

## **The place of DPP-4 inhibitors in the treatment algorithm of diabetes type 2: a Systematic Review of Cost-effectiveness Studies**

This is a project elaborated with the objective of producing an original dissertation in the Course of Epidemiology of the Faculty of Medicine of the University of Lisbon by Alexandre de Sousa Calaça Pereira Baptista under the supervision of Prof. Dr. Julien Perelman and co-supervision of Prof. Dr. Antonio Vaz Carneiro.

**Introduction:** Diabetes mellitus is classified into 3 broad categories: type 1, type 2 and gestational diabetes. Type 2 diabetes, known as noninsulin-dependent diabetes, is a chronic condition that affects the way the body metabolizes glucose. Globally, as of 2012, an estimated 371 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of high fasting blood sugar. More than 80% of diabetes deaths occur in low- and middle-income countries. WHO projects that diabetes will be the 7th leading cause of death in 2030. Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use can prevent or delay the onset of type 2 diabetes. In Portugal about 90% of all diabetics have diabetes type 2. Treatment of diabetes type 2 is initially with diet and exercise, with oral drugs being added if that is insufficient, or when the condition progresses, as is common. The UK Prospective Diabetes Study (UKPDS) showed that in many patients, T2DM, is a progressive disorder with diminishing beta cell function over time. Many patients progress from lifestyle changes to oral monotherapy, then to continuation of tablets, and in a third of cases, to insulin therapy, with or without continued tablet treatment such as metformin. Inhibitors of dipeptidyl peptidase 4, also called DPP-4 inhibitors or gliptins, are a class of oral hypoglycemics that block DPP-4. They can be used to treat diabetes mellitus type 2. DPP-4 inhibitors are relatively new oral hypoglycaemic drugs. Sitagliptin, vildagliptin, saxagliptin, linagliptin and alogliptin are currently approved by the US Food and Drug Administration or the European Medicines Agency, while others are awaiting approval or are in development. The DPP 4 class was considered due to its economic impact in the national health systems expenses.

**Objectives:** To conduct a systematic review of cost-effectiveness and cost-utility studies of DPP4-inhibitors as treatment of diabetes type 2 and understand its implications for policy and for further research.

**Methods:** This review will follow the methodology recommended by the Centre for Reviews and Dissemination of the University of York for systematic reviews of economic evaluations.

The Literature Review will be based on a search for journal articles and abstracts in Medline from 1996 to present, CRD Database from 1996 to present, Medline (Dialog Datastar) 1996 to present, Embase (Dialog Datastar) 1996 to present, Cinahl (Dialog Datastar) 1996 to present, the Cochrane (including NHS EED) to present, and the Health Economic and Evaluations Database (HEED) to present and in Tufts CEA Registry. Searches for economic outcomes will be conducted using a variety of terms used in the medical literature to describe the intervention, the comparator, the target patient population, the outcomes and the study designs. A combination of these search terms will also be used for interrogating the databases. In addition, a hand search of the references in paper retrieved from the literature search will be conducted and additional relevant papers retrieved. The Internet will also be searched to identify relevant guidelines and reports. Based on this search, publications from the sites of:

- National Institute of Health and Clinical Excellence (NICE) ([www.nice.org.uk](http://www.nice.org.uk))

will also be retrieved. Inclusion criteria will follow PICOS approach. Models will have to be freely available as a full-text publication and be published in English language.

**Conflicts of Interest:** The author has no affiliations or financial involvement that conflicts with the material presented in this paper. The author is not employed in the pharmaceutical industry.