#### ORIGINAL ARTICLE

Clinical Trials and Investigations



# Three-dimensional optical body shape and features improve prediction of metabolic disease risk in a diverse sample of adults

Jonathan P. Bennett<sup>1,2</sup> | Yong En Liu<sup>2</sup> | Brandon K. Quon<sup>2</sup> | Nisa N. Kelly<sup>2</sup> | Lambert T. Leong<sup>2</sup> | Michael C. Wong<sup>1,2</sup> | Samantha F. Kennedy<sup>3</sup> | Dominic C. Chow<sup>4</sup> | Andrea K. Garber<sup>5</sup> | Ethan J. Weiss<sup>6</sup> | Steven B. Heymsfield<sup>3</sup> | John A. Shepherd<sup>1,2</sup>

# Correspondence

John A. Shepherd, University of Hawai'i Cancer Center, 701 Ilalo St., Honolulu, Hawaii 96813. USA

Email: johnshep@hawaii.edu

# Funding information

National Institutes of Health, Grant/Award Number: R01 DK109008

#### **Abstract**

Objective: This study examined whether body shape and composition obtained by three-dimensional optical (3DO) scanning improved the prediction of metabolic syndrome (MetS) prevalence compared with BMI and demographics.

Methods: A diverse ambulatory adult population underwent whole-body 3DO scanning, blood tests, manual anthropometrics, and blood pressure assessment in the Shape Up! Adults study. MetS prevalence was evaluated based on 2005 National Cholesterol Education Program criteria, and prediction of MetS involved logistic regression to assess (1) BMI, (2) demographics-adjusted BMI, (3) 85 3DO anthropometry and body composition measures, and (4) BMI + 3DO + demographics models. Receiver operating characteristic area under the curve (AUC) values were generated for each predictive model.

Results: A total of 501 participants (280 female) were recruited, with 87 meeting the criteria for MetS. Compared with the BMI model (AUC = 0.819), inclusion of age, sex, and race increased the AUC to 0.861, and inclusion of 3DO measures further increased the AUC to 0.917. The overall integrated discrimination improvement between the 3DO + demographics and the BMI model was 0.290 (p < 0.0001) with a net reclassification improvement of 0.214 (p < 0.0001).

Conclusions: Body shape measures from an accessible 3DO scan, adjusted for demographics, predicted MetS better than demographics and/or BMI alone. Risk classification in this population increased by 29% when using 3DO scanning.

# INTRODUCTION

Noncommunicable diseases and related conditions such as metabolic syndrome (MetS) continue to grow in prevalence, with prevalence reaching one-third of the adult population in countries such as the United States and Spain [1, 2]. Individuals diagnosed

with MetS have a five times greater risk of developing diabetes and a three times greater risk of cardiovascular disease (CVD) [3, 4]. As rates of MetS increase, staging of disease risk in children and adults can aid in identifying factors contributing to increasing disease risk [5]. Monitoring the underlying risk factors associated with changes in metabolic status also remains a cornerstone of routine clinical practice in an effort to reduce lifetime health care expenditures [6].

<sup>&</sup>lt;sup>1</sup>Graduate Program in Human Nutrition, University of Hawai'i Manoa, Honolulu, Hawaii, USA

<sup>&</sup>lt;sup>2</sup>Department of Epidemiology, University of Hawai'i Cancer Center, Honolulu, Hawaii, USA

<sup>&</sup>lt;sup>3</sup>Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana, USA

<sup>&</sup>lt;sup>4</sup>John A. Burns School of Medicine, University of Hawai'i Manoa, Honolulu, Hawaii, USA

<sup>&</sup>lt;sup>5</sup>Division of Adolescent & Young Adult Medicine, University of California, San Francisco, California, USA

<sup>&</sup>lt;sup>6</sup>Division of Cardiology, University of California School of Medicine, San Francisco, California, USA

MetS is a cluster of clinical findings that reflect overnutrition, sedentary lifestyle, and excess adiposity [7]. Specifically, MetS is defined as possessing three or more directionally unhealthy measures, including waist circumference (WC), plasma triglycerides, blood pressure (BP), fasting blood glucose, and highdensity lipoprotein (HDL) cholesterol. These clinically accessible measures are linked with underlying risk factors that promote coronary heart disease, CVD, and all-cause mortality [7, 8]. Whereas each of these measures is independently associated with a variety of adverse health outcomes, including CVD and cancers, each additional risk factor is also associated with a 24% increase in health care costs [4, 9]. Owing to the fact that metabolic dysregulation occurs over time, the ability to monitor and treat symptoms related to MetS is necessary to reduce the overall health care burden [8].

