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Decreasing incidence of pharmacologically treated Type 2 diabetes in Hungary from 2001 to 2016: A nationwide cohort study

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ABSTRACT

Aims: Incidence and prevalence of Type 2 diabetes mellitus (T2DM) vary in different regions. Long-term nationwide epidemiological data are useful to assess trends over time. The aim of the study was to analyze the epidemiological changes of pharmacologically treated T2DM among people aged over 18 years in Hungary between 2001 and 2016.

Methods: Annual incidence, prevalence and all-cause mortality rate of pharmacologically treated T2DM patients were evaluated from 2001 to 2016 using the central database of the National Institute of Health Insurance Fund Management. Data were adjusted to age using the 2013 European Standard Population.

Results: Incident rate of pharmacologically treated T2DM decreased from 931.6 cases/100,000 person-years to 350.7 cases/100,000 person-years resulting in a −62.4% change (annual average change: −6.46% [95% CI: −7.64%; −5.67%]) between 2001 and 2016. The prevalence rate continuously increased from 4949.9 cases/100,000 persons in 2001 to the highest rate (8135.0 cases/100,000 persons) in 2011, which plateaued during the next 3 years and slightly decreased thereafter. Standardized all-cause mortality rate in people with T2DM decreased between 2001 and 2016 by 11.9% (annual average change: −0.84% [95% CI: −1.22%; −0.39%]).

Conclusions: Despite a clearly decreasing incidence of pharmacologically treated T2DM in patients aged over 18 years, the prevalence rate increased from 2001 to 2011 followed by a 3-year-long plateau and a slight decrease thereafter. These long-term trends with the reduced mortality rate may indicate favorable effects of health promotional activities for preventing and treating T2DM.

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1. Introduction

The burden of diabetes mellitus has been widely recognized. The latest publication from the International Diabetes Federation (IDF) estimated that in 2017 there were 451 million adult people (age 18–99 years) with diabetes worldwide and this number was expected to increase to 693 million by 2045 [1]. The large increase in prevalence of diabetes carries serious social and economic consequences in all regions of the world [2]. At population level, the burden of Type 2 diabetes mellitus (T2DM) far exceeds that of Type 1 diabetes due to substantially higher number of patients with T2DM. In addition, late complications and comorbidities of T2DM in adulthood create further difficulties for health care providers.

Estimation of annual incidence of T2DM over time in a nationwide cohort could provide valuable information regarding prevention, diabetes care and treatment, especially if coexisting data on prevalence and mortality are also available. Importantly, evaluation of incidence is the only way to truly understand the nature of the evolving epidemic of T2DM as its prevalence will increase in an ageing population which improves with medical treatment.

Unfortunately, only few studies were published so far about simultaneous evaluation of incidence, prevalence and mortality rates of T2DM at national level. Recently, a nationwide study from Norway documented that despite a decreasing incidence of T2DM, the prevalence continues to rise in the period of 2009–2014 [3]. As for mortality trends, a very recent review summarized all-cause mortality data from 11 countries worldwide: a consistent reduction in mortality was observed among people with diabetes since the late 1980s, ranging from 4% to 37% relative decline [4]. Studies about epidemiological changes of T2DM over time in Central-European countries are lacking and nationwide, long-term investigation for evaluating basic epidemiological trends of T2DM was not performed in Hungary up to present.

Therefore, we decided to analyze the annual epidemiological data of pharmacologically treated T2DM among people aged over 18 years in Hungary between 2001 and 2016. We evaluated annual incidence, prevalence and all-cause mortality rates in pharmacologically treated T2DM using the central database enabling us to perform a nationwide cohort study.

