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Obesity

Walking in the Light: How History of Physical Activity, Sunlight, and Vitamin D Account for Body Fat—A UK Biobank Study

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Objective: The high prevalence of vitamin D deficiency and obesity drives the need for successful strategies that elevate vitamin D levels, prevent adipogenesis, and stimulate lipolysis. This study provides a theoretical model to evaluate how physical activity (PA) and sunlight exposure influence serum vitamin D levels and regional adiposity. This study hypothesized a posteriori that sunlight is associated with undifferentiated visceral adiposity by increasing the ratio of brown to white adipose tissue.

Methods: Using 10-year longitudinal data, accelerometry, a sun-exposure questionnaire, and regional adiposity quantified by dual-energy x-ray absorptiometry imaging, a structural-equation mediation model of growth curves was constructed with a data-driven methodology.

Results: Sunlight and PA conjointly increased serum vitamin D. Changes in vitamin D levels partially mediated how sunlight and PA impacted adiposity in visceral and subcutaneous regions within a subjective PA model. In an objective PA model, vitamin D was a mediator for subcutaneous regions only. Interestingly, sunlight was associated with less adiposity in subcutaneous regions but greater adiposity in visceral regions.

Conclusions: Sunlight and PA may increase vitamin D levels. For the first time, this study characterizes a positive association between sunlight and visceral adiposity. Further investigation and experimentation are necessary to clarify the physiological role of sunlight exposure on adipose tissue.

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Study Importance

What is already known?

- Obesity and vitamin D deficiency are prevalent among most age cohorts.
- Both physical activity (PA) and sunlight exposure are independently linked to increased vitamin D and reduced obesity.

What does this study add?

- When tested conjointly, PA was associated with elevated vitamin D levels above and beyond the effects of sunlight.
- Greater sunlight exposure was associated with more visceral fat mass but not with subcutaneous fat mass.
- Mediation results suggest separate photic and vitamin D–related effects on adipose tissue from exposure to sunlight.

How might these results change the direction of research?

- Because of correlations between sunlight and PA, it may be best to consider them together in future studies.
- If there are separate vitamin D and photic effects, supplementing vitamin D alone may not adequately replace effects from sunlight exposure.

Introduction

Despite a century of advancements in life expectancy, longevity in the United States has been on the decline since 2014 (1). Both an aging baby-boomer generation and an alarming acceleration in mortality among adults in midlife are responsible for this trend (2). Although the nature of this bleak trajectory is multifactorial, the prevalence of obesity has consistently risen since the early 1990s and has been shown to have a profoundly detrimental effect, not only on the prevalence of cardiovascular diseases but also on that of neurological disorders (3,4).

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Vitamin D serum levels are thought to operate as a central control mechanism of body composition, in which lower systemic concentrations stimulate adipogenesis. This would, in turn, maximize survival in energy-scarce seasons, including winter (5). For decades, however, vitamin D levels among infants and toddlers (6), adolescents (7), and adults (8) have remained chronically low in the general population. This chronic, multigenerational deficiency in vitamin D could compound or in part give rise to obesity and its sequelae, including gut inflammation, hyperglycemia, and progressive deficits in immunometabolic signaling in the brain that hinder cognitive function (9).

Physical activity (PA) has a myriad of positive health effects, including aiding in the reduction of adipose tissue volume while maintaining or increasing muscle mass (10,11). Recent studies have further suggested that engagement in greater levels of PA is associated with higher circulating vitamin D levels (12), even from exercise done exclusively indoors (13). Ultraviolet (UV) radiation from sunlight exposure increases endogenous production of vitamin D, with subsequent reduction in adiposity (14). In experimental mouse models, exposure to summer-related UV wavelengths has been shown to enhance lipolysis of white adipose tissue and activate brown adipose tissue deposition (15).

PA frequently coincides with increased sunlight exposure; however, it is difficult to disentangle independent and additive effects of these two variables on abdominal adipose mass. Although cross-sectional studies have observed greater mean levels of serum vitamin D with outdoor activities in contrast to indoor activities (16), it is important to examine further how vitamin D levels, PA, and sunlight exposure interact with one another to influence body fat composition. Few studies to date have conjointly estimated the extent to which accelerometer-based PA and long-term sun exposure raise vitamin D levels and impact obesity from middle-to-late adulthood. It is also critical to understand these relationships for individuals located in the northernmost and southernmost regions of the world, where little UV radiation–induced vitamin D occurs outside of the summer months, as well as in aged adults who synthesize vitamin D less efficiently compared with younger counterparts (17).

Our objectives in the present study were (1) to establish how PA and sunlight exposure are conjointly related to abdominal fat mass using dual-energy x-ray absorptiometry (DEXA), as well as (2) to characterize how serum vitamin D may underlie and describe these associations. We also considered subcutaneous fat mass and compared questionnaire- and accelerometry-based models. Potentially confounding dietary variables were controlled to ensure that effects from PA and sunlight were not stemming from correlations between these variables and diet.

Methods

Cohort

Participants were a part of the UK Biobank study (18). This prospective cohort study collected baseline data in a half-million individuals from 22 assessment centers located in the United Kingdom north of 53° latitude, starting in 2006. Each participant had baseline measurements taken between 2006 and 2010, when genetic, behavioral, and biological data were collected. A visit to the assessment center involved six consecutive steps: (1) consent, (2) touch-screen questionnaire, (3) verbal interview, (4) eye measures, (5) physical measures, and (6) blood/urine sample collection. The touch-screen questionnaire collected data on sociodemographic information, occupation, lifestyle, early-life exposure, cognitive function, and family history of illness. Informed consent to participate was given at baseline. Longitudinal assessments are ongoing in a subset of participants. The UK Biobank protocol was approved by the North West Multicentre Research Ethics Committee. Because of power and generalizability considerations, only participants of European ancestry were considered. As noted in Supporting Information Figure S1, a total sample of 1,853 participants was available for self-reported assessment of PA (i.e., the subjective model), and a subset of 1,353 participants was available for accelerometry-based assessment of PA (i.e., the objective model). As noted in Supporting Information Figure S2, participants were aged 48 to 80 years old at the completion of this study.

