NAS roundtable
BMI and Beyond – Considering Context in Measuring Obesity

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Clinical Context: How Can We Measure a Disease in Order To Track its Improvement?

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Disclosures
Donna Ryan, MD

- *Advisor/consultant*: Altimmune, Amgen, Biohaven, Calibrate, Carmot, Epitomee, Gila, Lilly, Novo Nordisk, Scientific Intake, Structure Therapeutics, Wondr Health, Xeno Bioscience, YSOPIA, Zealand
- *Speaker's Bureau:* Novo Nordisk
- *Stock Options:* Epitomee, Calibrate, Roman, Scientific Intake
- *Research:* SELECT Steering Committee (Novo Nordisk)
- *DSMB:* setmelanotide (2); tirzepatide (1)

When did obesity become a disease? (in the US)

20th Century

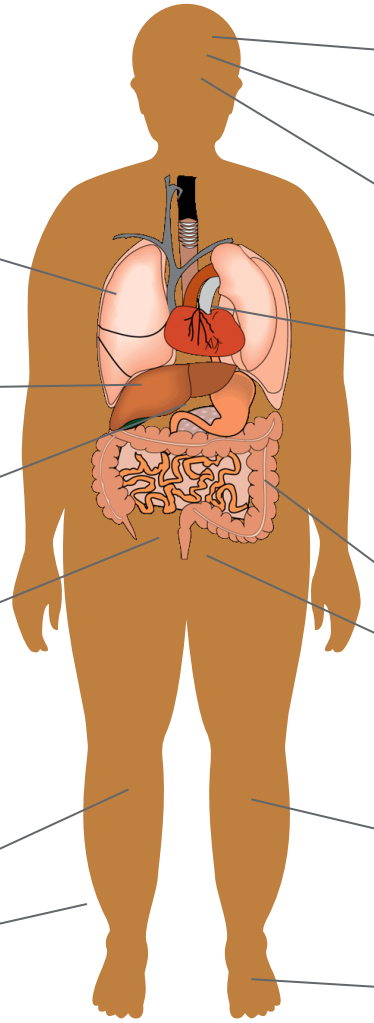
- US HCFA and CMS *Coverage Issues Manual* statement "Obesity is not a disease" was only removed in 2004

21st Century

- NIH Guidelines (1998), Obesity Society White Paper (2008), AACE position Statement (2012) declare obesity a chronic disease
- IRS allows obesity treatment deductions (2002), CMS covers bariatric surgery (2006)
- AMA resolution "Obesity is a disease." The tipping point - 2013

Kyle TK et al. Endocrinol Metab Clin North Am. 2016 September; 45(3): 511–520.
HCFA Healthcare Financing Administration; CMS Center for Medicare & Medicaid Services; NIH National Institutes of Health; AACE American Association of Clinical Endocrinologists; IRS Internal Revenue Service

If obesity is a disease, what is the pathogenesis?



Pulmonary disease
Abnormal function
Obstructive sleep apnea
Hypoventilation syndrome

Nonalcoholic fatty liver disease
Steatosis
Steatohepatitis
Cirrhosis

Gall bladder disease

Gynecologic abnormalities
Abnormal menses
Infertility
Polycystic ovarian syndrome
Urinary incontinence

Osteoarthritis

Skin

Idiopathic intracranial hypertension

Stroke

Cataracts

Coronary heart disease

Diabetes

Dyslipidemia

Hypertension

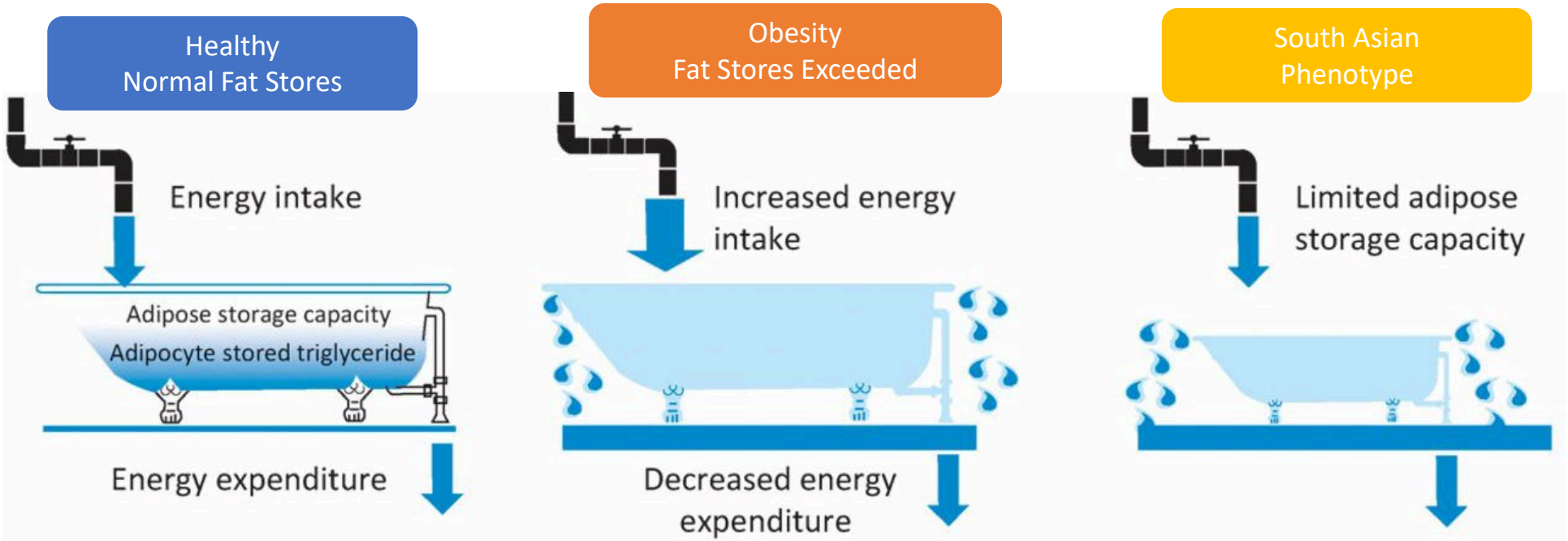
Cancer
Breast, uterus, cervix, colon, esophagus, pancreas, kidney, prostate

Phlebitis
Venous stasis

Gout

Adapted from European Practical and Patient-Centred Guidelines for Adult Obesity Management in Primary Care. January 2019. Obesity Facts 12(1):40-66

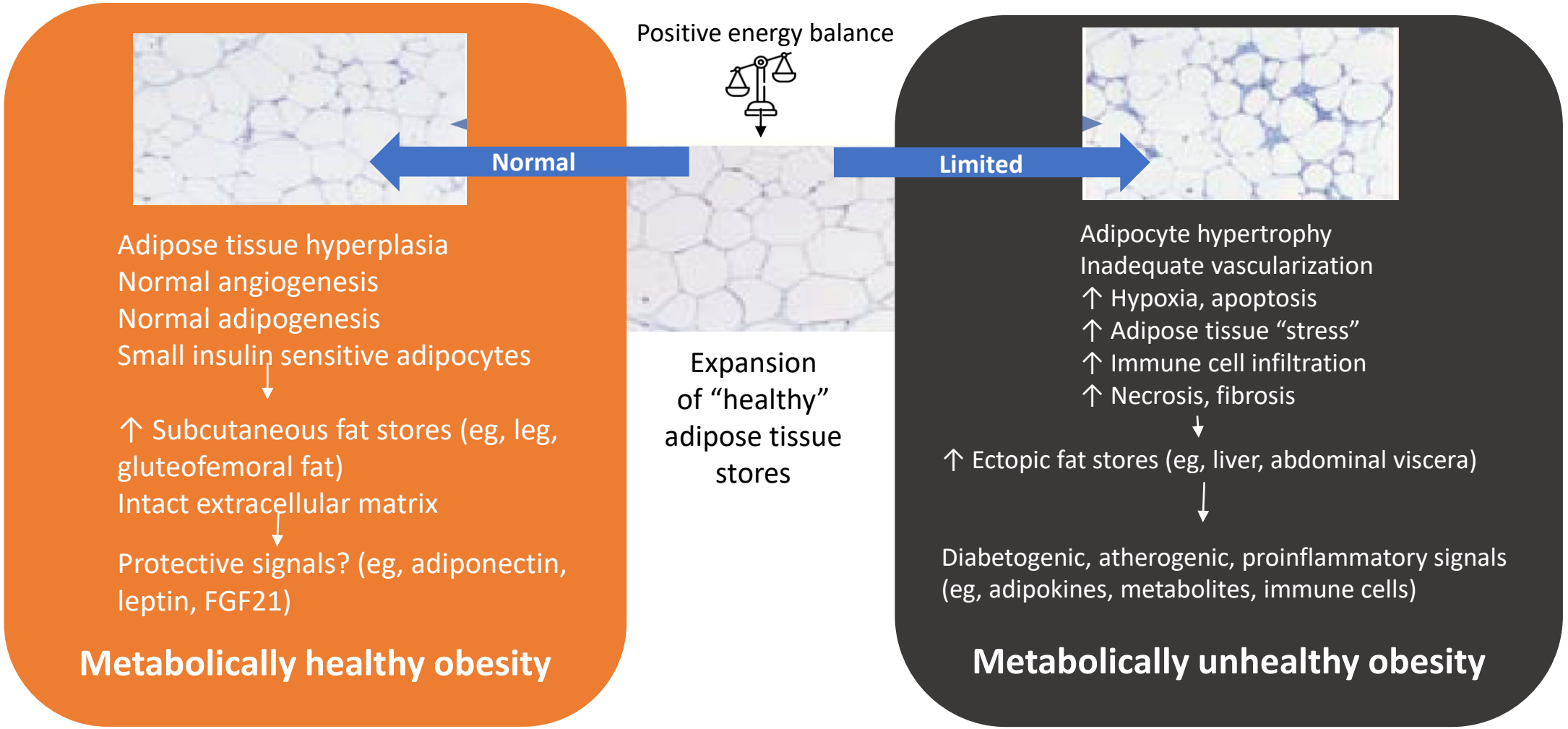
The Soggy Bathroom Carpet Model of Over-Nutrition–Related Metabolic Disease[1]



