

## CHAPTER 5

### STUDY 2: EFFICACY OF A YOGA-BASED LIFESTYLE PROGRAM ON DIABETES RISK REDUCTION AMONG HIGH-RISK INDIANS

#### 5.1 AIM AND OBJECTIVES

##### 5.1.1 Aim of the study

To study the effect of the YLP on diabetes risk among normoglycemic Indians who are at increased risk of getting diabetes (as measured by IDRS  $\geq 60$ )

##### 5.1.2 Objectives

- To study the risk of diabetes progression among high-risk Indians who are not yet in the prediabetes stage
- To analyse the effects of 12 weeks of YLP on the risk of diabetes progression

##### 5.1.3 Rationale for the study

There is a lot of evidence that the practice of Yoga mitigates the underlying risk factors for insulin resistance, such as obesity and stress; there is also evidence that shows the efficacy of Yoga to produce sustainable behavioural changes that foster a more active lifestyle and better nutritional choices, both of which mitigate diabetes risk. However, this has not been studied in a large community setting.

##### 5.1.4 Hypothesis and Null Hypothesis

$H_0: R_C = R_Y$

$H_1: R_C \neq R_Y$

Where  $R_C$  is the risk of diabetes progression in the control group, and  $R_Y$  is the risk of diabetes progression in the Yoga group.

## **5.2 DESIGN OF THE STUDY**

The details of NMB-2017 study, whose data is being analyzed here, have been given above in Section 4.2., and the full details of both phases of the study protocol have been reported elsewhere (Nagarathna et al., 2019; Nagendra et al., 2019). Given here is a brief description of the randomized controlled trial (RCT) phase of the study. The aim of the RCT was to assess the efficacy of a yoga-based lifestyle intervention as a primary prevention strategy for diabetes on high diabetes risk Indians, in a large community setting. The trial was executed as a 2-armed cluster randomized translation trial; a cluster design approach was adopted to minimize the exposure of the control group to the intervention effects. Intervention included practice of yoga-based lifestyle modification protocol (YLP) for 9 consecutive days, followed by daily home and weekly supervised practices for 3 months. The control-cluster received standard of care advice for diabetes prevention. An International Research Advisory Committee with subject experts provided guidance at all stages of the study. The protocol was approved by the Ethics Committee of the Indian yoga association (IYA). The study was registered in Clinical Trials Registry- India (CTRI) Trial Registration Number: CTRI/2018/03/012804.

### **5.2.1 Study Enrolment and Follow-up**

The community level recruitment in Phase 1 of the screening for IDRS values included 240 clusters with 162,330 adult respondents. Of these 49,226 individuals belonging to 130 clusters (urban/rural) were found to eligible with high  $\geq 60$  IDRS scores; further 27,611 individuals responded to biochemical assessments. Among these, clusters with cohort population of an average of 50 individuals were invited for study. Accounting for a 24% loss for follow up, the final analyzed number was 4460, with 2396 in yoga and 2064 in the control arms of the study.

The reasons for drop out were mostly time or work constraints, or unavailability of participants due to weather conditions.

### **5.2.2 Randomization and blinding**

Overall, 80 clusters were randomly assigned in a 1:1 ratio to the control or the intervention arms by an independent statistician using a computer-generated randomization sequence. A total of 2396 (40 clusters) and 2064 (40 clusters) individuals were included in the intervention and control arms, respectively; an overall equivalent ratio of rural and urban location distributions was maintained (44 rural and 36 urban centers). Group allocation was concealed to the participants until the completion of the baseline assessment. Based on the nature of the intervention, other than the statisticians and the baseline data collection staff, the study participants or the field intervention yoga therapists or other investigators could not be blinded.

### **5.2.3 Data Collection**

Assessments at baseline and after 3 months included study questionnaires, anthropometric measurements, and blood draw. IDRS was used as a validated instrument [with 4 factors and score ranging from 0-100 for baseline screening of high diabetes risk individuals (Mohan, Deepa, Anjana, Lanthorn, & Deepa, 2008)]. Covariates included age, gender, family history of diabetes, baseline values of BMI and physical activity and medication. Details of self-reported physical activity including mean minutes of weekly activity were estimated based on the questions on frequency and duration of exercise sessions. Details of any adverse reactions or events were recorded including their severity, duration, and time of occurrence.

