

## THIN FAT OBESITY: THE TROPICAL PHENOTYPE OF OBESITY

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### ABSTRACT

Disorders like diabetes and obesity have reached pandemic proportions globally. However, this problem is a little different in some tropical countries especially in the south Asian region. Countries like India and China have the leading number of people living with type 2 diabetes mellitus but paradoxically a much lower number of people with obesity (as defined by body mass index). This paradox is partly explained by the unique thin-fat phenotype prevalent in this region. Though this concept was described about 15 years ago, further evidence regarding its prevalence, pathophysiology, diagnosis, cardiometabolic risks, treatment, and implications for policy change are still emerging. The thin-fat phenotype is known by several other names in the scientific literature including normal weight obesity, metabolic obesity, metabolically unhealthy non-obese, etc. It is defined as an individual who has normal body weight (as measured by body mass index) but a disproportionately high body fat percentage (based on ethnicity and gender specific cutoffs). This phenotype is found to be very common in tropical countries and associated with a high cardiometabolic risk, which is similar to individuals with overt obesity. Moreover, the mortality associated with this phenotype is also significantly higher than nonobese subjects and thus this phenotype needs to be identified as a distinct entity. While evidence for the best therapeutic protocols is still emerging, an improvement in lifestyle intervention shows a slow but a positive trend in improving the cardiometabolic risk of this phenotype. The role of examining the underlying genetic makeup and the use of surrogate measures to estimate body fat could be useful adjuncts in the further characterization of this unique phenotype. In this chapter we summarize the current existing literature of this unique disorder and its importance in tropical countries.

### INTRODUCTION

Developing countries in the south Asian region are undergoing a rapid transition towards an increasing prevalence of non-communicable diseases but at the same time still grappling with undernutrition and infectious diseases. This dual burden of disease may appear as a transient phenomenon but may have deeper implications in determining the phenotype of cardiometabolic diseases in this population (1). One such example is of obesity and diabetes (2, 3). Though countries like India and China are the leading countries with the largest number of people with diabetes there is paradoxically a much smaller number of people with obesity in these countries (4). This paradox is largely due to the altered body composition with increased visceral adipose tissue and decreased lean mass leading to this unique thin fat phenotype that has been described in individuals of south Asian descent (5).

Moreover, this problem is further compounded by a younger age of development of these cardiometabolic disorders, a rapidly increasing prevalence, and significant financial constraints for most people to afford good healthcare in these countries (6). This complex situation highlights the need to appropriately identify at risk individuals and intervene in those who have a high cardiometabolic risk irrespective of their apparently lean phenotype. In this review, we discuss this unique thin fat phenotype seen in tropical countries, its prevalence, pathogenesis, clinical implications, and discuss the current evidence-based management.

This unique south Asian phenotype was classically described in a seminal paper published in the Lancet in the year 2004 called the YY Paradox (7). This pictorial abstract compared the body mass index and body composition of a Caucasian and an Indian physician. It showed how despite both having a similar normal body mass index (22.3 kg/m<sup>2</sup>), the body fat content was much higher in the Indian doctor. (21.2% vs 9.1%). Following this, several studies have examined the underlying pathophysiology of this phenotype (8, 9); however, better understanding of the utility and role of the conventional obesity indicators in this phenotype is needed. Furthermore, there is also a need to validate novel clinical and genetic indicators that can be used for mass screening such that the burden of non-communicable disorders in this region can be decreased (10).

### **DEFINITION OF THIN FAT OBESITY**

Thin fat obesity has been known by several names in the scientific literature. Names such as normal weight obesity, metabolic obesity, metabolically unhealthy non-obese, skinny fat, and sarcopenic obesity(especially in elderly) have been used in the past (5, 11). However, the term normal weight obesity was first described in 2006, by De Lorenzo as an individual with a high body fat despite normal weight (12). Simultaneously it was also observed that the Asian phenotype was very different from the West and the "thin fat phenotype" was commonly found in the Indian ethnicity, both those residing in India and overseas (7, 13).