- When the ability to store healthy fat is exceeded by a continuous positive energy balance, ectopic and abnormal fat stores give rise to metabolic disease
- The ability to store fat in healthy depots is determined by genetics, hormones, and other factors
- Some individuals, such as those of South Asian descent, have little capacity to store excess fat in healthy depots and develop ectopic and abnormal fat stores at lower BMI levels

1. O'Rahilly S. *Diabetes*. 2021;70:29-38.

When the body exceeds healthy adipose tissue stores, excess abnormal body fat occurs[1]

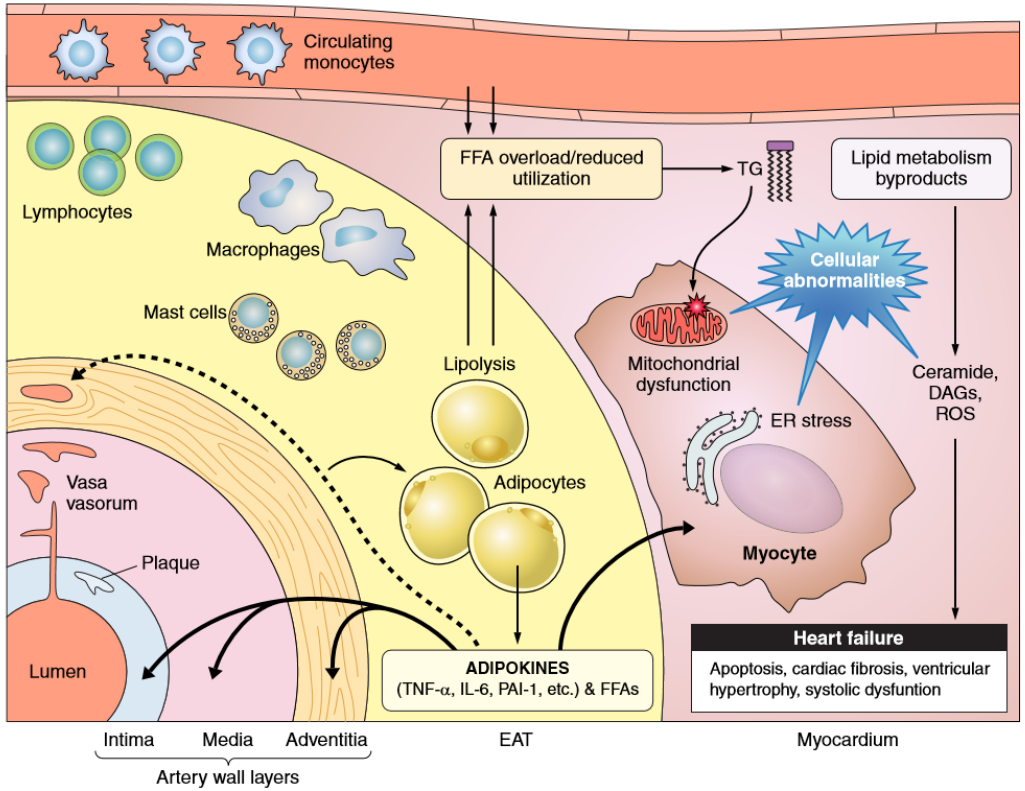


1. Blüher M. *Endocr Rev*. 2020;41:405-420.

Location, Location, Location

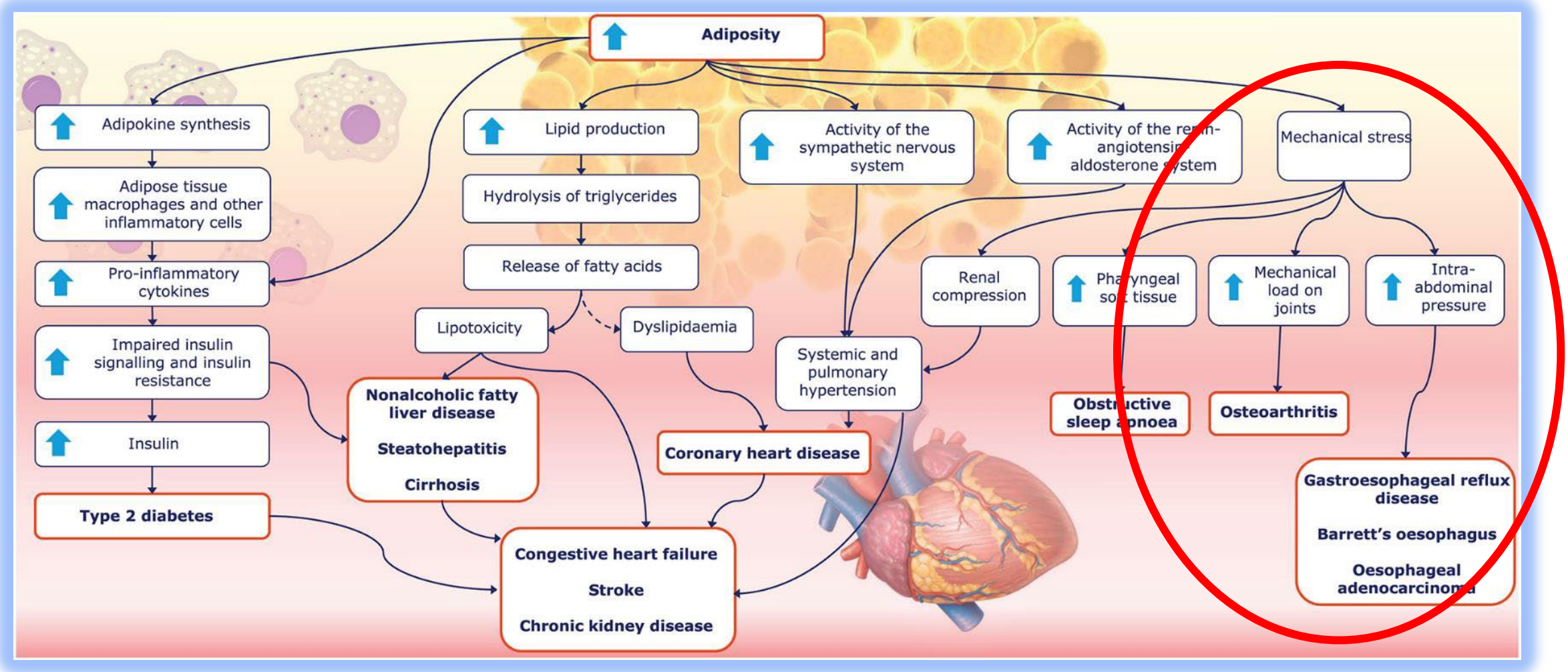
- Visceral and ectopic (muscle, liver, pancreas, epicardial) adipose tissue produces more pro-inflammatory and pro-thrombotic cytokines.
- Visceral and ectopic fat are mobilized first with weight loss.

