Disparity in Adiposity among Adults with Normal Body Mass Index and Waist-to-Height Ratio

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HIGHLIGHTS
BMI > 30 reliably defines obesity regardless of age and sex
People with BMI of 20–25 and WHtR < 0.5 showed age-dependent hidden obesity
Subjects with excess body fat and BMI range of 20–25 showed increased WHtR with increased age
The present study supports the new notion of normal-weight central obesity

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Disparity in Adiposity among Adults with Normal Body Mass Index and Waist-to-Height Ratio

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SUMMARY
Body mass index (BMI) is commonly used to define obesity. However, concerns about its accuracy in predicting adiposity have been raised. The feasibility of using BMI as well as waist-height ratio (WHtR) in assessing adiposity was examined in relation to a more direct measurement of percent body fat (%BF). We analyzed the relation between dual-energy X-ray absorptiometry (DXA)-measured fat mass and BMI and WHtR using the US 1999–2004 National Health and Nutrition Examination Survey (NHANES) data. A considerable proportion of subjects in the healthy BMI range 20–25 were found to have excess adiposity, including 33.1% of males and 51.9% of females. The use of WHtR also supports the notion of normal-weight central obesity (NWCO), which increases with age. These findings have important implications not only for clinical practice but also for many comparative studies where control subjects are usually selected based on age, sex, and BMI.

INTRODUCTION
Concerns about the use of body mass index (BMI) to assess obesity have recently been raised even in public (“Calling BS on BMI: How Can We Tell How Fat We Are?,” 2018). BMI as the ratio of weight to height squared (W/H²) was first termed in an epidemiological study comparing several indices published in 1972 by Keys et al. (Keys et al., 1972), which was known as the Quetelet Index since 1832 (Quetelet, 1832). The study recommended BMI to simply be better than weight/height (W/H) ratios. Furthermore, it was pointed out that any anthropometry-based index would best fit for growth but not for the evaluation of body composition, nutritional status, or adiposity.

BMI has two serious limitations in that [1] it does not distinguish between fat and muscle and [2] fails to differentiate between central and peripheral obesity and thus, BMI alone cannot be used as a diagnostic tool for assessing adiposity. However, anthropometry-based indices are excellent in their use of simple and practical parameters. In light of the prevalence of increased abdominal adiposity in adults (Araujo de França et al., 2014; Aune et al., 2017) as well as childhood (Okosun et al., 2006; Garnett et al., 2011), it has been suggested that WHtR should be clinically more useful than BMI (Savva et al., 2000; Ashwell and Hsieh, 2005; Maffetone et al., 2017). Nonetheless, BMI has still been widely used in medicine as well as in clinical and basic studies, where control subjects are usually defined as age, sex, and BMI matched. There has been no alternative matrix identified to replace BMI to date.

In this study, we examine the extent of the relationship between adiposity assessed by %BF and BMI/WHtR. Specifically, we aim to identify reliable ranges versus problematic ranges of BMI and WHtR in assessing adiposity and explore the possible merits of using BMI according to age ranges as well as for research and clinical practice.

