CHAPTER 7

DISCUSSION

7.1 WAIST CIRCUMFERENCE VS. BMI AS A RISK FACTOR FOR T2DM

Although obesity is an established risk factor for type 2 diabetes, it is unclear what the best anthropometric measure for this is. Current studies in this area have focused on two metrics – WC (for central fat), and BMI (for general adiposity). While there are many studies that have investigated the link between WC, BMI, and Diabetes, the result of these studies paints a confusing picture.

Some studies have found that WC is a better predictor of Diabetes than BMI. A 2016 (Alperet et al., 2016) study of Chinese, Malays, Asian Indians found that “Abdominal adiposity measures generally performed better than BMI in identifying undiagnosed diabetes.”. A 2016 (Hartwig et al., 2016) pooled analysis of four German population-based cohort studies found that “there were stronger associations between anthropometric markers that reflect abdominal obesity (WC and WHR) and incident type-2 diabetes than for BMI and weight.” A 1991 (McKeigue et al., 1991) study of South Asians settled in London found that “Insulin resistance syndrome, prevalent in South Asian populations is associated with a pronounced tendency to central obesity.” A 2008 (Nyamdorj, 2008) collaborative analysis of cross-sectional data from 16 cohorts from the DECODA study, which involved multiple Asian ethnicities, found that “WSR (Waist to Stature Ratio, a measure of central fat) was stronger than BMI in association with diabetes.”

Other studies have found BMI to be a better predictor of Diabetes than WC. A 2018 (Qiao & Nyamdorj, 2010) five-year prospective study of elderly Chinese found that “BMI was the strongest predictor of diabetes among both men and women." A 2015 (He et al., 2015) study of Asian Indian, Chinese, and Japanese found that "Population Attributable Risk (PAR) for BMI was high among Indians."

Still other studies have concluded that neither WC nor BMI are reliable predictors of Diabetes. A 2000 (Okosun et al., 2000) study of White, Black, Hispanic Americans found that "the positive predictive value (PPV) of WC for diabetes was low." A 2018 (Kobayashi et al., 2018) study of Asian Americans found that "one in seventeen Asian Americans with BMI less than 17 has diabetes." The authors concluded that regular screening for diabetes was required within this group.

It is clear that neither metric adequately measures obesity as it is related to diabetes risk. One reason could be confounding factors that are inherent to each metric: a tall individual is likely to have a higher WC and a muscular individual will have a higher BMI, without being more obese. There could be deeper, yet to be understood reasons as well.

Our approach was to study if a composite metric, which combines both WC and BMI, would perform better as a risk factor for type 2 diabetes. Following the suggestion of the WHO expert consultation (Nishida et al., 2004), our metric uses BMI as the base metric and gives "credit" to individuals who had low WC – i.e. reduce their risk level.

We have shown, through χ^2 analysis, that there is a statistically significant association BMI_{WC} and the outcome (type 2 diabetes). We have also shown that BMI_{WC} is superior to WC or BMI in predicting type 2 diabetes risk, as demonstrated by higher values of OR at every risk category. We can thus conclude that BMI_{WC} is a better risk factor for type 2 diabetes either central or general fat.

We also found WC, BMI, and BMI_{WC} are similar in their ability to pick individuals with type 2 diabetes from a population (this is measured by Sensitivity): 81% of people with moderate or higher BMI, 75% of people with moderate or higher WC, and 70% of the people with moderate or higher BMI_{WC} had type 2 diabetes. Thus, individuals with type 2 diabetes are likely to be higher on the obesity scale, regardless of which metric is used.

But, to be useful as a risk factor measure, WC, BMI, and BMI_{WC} should be lower in individuals without type 2 diabetes (this is measured by Specificity). We found that WC and BMI have low Specificity: among people who did not have type 2 diabetes, only 27% had lower than moderate WC or BMI. However, BMI_{WC} was significantly more Specific, as 36% of people without type 2 diabetes had lower than moderate BMI_{WC}. It follows that BMI_{WC} is a better risk measurement for type 2 diabetes than just WC or BMI.

We can also infer from this that individuals who have either high central fat or general adiposity are at higher risk of diabetes, while individuals with both low central fat and low general adiposity are at lower risk of diabetes. This suggests that the relationship between obesity and diabetes risk cannot be narrowed down to central fat alone (as has been suggested by various researchers), nor can is it entirely dependent on the proportion of height and weight. Future research, more targeted to the interplay between both types of fat as factors of T2DM incidence, is necessary to unravel a more precise connection.