Role of epicardial adipose tissue in cardiovascular risk



Cherian S et al. *Am J Physiol Endocrinol Metab*. 2012;303:E937-E949.

Growing Understanding of How Excess Abnormal Fat Drives Disease



Heymsfield SB & Wadden T. NEJM 2017; Adapted in Wilding, JPH, Jacob, S. Obesity Reviews. 2021

The Way Up and the Way Down…

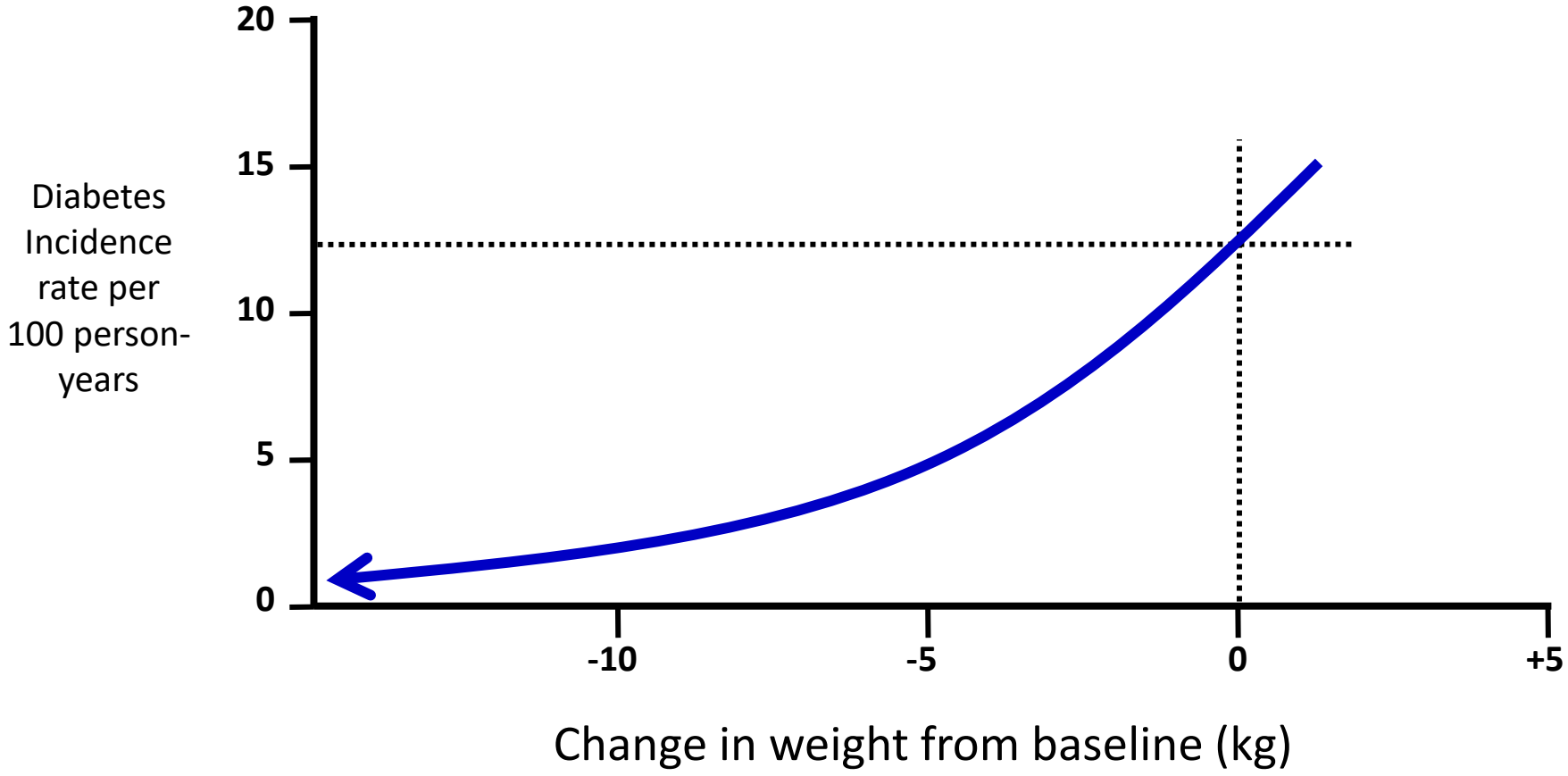
Image Open Access.

The Good News

- It is not necessary to achieve a “normal” body weight to achieve health benefits.
- For BMI categories >30 kg/m^2 the same percentage weight loss produces the same improvements in health indices. (time limits me showing the evidence)
- Moderate weight loss is more achievable and more sustainable.
- Ectopic and visceral body fat is mobilized preferentially during weight loss, so modest and moderate weight loss brings health benefits.
- More proportional weight loss may be needed for some complications. (time limits me showing the evidence)

The DPP Experience: Every Kilogram Lost Reduced Risk of Diabetes by 16%

After 10 Kg (~10%) weight loss, there was no additional benefit in diabetes prevention in persons with TGY.



Adapted from Hamman et al., *Diabetes Care (2006)* 29: 2102-2107.

What Happens In the Clinic for Obesity Diagnosis?

- BMI is a Core Measure – reported at every visit

For Europids:
Overweight BMI >25 kg/m^2
Obesity BMI >30 kg/m^2
Waist circumference 35 in for women and 40 in for men
Jensen MD, et al. Guidelines (2013) *Obesity.* 2014;22(S2):S1-S410.

For Asians:
Overweight BMI >23 kg/m^2
Obesity BMI >25 kg/m^2
Waist circumference 31.5 in for women and 35 in for men
WHO/IASO/IOTF, 2000.
(http://www.idi.org.au/obesity_report.htm)

- ICD-10 Codes for billing

CDC estimates of BMI >30 kg/m^2 41.5%
Medicare claims with obesity diagnosis 21%
N Engl J Med 2023; 388:961-963

Codes
- E66 Overweight and obesity
  - E66.0 Obesity due to excess calories
    - E66.01 Morbid (severe) obesity due to excess calories
    - E66.09 Other obesity due to excess calories
  - E66.1 Drug-induced obesity
  - E66.2 Morbid (severe) obesity with alveolar hypoventilation
  - E66.3 Overweight
  - E66.8 Other obesity
  - E66.9 Obesity, unspecified

BODY SIZE ≠ BODY HEALTH

Valid Criticism of BMI for Clinical Diagnosis of Obesity
Body Size (BMI) vs Excess Abnormal Body Fat

Metabolically Healthy Obesity

- BMI >30 kg/m^2
- Normal waist circumference
- Normal glycemic and cardiovascular risk factors
- Younger; tends to destabilize with aging

Normal Weight Obesity

- BMI <25 kg/m^2
- Increased waist circumference
- Increased visceral and ectopic fat
- Dysglycemia, diabetes, cardiovascular risk factors and disease.

https://www.ncbi.nlm.nih.gov/books/NBK568563/

What We Teach Clinicians About the Clinical Diagnosis of Obesity

Clinical Medicine

- *WHO*: "Condition where excess of abnormal body fat impairs health"
- Cut points are used as screening, and
- Diagnosis = cut-points + health risk assessment

Action item for clinicians: BMI is a screening tool. Assess waist circumference and obesity-related risk factors and comorbidities to make a clinical diagnosis of obesity.

WHO = World Health Organization.

Sharma AM, et al. Redefining obesity: beyond the numbers. *Obesity (Silver Spring).* 2017;25(4):660-1.
Ryan DH, et al. Keeping the baby and throwing out the bathwater. *Obesity (Silver Spring).* 2017;25(4):659.

