# PHARMACOECONOMIC EVALUATION OF ANTIDIABETIC AGENTS: SOCIETAL PERSPECTIVE

Dissertation submitted to

**The Tamil Nadu Dr. M.G.R. Medical University, Chennai**

in partial fulfillment of the requirements for the award of degree in

**MASTER OF PHARMACY**

**In**

**PHARMACY PRACTICE**


**Submitted by**

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**Under the Guidance of**

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**DEPARTMENT OF PHARMACY PRACTICE**

**J.K.K. NATTRAJA COLLEGE OF PHARMACY**

**KOMARAPALAYAM – 638183**

**TAMILNADU**

# CERTIFICATE

This is to certify that the work embodied in this dissertation entitled **"Pharmacoeconomic Evaluation of Antidiabetic agents: Societal Perspective",** submitted to "The Tamil Nadu Dr. M.G.R. Medical University", Chennai, in partial fulfillment to the requirement for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice**, is a bonafide work carried out by **Miss. GAYATHRI M, [Reg.No: 26103183],** during the academic year 2011-2012, under the guidance and supervision of **Mr. N. VENKATESWARAMURTHY,** Professor and Head, Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Komarapalayam.

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# DECLARATION CERTIFICATE

I do here by declare that the dissertation work entitled **"Pharmacoeconomic Evaluation of Antidiabetic Agents: Societal Perspective",** submitted to "The Tamil Nadu Dr. M.G.R. Medical University", Chennai, in partial fulfillment to the requirement for the award of degree of **Master of Pharmacy** in **Pharmacy Practice**, is a bonafide work carried out by me during the academic year 2011-2012, under the guidance and supervision of **Mr. N. Venkateswaramurthy, M.Pharm.,** Professor and Head, Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Komarapalayam.

I further declare that, this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship.

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*Dedicated to my*

*Family, Teachers*

*& Almighty*

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# Abbreviations

## *ABBREVATIONS*

| | |
|---|---|
| AGI | Alpha glucosidase inhibitors |
| BGS | Biguanides |
| CEA | Cost Effectiveness Analysis |
| CMA | Cost Minimisation Analysis |
| DM | Diabetes Mellitus |
| DPP IV | DPP IV inhibitors |
| HRQoL | Health related quality of life |
| INR | Indian Rupee |
| INS | Insulins |
| M.Fq. | Mean Frequency of Administration |
| SUS | Sulphonylureas |
| TGZ | Thiaglitazones |
| WHO | World Health Organization |

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# Introduction

# I. INTRODUCTION

## 1. PREVALENCE OF TYPE 2 DIABETES MELLITUS

### 1.1 Global scenario

Diabetes is a high incidence, chronic, globally, occurring disease that seriously trailing ground quality of the life[1]. Even today type 2 diabetes is one of the principal health care problems worldwide, and its scale is forecast to grow in the near future[2]. There is likely one person undiagnosed for every three persons presently diagnosed with the disease[3].The global increase in dominance of diabetes is due to population growth, aging, urbanization and increase of obesity and physical inactivity[4].

According to recent estimates, approximately 285 million people worldwide (6.6%) in 20-79 years age fraction have diabetes in 2010 and by 2030, 438 million people 7.8% of adult inhabitants is expected to have diabetes[4]. The total number of individuals with diabetes worldwide is anticipated to rise from about 170 million (2.8%) in 2000 to about 370 million (4.4%) in 2030[5, 6]. At both time points of 2010 and 2030 the three countries with prevalent number of people with diabetes are India, china and US respectively[4]. Although no nation or cultures are off the hook from this devastating disease, developing countries will account for 150% of the increase[7]. Type 2 diabetes is the commonest form of diabetes constituting 90% of diabetic populace in any country[8, 9].

Diabetes shortens the life bated breath by about 15 years [10]. Diabetes mellitus is the foremost cause of blindness in adults aged 20 to 74 years and leading contributor to advance of end stage renal disease[3]. It accounts for around 82,000 lower extremity amputations annually[3]. Approximately 4 million deaths each year are caused by diabetes related complications, adding up an astounding 9% of deaths worldwide[7]. Annual deaths attributable to diabetes are perhaps as high as 3 million (54% of deaths which is predicted to rise by 65% by 2030) with more than 80% occur in developing countries [11]. Macro vascular complications are the most widespread and are responsible for almost 70% of the deaths in chronic kidney disease exceeded 20% per year in patients with diabetes and that cardio vascular disease is in charge for two third of deaths amongdiabetic patients with end stage renal disease [3, 12, 13]. Low prevalence of peripheral vascular disease was verified in Indian patient as 4.0% [9].

Currently it is calculated that the population with diabetes consumes 4-14% of the global health expenses in western countries and that a patient with diabetes consumes 2-6 more direct resources than individuals of similar age and gender with other chronic diseases[2]. Health expenditure on diabetes is to account for 11.6% of total health care outflow in the world in 2010[4]. It has been estimated that diabetic patient consumes at least more or less 5-6% of health care expenditures in developed countries and that a diabetic patient consumes more resources than does a non-diabetic patient[1]. Estimated global health care expenditures to treat and prevent diabetes and its complications are likely to total at least 376 billion USD in 2010, by 2030, the number is predictable to exceed some USD 490 billion[4].

### 1.2 Indian scenario

Diabetes mellitus is rapidly rising as major health care challenge in India, especially in urban areas[14]. Although poor Indians are currently at lower risk than affluent Indians, the rapid spread of fast food exposes even urban Indian slum dwellers to the peril of diabetes[15]. More over there is uniformly large pool of persons with impaired glucose tolerance (IGT) many of whom will develop type 2 diabetes in future[14]. The lack of ample facilities and financial capacity indirectly worsens long term prognosis[8]. The prevailing poverty, unawareness, illiteracy and poor health consciousness further adds to the problem[8, 14].

The WHO recently revised its estimates of the persons with diabetes in India in 2000 as 31.7 million, the number is prone to increase to 79.4 million in 2030 [14, 16]. Prevalence of impaired glucose tolerance was also elevated as 14.0%[9]. A countrywide survey of diabetes conducted in six major cities in India in year 2000 showed that the prevalence of diabetes in urban adults was 12.1% [9]. Crude estimate suggest that type 2 diabetes pervasiveness in rural areas is much lower (approximately 25-50%) than in urban areas is rapidly catching up with the urban areas[17]. Prevalence is only 0.7% for non-obese physically active rural Indians, but it reaches 11% for obese, deskbound and urban Indians[4]. The exact age of onset of T2DM subjects is not clear because many folks in this population do not undergo regular checkup until symptoms appear; thus, diabetes may remain undiagnosed for 4 to 7 years[18]. Studies in India point out that more than 50% of people with diabetes have poor glycemic control (HbAIc >8%), uncontrolled hypertension, dyslipidemia and a large proportion have diabetic vascular complications[4]. It is found faintly more in men with age <60 years and in women at older age[16]. The ages of inception in India has been shifting

towards even younger people within the past decade and are more likely to fall in prey to complications ranging from heart attack and strokes to blindness and sexual dysfunction[15, 19].

In urban India, there are spacious social and economic disparities[9]. Free health care facilities are available for the economically backward classes, but due to low level of education and job-related problems, the facilities are not always used[9]. Management of diabetes involves finest glucose control which can be achieved through strict adherence to medications, diet and exercise which in turn minimizes long term complications[16]. Emerging therapies are designed to offer an option to standard therapies, which may get better glycemic control and help reduce incidence or the severity of complications and hence, the cost of type 2 diabetes[20].

Diabetes being a lifelong disorder is an expensive ailment for a very large fraction of subjects in developing societies[9]. Considering a rather low estimate of approximately 20 million diabetic patients in India, the annual projected cost could be Rs. 90,200/- million (USD 2.2 billion) for diabetic health care[9]. In Indian perspective the financial burden is often shared by relatives of the patient[9]. The currency spent was from family's financial resources[9]. Studies in India estimate that for a low income Indian family an adult with diabetes, as much as 25% of family income may be committed to diabetes care and India will suffer cumulative gross domestic product loss of 16.7 % over 10 year period[11, 21]. Many socioeconomic factors and health care delivery related issues impact the outcome of diabetes and therefore the costs and vice versa [14]. Persons with diabetes use higher health care funds and excess cost are related to higher cost to treat complications [14]. In India, direct expenditure correlated to diabetes care is presently Rs 10,000 crores which is likely to scale up to Rs 1, 25,000 crores by 2025[16].

In view of towering prevalence of diabetes and the vascular complications in Indians, emphasis must be given on primary prevention of diabetes as major combat the disorder[9]. Serious efforts should be made to spotlight and upscale activities on health promotion and prevention of diabetes which could provide a more cost effective solution to this condition with huge and increasing economic loss[11]. Overall diabetes care in India leaves much to be preferred [5].

## 2. DIABETES MELLITUS

Diabetes is a group of carbohydrate metabolic disorder characterized by resistance to the action of insulin, inadequate insulin secretion, or both. The medical manifestation of these disorders is hyperglycemia [3, 22]. Very high glucose levels can cause fatigue, dehydration, and even death. Long standing diabetes is associated with increased incidence of micro vascular and macro vascular disease[9]. As the disease progresses tissue or vascular damage ensues leading to harsh complications such as retinopathy, nephropathy, neuropathy, cardiovascular disease, and foot ulceration [22, 23]. Long term clinical follow up studies have shown that improvements in glycemic control, Blood Pressure, and Cholesterol level lead to fewer micro & macro vascular complications and progress health outcomes[24].

## 2.1 Epidemiology

Diabetes is a chronic extensive devastating metabolic disease which can affect every organ in the body and is an important cause of premature death and disability [10, 13, 19]. Diabetes is prevailed in parallel proportion in both men and women [16]. It is the most leading reason of morbidity and mortality in most developed countries [10, 13]. Poor management leads to several complications and end organ damage that finally impairs the health related quality of life in individuals [16]. Long term thorough glycemic control is essential to manage and prevent complications [10, 19]. People with diabetes are at amplified risk of developing long term complications related to micro vascular (ex: retinopathy, neuropathy, nephropathy, foot ulcer) and macro vascular (ex: heart, cerebral and peripheral vascular diseases) [12, 13], when compared with non diabetic patient in the same age group [1]. Typical type 1 diabetes accounts for 5-10% of all cases of diabetes and is an auto immune disorder mounting in childhood or early adulthood although some latent forms do occurs [3]. Type 2 diabetes is a chronic disease characterized by hyperglycemia and dyslipidemia due to underlying insulin resistance [13].

### 2.1.1 *Risk factors leading to Diabetes Mellitus.*

- A genetic predisposition (i.e parents or siblings with diabetes) [3, 15].
- Lifestyle factors, especially those of so called westernized way of life, characterized by high calorie intake and little exercise [15].
- Central obesity (i.e $\geq$ 20% over ideal body weight or Body mass index $\geq$ 25 kg/m$^2$) [3, 10].
- Habitual physical inactivity [3].

- Race or ethinicity (previously identified impaired glucose tolerance or impaired fasting glucose) [3].
- Hypertension (≥140/90 mm Hg in adults) [3].
- HDL cholesterol ≤ 35 mg/dL and/or triglycerides ≥ 250mg/dL[3].
- History of gestational diabetes or delivery of a baby weighing >4 Kg [3].
- History of vascular disease [3].
- Presence of acanthosisnigricans; and polycystic ovary disease [3].

## 2.2 Classification of Diabetes

DM may be categorized into numerous types but the two major types are:-

***Type 1 Diabetes***(insulin-dependent diabetes mellitus (IDDM) / Juvenile-onset diabetes)**:** This form of the disease has an auto-immune basis of destruction of β cells of the pancreas in most cases, and generally occurs in children, adolescents and it can occur at any age [3, 22]. Itis present with little or no endogenous insulin secretory capacity and hence requires exogenous insulin therapy for survival. The coupled hypoinsulinaemia and hyperglucagonaemia put such patients at risk of ketosis and ketoacidosis [22].

***Type 2 Diabetes***(non-insulin-dependent diabetes mellitus (NIDDM) / maturity onset diabetes)**:** This disease classically develops in later life [22]. Insulin secretion may appear normal or even excessive but it is in short supply to compensate for insulin resistance, due to cluster of abnormalities like obesity, hypertension, dyslipidemia, and elevated plasminogen activator inhibitor type 1 (PAI-1) levels collectively referred as the *insulin resistancesyndrome* or *metabolic syndrome* [3, 22]. Type 2 diabetes has a strong genetic predisposition and patients with type 2 diabetes are at augmented risk of developing macrovascular complications [3].

| **Type I DM** [25] | **Type II DM**[25] |
|---|---|
| Formerly called insulin-dependent (IDDM), juvenile-onset, or brittle DM[25] | Formerly called non–insulin-dependent [NIDDM] or adult-onset DM[25] |
| Represents 5%–10% of diabetic patients[25] | Represents 90%–95% of diabetic patients[25] |
| Autoimmune disease in which pancreatic beta islet cell are targets of destruction[25] | Varies from predominantly insulin resistance in muscle and fat with relative deficiency to predominantly insulin |

| | |
|---|---|
| | secretory defect with insulin resistance. Relative rather than absolute insulin deficiency[25] |
| Autoantibodies are present in 85%–90% of cases. Other autoimmune disorders may be present (e.g., Graves disease, Hashimoto thyroiditis, Addison disease, pernicious anemia) [25] | Associated with dyslipidemia, obesity (in 80%–90% of cases), increasing age, hypertension, family history[25] |
| Insulin secretion is virtually absent Plasma C-peptide is low or undetectable in contrast to Type 2[25] | Plasma insulin may be normal or increased but is expected to be higher relative to blood glucose concentration[25] |
| Ketosis prone[25] | Ketosis occurs with stress (e.g., infection), but seldom spontaneously[25] |

## 2.3 Pathogenesis

The islets of Langerhans are the endocrine component of the pancreas [26]. Insulin is synthesized in the pancreatic β- cells, initially as a polypeptide precursor, pre-proinsulin [26]. The latter is rapidly transformed in the pancreas to proinsulin [26]. This forms equal amounts of insulin and C-peptide through removal of four amino acid residues [26]. Insulin consists of 51 amino acids in two chains (A chain contains 21 amino acids and B chain contains 30), linked by two disulfide bridges [26]. In islets, insulin and C-peptide are crammed into granules. Insulin associates impulsively into a hexamer containing two zinc ions and calcium ions [26].Glucose is the major stimulant to insulin release [26]. The response is triggered both by the intake of nutrients and the discharge of gastrointestinal peptide hormones [26].

Once released from the pancreas, insulin enters the portal circulation [26]. In basal state, insulin secretion is at a rate of approximately 1 unit per hour [26]. Total daily secretion is approximately 40 units [26]. Insulin circulates free as a monomer, has a half-life of 4-5 minutes and is principally metabolized by the liver and kidneys [26]. In kidneys, insulin is filtered by the glomeruli and reabsorbed by the tubules and degraded [26]. Peripheral tissues

such as muscle and fat also degrade insulin but this is of minor quantitative significance [26]. The interaction of insulin with the receptor on the cell of surface sets off a chain of messengers within the cell [26]. This opens up transport processes for glucose, amino acids, and electrolytes [26].

Type 1 DM is characterized by an utter deficiency of pancreatic β-cell function resulting of an immune-mediated destruction of pancreatic β cells mediated by macrophages and T-lymphocytes with circulating auto-antibodies to various β-cell antigens, but rare unknown or idiopathic processes can throw in [3]. Destruction of pancreatic β-cell function causes hyperglycemia because of an absolute deficiency of both insulin and amylin [3]. Also glucose uptake is decreased in insulin- sensitive tissues, hence hyperglycemia ensues that leads to unrestrained hepatic glycogenolysis and gluconeogenesis with a ensuing increase in hepatic glucose output [26]. Insulin lowers blood glucose by a variety of mechanisms including: stimulation of tissue glucose uptake, suppression of glucose production by the liver, and suppression of free fatty acid release from fat cells[3]. The suppression of free fatty acids plays an important role in glucose homeostasis[3]. Increased levels of free fatty acids inhibit the uptake of glucose by muscle and stimulate hepatic gluconeogenesis[3]. Amylin, a glucoregulatory peptide hormone cosecreted with insulin, plays a role in lowering blood glucose by slowing gastric emptying, suppressing glucagon output from pancreatic α cells, and increasing satiety [3].

In type II diabetes the process is usually less acute, since insulin production decreases over a sustained period of time [26]. Glucagon, produced by pancreatic α cells, is secreted in the fasting state to oppose the action of insulin and stimulate hepatic glucose production [3]. Thus, glucagon prevents hypoglycemia or restores normoglycemia if hypoglycemia has occurred [3]. The resultant hyperinsulinemia (1) suppresses hepatic glucose production and (2) stimulates glucose uptake by peripheral tissues [3].Hyperinsulinnemia is able to maintain glucose levels for a period of time but eventually β-cell function deteriorates and hyperglycemia ensues [26]. If this cycle is not interrupted, type 2 diabetes develops [26]. Type 2diabetes is also associated with metabolic syndrome, which is a group of risk factors frequently found in those with type 2 diabetes, including insulin resistance, glucose intolerance, hyperinsulinnemia, hypertension, dyslipidemia, central obesity, artherosclerosis and increased levels of procoagulant factors, ex: plasminogen activator inhibitor-I and fibrinogen [26]. Small increments in the plasma insulin concentration exert a potent antilipolytic effect, leading to a marked reduction in the plasma free fatty acid (FFA) level [3]. The decline

in plasma FFA concentration results in increased glucose uptake in muscle [3]. Thus a decrease in the plasma FFA concentration lowers plasma glucose by both decreasing its production and enhancing the uptake in muscle [3].

## 2.4 Pathophysiology

Hepatic insulin resistance and hyperglucagonemia result in continued production of glucose by the liver, a shortened gastric emptying time can result in marked hyperglycemia [3]. Increased insulin concentration, causes muscle glucose uptake. In lean type 2 diabetic subjects, the onset of insulin action is delayed and the ability of insulin to stimulate leg glucose uptake is reduced[3]. Therefore the primary site of insulin resistance in type 2 diabetic subjects resides in muscle tissue[3]. Insulin is a potent inhibitor of lipolysis, and restrains the release of FFAs from the adipocyte by inhibiting the hormone-sensitive lipase enzyme [3]. Chronically elevated plasma FFA concentrations can lead to insulin resistance in muscle and liver and impair insulin secretion [3]. Increased stores of triglycerides in muscle and liver and the increased fat content correlates closely with the presence of insulin resistance in these tissues [3].

### 1.4.1. *Cellular Mechanisms of Insulin Resistance*

#### 2.4.1.1 *Obesity and Insulin Resistance*

Abdominal fat is resistant to the anti-lipolytic effects of insulin, resulting in the release of excessive amounts of free fatty acids, which in turn lead to insulin resistance in the liver and muscles [26]. The effect is an increase in gluconeogenesis in the liver and an inhibition of insulin-mediated glucose uptake in the muscle [26]. These both result in increased levels of circulating glucose [26]. Furthermore, excess fat itself may contribute to insulin resistance because when adipocytes become too large they are unable to store additional fat, resulting in fat storage in the muscles, liver and pancrease, causing insulin resistance in these organs [26]. Adipose tissue causes the oversecreation of some cytokines associated with inflammation, endothelial dysfunction and thrombosis [26]. Adipose tissue is also thought to cause under secretion of a beneficial adipokine called adiponectin [26]. Adiponectin suppresses the attachment of monocytes to endothelial cells, thereby protecting against vascular damage [26]. People with diabetes have lower levels of adiponectin than those without diabetes and weight reduction increases with adiponectin levels [26].

## 2.5 Screening

***Type 1 Diabetes Mellitus*:** Because of the acuteness of symptoms, screening for type 1 DM is not recommended [3].

***Type 2 Diabetes Mellitus*:** Testing should be considered at an earlier age and more frequently in individuals with risk factors [3]. The recommended screening test is the fasting plasma glucose (FPG) or oral glucose tolerance test (OGTT) [3].Testing should be done every 2 years starting at 10 years of age or at the onset of puberty if it occurs at a younger age [3].

## 2.6 Clinical presentation

***Type 1 DM:*** It can occur at any age thin individuals and are prone to develop diabetic ketoacidosis after several days of polyuria, polydipsia, polyphagia, and weight loss [3].

***Type 2 DM:*** Patients are often diagnosed secondary to unrelated blood testing, as they fail to present with symptoms [3]. Lethargy, polyuria, nocturia, and polydipsia can be seen at diagnosis, but significant weightloss at diagnosis is less common [3].

## 2.7 Diagnosis of diabetes

Patients with either IFG or IGT are now commonly referred to as having "prediabetes" because of a higher risk of developing diabetes in the future [3]. Diagnosis is now based on any of the three criteria that follow:

- Classic symptoms of diabetes (polyuria, increased thirst, unexplained weight loss, blurred vision) and a random plasma glucose concentration of _200 mg/dL (11.1 mmol/L) [27].
- Impaired glucose tolerance (IGT), is defined as a 2-hour postload plasma glucose value ≥140 mg/dL (7.8 mmol/L), but less than 200 mg/dL (11.0 mmol/L) during a standard 75g OGTT [3, 27].
- Impaired fasting glucose (IFG) is plasma glucose of at least 100 mg/dL (5.6 mmol/L) but less than 126 mg/dL (7.0mmol/L) after an overnight (at least 8 h) fast (DM. 5) [3].
- The fasting glucose reflects hepatic glucose production, which depends on insulin secretory capacity of the pancreas [3].
- The postprandial glucose reflects uptake of glucose in peripheral tissues (muscle and fat) and depends on insulin sensitivity of these tissues [3].
- HbA1c measurements are the gold standard for following long-term glycemic control and risk of microvascular complications in persons with diabetes for the previous 2 to 3 months [3, 28].

## 2.8 Treatment

**2.8.1** ***Desired outcome***: The primary goals of DM management includes [3]

- To reduce risk for microvascular and macrovascular disease complications.
- To ameliorate symptoms.
- To reduce mortality and improve quality of life.
- To prevent poor wound healing & decreased white blood cell function.
- To prevent Diabetic ketoacidosis and hyperosmolar hyperglycemic state.
- To maintain blood pressure as near normal as possible.

**2.8.2** ***Monitoring complications***

Current recommendations continue to advocate yearly or less frequent eye examination implemented on the advice of an eye care specialist [3]. The feet should be examined and the blood pressure assessed at each visit [3]. Yearly testing for microalbumin in urine and lipid abnormalities (or more) if needed to achieve lipid goals, is recommended [3].

