TYPE 2 DIABETES MELLITUS IN INDIA

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1. Background

It has been estimated that the global burden of type 2 diabetes mellitus (T2DM) for 2010 would be 285 million people (2010) which is projected to increase to 438 million in 2030; a 65 % increase (Snehalatha and Ramachnadaran 2009). Similarly, for India this increase is estimated to be 58%, from 51 million people in 2010 to 87 million in 2030 (Snehalatha and Ramachnadaran 2009). The impacts of T2DM are considerable: as a lifelong disease, it increases morbidity and mortality and decreases the quality of life. (Hoskote and Joshi 2008). At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society. A better understanding about the cause of a predisposition of Indians to get T2DM is necessary for future planning of healthcare, policy and delivery in order to ensure that the burdens of disease are addressed (Hoskote and Joshi 2008).

This chapter on will focus on type T2DM and will provide a description of prevalence and incidence of T2DM in India; it will describe the health related complications, along with its various risk factors and recommended treatment. It will discuss current management practices and government policies for T2DM in India as well as identify policy and research gaps.

Morbidity and Mortality associated with Diabetes

Global Morbidity and Mortality associated with Diabetes

- Close to four million deaths in the age group of 20-79 years in 2010 (International Diabetes Federation (IDF) Report 2009)
- Accounting for 6.8% of global all-cause mortality in this age group in 2010 (IDF 2009). IDF 2006 reported >50 million diabetes people in South East Asia.
- 7.97 million DALYs were lost because of diabetes (Jönsson 1998)

Diabetes Morbidity and Mortality in India

- Responsible for 109 thousand deaths in 2004 (Venkataraman et al. 2009)
- 1.157 million years of life lost in 2004 (Venkataraman et al. 2009)
- 2.263 million disability adjusted life years (DALYs) in India during 2004 (ICMR 2006)

2. What is T2DM Mellitus?

T2DM is a non-autoimmune, complex, heterogeneous and polygenic metabolic disease condition in which the body fails to produce enough insulin, characterized by abnormal glucose homeostasis (Gupta et al. 2008). Its pathogenesis appears to involve complex interactions between genetic and environmental factors (Gupta et al. 2008). T2DM occurs when impaired insulin effectiveness (insulin resistance) is accompanied by the failure to produce sufficient β-cell insulin (Permutt et al. 2005).

2.1 Causes of T2DM

T2DM as a common and complex disease has been characterized by the following causes:

- Obesity: obesity is also considered a key risk factor for T2DM. The association between increasing body mass index (BMI) and greater weight gain and risk of diabetes is most pronounced among Asians, suggesting that lower cut off BMI values are needed to identify Asians at a higher risk of diabetes (Shai et al. 2006). BMI cut point for Indians for any cardio-metabolic risk factors is 23 kg/m^2 in both sexes, whereas that of waist circumference (WC) is 87cm for men and 82cm for women (Mohan et al. 2007).

- Abdominal adiposity: there is also a probable indication that there is a preferential abdominal adiposity in Indians irrespective of the degree of general adiposity (Ramachandran et al. 2002).

- Imbalance of human metabolism is associated with T2DM: Changes in work patterns from heavy labour to sedentary, the increase in computerization and mechanization, and improved transport are just a few of the changes that have had an impact on human metabolism (Zimmet et al., 2001).

- Genes: since 2007, genome-wide association studies has catalogued around 20 genes (like TCF7L2, HHEX, CDKAL1, SLC30A8 etc.) showing a strong association (with modest odds ratio ranges between 1.2 to 1.5) with T2DM (Sladek et al. 2007, WTCCC 2007, Scott et al. 2007, Zeggini et al. 2007).

- Ethnicity: the interethnic differences (like differences in prevalence of T2DM among Europeans, Americans, Chinese, and Asian Indians) in insulin resistance may have an environmental or genetic explanation. The main acquired factors that seemingly increase insulin resistance in all ethnic groups include obesity, sedentary lifestyle, diet rich in animal products, and aging (Abate and Chandalia 2001).

2.2 Complications of Diabetes in India

The burden of diabetes is to a large extent the consequence of macrovascular (coronary artery disease, peripheral vascular disease, and atherosclerosis) and microvascular (like retinopathy, neuropathy, and nephropathy) complications of the disease (Permutt et al, 2005) (table1).

Table-1: Studies on diabetes complications (Joshi et al. 2008)

Author (Reference)	Type of the study	City	Prevalence
RETINOPATHY			
Rema *et al*, 1996	Clinical based	Chennai	34.1%
Dandona *et al*, 1999	Population based	Hyderabad	22.6%
Ramachandran *et al*, 1999	Clinical based	Chennai	23.7%
Rema *et al*, 2000	Clinic based	Chennai	7.3%
Narendran *et al*, 2002	Population based	Palakkad	26.8
Rema *et al*, 2005	Population based	Chennai	17.6%
NEPHROPATHY			
John *et al*, 1991	Clinic based	Vellore	Microalbuminuria: 19.7% Diabetic nephropathy: 8.9%
Gupta *et al*, 1991	Clinical based	New Delhi	Microalbuminuria: 26.6%
Yajnik *et al*, 1992	Clinic based	Pune	Microalbuminuria: 23.0%
Vijay *et al*, 1994	Clinical based	Chennai	Proteinuria: 18.7%
Mohan *et al*, 2000	Clinical based	Chennai	Macroproteinuria with retinopathy: 6.9%
Varghese *et al*, 2001	Clinical based	Chennai	Microalbuminuria: 36.3%
CORONARY ARTERY DISEASE			
Mohan *et al*, 1995	Clinical based	Chennai	17.8%
Ramachandran *et al*, 1999	Clinical based	Chennai	11.4%
Mohan *et al*, 2001	Population based	Chennai	21.4%
PERIPHERAL VASCULAR DISEASE			
Premalatha *et al*, 2000	Population based	Chennai	6.3%
PERIPHERAL NEUROPATHY			
Ramachandran *et al*, 1999	Clinical based	Chennai	27.5%
Ashok *et al*, 2002	Clinical based	Chennai	19.1%
Pradeepa *et al*	Population based	Chennai	26.10%
CAROTID ATHEROSCLEROSIS			
Mohan *et al*, 2001	Population based	Chennai	20%

3. Prevalence of T2DM

Global Prevalence: The number of cases of diabetes worldwide in the year 2000 among adults (≥20 years) was estimated to be 171 million and will rise to 366 million by 2030 (Wild et al. 2009). In terms of rank of countries for T2DM prevalence, Ukraine (3.2 million) is at the bottom of the list, Pakistan (5.2 million) comes at number six, China is second with 20.8 million people and India has the highest number (31.7 million) of people with rate of 3% for T2DM (see Table-2).. The Pima Indians of Arizona in the United States (US) and have the highest prevalence rates (21%) of T2DM (King et al. 1998; Knowler et al. 1978). A study by Ravussin et al. (1994) compared the prevalence of T2DM in Pima Indians living in Arizona to members of a population of Pima ancestry living in northwestern Mexico. In association with marked lifestyle differences, the two genetically related populations had very different prevalence of diabetes. The Pima Indians living in Mexico were found to have a prevalence of 6% and 11%, for men and women, respectively, as compared to the frequency of 54% and 37% reported in the Pima Indians living in Arizona.