7.2 IMPROVING IDRS THROUGH BMI_{WC}

It is to be noted that a viable screening score considers not just obesity, but also other risk factors such as age, family history, and physical activity. As mentioned in Section 1, IDRS is an effective screening technique used in India which considers all of these risk factors. We validated our conclusion that BMI_{WC} is a better measure of obesity by modifying IDRS to replace WC with BMI ($IDRS_{BMI}$) and then with BMI_{WC} ($IDRS_{BMIWC}$). All three variants were highly Sensitive: among people with type 2 diabetes, 88% had $IDRS_{BMI}$ of 60 or more; 87% had $IDRS_{WC}$ of 60 or more, while 82% had $IDRS_{BMIWC}$ of 70 or more. However, when selecting

ONLY people with type 2 diabetes from within a high-risk population (Specificity), $IDRS_{BMIWC}$ significantly outperformed $IDRS_{WC}$ by 26·61% and $IDRS_{BMI}$ by 24·31%.

This is an important result from both public health and clinical perspectives. Height, weight, and WC are typically available for a patient (or are easily measured). Thus, there is no added cost to calculating BMI_{WC}, and $IDRS_{BMIWC}$. Given the significantly better Specificity of $IDRS_{BMIWC}$, it should be used as a screening test in both public health and clinical situations. Table 15 shows the scoring key for the new IDRS, side-by-side with the old.

Table 15: Scoring key for current and new IDRS

Current IDRS (≥ 60 indicates diabetes risk)		**New IDRS (≥ 70 indicates diabetes risk)**		
Criterion	**Score**	**Criterion**		**Score**
Age		Age		
< 35 years	0	< 35 years		0
35-49 years	20	35-49 years		20
≥ 50	30	≥ 50		30
Physical Activity		Physical Activity		
Exercise [regular] & strenuous work	0	Exercise [regular] & strenuous work		0
Exercise [regular] or strenuous work	20	Exercise [regular] or strenuous work		20
No exercise and sedentary work	30	No exercise and sedentary work		30
Family History		Family History		
No family history	0	No family history		0
Either parent	10	Either parent		10
Both parents	20	Both parents		20
Obesity (WC in cm)		Obesity (composite of WC in cm and BMI in kg/m^2)		
≤ 79·99 (f)^a, ≤ 89·99 (m)^b	0	WC ≤79·99 (f)^a, ≤89·99 (m)^b	WC >80 (f)^a, > 90(m)^b	
80 - 89·99 (f)^a, 90 - 99·99 (m)^b	10	BMI ≤ 22.9		0
≥ 90 (f)^a, ≥ 100 (m)^b	20	23 ≤ BMI ≤ 27.49	BMI ≤ 22.9	10
		BMI ≥ 27.5	23 ≤ BMI ≤ 27.49	20
			BMI ≥ 27.5	30
Range	**0-100**			**0-110**

a Female
b Male

7.3 YLP FOR DIABETES PREVENTION

The study provides a strong preliminary first evidence towards the effectiveness of yoga based lifestyle change in reducing the incidence of diabetes in high risk individuals who are not diagnosed with T2DM and are normoglycemic, as indicated by both absolute risk reduction of 8.76% and relative risk reduction of 50.23%, as compared to the standard care.

In trying to assess the efficacy of YLP as compared to other forms of lifestyle interventions, we found that most lifestyle-based diabetes prevention trials have been conducted among individuals with prediabetes, rather than among high-risk individuals who are still normoglycemic (as we have done in this study). Amongst the reported lifestyle-based diabetes prevention trials, the most substantial findings have been derived from the Finnish Diabetes Prevention Study (DPS) [RRR of 58% at 4 years of follow-up] (Tuomilehto et al., 2001), Diabetes Prevention Program (DPP) [RRR of 56% at 2.8 years of follow-up] (Knowler et al., 2002), Da Qing IGT and Diabetes Study [RRR of 46% at 6 years for the exercise intervention] (Pan et al., 1997), and Japanese lifestyle intervention trial [RRR of 67.4% at 4 years] (Kosaka, Noda, & Kuzuya, 2005). The samples were selected from Finnish, American, Chinese, and Japanese populations. Among studies done on Asian Indian cohorts, the recent “Diabetes Community Lifestyle Improvement Program (D-CLIP) on 578 overweight/obese Asian Indian adults with prediabetes reported a relative risk reduction (RRR) of 32% (95% CI 7–50) at the 3-years of follow-up (Weber et al., 2016). However, RRR of only 28.5% at 3 years of follow-up has been previously reported by a lifestyle intervention trial on Indian population (Ramachandran et al., 2006). Our sister study, which was an RCT of YLP intervention among Asian Indians with prediabetes, reported an RRR of 68.29% over the 3-month duration of the trial (Nagarathna, et al., 2019).