**2.8.3** ***Self-monitoring of blood glucose***

Frequent SMBG enables patients to know their blood glucose concentration at any moment easily and relatively inexpensively to achieve near-normal blood glucose concentrations and to assess for hypoglycemia [3].

**2.8.4** ***Non pharmacologic therapy***

Medical nutrition therapy is recommended for regulating drug administration with a balanced diet (<7% of total calories) to achieve and maintain a healthy body weight in diabetic patients [3].All diabetic patients should be encouraged to exercise, according to their age and physical capability [22]. Exercise improves carbohydrate metabolism, insulin sensitivity and cardiovascular function, contributes to weight loss or maintenance, and improves well-being [22]. It is also a useful component of any weight reduction program although diet may be more effective in promoting weight loss and metabolic control [22].

**2.8.5** ***Pharmacologic therapy***

Currently, six classes of oral agents are approved for the treatment of type 2 diabetes: sulphonyl ureas, Thiazolidinones, Aldose reductase inhibitors, α- glucosidase inhibitors, Biguanides, Dipeptidyl peptidase -4- inhibitors, Meglitinides, Micellaneous agents

[22]. Oral antidiabetic agents are often grouped according to their glucose-lowering mechanism of action [3].

- Insulin sensitizers (that has ability to reduce insulin resistance): Biguanides & thiazolidinediones [TZDs] or glitazones [3].
- Insulin secretagogues (that enhances endogenous insulin release): Sulfonylureas, Meglitinides[3].

## 2. PHARMACOECONOMICS

"Pharmacoeconomics is the description and analysis of the costs of drug therapy to health care systems and society"[30]. It is a branch of health economics dealing with costs and benefits of drug therapy applied to the health care industry[31, 32]. It is taking on greater prominence in our health care system as costs continue to increase rapidly[31]. However, assessing the clinical data is the first part of economic evaluation and judgments about the role of new and existing drug therapies will often be based primarily on the clinical evidence of benefits and harm[33].

Cost outcome analyses are based on clinical studies of efficacy or effectiveness[31]. Before a cost outcome analysis is performed, the clinical issue (ex: Symptom management) must be identified and potential solutions measured for effectiveness[31]. Effectiveness refers to the benefit of an intervention when used in the "real world" where patient may have other co-existing conditions, take other medications, or may not be as compliant[31]. It is concerned with three areas of analysis: [30]

1. Comparison of drug therapy with other treatment modalities.
2. Cost effectiveness of alternative drugs.
3. Methods and procedures to improve cost effectiveness.

### 3.1 Specific tools in Pharmacoeconomic analysis to allow the orderly and comprehensive collection of data.[30]

1. Cost-Benefit Analysis
2. Cost-Effectiveness Analysis
3. Cost-of-Illness Analysis
4. Cost Minimization Analysis
5. Cost Utility Analysis

6. Cost Consequences analysis

***3.1.1 Cost-Benefit Analysis:***Cost benefit studies provide the most direct comparisons of costs with benefit; but they can also be most controversial[31]. All outcomes are valued in dollars, thus the study asks whether the dollar value of benefit is larger than the dollar value of the costs[31]. Cost benefit studies may place dollar values on medical care costs saved, in addition to days off from work, days of reduced productivity at work because of illness[31]. It is appreciated that while the costs of specific treatment are easy to obtain (drug costs) that of the consequences (eventual therapy, support costs) are variable and difficult to estimate [30].

***3.1.2 Cost-Effectiveness Analysis:*** Cost effectiveness is broadly used term inside and outside the healthcare community [31].The costs of treatment to achieve specific therapeutic objectives are assessed[30]. In pharmacoeconomics, these studies measure dollars spent per outcome achieved, in which the outcomes (ie. Effectiveness) are measured in natural units [31].

***3.1.3 Cost-of-Illness Analysis:*** Cost of illness studies measure the lifetime cost for an incident case of a condition (i.e cost over a lifetime for individuals with a condition, even if the condition is not lifelong) [31].

***3.1.4 Cost Minimization Analysis****:* Cost minimization studies compare two or more treatment options that achieve the same or a defined minimum outcome [31], (costs of alternative equivalent treatments) [30].

***3.1.5 Cost Utility Analysis:*** Cost utility studies are a specific type cost effectiveness analysis in which two interventions are compared on preferences for different health states[31]. The health states are measured by morbidity & mortality[31]. Morbidity is defined based on quality of life measures and for cost utility studies, morbidity is combined with mortality to create a QALY[31]. The outcome of treatment is measured in terms ofquality of life, willingness to pay or patient preferencefor one treatment over another[30]. Although this appearsto be an index of consumer satisfaction, choices areinfluenced by several factors[31]. Attempts atdefining outcome in terms of quality of life per additional year of life (QALYs) may be suitable in measuringthe effect of treatment of a fatal disease [30].

***3.1.6 Cost consequence analysis:*** Cost consequence studies compares the cost of an intervention with the consequences or outcomes; however the consequences are not considered based on monetary value (ex: dollars per outcome), and there is no summary

measure[31]. Each consequence is considered individually[31]. The collection of all costs of treatment (drugs, personnel, process) and their consequences (return to employment, cost of nontreatment or eventual therapy), both measures is expressed in financial terms[30].

### 3.2 Perspective

Perspective is the key point that is to be considered for any economic evaluation[34]. Here it is mandatory from whose point of view the evaluation should be considered, from health care perspective involve (direct cost) or societal perspective (involves indirect cost) [34]. How much a drug cost depends on your point of view?

From:-

1. *Patient's perspective*: out-of-pocket expenses are cost [33].
2. *Societal perspective*: It is the most comprehensive, as it includes all cost and benefit irrespective of who pays and who benefits, but often more limited perspectives are adopted [33].

### 3.3 Costs

Costs are clearly an important component of cost outcome analysis, thus it is critical to understand how costs are defined[31]. The costs of an intervention include the quantities of intervention used, the price of the intervention, the "labor" is administering the interventions, preparations and evaluation and other ongoing costs[31]. Clearly, cost calculations need to be transparent in a published cost outcome analysis because determining which costs to include can significantly affect the results[31].

1. *Direct cost:* - Direct cost are those associated directly with the delivery of medical care[33].
2. *Indirect cost*: - Indirect costs are those associated with lost production capacity (ex: time cost from work due to illness or death) [33].

Most recently, an alternative costing terminology has been proposed cost may be classified as:-

1. *Health care sector costs:* - resources used in providing initial and continuing care [33].
2. *Patient and Family sector costs*: - Out-of-pocket expenses, cost associated with seeking care, time lost by patient and family[33].
3. *Other sector cost*: - home care and volunteer services[33].

### 3.4 Incremental costs

This is the incremental cost of treatment with new therapy compared with the alternative what goes into calculation varies with the perspective of analysis, but the focus is on what is different between the two therapies rather than concentrating efforts on calculating the total costs of treatment with drug A and cost of treatment with alternative B in detail[33].

### 3.5 Discounting

When cost and benefits extend over a number of years, discounting is used to reflect the fact that values from today's perspective depend on when costs are paid and benefit accrue[33]. Typical discount rates applied range from 3-6% [33]. Other rates can be tested in sensitivity analysis[33]. NICE guidance recommends discounting rates of 6% of costs and 1-5% for benefits with equal discounting benefits (6% costs, 0% benefits) tested in sensitivity analysis[33].

## 4. ADVANTAGES OF PHARMACOECONOMIC ANALYSIS

WHO defines health as being at only the absence of the disease and infirmity but also presence of physical, mental and social well being[16]. Health and economic development are positively linked and external investment is needed to break the vicious cycle of poor health and poverty that afflicts the less developed countries [36]. Good health is a pre requisite to successful human endeavor and therefore core to economic growth and activity[14]. The demand for and the cost of the health care are increasing in all countries as the improvement in and sophistication of health technologies[37].The increase in health care spending is mainly because of increased life expectance, increased technology, increased standard of living and increased demand in health care quality and services[37].

Medicines form a small but significant proportion of total health care cost[37]. Cost of medicines are marketed and are under patent law, preference of drug therapy over invasive therapy, discovering various labels uses of existing drugs and the irrational drug prescription[37]. Since 1961, pharmaceuticals are fallen under price regulation in India[37]. A total of 43 drugs accounting for 85% of the drug market were under price control in 1979[37]. With successive polices, the number diminished and now a mere 15-20% of the drug market is under price control[37]. All over the world patients are affected by high price of medicines[37].

Health related quality of life (HRQoL) is increasingly used as an outcome indicator alongside conventional biomedical measures [23]. QoL assessment focuses attention on patients's life beyond symptoms and signs [40]. QoL also helps in policy research including programme evaluation and resource allocation [40]. HRQoL is considered a patient assessed or patient centered outcome that relates to the individula's health perceptions, wellbeing and functioning rather than of diseases and disorders, hence is more comprehensive and compatible with WHO's (World Health Organization) concept [23, 40]. Since complications are known to reduce HRQoL, intensified glycemic control is an important way to reduce the risk of complications and improve HRQoL. Rising health care costs have led to more focus on the need to prevent disease and to promote health as a longer term strategy for cost-containment [42]. These tools are potentially helpful to help to 'do the right things right" but this objective is easier said than done [42].

## 5. NEED FOR PHARMACOECONOMIC ANALYSIS IN INDIA

In a developing country like India 85% of total health expenditure is financed by house hold out-of-pocket expenditure on drug imposes a major financial burden on households[37]. A major portion of private health care spending goes to drug and per capita private drug spending in India is estimated as USD 16[37]. Hence many poor people frequently face a choice between buying medicines or buying food or other necessities due to limited resources and high pricing of drug. So medicine prices do matter[37].

Diabetes is traditionally known as a 'Silent disease' exhibiting no symptoms until it progresses to severe target organ damage[17]. Because of its adverse effects and the associated economic burden on the health care system for individuals & society, diabetes is a major public health problem [38, 39]. The prevalence of DM is rapidly rising all over the globe at an alarming rate [40.] The expenses associated with caring for persons with diabetes are staggering[7]. Medical expenditure for people with DM is 2-3 times higher than those not affected by DM [39]. Every year a large percentage of total health care budgets are spent on DM related costs[24]. Proper treatment of diabetes is not costly; not treating diabetes is very costly[14]. Although efforts to control hyperglycemia and associated symptoms are important, the major challenges in optimally managing the patient with diabetes are targeted at reducing or preventing complications and improving life expectancy and quality of life [3]. Good glycemic control can delay the onset and slow progression of diabetic complication and

thereby help in avoiding health expenditures [41]. Intensive treatment, based on current guidelines, might lead to lower health care costs [24].

The diabetes economics literature is extensive and diverse [39].Despite several advances in the approach to estimating the costs of DM, there is no standard for estimating these costs [39]. It is well established that the care and treatment of DM patients consumes large amounts of health care resources, pharmacoeconomics on diabetes enables health care payers to budget appropriately, estimating the burden of illness and cost of treatment for DM becomes more important [43]. Qualifying prevalence of DM and the number of people affected by DM, now and in future, is important to allow rational planning and allocation of resources [44]. The significance of the epidemiological burden of DM lies in the complexity of these metabolic diseases which, if left untreated or not appropriately treated, may develop into complications, many of which are life- threatening, that inevitably resulting in different costs of treatment of complications [43].

Pharmacoeconomics serves as a link between medicine and market economy[32]. The term pharmacoeconomics implies the application of economic principles to evaluation of pharmaceuticals[33]. Pharmacoeconomics offers reliable and meaningful information and serves as a tool for decision making in the choice of therapeutic approach[32]. The aim is to maximize health benefit for the community to be delivered considering the existing limited financial resources[32].

# Literature Review

## II. LITERATURE REVIEW

**Guillermin *et al.*, (2011)** has conducted a cost minimization analysis comparing the long-term costs of insulin glargine once daily versus insulin detemir once or twice daily (for type 1 (T1DM) and type 2 (T2DM) diabetes mellitus using a validated computer simulation model, the CORE Diabetes Model from a Canadian provincial government's perspective. Costs were discounted at 5% per annum. Lifetime direct medical costs including costs of insulin treatment and diabetes complications were projected, assuming that all patients stay on the same treatment for life. T1DM and T2DM patients' daily insulin dose was derived from a meta-analysis of randomized trials. The meta-analysis showed T1DM and T2DM patients had similar HbA1c change from baseline when receiving IGlarg compared to IDet. Treatment of T1DM patients with IGlarg versus IDet BID resulted in lifetime cost savings of $4231 per patient. Treatment of T2DM patients with IGlarg resulted in lifetime cost savings of $4659 per patient versus IDet QD and cost savings of $8709 per patient versus IDet BID. Similar HbA1c change from baseline can be achieved with a lower IGlarg than IDet dose showing that with IGlarg instead of IDet can generate long-term cost savings[45].

**Lee *et al.*, (2011)** estimated the cost-effectiveness of a once-daily GLP-1 analog Victoza [Novo Nordisk] versus a thiazolidinedione, rosiglitazone in patients with T2DM including background therapy with glimepiride. The CORE Diabetes Model was used to compare 35-year clinical and economic outcomes associated with liraglutide 1.2 mg & glimepiride and liraglutide 1.8 mg & glimepiride versus rosiglitazone 4mgþ glimepiride. Baseline cohort characteristics were based on the Liraglutide Effect and Action in Diabetes-1 trial and primary outcomes included life expectancy (LE), quality-adjusted life-years (QALYs), total costs and incremental cost-effectiveness ratios (ICERs). When compared to rosiglitazone, liraglutide 1.2 mg and 1.8 mg increased mean LE by 0.968 and 1.041 years, and QALYs by 0.764 and 0.837, respectively. Total lifetime costs increased by $26 094 for liraglutide 1.2 mg versus rosiglitazone, and by $47 041 for liraglutide 1.8 mg versus rosiglitazone. ICERs for liraglutide 1.2 mg versus rosiglitazone and 1.8 mg versus rosiglitazone were $34 147 and $56 190, respectively. Compared to rosiglitazone 4 mg plus glimepiride, liraglutide (at the 1.2-mg dose) plus glimepiride is a cost-effective treatment option for improving glucose control in T2DM[46].

**Francis *et al*., (2011)** has examined progression to type 2 diabetes and compared healthcare utilization and costs among patients with pre-diabetes, with or without comorbid hypertension, from a large national claims database (2003–2008). Patients were ≥ 18 years of age with a medical claim or lab value indicating the presence of pre-diabetes. The index date was the first pre-diabetes diagnosis or qualifying lab value of fasting plasma glucose or impaired glucose intolerance. Multivariate analysis was conducted to identify risk factors affecting progression to type 2 diabetes, and to estimate the impact of hypertension status and diabetes progression on healthcare utilization and cost. 144,410 patients met study criteria, with an average follow-up of 802 days. Among participants, 30.7% progressed to diabetes, with a mean 288 days from pre-diabetes identification to diabetes diagnosis. Compared with patients who did not progress, the total adjusted medical costs for patients who developed diabetes increased by $1429 in 1 year, $2451 in 2 years, and $3621 in 3 years. Patients with concomitant hypertension were significantly more likely to progress to type 2 diabetes, and had higher total medical costs compared to patients without hypertension. Patients with pre-diabetes who progressed to type 2 diabetes had higher healthcare utilization and costs compared with patients who did not. The presence of hypertension substantially increased costs and was associated with higher likelihood of diabetes progression[47].

**Cleveringa *et al*., (2010)** has performed a cluster randomized trial on cost-effectiveness analysis of Diabetes Care Protocol versus usual care from a Dutch health care perspective with 1-year follow up and data were extrapolated using a modified micro simulation diabetes model, computing individual lifetime health-related costs, and health effects. Incremental cost-effectiveness ratios (ICERs) and cost-effectiveness (QALYs) were estimated using multivariate generalized estimating equations and acceptability curves were created. DCP patients lived longer, experiencedmore QALYs, and incurred higher total costs, per QALY gained. DCP had a more favorable effect on CVD+ patients than for CVD- patients. Coronary heart diseasecosts were reduced.DCP reduces cardiovascular risk, resulting in only a slight improvementin QALYs, lower CVD costs, but higher total costs, with a high cost-effectiveness ratio. Cost effectivecare can be achieved by focusing on cardiovascular risk factors in type 2 diabeticpatients with a history of CVD[24].

**Palmer*et al*., (2010)**has estimated the cost-effectiveness of BIAsp 30 versus IGlarg in the Chinese setting using validated and peer reviewed CORE Diabetes Model. The nephropathy, retinopathy, and stroke sub models were modified to incorporate available clinical data. Diabetes complication costs were derived from hospital surveys. Simulated

cohorts and insulin treatment effects were based on the Once Mix study for once-daily BIAsp 30 versus IGlarg and on the INITIATE study for twice-daily BIAsp 30 versus IGlarg. Life expectancy and direct medical costs were calculated and projections were made over 30-year time horizons, with a discount at 3% annually. Extensive sensitivity analyses were performed, including adjustments to cardiovascular risk. Once-daily BIAsp 30 increased life expectancy by 0.04 years and reduced direct medical costs (Chinese Yuan (CNY)) compared with IGlarg in the OnceMix-based analysis. Twice daily BIAsp 30 increased life expectancy by 0.08 years and reduced direct medical costs compared with IGlarg in the INITIATE-based analysis. Cost savings were attributable to lower lifetime insulin costs for BIAsp 30 compared with IGlarg. Lowered risk of cardiovascular, reduced the projected clinical improvements for BIAsp 30 but increased treatment-related lifetime cost savings. BIAsp 30, either once- or twice-daily, improved projected life expectancy or reduced projected costs compared with IGlarg in the Chinese setting[48].

**Tunceli *et al.*, (2010)** has performed a cohort study using the Health Core Integrated Research Database identified T1DM and T2DM patients age ≥18 and ≤ 65 years between 1/1/2006 – 12/31/2006 to compared the annual direct healthcare cost among T1DM and T2DM patients using two cost estimation methods: (1) DM-attributable cost and (2) all cause case–control cost. DM-attributable cost was assessed by summing medical claims for DM and pharmacy claims for antihyperglycemic agents, and all cause health care cost was assessed for cases and controls. A total of 12,096 T1DM and 256,245 T2DM cases and matched controls were identified. T1DM and T2DM cases had significantly higher average baseline comorbidities and Deyo–Charleson Comorbidity scores than controls. While DM attributable cost estimation resulted in a mean annual cost of $6247 for T1DM and $3002 for T2DM in 2007, the mean annual (per patient) all-cause total cost estimation using the case–control method resulted in a difference of $10,837 for T1DM; and $4217 for T2DM. DM-attributable cost method underestimated costs by 42% for T1DM and 29% for T2DM compared to the case–control method. The difference was smaller but still significant when multivariate technique was used. Patients with DM may use a substantial amount of medical & pharmacy services and attributable cost method may underestimate the total cost[49].

**Menzin *et al.*, (2010)** has conducted a retrospective cohort analysis to asses the potential relationships between glycemic levels, diabetes-related hospitalizations, and costs among adult patients with either type 1 or type 2 diabetes mellitus who were assigned to a primary care provider (PCP) in a clinic. Data from approximately 200,000 members of the

Fallon Clinic Health Plan who were assigned to a clinic PCP at any time during a 5-year study period beginning starting with each patient's first A1c test and continued until plan disenrollment. In the logistic regression analysis, odds of having at least 1 diabetes-related hospital stay did not significantly differ for patients with mean A1c of < 7% compared with patients in most higher mean A1c categories; however, odds of having a diabetes-related hospitalization were significantly higher for patients with mean A1c of 10% or more compared with patients with mean A1c of < 7%. In the negative binomial regression analysis of those with at least 1 hospital admission, estimated costs per hospitalized patient increased by mean HbA1c level. In the Poisson regression analysis, the rate of diabetes-related hospitalizations significantly increased by A1c level. In the 2-part model results, adjusted mean estimated costs of diabetes-related hospitalizations per study patient were $2,792 among those with mean A1c of < 7% and $6,759 among those with mean A1c of 10% or more. In this managed-care plan, the odds of having at least 1diabetes-related hospitalization were not significantly associated with higher mean A1c except for patients with mean A1c of at least 10%, however, higher mean A1c levels were associated with significantly higher estimated hospitalization costs among those with at least 1 hospitalization and with higher rates of diabetes-related hospital utilization per 100 patient-years[50].

**Al-Maskari *et al*., (2010)** has estimated the direct annual treatment costs of DM and its related complications among patients in Al-Ain city, UAE. A sample of 150 DM patients were enrolled during 2004-2005, and their medical costs over the ensuing 12 months was measured, quantified, analyzed and extrapolated using conventional and inference statistics. The total annual direct treatment costs of DM among patients without complications, was US $1,605 which is 3.2 times higher than the per capita expenditure for health care in the UAE during 2004. However, this cost increased 2.2 times with the presence of DM related complications for patients with microvascular, 6.4 times for patients with macrovascular and 9.4 times for patients with both micro and macrovascular complications. Likewise, the annual direct hospitalization costs of DM patients increased by 3.7 times for patients with microvascular complications, by 6.6 times for patients with macrovascular complications and by 5 times for patients with both micro and macrovascualr complications. Hospitalisation costs constituted a large proportion and were increasingly higher with the presence and progression of DM related complications. To reduce the impact on healthcare resources, efforts should be made to prevent progression to DM complications, by

implementing guidelines for diabetes care, screening for complications and better management[51].

**Kapoor*et al.*, (2010)** performed a cross-sectional study was conducted among adult Saharia, a primitive tribal group of Madhya Pradesh. A total of 364 subjects ranging in age group 18 - 60 years were divided into two groups based on their random blood sugar level. Stature, weight, waist circumference, hip circumference, skin fold thicknesses, fat percent, blood pressure and blood sugar level were measured for all the subjects. 8.9% males and 7.1% females were found to be having more than 140 mg/dl random sugar level. All the skin fold thicknesses, body circumference, indices of adiposity, fat percentage and blood pressure were found to be significantly higher among the 'pre-diabetic males'. The picture was not so clear among females. Saharia is a socio-economically weaker population with very low literacy level but the clustering of higher blood sugar level, higher blood pressure and higher fat percentage is an indicator of a beginning of metabolic syndrome among this primitive tribal group showing a paradoxical situation[52].

