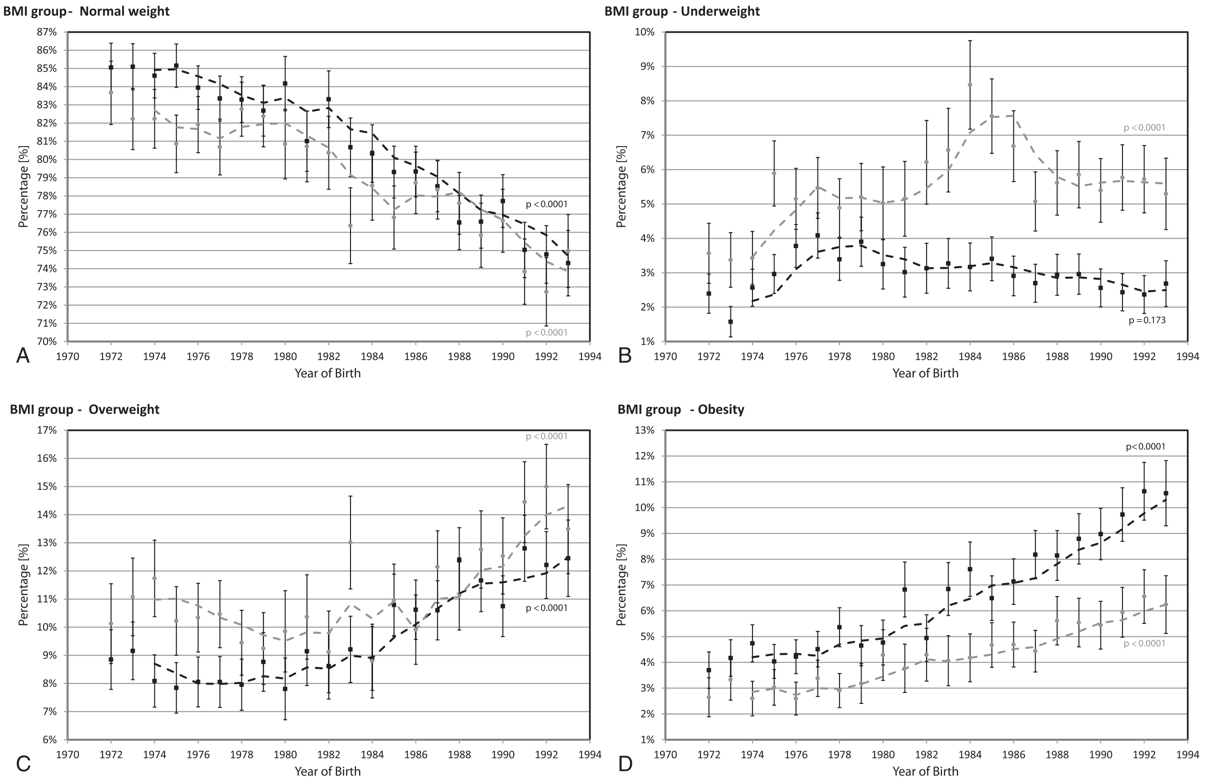

FIGURE 2. Trends of normal (A), underweight (B), overweight (C), and obesity (D) body mass index among adolescent males (black square) and females (gray square) who were born between the years 1972 and 1993. Data are shown as prevalence, I bars indicate 95% confidence intervals (CIs), while *P* value for trend is also indicated. A moving average trendline of 3 y period is presented.

revealed significant differences in average BMI among both genders. Differences were mainly evident in the females' prevalence rates of underweight, which were higher among those born during the spring and summer.

Most male (~84%) and female (~95%) conscripts were Jewish. In males, the prevalence of overweight and obesity was lowest in the Druze recruits and highest in the Arab ones, whereas the prevalence of underweight was almost 10 times higher in the former compared to Arabs and Christians. A higher prevalence of obesity and overweight was observed among Jewish females (compared to all non-Jewish females). It should be noted that only a small proportion of the Arab and Bedouin populations was represented in the study population, since their draft into the IDF is voluntary (see Supplemental Content 1, http://links.lww.com/MD/A755, which describes the IDF's service law and the populations that are exempt from service).

The higher mean BMI of both male and female rural conscripts stem mainly from a lower prevalence of being underweight in the rural population. Low SES in females (and to a lesser extent, medium SES in males) is characterized by a higher prevalence of all abnormal BMI categories. A strong association between BMI and education was evident. A higher education score was associated with increased prevalence of normal BMI in both genders. A lower education score was associated with a higher prevalence of obesity, underweight (in both genders), and overweight (only in females).

An association between parent- and family-related parameters and BMI, especially in males, was also noted. In general, as the number of children in the family increased, the prevalence of normal BMI and underweight increased and that of overweight and obesity decreased. Single-offspring status was associated with higher BMI and higher prevalence of obesity and overweight. Younger and elder offspring in the family were associated with a higher prevalence of obesity and overweight and a lower prevalence of underweight.

The prevalence of normal BMI was almost identical among native Israelis and immigrants. Nevertheless, male immigrants were less likely to be underweight and more likely to be overweight or obese—a mirror image of female immigrants. Males of Asian and African origin and females of Asian and former Union of Soviet Socialist Republics (FUSSR) origin had lower mean BMI, mainly due to a lower prevalence of obesity and overweight (only in the males) and higher prevalence of underweight. The reverse was true among males and females of American origin.