RESULTS
Distribution of %BF by BMI Range
To define feasibility of BMI in assessing adiposity, we examined the correlation between BMI and DXA-measured %BF in adults; male (n = 6,400, age 18–85 years, mean 44.6 ± 20.0 years) and female (n = 6,239, age 18–85 years, mean 45.9 ± 20.1 years) (Figure 1A). Coefficient of determination (r²) was modest for both groups (0.58 and 0.63, respectively). The population was then classified into five BMI groups: BMI < 20 (under to normal weight; see the rationale in the Discussion), BMI = 20–25 (normal weight), BMI = 25–30 (overweight), BMI = 30–35 (obese), and BMI > 35 (morbidly obese). Distribution of %BF was plotted according to these BMI ranges (Figure 1B). The overall...
Figure 1. Distribution of %BF by BMI Range
(A) DXA-measured percentage of body fat (%BF) compared with BMI in non-diabetic adults; males (n = 6,548) and females (n = 6,403).
(B) Distribution of %BF plotted according to BMI ranges. The population was classified into five BMI groups: BMI < 20 (underweight, pink), BMI = 20–25 (normal weight, orange), BMI = 25–30 (overweight, green), BMI = 30–35 (obese, blue), and BMI > 35 (morbidly obese, purple). The red line depicts the proportion of individuals with a given %BF for all subjects. The cutoff for obesity as determined by %BF is shown by the gray bar (25% for males and 35% for females).
(C) The distribution of %BF compared with BMI was examined in three race/ethnicity groups: Black, Hispanic, and White.
(D) The distribution of %BF for normal weight subjects (BMI 20–25) was plotted for all race/ethnicity groups. The blue shaded area represents normal-weight individuals from all race/ethnicity groups.
Hispanic and White subjects. Black individuals generally had lower %BF among those with normal weight compared with individuals, as defined by BMI 20–25, had obesity by %BF standards (blue area, Figure 1D). For both groups in this population with normal weight (BMI = 20–25) is highlighted in Figure 1D. A striking proportion of normal-weight individuals in WHtR ranges from below 0.4 to greater than 0.6 were sorted by age range and analyzed for Proportion of Individuals with Excess Body Fat by WHtR

Various BMI ranges from lean (BMI < 20) to morbid obesity (BMI > 35) were sorted by age range and analyzed for incidence of excess body fat, as defined by >25% in males and >35% in females (Figure 2). Among individuals with BMI < 20, males tended to carry excess body fat most often in the age range of 80–85 years (27.8% of 18 individuals). Whereas, females with BMI < 20 tended to carry excess body fat most often in the 60–69 years age range (20% of 25 individuals). Overall, 94.3% of 358 males and 91.8% of 468 females with BMI < 20 were not found to have excess adiposity. Similarly, in the groups with a BMI of 20–25, incidence of excess adiposity tended to rise as age increased. Starting with the youngest male age group, incidence of excess body fat increased with each incremental increase in age. Among males, the youngest age group (18–29 years) had the lowest incidence of excess adiposity, occurring in 15.9% of 792 individuals. The eldest age group (80–85 years) had the highest incidence of excess adiposity, which occurred in 78.8% of 146 individuals. In females, rates of excess adiposity increased with age, peaking in the 70–79 years age group, before declining slightly in the 80–85 years age group. In the youngest age range, 18–29 years, 26.4% of 794 females had excess adiposity, as compared with a rate of 78.7% in 141 individuals aged 70–79 years. This trend of increased body fat with age was observed in the BMI range of 25–30 as well, with males aged 18–29 years having the lowest incidence of excess body fat (65.5% of 545 individuals) and males aged 80–85 years having the highest incidence (96.0% of 177 subjects). A similar pattern was observed in females, although excess adiposity peaked again at a younger age range than in males. The rate of excess adiposity in the youngest group of females was 58.2% and was highest in those aged 60–69 years at 98.6% of 291 individuals. A vast majority (97.3%) of males of all ages had excess body fat among those in the BMI range of 30–35, as did a similarly high proportion of females (99.7%) in the same BMI range.

Proportion of Individuals with Excess Body Fat by BMI

Proportion of Individuals with Excess Body Fat by WHtR

Individuals in WHtR ranges from below 0.4 to greater than 0.6 were sorted by age range and analyzed for incidence of excess body fat (Figure 3). The WHtR cutoff values were chosen based on the Ashwell Shape Chart, which provides a framework for assessing adult and child (>5 years old) body shape in terms of WHtR thresholds of 0.4, 0.5, and 0.6 (Ashwell, 2011). Among 94 adult males of all age ranges with WHtR < 0.4, none was found to have excess adiposity, and 1 female of 50 from all ages with WHtR < 0.4 had excess adiposity. Among adult males with a WHtR < 0.5, the vast majority (90.0%) of subjects in all age ranges had no excess body fat, with the lowest incidence of excess adiposity occurring in the youngest age range (7.9% of 1,004 individuals) and the highest incidence in the eldest age range (33.3% of 36 subjects). Similarly, in females with a WHtR < 0.5, the majority of individuals in all age ranges had no excess body fat, with the youngest age group having the lowest rate of excess body fat (18.5% of 685 subjects). The age group with the highest incidence of excess adiposity in females with a WHtR < 0.5 was 50–59 years (47.8% of 138 subjects). Interestingly, the trend of increased adiposity with age in males continued in those with WHtR > 0.5, with those aged 80–85 years having the highest incidence of excess body fat (92.2% of 270 subjects) and subjects aged 30–39 years with the lowest incidence (79.0% of subjects). Incidence of excess adiposity
Figure 2. Proportion of Individuals with Excess fat by BMI.
(A) Proportion of adults with excess body fat and BMI < 20 sorted by age bins: 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80–85 years.
(B) BMI 20–25.
(C) BMI 25–30.
(D) BMI 30–35.
(E) BMI >35.
among individuals of both sexes with WHtR > 0.6 was overwhelmingly high. Overall, 99.4% of 1,807 males with WHtR > 0.6 and 99.1% of 2,328 females with WHtR > 0.6 had excess adiposity.