Normal weight obesity or the thin fat phenotype is defined as the presence of an increased body fat percentage in an individual with normal body mass index (5, 14, 15). Though there has been a consensus to use a lower body mass index cutoff for the south Asian population ( $\geq 25 \text{ kg/m}^2$  defined as obesity instead of  $\geq$  30 kg/m<sup>2</sup> as proposed for Western populations), there has been a significant differences in the defining the thresholds for body fat percentages to overall define this phenotype (16). The most widely used cutoff for body fat percentage in the Asian population is  $\geq$  20.6 kg/m<sup>2</sup> for men and 33.4% in women, which has been rounded to the closest decimal in the table below (4). It is thus important to note, that in addition to the type of obesity indicator used for defining obesity, it is equally critical to use an appropriate ethnicity specific threshold of a given indicator. The cut points for different obesity indicators in India compared to that for Western population is summarized in Table 1.

Table 1. Cutpoints Used for Different Obesity indicators in South Asian and Western						
Populations						
	South Asians	Western Population				
Body Mass Index						
Underweight	< 18.5 kg/m <sup>2</sup>	< 18.5 kg/m²				
Normal Weight	18.5 to 22.9 kg/m <sup>2</sup>	18.5 to 24.9 kg/m <sup>2</sup>				
Overweight	23 to 24.9 kg/m <sup>2</sup>	25 to 29.9 kg/m <sup>2</sup>				
Obese I	25 to 29.9 kg/m <sup>2</sup>	30 to 34.9 kg/m <sup>2</sup>				
Obese II	30 to 34.9 kg/m <sup>2</sup>	35 to 39.9 kg/m <sup>2</sup>				
Obese III	35 to 39.9 kg/m <sup>2</sup>	<u>&gt;</u> 40 kg/m²				
Waist Circumference:						
Men	<u>&gt;</u> 90cm	<u>&gt;</u> 102cm				
Women	<u>&gt;</u> 80cm	<u>&gt;</u> 88cm				
Waist Hip Ratio:						
Men	<u>&gt;</u> 0.9	<u>&gt;</u> 0.9				
Women	<u>&gt;</u> 0.8	<u>&gt;</u> 0.8				
Body Fat percentage:						
Men	<u>&gt;</u> 20%	<u>&gt;</u> 25%				
Women	<u>&gt;</u> 33%	<u>&gt;</u> 35 %				

### UTILITY OF ETHNICITY SPECIFIC OBESITY INDICATORS

Assessment of obesity in any given patient would depend on two factors. The obesity indicator chosen to assess the obesity status and the cut-off used to define the threshold of obesity (17). Though several obesity indicators have been used for the evaluation of obesity, over the year's focus had changed to use ethnicity specific cut-offs (10). In addition to the conventionally used indicators like body mass index, waist circumference, and waist hip ratio, more recently neck circumference, waist height ratio, and body fat estimation have been added to the diagnostic armamentarium (18, 19). If more sophisticated

imaging is available, visceral fat estimation is now considered the most reliable obesity indicator that may accurately predict underlying cardiometabolic risk factors (19, 20).

The key merits and disadvantages of different clinical/ imaging-based obesity indicators are summarized in Table 2. In addition to these other methods such as bio-electrical impedance, potassium counter, and underwater weighing have also been used. Data is still emerging with respect to ethnicity specific cutoffs for these indicators and no universally acceptable thresholds have been defined for different ethnicities.(21)