To analyze the environmental effect, we focused on conscripts of either FUSSR or Ethiopian origin, representing the most recent main immigration waves to Israel. The population was divided into 3 groups based on origin, place of birth, and age of immigration (Table 2). Among both genders, a longer period spent in Ethiopia (immigration age, compared to Israeli origin) was associated with a lower mean BMI, and a decreasing prevalence of all abnormal BMI categories, mainly in males. A much higher prevalence of abnormal BMI was observed in males and females of Ethiopian origin born in Israel compared to those born in Ethiopia. Among conscripts born in Israel, the prevalence of below- and above-normal BMI was higher and lower, respectively, in ethnic Ethiopians compared to native

TABLE 1. Mean Body Mass Index and Prevalence of Body Mass Index Categories Among Adolescent Males and Females Stratified by Diverse Socio-Demographic Variables

Parameter	Categories	Males							Females						
		n	Mean (SD)	95 of CI	Prevalence (%) of BMI categories				n	Mean (SD)	95 of CI	Prevalence (%) of BMI categories			
					Normal weight	Under weight	Over weight	Obesity				Normal weight	Under weight	Over weight	Obesity
Year of birth	<=1975	14,085	21.68 (3.12)	21.63-21.73	85.2	2.4	8.3	4.1	8,977	21.90 (3.24)	21.84-21.97	82.2	4.1	10.7	3.0
	1976-1980	15,644	21.57 (3.26)	21.52-21.62	83.5	3.7	8.1	4.7	11,022	21.70 (3.32)	21.64-21.76	81.7	5.2	9.9	3.2
	1981-1985	12,225	21.96 (3.59)	21.90-22.03	80.8	3.2	9.4	6.6	8,790	21.79 (3.68)	21.72-21.87	78.4	6.9	10.5	4.2
	1986-1990	16,069	22.44 (3.96)	22.38-22.50	77.8	2.8	11.2	8.2	11,649	22.15 (3.90)	22.08-22.22	77.4	5.7	11.7	5.1
	=>1991	8,546	22.81 (4.21)	22.73-22.91	74.7	2.5	12.5	10.3	6,687	22.50 (4.19)	22.40-22.60	73.9	5.6	14.3	6.2
	P value for trend (Linear-by-Linear Association):				<0.0001	0.247	<0.0001	<0.0001				<0.0001	<0.0001	<0.0001	<0.0001
Season of birth	Autumn	16,581	22.11 (3.63)	22.05-22.16	80.8	2.8	10.0	6.4	11,659	22.05 (3.64)	21.99-22.12	79.2	5.1	11.3	4.4
	Winter	16,603	21.99 (3.58)	21.94-22.05	80.8	3.1	9.7	6.4	11,646	22.05 (3.61)	21.99-22.12	79.4	5.0	11.4	4.2
	Spring	16,344	22.07 (3.67)	22.01-22.12	80.8	2.8	9.7	6.7	11,680	21.91 (3.68)	21.85-21.98	78.6	5.9	11.2	4.2
	Summer	17,041	21.98 (3.61)	21.93-22.04	81.0	3.1	9.4	6.4	12,140	21.91 (3.69)	21.84-21.97	78.9	5.9	11.0	4.2
Religion	Jews	55,311	22.04 (3.62)	22.01-22.07	80.9	3.0	9.7	6.4	44,337	22.00 (3.66)	21.96-22.03	78.9	5.5	11.3	4.3
	Druze	3,374	21.22 (3.40)	21.11-21.34	83.0	5.4	6.9	4.7	2	22.18 (2.16)	2.78-41.59	100.0	0.0	0.0	0.0
	Bedouins	2,787	22.00 (3.61)	21.87-22.14	81.7	2.1	9.4	6.7	12	22.06 (3.39)	19.91-24.22	75.0	0.0	25.0	0.0
	Muslims	968	22.86 (3.75)	22.62-23.10	76.1	1.1	13.2	9.5	17	22.98 (5.76)	20.02-25.95	52.9	11.8	17.6	17.6
	Circassians	505	22.55 (3.62)	22.23-22.87	77.4	1.6	14.5	6.5	0						
	Christians	488	22.98 (3.36)	22.68-23.28	76.6	0.6	15.0	7.8	70	22.38 (3.22)	21.61-23.15	77.1	4.3	15.7	2.9
	Arabs	364	24.37 (4.68)	23.89-24.85	63.2	0.5	19.5	16.8	27	25.49 (5.46)	23.33-27.65	59.3	0.0	14.8	25.9
	Others	238	21.43 (3.05)	21.04-21.82	88.7	2.5	5.0	3.8	218	21.02 (2.58)	20.68-21.37	86.2	6.9	6.4	0.5
	Unknown	2,017	22.27 (3.66)	22.11-22.43	81.0	2.1	9.9	7.1	1,865	21.61 (3.60)	21.45-21.78	81.3	6.2	9.3	3.2
Residential environment	Urban	32,378	21.97 (3.68)	21.93-22.01	80.5	3.5	9.5	6.6	24,352	21.92 (3.72)	21.87-21.96	78.3	6.1	11.3	4.3
	Rural	34,191	22.10 (3.57)	22.06-22.14	81.2	2.5	9.9	6.4	22,773	22.05 (3.58)	22.00-22.10	79.9	4.8	11.1	4.2
Socio-economic status (SES)	Low	5,508	22.33 (3.95)	22.23-22.44	77.9	2.8	11.1	8.1	1,918	22.30 (4.12)	22.11-22.48	73.0	7.1	14.0	5.8
	Medium	16,395	22.32 (4.00)	22.25-22.38	77.3	3.4	10.8	8.5	13,213	22.07 (4.02)	22.00-22.14	76.0	6.8	11.9	5.3
	High	561	22.36 (3.88)	22.04-22.68	80.4	2.3	9.4	7.8	623	22.04 (3.67)	21.75-22.33	76.6	6.3	13.2	4.0
Education	1-6	2,000	22.19 (4.20)	22.00-22.37	77.7	4.4	8.8	9.1	284	23.15 (4.59)	22.61-23.69	70.4	4.2	16.5	8.8
	7-9	3,514	21.95 (3.62)	21.83-22.07	80.4	3.2	9.8	6.6	539	22.04 (4.20)	22.05-22.76	74.2	5.8	13.2	6.9
	10-11	16,679	22.06 (3.81)	22.00-22.12	79.5	3.3	9.6	7.6	6,179	22.27 (4.02)	22.17-22.37	75.1	6.0	13.2	5.7
	12	42,351	22.03 (3.52)	22.00-22.06	81.5	2.7	9.8	5.9	39,096	21.91 (3.57)	21.88-21.95	79.8	5.4	10.8	3.9
	≥13	2,004	21.99 (3.46)	21.84-22.15	81.0	3.0	9.6	6.3	1,019	22.20 (3.70)	21.98-22.43	77.4	5.4	12.2	5.0
Number of children in family	1	2,629	22.61 (3.86)	22.46-22.76	77.4	2.2	11.8	8.5	2,423	22.02 (3.79)	21.87-22.17	77.9	6.0	12.3	3.8
	2-3	25,257	22.29 (3.72)	22.24-22.33	79.3	2.7	10.7	7.3	21,718	22.09 (3.74)	22.04-22.14	78.2	5.4	11.6	4.8
	4-5	24,901	21.99 (3.58)	21.94-22.03	81.2	2.9	9.5	6.4	18,456	21.91 (3.58)	21.86-21.96	79.8	5.3	10.9	4.0
	≥6	13,656	21.56 (3.40)	21.50-21.62	83.6	3.8	7.9	4.8	4,525	21.72 (3.44)	21.62-21.82	80.3	6.3	10.3	3.2