What Might Be Better? Clinically Applicable Body Composition Methods

DXA

Attenuation of 2 energy level x-ray transmissions (absorbed or scattered). Measures bone and soft tissue

MF-BIA

Uses electrical properties of body to estimate TBW and from that the body fat mass. Body is modeled as 5 cylindrical compartment

ADP

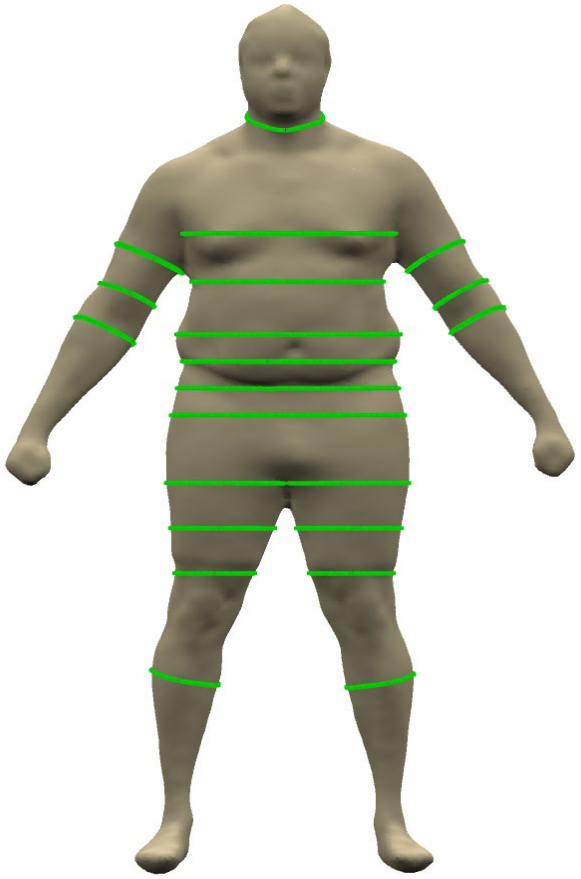
Assumes two compartment model (fat and lean) with different density. Volume of displaced air determined from changes in air pressure

DA

Smartphone app scans and quantifies body anthropometric dimensions and volume, estimates body fat by algorithm

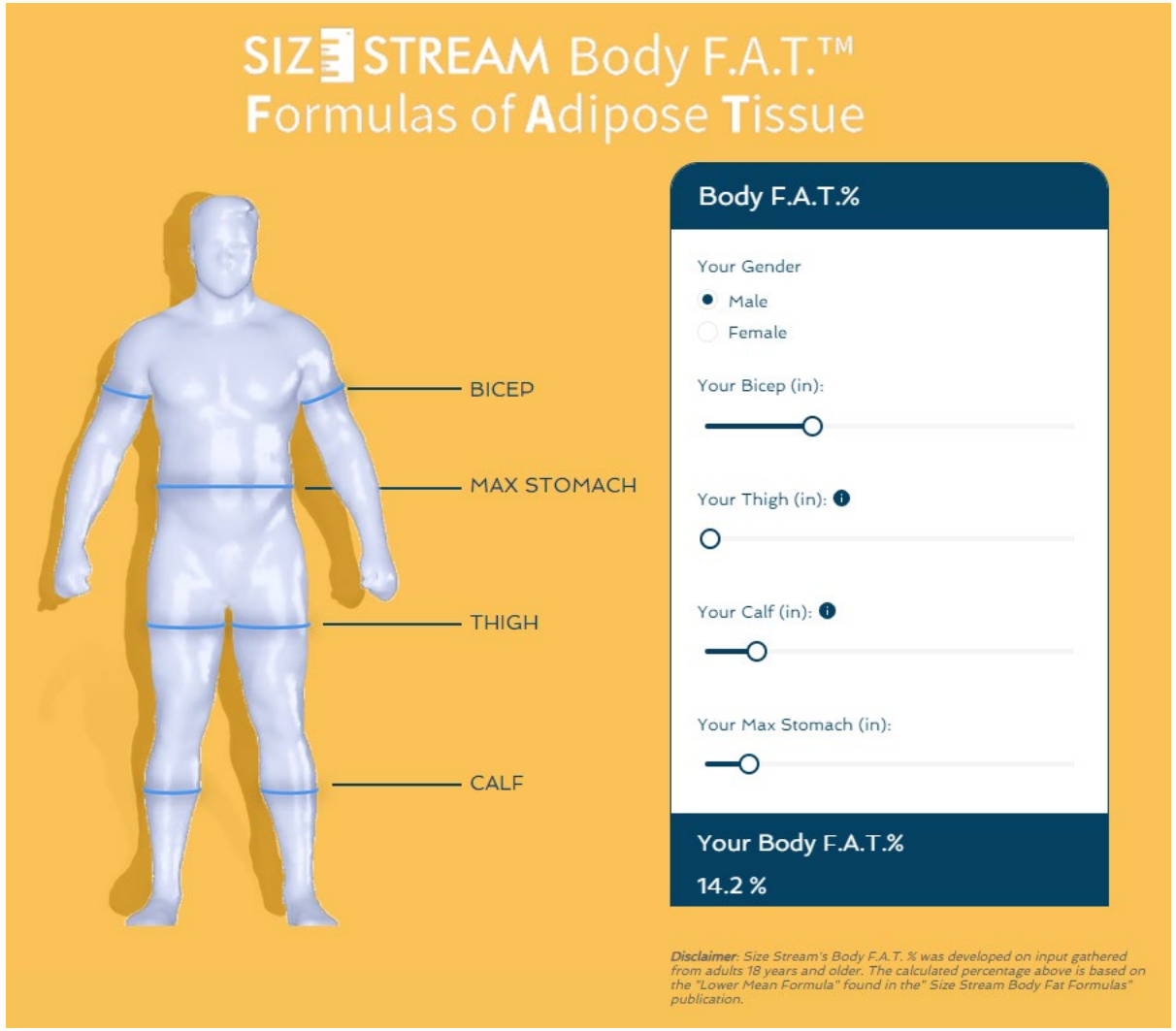
DXA = Dual x-ray absorptiometry; MF-BIA = multiple frequency Bioimpedance analysis; ADP = Air displacement plethysmography
DA = Digital anthropometry

Digital Anthropometry

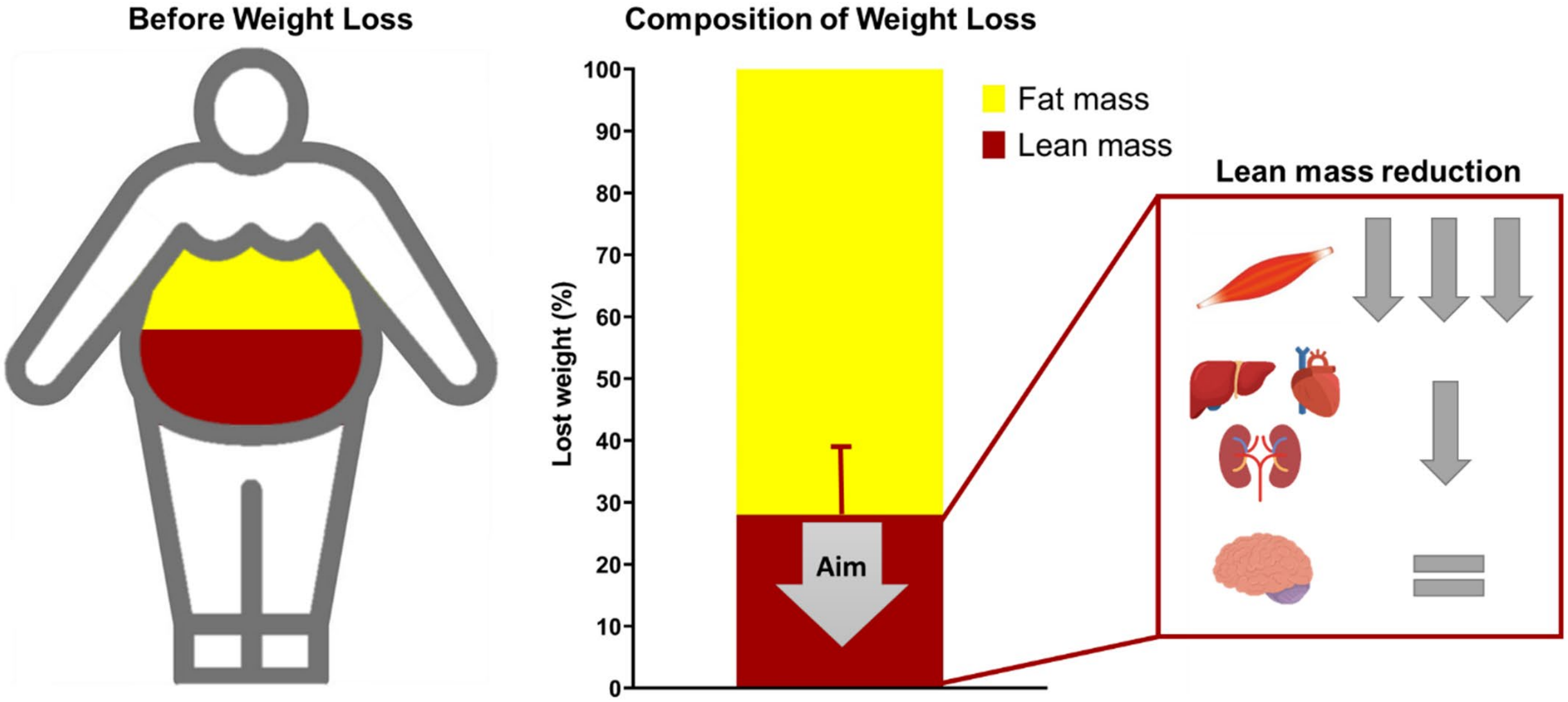


Courtesy of S Heymsfield

Body Measurements (in)	
Bicep Left Lower	12.12
Bicep Right Lower	12.53
Bicep Left	13.97
Bicep Right	15.19
Calf Left	14.68
Calf Right	14.67
Chest	44.33
Forearm Left	11.71
Forearm Right	12.04
High Hip	41.75
Hip	44.16
Neck	16.11
Thigh Left Lower	18.85
Thigh Right Lower	17.96
Mid-Thigh Left	25.42
Mid-Thigh Right	24.90
Thigh Left Upper	27.61
Thigh Right Upper	27.23
Waist (Abdominal)	41.52
Waist (Lower)	42.80
Waist (Narrowest)	38.81



Body Visualizer| MeThreeSixty



Christoffersen, BØ, et al. *Obesity (Silver Spring)*. 2022; 30: 841– 857.