Table 2. Comparison of Different Clinical/Imaging Based Obesity Indicators					
Obesity Indicators	Advantages	Disadvantages			
Body Mass Index	Easy to measure	Does not distinguish between			
	Inexpensive	body fat and lean body mass			
	Strongly correlated with body	Not a good predictor of body			
	fat levels.	fat in the elderly			
	Conventionally used for	Gender and ethnicity-based			
	many years.	differences are not detected.			
Waist circumference	Easy to measure	Measurement procedure not			
	Inexpensive	standardized			
	Strongly correlated with body	Lack of good reference data			
	fat in adults	for children			
	Shown to predict mortality	Difficult to measure in			
		individuals with morbid obesity.			
Skin fold thickness	Convenient	Not as accurate or			
	Safe	reproducible as other methods			
	Inexpensive	Very hard to measure in			
	Portable	individuals with a BMI of 35 or			
	Fast and easy	higher			
Dual Energy X-ray	Accurate	Expensive and currently used			
Absorptiometry (DXA)	Can measure visceral	in research settings			
	adiposity	Not portable			
	Very low radiation exposure	Limited availability			
	Can precisely estimate lean	Cannot be used with pregnant			
	mass and fat.	women			
Magnetic Resonance	Accurate	This is expensive and only			
Imaging (MRI)	Allows for measurement of	used in research settings.			
	specific body fat	Equipment is very heavy and			
	compartments, such as	cannot be moved.			
	Visceral fat and				
	subcutaneous fat				

In a recent study from southern India, we found that waist circumference, waist height ratio, and waist hip ratio were the best indicators to detect underlying type 2 diabetes mellitus in the Indian population (18). More importantly, body mass index. which is the most common obesity indicator used in many south Asian countries, did not perform well in detecting undiagnosed type 2 diabetes mellitus. Though waist circumference is now advocated as a good indicator of centripetal obesity and an indirect measure of visceral adipose tissue, its widespread use in clinical practice is still not routine (22). Furthermore, in recent guidelines assessment of obesity is now advocated to be measured beyond the lens of mere calculated numbers but rather to focus on a more holistic assessment of comorbidities, mental health, and quality of life (23-25).

### **PROBLEM STATEMENT**

Globally, there is limited data on the prevalence of normal weight obesity and this is further compounded by the different diagnostic cutoffs that have been used to define it. Furthermore, the method of body fat estimation may further augment the problem. Table 3 summarizes the prevalence of normal weight obesity in different tropical countries and the cutoffs used.

Table 3. Prevalence of Normal Weight Obesity in Different Tropical Countries						
Study	Body fat	Body fat % -	Prevalence	Country		
	assessment	criteria				
Kapoor et	Bio impedance	≥ 20.6% in men;	32% [95% confidence	India		
al		≥ 33.4% in women	interval (CI) 29.1-			
2020(14)			34.5].			
Kim et al	Bio impedance	≥ 20.6% in men;	In normal BMI	Korea		
2014 (26)		≥ 33.4% in women	Subjects - 36% in			
			men; 29% in women			
Madeira et	Skin fold	TSF + þSSF ≥	9.2% in men; 9.0% in	Brazil		
al.	thickness	P90 ~ 23.1% in	women			
2013(27)		men; 33.3% in				
		women				
Marques-	Bio impedance	≥ 30% overall	3.2% in men; 10.1%	Caucasians		
Vidal et al.			in women			
2010 (28)						
Romero-	Bio impedance	≥ 20.6% in men;	Among normal-BMI	North		
Corral et al.		≥ 33.4% in women	subjects: 33.4%	Americans		
2010(29)						
Ramsaran	Bio impedance	≥23.1% males,	19.9% [95%	Trinidad		
C et al		≥33.3% females	confidence interval	and		
2017(30)			(CI) 15.1-25.7].	Tobago		
Ji T et al	Bio impedance	male ≥25% and	10.7%	China		
2020 (31)		female ≥35%)				

In a recently published study from southern India, it was found that about two third of participants who had a non-obese BMI (<  $25 \text{ k/m}^2$ ), actually had a high body fat percentage. These individuals with normal weight obesity, accounted for about one third of the entire study population. (14)

As shown in table 3 there is a wide variation in the prevalence of normal weight obesity across different tropical countries but appears to higher than observed in North America. The key reasons for the wide variation in the prevalence of normal weight obesity across the world are multifactorial. In addition to the role played by the genetic background and ethnicity, the method of body fat assessment, the body fat thresholds used to define obesity, the prevalence of overt obesity in that community, and other factors like low birth weight may be responsible for the variation (32). These are discussed in greater detail in the pathophysiology section of this chapter.