**Lage *et al*., (2009)** has compared costs of Exenatide and sitagliptin among patients with type 2 diabetes treated with either of these agents. Data with dates of service from September 1, 2005 through August 31, 2007, were obtained from a large US retrospective claims database. Intent-to-treat cohorts of adults diagnosed with T2D who began taking either exenatide ($n$=1885) or sitagliptin ($n$=2482) and did not use the alternate medication in the 6-month follow-up period were created. Six-month total medical costs were estimated and examined using either stepwise multivariate regressions or a two-part model that controlled for the probability of using the medical service. The analysis controlled for the potential impact of patient demographics, general health, prior resource use, co-morbidities, and timing of treatment initiation. Exenatide was associated with lower total 6-month direct medical costs and outpatient costs, despite some component costs being slightly higher with exenatide: diabetes-related drug costs, diabetes-related medical costs, and emergency room costs. Compared with the use of sitagliptin, exenatide was associated with lower total medical costs (difference of $655) despite higher total diabetes-related costs (difference of $140). As a result, there appears to be overall cost savings associated with the use of exenatide relative to sitagliptin[53].

**Afkhami-Ardekani *et al.*, (2009)** has conducted a cross sectional study to assess the prevalence of type 2 diabetes complications and their contributing factors, carried

out on 1000 the type 2 diabetic patients referred to Yazd Diabetes Research Center. All diabetic patients underwent the specific tests for retinopathy, nephropathy, neuropathy, peripheral vascular diseases and cardiovascular diseases. Logistic regression analysis was used to find out strength of association of risk factors with a specific complication. In this study 1000 type 2 diabetic patients were studied. Nephropathy was diagnosed in 285, retinopathy in 519, CAD in 251, PVD in 143, CVA in 109 and foot ulcer in 84 patients.In this study the most important contributing factors in diabetic complications were age, duration of diabetes, blood pressure, glycated hemoglobin and Body Mass Index. So glycemic and blood pressure control can prevent diabetic complications or at least delay them[54].

**Ramesh *et al*., (2009)** has conducted a prospective, open label, randomized study in a South Indian state for nine months to assess the impact of pharmacist provided patient education on knowledge, attitude, practice (KAP) and quality of life in Type 2 diabetes mellitus patients. 78 patients meeting the study criteria were randomized into control and test group through envelope method. 70 patients completed all the follow-ups of the study. Content and translation validated KAP questionnaire and Ferrans and Powers quality of life questionnaire were administered to assess the influence of education. The validated F & P questionnaire was supported by an internal consistency á = 0.96 and a temporal stability r = 0.89 and construct validity r = 0.88. The test group patients received pharmacist provided patient education regarding drug therapy, diet, exercise and life style modifications through the verbal and written education material (PIL) in regional language. The control group patients received patient education at the end of the study. A significant improvement was observed with respect to knowledge, practice and attitude towards disease management, QOL scores in various domains and a significant decrease in blood glucose ($P < 0.05$) was observed in test group patients[41].

**Palmer *et al*., (2008)** has studied the long-term clinical and cost-effectiveness of switching to Biphasic Insulin Aspart in poorly- controlled Type 2 Diabetes Patient in Chinese setting using a computer simulation CORE Diabetes Model. Previous data on treatment effects and patient characteristics were obtained from Physicians' Routine Evaluation of Safety and Efficacy of NovoMix 30 Therapy, a multi country, single-arm, observational study where type 2 diabetes patients poorly controlled with biphasic human insulin were converted to biphasic insulin aspart 30; the Chinese subgroup experienced an improvement in HbA1c and a reduction in hypoglycemic events. Extensive sensitivity analyses were performed. Conversion to BIAsp30 was associated with increased direct

medical costs of Chinese Yuan (CNY) 1751 per patient, due to higher pharmacy and management costs (CNY+19,007), offset by reduced diabetes-related complication costs (CNY –17,254) over patient lifetimes. BIAsp30 was associated with an incremental cost-effectiveness ratio of CNY 1926 per QALY gained and clinical outcomes was improved but associated with increased lifetime medical costs. BIAsp30 would be considered cost-effective in China given a willingness-to-pay threshold of CNY 100,000 per QALY gained in type 2 diabetes patients poorly controlled on BHI[55].

**Tunis *et al.*, (2008)** has evaluated the long-term cost-effectiveness of pioglitazone compared to rosiglitazone in treating patients with T2DM and dyslipidemia, and determine the extent to which reported beneficial lipid effects of pioglitazone would improve clinical and economic outcomes through reduced macrovascular complications. The validated CORE Diabetes Model was used to simulate changes in glycosylated hemoglobin, complications, and direct medical costs, double-blind trial comparing lipid and glycemic effects of pioglitazone and rosiglitazone among individuals with T2DM and untreated dyslipidemia. Sensitivity analyses examined the impact of cohort, clinical, and cost inputs on incremental cost effectiveness ratios (ICERs). In the base case, pioglitazone was associated with mean quality-adjusted lif years (QALYs) of 7.476 (0.123) vs. 7.326 (0.128) for rosiglitazone. Pioglitazone had $3038 higher total direct costs, but $580 lower complication costs. Risks of four cardiovascular complications were reduced with pioglitazone, while risks of 17 other complications were slightly higher. The ICER for pioglitazone treatment was $20 171/QALY. Results were most sensitive to the effects of HbA1c, high-density lipoprotein-cholesterol, overall lipid effects, and pioglitazone acquisition costs[56].

**Schofield *et al.*, (2008)** has examined the association between long-term health conditions and being out of the labour force among older Australians. Retrospective analysis of cross-sectional data from the Australian Bureau of Statistics 2003 Survey of Disability, Ageing and Carers for people aged 45–64 years. Main outcome measuresof gross domestic product lost as a result of premature retirement associated with ill health. 9198 people surveyed were aged 45–64 years, 3010 of whom were not in the labour force. Of these, 1373 had retired because of a chronic health condition, most commonly a back problem, or arthritis and related disorders. When adjusted for age and sex, all conditions studied except diseases of the ear and mastoid process, other endocrine/nutritional and metabolic disorders, noise-induced deafness or hearing loss, and high cholesterol were significantly associated with being out of the labour force. Extrapolating from these results,

an estimated 663 235 older Australians were not working because of ill health, reducing Australia's gross domestic product by around $14.7 billion per annum. Prevention of long-term health conditions may help older Australians remain in the labour force longer, thereby increasing revenue to fund health care for the ageing population[57].

**Crivera *et al*., (2006)** has estimated the incremental medication cost of providing optimal therapy to reach recommended goals versus actual therapy in patients with T2DM. A total of 601 type 2 diabetes patients receiving care from the outpatient clinics from March 1, 1996–August 31, 1997, selected randomly and abstracted clinical- medication data. Treatment algorithms based on 2004 clinical practice guidelines were applied for hyperglycemia, hyperlipidemia, and hypertension to patients' current medication therapy to determine how medication regimens could be improved to attain recommended treatment goals to assess the Mean incremental medication costs, the cost differences between current and recommended therapies. Average annual medication cost/patient would increase from $1525 to $2164 and annual incremental costs/patient increased by $168 for antihyperglycemic medications, $75 for antihypertensive medications, $392 for antihyperlipidemic medications, and $3 for aspirin prophylaxis. Average yearly incremental cost of recommended laboratory testing ranged from $77–$189/patient, optimizing drug regimens to achieve recommended treatment goals for type 2 diabetes was approximately $600/patient. These results provide valuable input for assessing the cost-effectiveness of improving comprehensive diabetes care[58].

**Esposti *et al*., (2004)** performed a clinical practice-based analysis of how long patients remain on various antihypertensive drugs. An administrative database listing of patient baseline characteristics, drug prescriptions, and hospital admissions was used. All new users of antihypertensive drugs, ≥20 years of age, receiving a first prescription for diuretics, β blockers, CCBs, ACE inhibitors, or ARB antagonists for an entire year of 2000, were included and observed. A total of 14,062 patients were included in the study, 39.7% of whom remained on treatment provided. Persistent patients (duration of therapy > 273 days) were more likely to be older, taking other drugs for concurrent disorders, hospitalized for cardiovascular diseases, and initially prescribed ARB antagonists, accounted for 80.6% of the overall cost for antihypertensive drugs. Factors associated with drug cost were age, pattern of persistence, number of prescribed classes, and specific medication at enrollment, is needed to evaluate the appropriateness and the cost-effectiveness of drug use[59].

**Palmer *et al*., (2004)** has observed the application of the CORE Diabetes Model in type 2 diabetes using a simulated the long-term cost-effectiveness of repaglinide/ metformin combination therapy versus nateglinide/metformin for treatment of individuals with type 2 diabetes with an inadequate response to sulphonylurea, metformin, or fixed dose glyburide/metformin. HbA1c changes for each regimen were taken from a comparative study. At the end of the study, changes in HbA1c from baseline were –1.28% points and –0.67% points for repaglinide/ metformin and nateglinide/metformin, respectively. Costs were calculated as the annual costs for drugs plus costs of complications over a 30-year period. Outcomes and costs were discounted at 3% annually.With repaglinide/metformin, improved glycaemic control led to projected decreases in complication rates, improvement of LE and QALE by 0.15 and 0.14 years respectively and total cost savings of $3,662/person over the 30-year period. Repaglinide/metformin had a 96% probability that the incremental costs per quality-adjusted life year gained would be $20,000 or less, and a 66% probability that repaglinide/metformin would be cost-saving compared to nateglinide/metformin. Sensitivity analyses supported the validity and reliability of the results. In the health economic context, repaglinide/metformin combination was dominant to nateglinide/metformin[60].

**Bottomley., (2001)** has performed a cross sectional postal T2ARDIS*survey and data were acquired from a random sample of people diagnosed with type 2 diabetes from population-wide diabetes registers. Aggregated resource use, implications for healthcare management, costs in the NHS and Social Services were considered. The data were compared to resource data in the general population to determine the impact of developing diabetic complications, particularly vascular disease. Implications for services were also considered. At a population level, on average one in four patients reported microvascular complications, one in 10 macrovascular complications and one in 14 reported both. Compared to the general population, people with T2DM were admitted to hospital more often and stayed longer as in-patients. This trend was similar for out-patient care. Across the whole cohort, more than 40% of the NHS cost was due to in-patient care. Diabetic complications increased costs in the NHS and Social Services, costs of insulin products and other drugs. The average annual spend on oral antidiabetic drugs accounted for only 2% of NHS costs for diabetes. Most of the costs of care for the person with type 2 diabetes are borne by the NHS and the hospital sector[61].

# Aim & Objectives

## III. AIM AND OBJECTIVES

Diabetes mellitus is a chronic potentially disabling disease commonly encountered by health care professionals that represents an important public health and clinical concern[12, 62]. Diabetes mellitus is a costly disease, both for the patient and the health care provider due to its chronicity and multi-organ involvement which resulted in frequent visit and admission to health facilities[11].

Pharmacoeconomics is a part of the tool bag; Pharmacist can be used to improve the efficacy of his profession. It adopts and applies the principles & methodology of health economics to the field of pharmaceutical policy [34]. The cost benefit analysis facilitates decision making regarding the implementing, withdrawing or continuing of a program. Net social gains or loss make it easy for making decisions. Furthermore, CEA studies facilitate comparisons between different programs with different outcomes, since all outcomes are converted into monetary values[63].

The large cost is associated with diabetes and its treatment is unsustainable of most health care systems and hence there is increasing use of economic evaluation as a tool to allocate resources. These evaluates can track the current costs and assess the future expenses and resources allocation, which leads to the improvement of the quality of healthcare [63]. Decisions about what treatment should be available within a healthcare system have always been influenced by the resources available to pay for them [34]. Economics are an issue in diabetes care because patients require continues medication care, monitoring supplies and equipment, regular office appointments and patient self management education to prevent acute complications and to reduce the risk of long term complications[23].

***Aim***

The aim of this study was to perform pharmacoeconomic evaluation of long term and clinical outcomes of patients receiving anti diabetic treatment and to compare the total direct medical costs with each drug treatment. This was a prospective study that included only the records of patient who received anti diabetic drugs to improve the quality of care and to improve the compliance of diabetes to the medical care provided.

***Objectives***

- To find the patient demographics of diabetic population
- To assess their adherence to therapy and Quality of health care
- To analyze their clinical data with ongoing therapy
- To study the prescribing pattern of the antidiabetic drugs
- To analyze their cost of therapy & beneficence
- To compare the cost and benefits among each drug used for treatment

# Plan of Work

## IV. PLAN OF WORK

The present study was carried out for an entire period of 6 months from August 2011 to January 2011 to achieve the objective. The study was designed as outlined below.

Stage I: Preparatory study to identify the scope of the work.

Stage II: Literature survey.

Stage III: Compose study protocol.

Stage IV: Attain permission from the hospital authority.

Stage V: Contrive a data entry form

Stage VI: Data collection.

Stage VII: Analysis of procured data.

Stage VIII: Perform cost minimization analysis.

Stage IX: Execute cost effectiveness analysis based on cost minimization analysis.

Stage X: Submission of report.

# Methodology

## V. METHODOLOGY

***Study site***

The study was conducted at Monika Diabetic Care Centre, Erode.

***Consent from hospital authorities***

The proposal of the study including the aim, objectives, and plan of work was submitted to the director of the hospital and consent was obtained.

***Study duration***

The study duration was between August to December 2011.

**Analysis**

The duration of therapy (days elapsing between the 1st and the last prescription) and the mean daily dose were calculated[45].

***Literature survey***

The extensive survey of literatures was carried out about the pharmacoeconomics of the anti-diabetic drugs, extensively prescribed. The literature was procured from primary, secondary and tertiary sources of drug information.

***Study design***

The study was performed as a retrospective method to analyze the pharmacoeconomics of drugs prescribed widely for their cost minimization and cost effectiveness, in management of diabetes mellitus.

***Sources of data***

All the indispensible and pertinent information are procured from the patient medication profile and direct interview with patients.

***Data entry form***

A distinctly contrived data entry form was used to enter patient's details like age, sex, food habits, occupational status, co morbid diseases, clinical data, diabetic complications and drugs used for treatment. The data collected for the study were analyzed and the report was submitted.

***Data procurement***

All the needful and applicable information are collected in a distinctive data entry form, while patients were waiting to see the Diabetician. Ethical approval for the study was obtained from the institutional ethics committee. Anonymity and confidentiality of the information provided by the patient was maintained throughout and after the present study.

**Study variables**

This was operationalised by assessing the usefulness of antidiabetics in diabetes management (International classification of diseases nineth revision (ICD-9) Code 250xx); using QALY achieved from each type of drug administrated was obtained by "The Quality of Life Health Questionnaire" by Hadorn and Uebersax[68]. Incremental cost effectiveness ratio (ICER) is calculated based on the discounted incremental cost to discounted quality adjusted life in years.

**Cost analysis**

Direct costs of anti diabetic drugs were taken into account and evaluated at MIMS- Asia purchase price. Costs were expressed as overall and average values. The currency reference was the Indian rupees (₹). The mean price of the drugs belonging to the '5'pharmacological classes and their combinations available in market, weighed for the number of drugs administered for each individual drug was ₹ for Insulins, ₹ for Biguanides etc [45].

**Discounting**

Discounting of future costs and clinical outcomes (in terms of life in years) was performed with a discount rate of 3% per annum applied in the base case analysis based on WHO guidelines for cost effectiveness analysis[48].

# *Observations*

## VI. OBSERVATIONS

**Table- 1: Data on patients enrolled for study.**

| | | |
|---|---|---|
| Number of Male patients | 229 | 54.39% |
| Number of Female patients | 192 | 45.61% |
| Total number of patients enrolled | 421 | 100% |

**Characteristics of patients with Diabetes: Age wise distribution**

**Table- 2: Age wise distribution of Diabetes with Average duration and Body Mass Index (n= 407)**

| Age Group (*in years*) | Total (%) | Duration (yrs range) | BMI ($Kg/m^2$) | Male (%) | Female (%) |
|---|---|---|---|---|---|
| Below 20 | 0.74 | 1-5 | 11.27 | 0.25 | 0.49 |
| 21-30 | 1.72 | 1-5 | 23.88 | 1.23 | 0.74 |
| 31-40 | 9.58 | 1-5 | 24.62 | 6.88 | 2.70 |
| 41-50 | 27.52 | 6-10 | 25.82 | 15.23 | 12.29 |
| 51-60 | 33.66 | 6-10 | 26.19 | 17.44 | 16.22 |
| 61-70 | 21.13 | 6-10 | 25.5 | 11.30 | 10.07 |
| 71-80 | 5.16 | 11-15 | 25.34 | 2.70 | 2.46 |
| Above 80 | 0.25 | 1-5 | 21.46 | 0.25 | 0 |

**Table- 3: Occupational status and Weight variations of patients with Age wise Distribution (n= 407)**

| Age Group | Sedentary | Active | Pensioner | Wt gain | Wt loss |
|---|---|---|---|---|---|

| (*in years*) | (%) | (%) | (%) | (%) | (%) |
|---|---|---|---|---|---|
| Below 20 | 0.25 | 0.49 | 0 | 0 | 0 |
| 21-30 | 0.49 | 0.98 | 0 | 0 | 0.49 |
| 31-40 | 3.93 | 4.42 | 0 | 1.23 | 4.67 |
| 41-50 | 13.27 | 11.06 | 0.98 | 2.21 | 11.30 |
| 51-60 | 19.90 | 8.85 | 1.22 | 3.19 | 15.48 |
| 61-70 | 14.99 | 2.95 | 2.21 | 2.21 | 9.34 |
| 71-80 | 3.69 | 0.25 | 0.98 | 0.25 | 2.70 |
| Above 80 | 0.25 | 0 | 0 | 0 | 0 |

**Characteristics of patients with Diabetes: Duration wise distribution**

**Table- 4. Duration wise distribution of Diabetes with Average Age and Body Mass Index (n= 407)**

| Duration Group (*in years*) | Total (%) | Age (yrs range) | BMI ($Kg/m^2$) | Male | | Female | |
|---|---|---|---|---|---|---|---|
| | | | | No: | (%) | No: | (%) |
| New 0-1 | 13.26 | 41-50 | 24.52 | 38 | 9.34 | 16 | 3.93 |
| 1-5 | 39.80 | 51-60 | 26.00 | 93 | 22.60 | 68 | 16.71 |
| 6-10 | 24.32 | 51-60 | 24.83 | 44 | 10.81 | 56 | 13.71 |
| 11-15 | 13.26 | 51-60 | 25.80 | 27 | 6.34 | 26 | 6.34 |
| 16-20 | 6.88 | 51-60 | 25.97 | 15 | 3.69 | 13 | 3.19 |
| 21-25 | 1.97 | 51-60 | 31.24 | 5 | 0.998 | 4 | 0.98 |
| Above 25 | 0.49 | 71-80 | 26.95 | 1 | 0.25 | 1 | 0.25 |

**Table- 5: Occupational status and Weight variations of patients with Age wise Distribution (n= 407)**

| Duration Group (*in years*) | Sedentary (%) | Active (%) | Pensioner (%) | Wt gain (%) | Wt loss (%) |
|---|---|---|---|---|---|
| New 0-1 | 6.88 | 5.90 | 0.25 | 0.98 | 7.86 |

| | | | | | |
|---|---|---|---|---|---|
| 1-5 | 20.64 | 14.50 | 1.47 | 4.67 | 14.00 |
| 6-10 | 15.72 | 6.39 | 1.47 | 1.72 | 11.55 |
| 11-15 | 9.09 | 2.46 | 1.47 | 0.49 | 7.37 |
| 16-20 | 4.67 | 0.74 | 0.74 | 0.25 | 2.70 |
| 21-25 | 1.47 | 0.25 | 0.25 | 0.25 | 0.74 |
| Above 25 | 0.25 | 0.25 | 0 | 0.25 | 0.25 |

**Co-existing illness of patients with Diabetes: Age wise distribution**

**Table- 6: Micro vascular complications (n= 407)**

| **Age Group (*in years*)** | **Retinopathy (%)** | **Foot ulcer (%)** | **Nephropathy (%)** | **Neuropathy (%)** |
|---|---|---|---|---|
| Below 20 | 0 | 0 | 0.49 | 0 |
| 21-30 | 0.49 | 0 | 0.49 | 0.49 |
| 31-40 | 2.70 | 0.98 | 3.44 | 3.44 |
| 41-50 | 12.53 | 4.91 | 10.07 | 11.55 |
| 51-60 | 15.97 | 7.62 | 14.50 | 18.67 |
| 61-70 | 13.76 | 6.14 | 10.32 | 12.29 |
| 71-80 | 4.18 | 1.97 | 2.21 | 2.70 |
| Above 80 | 0 | 0.25 | 0 | 0 |

**Table- 7: Macro vascular complications (n= 407)**

| **Age Group (*in years*)** | **Hypertension (%)** | **Dyslipidemia (%)** | **Cardio Vascular Diseases (%)** | **Peripheral Vascular Diseases (%)** |
|---|---|---|---|---|
| Below 20 | 0 | 0 | 0 | 0 |
| 21-30 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| 31-40 | 2.21 | 1.97 | 0 | 0.49 |
| 41-50 | 11.30 | 5.65 | 0.49 | 0.49 |
| 51-60 | 15.48 | 7.37 | 3.19 | 0.98 |
| 61-70 | 16.22 | 7.37 | 1.72 | 0.49 |
| 71-80 | 3.44 | 0.98 | 0.49 | 0.25 |
| Above 80 | 0 | 0 | 0 | 0 |

**Co-existing illness of patients with Diabetes: Duration wise distribution**

**Table- 8: Micro vascular complications (n= 407)**

| **Duration Group (*in years*)** | **Retinopathy (%)** | **Foot ulcer (%)** | **Nephropathy (%)** | **Neuropathy (%)** |
|---|---|---|---|---|
| New 0-1 | 4.18 | 1.72 | 5.65 | 4.67 |
| 1-5 | 18.43 | 7.86 | 17.20 | 19.90 |
| 6-10 | 13.02 | 5.65 | 11.30 | 12.53 |
| 11-15 | 8.11 | 3.69 | 4.91 | 7.37 |
| 16-20 | 4.91 | 3.19 | 2.95 | 3.19 |
| 21-25 | 1.72 | 0.74 | 0.74 | 1.72 |
| Above 25 | 0 | 0.25 | 0 | 0.49 |

**Table- 9: Macro vascular complications (n= 407)**

| **Duration Group (*in years*)** | **Hypertension (%)** | **Dyslipidemia (%)** | **Cardio Vascular Diseases (%)** | **Peripheral Vascular Diseases (%)** |
|---|---|---|---|---|
| New 0-1 | 4.18 | 1.97 | 0.25 | 0.49 |
| 1-5 | 18.92 | 9.34 | 2.95 | 0.74 |
| 6-10 | 11.79 | 5.90 | 0.49 | 0.98 |
| 11-15 | 7.86 | 3.19 | 0.74 | 0.25 |

| | | | | |
|---|---|---|---|---|
| 16-20 | 3.44 | 2.21 | 1.23 | 0.49 |
| 21-25 | 1.47 | 0.98 | 0.25 | 0 |
| Above 25 | 0.49 | 0 | 0 | 0 |