Summing up: There is a need for clarity on the clinical diagnosis of obesity

But, for the immediate future

- BMI is here to stay
- Clinical judgment will be part of the clinical diagnosis, perhaps with more sophisticated staging
- No existing measures are ideal to replace BMI as a diagnostic screening tool
- % Weight loss as a surrogate for clinical outcomes is not ideal, but has some evidence to support it
- Digital anthropometry (providing % fat and % fat free mass) is likely to emerge as a tool to aid in weight management, provided we develop evidence for it in large studies.

Suggested topics I touched on.

- Historical view of obesity from anthropological perspective

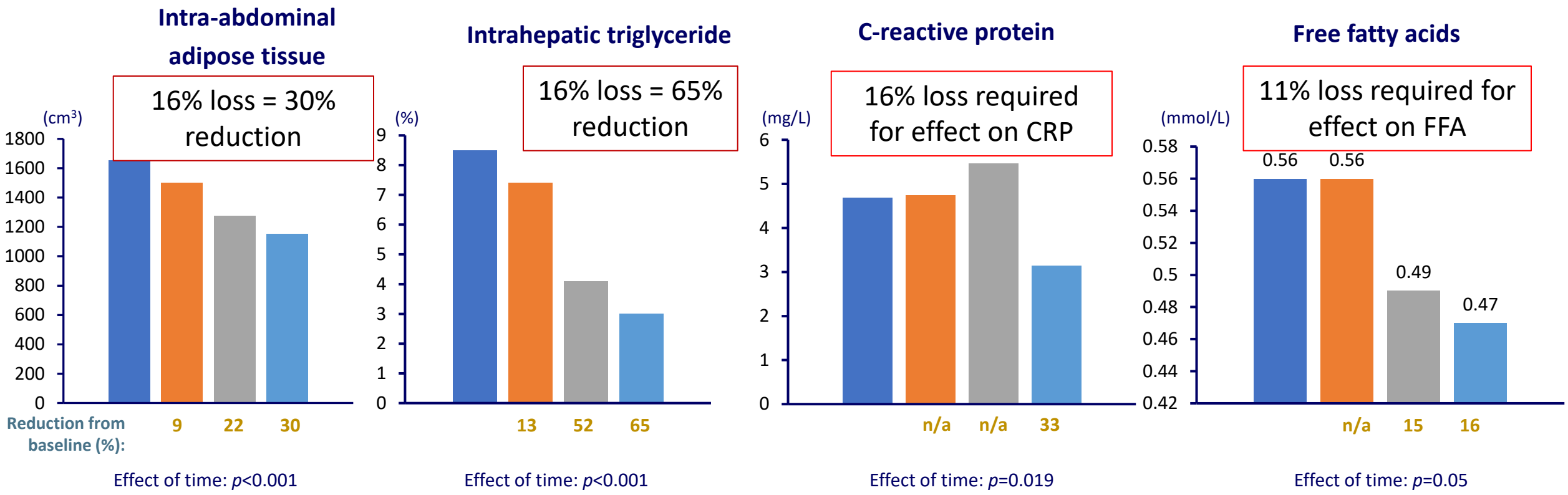
✓ Changes in the understanding of the pathophysiology of obesity over time
✓ Defining body composition and science behind it (e.g., obesity, adiposity)
✓ Common body composition measurements (include BMI and other measurements) --- what are they and what do they measure?

- Origins of BMI and its use today; evolution of BMI over time (and benefits and drawback of this evolution)

✓ Reasons for why we need a broad, inclusive definition of obesity
✓ Implications for the diagnosis and management of obesity

Question: You said different tissues respond differently to weight loss. How much weight do we need to lose?

Why does modest weight loss produce health benefit?
Effect of weight loss on metabolic function and adipose tissue biology



Magkos F et al. Cell Metabolism 2016;23:591–601

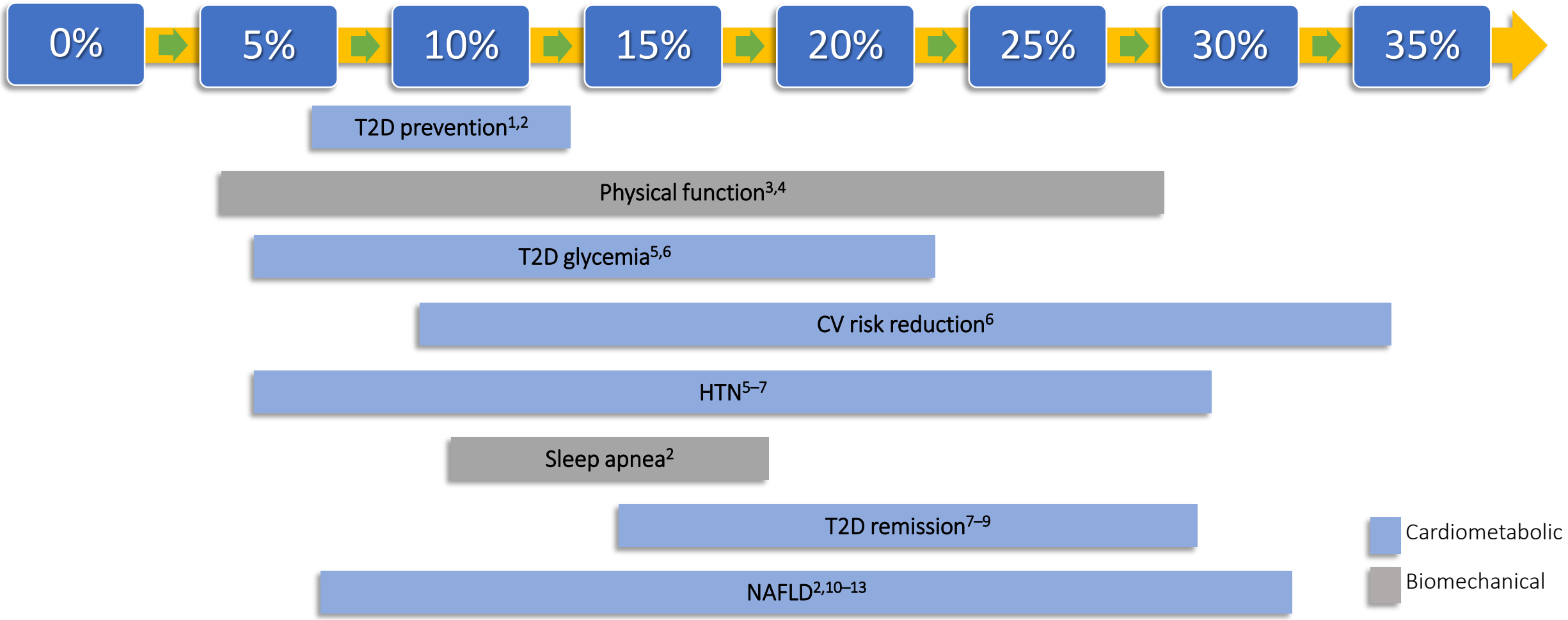
PROGRESSIVE WEIGHT LOSS HAS DOSE-DEPENDENT AND TISSUE-DEPENDENT BIOLOGIC EFFECTS

	5% weight loss	11% weight loss	16% weight loss
Improvement in glucose, insulin, triglycerides, alanine transaminase	+	++	+++
Improvement LDL & HDL cholesterol, adiponectin, free fatty acids		+	++
Improvement in C-Reactive Protein			+
Adipose tissue insulin sensitivity	+++	+++	+++
Liver insulin sensitivity	+++	+++	+++
Muscle insulin sensitivity	+	++	+++
Beta Cell function	+	++	+++
Adipose tissue biology*		+	++

*Upregulation of genes involved in cholesterol flux downregulation of genes involved in lipid synthesis, extracellular matrix remodeling and oxidative stress

Magkos F et al. Cell Metabolism 2016;23:591–601

How Much Weight Loss is Needed?