The high prevalence of normal weight obesity, across different continents calls for better screening and early identification of this poorly recognized phenotype. Many of these patients may go unnoticed by the treating physician and the high risk of metabolic abnormalities such as type 2 diabetes mellitus and hypertension that may lead to severe complications not appreciated. Moreover, a unified diagnostic criterion for establishing a diagnosis of normal weight obesity is needed for being able to compare the prevalence of this phenotype across different populations. However, there a need for ethnicity specific cutoffs and recently countries from the south Asian region have used the body fat percentage cutoff as ~20% for men and 33% for women (4, 5, 10) (Table 1).

### INSIGHTS INTO THE PATHOPHYSIOLOGY

Several factors have been implicated in the pathogenesis of the thin fat phenotype in the south Asian population. (Figure 1). Though overall, there has been in an increase in the prevalence of overt obesity in south Asian countries, which could be attributed to the increased urbanization and reduced physical activity, there still remains a paradox between the disproportionately large number of people with type 2 diabetes and the relatively small number of individuals with overt obesity. The intake of high fat - high sugar meals, easy access to energy dense foods, and activity have limited physical been further compounded by the occurrence of the COVID-19 pandemic (Figure 2) (33-35). Overall, a rapid economic transition in many tropical countries has led to an increased availability of processed foods, more

environmental pollution, mechanization of lifestyle and limited time to do physical activity contributing to a rapid increase in the prevalence of obesity in these countries. (36-38).

Though urbanization is known to increase the risk of obesity, for the development of the thin-fat phenotype there have been speculations that migration of people from a rural to the urban setting may play a significant role especially in the Indian setting. In a study by Kinra et al, it was found that body fat percentage increased rapidly in the first decade following migration unlike many other cardiometabolic parameters which changed more gradually (39).

Low birth weight has also been implicated in the development of this "thin fat" phenotype described in the Indian population. In 2003, Yajnik et al, published findings to support that the thin fat Indian phenotype is present even in newborns. Neonates from Indian origin were compared to those born from a European ancestry in the United Kingdom (40). The authors found the Indian newborn babies were thin in terms of their skeletal mass but had a relatively high amount of subcutaneous fat. This led to term "thin fat neonate" and was in line with the previous thrifty phenotype suggested by Barker (41). These findings provided further impetus to ongoing studies of nutritional programming as a basis for Developmental Origins of Health and Disease (DOHaD).





# Figure 1: The key factors implicated in the pathogenesis for the development of the thin-fat phenotype in the south Asian population

Stress associated with maternal malnutrition and a consequent maternal glucocorticoid surge could lead to intrauterine growth retardation and subsequent changes in the fetal hypothalamic pituitary adrenal axis could cause altered ectopic fat deposits, including in the pancreas (42). There is also a possible role of maternal vitamin B12 in influencing fetal growth and programming for chronic diseases, explained through several interlinking metabolic pathways involving methionine and folate cycles collectively called the once carbon hypothesis (43).

In a previously published study from our center, we found that individuals with a low birth weight showed trends towards an unhealthy body fat distribution, lower lean body mass, impaired glucose tolerance, and an elevated diastolic blood pressure, even while they were just in their second decade of life (44). More recent evidence from basic science experiments have revealed that not only the birthweight but even the post-natal diet could play an important role in developing normal weight obesity (45).