### **5.2.4 Procedure for biochemical measures**

HbA1c assessment was done by high-pressure liquid chromatography using the Variant™ II Turbo machine (Bio-Rad, Hercules, CA) certified by the National Glycohemoglobin

Standardization Program. The intra- and inter-assay coefficients of variation for the biochemical assays ranged within the target goals set by ADA's Standards of Medical Care.

## **5.3 METHODS**

### **5.3.1 Participants and Outcomes**

The study included individuals (age 18 - 81 years) with IDRS  $\geq$  60 who had never been diagnosed with diabetes and whose blood HbA1c values were  $<$  5.7%. Individuals with diabetes or prediabetes (known and newly diagnosed), severe obesity (BMI $>$ 40 Kg/m<sup>2</sup>), history of uncontrolled hypertension, coronary artery disease, renal disease, diabetes retinopathy, head injury, tuberculosis, reported psychiatric problems, major surgery, pregnancy in case of women, those planning to move out of the area within the next 3 months and those who had already done yoga for  $\geq$  3 months just before the dates of recruitment, were excluded from the study.

Informed consent was obtained from all the participants before screening and randomization. Details of recruitment of participants have been discussed in section Chapter 4, Section 1. and in earlier reports (Nagarathna, et al., 2019; Nagendra et al., 2019).

The outcome was the conversion from normoglycemia (HbA1c  $<$  5.7) to diabetes (HbA1c  $\geq$  6.5%) after 3 months of intervention. The outcome was diagnosed based upon single time point assessment of blood HbA1c levels.

### **5.3.2 Sample Size**

NMB-2017 was a study with multiple objectives, the sample size calculations for which have been detailed in section 4.3.2. To verify the sufficiency of sample size for our study, we looked at the results of the Finnish Diabetes Prevention Study (Lindström et al., 2003), which studied the effects of lifestyle intervention to postpone T2DM among high-risk individuals. They

reported that 9% of the intervention group (22 individuals) developed T2DM in a 3 year period, while this number for 20% (51 individuals) for the control group. This provided a conversion rate at a 3 month follow-up to 0.75% in the intervention condition and 1.67% in the control condition. Following the method described by Hajian-Tilaki K in (Hajian-Tilaki, 2011), the required sample size was calculated to be 2228 in each group.

### **5.3.3 Analysis**

To analyze the occurrence of primary outcome, absolute risk reduction (ARR), relative risk (RR), and relative risk reduction (RRR) were derived from the marginal probabilities based on contingency tables. Standard errors and 95% confidence intervals were calculated using the methods described by Altman (Altman, 1991; Altman & Bland, 2003). A *P* value <0.05 was considered statistically significant for all analyses. *P*-values were calculated based on standard errors of proportions (for RR and RRR), and differences (for ARR). The results were considered statistically significant if the 95% confidence interval didn't include the reference values of 0 (for ARR/RRR) or 1 (for RR) for these measures.

Intervention adherence was assessed by evaluating (a) class attendance and (b) regularity of practice of yoga during the period of study.

All analyses were done using Python v.3.7. Pandas v.0.23 was used to import data. Contingency table creation and calculation of risk measures were done using Statsmodels v.0.10.1.

## **5.4 INTERVENTION**

All participants in the intervention group received core initiation camps of 2-hours daily for 9 days. The intervention group received the standardized yoga-based lifestyle modification protocol (YLP) along with educational meetings to emphasize the role of adherence to yoga-based lifestyle to prevent diabetes. The intervention protocol was developed by a team of 16

experts including senior yoga masters from different yoga traditions (member institutions of Indian Yoga Association [IYA]), yoga researchers and diabetologists (Nagarathna, et al., 2019). The protocol (Appendices 3 and 4) comprised of selected practices for lifestyle diseases, extracted from traditional sources. It included 30 minutes of physical postures (sun salutation and asanas) equivalent to mild to moderate physical activity and 30 minutes of breathing practices (kapalabhati kriya and pranayama), meditation and relaxation techniques. Evidence-based dietetic advice was also provided to promote healthy choices, rich in fiber and lower in fat and carbohydrate content. Group/individual lectures on concepts of ethical principles (yamas and niyamas), stress and nutrition for diabetes management were also held for 20 minutes.