**Sensitivity and Specificity of BMI and WHtR**

The correlation between %BF and BMI in the healthy range and WHtR greater than or less than 0.5 was assessed for adult males and females (Figure 4A). We show an age-dependent color gradient of data points,

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**Figure 3. Proportion of Individuals with Excess Fat by WHtR**

(A) Proportion of adults with excess body fat and a WHtR < 0.4, sorted by age bins: 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80–85 years.

(B) WHtR 0.4–0.5.

(C) WHtR 0.5–0.6.

(D) WHtR > 0.6.
Figure 4. Sensitivity and Specificity of BMI and WHtR

(A) Correlation between BMI/WHtR and %BF among adults with BMI 20–25 and WHtR < 0.5. Individual data points are continuously color coded by age, ranging from 18 (blue) to 85 years (red). R-squared values for each correlation are indicated.

(B) Sensitivity calculations for BMI < 20 and BMI 20–25 and specificity calculations for BMI >25 among male and female adults for assessing %BF. Sensitivity was calculated by dividing the number of individuals with BMI < 20 or <25 and %BF below the healthy threshold (25% in males, 35% in females; blue dots) by the number of all individuals with BMI < 20 or <25. Specificity was calculated by dividing the number of individuals with BMI >25 and elevated %BF (above 25% in males, above 35% in females; red dots) by the number of all individuals with BMI > 25.

(C) Sensitivity and specificity calculations for assessing %BF using WHtR, using 0.5 as a sensitivity and specificity threshold. Sensitivity was calculated by dividing the number of individuals with WHtR < 0.5 and %BF below the healthy threshold (blue dots) by the number of all individuals with WHtR < 0.5. Specificity was calculated by dividing the number of individuals with WHtR > 0.5 and %BF above the healthy range (red dots) by the number of all individuals with WHtR > 0.5.
with blue representing the youngest subjects (18 years) and red representing the eldest (85 years). Lines of least-squares regression are shown. We found the correlation between %BF and BMI of 20–25 to have a coefficient of determination, $r^2$, of 0.17 in males and 0.23 in females. The $r^2$ value in the correlation between %BF and WHtR in individuals with WHtR < 0.5 was 0.45 for males and 0.14 for females. With regard to age-dependent color coding, we interestingly found that the average age of adult males with BMI of 20–25 and excess adiposity was 54.6 years compared with the average age of males with BMI of 20–25 but without excess adiposity, which was 34.6 years. A similar but less extreme pattern was observed in females, where the average age of subjects with BMI of 20–25 and excess adiposity was 43.9 years compared with the average age of those with BMI of 20–25 and without excess adiposity, which is 35 years. Sensitivity and specificity in predicting adiposity in terms of %BF was also analyzed. Individuals were separated by sex, and all subjects aged 18 years and older were included. The sensitivity of BMI < 20 was found to be 94.3% in male adults and 91.8% in female adults. The average age in this group was 34.9 years for males and 39.0 years for females. The sensitivity of BMI < 25 was calculated to be 71.1% in male adults and 56.6% in female adults. The mean age of males in this group was 40.3 years, and the mean age of females was 42.8 years. The specificity of BMI > 25 was calculated to be 87.3% in males and 96.6% in females. The mean age for males with BMI > 25 was 47.1 years, and the mean age for females with BMI > 25 was 47.8 years. Similarly, the sensitivity and specificity for WHtR were calculated. The sensitivity for a WHtR < 0.5 was 90.0% in males (mean age: 31.9 years) and 71.7% in females (mean age: 36.2 years). Additionally, the specificity for a WHtR > 0.5 was 86.1% in males (mean age: 49.3 years) and 91.6% in females (mean age: 49.0 years).