### Figure 2: The bidirectional impact of obesity and COVID-19

A higher visceral adipose tissue content which is now considered the most important predictor of cardiometabolic disorders is also said to be higher in individuals from the south Asian region (46). The classical thin fat phenotype is also well explained in this population by the fat overflow hypothesis. This states that south Asians have a much lower capacity of storing fat in the subcutaneous region. Thereby when exposed to high calorie intake the subcutaneous tissue is overwhelmed and the extra fat content then spills into ectopic sites. The classic ectopic sites include the omentum (visceral adipose tissue), kidney, heart, intestine and liver. This then leads to higher amount of VAT despite similar total body fat compared to the European population and therefore the development of normal weight obesity (47).

Several genetic variations have also been studied to understand the origins of the thin fat phenotype in the Indian population. Several variants of the FTO and MC4R gene have been implicated in development of this phenotype but further studies are needed in this regard (48). Moreover, the presence of monogenic causes of obesity is higher in the south Asian population due to a higher prevalence of consanguinity (49, 50).

### **CLINICAL IMPLICATIONS**

This poorly recognized thin fat phenotype is not only common in the south Asian region but also has significant clinical implications with respect to cardio metabolic risk. This is important not only for health care providers practicing in south Asia but is also applicable to the health care of south Asian individuals who have migrated to different countries (51).



Figure 3. Prevalence of diabetes, hypertension, and dyslipidemia in individuals with normal weight obesity as compared to non-obese and overtly obese individuals

In a recent study done in south India it was found that individuals with normal weight obesity had a significantly higher prevalence of diabetes. hypertension, and dyslipidemia (defined by the NCEP-ATP III guidelines (52)) as compared to those without obesity. More importantly, the prevalence of these cardiometabolic risk factors were similar to individuals with obesity (Figure 3). After adjusting for other risk factors the odds of normal weight obese individuals having type 2 diabetes mellitus was found to be 2.72 (95% CI:1.46-5.08) as compared to non-obese individuals (53). A similar study from China found that individuals with normal weight obesity also had a significantly higher prevalence of metabolic syndrome when compared to non-obese individuals (54).

In the Women's Health Initiative study including 161,808 postmenopausal women between 50 to 74 years, it was found that women with normal weight obesity had a twofold higher risk of developing type 2 diabetes mellitus (55). When compared to non-obese individuals, those with normal weight obesity have not only been found to have a higher risk of atherosclerosis but normal weight obesity has been

found to be an independent risk predictor for presence of soft plaques in blood vessels after adjustment for blood pressure, blood glucose, lipid level, c-reactive protein, medications, smoking status, and physical activity (56). In another study involving 23,748 individuals, people with normal weight obesity had a significantly higher odds of having a high Framingham risk score for cardiovascular disease (OR 1.973, 95% Cl 1.596-2.439) as compared to normal individuals (57). Similar findings have been found in either sex and even in children, adolescents, and younger adults (58-60).

Another important clinically relevant subject related to the thin fat phenotype especially in tropical countries comes with the intersection of non-communicable diseases with chronic cachectic infectious disease. A classic example of this would be the presence of cardiometabolic disorders with an infectious disease like AIDS. We recently reviewed the association of HIV-AIDS with nonalcoholic fatty liver disease in south Asian countries (61). With better treatment of HIV infected individuals, the life expectancy and morbidity due to the virus per se has greatly improved. However, in most tropical countries there is limited screening facilities, widespread use of non-metabolic friendly antiviral drugs, and an existing thin fat phenotype making the prevalence of NAFLD much higher and yet very obscure.

In the recent ongoing COVID-19 pandemic, obesity has been considered as one of the key risk factors for increased mortality in the younger population. However, there is emerging evidence that individuals with normal weight obesity especially in the south Asian countries are also more likely to develop severe disease (35). There are several risk factors that have been described to associate the bidirectional relationship between COVID 19 and normal weight obesity (Figure 2).