BMI, a measure of body weight for size, serves as an indirect estimation of body fatness closely tied to each metabolic risk factor. As a predictor of MetS, increasing BMI is directly related to disease risk in adults with normal weight and adults who have overweight [5]. However, BMI cannot differentiate the weight of fat mass and fat-free mass, with both muscle and fat having an important role in disease risk [10, 11]. These limitations in the predictive ability of BMI mean that those with higher muscle mass or normal weight obesity (normal BMI with low muscle and high fat mass) may be inappropriately evaluated for disease risk [12, 13]. For example, 30% of people with obesity are metabolically healthy, whereas a recent analysis of National Health and Nutrition Examination Survey (NHANES) data showed that 8.6% of adults in the normal weight category have MetS [14, 15]. BMI is also limited in that it is not representative of overall body fatness across age (in children and adults), sex, and ethnicity, meaning that specific cut points for disease-risk identification are limited [16, 17].

Body shape and body composition are increasingly being linked to obesity-related metabolic risk [18]. Body shape change, often measured via anthropometric WC or waist-hip ratio (WHR), reflects alterations in total and regional fat and muscle, with these shape factors being linked to vascular aging and risk of diabetes and mortality [19, 20]. These markers of fat and tissue distribution, with further emphasis on central obesity, can now be captured noninvasively, with much greater frequency, using three-dimensional optical (3DO) imaging scanners in individuals of all ages, provided that they are capable of standing in the required pose for the duration of the test [21, 22]. 3DO scanners are also capable of quickly capturing these anthropometrics along with additional body shape (volumes and circumferences) and composition (fat-free mass, fat mass, visceral fat mass) metrics that are also linked to MetS risk [10, 20, 23]. Ng et al. [24] showed the ability for 3DO body shape by principal components analysis to predict serum lipid and diabetes markers, whereas a recent meta-analysis highlighted the impact of markers of central fatness, such as WC being associated with higher all-cause mortality risk [25].

Given the relative affordability and convenience of 3DO scanning for body composition assessment, rapid expansion of this technology has occurred in clinical practice [23]. With its ease of use and ability to track body composition trajectories with repeated measurements, these tools have the potential to inform patient education regarding disease risk and aid medical professionals in mitigating risk. With an

## **Study Importance**

#### What is already known?

- Metabolic abnormalities can occur in individuals with normal weight, whereas some individuals who have overweight do not meet the criteria for metabolic syndrome (MetS), highlighting the limitations of using BMI for disease-risk identification.
- Body shape features, as measured through three-dimensional optical (3DO) body scans, correlate to serum lipid markers linked to MetS.

## What does this study add?

 Body shape and composition from 3DO scans improve the modeling of MetS over BMI and demographics. The prediction model successfully identifies individuals with normal weight with MetS and improves identification of individuals who have overweight without MetS.

How might these results change the direction of research or the focus of clinical practice?

 Accessible optical body shape and composition scans can improve clinical detection of MetS and aid in clinical guidance of disease risk or management.

increasing number of shape and composition features being individually linked to disease risk, it is of interest to explore whether the combination of these features can improve the prediction of MetS risk over anthropometry or demographics alone. However, we are unaware of any studies looking at the ability for 3DO measures of body shape and body composition to improve the prediction of MetS. The current study aims to explore the ability for 3DO, without the need for manual measurements or the use of more expensive clinical measurement methods, to improve MetS identification in comparison with BMI in routine clinical practice. We hypothesize that the combination of measures obtained from a 3DO scan can improve the prediction of MetS over BMI or anthropometry.

# **METHODS**

#### Overview

We performed a cross-sectional analysis to determine how body shape and body composition, as reported by 3DO, predicted MetS status in a healthy and diverse cohort of adults. Details of the entire protocol can be found in Ng et al. [24], and they are briefly described in this paper. Participants received criterion measures for MetS as

well as exploratory measures using a commercial 3DO system. Models with and without the 3DO measures were created to explore the relationship between the >80 circumferences, regional and whole-body volumes, and body composition variables and MetS. To assess the impact of body shape and composition variables on disease risk, models were compared using logistic regression and areas under the receiver operating characteristic (ROC) curves.