Parameter	Categories	Males							Females						
					Prevalence (%) of BMI categories							Prevalence (%) of BMI categories			
		n	Mean (SD)	95 of CI	Normal weight	Under weight	Over weight	Obesity	n	Mean (SD)	95 of CI	Normal weight	Under weight	Over weight	Obesity
Birth's order	A single offspring	2,629	**22.61 (3.86)**	**22.46-22.76**	**77.4**	**2.2**	**11.8**	**8.5**	2,423	22.02 (3.79)	21.87-22.17	77.9	6.0	12.3	3.8
	Multiple offspring	63,938	**22.01 (3.61)**	**21.99-22.05**	**81.0**	**3.0**	**9.6**	**6.4**	44,702	21.98 (3.65)	21.94-22.01	79.1	5.4	11.2	4.3
	Youngest offspring	18,991	**22.29 (3.80)**	**22.24-22.34**	**78.9**	**2.7**	**10.8**	**7.6**	15,204	**22.06 (3.77)**	**22.00-22.12**	**78.7**	**5.4**	**11.3**	**4.7**
	Non-youngest offspring	47,452	**21.94 (3.55)**	**21.91-21.97**	**81.6**	**3.1**	**9.3**	**6.0**	31,918	**21.94 (3.60)**	**21.90-21.98**	**79.2**	**5.5**	**11.2**	**4.1**
	Elder offspring	21,333	**22.23 (3.70)**	**22.18-22.28**	**79.8**	**2.7**	**10.3**	**7.3**	16,495	**22.04 (3.69)**	**21.98-22.09**	78.6	5.4	11.6	4.4
	Non-elder offspring	45,236	**21.95 (3.58)**	**21.91-21.98**	**81.3**	**3.1**	**9.4**	**6.1**	30,630	**21.95 (3.64)**	**21.91-21.99**	79.3	5.5	11.1	4.2
Blood pressure	Normal	16,629	**20.96 (2.98)**	**20.92-21.01**	**86.4**	**5.1**	**5.8**	**2.7**	23,108	**21.24 (3.08)**	**21.20-21-28**	**83.7**	**6.9**	**7.7**	**1.8**
	Hypotension	118	**21.25 (3.39)**	**20.64-21.87**	**83.1**	**5.9**	**6.8**	**4.2**	125	**21.50 (4.30)**	**20.73-22.26**	**78.4**	**10.4**	**6.4**	**4.8**
	Pre-hypertension	32,721	**22.02 (3.50)**	**21.98-22.06**	**81.9**	**2.6**	**9.7**	**5.9**	13,893	**22.20 (3.61)**	**22.14-22-26**	**78.5**	**4.6**	**12.6**	**4.3**
	Hypertension type I-II	16,856	**23.11 (4.07)**	**23.05-23.18**	**73.5**	**1.7**	**13.6**	**11.2**	9,858	**23.41 (4.40)**	**23.32-23.49**	**69.1**	**3.3**	**17.6**	**9.9**
Country of origin	Sabra	56,739	**22.01 (3.61)**	**21.98-22.04**	**80.9**	**3.1**	**9.6**	**6.4**	38,923	**22.01 (3.66)**	**21.97-22.04**	**79.0**	**5.3**	**11.3**	**4.4**
	Immigrants	9,830	**22.18 (3.69)**	**22.11-22.26**	**80.8**	**2.5**	**10.0**	**6.8**	8,202	**21.85 (3.62)**	**21.77-21.93**	**79.2**	**6.3**	**10.8**	**3.6**
Continent of origin	Israel	12,183	**22.02 (3.63)**	**21.95-22.08**	**80.8**	**3.0**	**9.6**	**6.6**	3,509	**22.07 (3.75)**	**21.95-22.20**	**79.1**	**4.9**	**10.9**	**5.1**
	Former USSR	9,967	**22.31 (3.71)**	**22.24-22.38**	**80.0**	**2.2**	**10.7**	**7.1**	8,649	**21.84 (3.53)**	**21.77-21.92**	**79.6**	**6.0**	**10.9**	**3.5**
	Europe	12,275	**22.11 (3.58)**	**22.05-22.18**	**81.3**	**2.4**	**9.8**	**6.5**	10,676	**22.10 (3.63)**	**22.03-22.17**	**79.9**	**4.5**	**11.1**	**4.6**
	Asia	9,362	**21.87 (3.63)**	**21.80-21.95**	**80.9**	**3.8**	**9.0**	**6.2**	7,327	**21.78 (3.60)**	**21.70-21.87**	**78.7**	**6.4**	**11.2**	**3.6**
	Africa	19,911	**21.89 (3.60)**	**21.84-21.94**	**81.0**	**3.5**	**9.3**	**6.2**	14,589	**21.98 (3.74)**	**21.92-22.04**	**78.3**	**5.9**	**11.3**	**4.4**
	America	2,352	**22.41 (3.56)**	**22.27-22.56**	**80.2**	**1.7**	**10.9**	**7.2**	1,989	**22.42 (3.70)**	**22.26-22.58**	**78.5**	**3.2**	**13.2**	**5.1**
	Oceania	59	**21.90 (2.93)**	**21.13-22.66**	**76.3**	**5.1**	**16.9**	**1.7**	55	**22.39 (3.43)**	**21.46-23.32**	**80.0**	**3.6**	**10.9**	**5.5**
	Unknown	460	**22.14 (3.36)**	**21.83-22.44**	**82.2**	**2.0**	**11.5**	**4.3**	331	**22.19 (3.67)**	**21-79-22.59**	**78.9**	**3.3**	**14.2**	**3.6**