### Mortality Associated with Normal Weight Obesity

Individuals with normal weight obesity have been found to have a higher all-cause mortality and major adverse cardiac and cerebrovascular events after an acute coronary syndrome when compared to those without normal weight obesity (adjusted (HR 1.83; 95% CI: 1.04-3.31) (62). In another recent study from the Women's Health Initiative study cohort, which involved 156,624 women followed for a total of 2,811,187 patient years, it was found that women with normal weight obesity were found to have a higher allcause mortality (HR 1.31; 95% CI, 1.20-1.42) and higher cardiovascular mortality (HR 1.25; 95% CI, 1.05-1.46). There was no difference in the mortality risk between women who had normal weight obesity as compared to those who had overt obesity. Moreover, this is the first study to show that cancer related mortality was also higher in women with normal weight obesity as compared to those who were normal weight without centripetal obesity (HR 1.20; 95% CI, 1.01-1.43) (63).

Considering the higher risk of cardiometabolic disease and the higher mortality in people with normal weight obesity, there has been a recent concern in army recruits as they are predominantly deemed fit from an obesity perspective based only on body mass index measurements (64).

### BODY FAT ESTIMATION

Accurate assessment of body fat is one of the key methods of identifying at-risk individuals in the south Asian population. More specifically detection of visceral adipose tissue is clinically more relevant. However, the gold standard for assessment of total body fat and ectopic fat depots is by using a magnetic resonance imaging (MRI), which is limited by the cost, availability, and the expertise required in tropical countries. Several other methods of assessing body fat have been described in literature. These include Dual energy x ray absorptiometry (DXA) scan, bioelectrical impedance, computed tomography (CT), body plethysmography, skin fold thickness, etc. (4, 10). The advantages of using DXA scans is that there is minimal radiation exposure, provides estimates of visceral adipose tissue, and is relatively easy to interpret. However, it is still costly and not widely available in many south Asian countries. DXA scans also cannot be used in community-based studies due to the large size of the DXA scanner compared to other portable machines that estimate fat such as bioelectrical impedance. Though there has been a good concordance between the fat estimation between bioimpedance and DXA scan, it is important to note that this concordance has been seen in normal ranges of body fat. Bio-impedance tends to over-estimate lower body fat percentages and under estimate higher values of body fat percentage (65). Nevertheless, its safe, rapid, and inexpensive. It is important to standardize for the variables that can modify the impedance values. These include room temperature, body position, electrode placement, quantity of urine in the bladder, food and water consumption, and proximity of exercise to time of evaluation.

In a large study from rural China involving more than 7000 participants waist circumference was found to be a better tool than body adiposity index to predict body fat percentage (measured by DXA), however the correlation coefficients between waist circumference and body fat percentage ranged between 0.24 to 0.66 in men and 0.12 to 0.77 in women, across different age groups. (66)

Apart from the method of estimation, it is also important to use the appropriate threshold for diagnosing abnormal body fat percentage. The impact of using different cut points for the diagnosis of normal weight obesity has been mentioned before. As per the American Association of Clinical Endocrinology guidelines a body fat percentage of more than 35% for women and 25% for men was set as a threshold for the diagnosis of obesity. However, for Asian countries a cut off of 33.4% for women and 20.6% for men, has been commonly used (4, 10).

Though measures of body fat estimation are helpful in clinical practice their widespread use in low -middle income countries may not be possible and good surrogate measures of visceral fat estimation may be the better way forward in such cost restrained settings. We recently studied the utility of using METS-VF, a novel surrogate measure to estimate visceral adipose tissue in Indian subjects with morbid obesity. This performed better than all other common clinically used obesity indicators and had the highest area under the curve 0.78 (95% CI: 0.72-0.85) for predicting VAT. At a cutoff of 7.3, METS-VF was found to have a good sensitivity and reasonable specificity in predicting high visceral adipose tissue in this population (6). Other surrogate measures of FAT assessment that have been used include 'VAT=TAAT-SAAT model and ap VAT (anthropometrically predicted VAT). Though they have been shown to be useful in selected populations, they have not been validated in many tropical countries (6).