## **Participants**

Participants were recruited as part of the Shape Up! Adults cohort at University of Hawaii Cancer Center in Honolulu, University of California, San Francisco (UCSF), and Pennington Biomedical Research Center in Baton Rouge, Louisiana, between October 2016 and January 2020. Shape Up! Adults (NIH R01 DK109008, ClinicalTrials.gov identifier NCT03637855) is a cross-sectional sample of healthy adults with the goal to represent the breadth of body shape in the US population. The recruitment goals were for equal cells by age (18-40 years, 40-60 years, >60 years), ethnicity, and BMI (weight in kilograms divided by height in meters squared; <20, 20-24.9, 25-30, >30). Participants were excluded if they could not stand for 2 minutes without aid or if they had significant body shape-altering procedures (e.g., liposuction, amputations, breast augmentation or reduction). Female participants were also excluded if pregnant or breastfeeding. The study protocols were approved by institutional review boards at all sites, and participants provided written informed consent.

# **Anthropometric measurements**

Anthropometry was measured using the NHANES protocol [26]. Height and mass to the nearest 0.1 cm and 0.1 kg was measured

using a stadiometer and digital scale (Seca GmbH). Flexible measuring tapes were used to collect WC. WC measurements were taken using marks placed on the top of the iliac crest as reference while the participant stood up straight with their arms crossed. Measurements were recorded in triplicate to the nearest 0.1 cm and averaged. Although WC was measured and used in the MetS diagnosis, the aim was to explore the use of variables measured via 3DO, including 3DO WC, to improve the prediction of MetS. This allowed for the investigation of this simplified approach of 3DO and readily available demographic data, although we also explored the prediction of MetS using demographics and anthropometric WC (data not shown).

# **Blood measurements**

Blood samples were collected from participants after an overnight fast. Biochemical analysis was performed at Pennington Biomedical Research Center. Measurements included serum triglycerides, fasting glucose, and HDL cholesterol. Systolic and diastolic BP were measured by a certified technologist in a seated position after 5-minute rest.

#### 3DO scans

3DO scans were obtained using a commercial scanner comprised of a single depth camera incorporated into a sensor tower that stands approximately 6 feet in front of a rotating platform (S100 Body Scanner, Styku LLC, software version 4.1, using "Styku Advanced Phoenix Model for Body Composition" setting). Participants wore form-fitting shorts (female participants wore a sports bra) and a swim cap and stood on the turntable with legs separated, arms away from the body at a 45-degree angle, and hands closed into fists as recommended by the manufacturer. Each scan

**TABLE 1** Participant characteristics (n = 501 [280 female])

					Total (n = 501)		
Variable	Male ( $n=221$ ), mean (SD)		Female ( $n=280$ ), mean (SD)		Mean (SD)	Min.	Max.
Age (y)	45.0 (16.6	5)	46.7 (16.2)		46.2 (16.5)	18.0	89.0
Height (cm)	175.3 (8.0)		162.7 (6.4)		167.7 (10.0)	144.1	202.1
Weight (kg)	86.0 (21.0	0)	73.5 (21.6)		77.8 (22.2)	35.4	173.5
BMI (kg/m <sup>2</sup> )	27.9 (6.2)		27.8 (8.0)		27.5 (7.0)	14.2	52.6
3DO PBF (%)	20.8 (6.5)		31.0 (7.9)		26.2 (8.9)	2.0	48.0
Ethnicity	Count	MetS+ <sup>a</sup>	Count	MetS+ <sup>a</sup>	Count	%	MetS+ <sup>a</sup>
Asian	46	6	65	16	111	22.2	22
NH Black	63	8	68	5	131	26.1	13
Hispanic	30	2	39	5	69	13.8	7
NHOPI	17	6	27	10	44	8.8	16
NH White	65	11	81	18	146	29.1	29

Note: Percentage values are rounded.

Abbreviations: 3DO, three-dimensional optical; PBF, percentage body fat; MetS, metabolic syndrome; NH, non-Hispanic; NHOPI, native Hawaiian or Pacific Islander.

<sup>&</sup>lt;sup>a</sup>MetS positive (+) using National Cholesterol Education Program Adult Treatment Panel III criteria.

TABLE 2 Prediction equations derived using logistic regression to predict MetS

Model	Name	Test variables	AUC	Equation <sup>a</sup>
1	BMI	BMI	0.819	$-5.768 + 0.143 \times BMI$
2	BMI + demographics	BMI, age, race, sex	0.861	$-9.643 + 0.177 \times ^*\text{BMI} + 0.059 \times \text{Age} - 0.059 \times \text{NH}$ Black $+1.159 \times \text{NHOPI}$
3	3DO	3DO	0.889	$-12.583+0.073\times3\text{DO}$ Body Fat Percentage $+$ 0.009 $\times$ 3DO Chest Volume $-$ 0.046 $\times$ 3DO Left Arm Area $+$ 0.025 $\times$ 3DO Left Arm Volume $+$ 14.516 $\times$ 3DO WHR
4	BMI + demographics + 3DO	BMI, age, race, sex, 3DO	0.917	$-17.328 + 0.192 \times \text{BMI} + 0.033 \times \\ \text{Age} + 1.569*\text{Sex} - 1.131 \times \text{NH Black} + 0.986 \times \\ \text{NHOPI} - 1.061 \times 3\text{DO Bone Mass Percentage} - 0.015 \\ \times 3\text{DO Left Calf Volume} - 0.157 \times 3\text{DO WC} + 19.887 \\ \times 3\text{DO WHR}$