Univariate analysis: 1-way ANOVA or Kruskal–Wallis tests were used to compare means of categories within each variable. Chi-squared test was used to compare prevalence rates of categorical variables between BMI categories.

ANOVA = analysis of variance, BMI = body mass index, CI = confidence intervals, SD = standard deviation, USSR = Union of Soviet Socialist Republics.

Significance code: all significant differences marked in bold, and level of significance is color coded: $P < 0.05$; $P < 0.01$; $P < 0.0001$.

TABLE 2. Mean Body Mass Index and Prevalence of Body-Mass Index Categories Among Adolescent Males and Females Stratified by Origin Place of Birth and Age of Immigration

Categories		Males							Females						
					Prevalence (%) of BMI categories							Prevalence (%) of BMI categories			
		n	Mean (SD)	95% of CI	Normal weight	Under weight	Over weight	Obesity	n	Mean (SD)	95% of CI	Normal weight	Under weight	Over weight	Obesity
Birth: Israel AND Origin: Israel		12,064	22.01 (3.63)	21.95-22.08	80.7%	3.0%	9.7%	6.6%	3,414	22.05 (3.74)	21.93-22.18	79.0%	5.0%	10.9%	5.1%
Ethiopia	Birth: Israel (AND Origin: Ethiopia	366	20.28 (3.64)	19.91-20.66	**73.5%**	**17.5%**	**5.7%**	**3.3%**	324	21.20 (4.15)	20.75-21.65	68.8%	16.7%	9.9%	4.6%
	Birth: Ethiopia (Immigrated at the age of 0-7 years old	327	20.03 (2.57)	19.75-20.30	**86.9%**	**8.3%**	**4.3%**	**0.6%**	222	20.59 (3.64)	20.11-21.07	77.0%	14.9%	5.4%	2.7%
	Birth: Ethiopia (Immigrated at the age of >7 years old	372	19.84 (1.93)	19.65-20.04	**92.5%**	**6.2%**	**1.1%**	**0.3%**	124	20.38 (2.88)	19.86-20.89	79.8%	12.9%	6.5%	0.8%
	Total Ethiopia	1,065	20.05 (2.81)	19.88-20.22	**84.2%**	**10.7%**	**3.7%**	**1.4%**	670	20.85 (3.78)	20.56-21.13	73.6%	15.4%	7.8%	3.3%
Former USSR (FUSSR)	Birth: Israel AND Origin: FUSSR	2,734	**22.41 (3.76)**	**22.27-22.55**	**79.3%**	**1.7%**	**11.7%**	**7.4%**	2,416	**22.11 (3.57)**	**21.97-22.26**	**78.8%**	**4.4%**	**12.6%**	**4.2%**
	Birth: FUSSR (Immigrated at the age of 0-7 years old	2,520	**22.52 (4.04)**	**22.36-22.67**	**78.8%**	**2.4%**	**10.3%**	**8.6%**	2,284	**21.90 (3.88)**	**21.74-22.06**	**77.5%**	**7.0%**	**11.3%**	**4.3%**
	Birth: FUSSR (Immigrated at the age of >7 years old	4,880	**22.14 (3.48)**	**22.05-22.24**	**81.3%**	**2.3%**	**10.5%**	**5.9%**	4,091	**21.63 (3.29)**	**21.53-21.73**	**81.3%**	**6.4%**	**9.7%**	**2.7%**
	Total FUSSR	10,134	**22.31 (3.71)**	**22.24-22.38**	**80.1%**	**2.2%**	**10.7%**	**7.0%**	8,791	**21.83 (3.53)**	**21.76-21.91**	**79.6%**	**6.0%**	**10.9%**	**3.5%**

Univariate analysis: One way ANOVA or Kruskal-Wallis tests were used to compare means of categories within each variable. Chi-square test was used to compare prevalence rates of categorical variables between BMI categories.