Measures

A timeline of all measures and their assessment dates is illustrated in Supporting Information Figure S3.

Body composition. A subset of participants had body-composition imaging data collected in 2015 to 2016. Compartment measurements of body composition (lean muscle mass in kilograms, subcutaneous adipose mass in kilograms, visceral adipose mass in kilograms, and bone density in grams per centimeter squared) were determined by a trained radiographer delivering a 5-minute, full-body DEXA scan (Lunar iDXA, GE Healthcare, Madison, Wisconsin) to each participant while they lay supine (19). To enhance the value of DEXA as a prospective outcome measure, imaging started in May 2014 after collection of the lifestyle data.

Subjective PA levels. Subjective PA was assessed using adapted questions from the validated short International Physical Activity Questionnaire (20), which covered the frequency, intensity, and duration of moderate and vigorous activity. Values were quantified in mean minutes per day. Data processing rules published by the International Physical Activity Questionnaire were followed (21).

Objective PA levels. Invitations were mailed to 236,519 eligible participants to participate in the substudy of objective PA. Participants in the northwest region who had been involved in other substudies were not invited for accelerometer measurement because of potential participant burden. A total of 1,422 participants had complete data. Eligible participants were mailed a triaxial accelerometer (AX3; Axivity, Newcastle upon Tyne, United Kingdom), which was set to capture 3-dimensional acceleration at 100 Hz with a dynamic range of ±8 g to quantify PA in meters per second squared. Instructions on proper use of the accelerometer were provided. Consenting participants wore the device on their dominant wrist for 7 consecutive days. Device programming automatically started and stopped recording at predefined times. A prepaid envelope was provided to return the equipment after use. Nonwear was identified as time periods of >60 minutes, in which SDs of all 3 axes were <13.0 milli-g (1 milli-g = 0.001 g-forces). Participants with <72 hours of wear time (n = 69) were excluded from the analyses. In the remaining 1,353 participants, the device was worn for an average of 6.69 days. To describe the overall level and distribution of PA intensity, the sample-level data were combined into 5-second epochs for summary data analysis, maintaining the mean vector magnitude value over the epoch. To represent the distribution of time spent by an individual in different levels of PA intensity, an empirical cumulative distribution function from all available 5-second epochs was generated (22). Data processing has been described in detail elsewhere (23).

Sunlight exposure and sun protection. Participants answered the question "In a typical day in summer, how many hours do you spend outdoors?" as part of the touch-screen questionnaire at three separate occasions. Responses were recorded as integers between 0 and 12. As there are approximately 6 hours maximum of meaningful UV radiation at the peak of summer in the United Kingdom, values above 6 were set to 6. Participants also answered the question "Do you wear sun protection (e.g., sunscreen lotion, hat) when you spend time outdoors in the summer?" Responses were recorded as one of four ordinal categories ("Never/rarely," "Sometimes," "Most of the time," and "Always").

Serum biomarker levels. At two separate visits (2006-2010 and 2012-2013), plasma samples were collected in 4-mL EDTA vacutainers and analyzed within 24 hours of sampling using 4 LH750 instruments (Beckman Coulter, Brea, California) (Elliott & Peakman, (23)). Serum samples were analyzed for levels of vitamin D (nanomoles per liter) and 24 other biomarkers, as listed in Supporting Information Text S1. All serum biomarkers were tested in a backward-elimination approach to reduce bias (see Statistical Analysis section). Vitamin D serum levels were corrected for seasonal effects on the basis of the time of the year. The serum samples were collected in spring, summer, autumn, or winter.

Dietary composition and alcohol consumption. To ensure that associations of PA and sunlight were not confounded by correlations with diet, we covaried several aspects of dietary composition. This analysis focused on total dietary composition rather than on specific nutrients like protein, crude fiber, or moisture. Participants completed a Food Frequency Questionnaire (24), including 18 questions about commonly eaten food groups, as part of the touch-screen questionnaire at 3 separate assessments. More information is available in Supporting Information Text S2.

Covariates. Covariates included sex, age, education, socioeconomic status, and tobacco smoking. Age was measured in years at baseline. A categorical variable was used to capture education level at baseline. Education categories were considered sequentially and included the following: college or other higher-level qualification, postsecondary or vocational qualification, secondary qualification, or none of the previous education levels listed. Socioeconomic status was considered sequentially and based on the participant's average total household income between 2006 and 2014. Responses were recorded as 1 of 5 ordinal categories in British pounds (<£18,000, £18,000-£30,999, £31,000-£51,999, £52,000-£100,000, or >£100,000), in which the lowest 2 categories were classified as lower class, the next 2 categories were classified as middle class, and the greatest category was classified as upper class. Tobacco smoking indicated who has never smoked, who used to smoke, and who is currently a smoker.

Statistics

Longitudinal modeling. For longitudinally observed variables, we computed individual, across-time averages and nonlinear changes over time to enhance model fit using difference equations (25). We then integrated these values to derive average levels and the sum of changes for each longitudinally assessed variable (26). Serum biomarkers were computed as average individual levels over 2 visits spanning 4 years. As we have recently demonstrated (27), this method produces superior goodness-of-fit while increasing testing power and elucidating relationships between variables more robustly by capturing both within-participant variation (28) and between-participant variation over time (29,30).