Note: Where sex (male = 0, female = 1); NH Black (all other = 0, NH Black = 1); NHOPI (all other = 0, NHOPI = 1). Abbreviations: 3DO, three-dimensional optical; MetS, metabolic syndrome; NH, non-Hispanic; NHOPI, native Hawaiian or Pacific Islander; WC, waist circumference; WHR, waist-hip ratio.

**TABLE 3** Variables included in BMI + demographics + 3DO MetS prediction model (model 4) compared with BMI models (models 1 and 2)

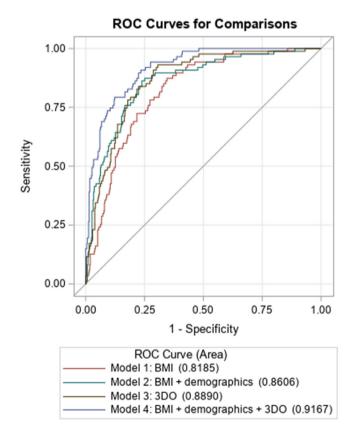
	AUC	AUC improvement
BMI (model 1)	0.819	
BMI + demographics (model 2)		0.042
3DO WHR		0.022
3DO bone mass percentage		0.006
3DO WC		0.006
3DO calf volume (left)		0.004
BMI + demographics + 3DO (model 4)	0.917	

Abbreviations: 3DO, three-dimensional optical; AUC, area under the curve; WC, waist circumference; WHR, waist-hip ratio.

took 30 to 40 seconds to complete. The reports include 65 whole-body and segmental surface areas, volumes, and circumferences, along with three circumference ratios. Seventeen body composition estimates are also derived from these measures using proprietary algorithms built into the system software. Bennett et al. [23] described the accuracy (Lin's concordance correlation coefficient, CCC) and precision (coefficient of variation, CV) of fat and fat-free mass (CCC > 0.95; CV < 1.94%), whole-body volume (CCC = 0.99; CV = 1.45%), and circumference measurements (CCC > 0.97; CV < 0.63%) in a sample of adults (age 18-89 years) stratified by BMI and ethnicity [23]. With the 3DO shown to be accurate compared with criterion measures for body composition and anthropometry, we aimed to use the 3DO variables exclusively as a simplified assessment technique to improve the prediction of MetS.

# MetS

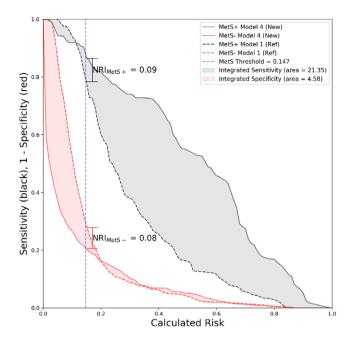
MetS was defined using the 2005 National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines as having



**FIGURE 1** Stepwise receiver operating characteristic (ROC) curves for MetS prediction. 3DO, three-dimensional optical scan variables [Color figure can be viewed at wileyonlinelibrary.com]

 $\geq$ 3 of the following: high WC (as measured by manual anthropometry;  $\geq$ 102 cm in men,  $\geq$ 88 cm in women), elevated triglycerides ( $\geq$ 150 mg/dL), elevated BP ( $\geq$ 130 mm Hg systolic or  $\geq$ 85 mm Hg diastolic), elevated fasting glucose ( $\geq$ 100 mg/dL), and/or reduced HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women) [8]. For individuals with missing data points, presence or absence of MetS was defined if at least three of the available variables were met or if they were less

<sup>&</sup>lt;sup>a</sup>Probability of MetS calculated using =  $\frac{1}{1 + \exp^{-(equation)}}$ 



**FIGURE 2** IDI and NRI for MetS prediction when comparing model 4 with model 1. The integrated sensitivity (IS), black shaded region, indicates the change in sensitivity model 4 compared with model 1 across all risk thresholds. The integrated 1-specificity (IP), red shaded region, indicates the change in specificity with the addition of the 3DO model. Using a threshold of 0.147, model 4 was able to identify 9% more MetS positive individuals than model 1. The IDI is the sum of the IS and IP and the positive IDI indicates that predictive models benefit from the addition of 3DO. NRI are presented for prediction of MetS (black) and non-events (red). 3DO, three-dimensional optical; IDI, integrated discrimination improvement; MetS, metabolic syndrome; NRI, net reclassification index [Color figure can be viewed at wileyonlinelibrary.com]

than the criteria for diagnosis, respectively. Individuals with four available measures, with two variables above and two variables below the cut points, were excluded from the data set because of insufficient data to make an accurate diagnosis.