Table-2: Top ten countries for number of persons with Diabetes *(Wild et al. 2009)*

Rank		Year 2000	Rank		Year 2030
	Country	People with T2DM (million)		No. Country	People with T2DM (million)
1.	India	31.7	**1.**	India	79.4
2.	China	20.8	**2.**	China	42.3
3.	USA	17.7	**3.**	USA	30.3
4.	Indonesia	8.4	**4.**	Indonesia	21.3
5.	Japan	6.8	**5.**	Pakistan	13.9
6.	Pakistan	5.2	**6.**	Brazil	11.3
7.	Russia Fed	4.6	**7.**	Bangladesh	11.1
8.	Brazil	4.6	**8.**	Japan	8.9
9.	Italy	4.3	**9.**	Philippines	7.8
10.	Ukraine	3.2	**10.**	Egypt	6.7

3.1 Prevalence of T2DM in India:

Estimated prevalence rates in for urban and rural India are based on national surveys and individual studies. (Tables 3+4) Estimates vary depending on geographical location and year of study.

3.1.1 Urban India: In the urban population, an Indian Council of Medical Research (ICMR) study in 1972 reported a prevalence of 2.3% (Ahuja 1979) which rose to 12.1% in the year 2000 (Ramachandran et al. 2001). More recently, Mohan et al. (2008a) provided estimates from a nation-wide surveillance study of T2DM and found that in urban areas there was a prevalence 7.3% of known T2DM and a prevalence of 3.2% in peri-urban/slum areas (urban fringes).

Table-3: Prevalence of Diabetes in Urban Cities of India

Place	Year	Author	Area	Prevalence (%)
Kashmir	2000	Zargar et al. 2000.	North	**6.1**
New Delhi	1972	Ramachandran et al. 2005	North	**2.3**
New Delhi	1991	Ramachandran et al. 2005	North	**6.7**
New Delhi	2001	Ramachandran et al. 2005	North	**10.3**
New Delhi	2005	Prabhakarn et al. 2005	North	**15.0**
Mumbai	2001	Ramachandran et al. 2001	West	**9.3**
Jaipur	2003	Gupta et al. 2003	West	**8.6**
Guwahati	1999	Shah et al. 1999	East	**8.3**
Kolkata	2001	Ramachandran et al. 2001	East	**11.7**
Thriuvananthapuram	1999	Raman et al. 1999	South	**16.3**
Hyderabad	2001	Ramachandran et al. 2001	South	**16.6**
Bengaluru	2001	Ramachandran et al. 2001	South	**12.4**
Chennai	2001 2006	Ramachandran et al. 2001 Mohan et al. 2006	South	**13.5** **14.3**
Ernakulam	2006	Menon et al. 2006	South	**19.5**
Vellore		Raghupathy et al. 2007	South	**3.7**
Tamil Nadu	2008	Ramachandran et al. 2008	South	**18.6**
India	2001	Sadikot et al. 2004	NA	**5.6**
Multi-centric	2008	Mohan et al. 2008 (WHO-ICMR)	Multi-centric	**7.1**

3.1.2 Rural India: An early study in 1991 of rural areas in Delhi indicated that the prevalence rate for T2DM ranged from 0.4-1.5% (Ahuja et al. 1991) (table 4). Prevalence rates vary according to measuring criteria used e.g. using the American diabetes association criteria, it has recently been estimated to be 1.9% in the rural areas; but with using the WHO criteria the estimate increased to 2.7% (Sadikot et al. 2004).

Other studies indicate higher rates. Data from a large-scale survey on 4,535 individuals aged ≥30 years from 20 villages of Godavari, a developing rural area of Andhra Pradesh, suggests that rural India may soon experience the urban epidemic of T2DM. (Chow et al. 2006) Estimates of T2DM prevalence were calculated by applying sampling weights derived from the 2004 census where T2DM was defined by disease history and/or fasting glucose of 7.0 mmol or over. The results indicated that the prevalence for known T2DM was of 6.4%, for undiagnosed T2DM 6.8%, and that 15.5% had

Table-4: Prevalence of Diabetes in Rural India

Place	Year	Prevalence (%)	References
Delhi	1991	1.5	Ahuja 1991
Delhi	1991	0.4	Ahuja 1991
Punjab	1994	4.6	Wander et al. 1994
Srinagar	2000	4.0	Zargar et al. 2000
India	2001	2.7	Sadikot et al. 2004
Rajasthan	2004	1.8	Aggarwal et al. 2004
Mysore	2005	3.8	Basavanagowdappa et al. 2005
Maharashtra	2006	9.3	Deo et al. 2006
Nagpur	2007	3.7	Kokiwar et al.2007
Vellore	2007	2.1	Raghupathy et al. 2007
Tamil nadu	2008	9.1	Ramachandran et al. 2008
Multi-centric	2008	3.1	Mohan et al. 2008

impaired fasting glucose. While these data are by no means representative of rural India as a whole, they imply increases of T2DM. Figures based on National Family Health Survey (NFHS) in 2005-06 suggest the prevalence of T2DM in rural India are highest in Kerala, Tripura, West Bengal, Goa and Sikkim, (1500 to >2000 individuals per 100,000 individuals) and least in central India (<500 individuals per 100,000 individuals). (See figure below)

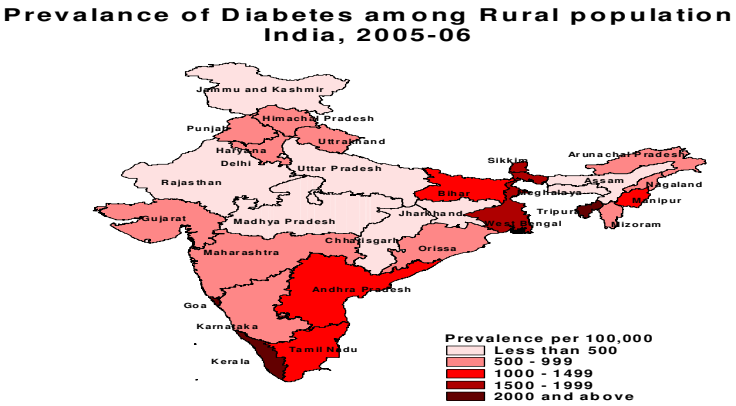
3.1.3 Sex and Socio-economic status based prevalence of T2DM

Data from the NFHS of 2005-06 suggested that the number of women who have diabetes ranges from 0.28% women in Rajasthan to 2.54% women in Kerala. Five states (Tamil Nadu, Goa, Tripura, West Bengal, and Delhi) have relatively high (>1.5%) number of women with T2DM. Rajasthan, Uttar Pradesh, and Assam, and Maharashtra have T2DM prevalence levels below 0.5%. Among men, six states: Kerala, Goa, Tripura, West Bengal, Andhra Pradesh, and Sikkim, have prevalence level >1.5%. Five states: Kashmir, Mizoram, Himachal Pradesh, Rajasthan, Uttar Pradesh have prevalence below 0.5% from men.