Slide courtesy of Tim Garvey MD

1. Knowler WC, et al. N Engl J Med 2002;346:393–403. 2. Cefalu WT, et al. Diabetes Care 2015;38:1567–82. 3. Christensen R, et al. Osteoarthritis Cartilage 2005;13:20–7. 4. Bliddal H, et al. Obes Revs 2014:15:578–86. 5. Wing RR, et al. Diabetes Care 2011;34:1481–6. 6. Ooi GJ, et al. Int J Obes 2017;41:902–8. 7. Courcoulas AP, et al. JAMA Surg. 2018;153:427–34. 8. Lean ME, et al. Lancet 2018;391:541–51. 9. Dambha-Miller H, et al. Diabet Med. 2020;37:681–8. 10. Vilar Gomez E, et al. Gastroenterology 2015;149:367–78. 11. Koutoukidis DA, et al. Metabolism 2021;115:154455. 12. Promrat K, et al. Hepatology 2010;51:121–9. 13. Liu X, et al. Obesity Surgery 2007;17:486–92.

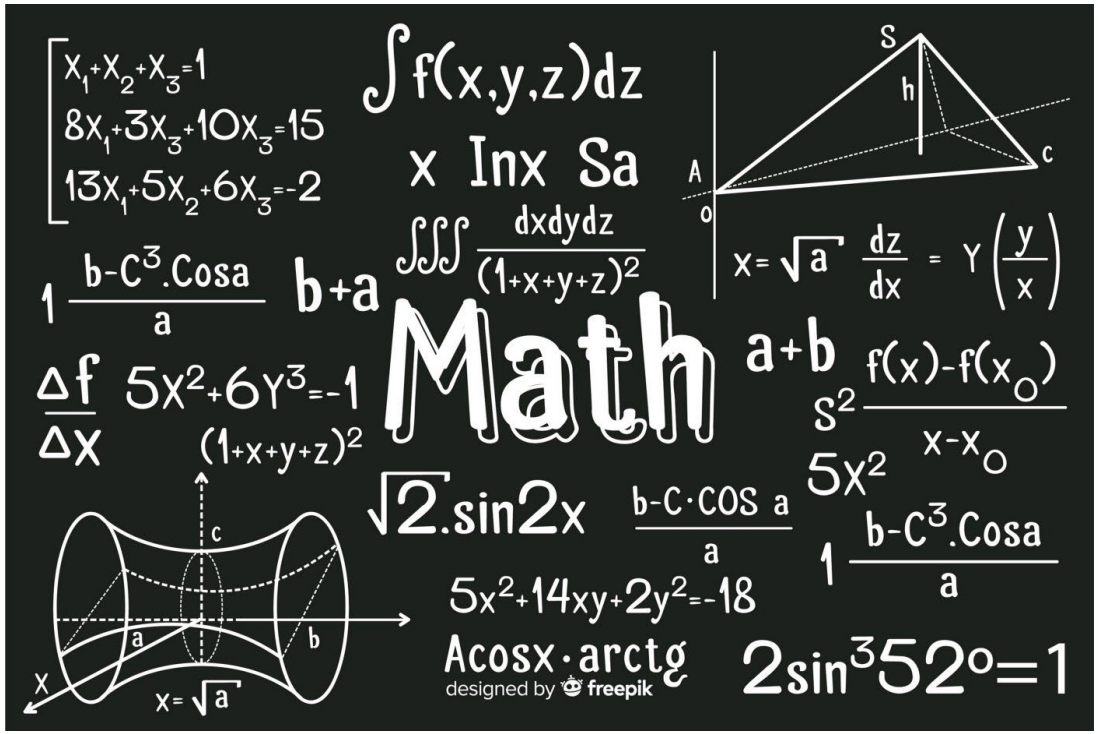
Question: How does digital anthropomenty measure % body fat and fat free mass?

How is body composition calculated from volume measurements?

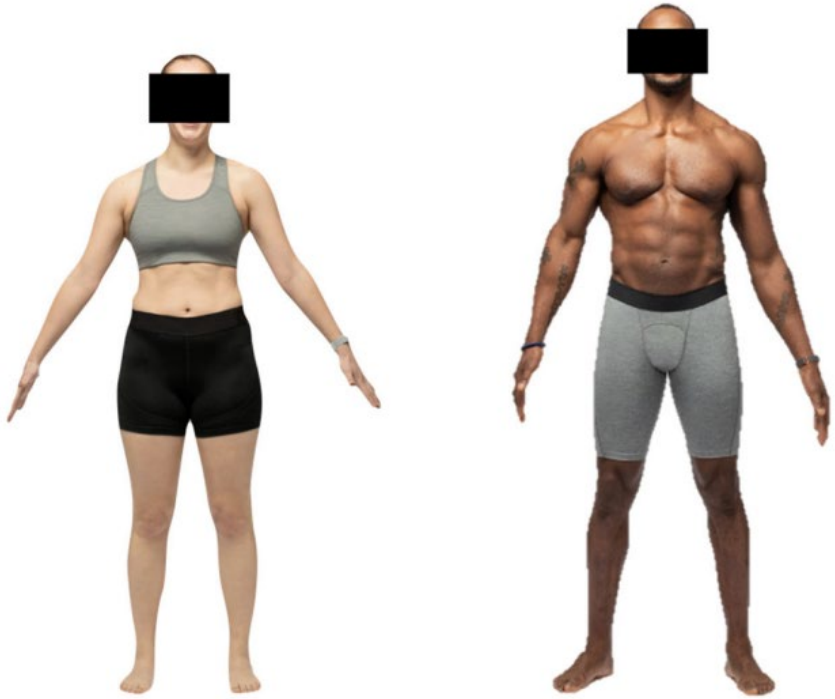
Body density (BD) = body mass (kg)/body volume (L)

The Siri equation is used to compute body fat mass using body density:

Body fat mass (BFM) = (4.95/BD – 4.5) x 100



Visual Body Composition Technology had the Best Concordance with DEXA for Body Fat Assessment



Example of smart phone images

npj | digital medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Check for updates

Smartphone camera based assessment of adiposity: a validation study

Maulik D. Majmudar[1]✉, Siddhartha Chandra[1], Kiran Yakkala[1], Samantha Kennedy[2], Amit Agrawal[1], Mark Sippel[1], Prakash Ramu[1], Apoorv Chaudhri[1], Brooke Smith[2], Antonio Criminisi[1], Steven B. Heymsfield[2] and Fatima Cody Stanford[3]

Body composition is a key component of health in both individuals and populations, and excess adiposity is associated with an increased risk of developing chronic diseases. Body mass index (BMI) and other clinical or commercially available tools for quantifying body fat (BF) such as DXA, MRI, CT, and photonic scanners (3DPS) are often inaccurate, cost prohibitive, or cumbersome to use. The aim of the current study was to evaluate the performance of a novel automated computer vision method, visual body composition (VBC), that uses two-dimensional photographs captured via a conventional smartphone camera to estimate percentage total body fat (%BF). The VBC algorithm is based on a state-of-the-art convolutional neural network (CNN). The hypothesis is that VBC yields better accuracy than other consumer-grade fat measurements devices. 134 healthy adults ranging in age (21–76 years), sex (61.2% women), race (60.4% White; 23.9% Black), and body mass index (BMI, 18.5–51.6 kg/m^2) were evaluated at two clinical sites ($N = 64$ at MGH, $N = 70$ at PBRC). Each participant had %BF measured with VBC, three consumer and two professional bioimpedance analysis (BIA) systems. The PBRC participants also had air displacement plethysmography (ADP) measured. %BF measured by dual-energy x-ray absorptiometry (DXA) was set as the reference against which all other %BF measurements were compared. To test our scientific hypothesis we run multiple, pair-wise Wilcoxon signed rank tests where we compare each competing measurement tool (VBC, BIA, …) with respect to the same ground-truth (DXA). Relative to DXA, VBC had the lowest mean absolute error and standard deviation (2.16 ± 1.54%) compared to all of the other evaluated methods ($p < 0.05$ for all comparisons). %BF measured by VBC also had good concordance with DXA (Lin's concordance correlation coefficient, CCC: all 0.96; women 0.93; men 0.94), whereas BMI had very poor concordance (CCC: all 0.45; women 0.40; men 0.74). Bland-Altman analysis of VBC revealed the tightest limits of agreement (LOA) and absence of significant bias relative to DXA (bias −0.42%, $R^2 = 0.03$; $p = 0.062$; LOA −5.5% to +4.7%), whereas all other evaluated methods had significant ($p < 0.01$) bias and wider limits of agreement. Bias in Bland-Altman analyses is defined as the discordance between the y = 0 axis and the regressed line computed from the data in the plot. In this first validation study of a novel, accessible, and easy-to-use system, VBC body fat estimates were accurate and without significant bias compared to DXA as the reference; VBC performance exceeded those of all other BIA and ADP methods evaluated. The wide availability of smartphones suggests that the VBC method for evaluating %BF could play an important role in quantifying adiposity levels in a wide range of settings.