# Statistical methods

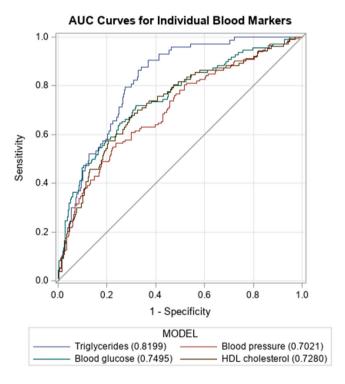
Logistic regression was performed to create the following models to predict MetS: BMI (model 1), BMI + demographics (age + sex + race; model 2), 3DO body shape variables (model 3), and model 2 + model 3 (BMI + demographics + 3DO; model 4). Selection of 3DO variables in model 3 and model 4 was performed using step forward logistic regression (proc LOGISTIC with stepwise option, SAS Institute Inc.). Variables were selected if they were significantly associated to MetS (p < 0.10) and kept in the final model if their significance was p < 0.05 to ensure the optimum fit while limiting risk of model overfitting. An ROC curve with its associated area under the curve (AUC) and concordance index measures were generated for each model. To determine the appropriate cut point, the highest Youden index (sensitivity + specificity – 1) was calculated [27]. Integrated discrimination improvement (IDI) was used to visualize the separate improvements in sensitivity and specificity

A RELEA Confusion matrix of prediction model using optimal

**TABLE 4** Confusion matrix of prediction model using optimal cutoff by minimizing difference between sensitivity and specificity

	MetS +	MetS-	
Predicted +	78	65	
Predicted –	9	349	
Total	87	414	501

Note: MetS+ is diagnosed as MetS positive by National Cholesterol Education Program Adult Treatment Panel III (criterion measure). Abbreviation: MetS, metabolic syndrome.



**FIGURE 3** Stepwise receiver operating characteristic (ROC) curves for individual blood markers. AUC, area under the curve [Color figure can be viewed at wileyonlinelibrary.com]

between model 1 and model 4 [28]. Net reclassification index (NRI) was computed with 1,000 rounds of bootstrapping for specific cut points in the prediction probability [28]. The model 4 MetS prediction equation was used to generate AUC values for each of the individual MetS blood parameter cutoffs. Statistical analysis was performed using SAS version 9.4 (SAS Institute) and Scitkit Learn (Python Software 3.10).

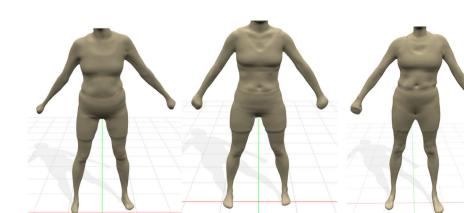
#### **RESULTS**

A total of 619 adults were available for this study. Of this sample, 3DO scans were missing for 105 participants (owing to the later inclusion of the 3DO scanner into the study protocol), and, of the remaining participants, 12 did not have serum markers available to make a diagnosis. See the Consolidated Standards of Reporting Trials

(CONSORT; Supporting Information Figure S1) flowchart and Strengthening the Reporting of Observational studies in Epidemiology (STROBE; Supporting Information Figure S2) checklist for further details of exclusions. After these exclusions, 501 participants had 3DO scans and available parameters. Of those, 87 (17.4% of the total population) met the criteria for MetS. Individuals with MetS tended to be older and female and to have a higher BMI, WC, and percentage

body fat (all p < 0.05). Summary characteristics and participant counts by ethnicity are presented in Table 1.

Each model is presented in Table 2, which shows the progressive AUC improvement with each model. A total of eight variables (four 3DO variables) were included in model 4. The contribution of each variable to the AUC is shown in Table 3. Overall, WHR (AUC improvement of 0.022) showed the greatest improvement.