The highest prevalence of T2DM in developing countries occurs in the higher socio-economic groups and this also true for the Indian population. For example, Boddula et al. in 2008 in their research on 1,112 affluent adult Indian subjects found the prevalence of T2DM to be 21.1%, the highest prevalence of T2DM reported from within India to date.

3.2 Incidence of T2DM in India

Mohan et al. 2008 found that the incidence of:
(1) T2DM in the urban south Indian population was 20.2 per 1,000 person years,
(2) Pre-T2DM was 13.1 per 1,000 person years,
(3) T2DM among subjects with impaired glucose tolerance (IGT) at baseline was higher compared to those with normal glucose tolerance (NGT).
This research team recommended that Indian Diabetes Risk Score (IDRS) was best predictive tool of estimating incidence of T2DM in Asian Indians.



4. Economic Burden of Diabetes in India

Despite diabetes being a life-long disorder and is expensive to manage and treat for the large proportion of subjects in developing societies, there is lack of data on its economic burden in India. In the Indian context the financial burden is often shared by relatives of the patients (Ramachandran 2007). The health care budget of the government in India is a meager 2% (Shobhana and Ramachandaran 2007) compared to 14% to defense (Indian Budget 2010: *http://indiabudget.nic.in/*). The total amount needed for India to treat T2DM is estimated to around 2.2 billion USD. (Ramachandran 2007). In India the direct medical cost to identify one subject with insulin glucose tolerance is INR 5,278 (Ramachandaran et al. 2007a). The cost of insulin amounts to 350.00 USD (16,000 Indian Rupees) per year, while medication for non-insulin-requiring patients costs about 70.00 USD per year (Shobhana and Ramachandaran 2007). In the Indian context these costs are prohibitive: 75.5% of the Indian population is earning less than $2 per day and 41.6% less than $1.25 per day (Prabhakaran and Ajay 2009).

Kumar et al. 2008 analyzed the community based data available from the middle and high income groups in Delhi (DEDICOM survey) to determine the direct cost of ambulatory diabetes care, to evaluate the socio-demographic associates of spending, and to ascertain the relationship of spending with the delivered quality of diabetes care. They concluded that a majority of diabetes patients spend a significant proportion of their family income on diabetes related expenditure (~Rs. 6000 i.e. ~US$ 150) per year. The cost is higher for subjects with longer duration since diagnosis, those with higher education or income, those with co-morbidities and those requiring oral hypoglycemic agents or insulin.

In developing countries like India, the brunt of diabetes and cardiovascular disease occurs among the economically productive age group (20-45 year olds) (WHO 2005). Diabetes mellitus is responsible for 1157 thousand years of life lost due to the disease, and for 2263 thousand DALYs during 2004 (ICMR 2006).

Table-5: Cost of diabetes borne by in and out-patient subjects and subjects needing surgical care. (*Ramachandran 2007*)

Variables	Inpatient Care N = 122 (1)	Outpatient Care N = 260 (2)	Patients Needing Surgical Care, N = 40 (3)
Annual Family Income	**48,000 (3,600-6,00,000)**	**48,000 (2,400-10,80,000)**	**45,000 (2,400-6,00,000)**
Money spent on DM* Investigations, Physicians fees and Medicine	**6,725 (620-41,000)**	**3,050 (364-48,450)**	**5,395 (350-73,700)**
Expenditure on Hospitalization	**5,000 (300-30,000)**	**Nil**	**9,000 (2,800-3,10,000)**
Expenditure on Transport	**300 (3-30,000)**	**200 (4-12,000)**	**200 (5-50,000)**
Average expenditure**	**7,505 (400-75,200)**	**3,310 (360-48,600)**	**13,880 (550-75,200)**
Proportion of Income spent on DM#	**17.5%**	**7.7%**	**16.3%**
*** 1 vs 2 P = 0.0001; 2 vs 3 P = 0.01; 3 vs 1 P = 0.36 ** 1 vs 2 P = 0.0001; 2 vs 3 P = 0.004; 3 vs 1 P = 0.10 # 1 vs 2 P = 0.0001; 2 vs 3 P = 0.0013; 3 vs 1 P = 0.86**			

Data are median values in Indian rupees-range given in brackets.

5. Risk factors of Diabetes

The known risks factors of T2DM embedded in nature (genetic) as well as nurture (i.e. environmental factors including intrauterine environment) are as follows:

Modifiable Risk Factors	Studies
Obesity (via BMI and WHR)	Meta-analysis done by Vazquez et al. 2007 demonstrated the pooled relative risks for incident diabetes of 1.87 (95% confidence interval (CI): 1.67-2.10), 1.87 (95% CI: 1.58-2.20), and 1.88 (95% CI: 1.61-2.19) per standard deviation of body mass index, waist circumference, and waist/hip ratio, respectively, demonstrating that these three obesity indicators are the important risk factor for diabetes.
Physical Inactivity	The protective effect of physical activity in subjects with an excessive BMI and elevated glucose levels; physical activity and weight control are critical factors in diabetes prevention in subjects with both normal and impaired blood glucose regulation (Hu et al. 2004**).**
Plasma Lipids and Lipoproteins Level	It has been reported by various workers that T2DM patients have elevated levels of total cholesterol, LDL-Chol, VLDL-Chol, hypertriglyceridemia and reduced levels of HDLChol (Laasko et al., 1987; Demant, 2001; Petersen et al., 2002; Eschwege, 2003). American Diabeets Association recommends that LDL Cholesterol should be <100 mg/dL; HDL Cholesterol: >60 mg/dL; and Triglycerides: <150 mg/dL (http://www.diabetes.org/diabetes-basics/prevention/checkup-america/cholesterol.html).
Hypertension	In San Antonio Heart Study, the odds of incident diabetes were 2.21 greater for individuals with prehypertension than for those with normal blood pressure (95% CI 1.63–2.98) after adjusting for age, sex, and ethnicity (Mullican et al. 2009). The prospective cohort study found that T2DM mellitus was almost 2.5 times as likely to develop in subjects with hypertension as in subjects with normal blood pressure (Gress et al. 2000).
Dietary Habits	Mohan et al. 2009 found an odds ratio (OR) of 5.3 (2.98-9.45), p-vale<.001 for Refined Grains and an OR of 0·31 (0·15, 0·62), p-vale<.001 for dietary fiber intake (inversely related). Misra et al. 2009 suggested that whole grains are rich in components like dietary fiber, starch, fat, antioxidant nutrients, minerals, vitamin, lignans, and phenolic compounds that have been linked to the reduced risk of obesity, insulin resistance, dyslipidemia, T2DM, heart diseases. Intervention study of Stanhope et al. 2009 found dietary fructose specifically increases de novo lipogenesis, promotes dyslipidemia, decreases insulin sensitivity, and increases visceral adiposity in overweight/obese adults. This study proves fasting plasma glucose and insulin levels increases during fructose but not glucose consumption.