**Quality of Life of patients with Diabetes: Age wise distribution**

**(Hadorn & Uebersax Scale[68], Appendix II)**

**Table- 10: Suffering of patients (n= 407)**

| **Age Group (*in years*)** | **None (%)** | **Mild (%)** | **Moderate (%)** | **Severe (%)** |
|---|---|---|---|---|
| Below 20 | 0.49 | 0 | 0.25 | 0 |
| 21-30 | 0.98 | 0.25 | 0 | 0 |
| 31-40 | 5.90 | 1.47 | 0.25 | 0 |
| 41-50 | 16.46 | 6.14 | 1.47 | 0 |
| 51-60 | 23.59 | 5.90 | 0.98 | 0 |
| 61-70 | 14.00 | 4.42 | 1.23 | 0 |
| 71-80 | 2.70 | 1.47 | 0.49 | 0.25 |
| Above 80 | 0.25 | 0 | 0 | 0 |

**Table- 11: Physical Activity restriction of patients (n= 407)**

| **Age Group (*in years*)** | **None (%)** | **Mild (%)** | **Moderate (%)** | **Severe (%)** |
|---|---|---|---|---|
| Below 20 | 0 | 0.74 | 0 | 0 |
| 21-30 | 0.49 | 0.74 | 0 | 0 |
| 31-40 | 3.44 | 3.19 | 0.49 | 0.49 |
| 41-50 | 9.34 | 9.82 | 2.21 | 2.95 |
| 51-60 | 10.32 | 13.76 | 4.18 | 2.46 |
| 61-70 | 7.37 | 8.11 | 2.95 | 1.23 |
| 71-80 | 1.97 | 2.21 | 0.49 | 0.25 |
| Above 80 | 0.25 | 0 | 0 | 0 |

**Quality of Life of patients with Diabetes: Duration wise distribution**

**(Hadorn & Uebersax Scale[68], Appendix II)**

**Table- 12: Suffering of patients (n= 407)**

| **Duration Group (*in years*)** | **None (%)** | **Mild (%)** | **Moderate (%)** | **Severe (%)** |
|---|---|---|---|---|
| New 0-1 | 9.09 | 2.21 | 0.49 | 0 |
| 1-5 | 24.82 | 8.85 | 1.97 | 0 |
| 6-10 | 16.71 | 3.93 | 1.72 | 0 |
| 11-15 | 8.85 | 2.70 | 0.49 | 0.25 |
| 16-20 | 4.67 | 1.23 | 0.25 | 0 |
| 21-25 | 1.23 | 0.74 | 0 | 0 |
| Above 25 | 0.25 | 0.25 | 0 | 0 |

**Table- 13: Physical Activity restriction of patients (n= 407)**

| **Duration Group (*in years*)** | **None (%)** | **Mild (%)** | **Moderate (%)** | **Severe (%)** |
|---|---|---|---|---|
| New 0-1 | 5.90 | 5.16 | 0.74 | 0.25 |
| 1-5 | 12.04 | 14.74 | 6.14 | 2.70 |
| 6-10 | 8.60 | 10.07 | 1.72 | 1.97 |
| 11-15 | 4.42 | 5.16 | 1.23 | 1.23 |
| 16-20 | 1.72 | 2.46 | 0.74 | 1.23 |
| 21-25 | 0.49 | 0.98 | 0.25 | 1.23 |
| Above 25 | 0.49 | 0 | 0 | 0 |

**Table- 14: Therapy provided to selected patients (n= 388)**

| Therapy | Percentage of patients received treatment (%) |
|---|---|
| Single Drug therapy | 8.76 |
| 2-Drug Combination therapy | 38.92 |
| 3-Drug Combination therapy | 30.15 |
| 4-Drug Combination therapy | 15.21 |
| >4- Drug Combination Therapy | 6.96 |

**Figure- 1: Therapy provided to selected patients (n= 388)**

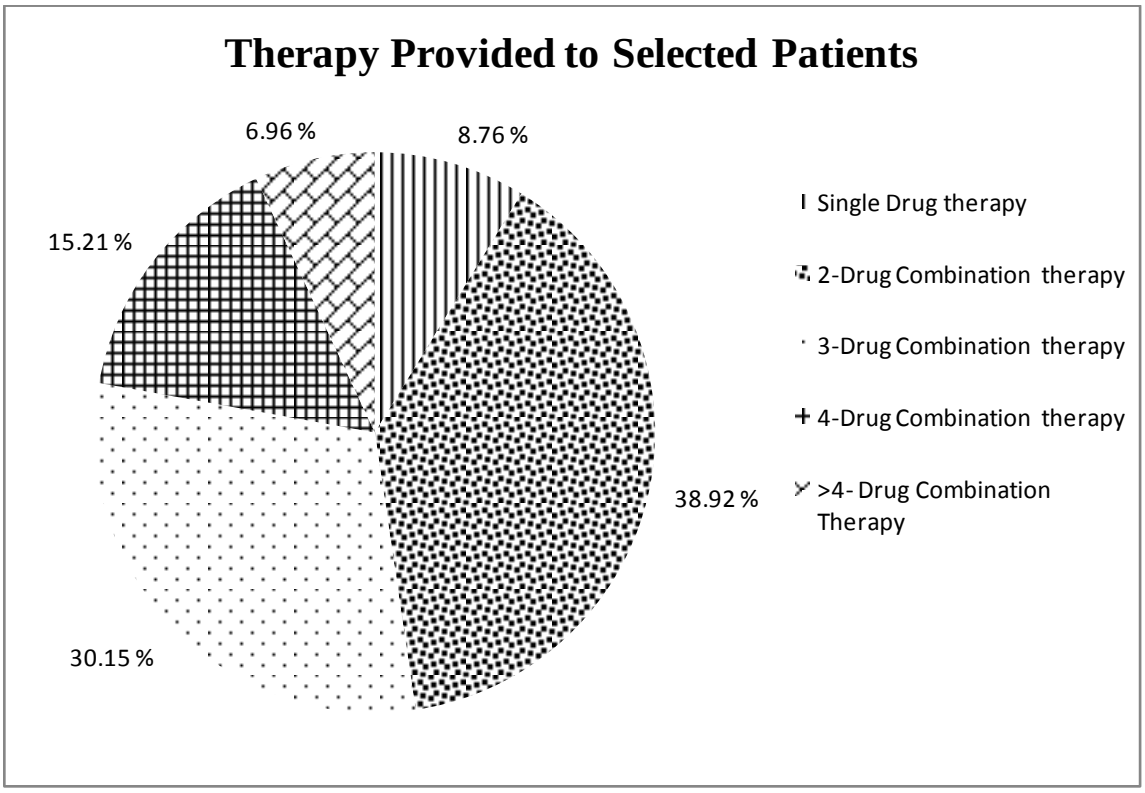


**Table- 15: Drugs provided to patients receiving Single Drug therapy (n= 388)**

| Therapy | Percentage of patients received treatment (%) |
|---|---|
| Total | 8.76 |
| BGS | 5.67 |
| TGZ | 0.26 |
| SUS | 2.32 |
| INS | 0.52 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

**Table- 16: Drugs provided to patients receiving 2-Drug Combination therapy (n= 388)**

| Therapy | Percentage of patients received treatment (%) |
|---|---|
| Total | 38.92 |
| 1 AGI + 1 BGS | 0.26 |
| 1 AGI + 1 SUS | 1.03 |
| 1 BGS + 1 DPP IV | 0.26 |
| 1 BGS + 1 SUS | 27.84 |
| 1BGS + 2 SUS | 2.32 |
| 1 BGS + 1 TGZ | 0.52 |
| 1 AGI + 2 INS | 1.03 |
| 1 AGI + 1 INS | 0.77 |
| 1 BGS + 1 INS | 0.26 |
| 1 SUS + 1 INS | 2.32 |
| 1 INS + 2 SUS | 0.26 |
| 3 INS + 1 SUS | 0.52 |
| 1 SUS + 1 TGZ | 1.55 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 17: Drugs provided to patients receiving 3-Drug Combination therapy (n= 388)**

| **Therapy** | **Percentage of patients received treatment (%)** |
|---|---|
| Total | 30.15 |
| 1 AGI + 1 BGS + 1 DPP IV | 0.26 |
| 1 AGI+ 1 BGS+ 1 SUS | 6.70 |
| 1 AGI + 1 BGS + 2 SUS | 2.32 |
| 1 AGI + 1 BGS + 3 SUS | 0.26 |
| 1 BGS + 1 SUS + 2 DPP IV | 0.77 |
| 1 BGS + 1 SUS + 1 DPP IV | 4.12 |
| 1 BGS + 1 SUS + 1 TGZ | 1.29 |
| 1 BGS + 2 SUS + 1 TGZ | 1.55 |
| 1 INS + 1 BGS + 1 AGI | 0.26 |
| 2 INS + 1 BGS + 1 AGI | 0.26 |
| 1 INS + 1 AGI + 1 SUS | 0.77 |
| 2 INS + 1 AGI + 2 SUS | 0.26 |
| 2 INS + 1 AGI + 1 SUS | 0.52 |
| 3 INS + 1 AGI + 1 SUS | 0.26 |
| 1 INS + 1 AGI + 2 SUS | 0.26 |
| 3 INS + 1 BGS + 1 DPP IV | 0.26 |
| 1 INS + 1 BGS + 1 SUS | 7.99 |
| 4 INS + 1 BGS + 2 SUS | 0.26 |
| 2 INS + 1 BGS + 2 SUS | 0.26 |
| 2 INS + 1 BGS + 1 SUS | 0.52 |
| 1 INS + 1 BGS + 2 SUS | 0.77 |
| 1 INS + 1 DPP IV+ 1 SUS | 0.26 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 18: Drugs provided to patients receiving 4-Drug Combination therapy (n= 388)**

| Therapy | Percentage of patients received treatment (%) |
|---|---|
| Total | 15.21 |
| 1 AGI + 1 BGS + 1 DPP IV + 1 SUS | 2.84 |
| 1 AGI + 1 BGS + 2 DPP IV + 1 SUS | 1.03 |
| 1 AGI + 1 BGS + 1 SUS + 1 TGZ | 0.77 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS | 2.58 |
| 2 INS + 1 AGI + 1 BGS + 1 SUS | 0.77 |
| 3 INS + 1 AGI + 1 BGS + 1 SUS | 1.29 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS | 1.03 |
| 2 INS + 1 AGI + 1 BGS + 2 SUS | 0.52 |
| 1 INS + 1 AGI + 1 BGS + 3 SUS | 0.52 |
| 1 INS +1 SUS + 1 AGI +1 DPP IV | 0.52 |
| 1 INS + 1 AGI + 1 SUS + 1TGZ | 0.26 |
| 1 INS + 1 BGS + 1 DPP IV + 1 SUS | 0.52 |
| 1 INS + 1 BGS + 1 DPP IV + 2 SUS | 1.55 |
| 1 INS + 1 BGS + 2 DPP IV + 1 SUS | 0.26 |
| 2 INS + 1 BGS + 1 DPP IV + 1 SUS | 0.26 |
| 1 BGS + 2 SUS+ 1 TGZ + 1 INS | 0.26 |
| 1 BGS + 3 SUS+ 1 TGZ + 1 INS | 0.26 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 19: Drugs provided to patients receiving >4-Drug Combination therapy (n= 388)**

| Therapy | Percentage of patients received treatment (%) |
|---|---|
| Total | 6.96 |
| 1 AGI + 1 BGS + 1 DPP IV + 1 SUS + 1 TGZ | 0.26 |
| 1 AGI + 1 BGS + 2 DPP IV + 3 SUS + 1 TGZ | 0.26 |
| 1 AGI + 1 BGS + 1 DPP IV + 2 SUS + 1 TGZ | 0.26 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 2 SUS | 0.77 |
| 2 INS + 1 AGI + 1 BGS + 1 DPP IV + 2 SUS | 0.26 |
| 3 INS + 1 AGI + 1 BGS + 1 DPP IV + 2 SUS | 0.26 |
| 1 INS + 1 AGI + 1 BGS + 2 DPP IV + 2 SUS | 0.77 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 1 SUS | 3.09 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS + 1 TGZ | 0.26 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS + 1 TGZ | 0.26 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 1 SUS + 1 TGZ | 0.26 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 2 SUS + 1 TGZ | 0.26 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

## COST MINIMISATION ANALYSIS OF PRESCRIBED DRUGS

**Table- 20: Cost analysis of Drug category of prescribed brands per unit**

| **Therapy** | **Average Lowest cost (₹)** | **Average Highest cost (₹)** | **Difference in costs (₹)** |
|---|---|---|---|
| AGI | 4.71 | 13.85 | 9.14 |
| SUS | 1.55 | 6.12 | 4.57 |
| TGZ | 1.5 | 8.12 | 6.62 |
| INS | 0.49 | 0.49 | 0 |
| DPPI | 37.24 | 27.24 | 0 |
| BGS | 1.15 | 2.48 | 1.33 |

**Figure 2: Cost analysis of Drug Category of prescribed brands in INR (₹)**

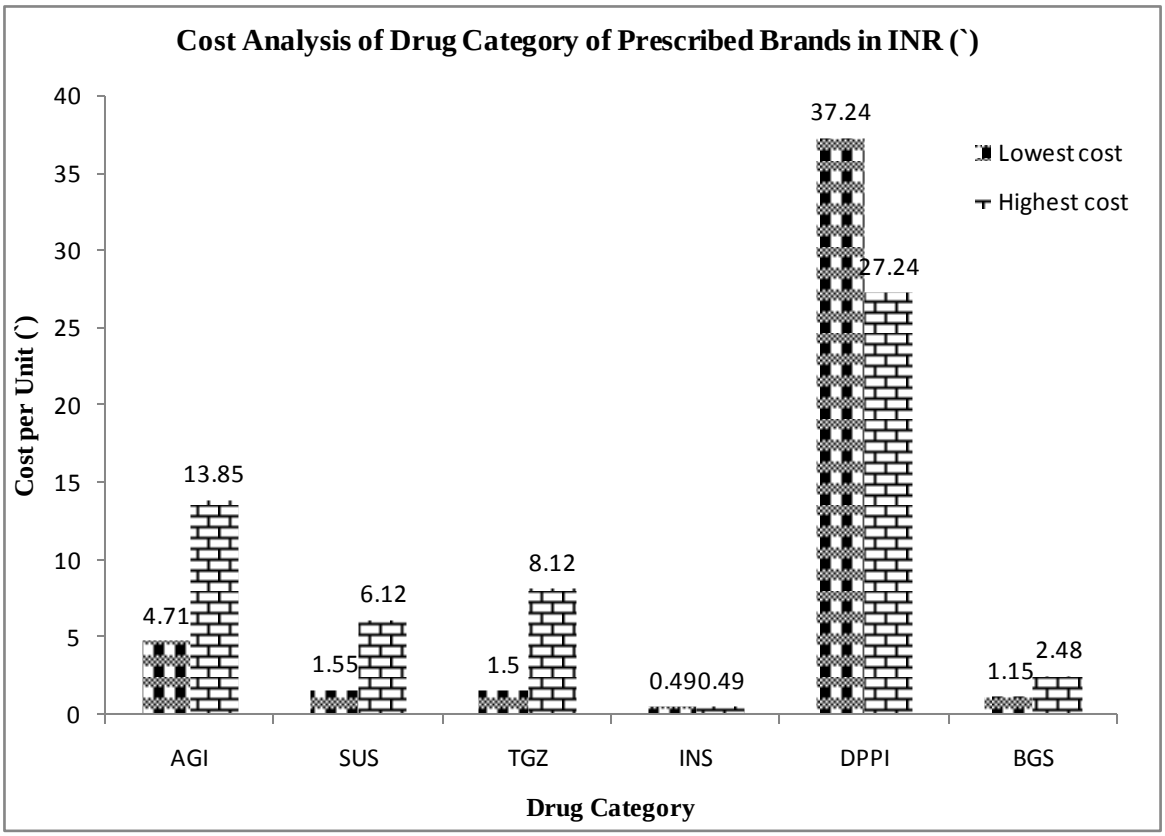



**Table- 21: Cost analysis of combination drugs of prescribed brands available in Market per unit**

| Therapy | Average Lowest cost (₹) | Average Highest cost (₹) | Difference in costs (₹) |
|---|---|---|---|
| AGI+BGS | 6.91 | 8.11 | 1.2 |
| SUS+BGS | 3.63 | 4.81 | 1.18 |
| DPP IV +BGS | 20.35 | 20.35 | 0 |
| TGZ+BGS | 4.56 | 5.84 | 1.28 |
| BGS+SUS+TGZ | 4.98 | 6.63 | 1.65 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 3: Cost analysis of combination drugs of prescribed brands in INR (₹)**

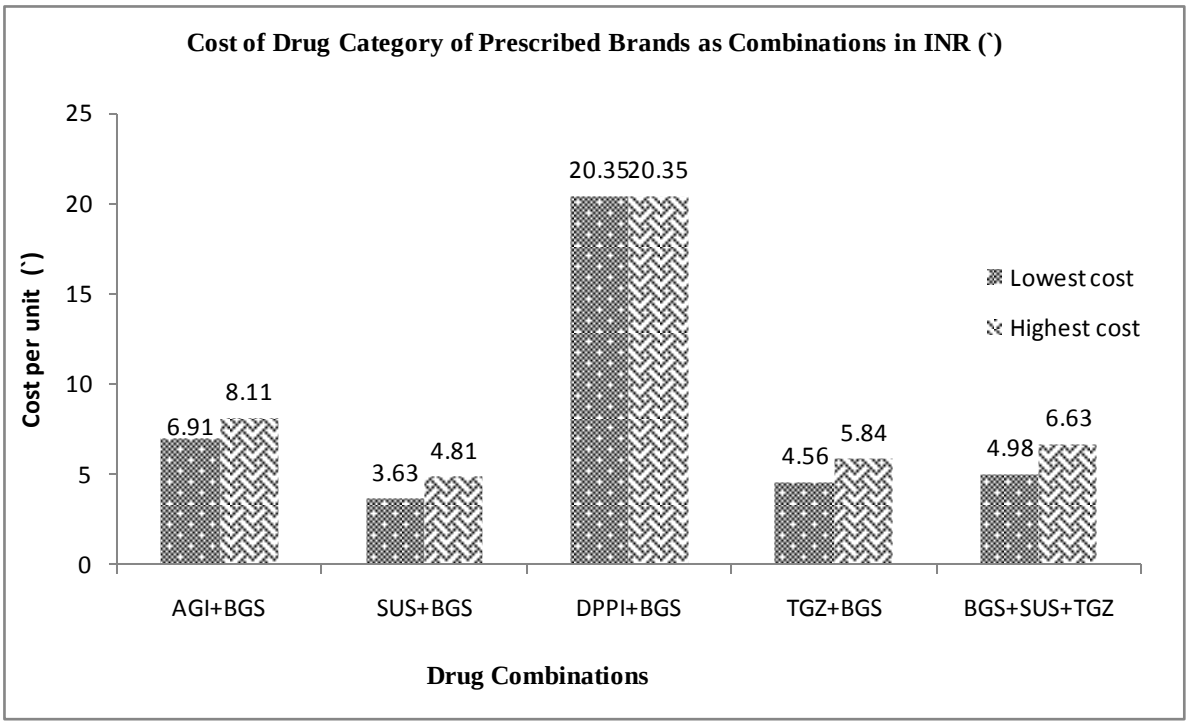



**Table- 22: Cost analysis of individual drug category combinations of prescribed Brands with market available combinations**

| Therapy | Lowest cost of individual drugs | Lowest cost of combination drugs | Difference |
|---|---|---|---|
| AGI+BGS | 5.86 | 6.91 | 1.05 |
| AGI+SUS | 6.26 | - | - |
| AGI+INS | 5.2 | - | - |
| BGS+DPPI | 38.39 | 20.35 | 18.04 |
| BGS+SUS | 2.70 | 3.63 | 0.93 |
| BGS+TGZ | 2.65 | 4.56 | 1.91 |
| INS+BGS | 1.64 | - | - |
| INS+SUS | 2.04 | - | - |
| SUS+TGZ | 3.05 | - | - |
| BGS+ SUS+ TGZ | 4.20 | 4.98 | 0.78 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

**Figure 4: Cost analysis of combination drugs prescribed brands available in Market in INR (₹)**

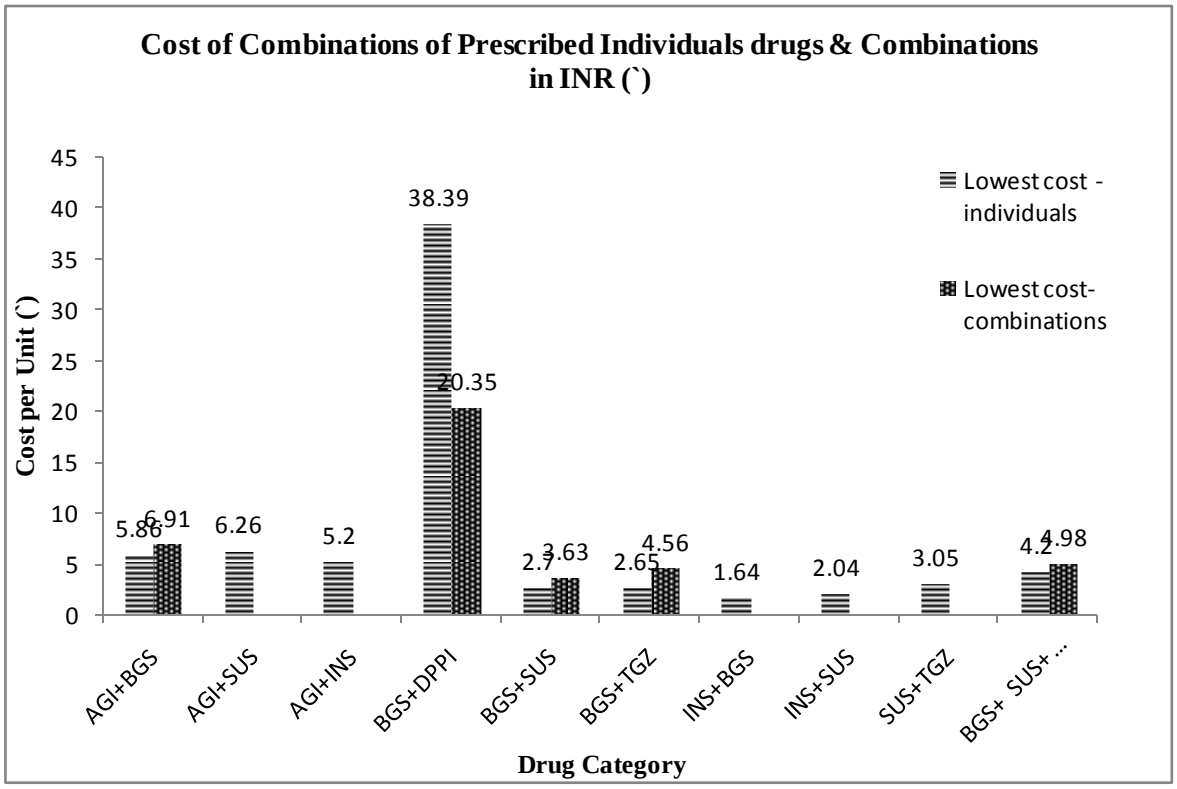



**Table- 23: Annual treatment cost analysis for single drug therapy**

| Therapy | M.Fq. | Unit cost **(₹)** | Cost/Day **(₹)** | Annual cost **(₹)** |
|---|---|---|---|---|
| BGS | BD | 1.15 | 2.30 | 840 |
| SUS | BD | 1.55 | 3.10 | 1132 |
| TGZ | BD | 1.5 | 3.00 | 1095 |
| INS | 27 units | 0.49 | 13.23 | 4830 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