Height: 150 cm Weight: 44.2 kg Age: 49

BMI: 19.7 kg/m<sup>2</sup> 3DO PBF: 30.6% Ethnicity: Asian

MetS: +

Height: 158 cm Weight: 52.0 kg

Age: 63

BMI: 20.7 kg/m<sup>2</sup> 3DO PBF: 21.6% Ethnicity: Asian

MetS: -

Height: 175 cm Weight: 74.2 kg

Age: 57

BMI: 24.3 kg/m<sup>2</sup> 3DO PBF: 24.1% Ethnicity: NH Black

MetS: +

Height: 169 cm Weight: 69.0 kg

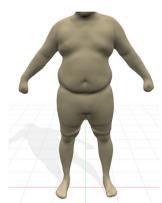
Age: 47

BMI: 24.2 kg/m<sup>2</sup> 3DO PBF: 27.4% Ethnicity: NH Black

MetS: -









Height: 159 cm Weight: 72.5 kg

Age: 49

BMI: 28.6 kg/m<sup>2</sup> 3DO PBF: 35.7% Ethnicity: Asian

MetS: +

Height: 160 cm Weight: 73.5 kg

Age: 57

BMI: 28.9 kg/m<sup>2</sup> 3DO PBF: 27.8% Ethnicity: Asian

MetS: -

Height: 173 cm Weight: 119.5 kg

Age: 29

BMI: 39.9 kg/m<sup>2</sup> 3DO PBF: 30.2% Ethnicity: NHOPI

MetS: +

Height: 185 cm Weight: 116.0 kg

Age: 55

BMI: 33.8 kg/m<sup>2</sup> 3DO PBF: 25.2% Ethnicity: NH Black

MetS: -

FIGURE 4 Sample images of MetS positive (+) versus negative (-) participants. Example 1: similar BMI (normal), higher PBF, WC, and WHR in MetS+. Example 2: same BMI (normal), higher PBF in MetS- but greater WC and WHR in MetS+. Example 3: same BMI (overweight), different PBF with greater WC and WHR in MetS+. Example 4: same WC, greater WHR in MetS+. MetS, metabolic syndrome; PBF, percentage body fat; WC, waist circumference; WHR, waist-hip ratio; 3DO, three-dimensional optical; NH, non-Hispanic; NHOPI, native Hawaiian or Pacific Islander [Color figure can be viewed at wileyonlinelibrary.com]

The ROC curves for each model are presented in Figure 1. We found a progressive improvement in the AUC values from model 1 (AUC = 0.819, 95% CI: 0.775-0.862) to model 4 (AUC = 0.917, 95% CI: 0.889-0.945). The combination of BMI and demographic variables with 3DO scans (model 4) made for the best model with high discriminatory power, as shown in Table 2.

The results of the IDI curve comparing the final BMI + demographics + 3DO model (model 4) with the BMI-only model (model 1) are presented in Figure 2. Adding the additional variables used in model 4 resulted in an average predicted probability of MetS increase of 71.8% and a 31.7% decrease in average predicted probability of nonevents. Overall, the model increased the IDI by 26.0% (95% CI: 23.5%-34.5%, p < 0.0001) and NRI by 19.4% (95% CI: 2.8%-40.0%, p < 0.0001).

The optimal cutoff used to derive a confusion matrix of results, presented in Table 4, showed that 78 (89.7%) of the 87 positive cases (MetS+) were correctly identified. Of the negative cases (MetS-), 349 (84.3%) of the 414 cases were properly classified. Importantly, this cutoff correctly identified all seven normal BMI MetS+ participants. Model 4 also improved prediction of MetS compared with a demographics + anthropometric WC (AUC = 0.888, 95% CI: 0.804-0.906; data not shown). Furthermore, the demographics + anthropometric WC model successfully predicted only two of the seven normal BMI MetS+ participants and failed to capture eleven of the high BMI MetS- participants, highlighting the significance of the 3DO system over a simplified WC assessment to identify disease risk.

Using the prediction equation generated by model 4, we examined the relationship to each individual blood parameter cutoff used in MetS diagnosis, presented in Figure 3. Generated AUC values for each blood parameter ranged from 0.702 for BP to 0.820 for blood triglycerides, ranging from acceptable to excellent [29]. In addition, we examined the relationship of model 4 to each individual blood parameter used in MetS diagnosis, presented in Supporting Information Table S1. We also included a correlation matrix for each 3DO measurement variable and MetS blood parameter in Supporting Information Figure S3.

In Figure 4, we matched MetS+ and MetS- participants with similar characteristics to highlight how shape and composition more accurately reflected disease risk and diagnosis.

# **DISCUSSION**

The purpose of the present study was to evaluate potential improvements in MetS prediction by incorporating demographic, body shape, and body composition parameters, easily obtained using clinically accessible 3DO technology. We found that our model resulted in a significant improvement in the prediction of MetS, further highlighting the importance of body shape and composition in disease prediction. Furthermore, we confirmed our hypothesis that the combination of measures obtained from a 3DO scan provided a better diagnostic compared with simpler models or individual measurements.