Non-modifiable Risk Factors	
Family History	Viswanathan et al. 1996 in their study found nearly 75% of the T2DM patients have first degree family history of diabetes. The prevalence among offspring with one diabetic parent to be 36%, which increased to 54% when there was a positive family history of diabetes on the non-diabetic parental side also. When both parents had diabetes, the prevalence rate increased further (62%) Typical estimates of the heritability of T2DM and related continuous traits (beta-cell function, insulin sensitivity, BMI) lie in the 30-60% range (Stumvell et al. 2005). Most conservative estimates place long term concordance at about 60%, which is at least double to that of dizygotic twins (Elbein et al. 2002). Black children with a family history of T2DM have 25% lower insulin stimulated glucose disposal compared with black children without a family history of T2DM (Danadian et al. 1999).
Genetic factors	Since 2007, genome-wide association studies has catalogued around 20 genes (like TCF7L2, HHEX, FTO, CDKAL1, SLC30A8 etc.) showing strong association (with modest odds ratio ranges between 1.2 to 1.5) with type2 diabetes (Sladek et al. 2007, WTCCC 2007, Scott et al. 2007, Zeggini et al. 2007).
Low/High Birth Weight **(Intra-uterine Environment exposure)**	Low birth weight is implicated as a risk factor for T2DM. Meta-analysis done by Whincup et al. 2008 found a combined OR of 0.75 (95% CI, 0.70-0.81) per kilogram (increase in weight) of T2DM, adjusted for age and sex, in the 28 populations. The inverse association between birth weight and T2DM risk appeared graded in all studies, particularly at birth weights of 3 kg or less. In the same study the meta-analysis of the 16 studies with individual, ungrouped birth weight data, the OR of T2DM associated with a 1-kg increase in birth weight at birth weights above 3 kg was 0.85 (95% CI, 0.68-1.05). Harder et al. 2006 found that low birth weight (<2,500 g), as compared with a birth weight of >2,500 g, was associated with increased risk of T2DM (OR- 1.32, 95% CI: 1.06-1.64). High birth weight (>4,000 g), as compared with a birth weight of 4,000 g, was associated with increased risk to the same extent (OR- 1.27, 95% CI: 1.01-1.59). These findings indicate that there exists a relation between birth weight and later-life risk of T2DM which is not linearly inverse but U-shaped (Harder et al. 2006)

6. Prevention of T2DM in India

Due to the ssubstantial personal and economic burden of T2DM, the WHO Collaborating Centre for Diabetes in India (Chennai) is actively engaged in the primary prevention of diabetes, childhood obesity and other related disorders by the promotion of health and reduction of risk factors through the individual and on a community basis. There are two approaches for the prevention of diabetes:

1. **Population approach:** Aims to bring about important changes in the health of a large percentage of the population. Based on promoting healthy lifestyles that are effective in the prevention of T2DM (Alberti et al. 2007).
2. **High risk approach:** Identification of those who may be at higher risk the measurement of risk and intervention to prevent the development of T2DM (Alberti et al. 2007) in affected individuals (table-6).

Table-6: Five simple tools for Identifying risk category for T2DM

1	Age above 40 years	**High:** Positive family history with one or two risk factors
2	Positive family history of diabetes	**Moderate:** Increased Age with sedentary lifestyle and increased waist circumference
3	Increased abdominal fatness (Waist circumference Male >=90cms, Female >=85cms)	**Low:** Presence of any 1 risk fcator
4	Pre-diabetes	
5	Sedentary lifestyle	
Published by M. V. Hospital for Diabetes & Diabetes Research Centre (WHO Collaborating Centre for Diabetes)		

Targeting pre-diabetes for life-style interventions is another approach because the relation between glycaemia and incidence of diabetes is non-linear, with the risk threshold coinciding with the onset of pre-diabetes (Venkat et al. 2002). Trials have shown the benefits of prevention or delay for people with pre-diabetes (Venkat et al. 2002). An effective delivery of lifestyle intervention to pre-diabetics will ensure that most future cases of diabetes are targeted. Methods of creating awareness are listed in table 7:

Table-7: Methods of Creating Awareness (*Never be a One Time but a Regular Ongoing program*)

Methods	Channels
Camps – Screening and education Awareness Campaigns/ programs Exhibitions/Fair Seminars/Conferences Rallies/Walks Folk Arts	**1.** Distribution of pamphlets, manuals, cards **2.** Advertisements in magazines, newspapers and other commonly read books. **3.** T.V, Radio, Media **4.** Health education curriculum in schools, workplaces. **5.** Lectures in various places like, Public meetings, religious gatherings **6.** Awareness programs by lecture and counseling in schools, colleges, offices, women's organizations

(Developed from WHO Collaborating Centre for Diabetes, Chennai)

Somannavar et al. 2008 conducted a large scale community based "Prevention Awareness Counselling Evaluation" (PACE) Diabetes Project to increase awareness of diabetes and its complications in Chennai city (population : 4.7 million) through:
1. public education
2. media campaigns
3. general practitioner training
4. blood sugar screening and
5. community based "real life" prevention program.

Multiple television and radio shows were given and messages about diabetes sent as Short Message Service (SMS) through mobile phones. The research team estimated that the diabetes prevention messages reached nearly two million people in Chennai, making it one of the largest diabetes awareness and prevention programs ever conducted in India (Somannavar et al. 2008). But, It is not clear from their paper whether this awareness program really increased awareness or not.

6.1 Diagnosis of T2DM: In 1985, WHO classified diabetes in terms of insulin-dependency (i.e. requirement of insulin for survival). The terminology is thus: Insulin dependent diabetes mellitus (IDDM) and Non-insulin dependent diabetes mellitus (NIDDM) (Zimmet et al. 2002). The latest dichotomy is type 1 and T2DM mellitus (Zimmet et al. 2002). Importantly, the two terms impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG) are not synonymous and the two conditions may have different implications. They are now categorized as a stage in the natural history of disordered carbohydrate metabolism as the people with it are at higher risk for diabetes than general population (Zimmet et al. 2002).