ANOVA = analysis of variance, BMI = body mass index, CI = confidence intervals, OR = odds ratio, SD = standard deviation, USSR = union of soviet socialist republics.

Significance code: all significant differences marked in bold, and level of significance is color coded: $P < 0.05$; $P < 0.01$; $P < 0.0001$.

TABLE 3. Odds-Ratios for Diverse Medical Conditions in the Males and Females Stratified by Body Mass Index Categories

Medical condition	Males				Females			
	n (%)	OR (95% of CI)			n (%)	OR (95% of CI)		
		Under weight	Over weight	Obesity		Under weight	Over weight	Obesity
Pre-hypertension	32,721 (49.2)	**0.74 (0.68-0.81)**	0.98 (0.93-1.03)	**0.84 (0.79-0.90)**	13,893 (29.5)	**0.81 (0.74-0.89)**	**1.20 (1.13-1.28)**	1.03 (0.93-1.14)
Scoliosis/Kyphosis	19,720 (29.6)	**1.67 (1.52-1.84)**	**0.67 (0.63-0.71)**	**0.50 (0.46-0.55)**	11,949 (25.4)	**1.68 (1.54-1.83)**	**0.68 (0.63-0.74)**	**0.49 (0.43-0.56)**
Refractive errors	15,944 (24.0)	**1.23 (1.11-1.37)**	**1.13 (1.06-1.20)**	**1.31 (1.22-1.41)**	14,912 (31.6)	1.06 (0.97-1.16)	**1.12 (1.05-1.19)**	**1.21 (1.10-1.33)**
Hypertension type I+II	16,856 (25.3)	**0.58 (0.51-0.66)**	**1.80 (1.70-1.90)**	**2.57 (2.41-2.74)**	9,858 (20.9)	**0.68 (0.60-0.76)**	**2.18 (2.05-2.32)**	**4.31 (3.93-4.73)**
Flat foot	15,911 (23.9)	**0.61 (0.54-0.70)**	**1.45 (1.37-1.54)**	**1.88 (1.76-2.02)**	6,978 (14.8)	**0.75 (0.66-0.85)**	**1.58 (1.46-1.71)**	**1.62 (1.44-1.83)**
Mental disorders	3,652 (5.5)	**1.37 (1.15-1.59)**	1.02 (0.90-1.15)	**1.19 (1.03-1.36)**	1,058 (2.2)	**1.49 (1.18-1.88)**	1.00 (0.83-1.23)	1.06 (0.79-1.42)
Active Asthma	2,921 (4.4)	**1.43 (1.17-1.74)**	1.04 (0.91-1.18)	**1.69 (1.49-1.92)**	1,661 (3.5)	1.09 (0.88-1.35)	**1.18 (1.02-1.37)**	**1.56 (1.27-1.91)**
Knee disorders	2,751 (4.1)	**1.28 (1.02-1.59)**	**1.34 (1.18-1.52)**	**3.75 (3.39-4.17)**	1,391 (3.0)	0.99 (0.74-1.32)	**2.75 (2.39-3.17)**	**9.45 (8.20-10.88)**
Allergic rhinitis	2,081 (3.1)	**1.30 (1.02-1.67)**	1.05 (0.91-1.22)	1.12 (0.95-1.32)	1,384 (2.9)	1.05 (0.83-1.32)	1.00 (0.84-1.18)	1.13 (0.88-1.44)
Learning disorders	1,478 (2.2)	**1.39 (1.06-1.82)**	**1.39 (1.17-1.64)**	**1.99 (1.68-2.36)**	1,035 (2.2)	1.25 (0.96-1.62)	**1.32 (1.10-1.59)**	**2.13 (1.69-2.67)**
Gastrointestinal disorders	1,282 (1.9)	**1.37 (1.02-1.82)**	0.89 (0.73-1.08)	1.21 (0.98-1.49)	1,080 (2.3)	1.10 (0.85-1.42)	1.02 (0.84-1.23)	1.30 (0.99-1.71)
Cardiac anomalies	999 (1.5)	**2.58 (2.01-3.30)**	**0.72 (0.57-0.92)**	**0.65 (0.48-0.89)**	510 (1.1)	**1.48 (1.07-2.03)**	**0.51 (0.36-0.73)**	**0.30 (0.15-0.61)**
Micro-hematuria	492 (0.7)	**1.69 (1.11-2.59)**	1.24 (0.93-1.65)	1.36 (0.98-1.89)	284 (0.6)	1.05 (0.62-1.77)	**1.53 (1.11-2.11)**	**1.63 (1.00-2.64)**
Endocrine disorders	344 (0.5)	**6.70 (4.67-9.60)**	1.32 (0.90-1.93)	**5.86 (4.56-7.52)**	263 (0.6)	1.32 (0.80-2.18)	**1.58 (1.13-2.20)**	**2.08 (1.33-3.26)**
ADHD - Ritalin	163 (0.2)	1.62 (0.71-3.71)	**2.11 (1.40-3.17)**	**2.22 (1.42-3.48)**	126 (0.3)	1.29 (0.62-2.69)	1.06 (.062-1.81)	**2.53 (1.49-4.32)**
Proteinuria	161 (0.2)	**4.19 (2.55-6.90)**	0.56 (0.29-1.11)	1.07 (0.59-1.94)	69 (0.1)	1.22 (0.49-3.06)	0.35 (0.11-1.13)	0.92 (0.29-2.94)
Hyperlipidemia	57 (0.1)	2.89 (0.88-9.51)	1.28 (0.49-3.30)	**6.20 (3.37-11.41)**	58 (0.1)	0.38 (0.05-2.76)	**2.12 (1.11-4.06)**	2.39 (0.94-6.07)
Diabetes mellitus	47 (0.1)	1.09 (0.15-8.02)	**3.05 (1.52-6.15)**	**2.83 (1.23-6.51)**	38 (0.1)	1.73 (0.52-5.78)	**2.71 (1.26-5.87)**	2.29 (0.69-7.65)
Sleeping disorder	55 (0.1)	1.22 (0.30-5.03)	0.57 (0.18-1.84)	1.71 (0.73-4.02)	12 (0.0)	2.43 (0.29-20.17)	3.40 (0.85-13.62)	5.78 (1.16-28.88)