Trial registration: ClinicalTrials.gov Identifier: NCT04854421.

npj Digital Medicine (2022)5:79 ; https://doi.org/10.1038/s41746-022-00628-3

US Military has BMI and Body Fat Assessment for Active Duty Personnel (and Fitness)

Materials courtesy of Diana Thomas CIV diana.thomas@westpoint.edu

Headquarters
Department of the Army
Washington, DC
16 July 2019

***Army Regulation 600–9**

Effective 16 August 2019

Personnel-General

The Army Body Composition Program

By Order of the Secretary of the Army:

MARK A. MILLEY
General, United States Army
Chief of Staff

Official:

KATHLEEN S. MILLER
Administrative Assistant
to the Secretary of the Army

History. This publication is an expedited revision. The portions affected by this expedited revision are listed in the summary of change.

Summary. This regulation implements DODI 1308.3. It prescribes procedures governing fitness and weight and body fat standards.

Applicability. This regulation applies to the Regular Army, the Army National Guard/Army National Guard of the United States, and the U.S. Army Reserve, unless otherwise stated.

Proponent and exception authority. The proponent of this regulation is the Deputy Chief of Staff, G–1. The proponent has the authority to approve exceptions or waivers to this regulation that are consistent with controlling law and regulations. The proponent may delegate this approval authority, in writing, to a division chief within the proponent agency or its direct reporting unit or field operating agency in the grade of colonel or the civilian equivalent. Activities may request a waiver to this regulation by providing justification that includes a full analysis of the expected benefits and must include formal review by the activity's senior legal officer. All waiver requests will be endorsed by the commander or senior leader of the requesting activity and forwarded through their higher headquarters to the policy proponent. Refer to paragraph 3–17 of this regulation and AR 25–30 for specific guidance.

Army internal control process. This regulation contains internal control provisions in accordance with AR 11–2 and identifies key internal controls that must be evaluated (see appendix D).

Supplementation. Supplementation of this regulation and establishment of command and local forms are prohibited without prior approval from the Deputy Chief of Staff, G–1 (DAPE–HR), 300 Army Pentagon, Washington, DC 20310–0300.

Suggested improvements. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) directly to Deputy Chief of Staff, G–1 (DAPE–HR), 300 Army Pentagon, Washington, DC 20310–0300.

Distribution. This publication is available in electronic media only and is intended for the Regular Army, the Army National Guard/Army National Guard of the United States, and the U.S. Army Reserve.

3D scanners work well within BMI range

Time to Automate US Army Body Taping Using 3D Scanners

Ira Crofford[1], Ezra Grant[1], Anny Claude-Joseph[1], Michael McGurk[2], Brenda Bustillos[2], Brooke A. Sorrell[2], John Shepherd[3], Steven B. Heymsfield[4], Nicholas Gist[5], Diana M. Thomas[1]

[1]Department of Mathematical Sciences, United States Military Academy, West Point, NY

[2]Pennington Biomedical Research Center, Baton Rouge, LA

[3]University of Hawai'i Cancer Center, Honolulu.

[4]Research and Analysis Directorate, U.S. Army Center for Initial Military Training (CIMT), U.S. Army Training & Doctrine Command (TRADOC), Fort Eustis, VA

[5]Department of Physical Education, United States Military Academy, West Point, NY

Diagnosis of Clinical Obesity:

What can we use in the clinic to assess excess abnormal body fat?

Limitations

- Taping (for BMI <35 kg/m$^{2)}$) training challenge
- DEXA – ionizing radiation, requires technician
- MF-BIA – accuracy is problematic, requires standardized conditions and equations
- Air displacement – requires equipment, time, and staff
- MRI or CT – Gold standard but not clinically applicable

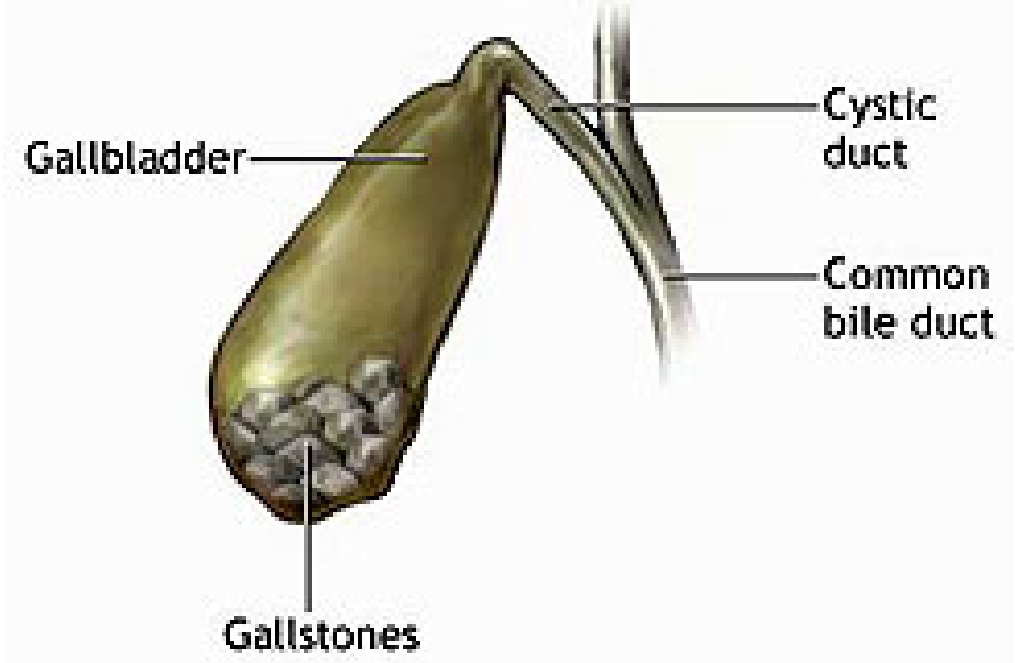
Shows promise

- Digital anthropometry
  - Rapidly emerging
  - Potentially affordable and scalable
  - Safe
  - Accurate at lower BMI ranges
  - Multiple techniques are being developed
  - Will need validation and longitudinal assessments

Could weight loss *per se* be bad for you?

Obesity, Weight Loss and Gall Bladder Disease

- Obesity increases risk for gall stones.
- Weight loss, especially rapid weight loss, increases risk for gall stones and acute gall bladder disease.



Gall Bladder Stones

Everhart JE. Contributions of obesity and weight loss to gallstone disease. Ann Intern Med. 1993 Nov 15;119(10):1029-35.