Roles and responsibilities of the study staff were discerned. The intervention was conducted at the study sites by the volunteers designated as yoga volunteers for diabetes movement (YVDM). These YVDMs were certified yoga instructors from different member organizations of Indian Yoga Association (IYA). After these core intervention camps, participants were asked to continue self-practice (group or individual) daily for 3 months. Supervised weekly follow up classes for 2-hours were also conducted. After 3 months, post data was collected from both groups. The YVDMs planned and conducted weekly 2-hours Sunday morning group classes where yoga camps were conducted and social media groups were also created. This facilitated the communications on interactive review follow-up classes, monitoring their compliance of daily practices, and their health-related issues. There were no major issues reported by the participants during the 3-month period.

Participants assigned to the control group received standard of care through printed handouts and one day interactive group presentation on structured lifestyle (diet physical activity, tobacco cessation etc.) change for diabetes prevention, by a team of physician, dietitian, and a fitness trainer. This was followed by weekly visit to the site by the volunteer to interact and

answer queries by the control group participants. Prescription of medication (metformin) for diabetes prevention was not the standard of care at the study site for either the intervention or the control group.

## 5.5 RESULTS

### 5.5.1 Description of Data

A total of 4460 individuals participated in the trial. They varied in age from 20 – 81 years ( $\mu = 48.95$ ,  $\sigma = 10.40$ ). 58.57% (n=2612) were females, and 41.43% (n=1848) were males; 60.09% (n=2680) were urban and 39.91% (n=1780) were rural. HbA1c levels varied from 3.90% to 5.69% ( $\mu = 5.21$ ,  $\sigma = 0.32$ ) (Table 9). The distribution of the demographic and clinical characteristics between the two arms was fairly even with non-significant difference between groups ( $p > 0.05$ ) (Table 9, Figs 11-14).

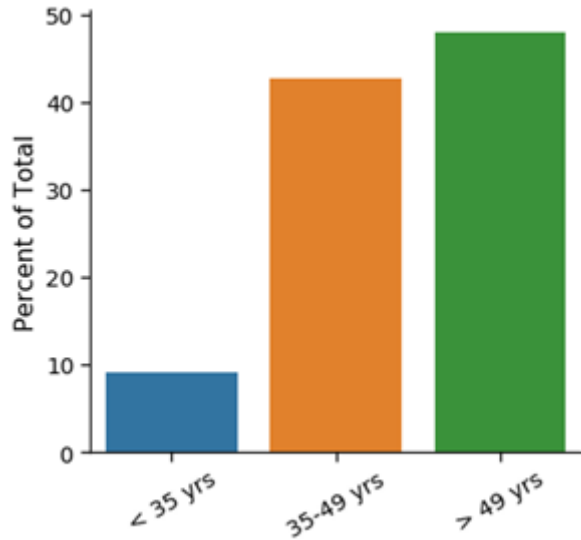
**Table 9. Baseline data for trial participants**

Characteristics	Overall (n=4460)	Control (n=2064)	Yoga (n=2396)
Age, years, $\mu \pm \sigma$	48.95 $\pm$ 10.40	48.88 $\pm$ 9.90	49.02 $\pm$ 10.82
HbA1c, $\mu \pm \sigma$	5.21 $\pm$ 0.32	5.16 $\pm$ 0.34	5.26 $\pm$ 0.29
Area, n (%)			
Urban	2680 (60.69)	1044 (50.58)	1636 (68.38)
Rural	1780 (39.91)	1020 (49.42)	760 (31.72)
Gender, n (%)			
Female	2670(60.00)	1414(61.05)	1256(58.86)
Male	1780(40.00)	902 (38.95)	878(41.14)

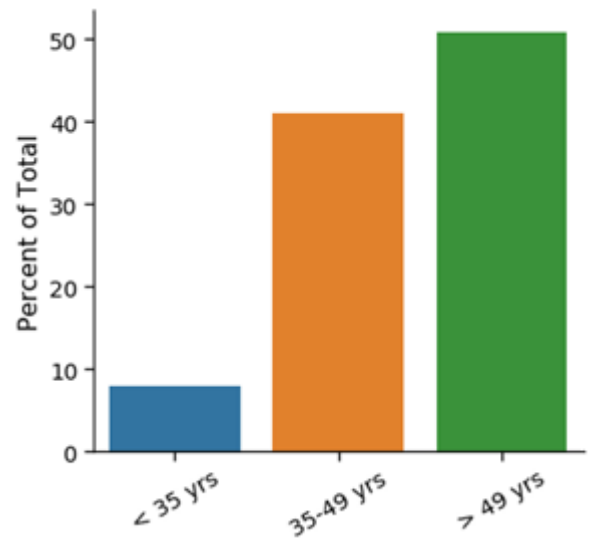
### 5.5.2 Conversion to Diabetes

Over a follow-up period of 3 months, a significantly smaller proportion of the intervention arm developed diabetes (n=208, 8.68%) compared to control arm (n=360, 17.44%), with an absolute risk reduction of 8.76%, 95% CI 6.77-10.75 The intervention group exhibited 0.50 times the risk of conversion (RR) from normal to diabetes (95% CI 0.42 – 0.58) compared to