**Excess Body Fat Compared with BMI and WHtR by Age**

Bar plots are presented showing the proportion of subjects with excess fat according to BMI and WHtR range, sorted by 10-year age bins (Figure 5). Here, we show the ability of BMI to predict adiposity in the range of BMI > 25 regardless of age or sex. Among all subjects with BMI > 25, 91.2% of 7,906 subjects had excess body fat. Similarly, subjects with BMI < 20 rarely had excess adiposity, as just 7.1% of all individuals in this BMI cohort had excess body fat as defined by %BF. This underscores the efficacy of the predictive ability of BMI in these ranges. In the BMI range of 20–25, variability in %BF was associated with age, and incidence of excess adiposity increased as age increased. This pattern was continuous in males and continuous in females until the age range of 70–79 years. Additionally, regardless of age, the vast majority of individuals with WHtR > 0.5 also had excess adiposity. A trend of increased body fat with increased age in females with 0.4 > WHtR > 0.5 was observed until the 60–69 years age range. In the 70–79 and 80–85 years age ranges in females, this trend was reversed, where the 80–85 years age group had a lower prevalence of excess adiposity compared with those in the 70–79 years age group. A similar trend was not observed in BMI for these same demographic groups, suggesting a unique change in body shape but not body composition in this demographic.

**Hidden Obesity Associated with Normal Weight and Aging**

The distribution of %BF among all adult individuals in BMI ranges from <20 to >35 was summarized (Figure 6A). The BMI range of 20–25 (red) is highlighted to emphasize the variance of %BF among individuals with BMI in this range. In both males and females, the group with BMI range of 20–25 had the largest variance, with an SD of 5.0 in males and 4.7 in females. The groups with the next largest variance included those with a BMI of 25–30 in males (SD 4.2) and <20 in females (SD 4.3). Variance in %BF was found to be significantly higher in males with a BMI of 20–25 than 25–30 (p < 0.05 by F-test of variance comparison) and variance in %BF among females with a BMI of 20–25 was also significantly higher than variance in %BF among females with BMI < 20 (p < 0.05). The distribution of BMI, WHtR, and %BF across wide age ranges (18–35, 36–65, and 66–85 years) was plotted in Figure 6B. Marked overlap in the distribution of BMI among the three groups was observed, whereas WHtR and %BF tended to increase with increased age ranges in both sexes. No such pattern was observed in BMI, suggesting an age-dependent relationship between WHtR and %BF but not BMI. Among individuals in the healthy BMI range, WHtR increased with increased age (Figure 6C). For each age group in both sexes, the WHtR of individuals with excess body fat was significantly greater than the WHtR of individuals without excess body fat (p < 0.05).

**DISCUSSION**

Obesity is defined as an excess of body fat mass. Currently, BMI is the most widely used and readily available metric for assessing obesity in studies of human subjects. However, since BMI is calculated solely by
Figure 5. Age Ranges and Proportion of Individuals with Excess Fat by BMI/WHR
Males (left) and females (right) according to age ranges of 18–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80–85 years.
height and weight parameters that do not distinguish between fat and muscle, the accuracy of BMI in detecting body adiposity at the individual level has been brought into question. One of the most cited articles regarding the inaccuracy of BMI in assessing obesity is that published by Romero-Corral et al., using a 1988-1994 US NHANES dataset (Romero-Corral et al., 2006). The authors questioned the "obesity paradox," or the enhanced survival and reduced cardiovascular events in individuals who had a mildly elevated BMI (25.0–29.9) (Romero-Corral et al., 2008; Flegal et al., 2007) and hypothesized that such "favorable
prognostic implications of higher BMI” would rather reflect intrinsic limitations of an overweight range of BMI. The study reported marked discrepancies between rates of BMI-defined obesity (>30) and %BF-defined obesity: 19.1% of men and 24.7% of women versus 43.9% of men and 52.3% of women, respectively. The authors concluded that the accuracy of BMI in diagnosing obesity was limited, particularly for individuals in the intermediate BMI ranges, in men and in the elderly. They further stated that a BMI cutoff of >30 had good specificity but missed more than half of people with excess fat. This assertion could be misleading, because there they lumped individuals from age 20–80 years into one category. Although they did recognize the influence of aging as a factor in assessing BMI’s efficacy in predicting %BF and concluded that “the diagnostic performance of BMI diminished as age increased” (2008), this is also overstated in general terms. Overall, such definite conclusions in the article might have been further interpreted excessively negatively about the usefulness of BMI beyond the authors’ intention.