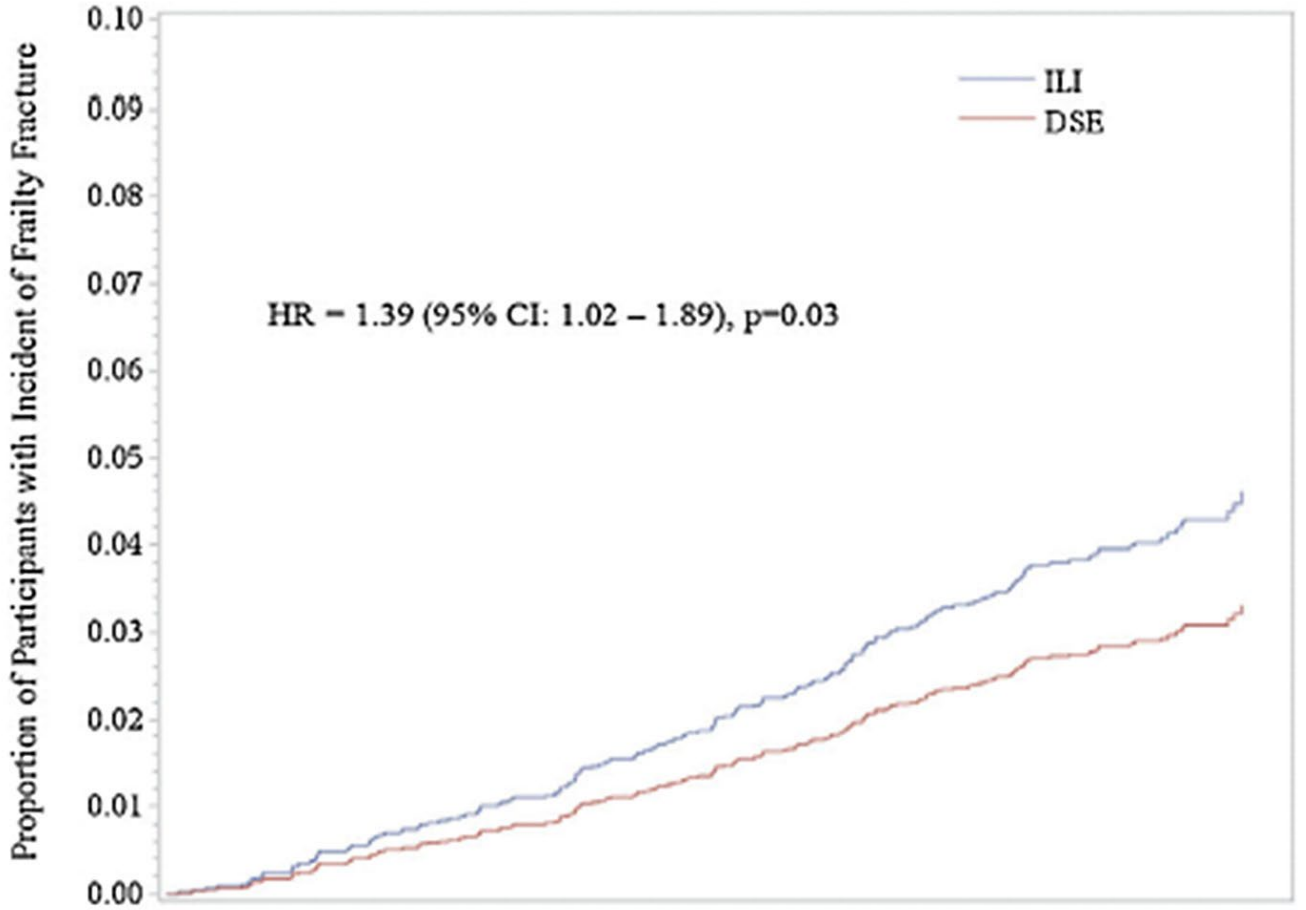
Key Findings From Look AHEAD Trial

Positive effects of ILI relative to DSE	NON-significant difference between ILI and DSE	Negative effects of ILI relative to DSE
A1C	Composite CVD outcomes	**Body composition**
Remission of diabetes	Cancer	**Bone density**
Nephropathy	Cognitive function	**Frailty fractures**
Neuropathy (self-report)	Cognitive impairment	
Depression	Total knee replacement	
Health-related quality of life		
Sleep apnea		
Health care costs		
Geriatric syndrome		
Incontinence		
Multimorbidity		
Disability/disability-free life years		
Brain structure (MRI)		

A1C = glycated hemoglobin; CVD = cardiovascular disease; DSE = diabetes support and education; ILI = intensive lifestyle intervention; MRI = magnetic resonance imaging.

Wing RR; Look AHEAD Research Group. Does Lifestyle Intervention Improve Health of Adults with Overweight/Obesity and Type 2 Diabetes? Findings from the Look AHEAD Randomized Trial. Obesity (Silver Spring). 2021 Aug;29(8):1246-1258.

Increased Risk of Frailty Fractures in Look AHEAD Intensive Lifestyle Intervention



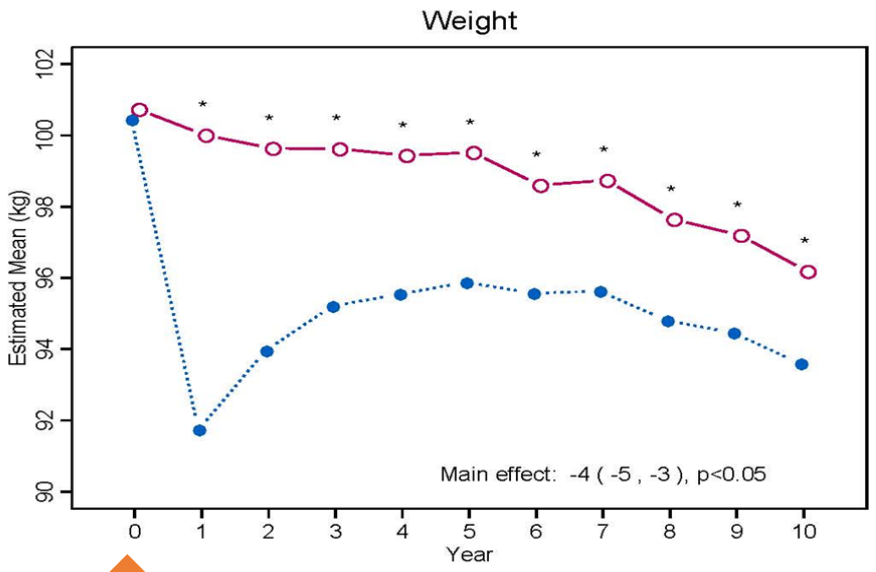
Time (Years)	0	1	2	3	4	5	6	7	8	9	10	11	12	13
Number at Risk														
DSE	2575	2526	2515	2477	2442	2407	2372	2336	2296	2228	2113	1810	1111	0
ILI	2570	2545	2499	2474	2452	2427	2391	2339	2299	2235	2184	1871	1173	0

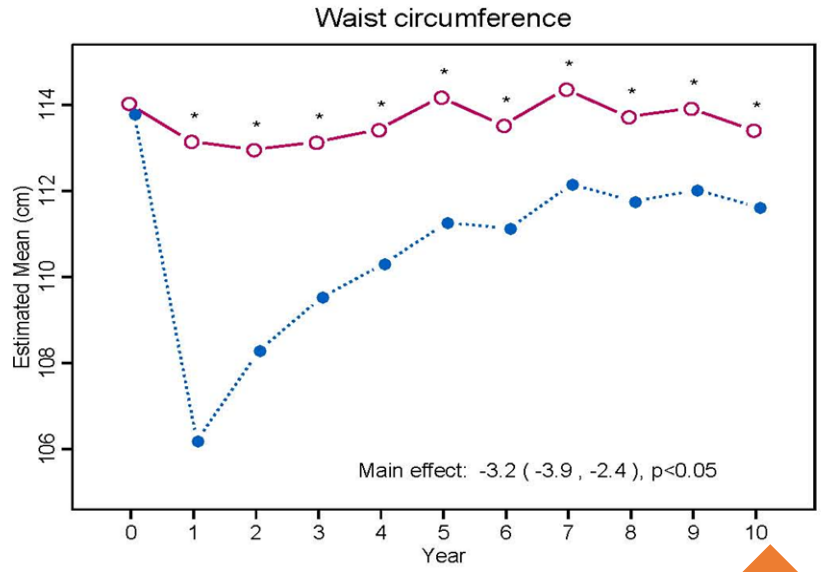
Johnson KC, Bray GA, Cheskin LJ, et al.; Look AHEAD Study Group. The effect of intentional weight loss on fracture risk in persons with diabetes: results from the Look AHEAD randomized clinical trial. *J Bone Miner Res* 2017;32:2278-2287.

Look AHEAD: Weight Loss Over 10 Years in 5145 Patients With T2DM

-o- support and education

…●… lifestyle intervention





Mean age 59 years

Mean age 69 years

T2DM = type 2 diabetes mellitus.

Look AHEAD Research Group, et al. *N Engl J Med.* 2013;369(2):145-154.

Mental Health Adverse Outcomes

Review of 32 studies

“Post-bariatric surgery patients had higher self-harm/suicide attempt risk compared to age-, sex-, and BMI-matched controls.”

Castaneda D, Popov VB, Wander P, Thompson CC. Risk of Suicide and Self-harm Is Increased After Bariatric Surgery-a Systematic Review and Meta-analysis. Obes Surg. 2019 Jan;29(1):322-333.