Table-8: WHO (1999) Criteria for the Diagnosis of Diabetes Mellitus (*ICMR guidelines also have the same diagnostic criteria for India*)

S.No.	Categories of Hyperglycemia	Glucose Concentrations mmol/l (mg/dl) Plasma
1.	Diabetes Mellitus	
	Fasting	>=7.0 (>=126)
	2-hour post glucose load (75g)	>=11.1 (>=200)
2.	Impaired Glucose Tolerance (IGT)	
	Fasting	<7.0 (<126)
	2-hour post glucose load (75g)	>=7.8 (>=140) and <11.1 (<200)
3.	Impaired Fasting Glycemia (IFG)	
	Fasting	>=6.1 (>=110) and <7.0 (<126)
	2-hour post glucose load (75g)	<7.8 (<140)

6.2 Treatment for Diabetes: Diabetes is a chronic condition that requires continuing medical care and self-management in order to minimize the risk of complications and mortality. The goals of treatment are (Norris et al. 2008),

1. To achieve optimal glycemic control;
2. To reduce other cardiovascular risk factors, including hypertension, hyperlipidemia, and overweight and obesity; and
3. To diminish complications such as heart disease, peripheral vascular disease, renal disease, and neuropathy.

T2DM may be treated by diet and exercise, often combined with 1 or more oral hypoglycemic agents. Optimal treatment, however, may require the use of insulin with or without oral agents. Among adults with diagnosed diabetes, the current distribution of types of treatment is as follows: 12% use both insulin and oral drugs, 16% use insulin only, 57% use oral agents only, and 15% do not use pharmacotherapy (Norris et al. 2008). The efficacy of drugs used in the treatment of T2DM are illustrated in table 9.

6.2.1 Alternative Treatments for T2DM: Systematic review of the published literature on the efficacy and safety of herbal therapies and vitamin/mineral supplements for glucose control in patients with diabetes suggest that there is still insufficient evidence to draw definitive conclusions about the efficacy of individual herbs and supplements for diabetes; however, they appear to be generally safe (Gloria et al. 2003). The best evidence for efficacy from adequately designed randomized controlled trials (RCTs) is available for *Coccinia indica* and American ginseng. Chromium has been the most widely studied supplement (Gloria et al. 2003). Other supplements with positive preliminary results include *Gymnema sylvestre*, *Aloe vera*, vanadium, *Momordica charantia*, (Gloria et al. 2003).

7. T2DM Management in India

The practical management of T2DM in developing countries is often made difficult by scarcity of health care personnel, monitoring equipment and drugs, especially in more remote areas (Ministry of family health and family welfare, 1984). In 2003, the ICMR conducted a workshop for the development of guidelines for the management of T2DM in consultation with WHO. They were published in 2005 (ICMR 2005) and are available on the internet (www.icmr.nic.in/guidelines-diabetes/).

Although, India has worked continuously to improve its health care system in recent decades and efforts have been made to expand the public health system and reduce the burden of disease, there remains no universal coverage (Rao et al. 2002). The healthcare delivery is shared by institutions run by state where free medical care is offered, private institutions where patients have to pay for the services and a large number of private medical practitioners (Ramachandran 2007).

It has been demonstrated that treatment outcome in diabetic patients is far from optimal in India (Raheja et al. 2001; Nagpal and Bhartia 2006). For example, Ramachandran et al. in 2008 analyzed and compared the clinical profile and glycaemic outcome in known diabetic cases in South Indian urban and peri-urban populations and found that the clinical outcome in known diabetic cases was far from satisfactory even in the city where specialized diabetes care was available [e.g. mean age at diagnosis was 45.3 years, prevalence of hypertension was 57.4% (32% known); 48% were obese and a larger percentage (63.3%) had abdominal obesity; Dyslipidaemia was present in nearly 50%].

Table-9: Efficacy of Drugs used in the Treatment of T2DM (*Padwal et al. 2005*)

Drug	Study	Population* (mean age or age range)	RR (95% CI)	Follow-up (years/rate†)
Metformin 1,700 mg (1,073; 22%) vs. placebo (1,082; 29%)	RCT, Diabetes Prevention Program, US	2,155 patients with IGT and a FPG level of 5.3–6.9 mmol/l (>25 years)	0.69 (0.57–0.83)	2.8/93%
Phenformin 50 mg (92; 14%) vs. placebo (89;16%)	RCT, Jarrett et al. (England)	204 men with IGT from the Whitehall Survey (56 years)	0.90 (0.45–1.80) ‡	5.0/89%
Troglitazone 400 mg (114; 20%) vs. placebo (122; 45%)	RCT, TRIPOD (U.S.)	266 Hispanic women with gestational diabetes (35 years)	0.45 (0.25–0.83)	2.5/67%
Tolbutamide 1,000 mg (123; 11%) vs. placebo (125; 9%)	RCT, Keen et al. (U.K.)	248 patients with IGT from the Bedford Diabetes Survey (57 years)	1.20 (0.56–2.6)‡	7.0/not specified
Troglitazone 400 mg daily then rosiglitazone 4 mg daily or pioglitazone 30 mg daily (101; 3.0%) vs. untreated comparison group (71; 26%)	Cohort, Durbin	172 patients with IGT (29–86 years) with a FPG level of 5.6–7.0 mmol/l and a 2-h postprandial glucose level between 7.8 mmol/l and 11.1 mmol/l	0.11 (0.03–0.36)	3.0/100%
Antiobesity Agent: Orlistat 360 mg (1,640; 6%) vs. placebo (1,637; 9%)	RCT, XENDOS (Sweden)	3,305 obese patients (30–60 years)	HR 0.63 (0.46–0.86)	4.0/43%
Antihypertensive agents: Verapamil-based therapy (8,098; 7.0%) vs. tenololbased therapy (8,078; 8.2%) Trandolapril and hydrocholorthiazide were second-line agents.	RCT, INVEST (North America, Europe, and Central America)	6,176 patients with hypertension and CAD (≥50 years)	0.85 (0.77–0.95)	2.7/97.5%
Statins—Pravastatin 40 mg (3,150; 4.0%) vs. placebo (3,067; 4.5%)	post hoc analysis of RCTs, LIPID (Australia and New Zealand)	6,997 patients with dyslipidemia (31–75 years)	0.89 (0.70–1.13)‡	6.0/100%
Simvastatin 40 mg (7,283; 4.6%) vs. placebo (7,325; 4.0%)	post hoc analysis of RCTs, Heart Protection Study (U.K.)	14,573 patients at high cardiovascular risk (40–80 years)	1.15 (0.99–1.34)‡	5.0/100%
Fibrates: Bezafibrate 400 mg (156; 42%) vs. placebo (147; 54%)	post hoc analysis of RCT, BIP (Israel)	303 patients with IGT from the Bezafibrate Infarction Prevention Trial	HR 0.70 (0.49–0.99)	6.2/100%
Estrogen replacement Therapy: Estrogen 0.625 mg/medroxyprogesterone. 2.5 mg (999; 6.2%) vs. placebo (1,030; 9.5%)	post hoc analysis of RCT, HERS (U.S)	2,029 postmenopausal Caucasian women with CAD (<80 years)	0.65 (0.48–0.89)	4.1/98%
Estrogen replacement Therapy: Current use (7,314; 2.3% vs. never used (9,761; 7.6%)	Cohort, studies, Nurses Health Study (U.S.)	21,028 postmenopausal women (mean age 50 years)	0.82 (0.7—0.96)	12/93%

*Excluding patients with T2DM at baseline. †Refers to the percentage of patients with complete follow-up. ‡RR and CI, calculated from the data presented using intention-to-treat analysis.