Multivariable logistic regression models were conducted to investigate the associations between body mass index and each one of the medical conditions tested in the study (separate model for each medical condition).

CI = confidence intervals; OR = odds ratio.

Significance code: all significant differences marked in bold, and level of significance is color coded: $P < 0.05$; $P < 0.01$; $P < 0.0001$.

Israelis. Adolescents of FUSSR origin who were born in Israel were more likely to be overweight and less likely to be underweight, compared to both adolescents of FUSSR origin who were born in the FUSSR, and native Israeli conscripts. Stratification by age of immigration of FUSSR conscripts showed a lower prevalence of obesity (in both genders) and overweight (only among females) among those who came to Israel at 8 years of age or older.

Coexistence of Medical Conditions

An increase in BP was correlated with an increasing tendency toward overweight or obesity (Table 1).

The association between BMI categories and the most common medical conditions,[56] where normal BMI category served as a reference, was analyzed (Table 3). Obesity and overweight were associated with diverse risks for medical conditions (11 and 7 conditions in males, 10 and 11 in females, respectively). Many of these associations were common to both BMI categories (in that case OR was usually higher in the obese category than in the overweight category). Obesity among males was associated with higher risk (arbitrarily defined as OR $>$ 2.5 and $P < 0.0001$) for hyperlipidemia (OR = 6.20), endocrine disorders (5.86), knee disorders (3.75), and hypertension type I + II (2.57). Knee disorders (9.45) and hypertension type I + II (4.31) were the only strong associations found in females with obesity. Being overweight was mainly associated with knee disorders (2.75) in females only. Being underweight was associated with higher risks for medical conditions, mainly in males (12 conditions, compared to only 3 in females), among which were endocrine disorders (6.7), proteinuria (4.19), and cardiac disorders (2.58). Most of the significant associations of higher risk for developing a medical condition (Table 3) observed in the above-normal BMI populations were found in both genders, whereas these in the underweight population were mainly observed among males. On the other hand, protective effects were also uncovered: lower rates of cardiac anomalies and scoliosis/kyphosis were obtained among males and females with above-normal BMI, whereas being underweight was associated with reduced risks of developing prehypertension, hypertension type I + II, and flat foot.

Hierarchical clustering analysis revealed the intricate relationships between gender and BMI with regard to medical signature. Two main clusters were obtained: one encompassed the underweight BMI categories of both genders, and the other, the above-normal BMI categories of both genders (Figure 3). The latter cluster was further divided into 2 sub-clusters based on gender classification.

It also uncovered clusters of medical conditions with distinctive associations to BMI categories and gender groups (Figure 3). In general, 2 main clusters were found in which a higher risk of developing a medical condition was manifested among either the underweight BMI category (Cluster #1) or the above-normal BMI categories (Cluster #2). Among the conditions in cluster #1 were cardiac anomalies, scoliosis/kyphosis and mental disorders (in both genders), allergic rhinitis, gastrointestinal disorders, proteinuria, micro-hematuria, asthma, and endocrine disorders (in males only, the last 3 conditions are also more prevalent among obese and overweight females). On the other hand, knee disorders, hypertension I + II and flatfoot, refractive errors, and learning disorders were among the conditions in cluster #2. These clusters were further divided into sub-clusters where the higher risk of developing a group of medical conditions was manifested among specific gender–BMI categories, solely or accompanied by increased risk or protective effect of developing these conditions by other gender–BMI category/ies (see Supplemental Content 6, http://links.lww.com/MD/A755, which describes and discusses in details the clusters of diseases).

