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## Original research

# Increased healthcare utilization costs following initiation of insulin treatment in type 2 diabetes: A long-term follow-up in clinical practice

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## ABSTRACT

**Aims:** To compare long-term changes in healthcare utilization and costs for type 2 diabetes patients before and after insulin initiation, as well as healthcare costs after insulin versus non-insulin anti-diabetic (NIAD) initiation.

**Methods:** Patients newly initiated on insulin ( $n = 2823$ ) were identified in primary health care records from 84 Swedish primary care centers, between 1999 to 2009. First, healthcare costs per patient were evaluated for primary care, hospitalizations and secondary outpatient care, before and up to seven years after insulin initiation. Second, patients prescribed insulin in second line were matched to patients prescribed NIAD in second line, and the healthcare costs of the matched groups were compared.

**Results:** The total mean annual healthcare cost increased from €1656 per patient 2 years before insulin initiation to €3814 seven years after insulin initiation. The total cumulative mean healthcare cost per patient at year 5 after second-line treatment was €13,823 in the insulin group compared to €9989 in the NIAD group.

**Conclusions:** Initiation of insulin in type 2 diabetes patients was followed by increased healthcare costs. The increases in costs were larger than those seen in a matched patient population initiated on NIAD treatment in second-line.

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## 1. Introduction

The prevalence of drug treated type 2 diabetes mellitus (T2DM) in Sweden is increasing and has recently been reported to be 4.4% [1]. T2DM is a major cause of morbidity and premature mortality, primarily through macrovascular and microvascular complications [1–5]. The disease and its complications increase the use of healthcare services with associated increases in total healthcare costs [6–8].

Glycemic control is a cornerstone in T2DM management to avoid diabetes related complications, where insulin is considered to be an effective HbA1c lowering intervention [9]. In Sweden, with a relatively high use of insulin compared to other European countries, insulin has now surpassed sulphonylurea as the most commonly dispensed drug in second-line add-on to metformin [10,11]. This “treatment ladder” is in line with the Swedish national guidelines, recommending second line insulin when metformin fails, only subsequently followed by other available glucose lowering drugs [12]. International T2DM guidelines however recommend several options as second line treatment, including also more innovative second line treatment options, such as dipeptidyl peptidase (DPP)-4 inhibitors, sodium glucose cotransporter 2 inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RA) [13,14].

In addition to the benefits on glucose levels, insulin also carries a number of unwanted side effects like weight gain, hypoglycemia, reactions from injections and increased treatment complexity [15–18]. Furthermore, recent studies report associations between insulin and increased risk of cancer, cardiovascular disease and all-cause mortality [18–20]. Thus, despite the low direct cost of insulin treatment, unwanted side effects and treatment complexity of insulin may lead to increased long-term health care costs [21–23]. Despite several studies on health care costs and T2DM [24–30] there are limited data on use of health care resource associated with insulin. Since insulin is widely used in Sweden, a cost analysis might contribute useful evidence to the understanding of the implications for the healthcare system of the insulin use. Recently, one study has reported increased health care costs after insulin initiation, but findings were limited to a highly selected group of patients with no hospitalization data, low representativity and short follow-up [31].

The aim of this study was to compare long-term changes in healthcare utilization and costs before and after insulin initiation in Sweden. In addition, also to compare healthcare costs after insulin versus non-insulin anti-diabetic (NIAD) initiation.

## 2. Material and methods

### 2.1. Study sample

Patients diagnosed with type 2 diabetes mellitus (ICD E11) and/or prescription of any blood glucose-lowering drug (ATC A10) were identified at 84 primary-care centers in Sweden between 1 January 1999 to 31 December 2009 ([www.clinicaltrials.gov](http://www.clinicaltrials.gov); NCT: 01121315). Effort was made to ensure a representative selection of primary care centers [8]. A total of 58 333 patients could be included, and data linked to

the Swedish National Patient-, Prescribed Drug- and Cause of Death registries by using the unique personal identification number, mandatory for all citizens from birth or immigration. Details on study design and the data extraction from primary care records and registers have been described elsewhere [2,4,8,22,32].

### 2.2. The insulin initiation cohort

This cohort is used to compare long-term changes in healthcare utilization and costs before and after insulin initiation in all patients. The cohort will also be important when assessing the representativity of the smaller matched second line cohort, see below. We identified all patients >30 years of age initiating insulin after having 15 months with no insulin prescription to be included. Patients were excluded if they had no registered visit or contact in the electronic patient record within two years prior to index treatment start. Any gap larger than 15 months between prescriptions was considered as discontinuation. In order to control for other cost driving comorbidities, we excluded all patients with history of CVD and cancer at baseline. Patients with any hospital visit (in hospital stay or outpatient clinic visit) within 90 days prior to insulin initiation were excluded. Patients were followed from two years prior to index date and until discontinuation, death or end of study period from electronic patient records.

### 2.3. Matched second line cohort

In order to compare healthcare costs after insulin initiation with healthcare costs after initiation of NIADs, we defined two similar groups. We identified patients with metformin monotherapy for at least 2 years and no gaps of more than 15 months between two prescriptions. They were indexed when they either were prescribed second line insulin (Insulin group) or second line non-insulin antidiabetic drug (NIAD group). To reduce the likelihood of rescue insulin treatment, only patients with two prescriptions within 15 months were included. Any gap larger than 15 months between second line prescriptions was considered as discontinuation.

### 2.4. Patient baseline characteristics

Baseline data were extracted from electronic patient records for the variables of systolic and diastolic blood pressure; total-, low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol; serum triglycerides; HbA1c values; lipid-lowering-, glucose-lowering- and blood pressure-lowering drugs; and estimated glomerular filtration rate (eGFR), age and sex. Data on HbA1c is reported in DCCT.

Disease history at baseline was collected by searching for diagnoses coded with International Classification of Diseases, 9th (ICD-9) and 10th (ICD-10) revision in primary care- and hospital data, defined in an earlier publication [8].

### 2.5. Healthcare resource use

All patient healthcare resource use (primary care, inpatient care (hospitalizations) and/or secondary outpatient care), both diabetes and non-diabetes related, was considered and

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