Despite the progressive rise in expenditure on diabetes care, the quality of diabetes care delivered to patients in India continues to be poor (Nagpal et al. 2006). Studies on spending on diabetes care from India do not segregate type 1 and T2DM patients and are restricted to patients who were being followed up in hospitals, clinics or health centers or who were known to community health workers (Ramachandran et al. 2007; Shobhana et al. 2000).

There is also lack of awareness and knowledge of T2DM. For example, the Chennai Urban Rural Epidemiology Study (CURES) reported that nearly 25% of the population was unaware of a condition called diabetes. Only around 40% of the participants felt that the prevalence of diabetes was increasing and only 22.2% of the population and 41% of known diabetic subjects felt that diabetes could be prevented (Deepa et al. 2005). The study of Balagopal et al. 2008 in a resource-poor village of Tamil Nadu indicated that an educational intervention reduced fasting blood glucose levels of pre-diabetic adults by 11%, pre-diabetic youth by 17%, and type 2 diabetic adults by 25%. The intervention consisted of some sessions on dietary modification (increasing fiber, reducing fat, and portion control), improving physical activity, simple relaxing breathing techniques, reduces risk factors like obesity and dietary patterns of individuals with pre-diabetes and diabetes.

To shed light on the doctors and patients' knowledge, expectations and to understand the barriers to achieving good glucose control among patients and health professionals, IMPROVE Control India (ICI) study was conducted. This study showed that though insulin therapy is accepted as one of the most effective and dependable treatment option in management of diabetes, there are several barriers to its usage among type 2 diabetic cases particularly the acceptance of insulin therapy. (Joshi et al. 2008)

Moreover, there are issues of access to diabetes health care services. Seventy per cent of the population live in rural areas is has been argued that to meet the diabetic patient's requirements and ensure easy approach to the health centers, patients needs easy access to primary services and transportation by ambulance to regional diabetes health center for further management (Rao et al. 2002). Unlike in the developed world, the availability of a trained workforce is a real deficiency in rural India (Fairoz 2007). It is difficult recruit current medical services in rural areas to offer diabetic patient a variety of services pertaining to diabetic care such as guidance on nutrition, lifestyle changes, family support and counselling, treatment, and appropriate referrals (Fairoz 2007). Evidence further suggests that low and middle income group of patients prefer private hospital care but that the expenses cause a severe financial burden (Ramachandran 2007).

7.1 Health programs in India

Mohan in 2004 suggested that India needs strategies to achieve healthy fetal and infant growth and a programme which encourages the use of traditional diets rich in fibres. Appropriate interventions should be attempted in those who are genetically predisposed to diabetes in order to tackle the explosion of, and thereby reduce the burden due to, diabetes within the Indian subcontinent (Mohan 2004)**.** Presently there a number of programmes to improve diabetes care in situ in India and they include the following:

A. Government programs

1. **Pilot phase of the National Programme for Prevention and Control of Diabetes, Cardiovascular Diseases and Stroke (NPDCS) started in 2008.** This has the objective of risk reduction for prevention of non-communicable chronic diseases (Diabetes, CVD and Stroke) and early diagnosis and appropriate management of Diabetes, Cardiovascular diseases and Stroke. The expected outcomes for the pilot phase are awareness generated on HEALTHY LIFE STYLES; Health promotion at School, Community & work places; Decrease in the incidence of Non –Communicable Diseases particularly, Diabetes, Cardiovascular Diseases and Stroke

2. **National Rural Health Mission (NHRM)** is also providing the services for diabetes care in rural India. NRHM seeks to provide effective healthcare to rural population throughout the country with special focus on 18 states, which have weak public health indicators and/or weak infrastructure. It aims at effective integration of health concerns with determinants of health like sanitation & hygiene, nutrition, and safe drinking water through a District Plan for Health. One of its goal is the prevention and control of communicable and non-communicable diseases, including locally endemic diseases.

Programs Initiated by Diabetes Foundation of India (private NGO) are

1. **"MARG" (The Path)** focuses on primary prevention with the aim of creating awareness about diabetes, obesity, lipid disorders and heart disease in children and adolescents in North India. In order to enable children of age 9-18 years to disseminate messages regarding healthy living to peers and family, they are teaching children optimal dietary and lifestyle practices for prevention of lifestyle diseases. In the programme, more than 50,000 school children of three major cities in North India; Delhi, Jaipur, and Agra, will be educated over a period of three years. Surveys are to be conducted at the beginning and end of the project to evaluate the impact of the programme.
2. **'CHETNA**' Childrens' Health Education Through Nutrition and Health Awareness" is a program which aims to impart health education on the prevention of obesity, diabetes, and heart disease in school children. Lectures, posters, group discussions with children, parents and teachers, and health camps are devised to create awareness among the children about healthy lifestyle so that obesity related disorders like diabetes and heart diseases later in life are reduced.
3. '**TEACHER**'(Trends in childhood nutrition and lifestyle factors in India) is a multi-center project that is currently being undertaken in schools in 4 major cities of India. The aim is to obtain an in-depth understanding of nutrition and lifestyle behaviors that affect the health and well being of urban Indians, particularly children. Data is being collected on knowledge and attitudes as well as anthropometric measurements of children and their mothers

A Major Health Education Program Focusing on Women's Health and Nutrition:

A nutritional education program in India focusing on middle aged and elderly women was started with the help of a grant from the Department of Science and Technology. This project has been initiated in 8 cities and the women of age >30 years are targeted for proper nutrition and lifestyle advice and early detection of various diseases such as diabetes, obesity, heart problems and cancer. Mass awareness camps towards early detection and proper treatment of diabetes among the general public as well as among the medical and para-medical fraternity has been initiated. With the aim of spreading awareness about early screening for diabetes, several diabetes health camps have been organized for the poor in Delhi, UP and Haryana. Medical counseling, medicines and insulin are provided free of charge.