Outlier analysis. To ensure that our models were generalizable to at least 99.9% of the sample population, 0.1% quantiles were computed, and 68 participants beyond 99.9% of the sample distribution of the mean among any variable were removed from further analysis.

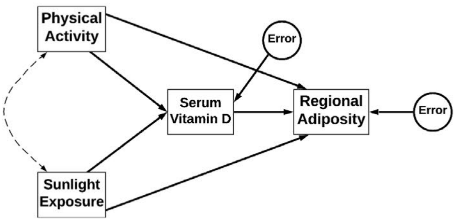
Structural-equation modeling. Structural-equation modeling (SEM) was done using R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) (31). Graphs were prepared in ggplot2 version 3.1.1 (https://ggplot2.tidyverse.org/) (32). SEM was initially used to determine model fit of two separate PA constructs: subjective activity using self-report and objective activity using accelerometry data. SEM-based mediation has more statistical power than the standard regression procedure (33). SEM has the additional benefit of easily extending to longitudinal data within a single framework (30), as was done in this report.

Variable selection. An empirical model-building approach was employed to select the most salient variables that predicted serum biomarker levels and visceral or subcutaneous adipose outcomes. In this backward-elimination approach, a full "all-variables-in" model was constructed, and the least significant variables were removed one at a time. The model was then recomputed until all variables remaining reached $P < 0.050$.

Parameter estimation, ANOVA, uncertainty analysis, and mediation. To establish predictors that significantly explained regional adiposity outcomes, a structural-equation model was used to comprehensively fit the covariance structure (34) of regional adiposity with vitamin D and 24 other available serum biomarkers, PA, sunlight exposure, and self-reported consumption of whole foods in the diet. See Figure 1 for a conceptual representation of the model. Standardized parameter estimates (β) were computed using maximum likelihood and interpreted as the mean potential effects of a variable. ANOVA is reported as the overall portion of variation in visceral or subcutaneous adiposity that is explained (R^2). Uncertainty analysis relied on standard errors and P values, in which results were considered significant at $^{***}P < 0.001$, $^{**}P < 0.01$, and $^{*}P < 0.05$ and considered trending at $^{\#}P < 0.10$. Mediation tested whether serum biomarker levels due to variation in PA and sunlight exposure explained visceral or subcutaneous adiposity associations. Specifically, parameter decomposition was used to distinguish indirect (λ) from direct (β) effects (35). To maintain an empirical data–driven analysis and ensure robustness, only participants with no data missingness were considered.

Post hoc analyses. To assess whether any observations were driving the results, the Cook distance was calculated for each observation in the subjective PA and objective PA models, and a threshold value of 1.0 was set. The largest value in the subjective PA model was 0.022, and in the objective PA model, we observed 0.024. As no values >1.0 were noted, we made no further adjustments to the models.

Sensitivity analysis. Given the sample size of 1,853, 30 predictors (the most observed here), and no a priori hypotheses ("two-tails"), G*Power version 3.1 (Heinrich Heine University Düsseldorf,



Subjective Physical Activity Model

$$\underset{[0,\ 5.5]}{\text{Visceral Adiposity}_{kg}} = -.13\ \Delta_1 \text{Vigorous Physical Activity}_{min/d} + .05\ \Delta_1 \text{Sunlight}_{h/d} - .12\ \Delta_2 \text{Vitamin D}_{nmol/L} + .10\ \text{Age}_y - .09\ \text{Education} + .82\ \text{Sex} + \sum_i^5 \Delta_1 \text{Diet} + \sum_i^{19} \Delta_2 \text{Biomarkers} + 44\%\ \textit{Uncertainty} \quad (1)$$

$$\underset{[4.8,\ 59.1]}{\text{Subcutaneous Adiposity}_{kg}} = -1.63\ \Delta_1 \text{Vigorous Physical Activity}_{min/d} - 1.8\ \Delta_2 \text{Vitamin D}_{nmol/L} - 1.22\ \text{Age}_y - .94\ \text{Education} - 3.5\ \text{Sex} + \sum_i^6 \Delta_1 \text{Diet} + \sum_i^{16} \Delta_2 \text{Biomarkers} + 66\%\ \textit{Uncertainty} \quad (2)$$

$$\underset{[10,\ 126]}{\text{Vitamin D}_{nmol/L}} = 4.12\ \Delta_1 \text{Vigorous Physical Activity}_{min/d} + 4.09\ \Delta_1 \text{Sunlight}_{h/d} + 3.22\ \text{Seasonal Variation}_{autumn} + 3.04\ \text{Age}_y - 1.96\ \text{Education} + \sum_i^1 \Delta_1 \text{Diet} + 96\%\ \textit{Uncertainty} \quad (3)$$

Objective Physical Activity Model

$$\underset{[0,\ 5.5]}{\text{Visceral Adiposity}_{kg}} = -.59\ \Delta_1 \text{Physical Activity}_{m/s^2} + .05\ \Delta_1 \text{Sunlight}_{h/d} - .12\ \Delta_2 \text{Vitamin D}_{nmol/L} + .83\ \text{Sex} + \sum_i^5 \Delta_1 \text{Diet} + \sum_i^{18} \Delta_2 \text{Biomarkers} + 41\%\ \textit{Uncertainty} \quad (4)$$

$$\underset{[4.8,\ 58.3]}{\text{Subcutaneous Adiposity}_{kg}} = -8.9\ \Delta_1 \text{Physical Activity}_{min/d} - 1.21\ \Delta_2 \text{Vitamin D}_{nmol/L} - 2.24\ \text{Age}_y - 4.01\ \text{Sex} + \sum_i^5 \Delta_1 \text{Diet} + \sum_i^{15} \Delta_2 \text{Biomarkers} + 56\%\ \textit{Uncertainty} \quad (5)$$

$$\underset{[11,\ 126]}{\text{Vitamin D}_{nmol/L}} = 11.97\ \Delta_1 \text{Physical Activity}_{m/s\wedge 2} + 2.69\ \Delta_1 \text{Sunlight}_{h/d} + 4.78\ \text{Age}_y - 2.04\ \text{Education} + 95\%\ \textit{Uncertainty} \quad (6)$$