**Figure 5: Annual treatment cost analysis for single drug therapy in INR (₹)**

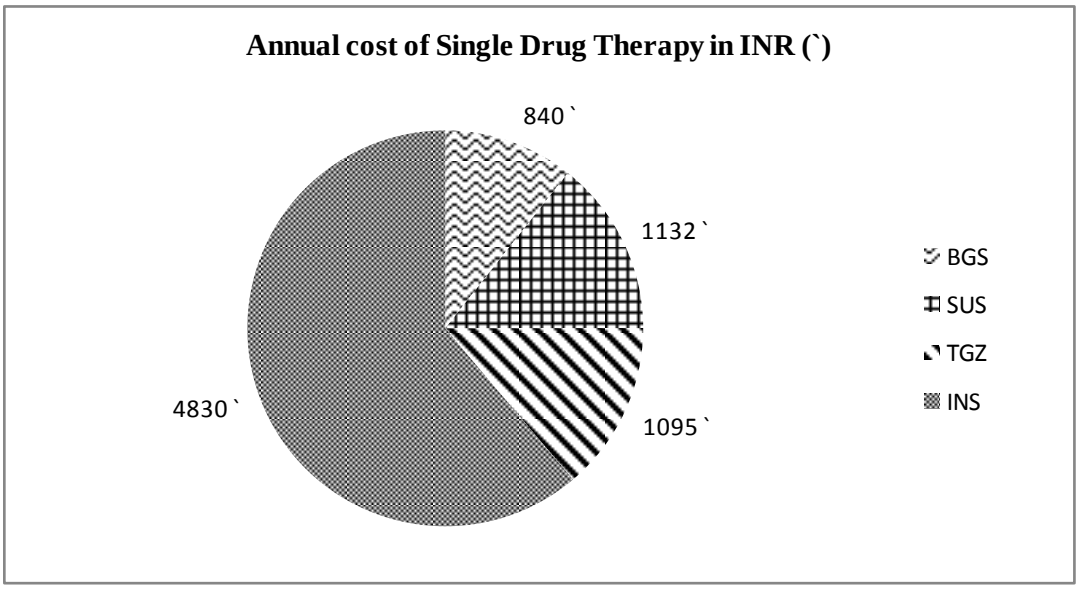



**Table- 24: Annual treatment cost analysis for 2- Drug Combination therapy**

| Therapy | M.Fq. | Unit cost (₹) | Cost/ Day (₹) | Annual cost (₹) |
|---|---|---|---|---|
| 1 AGI + 1 BGS | BD | 5.86 | 11.72 | 4278 |
| 1 AGI + 1 SUS | BD | 6.26 | 12.52 | 4570 |
| 1 BGS + 1 DPP IV | BD | 38.39 | 76.78 | 28025 |
| 1 BGS + 1 SUS | BD | 2.70 | 5.40 | 1971 |
| 1BGS + 2 SUS | BD | 4.25 | 8.50 | 3103 |
| 1 BGS + 1 TGZ | BD | 2.65 | 5.30 | 1935 |
| 1 AGI + 2 INS | BD | 31.17 | 35.88 | 13096 |
| 1 AGI + 1 INS | BD | 17.94 | 22.65 | 8267 |
| 1 BGS + 1 INS | BD | 14.38 | 15.27 | 5574 |
| 1 SUS + 1 INS | BD | 14.78 | 16.33 | 5961 |
| 1 INS + 2 SUS | BD | 16.33 | 19.43 | 7092 |
| 3 INS + 1 SUS | BD | 41.24 | 42.79 | 15618 |
| 1 SUS + 1 TGZ | BD | 3.05 | 6.10 | 2227 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

**Figure 6: Annual treatment cost analysis for 2- Drug Combination therapy in INR (₹)**

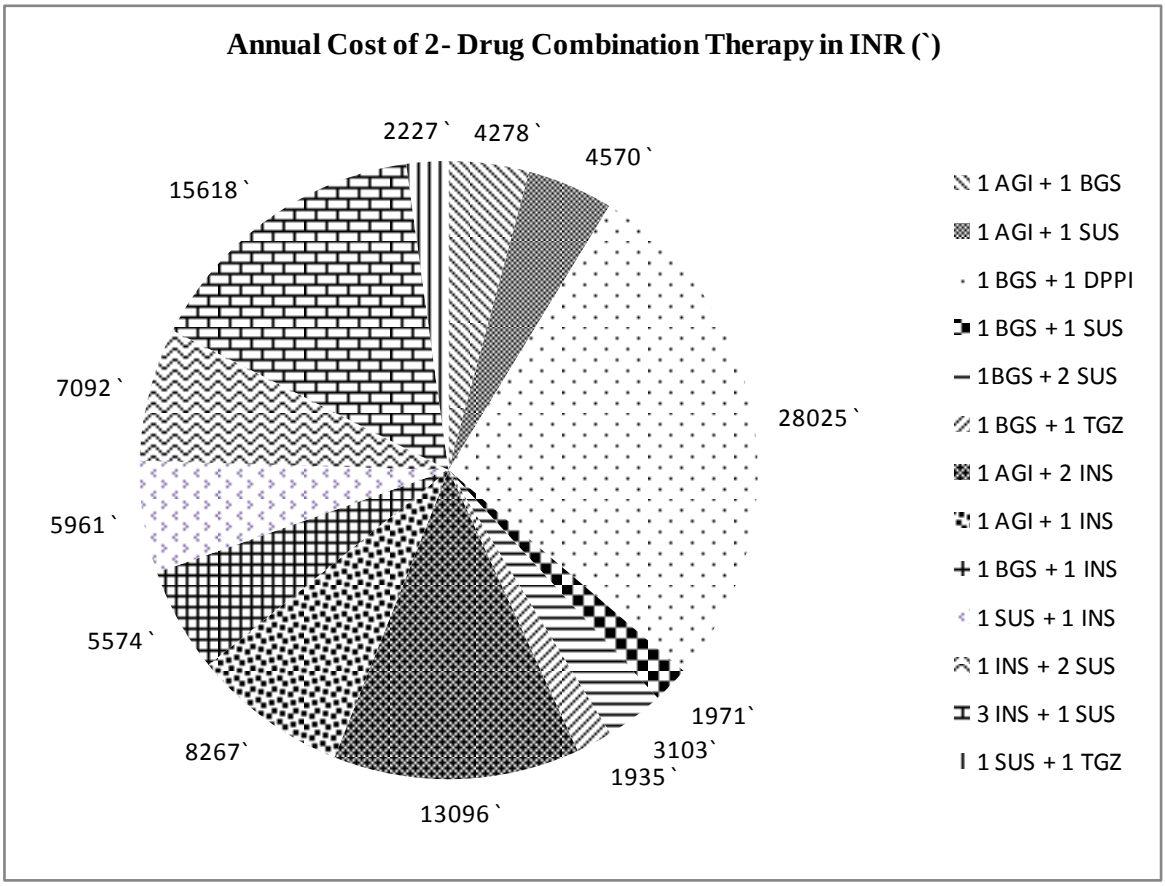


**Table- 25: Annual treatment cost analysis for 3- Drug Combination therapy**

| Therapy | M.Fq. | Unit cost (₹) | Cost/Day (₹) | Annual cost (₹) |
|---|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV | BD | 43.10 | 86.20 | 31463 |
| 1 AGI+ 1 BGS+ 1 SUS | BD | 7.41 | 14.82 | 5409 |
| 1 AGI + 1 BGS + 2 SUS | BD | 8.96 | 17.92 | 6541 |
| 1 AGI + 1 BGS + 3 SUS | BD | 10.51 | 21.02 | 7672 |
| 1 BGS + 1 SUS + 2 DPP IV | BD | 77.18 | 154.36 | 56341 |
| 1 BGS + 1 SUS + 1 DPP IV | BD | 39.94 | 79.88 | 29156 |
| 1 BGS + 1 SUS + 1 TGZ | BD | 4.20 | 8.40 | 3066 |
| 1 BGS + 2 SUS + 1 TGZ | BD | 5.75 | 11.5 | 4198 |
| 1 INS + 1 BGS + 1 AGI | BD | 19.09 | 24.95 | 9107 |
| 2 INS + 1 BGS + 1 AGI | BD | 32.32 | 38.18 | 13936 |
| 1 INS + 1 AGI + 1 SUS | BD | 19.49 | 25.75 | 9399 |
| 2 INS + 1 AGI + 2 SUS | BD | 34.27 | 42.08 | 15359 |
| 2 INS + 1 AGI + 1 SUS | BD | 32.72 | 38.98 | 14228 |
| 3 INS + 1 AGI + 1 SUS | BD | 45.95 | 52.21 | 19057 |
| 1 INS + 1 AGI + 2 SUS | BD | 21.04 | 28.85 | 10530 |
| 3 INS + 1 BGS + 1 DPP IV | BD | 78.08 | 116.47 | 42516 |
| 1 INS + 1 BGS + 1 SUS | BD | 15.93 | 18.63 | 6800 |
| 4 INS + 1 BGS + 2 SUS | BD | 55.62 | 58.32 | 21287 |
| 2 INS + 1 BGS + 2 SUS | BD | 30.71 | 34.96 | 12760 |
| 2 INS + 1 BGS + 1 SUS | BD | 29.16 | 31.86 | 11629 |
| 1 INS + 1 BGS + 2 SUS | BD | 17.48 | 21.73 | 7931 |
| 1 INS + 1 DPP IV + 1 SUS | BD | 52.02 | 90.81 | 33146 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 7: Annual treatment cost analysis for 3- Drug Combination therapy in INR (₹)**

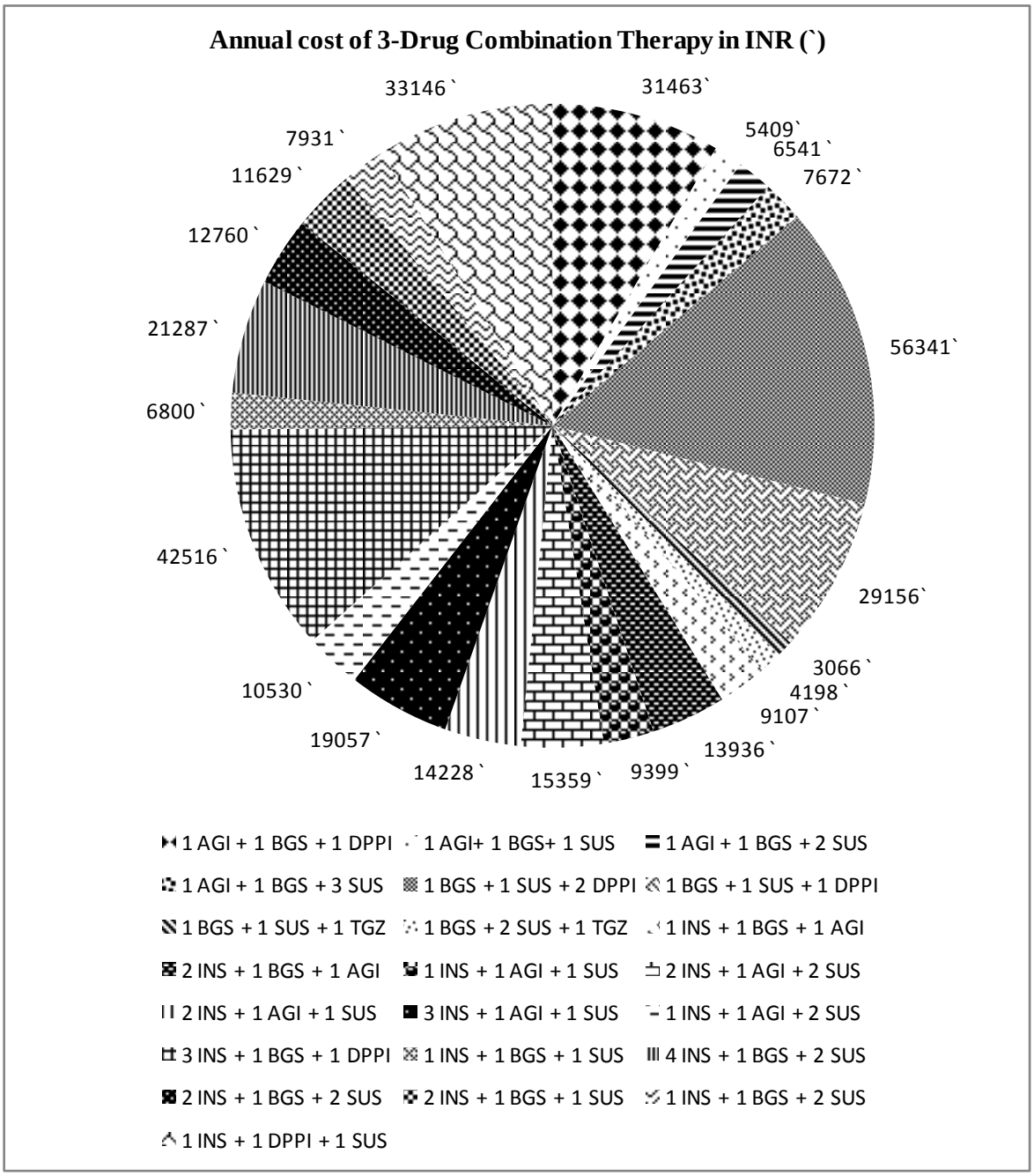


**Table- 26: Annual treatment cost analysis for 4- Drug Combination therapy**

| Therapy | M.Fq. | Unit cost (₹) | Cost/day (₹) | Annual cost (₹) |
|---|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV + 1 SUS | BD | 44.65 | 89.30 | 32595 |
| 1 AGI + 1 BGS + 2 DPP IV + 1 SUS | BD | 81.89 | 163.78 | 59780 |
| 1 AGI + 1 BGS + 1 SUS + 1 TGZ | BD | 8.91 | 17.82 | 6504 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS | BD | 20.64 | 28.05 | 94388 |
| 2 INS + 1 AGI + 1 BGS + 1 SUS | BD | 33.87 | 41.28 | 15067 |
| 3 INS + 1 AGI + 1 BGS + 1 SUS | BD | 47.10 | 54.51 | 19896 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS | BD | 22.19 | 31.15 | 11370 |
| 2 INS + 1 AGI + 1 BGS + 2 SUS | BD | 35.42 | 44.38 | 16199 |
| 1 INS + 1 AGI + 1 BGS + 3 SUS | BD | 23.74 | 34.25 | 12501 |
| 1 INS +1 SUS + 1 AGI +1 DPP IV | BD | 56.73 | 100.23 | 36584 |
| 1 INS + 1 AGI + 1 SUS + 1 TGZ | BD | 20.99 | 28.75 | 10494 |
| 1 INS + 1 BGS + 1 DPP IV + 1 SUS | BD | 53.17 | 93.11 | 33985 |
| 1 INS + 1 BGS + 1 DPP IV+ 2 SUS | BD | 54.72 | 96.21 | 35117 |
| 1 INS + 1 BGS + 2 DPP IV + 1 SUS | BD | 90.41 | 167.59 | 61170 |
| 2 INS + 1 BGS + 1 DPP IV + 1 SUS | BD | 66.40 | 106.34 | 38814 |
| 1 BGS + 2 SUS+ 1 TGZ + 1 INS | BD | 18.98 | 24.73 | 9027 |
| 1 BGS + 3 SUS+ 1 TGZ + 1 INS | BD | 20.53 | 27.83 | 10158 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 8: Annual treatment cost analysis for 4- Drug Combination therapy in INR (₹)**

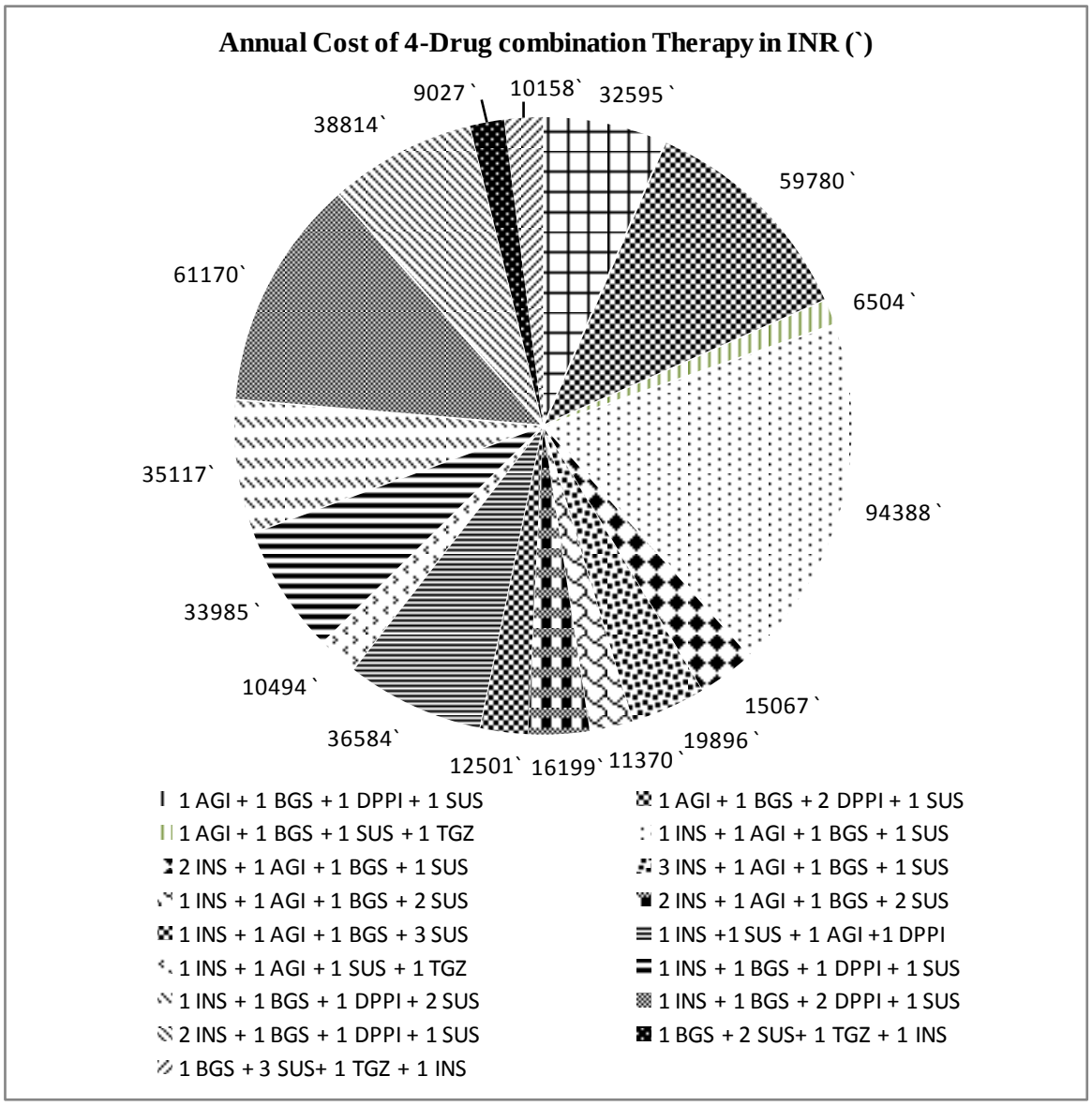


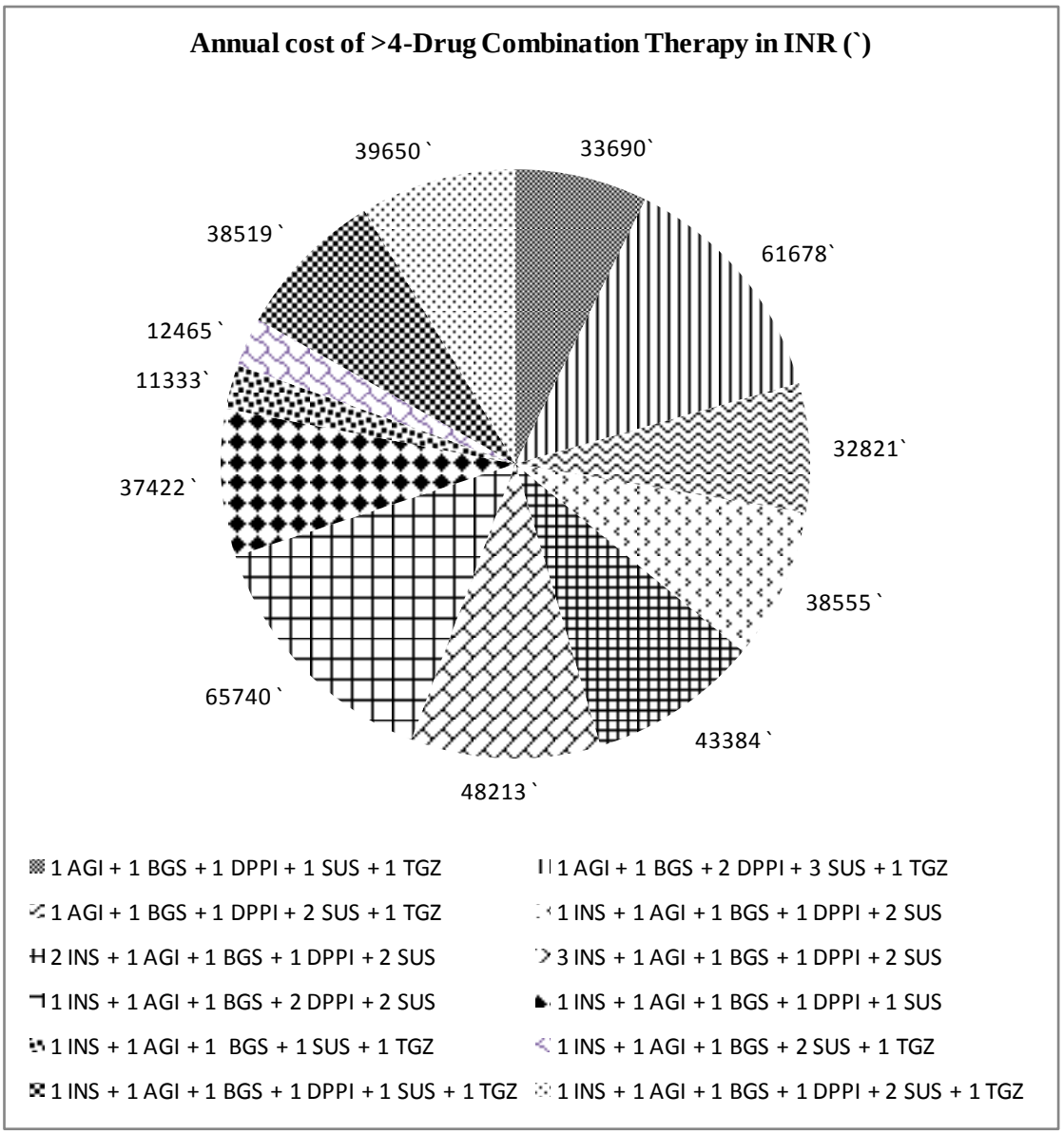
**Table- 27: Annual treatment cost analysis for >4- Drug Combination therapy**

