Progression of Physiological Measurements Over Time in Type 1 Diabetes Mellitus Patients in France

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Introduction

It is estimated that about 80,000 children under 15 years develop type 1 diabetes mellitus (T1DM) annually worldwide. The incidence continues to increase at a rate of 3% per year, and this trend is observed more markedly among younger children. This is associated with important consequences, since these patients will have to receive lifelong insulin therapy, combined with blood glucose monitoring, physical activity, and a healthy diet.

It is known that a tight control of blood glucose and other physiological parameters such as systolic blood pressure and cholesterol play an important role in preventing complications associated with T1DM. Consequently, many drugs and devices enabling continuous insulin infusion or continuous blood glucose monitoring devices are being developed.

Health economic modeling allows projection of healthcare benefits of medical interventions beyond the clinical trial period. To estimate the risk of microvascular and macrovascular complications, information about the progression of physiological parameters over time is required in order to make an accurate projection of the complications over a long period of time in the health economic model. It is therefore important to understand how these physiological parameters evolve over time in a modern cohort of adult T1DM patients.

Objectives

The objective of this study was to understand progression of physiological parameters T1DM patients to inform disease modeling. Physiological measurements of interest include HbA1c, body mass index (BMI), systolic blood pressure (SBP), total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides.

Methods

This is a cross-sectional analysis of T1DM patients based on the IMS LifeLink Diabetes Cohort in France, which consolidates patient-level data from general practitioners with additional data on diabetes patients via pop-up technology within electronic medical records to facilitate robust epidemiological studies. Currently, approximately 250 general practitioners in France which care for over nine thousand patients contribute to this database.

Variables collected include:

- Physician information (identification number, age, sex, region)
- Patient (identification number, birth year, sex, height, weight, blood pressure, comorbidities, hypoglycemic events)
- Diabetes information (diabetes type, time since diagnosis, HbA1c, complications)
- Drugs (prescription information, daily dose, stripes)
- Biological tests (date and results)
- Medical resource use (consultation date, specialist, and hospitalization).

Inclusion criteria included being an adult T1DM patient and having received at least an insulin prescription in the previous year.

Data were analyzed using R Studio. Descriptive statistics were presented. Physiological parameter evolutions over time were estimated by building multiple regression models using a backward elimination approach. Covariates of interest included sex, age, baseline blood pressure, HbA1c, BMI, cholesterol and smoking status. The goodness of fit was assessed based on the multiple R-squared.

Results

A cohort of 605 T1DM patients who visited their general practitioners between May 2011 and May 2014 were included in the analysis. Average patient age at inclusion in the cohort was 57.8 years of age. Forty-three percent of patients were male. Mean HbA1c was 7.84%, mean SBP was 132 mmHg, and mean BMI was 27.6 kg/m^2.

Changes in HbA1c and HDL-cholesterol over time were not statistically correlated with any of the variable studied.

Table 1) Cohorts baseline characteristics [1]

Patient Demographics	T1DM cohort Mean	SD
Mean age (years)	57.81	17.82
Duration of diabetes (years)	15.42	11.89
Proportion male	0.49	
Baseline Risk Factors		
HbA1c (%)	7.84	1.25
Systolic blood pressure (mmHg)	132.00	14.38
Total cholesterol (mg/dL)	183.00	16.50
HDL cholesterol (mg/dL)	54.30	8.09
LDL cholesterol (mg/dL)	97.30	14.15
Triglycerides (mg/dL)	134.00	82.30
Body mass index (kg/m2)	27.60	5.82
Proportion smoker	0.234	
Baseline Complications		
Proportion angina	0.170	
Proportion peripheral vascular disease	0.144	
Proportion stroke	0.078	
Proportion heart failure	0.115	
Proportion microalbuminuria	0.131	
Proportion background diabetic retinopathy	0.153	
Proportion history of amputation	0.064	
Proportion neuropathy	0.158	

Table 2) Regression models

Model 1: HbA1c regression model	Estimate (%)	Standard deviation (%)
Intercept	7.955	0.267
Covariates		
Age (years)	-0.002	0.004
Model 2: BMI regression model	**Estimate (kg/m^2)**	**Standard deviation (kg/m^2)**
Intercept	22.888	0.885
Covariates		
Time since diagnosis (years)*	-0.047	0.021
Age (years)***	0.092	0.015
Model 3: Systolic blood pressure regression model	**Estimate (mmHg)**	**Standard deviation (mmHg)**
Intercept	101.406	5.524
Covariates		
Age (years)***	0.248	0.047
HbA1c (%)***	2.170	0.598
Model 4: HDL-cholesterol regression model	**Estimate (mg/DL)**	**Standard deviation (mg/DL)**
Intercept	26.05	3.28
Covariates		
Age (years)	-0.085	0.053
Model 5: LDL-cholesterol regression model	**Estimate (mg/DL)**	**Standard deviation (mg/DL)**
Intercept	24.351	11.758
Covariates		
Age (years)*	-0.241	0.098
HbA1c (%)**	3.532	1.171
Model 6: Triglycerides regression model	**Estimate (mg/DL)**	**Standard deviation (mg/DL)**
Intercept	76.448	34.219
Covariates		
Age (Years)*	1.255	0.605
Time since diagnosis (years)*	2.243	0.718
Model 7: Total cholesterol regression model	**Estimate (mg/DL)**	**Standard deviation (mg/DL)**
Intercept	79.934	6.666
Covariates		
Age (Years)	-0.1555	0.108

*p value <0.05, ** p value <0,01, *** p value <0,0001

Conclusions

These results provide relevant inputs for the progression of physiological parameters to model the economic and clinical impacts of T1DM therapies over time.

Linear regression showed that BMI increased by 0.092 kg/m^2 (p<0.001) for each additional year of age. SBP was projected to increase by 0.248 mmHg (p<0.001) per additional year of age, LDL-cholesterol decreased by 0.624 mg/dL for each additional (p=0.017) year of age and triglycerides increased by 1.417 mg/dL for each additional (p=0.041) year of age.

Changes in HbA1c and HDL-cholesterol over time were not statistically correlated with any of the variable studied. Therefore, health economic modelers may assume that these parameters remain stable over time. One limitation of this study is that the data on time since diagnosis seemed underestimated when compared with the age of the patients. Repeating our analyses with other databases would allow to cross-validate our findings.

References

1. IDF Atlas, Sixth Edition
2. Le Jeunne P., IMS LifeLinkTM Cohorte Diabète : validité et utilité, La revue du praticien médecine-générale - Tome 26 I N° 889 I Novembre 2012

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