Figure 1 Top panel: Conceptual diagram of associations and their directionality between physical activity and sunlight exposure, serum vitamin D, and regional adipose tissue mass outcomes. Model is shown as exposure → mediator → outcome. Lower panels: Graphical equations algebraically summarize models illustrated in Figures 2, 3, and 4. First three equations (1-3) represent subjective model and last three equations (4-6) represent objective model. Because vitamin D is an outcome that is also nested within the prediction of regional adiposity, the equations that describes regional adiposity are computed sequentially after the vitamin D–related equation. The symbol Δ_1 is defined as average level and totality of changes observed over time, and Δ_2 is defined as average level over time. Each coefficient represents the change expected in the outcome if an individual progressed halfway (1.5 standard deviations) along the distribution of that predictor. To offer context for each coefficient, the range of each outcome is listed below the left-hand side of the equation.

Düsseldorf, Germany) (36) estimated the smallest effect that could be detected, while minimizing type 1 error to $\alpha = 0.05$ and type 2 error to $\beta = 0.20$, $\beta = 0.10$, $\beta = 0.05$, or $\beta = 0.01$; the size of effect was $f = 0.004$, $f = 0.006$, $f = 0.007$, or $f = 0.010$, respectively.

Results

Data summary

Demographics and summary data are listed in Table 1 and Supporting Information Table S1. As illustrated in Figure 1, two equivalent structural-equation models were determined to link subjective or objective PA and sun-exposure measures with regional adiposity. These models examined associations with (1) visceral and subcutaneous fat, (2) sunlight exposure and PA, (3) vitamin D, and (4) 24 serum biomarkers currently available in the UK Biobank. In the first model, subjective questionnaire-based PA was assessed. In the second model, objective accelerometer-based PA was assessed.

Subjective PA model: PA and adiposity mass

This model focused on the questionnaire-based subjective total (moderate/vigorous) PA or "subjective PA" (Table 2, Figure 2). Here, aging was associated with more visceral fat mass ($\beta = 0.049$, $P = 0.009$), whereas increasing vitamin D levels over time corresponded with less fat mass ($\beta_c = -0.051$, $P = 0.001$). Regarding subcutaneous adiposity (Table 2, Figure 3), aging was associated with less fat mass ($\beta = -0.076$, $P = 0.001$) and so were higher vitamin D levels over time ($\beta_c = -0.078$, $P < 0.001$).

TABLE 1 Demographics and data summary: participants with subjective PA

	Women	Men
Sample size, *n*	761	1,092
Age, y	63 ± 7.4	65 ± 7.2
Education level, *n* (%)		
College/other higher level	523 (67.9)	775 (70)
Postsecondary/vocational	108 (14.0)	196 (17.7)
Secondary	116 (15.0)	73 (6.6)
Other	23 (2.9)	60 (5.4)
Social class, *n* (%)		
Lower	331 (42.9)	429 (38.8)
Middle	396 (51.4)	618 (55.9)
Upper	43 (5.5)	57 (5.1)
Muscle mass, kg	39 ± 4.5	55 ± 6.2
Visceral adipose mass, kg	0.67 ± 0.51	1.59 ± 0.09
Subcutaneous adipose mass, kg	24 ± 8.1	22 ± 7.4
Bone mineral density, g/cm	1.13 ± 0.11	1.30 ± 0.11
Serum vitamin D, nmol/L	53.4 ± 19.5	53.3 ± 19.4
Subjective moderate PA, min/d	56 ± 47.9	59.6 ± 53.4
Subjective vigorous PA, min/d	38 ± 29.5	41 ± 33.6
Sunlight exposure, h/d	3.3 ± 1.6	3.8 ± 1.7

Data given as mean ± SD unless stated otherwise.
PA, physical activity.

For vigorous subjective PA, higher self-reported levels were associated with less visceral fat ($P = 0.009$). Serum biomarkers were able to account for 34% of the variance in this model. Specifically, vitamin D levels mediated 5% of subjective PA's effect on visceral adiposity ($P = 0.052$), as more subjective PA predicted more vitamin D ($\beta_b = 0.054$, $P = 0.019$). Higher levels of the liver enzyme alanine aminotransferase (ALT) separately explained 28% of the variance in this model.

In contrast, greater vigorous subjective PA predicted less subcutaneous fat ($P = 0.001$) (Figure 3). Vitamin D levels explained 5% of this effect ($P = 0.026$).

Subjective PA model: sunlight exposure and adiposity mass

For hours per day spent in sunlight, greater exposure was associated with more visceral fat mass ($P = 0.014$). Because of more sun exposure being related to higher vitamin D levels ($P < 0.001$), vitamin D reduced the association between greater sunlight and more visceral adiposity by 26% ($P = 0.014$). No other serum markers were found to be statistically significant.

In contrast, more sunlight exposure was related to less subcutaneous fat mass ($P = 0.001$), in which vitamin D levels accounted for 100% ($P = 0.001$) of the effects of sunlight on subcutaneous fat mass.

Objective PA model: PA and adiposity mass

This model focused on accelerometry-based "objective PA" (Table 3). For visceral adiposity, aging was not a significant covariate. Higher levels of objective PA strongly coincided with less visceral fat ($P < 0.001$). Many serum markers, particularly lipid fraction and transport proteins, accounted for 35% of the variance in this model.