A meta-analysis performed by Lee [30] showed that obesity was associated with a 62% greater MetS risk (risk ratio = 1.62, 95% CI: 1.32-1.98; p < 0.01), regardless of cardiovascular fitness level [30]. Body shape, as assessed by WC (a surrogate for abdominal obesity) and trunk to hip volume ratio (a surrogate for regional adiposity), has been shown to be an important metric for understanding the distribution of adipose tissue related to MetS disease risk [20, 25, 31]. The results of our study showed that both body composition and body shape parameters can provide valuable information regarding disease risk, WHR, an indirect marker of both abdominal and regional obesity. better predicted MetS risk compared with WC, which is consistent with findings of other studies that have looked at body shape and MetS risk [32-35]. Whereas WC is considered to be a strong predictor of MetS risk. WHR may better reflect adipose tissue storage in the gluteal subcutaneous region, which may be protective of MetS risk [34]. Our study showed that WC had an inverse association to MetS risk. Given the larger impact of the WHR on prediction risk, we believe the negative association observed may be a correction to address individuals with a high BMI who do not have MetS and, therefore, that it further highlights the benefits of body shape over BMI or WC assessment [35].

Body composition has a clear association with MetS risk [10, 14]. The 3DO model found two body composition variables to be predictive of MetS risk. Calf circumference, an indirect measure of muscle mass that is less affected by fat deposition, was associated with MetS risk using NHANES data sets [33]. We believe that the average calf volume reflects the leg musculature and, therefore, serves as a protective factor for MetS risk. Whereas bone mass is linked to MetS, the causal direction between these factors remains unclear [36]. Therefore, while low bone mass may be an independent predictor of MetS risk, a low proportion of body weight as bone mass may also reflect increased adiposity, a clear predictor of MetS risk [4]. This finding was supported by the strong positive correlation of bone mass percentage to lean mass percentage and strong negative correlation to body fat percentage (Supporting Information Figure S3).

Previous studies have explored the use of body composition by bioimpedance for the prediction of MetS; however, this method is unable to derive body shape measurements that reflect adipose tissue distribution and predict disease risk [32, 37]. Researchers have explored the utility of body shape using dual-energy x-ray absorptiometry; however, this technology is not accessible or cost-effective to be used for routine diagnostic purposes [20]. 3DO measures have added benefits for clinical practice by reducing measurement bias associated with manual anthropometry and providing rapid access to body composition and shape data. Given that these measures are low cost, easily accessible, and associated with disease risk, these findings support the use of 3DO measures as a novel and feasible approach for routine clinical risk assessment.

Body shape measures of WC have long been linked to visceral adiposity; WC has been validated using 3DO scanners previously [21, 22, 24]. In relation to blood, Jaeschke et al. [38] found that 3DO measures of WC were significantly associated with MetS blood parameters

[38]. Ng et al. [24] showed the relationship of principal components of 3DO scans and their individual relationships to blood metabolites [24]. Whereas these studies examined the relationship of body shape to individual blood parameters, our study was the first, to our knowledge, to examine disease risk by 3DO. The results showed that the final body shape and composition model as derived from 3DO (model 4) had a significant (all p < 0.05) relationship to MetS risk, as well as each MetS blood parameter, showing that 3DO is a useful metric to reflect adipose distribution and its relationship to blood markers and overall disease risk.

Because parameters of MetS can occur independently, it is important to develop metrics that are useful to evaluate the risk of disease in individuals with high weight as well as individuals with normal weight. Our study found that all seven individuals (4.7% of the normal-weight population, slightly below the 8.6% observed in the NHANES sample) with a normal BMI were properly identified as MetS+ using the derived model. Similarly, 201 of the 222 (90.5%) participants defined by BMI as possessing excess weight were correctly classified as MetS- using the final 3DO model. Owing to the fact that metabolic dysregulation develops over time, the ability to monitor progress is essential for guiding education and awareness as a strategy toward disease prevention [39]. As seen in the sample participant images, use of both body shape and composition can improve MetS modeling when compared between individuals. Furthermore, these images provide clinicians with easily accessible body shape images that can be used to educate patients on their current body composition, whereas tracking this information over time can serve as a potent indicator of change in disease risk for both the patient and clinician. Use of this information and the visuals provided by the 3DO system will allow medical professionals to monitor change over time, an essential aspect of monitoring disease risk [39].