These results are summarized in Table 16. The discrepancy in the findings of the prior reported diabetes prevention trials could be ascribed to the variations in the inclusion criteria for populations of high-risk (most were studies of individuals with prediabetes), varying baseline risk, genetic variability, variability in ethnic group (Finnish, United States, Chinese, Japanese, and Asian Indian), and responsivity to lifestyle interventions.

The outcome of the present short term YLP trial [RRR=50.23%, 95% CI 41.58 -57.60] are at par with those of the lengthy lifestyle modification-based trials cited above. The strength of the outcome despite the short duration of intervention could be attributed to high efficacy of YLP against diabetes prevention, high acceptance among Asian Indians of the culturally tailored yoga-based protocol (McDermott et al., 2014; Perreault et al., 2019), and elevated baseline risk of trial participants (IDRS ≥ 60).

Table 16: Comparison of various interventional studies among high-risk individuals[1]

Study	**Participant details**	**Duration, Intervention**	**Result**
NMB-2017 (This study)	4460 Asian Indians with high risk (IDRS ≥ 60) but normoglycemic	3 mo Yoga-based Lifestyle intervention protocol (YLP)	RRR 50.23%
NMB-2017	3336 Asian Indians with prediabetes	3 mo Yoga-based Lifestyle intervention protocol (YLP)	RRR 68.29%
Finnish Diabetes Prevention Study (DPS)	522 Finnish Middle aged, overweight with IGT	3y Nutrition counselling & resistance training	RRR 58%
Diabetes Prevention Research Group (DPP)	3324 American, obese adults with elevated FBS and/or PPBS	2.8y Metformin (MET) or Lifestyle modification (LSM)	RRR 31% (MET) RRR 58% (LSM)
Da Quing IGT and Diabetes Study	577 Chinese with IGT	6y Diet only (D), exercise only (E), diet and exercise (D+E)	RRR 31% (D) RRR 42% (E) RRR 46% (D+E)
Japanese Lifestyle Intervention	458 Japanese Males with IGT	4y Diet and exercise	RRR 67.4%
Diabetes Community Lifestyle Improvement Program (D-CLIP)	578 Asian Indian Overweight/obese adults with IGT and/or IFG	3y US-DPP-based lifestyle curriculum plus Metformin for highest risk participants	RRR 32%
Indian Diabetes prevention program	531 Asian Indians with IGT	3y Lifestyle modification (LSM) only, Metformin (MET) only, LSM and MET	RRR 28.5% (LSM) RRR 26.4% (MET) RRR 28.2% (LSM+MET)

1. All studies are RCT, and outcome measure is diabetes incidence.

The importance of this study is two-fold. First, given the well-known propensity for Asian Indian population to progress rapidly from prediabetes to diabetes, with the conversion rates being the highest among all studied populations (Dutta & Mukhopadhyay, 2016), this study has provided strong preliminary evidence that YLP intervention even before prediabetes can result in significant risk reduction of diabetic outcome. Combined with strong results reported in our sister study of individuals with prediabetes, the importance of YLP as an effective intervention is expanded to an even larger at-risk population.

The first study in this report has shown how to increase the efficacy of identifying individuals who are at risk of diabetes; this study shows how an intervention can be applied at the community level for such individuals, which will reduce their risk of progression down the path of impaired glucose tolerance and eventually to diabetes. The next study, to be discussed below, completes this picture with evidence for YLP intervention in bringing about glycemic control among individuals with diabetes.

7.4 YLP FOR GLYCEMIC CONTROL

Successful long-term diabetes self-management requires the integration of pharmacotherapy, proper nutrition, home blood glucose monitoring, increased physical activity, and surveillance for and prevention of complications. Exercise is one of the most valuable adjunct therapies “prescribed” to individuals with T2DM because its benefits are derived from multiple mechanisms including improving: insulin sensitivity, assist in maintaining a healthy body weight, improvement of lipid abnormalities, and beneficial redistribution of body fat (Joslin & Kahn, 2005). However, according to the results of DAWN study (Peyrot et al., 2005), adherence rates to exercise among individuals with T2DM has been reported to be as low as 37%.