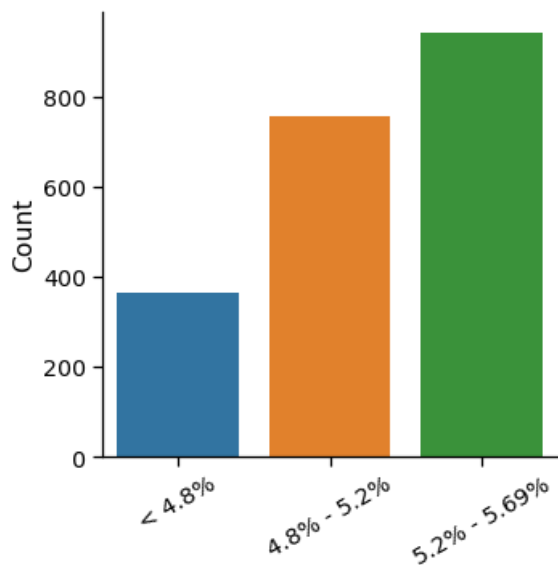
the control group, which corresponds to a relative risk reduction (RRR) of 50.23%, 95% CI 41.58-57.60.



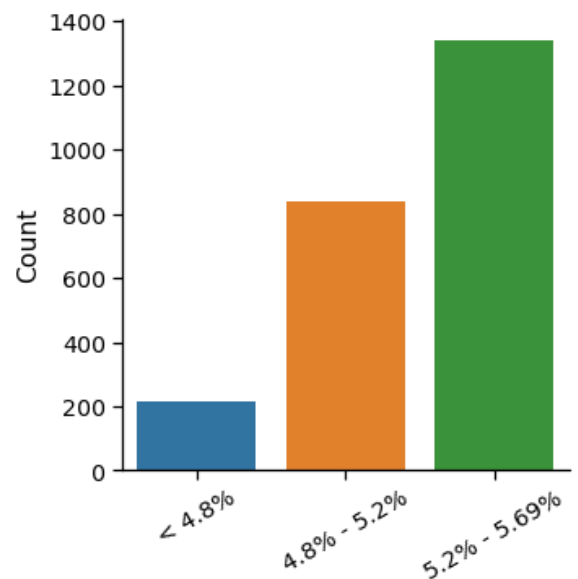
**Fig 11 Control group age distribution**



**Fig 12: Yoga group age distribution**



**Fig 13 Control group HbA1c distribution**



**Fig 14: Yoga group HbA1c distribution**

The 95% CI for ARR does not include the value 0, and neither does the 95% CI for RRR; similarly, the 95% CI for RR does not include the value 1. Thus, these results are statistically significant.

**Table 10: T2DM incidence in Yoga and Control groups**

Group	Total	Incidence of T2DM	Non-incidence of T2DM	Risk <sup>1</sup>
Intervention (Yoga)	2396	208	2188	8.68%
Control	2064	360	1704	17.44%

<sup>1</sup> Risk defined as proportion of incidences

**Table 11: Absolute and relative risk reduction of conversion to T2DM between Yoga and Control groups**

Measure	Value	95% CI	P <sup>1</sup>
Absolute Risk Reduction (ARR)	8.76%	6.77 – 10.75	< 0.0001
Relative Risk (RR)	0.498	0.42 – 0.58	< 0.0001
Relative Risk Reduction (RRR)	50.23%	41.58 – 57.60	< 0.0001

<sup>1</sup> CIs and P-values were calculated according to (Altman, 1991)

### 5.5.3 Adverse effects

There were no major adverse events or mortality during these 3 months of follow-up. Some participants reported mild pain in the lumbar or dorsal region during the yoga classes which was relieved by the end of the core practice session after practicing corrective posture (*pavanamuktasana* lumbar stretch for back pain), deep relaxation in supine posture, pranayama and meditation.