In the present study using a later (1999–2004) US NHANES dataset, after general analysis of several ranges of BMI in adult subjects, we examined proportion of individuals with excess body fat according to age ranges including WHtR. Our results demonstrate that BMI-defined obesity (>30) is reliable, except on extremely rare occasions, as in young athletes with muscular figures. It should not be an issue in clinical settings, where these subjects are examined individually. Similarly, almost all of the subjects with BMI under 20 were lean with %BF below obesity thresholds, except with a slight upward trend with increased age in both sexes. A vast majority of the subjects with BMI 25–30, defined as “overweight,” had excess body fat with a positively associated age-dependent tendency. Above all, the most problematic BMI range was 20–25, which is defined as “normal weight.” In both sexes, considerable proportions of the subjects were with excess body fat in a distinct age-dependent fashion. Here, the rationale for using the cut-off point of BMI 20 by not including subjects whose BMI being in the range of 18.5–19.9 in this study is that the majority of them are not obese. In a clinical setting, for example, such as for the donor selection for islet transplantation, those with BMI < 20.1 are declined (North America Islet Donor Score; Wang et al., 2016). Vlassopoulos et al. reported increasing obesity, in terms of BMI and waist circumference, over recent years comparing the Scottish and English Health Surveys of 1994–1996 and 2008–2010. It is indeed a worldwide trend that more young people enter adult life already obese and further that overweight and obesity are rising and are peaking later in life (Vlassopoulos et al., 2014).

It is noteworthy that the concept of obesity has been changing in recent years by challenging the historical and simplistic one as defined by BMI, particularly highlighted by the notion of “normal weight obesity (NWO)” (Oliveros et al., 2014). Individuals with normal BMI and high %BF show a high degree of metabolic dysregulation. NWO is associated with a significantly higher risk of developing metabolic syndrome, cardiometabolic dysfunction, and higher mortality. Further, the importance of fat distribution in NWO was demonstrated by Sahakyan et al. and reported that central obesity in NWO defined by BMI is at greater mortality risk than those with overweight or obesity (BMI ≥ 25) (Sahakyan et al., 2015), which has been termed as “normal weight central obesity (NWCO)” (Hamer et al., 2017; Owolabi et al., 2017; Sharma et al., 2016; Thaikruea and Thammasarot, 2006). We propose that the present study supports this new concept of NWCO with the accompanied %BF data. Indeed, we show that WHtR in the “healthy” range provided a better predictive value in assessing excess body fat in both sexes as compared with a BMI range of 20–25.

In conclusion, we have found that BMI is overall an accurate predictor of excess adiposity outside the normal BMI range and especially in BMI > 30, regardless of age and sex. Within the BMI range of 20–25, however, we report marked variability in adiposity in both sexes, with an age-dependent trend of increased adiposity with increased age. In many comparative studies, BMI is a common standard for matching control subjects along with age and sex. For example, in recent genetic studies of obesity such as genome-wide association study (Heid et al., 2010; Locke et al., 2015; Shungin et al., 2015; Wahl et al., 2017) and epigenome-wide association study (Sandholt et al., 2014; Demerath et al., 2015; Dhana et al., 2018), a potential concern would not be about targeted individuals with obesity but the comparison with “control” subjects who were classified simply by BMI. In the near future with more cost-effective accessibility to existing devices that accurately measure %BF, we propose that its primary application should be to normal-weight individuals to identify excess fat not detected by other widely used population measures.