TABLE 2 Subjective PA model

Mechanism of action	Effect size	Percentage of total effect, %
Visceral adiposity ~ vigorous PA	$\beta_{total} = -0.055$***	
Unspecified	$\beta_a = -0.039$**	71
ALT levels	$\gamma = -0.016$**	29
Subcutaneous adiposity ~ vigorous PA	$\beta_{total} = -0.074$***	
Unspecified	$\beta_a = -0.056$***	76
ALT levels	$\gamma = -0.017$**	23
Vitamin D levels	$\gamma_{b,c} = -0.004$*	5
GGT levels	$\gamma = 0.002$*	3
Subcutaneous adiposity ~ vigorous PA	$\beta_{total} = 0.023$#	
Unspecified	$\beta_e = 0.029$*	126
Vitamin D levels	$\gamma_{d,c} = -0.006$**	26
Subcutaneous adiposity ~ sunlight exposure	$\beta_{total} = -0.009$***	
Vitamin D levels	$\gamma_{d,c} = -0.009$***	100
Subcutaneous adiposity ~ moderate PA	$\beta_{total} = 0.008$*	
Creatinine	$\gamma = 0.008$*	100

All models shown as outcome ~ exposure. Percentage of effect for mediation effects (γ) are shown with respect to total effect that they compose. If mediation effects for one total oppose each other, percentages will not necessarily equal 100. Table does not include nonsignificant γ effects. Totals do not include nonsignificant γ pathways. Separate pathways are differentiated by subscript letters.
***$P < 0.001$.
**$P < 0.01$.
*$P < 0.05$.
#$P < 0.10$.
ALT, alanine aminotransferase; GGT, γ-glutamyltransferase; PA, physical activity.

For subcutaneous adiposity (Table 3, Figure 4), less fat mass was observed with age in years ($\beta = -0.131$, $P < 0.001$). Higher levels of objective PA ($P < 0.001$) and increased vitamin D ($\beta_c = -0.048$, $P = 0.006$) were related to less subcutaneous fat. The negative effect of PA on subcutaneous fat ($\beta_b = 0.152$, $P < 0.001$) was partially mediated by its impact on vitamin D ($\lambda_{b,c} = -0.007$, $P = 0.014$).

Objective PA model: sunlight exposure and adiposity mass

More sunlight exposure predicted more visceral fat mass ($\beta_{total} = 0.032$, $P = 0.018$). Unlike the subjective PA model, vitamin D levels did not mediate the relationship with visceral fat among those in our sample.

Conversely, more sun exposure predicted less subcutaneous fat ($\beta_{total} = -0.004$, $P = 0.046$). Vitamin D levels fully mediated the effects from sunlight ($\lambda_{d,c} = -0.004$, $P = 0.046$) because of the impact it had on serum levels ($\beta_d = 0.080$, $P = 0.004$).

Discussion

Typical changes in physique associated with aging, such as greater visceral fat, are associated with many negative health outcomes, like all-cause mortality, metabolic syndrome and type 2 diabetes,

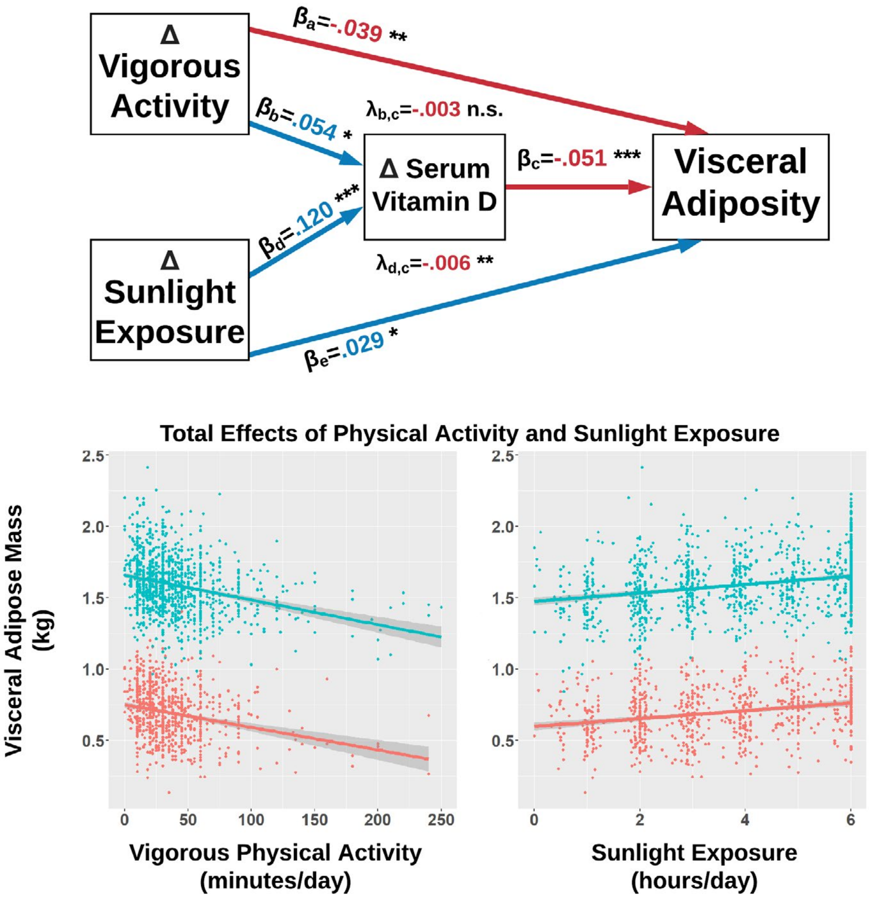


Figure 2 This snippet of the subjective structural-equation model illustrates which factors explain subcutaneous adipose mass. Model examined (1) metabolic biomarkers of the mechanisms of action, which explain associations between physical activity and sunlight exposure, and (2) remaining, unspecified effects (also called "direct effects") of physical activity and sunlight exposure. Delta symbol (Δ) is defined as average level and totality of changes in that variable observed over 6 years. Standardized β reflects average effect size of each path, and each path is denoted with a subscript letter. Each λ reflects the mediation effect resulting from the path analysis and is subscripted to illustrate the paths that compose it. ***$P < 0.001$, **$P < 0.010$, and *$P < 0.050$. Scatterplots illustrate intercept and slope among women (in red) and men (in blue), and gray band represents conditional standard error of the mean.