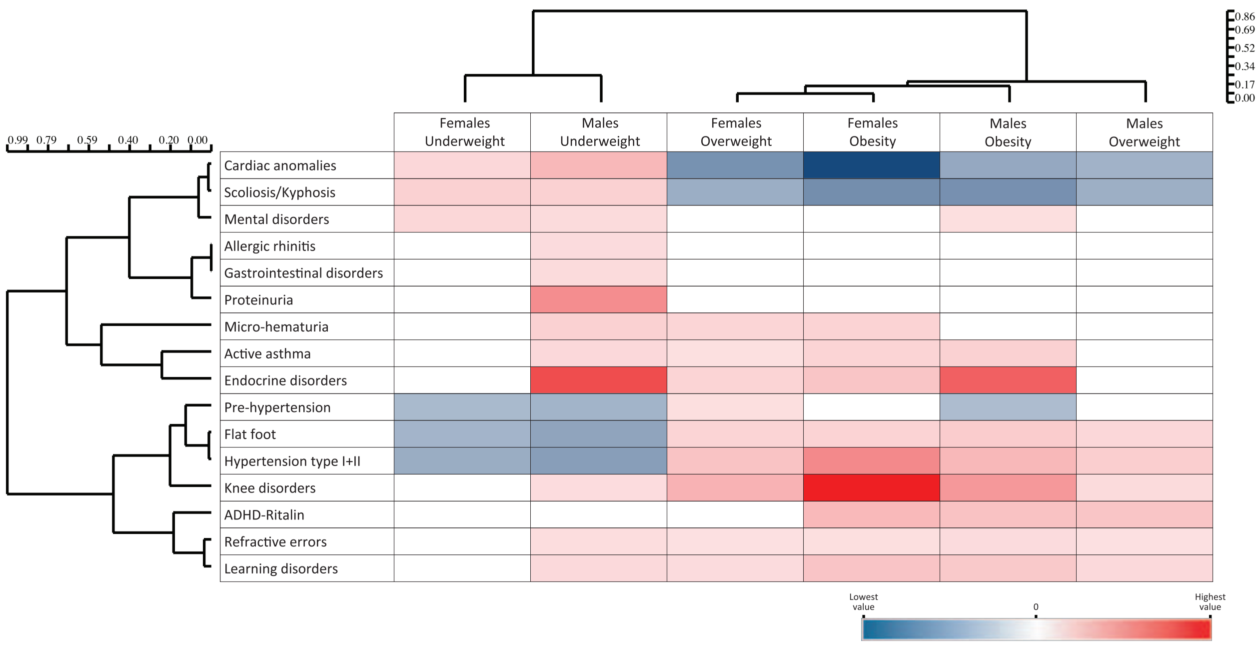

FIGURE 3. Hierarchical clustering of transformed odds rations of the different medical conditions and gender–body mass index groups. Statistically significant increased risks are denoted by red shades, while statistically significant reduced risks are denoted by blue shades, and white demarcates nonsignificant odds ratios.

DISCUSSION

Secular Trends

This study not only provides further support for the previously established upward trends in the prevalence of overweight and obesity among male and female adolescents but also uncovered downward trends in the prevalence of normal BMI and mainly increasing trend of underweight (the latter among females), mainly since the early to mid-1980s. This represents an increase in BMI extremes at the expense of normal BMI, resulting in an increase in the average BMI. The underlying mechanisms (such as lifestyle changes, historic events, etc.) that might explain these trends were not assessed in this study and require further investigation.

The rising prevalence of underweight among females may be explained, at least in part, by recently highlighted body image issues resulting in a tendency toward the ''ideal image'' of the thinner female,[62–64] coupled with a possible increase in dieting behavior and eating disorders, as implied here (Table 3, see mental disorders) and by others.[65] Preliminary analysis of the prevalence of eating disorders among females in our study population demonstrated a clear upward trend (from 0.00% to 0.10%, 0.23%, and 0.21% among females who were born before 1981, during 1981–1985, 1986–1990, and 1991 and later, respectively). However, the prevalence rate is low and thus can only partly explain the observed increase in underweight females. A milder spectrum of eating behaviors that are not diagnosed as overt eating disorders might further affect this trend. Since our study did not include dietary questionnaires, we cannot substantiate this hypothesis.

Interestingly, and somewhat speculatively, the 2 peaks observed in the underweight prevalence coincided with historical events: the Yom Kippur War (1973–1974) and the First Lebanon War (1982–1984), further compounded by the tense periods surrounding these wars. Children born during these periods were subjected to considerable stress or dietary factors (of pregnant mothers or babies) which affected their neonate length/weight measures or developmental process, which correlates to their 17-year-old anthropometric indices.[66] Furthermore, waves of immigrations to Israel might have influenced BMI measurements, as immigrants—depending on their country of origin—had different patterns of weight and disease prevalence.[67]

Socio-Demographic Parameters

Genetics, cultural habits, traditional/natural versus ''modern'' diet, physically active versus sedentary lifestyle, familial characteristics and parental education, exposure to fashion trends, belonging to SES, and even smoking habits[68] might be among the causes for differences between religious groups, rural versus urban residents, and different ethnic origins.[23,32,69,70] Such background and environmental factors, as well as lifestyle habits, are interrelated, but each may affect BMI independently, as they affect mortality.[71] This study further supports and extends our knowledge on socio-demographic variables and environmental effects related to BMI among adolescents. Not only were diverse variables tested (year and season of birth, religious and residential environments, education, family size, birth order, country, and continent of origin were all associated with BMI), but also gender similarities and differences were obtained.

The downward trend of females' average height correlates with a similar trend of mean age of menarche in Israeli females born after 1970.[72,73] Increased childhood and adolescent BMI may be associated with younger age of menarche.[74,75] Both BMI and early puberty were associated with socio-economic factors and may reflect the combined effect of genetics and environment.

Low SES and low education level were both associated with lower prevalence of normal BMI and a higher prevalence of obesity and also overweight, mainly in females. These findings further support previous studies.[23,25,32,44] Low SES has been associated with reduced physical activity,[76] poorer education, and a less healthy diet. The more unfavorable effect of low SES on females might be explained by a gender-specific decrease in height combined with increased weight which is common among adults of this SES sector.[70]

Stratification by country of origin and age of immigration allowed examination of environmental effects. Among individuals of Ethiopian origin, the effect on BMI was correlated with the time spent in Ethiopia. This can be explained, at least in part, by altered growth patterns due to nutritional and dietary habits and cultural differences in childhood.[77] As noted previously, even in the Israeli-born Ethiopian population, which generally belongs to lower education and SES, there was a decline in the prevalence of underweight. These findings are intriguing and deserve further investigation. In contrast to Ethiopian origin, no age of immigration dependency was found among FUSSR immigrants, which might imply difference in adaptation to Israel due to differences in either cultural or genetic background. Nevertheless, the prevalence of obesity (in both genders) was lower among those who came to Israel at 8 years of age or older, from either Ethiopia or FUSSR, compared to those of the corresponding origins (and also those of Israeli origin) who were born in Israel. This strongly points to a possible effect of lifestyle in Israel.