The practice of Yoga has a similar multi-factor benefit potential for diabetes care. Prior studies have suggested that Yoga can reduce obesity, help sustain an active lifestyle, improve nutritional choices, reduce stress, and improve insulin sensitivity (in addition to the scientific literature survey in Chapter 3, see also (Innes & Vincent, 2007)). Furthermore, it has been proposed that Yoga has a strong behavioral component, derived from the ethical principles of Yama and Niyama, which help an individual to pursue and maintain explicit goals and standards (Gard et al., 2014). Furthermore, the practice of Yoga is highly accessible because does not demand specialized equipment, requires minimal training, and can be practiced at home. These three aspects of Yoga – multi-factor benefit potential for diabetes care, behavioral component that might enhance the sustainability of lifestyle change, and easy accessibility – make it ideal as an adjunct to standard care in diabetes management.

Underlying all clinical goals of T2DM treatment is the desire to achieve sustainable and optimal levels of serum glucose so that long-term microvascular and macrovascular complications can be minimized. While several prior studies have shown positive effects of Yoga practice on glycemic control in T2DM (Agte & Tarwadi, 2004; Amita, Prabhakar, Manoj, Harminder, & Pavan, 2009; Jyotsna, Dhawan, Sreenivas, Deepak, & Singla, 2014; Mohta, Agrawal, Kochar, Kothari, & Sharma, 2009; Monro et al., 1992; Nagarathna et al., 2012; Pardasany, Shenoy, & Sandhu, 2010; S. Singh et al., 2008; Skoro-Kondza, Tai, Gadelrab, Drincevic, & Greenhalgh, 2009; Subramaniyan, Subramaniyan, & Chidambaram, 2012; Vaishali, Kumar, Adhikari, & UnniKrishnan, 2012), many of these studies present methodological limitations. A 2016 meta-analysis of 6 studies that had shown decrease in post-prandial glucose (PPG) in the yoga group compared to standard care, failed to show significant mean difference between yoga and control condition. Meta-analysis also noted a similar lack of significance in the mean difference between HbA1c between Yoga and control groups in 2 studies (Vizcaino & Stover, 2016).

This study has shown that even a short term practice of Yoga can beneficially impact glycemic control in individuals with T2DM as measured by HbA1c. The large sample size (n = 3392) ensures sufficient statistical power to back up the conclusions. The mean difference in HbA1c reduction between Yoga and control arms (0.86%, 95% CI 0.78 – 0.95), even within the short period of the study, is suggestive of a strong effect. Longer term studies with more frequent follow-ups are necessary to validate both the strength and sustainability of this effect. Self-regulation, one of the behavioral components of yoga, defined as a conscious ability to maintain stability of the physiological system by managing or altering adverse physiological or psychological states (Kumar et al., 2016), could have contributed significantly towards achievement of the observed improved glycemic control.

Of equal interest is the effect of Yoga on individuals with poor glycemic control (HbA1c $\geq$ 7.6) at baseline as compared to those with fair glycemic control (HbA1c < 7.6). It was found that in the group with poor control, Yoga was more effective in reducing serum glucose levels; the mean difference in HbA1c reduction between Yoga and control arms was 1.61%, (95% CI 1.47 – 1.75) for this group. The group with fair glycemic control benefited from Yoga, but the effect was less pronounced; the mean difference of the reduction in HbA1c levels for this group was 0.35% (95% CI 0.28 – 0.43). This result is clinically important because individuals with greater exposure to hyperglycemic load are more likely to have micro- and macro-vascular complications. Incorporating Yoga as an adjunct to standard care is especially effective in such populations.

7.5 YLP COMPARED TO OTHER LIFESTYLE INTERVENTIONS

Among its adherents, Yoga is usually referred to as a “holistic” practice. Scientifically, especially in the context of diabetes prevention and glycemic control, we may ascribe a precise meaning to the term “holistic”: the practices of Yoga provide mitigation via multiple pathways.

In fact, as our examination of current studies (see Chapter 3) have shown, there is evidence that Yoga mitigates almost every lifestyle factor and physiological dysfunction that comprise the heterogeneous disorder of diabetes. By its very nature, the YLP intervention addresses nutritional, psychological, and exercises aspects, and thus has the potential to be a more versatile life-style intervention when compared to those based on nutrition or exercise alone. The results reported in this thesis, combined with the results reported in (Nagarathna, et al., 2019), give a strong preliminary support to this assertion by demonstrating the efficacy of YLP to (a) reduce risk of progression to diabetes among high-risk but normoglycemic individuals (b) reduce risk of progression to diabetes among individuals with prediabetes (c) increase possibility of remission from prediabetes and (d) aid in glycemic control among individuals with diabetes.