| Therapy | M.Fq. | Unit cost (₹) | Cost/day (₹) | Annual cost (₹) |
|---|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPPI + 1 SUS + 1 TGZ | BD | 46.15 | 92.30 | 33690 |
| 1 AGI + 1 BGS + 2 DPPI + 3 SUS + 1 TGZ | BD | 86.49 | 168.98 | 61678 |
| 1 AGI + 1 BGS + 1 DPPI + 2 SUS + 1 TGZ | BD | 47.70 | 95.40 | 32821 |
| 1 INS + 1 AGI + 1 BGS +1 DPP IV + 2SUS | BD | 59.43 | 105.63 | 38555 |
| 2 INS + 1 AGI +1 BGS + 1 DPP IV + 2SUS | BD | 72.66 | 118.86 | 43384 |
| 3 INS + 1 AGI + 1 BGS + 1 DPP IV + 2SUS | BD | 85.89 | 132.09 | 48213 |
| 1 INS + 1 AGI + 1BGS + 2 DPP IV + 2 SUS | BD | 96.67 | 180.11 | 65740 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 1SUS | BD | 57.88 | 102.53 | 37422 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS + 1 TGZ | BD | 22.14 | 31.05 | 11333 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS + 1 TGZ | BD | 23.69 | 34.15 | 12465 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 1 SUS + 1 TGZ | BD | 59.38 | 105.53 | 38519 |
| 1 INS + 1 AGI + 1 BGS + 1 DPP IV + 2 SUS + 1 TGZ | BD | 60.93 | 108.63 | 39650 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 9: Annual treatment cost analysis for >4- Drug Combination therapy in INR (₹)**



## COST EFFECTIVENESS ANALYSIS

### Incremental Cost per Quality of Life in years gained for Single Drug therapy with Standard SUS (1.00 QALY; ₹ 1132) therapy

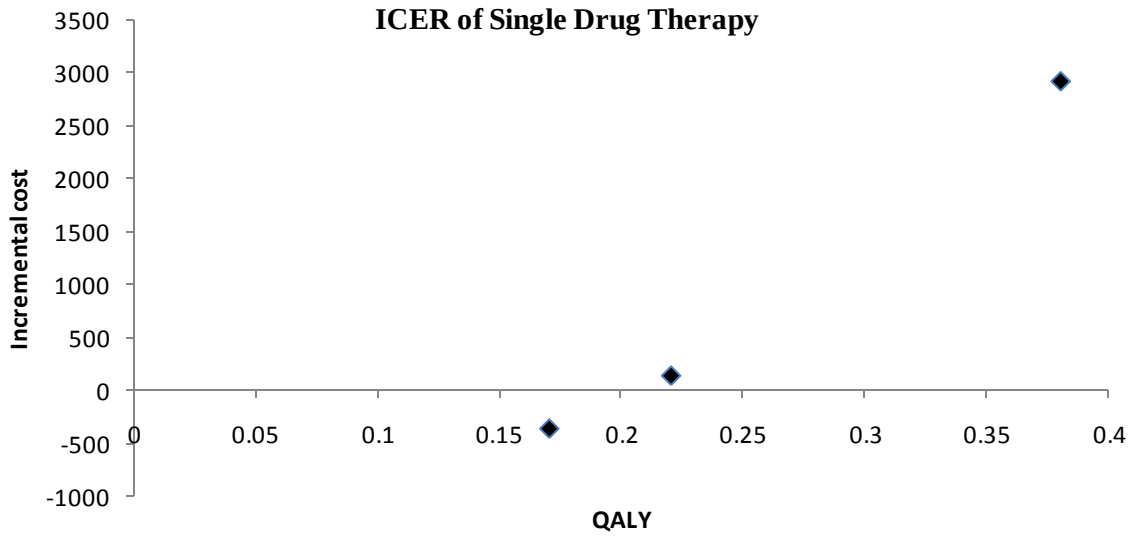
**Table- 28: Discounted QALY and IC with Standard therapy**

| Therapy | Difference in QALY | Difference in Annual cost (₹) | Discounted QALY | Discounted IC (₹) |
|---|---|---|---|---|
| BGS | 0.1 | 292 | 0.003 | 8.76 |
| TGZ | 0.26 | 37 | 0.0078 | 1.11 |
| INS | 0.31 | -110.91 | 0.0093 | -3.33 |

**Table- 29: ICER with Standard therapy**

| Therapy | QALY | Annual cost (₹) | ICER |
|---|---|---|---|
| BGS | 0.38 | 840 | 2920 |
| TGZ | 0.22 | 1095 | 142 |
| INS | 0.17 | 4829 | -358 |

**Figure 10: ICER with Standard therapy**




### Incremental Cost per Quality of Life in years gained for 2- Drug Combination therapy with Standard 1 BGS+ 1 TGZ: (1.00 QALY; ₹ 1935) therapy

**Table- 30: Discounted QALY and IC with Standard therapy**

| Therapy | Difference in QALY | Difference in Annual cost (₹) | Discounted QALY | Discounted IC (₹) |
|---|---|---|---|---|
| AGI + BGS | 0.89 | -2343 | 0.0267 | -70.29 |
| AGI + SUS | 0.30 | -2635 | 0.009 | -79.05 |
| BGS + DPP IV | 0.83 | -26090 | 0.0249 | -782.7 |
| 1 BGS + 1 SUS | 0.57 | -36 | 0.0171 | -1.08 |
| 1 BGS + 2 SUS | 0.48 | -1168 | 0.0144 | -350.64 |
| AGI + 2 INS | 0.72 | -11161 | 0.0216 | -334.83 |
| AGI + 1 INS | 0.89 | -6332 | 0.0267 | -189.96 |
| BGS + INS | 0.89 | -3639 | 0.0267 | -109.17 |
| SUS + INS | 0.57 | -4026 | 0.0171 | -120.78 |
| 1 INS + 2 SUS | 0.51 | -5157 | 0.0153 | -154.71 |
| 3 INS + 1 SUS | 0.58 | -13683 | 0.0174 | -410.49 |
| SUS + TGZ | 0.27 | -292 | 0.0081 | -8.76 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

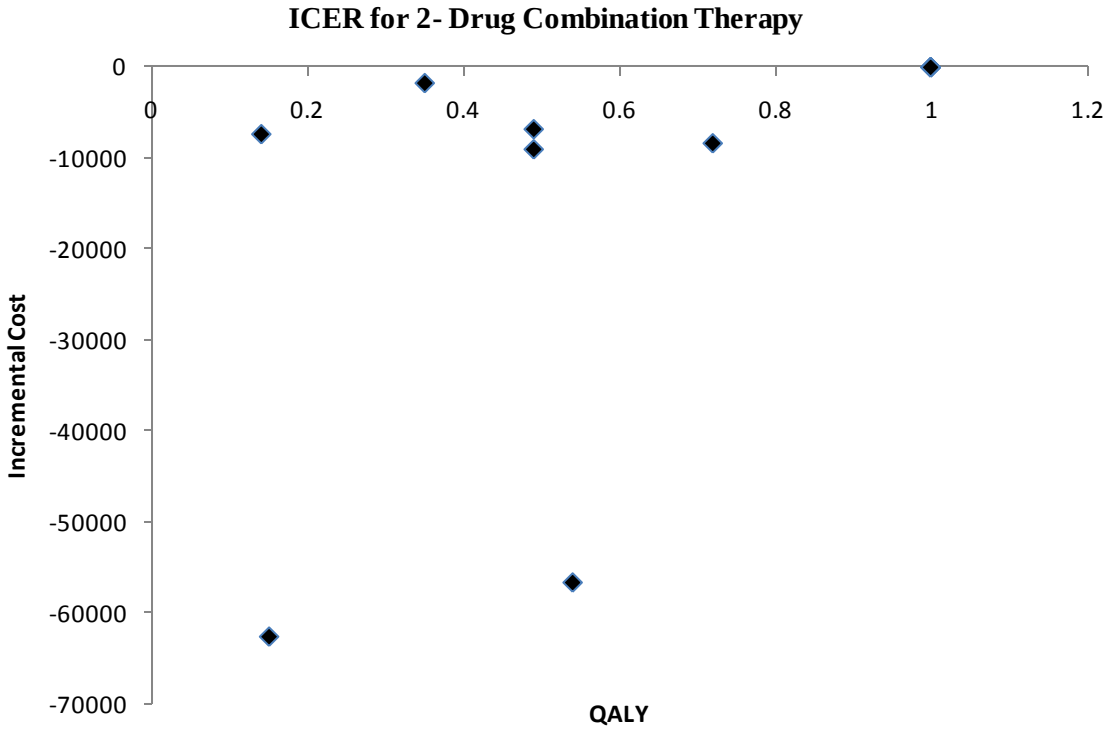
*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 31: ICER with Standard therapy**

| Therapy | QALY | Annual cost (₹) | ICER/QALY |
|---|---|---|---|
| AGI + BGS | 0.11 | 4278 | -2633 |
| AGI + SUS | 0.70 | 4570 | -8783 |
| BGS + DPP IV | 0.17 | 28025 | -31434 |
| 1 BGS + 1 SUS | 0.43 | 1971 | -63 |
| 1 BGS + 2 SUS | 0.52 | 3103 | -24350 |
| AGI + 2 INS | 0.28 | 13096 | -15501 |
| AGI + 1 INS | 0.11 | 8267 | -7114 |
| BGS + INS | 0.11 | 5574 | -4089 |
| SUS + INS | 0.43 | 5961 | -7063 |
| 1 INS + 2 SUS | 0.49 | 7092 | -10112 |
| 3 INS + 1 SUS | 0.42 | 15618 | -23591 |

| | | | |
|---|---|---|---|
| SUS + TGZ | 0.73 | 2227 | -1082 |

**Figure 11: ICER with Standard therapy**




**Incremental Cost per Quality of Life in years gained for 3- Drug Combination therapy with Standard 1 BGS + 1 SUS + 1 TGZ: (1.00 QALY; ₹ 3066) therapy**

**Table- 32: Discounted QALY and IC with Standard therapy**

| Therapy | Difference in QALY | Difference in Annual cost **(₹)** | Discounted QALY | Discounted IC **(₹)** |
|---|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV | 0 | -28397 | 0 | -851.91 |
| 1 AGI+ 1 BGS+ 1 SUS | 0.28 | -2343 | 0.0084 | -70.29 |
| 1 AGI + 1 BGS + 2 SUS | 0.51 | -3475 | 0.0153 | -104.25 |
| 1 AGI + 1 BGS + 3 SUS | 0.51 | -4606 | 0.0153 | -138.18 |
| 1 BGS + 1 SUS + 2 DPP IV | 0.85 | -53275 | 0.0255 | -1598.25 |
| 1 BGS + 1 SUS + 1 DPP IV | 0.46 | -26090 | 0.0138 | -782.7 |
| 1 BGS + 2 SUS + 1 TGZ | 0.65 | -1132 | 0.0195 | -33.96 |
| 1 INS + 1 BGS + 1 AGI | 0 | -6041 | 0 | -181.23 |
| 2 INS + 1 BGS + 1 AGI | 0 | -10870 | 0 | -326.1 |
| 1 INS + 1 AGI + 1 SUS | 0.86 | -6333 | 0.0258 | -189.99 |

| | | | | |
|---|---|---|---|---|
| 2 INS + 1 AGI + 2 SUS | 0 | -12293 | 0 | -368.79 |
| 2 INS + 1 AGI + 1 SUS | 0 | -11162 | 0 | -334.86 |
| 3 INS + 1 AGI + 1 SUS | 0.89 | -15991 | 0.0258 | -479.73 |
| 1 INS + 1 AGI + 2 SUS | 0.89 | -7464 | 0.0258 | -223.92 |
| 3 INS + 1 BGS + 1 DPP IV | 0.83 | -39446 | 0.0249 | -1183.38 |
| 1 INS + 1 BGS + 1 SUS | 0.72 | -3734 | 0.0216 | -112.02 |
| 4 INS + 1 BGS + 2 SUS | 0 | -18221 | 0 | -546.63 |
| 2 INS + 1 BGS + 2 SUS | 0.41 | -9694 | 0.0123 | -290.82 |
| 2 INS + 1 BGS + 1 SUS | 0.70 | -8563 | 0.021 | -256.89 |
| 1 INS + 1 BGS + 2 SUS | 0.67 | -4866 | 0.0201 | -145.98 |
| 1 INS + 1 DPP IV+ 1 SUS | 0.89 | -30080 | 0.0258 | -902.4 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 33: ICER with Standard therapy**

| Therapy | QALY | Annual cost (₹) | ICER/QALY |
|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV | 1.00 | 31463 | *** |
| 1 AGI+ 1 BGS+ 1 SUS | 0.72 | 5409 | -8368 |
| 1 AGI + 1 BGS + 2 SUS | 0.49 | 6541 | -6814 |
| 1 AGI + 1 BGS + 3 SUS | 0.49 | 7672 | -9031 |
| 1 BGS + 1 SUS + 2 DPP IV | 0.15 | 56341 | -62677 |
| 1 BGS + 1 SUS + 1 DPP IV | 0.54 | 29156 | -56717 |
| 1 BGS + 2 SUS + 1 TGZ | 0.35 | 4198 | -1742 |
| 1 INS + 1 BGS + 1 AGI | 1.00 | 9107 | *** |
| 2 INS + 1 BGS + 1 AGI | 1.00 | 13936 | *** |
| 1 INS + 1 AGI + 1 SUS | 0.14 | 9399 | -7364 |
| 2 INS + 1 AGI + 2 SUS | 1.00 | 15359 | *** |
| 2 INS + 1 AGI + 1 SUS | 1.00 | 14228 | *** |
| 3 INS + 1 AGI + 1 SUS | 0.11 | 19057 | -18594 |
| 1 INS + 1 AGI + 2 SUS | 0.11 | 10530 | -8679 |
| 3 INS + 1 BGS + 1 DPP IV | 0.17 | 42512 | -47525 |
| 1 INS + 1 BGS + 1 SUS | 0.28 | 6800 | -5186 |

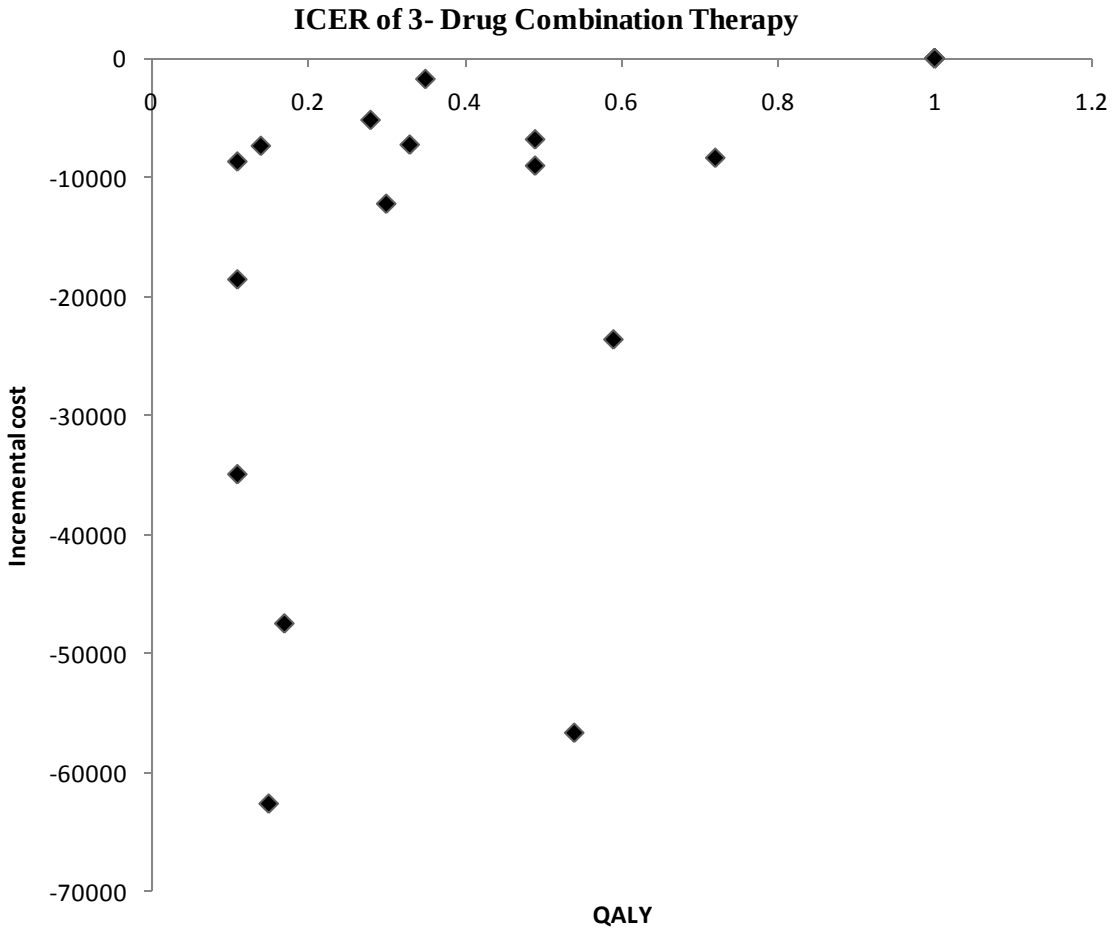
| | | | |
|---|---|---|---|
| 4 INS + 1 BGS + 2 SUS | 1.00 | 21287 | *** |
| 2 INS + 1 BGS + 2 SUS | 0.59 | 12760 | -23644 |
| 2 INS + 1 BGS + 1 SUS | 0.30 | 11629 | -12233 |
| 1 INS + 1 BGS + 2 SUS | 0.33 | 7932 | -7263 |
| 1 INS + 1 DPP IV + 1 SUS | 0.11 | 33146 | -34977 |

*****- Similar QALY as per Standard with increased Incremental Cost**

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 12: ICER with Standard therapy**



**Incremental Cost per Quality of Life in years gained for 4- Drug Combination therapy with Standard 1 INS + 1 BGS+ 1 DPPI + 1 SUS (1.00 QALY; ₹ 33985) therapy**

**Table- 34: Discounted QALY and IC with Standard therapy**

| Therapy | Difference in QALY | Difference in Annual cost **(₹)** | Discounted QALY | Discounted IC **(₹)** |
|---|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV + 1SUS | 0.61 | 1390 | 0.0183 | 41.7 |
| 1 AGI + 1 BGS + 2 DPP IV + 1SUS | 0.77 | -25795 | 0.0231 | -773.85 |
| 1 AGI + 1 BGS + 1 SUS + 1 TGZ | 0.64 | 27481 | 0.0192 | 824.43 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS | 0.36 | -60403 | 0.0108 | -1812.09 |
| 2 INS + 1 AGI + 1 BGS + 1 SUS | 0.87 | 18918 | 0.0261 | 567.54 |
| 3 INS + 1 AGI + 1 BGS + 1 SUS | 0.75 | 14089 | 0.0225 | 422.67 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS | 0.59 | 22615 | 0.0177 | 678.45 |
| 2 INS + 1 AGI + 1 BGS + 2 SUS | 0.89 | 17786 | 0.0267 | 533.58 |
| 1 INS + 1 AGI + 1 BGS + 3 SUS | 0.44 | 21484 | 0.0132 | 644.52 |
| 1 INS +1 SUS + 1 AGI + 1 DPP IV | 0 | -2599 | 0 | -77.97 |
| 1 INS + 1 AGI + 1 SUS + 1TGZ | 0.89 | 23491 | 0.0267 | 704.73 |
| 1 INS + 1 BGS + 1 DPP IV + 2 SUS | 0.56 | -1132 | 0.0168 | -33.96 |
| 1 INS + 1 BGS + 2 DPP IV + 1 SUS | 0.89 | -27185 | 0.0267 | -815.55 |
| 2 INS + 1 BGS + 1 DPP IV + 1 SUS | 0 | -4829 | 0 | -144.87 |
| 1 BGS + 2 SUS + 1 TGZ + 1 INS | 0.78 | 24958 | 0.0234 | 748.74 |
| 1 BGS + 3 SUS + 1 TGZ + 1 INS | 0.39 | 23827 | 0.0117 | 714.81 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 35: ICER with Standard therapy**