8. Indian Policy for Diabetes Management

The foundation of a diabetes health care system is central to that of public health care for diabetics. However, this will not occur unless the government and public health planners are aware of the potential problem (Rao et al. 2002). Progress in the control of T2DM is impeded by a health system that places a higher priority on communicable diseases and maternal and child health services and by a private health system driven by curative medicine (Siegel et al. 2008). However, prevention is cost-effective and should be a focus (Siegel et al. 2008). Although, diabetes action has been initiated, efforts are weak and fragmented (Siegel et al. 2008). Further, the variety of health care providers, lack of comprehensive national guidelines and protocol for health care services, including standards for health facilities, personnel and treatment protocols, makes it difficult to monitor and assure that quality services are provided universally (Venkataraman et al. 2009). More specifically the issues of providing improved care for diabetes center on the following:

Health system: Health care facilities are concentrated in large urban centers, are focused on tertiary care, and cater to the urban affluent. Government-run facilities are often crowded and under-resourced, so even low- and middle-income patients prefer private care or alternative medicine. For these populations, as much as 25% of income can be spent on diabetes care (Siegel et al. 2008). Initiatives such as National

Rural Health Mission (NRHM, which aims to improve rural health services), the NPCDS's health education components, the Public Health Foundation of India's (PHFI's) new public health schools, and the National Diabetes Control Program (which focuses on capacity building and rural health care delivery) are expected to increase capacity and resources (Siegel et al. 2008). However the success of this remains in its infant stages.

Food and nutrition: India has the worst stunting and iron deficiency in the world and also the largest number of people with diabetes, representing a failure in the nutrition governance system (Siegel et al. 2008). Many nutritional surveys are conducted throughout India, but they focus on under-nutrition; these should be expanded to include over-nutrition. Food consumption patterns and trade and agricultural policies have changed, encouraging over-consumption of unhealthy foods and under-consumption of healthy foods (Siegel et al. 2008).

Workforce: Unlike in the developed world, the availability of a trained workforce is a real deficiency in rural India (Fairoz 2007). It is difficult recruit current medical services in rural areas to offer diabetic patient a variety of services pertaining to diabetic care such as guidance on nutrition, lifestyle changes, family support and counselling, treatment, and appropriate referrals (Fairoz 2007). Recently, in order to compensate this gap, Medical Council of India jointly with Ministry of Health & Family Welfare (India) is planning to introduce a three-and-a-half year medical degree course (Bachelor in Rural Medicine and Surgery) to meet the shortage of doctors in rural areas (The Hindu, 7th February 2010: http://www.thehindu.com/2010/02/07/stories/2010020760601000.htm).

Urban design and transportation: India's urban design and transportation policies contribute to physical inactivity by encouraging the use of private cars and by making walking and cycling less feasible. Growth in the technology industry has encouraged the development of suburbs without adequate public transportation. More people are migrating to urban areas, straining urban infrastructure, but no national transportation survey has been conducted to identify needs (Siegel et al. 2008).

Economic Constraints: India needs a broader perspective and mission from the burgeoning health insurance industry to provide affordable access to its growing middle class, and construct care networks, including private hospitals, that can compete on quality and price (*Report on health systems in India, 2008*).

Table 10 below provides a blue print for addressing diabetes in India by illuminating opportunities and barriers for policy-makers and others.

Table-10: Blue print for addressing diabetes in India by illuminating opportunities and barriers for policy-makers and others (Siegel et al. 2008)

Examples of stakeholders	Roles	How capacity should be modified/ enhanced/ developed
Multilateral and bilateral organizations		
World Health Organization, World Bank, International Diabetes Federation	Technical capacity for prevention and for treatment, awareness, and capacity building Financial support for public policy NCD interventions (World Bank)	Implement UN Resolution on Diabetes. Build upon recent report
Central/state governments		
Indian Parliament, Ministry of Health and Family Welfare, Planning Commission of India, Ministry of Agriculture, Ministry of Urban Development, National Urban Renewal Mission	Prevention and treatment Develop better surveillance systems (improve Integrated Disease Surveillance program) Update dietary guidelines and ensure that available foods (and agricultural policies) reflect these guidelines. Promote active transportation Consider health effects of all economic development policies; use fiscal and regulatory mechanisms to influence individual behavior as well as that of industries	Develop multi stakeholder regulatory body to bring all players together (Planning Commission of India). Shift amount of resources allocated to "healthy policies"
Private sector (food industry, pharmaceuticals, and others)		
Confederation of Indian Industry	Provision of healthier foods and low-cost medicines and market innovation encouraging healthy eating and physical activity Increase access (via distribution expertise) to low-cost medicines	R&D investments, intersectoral collaboration to develop products for diabetes prevention and control. Pricing and marketing these products to reach those most in need and to ensure the profitability of companies that invest to promote health
National and international funding bodies		
World Diabetes Foundation, Gates Foundation	Sponsor demonstration projects and increased research (for example, Ovations/NHLBI Chronic Disease Initiative and the Community Interventions for Health program)	Fund research initiatives to identify future strategies for diabetes prevention and control
Nongovernmental organizations		
Oxford Health Alliance, Nutrition Foundation of India, Diabetes India, Center for Chronic Disease Control, Initiative for Cardiovascular Health Research in Developing Countries	Prevention and treatment, forming international networks and alliances to advocate for policy change Research, knowledge generation, and translation to policymakers	Funding, capacity building, advocacy, and development of educational resources Provide space for collaboration and come up with multi-sectoral solutions
Academics and researchers		
Indian Council of Medical Research, National Institute of Nutrition, academic institutions	Increase research and surveillance, train young professionals to tackle the issues	Hire public health professionals with experience-based knowledge of NCD issues to inspire and educate young students
Public-private partnerships		
HEAL Global Partnership, Public Health Foundation of India	Actionable research Ensure funding for promising ideas and proposals for diabetes prevention and control	Build upon current public-private partnership models
Health care sector		
Public and private health care Providers	Patient education and empowerment, develop guidelines for prevention and control	Increase in resources (human and financial)

9. Ongoing Research Programmes in Diabetes in India

Randomized Control Trials (RCTs) in Diabetes: Montori's et al. 2006 systematic assessment of RCTs in diabetes found that RCTs trend to be published in pertinent top journals, both general and specialized and, have important deficiencies in reporting of key methodological features (not closely adhering to CONSORT guidelines i.e. Consolidated Standards of Reporting Trails). These deficiencies are most common in laboratory investigations and RCTs that measured patient important outcomes showed better reporting. Many RCTs measured patient important outcomes, but very few of these assessed nonpharmacological interventions (Montori et al. 2006). Despite the worldwide explosion of diabetes as a major public health problem, most trials came from researchers working in the northern hemisphere.

Thus, to enhance the practice of evidence-based diabetes care, trialists need to pay closer attention to the rigorous implementation and reporting of important methodological safeguards against bias (Montori et al. 2006). Further, Gandhi et al. 2008 found that in their study sample of registered ongoing RCTs (worldwide) in diabetes, only 18% included patient-important outcomes (death and quality of life like morbidity, pain, function) as primary outcomes.