While METS-VF uses simple clinical and biochemical parameters, including - waist-height ratio (WHtr), age and sex. LDL cholesterol, serum triglycerides and fasting glucose the VAT=TAAT-SAAT model uses only clinical variables like Waist Circumference, proximal thigh circumference, age and body mass index. Ap VAT is derived from a regression-based model including height, body mass index, and circumferences of the waist and thigh (67-69).

### MANAGEMENT

At this point there is only limited information with respect to the management of the thin fat phenotype, which is widely prevalent in the south Asian population. Only a few intervention studies are available in the literature, and this is an important area of future research. The currently available literature is only based on life-style interventions.

A very recently published study exploring the effect of a 12 weeks eu-energetic but high protein diet in women with normal weight obesity in a randomized controlled fashion, revealed no change in body weight at 12 weeks but a favorable change in body composition was noted. The eu-energetic was defined as equal amount of energy content in both groups according to the resting metabolic rate based on the Harris–Benedict predictive formula. (70). In another exercise based intervention, It was found that interval exercise and short duration accumulated exercises (10 minutes x 3 times of cycling) were more favorable in individuals with normal weight obesity as compared to continuous exercises (1 cycling session of 30 minutes) (71).

We recently studied the impact of peer led Lifestyle based intervention in an unselected group of individuals including individuals with normal weight obesity at two years of follow-up. The intervention was based on specific targets in diet, physical activity, reduced tobacco and alcohol consumption, and was delivered through multiple sessions by trained peer leaders. Though there has been a significant improvement in reducing the overall cardiovascular risk of the entire study population and benefit in preventing diabetes in certain subgroups in the intervention arm, there was only a minimal improvement noted in the cardiometabolic parameters of individuals with normal weight obesity. The failure in this study to see benefit in patients with normal weight obesity was disappointing (53).

The clinical and policy implications of the normal weight obese phenotype are challenging and are summarized in Figure 4. With the limited information that it is currently available, it seems that this phenotype is either more resistant to change than the conventional obesity phenotype or requires more time to show significant improvement in metabolic parameters. The current practice recommendations may only be based on existing literature on overall populations where this phenotype is commonly prevalent. The Indian diabetes prevention study is one such example where individuals with prediabetes were randomized to an intensive lifestyle program targeting a weight reduction of about 7-10% of the original weight along with physical activity of at least 150 minutes per week to the intensity of brisk walking. The relative risk reduction to prevent diabetes was only 29% in this population as compared to 58% in the US prevention based. Diabetes Program (72).

Furthermore, addition of Metformin did not add a huge benefit in reducing the risk in this study population but bariatric surgery has been shown to be effective in achieving diabetes remission in another study including individuals with BMI between 22-35 Kg/m<sup>2</sup> individuals (73).

Thus, with existing literature it may be prudent to evaluate all individuals with normal weight obesity for underlying cardiometabolic risk factors like diabetes, hypertension and dyslipidemia. Treatment for these conditions could be started based on standard guidelines but probably warrant a closely monitored approach and long-term follow-up. It is of paramount importance to educate these patients about their potential cardiometabolic risks which may otherwise be overlooked due to an obscure phenotype. Further research is needed to study the impact of long-term lifestyle changes and other medications on cardiometabolic risk factors, in individuals with normal weight obesity.



Figure 4: The clinical and policy implications of the normal weight obese phenotype

### SUMMARY

To conclude the obesity phenotype in many tropical countries including several south Asian countries is very different from other populations. Given the large prevalence and significantly higher associated cardiometabolic disorders with the thin fat phenotype, it needs to be recognized as a distinct entity such that it can be identified and managed appropriately. While evidence for the best therapeutic protocols is still emerging, a good life style intervention focusing on healthy dietary practices, regular exercise, and reducing tobacco and alcohol consumption shows a positive trend in improving the cardiometabolic risk of this phenotype. The role of examining the underlying genetic makeup and use of surrogate measures to estimate body fat could be useful adjuncts in the further characterization of this unique phenotype.

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