Limitations of the Study

The NHANES dataset used in this study was collected in the years 1999–2004, and trends in obesity in the United States have increased in the years since these data were gathered. Specifically, prevalence of
obesity in adults in the United States has risen from 30.5% in 2000 to 39.6% in 2016 (Hales et al., 2017). Additionally, more recent editions of the NHANES dataset (conducted annually) do not contain data on whole-body %BF measures via DXA scan.

METHODS

All methods can be found in the accompanying Transparent Methods supplemental file.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.10.062.

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AUTHOR CONTRIBUTIONS

Study design, data analyses, and preparation of the manuscript: M.P.D. and M.H. Editing the manuscript: M.P.D., M.J.B., and M.H.

DECLARATION OF INTERESTS

The authors declare no conflicts of interest.

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Supplemental Information

Disparity in Adiposity among Adults
with Normal Body Mass Index
and Waist-to-Height Ratio

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Supplemental Document

Transparent Methods

Data Overview

We examined data from non-diabetic adult subjects from the US NHANES 1999-2004 data set. The NHANES survey data examines the health and nutrition status of individuals from across the United States and combines demographic, physical, and interview data. This dataset includes a nationally representative sample of the residential, noninstitutionalized, civilian population sampled using a multistage probability design. Subjects were measured \textit{in vivo} for regional body fat distributions by using DXA scanners, which was part of a comprehensive standardized physical examination. The data was retrieved using the R package "NHANES" (Krakauer and Krakauer, 2012) and analyzed with the R base package (R: A Language and Environment for Statistical Computing, 2008). The US NHANES 1999-2004 data set contained data on 31,126 subjects, including 15,184 male and 15,942 female adults, and 7,093 male and 6,972 female youth under 18 years old. Following exclusion for incomplete anthropometric data, including those without height, weight, waist circumference, and \%BF measurements. 6,400 male and 6,239 female adults had all required anthropometric data necessary for further analysis.

Body Composition Data

Body composition in the NHANES survey was collected via DXA and bioelectrical impedance analysis (BIA). DXA uses a laser to measure the thickness of a scanned body region and can differentiate bone mineral, lean soft tissue (blood, skin, water, and muscle), and adipose tissue from each other based on differing x-ray attenuating properties. Data were collected in a mobile examination center by a survey team consisting of a physician and several trained health
professionals. BMI is calculated as (mass in kilograms)/(height in meters)$^2$. WHtR is calculated as (waist circumference in meters)/(height in meters). %BF is the proportion of the entire body mass made up of adipose tissue, or (adipose tissue mass)/(entire body mass).

**Data Presentation**

Individual BMI, WHtR, and %BF data are grouped by decade age groups (except the youngest, 18-29 years) and separated by sex. Summary statistics, including mean and standard deviation, are provided by sex, age, and WHtR and BMI ranges. Males with %BF greater than 25 and females with %BF greater than were considered to have excess body fat. Standardized ranges of BMI and WHtR were implemented in assessing these metrics for ability to assess body composition in examined subjects. In order to make this assessment, proportions of individuals with excess body fat were compared to those without excess body fat among the same sex and across the same BMI, WHtR, and age ranges. Pearson correlations were performed to assess the relationship between BMI/WHtR and %BF and results are presented with a least squares line of regression to minimize the sum of residual values and $r^2$ as an indicator of variability in the relationship that is explained by such a linear model. Sensitivity and specificity calculations are performed such that BMI and WHtR are assessed as tools to predict an individual's %BF. Sensitivity was assessed separately for individual's with BMI<20 and BMI<25, and WHtR was evaluated for sensitivity in individuals with WHtR < 0.5. Specificity for BMI was assessed using BMI>25 as a cutoff, and specificity for WHtR were evaluated for individuals with WHtR > 0.5. The F-test for comparison of variance between two groups was employed to compare variance in %BF among different BMI groups at a significance level $\alpha$ of 0.05.
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