cardiovascular disease, sarcopenia, and osteoporosis (37). Regular PA helps in preventing or minimizing weight gain and obesity (11). Although sunlight exposure often coincides with PA, much less is known about its potential health effects (38). To the best of our knowledge, few studies have examined the extent to which accelerometer-based PA and history of sun exposure affect vitamin D levels and impact regional adiposity from middle-to-late adulthood, particularly at latitudes further from the equator. Briefly, we observed that higher levels of PA consistently corresponded to decreased adiposity. Interestingly, sunlight exposure was related to less subcutaneous fat but more visceral fat, which may be due to compensatory behaviors, such as feeling more hunger after a workout; present weight status (39); or the differential impact of sunlight on the mass of different adipose tissue types (5,15).

Our analysis of metabolic biomarkers suggests that PA and sunlight exposure are associated with regional adiposity, partially due to serum vitamin D levels. Vitamin D levels may regulate body composition, in which adipogenesis is stimulated during times when levels are depleted (5). Similar to Wanner et al. (12), we observed that serum vitamin D levels responded significantly to both PA and sunlight exposure. Although sunlight exposure had comparatively twice the effect on increasing vitamin D, importantly, PA further influences vitamin D above and beyond the sun exposure that often coincides with it.

PA levels may independently increase serum vitamin D levels. Our results showed that PA was associated with greater vitamin D levels, which remained significant even after considering sunlight exposure in our analysis. One study showed that each hourly increase in the level of moderate-to-vigorous PA engaged in per week was associated with a 1.54-ng/mL increase in 25(OH)D concentration, which is the predominant circulating, active form of vitamin D in the body and, consequently, the most common biomarker used to measure serum vitamin D levels (40). Some studies have shown that serum vitamin D levels

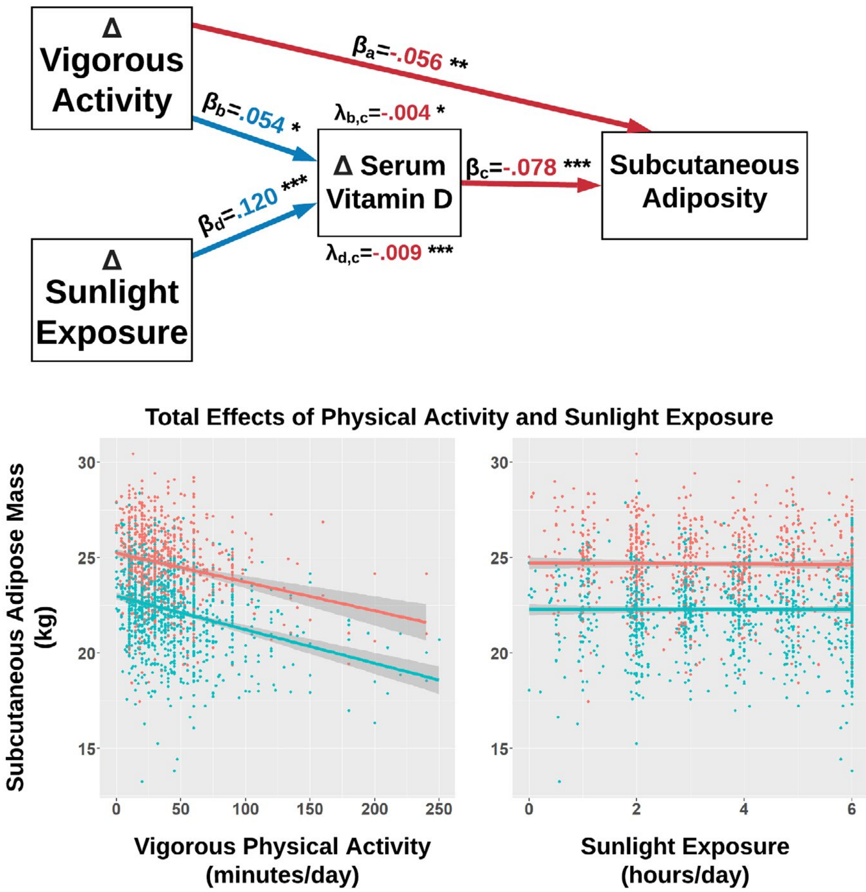


Figure 3 This snippet of the subjective structural-equation model illustrates which factors explain visceral adipose mass. Model examined (1) metabolic biomarkers of the mechanisms of action, which explain associations between physical activity and sunlight exposure, and (2) remaining, unspecified effects (also called "direct effects") of physical activity and sunlight exposure. Delta symbol (Δ) is defined as average level and totality of changes in that variable observed over 6 years. Standardized β reflects average effect size of each path and each path is denoted with a subscript letter. Each λ reflects the mediation effect resulting from the path analysis and is subscripted to illustrate the paths that compose it. ***P < 0.001, **P < 0.010, and *P < 0.050. Scatterplots illustrate intercept and slope among women (in red) and men (in blue), and gray band represents conditional standard error of the mean.

were increased in more physically active individuals compared with sedentary individuals, regardless of whether the PA was done indoors or outdoors (12,16). The association between greater PA and increased serum vitamin D levels independent of sunlight exposure could be elucidated by prior findings of increased plasma concentrations of vitamin D subsequent to engagement in PA. PA has been found to alter serum nutrient concentrations that relate to vitamin D status, including alterations in serum phosphate and ionized calcium levels (41,42). This suggests that PA may directly elevate circulating vitamin D metabolites in the blood (43).