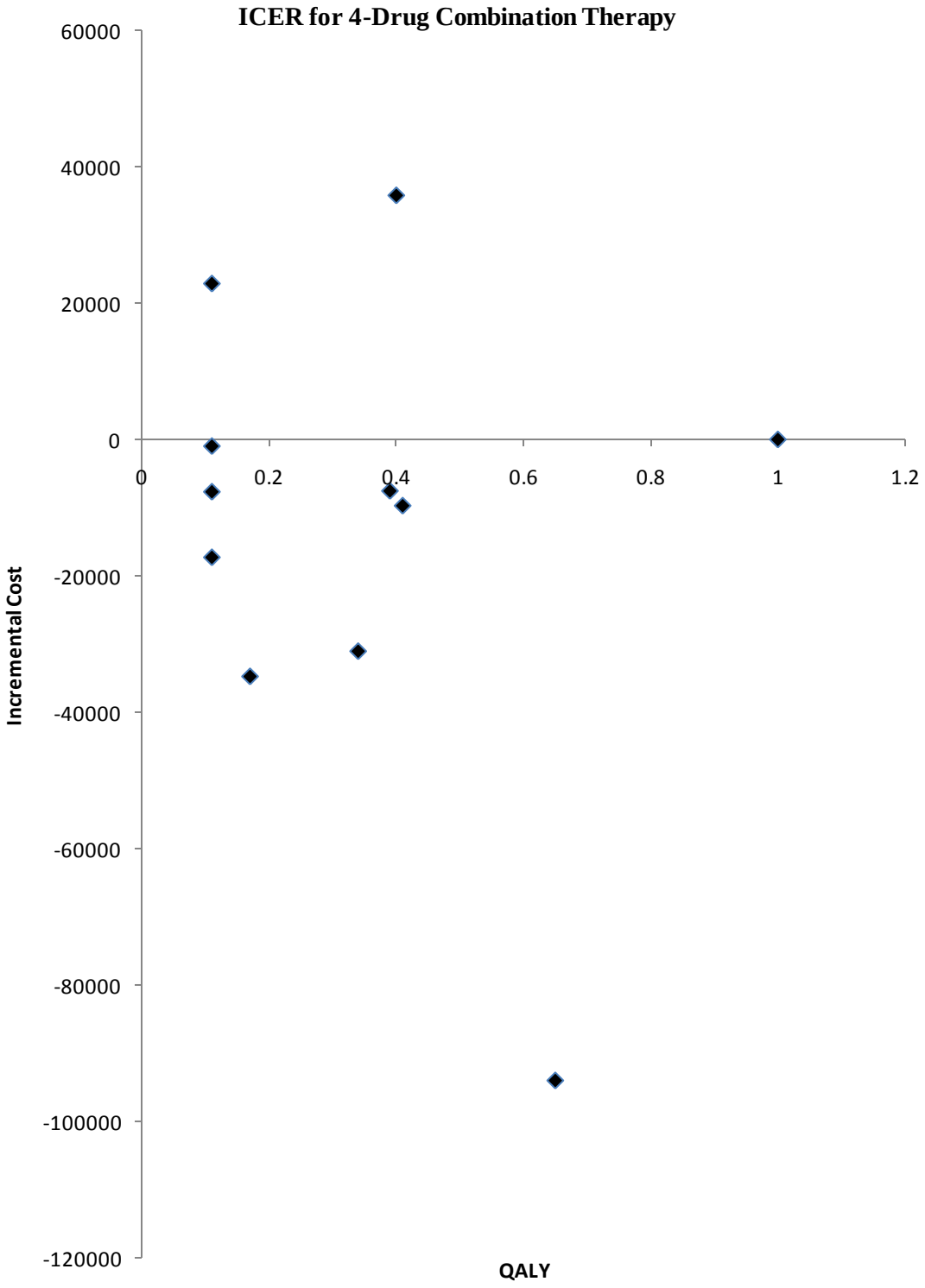
| Therapy | QALY | Annual cost (₹) | ICER/QALY |
|---|---|---|---|
| 1 AGI + 1 BGS + 1 DPP IV + 1SUS | 0.39 | 32595 | 2279 |
| 1 AGI + 1 BGS + 2 DPP IV + 1SUS | 0.23 | 59780 | -33500 |
| 1 AGI + 1 BGS + 1 SUS + 1 TGZ | 0.36 | 6504 | 42939 |
| 1 INS + 1 AGI + 1 BGS + 1 SUS | 0.64 | 94388 | -167786 |
| 2 INS + 1 AGI + 1 BGS + 1 SUS | 0.13 | 15067 | 21745 |
| 3 INS + 1 AGI + 1 BGS + 1 SUS | 0.25 | 19896 | 18785 |
| 1 INS + 1 AGI + 1 BGS + 2 SUS | 0.41 | 11370 | 38330.51 |
| 2 INS + 1 AGI + 1 BGS + 2 SUS | 0.11 | 16199 | 19984 |
| 1 INS + 1 AGI + 1 BGS + 3 SUS | 0.56 | 12501 | 48827 |
| 1 INS +1 SUS + 1 AGI + 1 DPP IV | 1.00 | 36584 | *** |
| 1 INS + 1 AGI + 1 SUS + 1TGZ | 0.11 | 10494 | 26394 |
| 1 INS + 1 BGS + 1 DPP IV + 2 SUS | 0.44 | 35117 | -2021 |
| 1 INS + 1 BGS + 2 DPP IV + 1 SUS | 0.11 | 61170 | -30545 |
| 2 INS + 1 BGS + 1 DPP IV + 1 SUS | 1.00 | 38814 | *** |
| 1 BGS + 2 SUS + 1 TGZ + 1 INS | 0.22 | 9027 | 31997 |
| 1 BGS + 3 SUS + 1 TGZ + 1 INS | 0.61 | 10158 | 61095 |

*****- Similar QALY as per Standard with increased Incremental Cost**

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 13: ICER with Standard therapy**




**Incremental Cost per Quality of Life in years gained for >4- Drug Combination therapy with Standard 1 AGI+ 1 BGS+ 1 DPPI+ 2 SUS+ 1 TGZ (1.00 QALY; ` 32821) therapy**

**Table- 36: Discounted QALY and IC with Standard therapy**

| Therapy | Difference in QALY | Difference In Annual cost (₹) | Discounted QALY | Discounted IC (₹) |
|---|---|---|---|---|
| 1 AGI+ 1 BGS+ 1 DPP IV+ 1 SUS + 1 TGZ | 0.89 | -869 | 0.0267 | -26.07 |
| 1 AGI+ 1 BGS+ 2 DPP IV+ 3 SUS + 1 TGZ | 0.83 | -28857 | 0.0249 | -865.71 |
| 1 INS+ 1 AGI + 1BGS + 1 DPP IV + 2 SUS | 0.59 | -5734 | 0.0177 | -172.02 |
| 2 INS+ 1 AGI + 1BGS + 1 DPP IV + 2 SUS | 0.34 | -10563 | 0.0102 | -316.89 |
| 3 INS+ 1 AGI + 1BGS + 1 DPP IV + 2 SUS | 0.89 | -15392 | 0.0267 | -461.76 |
| 1 INS+ 1 AGI + 1BGS + 2 DPP IV + 2 SUS | 0.35 | -32919 | 0.0105 | -987.57 |
| 1 INS+ 1 AGI + 1BGS + 1 DPP IV + 1 SUS | 0.61 | -4603 | 0.0183 | -138.09 |
| 1 INS+ 1 AGI+ 1 BGS+ 1 SUS + 1 TGZ | 0.60 | 21488 | 0.018 | 644.64 |
| 1 INS+ 1 AGI+ 1 BGS+ 2 SUS + 1 TGZ | 0.89 | 20356 | 0.0267 | 610.68 |
| 1 INS+1 AGI+1 BGS+1 DPP IV +1 SUS +1 TGZ | 0 | -5698 | 0 | -170.94 |
| 1 INS+1 AGI+1 BGS+1 DPP IV + 2 SUS+1 TGZ | 0.89 | -6829 | 0.0267 | -204.87 |

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Table- 37: ICER with Standard therapy**

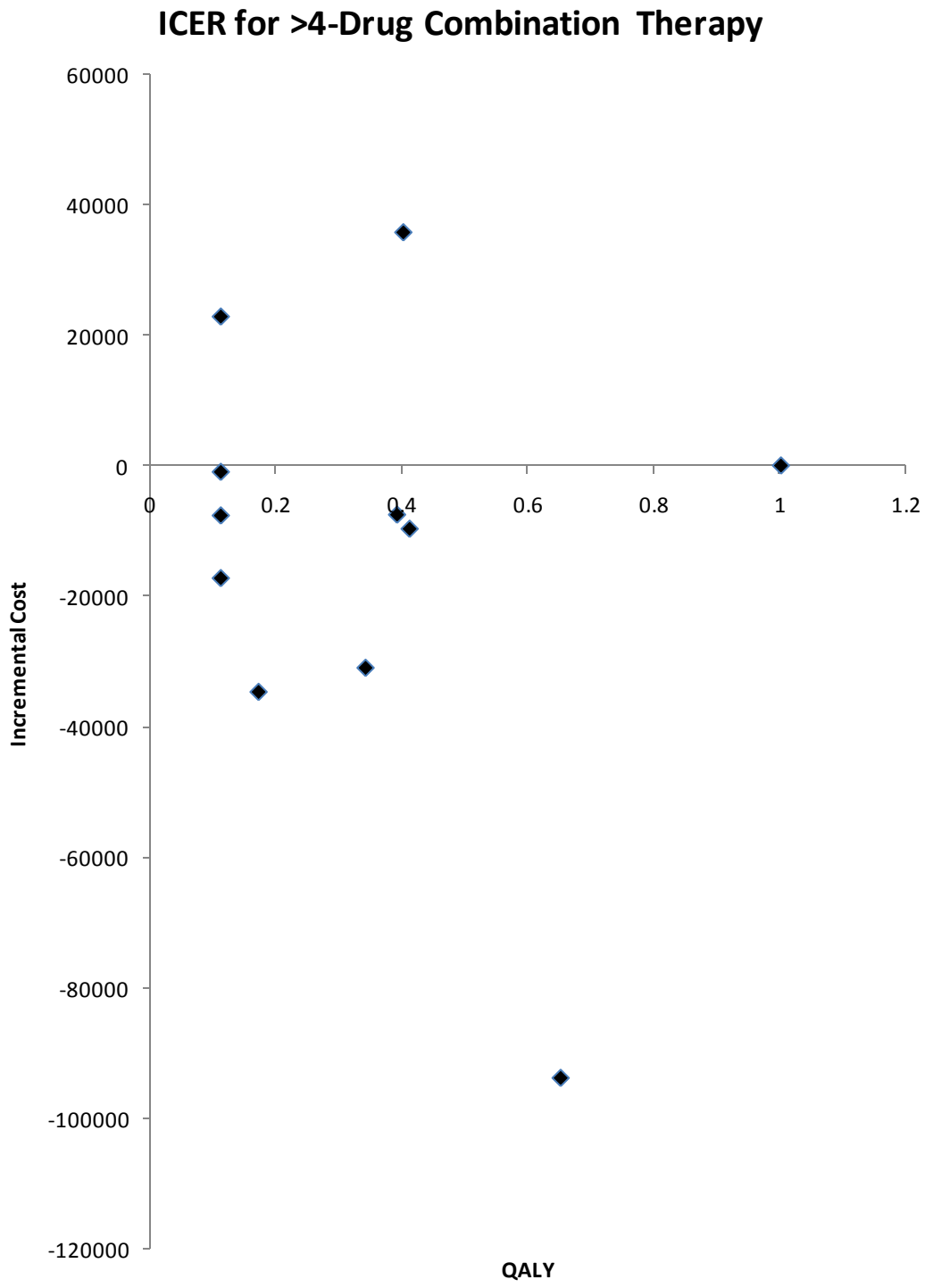
| Therapy | QALY | Annual cost (₹) | ICER/QALY |
|---|---|---|---|
| 1 AGI+ 1 BGS+ 1 DPP IV+ 1 SUS+ 1 TGZ | 0.11 | 33690 | -976 |
| 1 AGI+ 1 BGS+ 2 DPP IV + 3 SUS+ 1 TGZ | 0.17 | 61678 | -34768 |
| 1 INS+ 1 AGI + 1BGS + 1 DPP IV + 2 SUS | 0.41 | 38555 | -9719 |
| 2 INS+ 1 AGI + 1BGS + 1 DPP IV + 2 SUS | 0.34 | 43384 | -31068 |
| 3 INS+ 1 AGI + 1BGS + 1 DPP IV+ 2 SUS | 0.11 | 48213 | -17294 |
| 1 INS+ 1 AGI + 1BGS + 2 DPP IV + 2 SUS | 0.65 | 65740 | -94054 |
| 1 INS+ 1 AGI + 1BGS + 1 DPP IV + 1 SUS | 0.39 | 37424 | -7546 |
| 1 INS+ 1 AGI+ 1 BGS+ 1 SUS+ 1 TGZ | 0.40 | 11333 | 35813 |
| 1 INS+ 1 AGI+ 1 BGS+ 2 SUS+ 1 TGZ | 0.11 | 12465 | 22872 |
| 1 INS + 1 AGI + 1 BGS+ 1 DPP IV +1 SUS+1 TGZ | 1.00 | 38519 | *** |
| 1 INS+1 AGI+1 BGS+1 DPP IV +2 SUS+1 TGZ | 0.11 | 39650 | -7673 |

*****- Similar QALY as per Standard with increased Incremental Cost**

*BGS = Biguanides, TGZ = Thioglitazones, SUS = Sulphonyl Ureas, INS = Insulins*

*AGI = Alpha glucosidase inhibitors, DPP IV = DPP IV inhibitors*

**Figure 14: ICER with Standard therapy**



# Results & Discussion

## VII. RESULTS AND DISCUSSION

Diabetes is a chronic disease that requires continuing medical care to reduce the risk of long term complications. Self management education to prevent acute complications may improve patient well being; still the pharmaceutical management has an inevitable role. An economical analysis of antidiabetic agents has been performed in societal perspective to assess and evaluate those pharmaceuticals.

A total of 421 subjects were randomly enrolled in the study for a period of 12 months. Of these, 12 subjects (3.33% of enrollees) were excluded from survey regarding the prevalence of diabetes, and 33 (7.84% of enrollees) were excluded from economic analysis, because they moved away during the follow-up period. They were separately analyzed according to the age wise and duration wise distribution of diabetes. Table 1

Age wise distribution of diabetes was evaluated from a total of 407 patients enrolled that included 225 men (55.28%) and 182 women (44.72%). A sum of 137 patients (33.66%) present within the age group 51-60 years having an average duration of 6 years of diabetes and reaches a higher duration of 11-15 under 71-80 years of age which is similar to the data observed by Esposti *et al.*[59] and Bhatti *et al.*[18]. A higher population of 81.33% regular non-vegetarians was identified than 11.79% of patients were vegetarians falling under the age group 51-60 years with 27.52% and 4.42% respectively. Weight loss was reported by 43.98% of patients compared to 9.09% patients with weight gain with an increased level of 15.48 % and 3.19% respectively under the age group 51-60 years. Patients with higher Body Mass Index (BMI >25 $Kg/m^2$) were present in the age group 41-80 years out of which 51-60 years age group patients shown obese with a higher average BMI of 26.19 $Kg/m^2$. It was found that 14.25 % of tobacco users (4.91% under age group 41-50) and 13.51% of alcoholics were present with a significantly lower rate of physical activity 56.76 % of sedentary (19.90% under 51-60 years) and 5.41% pensioners (2.21 % under 61-70 years) than 28.99% active patients (11.06 % under 41-50 years) that complies with the report of Bhatti *et al.*[18] Table 2 & 3

Duration wise distribution pattern of diabetes was assessed from a population of 407 patients comprising 222 men (54.55%) and 185 women (45.45%). A total of 162 (39.80%) were present with a duration of 1-5 years, possessing an average age group of 57 years with increased number of patients age group of 51-60 under 1-5 years of duration which is parallel to the data observed by Esposti *et al.*[59], and Bhatti *et al*[18]. A total of 10.57%

vegetarians were over taken by 82.56% non-vegetarians with a group of 3.69 % under 6-10 years and 33.42% under 1-5 years of duration. Patients identified under duration of diabetes 1-5 years were noticed with 14% of weight loss and 4.67 % of weight gain. As a whole, weight gain was exercised by much less patients 8.60% than weight loss 44.47%. A higher number of obese patients with an average Body Mass Index (BMI) of 31.24 $Kg/m^2$ had duration of diabetes especially between 21-25 years, from a wide range of above 11 years. Tobacco users and alcoholics were present as 14.50% and 12.78% respectively which was been identified with a large population of 7.62% tobacco users and 14.5% alcoholics with a duration of 1-5 years. 30.47% of active diabetic patients (14.5 % under 1-5) were present, which was much less than 58.72% of sedentary (20.64% under 1-5) and 5.65% of pensioners (1.47 % under 1-15) similar to the figures provided by Bhatti *et al*[18]. Table 4 & 5

Microvascular complications were found very common in patients within the age group 51-60 years with 15.97% of Retinopathy, 7.62% of Foot ulcer, 14.50% of Nephropathy and 18.67% of Neuropathy. At the same time these complications are more persistent during 1-5 years of duration of diabetes, with a rate of retinopathy (18.43%), Foot ulcer (7.86%), nephropathy (17.20%), and neuropathy (19.90%). Among the macro vascular diseases, peripheral vascular disease is more common with duration of 6-10 years (0.98%). Other macro vascular complications are common with 1-5 years of duration of diabetes were hypertension (18.92%), Dyslipidemia (9.34%), and Cardio vascular diseases (2.95%). Hypertension leads foremost macro vascular complications of 16.22% within the age group 61-70 years. But, Dyslipidemia is a major disorder which shows its increased prevalence of 7.37% among the age group 51-70 years. Cardio vascular complications has its more prevalence within the age group 51-60 years, the same do the peripheral vascular diseases even with a small percentage of 0.98. Table 6-9

With ongoing treatment, no suffering was mostly experienced by patients within the age group 51-60 years (23.59%) and duration of 1-5 years (24.82%), Mild and moderate levels of suffering is faced by patients within the age group 41-50 years (6.14% and 1.47% respectively ) along with a duration of 1-5 years (8.85 and 1.97% respectively ). Severe suffering levels were noticed by patients with age group 71-80 years and 11-15 years of duration (0.25% each). Mild to moderate physical activity restriction was higher among patients with 51-60 years of age (13.76% and 4.18% respectively) and with a duration of 1-5 years (14.74% and 6.14% respectively) but no restriction to physical activity was noticed in patients with in the age group 51-60 years (10.32%)and duration 1-5 years (12.04%). Severe

restriction on physical activity was showed by patients among the age group 41-50 years (2.95 %) and with duration of 1-5 years (2.7%). Table 10 - 13

Cost analysis is performed by taking into account the direct costs of antidiabetic drugs and evaluated at MIMS-Asia purchase prices. Costs were expressed as overall and average values. The currency reference was the Indian Rupees (₹). Cost minimization analysis was performed using the evaluated purchase prices for each type of therapy provided to the patients. Cost effectiveness analysis was performed for each therapy provided based on the reports obtained from cost minimization analysis.

A total of 388 patients (92.16% of enrollees) were provided treatment with single and combining several classes of antidiabetic drugs at enrollment. Single drug therapy was provided to 8.76% of patients, 2- Drug combination therapy to 38.92% of patients, 3- Drug combination therapy to 30.15% of patients, 4- Drug combination therapy to 15.21% of patients, and >4- Drug combination therapy to 6.96% of patients. The average age and duration of the patients received each type of therapy is given in Table 15.

Biguanides were the class of drug most commonly prescribed for monotherapy (8.76%), followed by Sulphonyl ureas (2.32%), Insulins (0.52%), and Thioglitazones (0.26%). Patient age and duration of diabetes by class of drug prescribed at enrollment are presented in Table 15.