Coexistence of Medical Conditions

It is not uncommon today to encounter chronic diseases among adolescents that were once considered diseases of the fifth decade, such as type 2 diabetes mellitus, essential hypertension, hyperlipidemia, and others.[1] This study only provides a comprehensive analysis of the medical signatures of each of the BMI–gender groups, looking separately at a wide array of medical conditions and at the same time, the broader medical picture. The analysis further supported known associations and uncovered novel (and surprising) ones (see further on).

As demonstrated in our study, obesity in both genders was positively associated with hyperlipidemia, diabetes mellitus, endocrine disorders, hypertension, and active asthma. These associations can be explained by the more pro-inflammatory environment in obesity, as well as hormonal changes.[78–81] These associations might also pinpoint the work-up required for the obese patient to determine the presence of metabolic syndrome early on and treat subjects in that sub-group accordingly.[82] This and other medical signatures are discussed in detail in Supplementary Content 6, http://links.lww.com/MD/A755.

As most research on BMI has tended to focus on obesity, we characterized the medical signature of all BMI categories, including underweight, in male and female adolescents. While this study provided further support for the previously established associations, with the exception of cardiac anomalies, it also uncovered novel ones. Surprisingly, in both genders, obesity and overweight BMI were independently associated with lower rates of spinal deformities and cardiac anomalies. This could be related to either diagnostic issues, as these conditions are more apparent when examining thinner individuals, or medical implications, as underweight BMI may be more prevalent among those suffering from cardiac anomalies due to developmental implications. Further research, in the form of noncross-sectional studies, is needed to substantiate the findings and address the direction of this association and its underlying medical basis. Underweight habitus is associated with chronic (systemic) illnesses and disabling conditions including genetic syndromes and a spectrum of connective tissue abnormalities, such as Marfan syndrome[83] and homocystinuria, which are characterized by spinal deformities, cardiac anomalies (such as mitral valve prolapse, aortic valve abnormalities, and abnormalities of aortic root and arch), and findings in the urine.[83–88] Reduced fat mass and lower BMI are common in patients with classical homocystinuria, and in addition cysteine concentrations showed a positive correlation with BMI, while homocysteine and methionine levels were negatively correlated with BMI.[86,89]

On the other hand, in both genders, underweight BMI was associated with a reduced risk for flat foot, hypertension I + II, and prehypertension, whereas above-normal BMI was associated with an increased risk for the 2 former medical conditions. The associations to flat foot may be explained by the higher burden applied to the lower extremities in the overweight and obese categories, while lower burden is applied to the lower extremities among the thinner population.[90] Differences in flat foot and hypertension frequencies may also be a result of tissue thickness, which may affect diagnosis[91]: flat feet might be less and more apparent due to thinner and thicker tissue, respectively. Similarly, measuring BP of thin and obese subjects might lead to lower and higher values due to cuffs that are too wide or too tight, respectively. While a higher risk for hypertension among overweight and obese adolescents has already been widely observed, the reduced risk for prehypertension among males with obesity is surprising. As BMI increased from normal to overweight and obesity, the prevalence within the BMI category of hypertension I + II also increased (23.1%, 35.7%, and 44.1%, respectively), while the prevalence of prehypertension decreased (49.9%, 49.2%, and 45.3%, respectively). Namely, compared to normal BMI, both overweight and obese males tend to have higher BP, yet there is a higher shift toward hypertension I + II at the expense of prehypertension in males with obesity.

Despite the large sample size of the study population, of the study's limitations is that it was restricted to 1 recruitment center, with an under-representation of certain populations (see Supplemental Content 1, http://links.lww.com/MD/A755, which describes the IDF's service law and populations that are exempt from service). Moreover, additional information, such as waist circumference, physical activity, and other lifestyle factors, such as habits and dietary intake, were not available for analysis. We also lacked birth parameter records and genetic information of those born during the mentioned periods.

Nevertheless, the current findings of a very large nonselective study population of adolescents bring to light the importance of addressing not only the medical conditions associated with the obesity epidemic but also those related to an underweight BMI, mainly among young males. Moreover, the intricate interplay of BMI and gender further strengthens the value of gender- and weight-based approaches for research, diagnosis, intervention, and understanding the molecular, anatomical, behavioral, and sociological basis underlying the commonalities and differences.

A pilot project of information sharing between the recruitment center medical committee and the recruits' primary-care physician has been established to address the abnormal BMI epidemic and its short- and long-term morbidity.[92] The aims of the information exchange are education, prevention, and early intervention in target populations. Bidirectional information exchange between the recruitment center medical committee and the primary-care physician at the Health Maintenance Organizations leads to further and deeper investigation, while special attention is drawn to subjects at risk for current/future morbidity and mortality, for example, adolescents suffering from micro-hematuria, hypertension, or cardiac anomalies that are associated with an above- or below-normal BMI, as revealed by this study. This project has already proved fruitful as identification of subjects at risk has enabled further investigation, monitoring, appropriate intervention, and prevention. In the near future, educational activities will be undertaken to highlight the emerging significance and risks of an abnormal BMI. These activities will be held at schools and community centers in collaboration with the medical authorities and relevant Israeli medical associations (diabetes, cancer, and others), targeting both the general adolescent population and populations at risk.

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