Furthermore, we observed that liver enzymes and lipid-transport proteins mediated a significant portion of the effect of PA. A 2015 meta-analysis by Shephard and Johnson (44) stated that "the effect of PA on circulating aminotransferases is unclear." In our model, which examined long-term effects and not acute changes, levels of two liver enzymes, ALT and γ-glutamyl transferase, were lower when PA was greater, and a higher level of ALT was the strongest biomarker predictor of greater fat mass in visceral regions. ALT recycles nitrogen and carbon, particularly from muscle, whereas γ-glutamyl transferase catalyzes the synthesis of glutathione and plays a role in xenobiotic detoxification. Lawlor et al. (45) similarly reported in 2005 that PA decreased levels of ALT. Liver function has previously been associated with the distribution of regional fat (46). In results consistent with those of earlier studies, we also found that changes in the lipid-transport protein apolipoprotein A and high-density lipoprotein cholesterol from PA (47,48) were partially responsible for reductions in adipose tissue.

Unexpected and discordant relationships between sunlight exposure and regional adipose distribution were detected. The results from our model are consistent with previous work from Kim et al. (49), who proposed that UV light reduces lipid synthesis in subcutaneous fat by altering the transcription of lipogenic enzymes and the production of cytokines within keratinocytes and fibroblasts. However, our model is the first to characterize a positive relationship between sunlight exposure and visceral adiposity. It is surprising that contrasting associations

TABLE 3 Objective PA model

Mechanism of action	Effect size	Percentage of total effect, %
Visceral adiposity ~ PA	$\beta_{total} = -0.234^{***}$	
Unspecified	$\beta = -0.155^{***}$	66
HDL levels	$\gamma = -0.052^{***}$	22
ApoA levels	$\gamma = 0.031^{***}$	13
Urate levels	$\gamma = -0.017^{***}$	7
ALT levels	$\gamma = -0.016^{**}$	7
Cystatin C levels	$\gamma = -0.012^{***}$	5
SHBG levels	$\gamma = -0.010^{**}$	4
Triglycerides	$\gamma = -0.004^{*}$	2
Visceral adiposity ~ sunlight exposure	$\beta_{total} = 0.032^{*}$	
Unspecified	$\beta = 0.032^{*}$	100
Subcutaneous adiposity ~ PA	$\beta_{total} = -0.367^{***}$	
Unspecified	$\beta_{a} = -0.264^{***}$	72
HDL levels	$\gamma = -0.043^{***}$	12
ApoA levels	$\gamma = 0.025^{***}$	7
SHBG levels	$\gamma = -0.022^{***}$	6
Cystatin C levels	$\gamma = -0.021^{***}$	6
Urate levels	$\gamma = -0.017^{***}$	5
ALT levels	$\gamma = -0.014^{**}$	4
CRP levels	$\gamma = -0.008^{**}$	2
Vitamin D levels	$\gamma_{b,c} = -0.007^{*}$	2
GGT levels	$\gamma = 0.004^{*}$	1
Subcutaneous adiposity ~ sunlight exposure	$\beta_{total} = -0.004^{*}$	
Vitamin D levels	$\gamma_{d,c} = -0.004^{*}$	100%

All models shown as outcome ~ exposure. Percentage of effect for mediation effects (γ) are shown with respect to total effect that they compose. If mediation effects for one total oppose each other, percentages will not necessarily equal 100. Table does not include nonsignificant γ effects. Totals do not include nonsignificant γ pathways. Separate pathways differentiated by subscript letters.
$^{***}P < 0.001$.
$^{**}P < 0.01$.
$^{*}P < 0.05$.
$^{\#}P < 0.10$.
ALT, alanine aminotransferase; ApoA, apolipoprotein A; CRP, C-reactive protein; GGT, γ-glutamyltransferase; HDL, high-density lipoprotein; PA, physical activity; SHBG, sex hormone–binding globulin.

would be detected between regions, and yet we consider Leitner et al. (50), who showed that men with lean weight had greater brown adipose tissue than men who had obesity and that regions of visceral fat housed, on average, 70% of total brown adipose tissue. Comparatively, subcutaneous fat regions may contain as little as 10% to 15% of the total brown adipose tissue mass. Nayak et al. (15) demonstrated in mouse models that adipocytes contain opsin-3 receptors, which convert white adipose tissue into brown adipose tissue in response to summer UV wavelengths. Additionally, Foss (5) discussed the hypothesis that vitamin D levels act as a central regulator of body-fat composition by keeping the body informed about the time of year. Thus, there may be separate photic and vitamin D–related effects. Given prior findings and our data-driven results, we propose that sunlight is associated with undifferentiated visceral adiposity by increasing the ratio of brown to white adipose tissue in that region. If sunlight exposure and higher levels of serum vitamin D from PA could truly enhance adaptive thermogenesis, the implications here could be significant for the obesity epidemic because brown adipose tissue is associated with leaner body composition (51).

A comparison of the subjective PA and objective PA models showed important differences. Although the subjective PA model showed that vitamin D levels were related to both visceral and subcutaneous adiposity, the objective PA model only showed an association with subcutaneous adiposity. The effect of sunlight on vitamin D levels was stronger than effects from PA in the subjective PA model. This relationship was then reversed when accelerometry was used in the objective PA model. Last, several new relationships between PA and serum biomarkers were observed with accelerometry measures.