A strength of this study is that it used a diverse sample of adults of varying age, ethnicity, and BMI. The range of BMI values included is significant, as our sample included a strong sample of individuals with underweight, normal weight, and overweight/obesity. We also show the importance of age and gender adjustment and their importance in MetS diagnosis [40]. Owing to the relatively small sample of participants with MetS (n = 87), we were unable to separate training and test sets to examine the accuracy of our prediction model. That said, our sample (n = 501) was well above the amount required to detect differences between AUC values with a 95% probability (n = 58) [41]. Given the cross-sectional nature of the study, we were unable to examine the changes in body shape and their association with change in MetS risk, nor was our model able to tease out the impact of factors such as vitamin D and exercise on MetS risk [42, 43]. The review by Lee [30] shows the importance of cardiovascular fitness in the prevention of MetS [30]. However, because these individuals met the NCEP ATP III criteria for MetS, we believe the application of these findings remain, regardless of physical activity level.

It should be noted that, whereas 3DO systems are increasingly being used in clinical and field settings, their adoption in clinical practice is not universal, and access to 3DO technology may be limited in certain settings [23]. Although the WC  $_{\rm H}$  anthropometric model increased the AUC compared with model 1, the proper identification

of 16 individuals of the 3DO model 4 compared to a WC assessment further highlights the importance of other body shape variables as significant predictors of MetS disease risk. Given the increased reliability from the automated 3DO system, we believe the advantages noted earlier warrant the use of these systems when available. That said, we also included the BMI + demographics model for clinicians to use when 3DO scanning is unavailable.

Finally, the cutoffs for MetS continue to be debated based on a variety of factors, including body size, race/ethnicity, and cutoffs selected. For example, male patients can develop multiple metabolic risk factors when WC is only marginally elevated (94-102 cm) [8]. Given the criteria used by the NCEP ATP III, which focuses on MetS instead of focusing on obesity or insulin resistance being the primary cause of CVD, as well as the common use of these criteria, we believe this to be a strength of our study in our target population. That said. without including population-specific cut points such as those included in the International Diabetes Foundation criteria, the generalizability of these results to non-American populations is limited [44]. Further work should explore the predictive ability of these models in different populations to identify where the proposed model may be improved or identify limitations in the model based on the issues related to MetS risk discussed earlier. This work could also be expanded to youth populations in future works, as the rapid change in body size, shape, and composition may pose valuable information regarding changes to disease risk over time. Future studies should also look at the ability for 3DO to track body composition and shape changes longitudinally and their associations to MetS risk [45]. Prospective studies regarding MetS prediction over time, along with a greater understanding of how the information provided to patients informs clinical decision-making using this technology, will further improve the application of this technology as a tool for disease prevention and treatment. Monitoring the role of diet and exercise in the progression of MetS disease risk may also improve the application of 3DO technology in clinical practice.

## CONCLUSION

Our results confirm the findings of previous studies examining the link between body shape and composition with MetS disease risk. By building a prediction model with better predictive power, we show the usefulness of a 3DO scanner for routine clinical practice in the assessment of MetS disease risk that is accessible, noninvasive, and cost-effective O

# **AUTHOR CONTRIBUTIONS**

JPB: conceptualization, methodology, formal analysis, and writing (original draft preparation); YEL: resources, writing (review and editing), and investigation; BKQ: data curation; NNK: resources, writing (review and editing), and project administration; MCW: resources and writing (review and editing); LTL: resources and writing (review and editing); SFK: writing (review and editing); DCC: writing (review and editing); AKG: writing (review and editing);

EJW: writing (review and editing); SBH: conceptualization, writing (review and editing), and funding acquisition; JAS: conceptualization, methodology, supervision, writing (review and editing), and funding acquisition.

#### **ACKNOWLEDGMENTS**

The researchers are eternally grateful to the study participants for their participation in the Shape Up! Adults study. Deidentified data are available from the Shape Up! Studies for researchers who meet the criteria for access to confidential data. For details and to request an application, please contact Nisa Kelly, nnkelly@hawaii.edu, or visit www.shapeup.shepherdresearchlab.org.

#### CONFLICT OF INTEREST

The authors declared no conflict of interest.

#### ORCID

Jonathan P. Bennett https://orcid.org/0000-0003-1033-2343
Michael C. Wong https://orcid.org/0000-0003-2392-9253
Ethan J. Weiss https://orcid.org/0000-0001-9936-5816
Steven B. Heymsfield https://orcid.org/0000-0003-1127-9425
John A. Shepherd https://orcid.org/0000-0003-2280-2541

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Bennett JP, Liu YE, Quon BK, et al. Three-dimensional optical body shape and features improve prediction of metabolic disease risk in a diverse sample of adults. *Obesity (Silver Spring)*. 2022;30(8):1589-1598. doi:10.1002/oby.23470