In India there are currently a number of research programs in prognosis of diabetes and the most reputed research organization is "Madras Diabetes Research Foundation" (MDRF) *(http://mdrf.in/department/research_department.html),* and their most ambitious projects include:

World Health organization (WHO) Collaborating centre for Non-communicable diseases-Prevention & Control – designated by WHO, Geneva: MDRF carries out research on diabetes and other non-communicable chronic diseases like hypertension, obesity, dyslipidemia and cardiovascular diseases. The objectives of the WHO Collaborating Centre are to provide continuous surveillance, prevention and control of these diseases.

Establishment of a Centre for Prevention and Control of Diabetes and Cardio-metabolic Diseases in South Asia: Supported by The National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) and Ovations Chronic Disease Initiative of the United Health Group. Their main objective is to establish a multi-disciplinary, Centre of Excellence to address Cardio-metabolic diseases (CMD) in South Asia. This Centre will build world-class investigator and research capacity, produce and disseminate innovative, science-driven, and low-cost solutions. The Centre will study the burden and risk factors for cardiovascular disease and diabetes in India and Pakistan and investigate ways to prevent the diseases. In addition will also help train young scientists in these countries to conduct important diabetes and heart disease research.

More Specifically their research agenda includes the following studies:

1. **Chennai Rural Epidemiology Study (CURES)**
   CURES started in 2001 with objectives to estimate the prevalence of diabetes and its complications in urban Indian population and to identify the risk factors for NCDs. CURES is a large ongoing epidemiological cohort study involving a representative population of Chennai (screening 26,001 individuals from 46 corporation wards), in southern India.

2. **ICMR Advanced Centre for Genomics of Type 2 Diabetes**
   In the context of genomics of diabetes (and diabetic eye complications), this advanced centre aims to improve the quality and multidisciplinary nature of diabetes research by providing shared access to specialized technical expertise and resources. This centre will build capacity and develop basic infrastructure for carrying out genomic research related to diabetes. The overall goal is to bring together clinical and basic science investigators, from relevant disciplines, in a manner that will enhance and extend the effectiveness of research related to the genomics of diabetes and its complications.

3. A number of randomized control trials are also in progress and include the following as listed in table11;

Table-11: Randomized Control Trials

S. No.	Name of the RCTs	Objective
1	Dose Finding Safety and Efficacy of Monthly Subcutaneous Canakinumab administration for the treatment of hyperglycemia in metformin Monotherapy treated type 2 diabetic patients. (Phase III Interventional, Treatment, Randomized, Double Blind Placebo Control, Parallel Assignment, Safety Study)	Objective is to determine the optimal concentration for a monthly dose of canakinumab to be delivered subcutaneously. Canakinumab is expected to improve blood sugar levels in subjects in early stages of T2DM by neutralization of IL-1b activity in pancreatic islets.
2	A randomized, double-blind, placebo-controlled, parallel-group, multicenter study to determine the efficacy and safety of albiglutide when used in combination with pioglitazone with or without metformin in subjects with type 2 diabetes mellitu	A Phase III Clinical study to evaluate the efficacy and safety of albiglutide.
3	A Randomized, Placebo-Controlled Clinical Trial to Evaluate Cardiovascular Outcomes After Treatment With Sitagliptin in Patients With Type 2 Diabetes Mellitus and Inadequate Glycemic Control on Mono- and Dual Combination Oral Antihyperglycemic Therapy (TECOS STUDY)	To determine whether following treatment with sitagliptin oral (hypoglycemic agents) on a long term basis in patients with T2DM mellitus there is an increase or decrease the incidence of cardiovascular events (both fatal and non-fatal)
4	A randomized, double-blind, placebo-controlled, 2-arm parallel-group, multicenter study with a 24-week main treatment period followed by an extension assessing the efficacy and safety of AVE0010 in patients with T2DM insufficiently controlled with basal insulin.	To assess the efficacy of AVE0010, a GLP-1 analog, on glycemic control as an add on to insulin ± Metformin in comparison to a placebo in T2DM patients in terms of HbA1c reduction over a period of 24 weeks.
5	A multi-center, randomized, double-blind study to evaluate the efficacy and long-term safety of vildagliptin modified release (MR) as monotherapy in patients with T2DM.	To demonstrate the efficacy of vildagliptin MR 25 mg qd or 50 g qd as monotherapy in patients with T2DM mellitus.

4. **Market survey of foods from various retail outlets in the South Indian metro city of Chennai and its relevance to chronic disease epidemiology:** This study aims at providing the lacuna of information related to the profiling of foods in the urban market and their relevance to chronic diseases epidemiology with focus on T2DM. Unfortunately, no reported data on results has been provided yet.

5. **ORANGE Study (Obesity Reduction and Awareness of Non-communicable diseases through Group Education) 2008-2010:** Orange, is aimed at screening children in schools and colonies to determine the prevalence of obesity, diabetes, pre-diabetes, hypertension, dyslipidemias, metabolic syndrome and MODY. Unfortunately, no reported data on results has been provided yet.

6. **D-CLIP (Diabetes Community Lifestyle Improvement Program**) is a trial of a culturally specific lifestyle intervention program for diabetes prevention in India. It is three year project and was started in 2009.

9.1 Gaps in T2DM Research *(adapted from Walgate 2008)*

Gaps in research can never be completely fulfilled for any country or for any disease. Despite the increase of new diabetes research programmes in India they are far from adequate to address the emerging demand (corresponding increase in disease burden). The major diabetes related research gaps are as follows:

1. **Lack of large scale health surveillance;** to make accurate prediction of prevalence, incidence and related death rates is the major research gap for diabetes in India. Most of the aforementioned efforts in diabetes in India are regionalized or localized and cannot be easily generalized to the entire Indian population. Moreover, north Indian populations are highly neglected in all different kind of T2DM related research efforts. Therefore, to measure the scale of the problem there is a need of reliable population-based epidemiological studies in diabetes in the context of its existing and potential economic impact.

2. **Inadequate diabetic health care** prevention is apparent for the majority of people in India both in the primary and secondary care level. There is a need to establish evidence based services for effective prevention, diagnosis and care of T2DM, along with the need to evaluate these health systems in India.

3. **Evaluation and audit** of adherence to the national guidelines for T2DM are required to ensure appropriate care is provided, and if not, how this may be improved.

4. **Need of increased awareness of T2DM:** Awareness programs like MARG and CHETNA may not be sufficient in the light of T2DM burden in India because of low coverage. An awareness programme may develop means for the self-management of diabetes could be of value to lower resource settings, if account were taken of the relevant social and economic settings.

5. **Immediate need of well integrated translational research** designs to explore the research that takes diabetes' main causative factors and tests practical interventions against them which, if proven, might be adopted. This also includes infrastructure and equipment support for research on genetic markers for type 2 diabetes in the non-obese Indian population, although this has been catered by "ICMR Advanced Centre for Genomics of Type 2 Diabetes" but this may not be sufficient.

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