Our study had strengths to note. We examined quantified measures of adiposity in visceral and subcutaneous compartments by DEXA rather than relying on less accurate anthropometric measures like BMI. We furthermore covaried the effect of dietary intake, which can confound associations with PA and vitamin D levels. We also compared subjective versus objective PA to determine the degree to which results did or did not agree with self-reported data, which are often inaccurate compared with objective accelerometer data. Potential mechanisms of action via vitamin D were examined in this study and differed depending on visceral adipose mass versus subcutaneous adipose mass.

Several limitations of the study should also be noted. Although serum vitamin D and PA levels were obtained longitudinally, DEXA-based body morphometry was cross-sectional. It is therefore unclear whether changes over time in PA, sunlight exposure, or vitamin D correspond to changes over time in adipose mass. Consequently, we are unable to show the order of cause-to-effect relationships among the variables in our analyses. DEXA cannot distinguish between white versus brown adipose mass, which may explain discrepant findings with sunlight exposure. Exposure to sunlight was measured subjectively in a recall questionnaire and would be more accurately measured using objective measurements, such as dosimetry and surface area of exposed skin. We furthermore acknowledge that hours spent outdoors during the summer are more so a proxy of sunlight exposure because, for instance, of time spent in shade. However, the estimates of sunlight exposure in our study give additional insight into the body mass–sunlight relationship and provide a framework for future studies among human participants to expand on our findings. The mediational effects of vitamin D were in some cases modest, despite testing for it and 24 other serum biomarkers currently present in the UK Biobank. In this analysis, it was not possible to eliminate participants who were using vitamin D supplementation. It is possible that participants may have been taking unreported occasional or habitual vitamin D supplements during the times of data collection, which may account for some vitamin D–linked variation not explained by our model.

Despite these limitations, our data provide evidence and a theoretical model for the physiological roles of PA and sunlight in the aging body and describe vitamin D's biological mechanisms of action. PA levels and sunlight exposure conjointly influenced serum vitamin D levels in our sample population. Interestingly, although our results show that sunlight exposure was associated with increased visceral adiposity, our data suggest that vitamin D may provide protection against visceral adiposity with greater exposure to sunlight. Future studies that can use objective measures of sunlight exposure may be more sensitive to the detection of the influences of exposure on the amount and distribution of adipose tissue. Additional future directions include examining

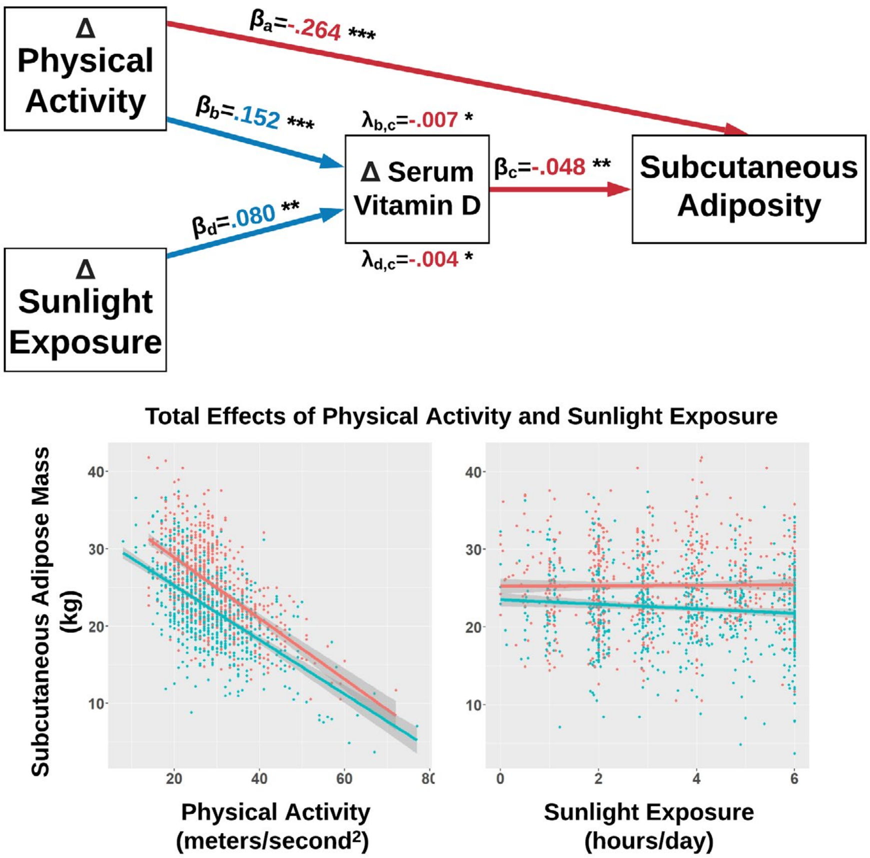


Figure 4 This snippet of the objective structural-equation model illustrates which factors explain subcutaneous adipose mass. Model examined (1) metabolic biomarkers of the mechanisms of action, which explain associations between physical activity and sunlight exposure, and (2) remaining, unspecified effects (also called "direct effects") of physical activity and sunlight exposure. Delta symbol (Δ) is defined as average level and totality of changes in that variable observed over 6 years. Standardized β reflects average effect size of each path and each path is denoted with a subscript letter. Each λ reflects the mediation effect resulting from the path analysis and is subscripted to illustrate the paths that compose it. ***$P < 0.001$, **$P < 0.010$, and *$P < 0.050$. Scatterplots illustrate intercept and slope among women (in red) and men (in blue), and gray band represents conditional standard error of the mean.

whether sunlight influences the brown-versus-white ratio of adipose tissue in both visceral and subcutaneous fat masses.

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Supporting information: Additional Supporting Information may be found in the online version of this article.

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