Therapy with combination of two drugs was provided to 151 patients (38.92%) in which patients fall within the age group 41-50 years with duration of 6-10 years of diabetes. The increased numbers of patients (27.84%) were treated with a combination of one Biguanide and one Sulphonyl ureas with age group 51-60 years and duration of 6-10 years followed by 2.32% each of the patients with one Biguanide plus two Sulphonyl ureas and one Sulphonyl ureas plus 27 units of Insulin, 1.03% each of the patients with one Alpha Glucosidase inhibitor plus 2 X 27 units of Insulin and one Alpha Glucosidase inhibitor plus one Sulphonyl ureas, 0.77% each of the patients with one Alpha Glucosidase inhibitor plus 27 units of Insulin, 0.52% each of the patients with one Biguanide plus one Thioglitazone and one Sulphonyl ureas plus 3 X 27 units of Insulin and one Sulphonyl ureas plus one Thioglitazone, 0.26% each of the patients with one Biguanide plus one DPP IV inhibitor, one Biguanide plus 27 units of Insulin, one Sulphonyl ureas plus 2 X 27 units of Insulin and one Alpha Glucosidase inhibitor plus one Biguanide. Table 16

Combination therapy of 3 drugs was given to 117 patients (30.15%) with duration of 11-15 years and age group of 51-60 years. The higher numbers of patients (7.99%) were treated with a combination of one Biguanide plus one Sulphonyl ureas and 27 units of Insulin with an average age group of 51-60 years and duration of 6-10 years, followed by 6.7% each of the patients with one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas, 4.12% each of the patients with one Biguanide plus one Sulphonyl ureas plus one DPP IV inhibitor, 2.32% each of the patients with one Alpha Glucosidase inhibitor, one Biguanide and two Sulphonyl ureas, 1.55% each of the patients with one Biguanide plus two Sulphonyl ureas plus one Thioglitazone, 1.29% each of the patients with one Biguanide plus one Sulphonyl ureas plus one Thioglitazone, 0.77% each of the patients with one Biguanide plus one Sulphonyl ureas plus two DPP IV inhibitors, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas, and 27 units of Insulin plus one Biguanide plus two Sulphonyl ureas, 0.52% each of the patients with 2 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas, 2 X 27 units of insulin plus one Biguanide plus one Sulphonyl ureas, 0.26% each of the patients with one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor, one Alpha Glucosidase inhibitor plus one Biguanide plus three Sulphonyl ureas, 2 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus two Sulphonyl ureas, 27 units of Insulin plus one Biguanide plus one Alpha Glucosidase inhibitor, 2 X 27 units of Insulin plus one Biguanide plus one Alpha Glucosidase inhibitor, 3 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus two Sulphonyl ureas, 3 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one DPP IV inhibitor, 4 X 27 units of Insulin plus one Biguanide plus two Sulphonyl ureas, 2 X 27 units of Insulin plus one Biguanide plus two Sulphonyl ureas and 27 units of Insulin plus one DPP IV inhibitors plus one Sulphonyl ureas. Table 17

The 4-drug combination therapy was provided to 59 patients (15.21%) with an age rgroup average of 51-60 years and duration of 6-10 years. A large population (2.84%) was treated with a combination of one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas with an age group of 51-60 years and an average duration of 6-10 years followed by 2.58% each of the patients with 27 units of insulin plus one Alpha Glucosidase inhibitors plus one Biguanide plus one Sulphonyl ureas, 1.55% each of the patients with 27 units of Insulin plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas, 1.29% each of the patients with 3 X 27 units of Insulin

plus one Alpha glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas, 1.03% each of the patients with one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas and 27 units of Insulin plus one Alpha glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas, 0.77% each of the patients with one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone and 2 X 27 units of Insulin plus one Alpha glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas, 0.52% each of the patients with 2 X 27 units of Insulin plus one Alpha glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas, 27 units of Insulin plus one Alpha glucosidase inhibitor plus one Biguanide plus three Sulphonyl ureas, 27 units of Insulin plus one Alpha glucosidase inhibitor plus one Sulphonyl ureas plus one DPP IV inhibitors and 27 units of Insulin plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas, 0.26% each of the patients with 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas plus one Thioglitazone, 27 units of Insulin plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas, 2 X 27 units of Insulin plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas, one Biguanide plus two Sulphonyl ureas plus one Thioglitazone plus 27 units of Insulin and one Biguanide plus three Sulphonyl ureas plus one Thioglitazone plus 27 units of Insulin. Table 18

Combination of >4 drugs was provided for (6.96%) of patients with an age group of 51-60 years and with duration of 6-10 years. A population of 3.09% of patients was treated with a combination of 5 drugs of 27 units of insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas with an average age group of 51-60 years and duration of 11-15 years followed by 0.77 % each of the patients with 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP Inhibitor plus two Sulphonyl ureas and 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP Inhibitors plus two Sulphonyl ureas, 0.26% each of the patients with one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP Inhibitor plus one Sulphonyl ureas plus one Thioglitazone, one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP Inhibitors plus three Sulphonyl ureas plus one Thioglitazone, one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP Inhibitor plus two Sulphonyl ureas plus one Thioglitazones, 2 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP Inhibitor two Sulphonyl ureas, 3 X 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP

Inhibitor two Sulphonyl ureas, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas plus one Thioglitazone, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone plus one DPP IV inhibitor and 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas plus one Thioglitazone plus one DPP IV inhibitors. Table 19

Cost minimization analysis was performed among each class of the drug in single drug prescription and for each type of combinations of drugs available in market which aids in combination therapy of the drugs which fall under the prescribed brands of drugs. Among the prescribed brands Lowest cost per unit of drug was Biguanides (₹ 1.15) and highest was for DPP IV inhibitors (₹ 37.24). The cost differences among the prescribed brand were more prominent among the drug under the class of Alpha Glucosidase inhibitors (₹ 9.14). Among the combination drugs available Lowest cost per unit was obtained for Sulphonyl ureas plus Biguanides (₹ 3.63) while the highest was for Biguanides plus DPP IV inhibitors (₹ 20.35). The increased cost variation among the prescribed brands was for a combination of Biguanides plus Sulphonyl ureas plus Thioglitazones. Mean daily dose taken by each patient was 2 doses per day as an average of prescribed frequency and 27 units of insulin were consumed by each patient per day for the entire year. Table 20 & 22

Annual treatment cost was calculated for each class of drug prescribed drug for monotherapy. The lowest annual cost was found to be spend by patients taking Biguanides (₹ 840), followed by Thioglitazones (₹ 1,095), Sulphonyl ureas (₹ 1,132) and Insulins (₹ 4,830). Table 23

Annul treatment cost for 2-drug combination therapy of prescribed drug was more when compared to single drug therapy. The lowest cost was spent by the population consuming one Biguanide plus one Thioglitazone (₹1,935) followed by one Biguanide plus one Sulphonyl ureas (₹ 1,971), one Sulphonyl ureas plus one Thioglitazone (₹ 2,227), one Biguanide plus two Sulphonyl ureas (₹ 3,103), one Alpha Glucosidase inhibitor plus one Biguanide (₹ 4,278), one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (₹ 4,570), one Biguanide plus 27 units of Insulin (₹ 5,574), one Sulphonyl ureas plus 27 units of Insulin (₹ 5,961), 27 units of Insulin plus two Sulphonyl ureas (₹ 7,092), one Alpha Glucosidase inhibitor plus 27 units of Insulin (₹ 8,267), one Alpha Glucosidase inhibitor plus 27 X 2 units

of Insulin (₹ 13,096), one Sulphonyl ureas plus 27 X 3 units of Insulin (₹ 15,618) and one Biguanide plus one DPP IV inhibitors (₹ 28,025). Table 24

Annul treatment cost for 3-drug combination therapy of prescribed drug was more when compared to single drug therapy and 2- drug combination therapy. The lowest cost was spent by the population consuming one Biguanide plus one Sulphonyl ureas plus one Thioglitazone (₹ 3,066) followed by one Biguanide plus two Sulphonyl ureas plus one Thioglitazone (₹ 4,198), one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (₹ 5,409), one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas (₹ 6,541), one Biguanides plus 27 units of Insulin plus one Sulphonyl ureas (₹ 6,800), one Alpha Glucosidase inhibitor plus one Biguanide plus three Sulphonyl ureas (₹ 7,672), one Biguanide plus 27 units of Insulin plus two Sulphonyl ureas (₹ 7,931), one Alpha Glucosidase inhibitor plus 27 units of Insulin plus one Biguanide (₹ 9,107), one Alpha Glucosidase inhibitor plus 27 units of Insulin plus one Sulphonyl ureas (₹ 9,399), one Alpha Glucosidase inhibitor plus 27 units of Insulin plus two Sulphonyl ureas (₹ 10,530), one Biguanide plus 27 X 2 units of Insulin plus one Sulphonyl ureas (₹ 11,629), one Biguanide plus 27 X 2 units of Insulin plus two Sulphonyl ureas (₹ 12,760), 27 X 2 units of Insulin plus one Biguanide plus one Alpha Glucosidase inhibitor (₹ 13,936), 27 X 2 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (₹ 14,228), 27 X 2 units of Insulin plus one Alpha Glucosidase inhibitor plus two Sulphonyl ureas (₹ 15,359), 27 X 3 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (₹ 19,057), 27 X 4 units of Insulin plus one Biguanide plus two Sulphonyl ureas (` 21,287), one Biguanide plus one Sulphonyl ureas plus one DPP IV inhibitor (₹ 29,156), one Biguanide plus one DPP IV inhibitor plus one Alpha Glucosidase inhibitor (₹ 31,463), 27 units of Insulin plus one Sulphonyl ureas plus one DPP IV inhibitor (₹ 33,146), 27 units of Insulin plus one Biguanide plus one DPP IV inhibitor (₹ 42,516) and one Biguanide plus one Sulphonyl ureas plus two DPP IV inhibitors (₹ 56,341). Table 25

In annul treatment cost for 4-drug combination therapy, the lowest cost was spent by the population consuming one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone (₹ 6,504) followed by 27 units of Insulin plus one Biguanide plus two Sulphonyl ureas plus one Thioglitazone (₹ 9,027), 27 units of Insulin plus one Biguanide plus three Sulphonyl ureas plus one Thioglitazone (₹ 10,158), 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas plus one

Thioglitazone (₹ 10,494), 27 units of Insulin plus one Alpha Glucosidase inhibitor one Biguanide plus two Sulphonyl ureas (₹ 11,370), 27 units of Insulin plus one Alpha Glucosidase inhibitor one Biguanide plus three Sulphonyl ureas (₹ 12,501), 27 X 2 units of Insulin plus one Alpha Glucosidase inhibitor one Biguanide plus one Sulphonyl ureas (₹ 15,067), 27 X 2 units of Insulin plus one Alpha Glucosidase inhibitor one Biguanide plus two Sulphonyl ureas (₹ 16,199), 27 X 3 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (₹ 19,896), one Alpha Glucosidase inhibitor one Biguanide plus one Sulphonyl ureas plus one DPP IV inhibitor (₹ 32,595), 27 units of Insulin plus one Biguanide plus one Sulphonyl ureas plus one DPP IV inhibitor (₹ 33,985), 27 units of Insulin plus one Biguanide plus two Sulphonyl ureas plus one DPP IV inhibitor (₹ 35,117), 27 units of Insulin plus one Sulphonyl ureas plus one Alpha Glucosidase inhibitor plus one DPP IV inhibitor (₹ 36,584), 27 X 2 units of Insulin plus one Biguanide plus one Sulphonyl ureas plus one DPP IV inhibitor (₹ 38,814), one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas (₹ 59,780), 27 units of Insulin plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas (₹ 61,170) and 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanides plu one Sulphonyl ureas (₹ 94,388). Table 26

In annul treatment cost for >4- drug combination therapy; the lowest cost was spent by the population consuming one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitors one Sulphonyl ureas plus one Thioglitazone (₹ 11,333) followed by 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone (₹ 12,465), one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas plus one Thioglitazone (₹ 32,821), one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas plus one Thioglitazone (₹ 33,690), 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (₹ 37,422), 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanides plus one DPP IV inhibitors plus one Sulphonyl ureas plus one Thioglitazone (₹ 38,519), 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (₹ 38,555), 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas plus one Thioglitazone (₹ 39,650), 27 X 2 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (₹ 43,384),

27 X 3 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (₹ 48,213), one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus three Sulphonyl ureas plus one Thioglitazone (₹ 61,678) and 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus two Sulphonyl ureas (₹ 65,740). Table 27

Cost effectiveness analysis was performed for each type of therapy taking the drug which elicited a higher Quality Adjusted Life in years (QALY). The negative costs indicates the increased incremental cost already spend by the patient to achieve the QALY similar to the standard drug or the QALY which is still less than that of the standard, while the positive cost estimates the incremental cost that has to be invested to obtain the QALY similar to that of the QALY.

Sulphonyl ureas have shown to provide a higher QALY (1.00) with lower annual cost ₹ 840, in the study period which has been taken as a standard to analyze the CE of other mono therapy. Patients using Biguanides and Thioglitazones mono therapy have to pay an incremental cost of ₹ 2,920 /QALY and ₹ 142 /QALY to gain the increased QALY similar to that of Sulphonyl ureas. In case of insulin monotherapy the Sulphonyl ureas will dominate in both QALY and less amount paid per year. Table 29

The standard for 2-drug therapy was combination of each dose of one Bigunide and one Thioglitazone that has shown to have an increased QALY (1.00) with an annual cost of ₹ 1,935. The standard combination was found to the dominant with less annual cost than any other drug combinations of one Biguanide plus one Sulphonyl ureas (-₹ 63 / QALY), one Sulphonyl ureas plus one Thioglitazone (-₹ 1,082 / QALY), one Biguanide plus one Alpha Glucosidase inhibitor (-₹ 2633 / QALY), 27 units of insulin plus one Biguanide (-₹ 4089 INR/ QALY), 27 units of insulin plus one Sulphonyl ureas (-₹ 7,063 / QALY), 27 units of insulin plus one Alpha Glucosidase inhibitor (-₹ 7,114/ QALY), one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (-₹ 8,783 / QALY), 27 units of insulin plus one Sulphonyl ureas (-₹ 10112 / QALY), 27 X 2 units of insulin plus one Alpha Glucosidase inhibitor (-₹15,501 / QALY), 27 X 3 units of insulin plus one Sulphonyl ureas (-₹ 23,591 INR/ QALY), one Biguanide plus two Sulphonyl ureas ( -₹ 24,350 / QALY) and one Biguanide plus one DPP IV inhibitor (-₹ 31,434 / QALY). Table 31

A combination of one Biguanide plus one Sulphonyl ureas plus one Thioglitazone with a QALY of 1.00 and ₹ 3066 as total annual cost which stands the top among all the 3- drug combinations in case of discounted Incremental cost also. The standard combination had a QALY which was similar to other 6 drug combinations prescribed, but their increased discounted incremental cost than the standard can have an economical impact on the use of those drugs that includes 27 units of insulin plus one Biguanide plus one Alpha Glucosidase inhibitor (-₹ 181.23) 27 X 2 units of insulin plus one Biguanide plus one Alpha Glucosidase inhibitor (-₹ 326.1) 27 X 2 units of insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (-₹ 334.86) 27 X 2 units of insulin plus one Alpha Glucosidase inhibitor plus two Sulphonyl ureas (-₹ 368.79) one Biguanide plus two Sulphonyl ureas plus 27 X 4 units of insulin (-₹ 546.63) and one Alpha Glucosidase inhibitor plus one DPP IV inhibitors plus one Biguanide (-₹ 851.91). Incremental cost effectiveness ratio of the other drugs in which the standard dominates includes one Biguanide plus two Sulphonyl ureas plus one Thioglitazone (-₹ 1,742 / QALY), 27 units of insulin plus one Biguanide plus one Sulphonyl ureas (-₹ 5,186 / QALY), one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas (-₹ 6,814 / QALY), 27 units of insulin plus one Biguanide plus two Sulphonyl ureas (-₹ 7,263 / QALY), 27 units of insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (-₹ 7,364 / QALY), one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (-₹ 8,368 / QALY), 27 units of insulin plus one Alpha Glucosidase inhibitor plus two Sulphonyl ureas (-₹ 8,679 / QALY), one Alpha Glucosidase inhibitor plus one Biguanide plus three Sulphonyl ureas (-₹ 9,031 / QALY), 27 X 2 units of insulin plus one Biguanide plus one Sulphonyl ureas (-₹ 12,233/ QALY), 27 X 3 units of insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas (-₹ 18,594 / QALY), 27 X 2 units of insulin plus one Biguanide plus two Sulphonyl ureas (-₹ 23,644 / QALY), 27 units of insulin plus one Sulphonyl ureas plus one DPP IV inhibitor (-₹ 34,977 / QALY), 27 X 3 units of insulin plus one Biguanide plus one DPP IV inhibitors (-₹ 47,525 / QALY), one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas (-₹ 56,717 / QALY) and one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas (-₹ 62,677 / QALY). Table 33

In the cost effectiveness analysis of 4-drug therapy with a combination of 27 units of Insulin plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas was taken as the standard as it poses a higher QALY (1.00) with a minimal annual expenditure of ₹ 33,985 than others. A combination of 27 units insulin plus one Sulphonyl ureas plus one

Alpha Glucosidase inhibitor plus one DPP IV inhibitors and 27 units insulin plus one Sulphonyl ureas plus one Biguanide plus one DPP IV inhibitor effectively produced the similar QALY with an annual discounted incremental cost of -₹ 2,599 and -₹ 4,829 respectively, which is still a higher cost than that of the standard. The incremental cost effectiveness ratio of the other combinations where the standard dominates includes were 27 units insulin plus three Sulphonyl ureas plus one Thioglitazone plus one Biguanide (₹ 61,095), 27 units insulin plus three Sulphonyl ureas plus one Alpha Glucosidase inhibitor plus one Biguanide (₹ 48,827), one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one Thioglitazone (₹ 42,939), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas (₹ 38,331), 27 units insulin plus two Sulphonyl ureas plus one Thioglitazone plus one Biguanide (₹ 31,997), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Sulphonyl ureas plus one Thioglitazone (₹ 26,394), 27 X 2 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (₹ 21,745), 27 X 2 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas (₹ 19,984), 27 X 3 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (₹ 18,785), one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas (₹ 2,279), 27 units insulin plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (-₹ 2,021), 27 units insulin plus one Biguanide plus two DPP IV inhibitors plus one Sulphonyl ureas (-₹ 30,545), one Alpha Glucosidase inhibitor plus one Biguanide plus 2 DPP IV inhibitors plus one Sulphonyl ureas (-₹ 33,500), and 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas (-₹ 1,67,786). Table 35

Assessment of incremental cost to be spent to obtain the QALY in case of combination therapy was calculated taking a standard combination of one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Thioglitazone plus two Sulphonyl ureas as they have shown to elicit the QALY of 1.00 with an annual expenditure of ₹ 32,821. The drugs showing similar QALY with an increased discounted incremental cost (-₹ 5,698) spend annually was a combination of 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas plus one Thioglitazone with an increased discounted incremental cost (-₹ 5,698). The standard combination dominates the ICER of the other drugs that includes 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl ureas plus one

Thioglitazone (₹ 35,813), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two Sulphonyl ureas plus one Thioglitazone (₹ 22,872), one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas plus one Thioglitazone (-₹ 976), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas (-₹ 7,546), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl ureas plus one Thioglitazone (-₹ 7,673), 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (-₹ 9,719), 27 X 3 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (-₹ 17,294), 27 X 2 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus two Sulphonyl ureas (-₹ 31,068), one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus three Sulphonyl ureas plus one Thioglitazone (-₹ 34,768), and 27 units insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus two DPP IV inhibitors plus two Sulphonyl ureas (-₹ 94,054).Table 37

Using individual brands of drugs for combination therapy will be more economical than using market available combinations. By using fewer combination products with individual drugs may help to reduce the total expenditure of Diabetes per year.

# Conclusion

## VII. CONCLUSION

The aim of the present study was to perform pharmacoeconomic analysis of antidiabetic drugs in a diabetology outpatient setting. Out of a total number of 421 patients enrolled in this study, 407 patients were analyzed for demographic study and the cost minimization and cost effectiveness analysis was performed for 388 patients. The study has estimated the following results.

- Males are found to be more affected by diabetes than do with females, with an average age in the range of 51-60 years of age and 1-5 years of duration.
- Population within the range of 51-60 years and 1-5 years duration was found have increased percentage of non-vegetarians, Obese, Sedentary, Alcoholics and tobacco users either as smokers or as chewers with increased weight loss.
- Micro vascular complications such as Retinopathy, Foot ulcer, Nephropathy and Neuropathy was very common with patients under 51-60 years of age and 1-5 years of diabetes duration, whereas with 1-5 years of diabetic duration, Hypertension, Dyslipidemia, and Cardio vascular disease are common macro vascular complications with 61-70 years, 51-70 years and 51-60 years of age, but Peripheral vascular diseases was common with 6-10 years of duration and 51-60 years of age,
- Suffering and Physical activity restriction was much lower with 51-60 years of age and 1-5 years of duration, at the same time population with 1-5 years of duration had a mild to moderate suffering and physical activity restriction with 41-50 years and 51-60 years of age respectively. Severe suffering was noticed with 11-15 years of duration and 71-80 years of age, while physical activity restriction was severe among patients with 41-50 years of age and 1-5 years of duration.
- Increased numbers of patients were treated effectively with a combination of 2- drug combination therapy.

- Single drug therapy was shown to be not advisable for treatment as it failed to posses the increased QALY. Sulphonyl ureas shown to provide a superior ICER than, Biguanides which was most commonly prescribed for single drug therapy and hold the lowest cost.
- A combination of one Biguanide plus one Sulphonyl ureas was prescribed mostly for 2- Drug combination therapy, than one Biguanide plus one Thioglitazones with improved ICER hold the lowest cost.
- A higher number of patients were administered with a one Biguanide plus one Sulphonyl urea plus 27 units of Insulin for 3- Drug combination therapy, but the successful rate of ICER and lowest cost was for treatment was found with one Biguanide plus one Thioglitazone plus one Sulphonyl urea.
- With 4- Drug combination therapy, a combination of one Biguanide plus one DPP IV inhibitor plus one Sulphonyl urea plus insulin with an average dose of 27 units/ day had much better ICER than those treated with one each of Alpha Glucosidase inhibitors, Biguanides, DPP IV inhibitors and Sulphonyl ureas which was prescribed for a large population, but lowest cost was used up was for one Alpha Glucosidase inhibitor plus one Biguanide plus one Sulphonyl urea plus one Thioglitazone.
- Using Combination therapy with >4 drugs, 27 units of Insulin plus one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl urea was prescribed for higher group of patients, while the lowest cost of therapy was for one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Sulphonyl urea plus one Thioglitazone which had a less efficacy than the combination of one Alpha Glucosidase inhibitor plus one Biguanide plus one DPP IV inhibitor plus one Thioglitazones plus two Sulphonyl ureas having a beneficial ICER.

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# Annexure

# ANNEXURE I

# DATA ENTRY FORM

**Form No:** **Date:**

| **DEMOGRAPHICS** | | | | | |
|---|---|---|---|---|---|
| Patient name: | | Age: | | Sex: | |
| Diabetic duration: | | Smoker: | | Food habits: | |
| ***Occupational situation*:** | | ***Existing co-morbidities:*** | | | |
| Active | | Hypertension | | | |
| Pensioner | | Dyslipidemia | | | |
| Non worker | | Weight Gain/Loss | | | |

| **CLINICAL DATA** | | | | | |
|---|---|---|---|---|---|
| ***Tests*** | ***Index*** | ***Final*** | ***Tests*** | ***Index*** | ***Final*** |
| HbA1C: | | | BMI: | | |
| Fasting BS: | | | Total cholesterol: | | |
| Random BS: | | | HDL: | | |
| Post prandial: | | | LDL: | | |
| BP: | | | Triglycerides: | | |

| **DIABETIC COMPLICATIONS** | | | |
|---|---|---|---|
| ***Micro vascular*** | | ***Macro vascular*** | |
| Retinopathy | | Cardio VD | |
| Foot ulcer | | Cerebral VD | |
| Nephropathy | | Peripheral VD | |
| Neuropathy | | | |

| **QUALITY OF LIFE HEALTH QUESTIONNAIRE** | | | |
|---|---|---|---|
| ***Suffering*** | | ***Daily activity limitation*** | |
| None | | None | |
| Mild | | Mild | |
| Moderate | | Moderate | |
| Severe | | Severe | |

| **DRUGS USED FOR TREATMENT:** | | | |
|---|---|---|---|
| ***Date*** | ***Drugs*** | ***Dose*** | ***Frequency*** |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

## ANNEXURE II

## HADORN & UEBERSAX's

## "THE QUALITY OF LIFE HEALTH QUESTIONAIRE"

| Suffering | Daily Activity Limitations | Ratings |
|---|---|---|
| None | None | 1.00 |
| None | Mild | 0.89 |
| None | Moderate | 0.66 |
| None | Severe | 0.41 |
| Mild | None | 0.83 |
| Mild | Mild | 0.78 |
| Mild | Moderate | 0.60 |
| Mild | Severe | 0.39 |
| Moderate | None | 0.63 |
| Moderate | Mild | 0.61 |
| Moderate | Moderate | 0.51 |
| Moderate | Severe | 0.34 |
| Severe | None | 0.41 |
| Severe | Mild | 0.37 |
| Severe | Moderate | 0.32 |
| Severe | Severe | 0.18 |
| (Death) | - | 0.00 |