2. Materials and methods

In this study we used the database of the National Institute of Health Insurance Fund Management (Hungary) (study license number: S04/227/2016). In this central database – operating as the only one in Hungary – all antidiabetic drugs prescribed with reimbursement and dispensed in pharmacies nationwide are regularly registered. Actually, we retrospective investigated a 16-year long period from 2001 to 2016, inclusive. Importantly, all insulin derivatives (vials and pens, human insulins or insulin-analogues) are reimbursed from 50% to 100% while oral antidiabetic drugs are reimbursed from 55% to 70%. Accordingly, the central registry contains data of all T2DM patients treated pharmacologically with antihyperglycaemic agents. Of note, a small change was introduced in Oct 2014 when the reimbursement of a single generic metformin was discontinued due to financial reason and, consequently, new patients treated only with this generic metformin in monotherapy were not registered and, therefore, we could not capture them. We estimated the potential number of these specific patients using IMS (Intercontinental Marketing Statistics) Health data and trends in our cohort. In this way we concluded that not more than 3000–3500 T2DM patients should be accounted for this reason in 2015 and 2016.

The central registry contains basic data about all subjects with pharmacologically treated diabetes but in this study we investigated subjects with T2DM and age of >18 years only. People starting with antidiabetic therapy (oral drugs, insulin, non-insulin injectables; ATC A10 class; at least one prescription) from January 1, 2001 were enrolled in this study. The year of 2000 was used as reference year in order to detect only the real starting therapy in 2001. Each person was followed until December 31, 2016 or death.

Only subjects with pharmacologically treated T2DM were involved in the current study. All patients had a special social security number. Diseases were qualified by using ICD codes (International Classification of Diseases, 10th version). Women with gestational diabetes (ICD-10: O24.4) and those with polycystic ovary syndrome (ICD-10: E28.2) were excluded from the analysis and only patients with T1DM or T2DM were considered (T1DM ICD-10: E10, T2DM ICD-10: E11). First, we identified patients with T1DM, and afterwards, patients who did not meet criteria for T1DM were considered as patients with T2DM.

For identification of subjects with T1DM, we used a hierarchical algorithm with 6 steps including a basic definition and 5 further, hierarchical, stepwise definitions. Identification process was stopped, and T1DM was established if the basic definition or the first hierarchical definition fulfilled (Table S1). The details with the classification system of our analysis can be found in our design paper [5]. All data were anonymized at data extraction and we used non-identifiable data for further analyses.

Population size data for Hungary given by age and sex and, in addition, verifications of death in subjects with diabetes registered in the central database were obtained from the Hungarian Central Statistical Office.

We investigated annual changes in incidence and period prevalence of pharmacologically treated T2DM. We also analyzed all-cause mortality rates of pharmacologically treated T2DM patients, and we compared mortality rates between those with and without pharmacologically treated T2DM.

2.1. *Incidence*

Annual numbers of subjects with newly registered T2DM are given as crude numbers (n), new cases were counted for each calendar year, i.e. from 1st Jan to 31st Dec. Annual incidence rates are expressed as standardized rate (per 100,000 person-years). In addition, we calculated the crude incidence as per cent (%) in total population at risk. Total population at risk was determined by subtraction of number of prevalent T2DM cases known on the 1st of January from total annual population (based on annual mid-year population estimates from Central Statistics Office). We used standardized incidence rates for evaluating changes in incidence over time.

2.2. Prevalence

Period prevalence per calendar year (from 1st Jan to 31st Dec) was calculated which reflects the annual total number of people with pharmacologically treated T2DM. Period prevalence was counted as number of people with prevalent and newly detected T2DM each calendar year. In this way period prevalence was considered as the sum of T2DM patients alive on the 1st of Jan in the particular year with previous registration with T2DM in the database and newly detected T2DM patients in the corresponding entire year. Annual prevalence was expressed as crude numbers (n) and standardized rate (per 100.000 persons). In addition, we calculated the crude prevalence as per cent (%) in the total population. We considered standardized prevalence rates for evaluating changes over time.

2.3. All-cause mortality

The number of patients with T2DM who died from 1st Jan to 31st Dec was counted as the number of deaths in people with T2DM for each year. All-cause mortality was expressed as crude numbers (n) and standardized rate per 100,000 T2DM patients per year. We also calculated crude all-cause mortality as per cent (%) in T2DM population. We evaluated changes over time by using standardized mortality rates.

We also calculated the mortality risk in the non-T2DM population. Number of non-T2DM population was determined by subtraction of number of T2DM people from total population (based on annual mid-year population estimates from Central Statistics Office). Annual number (n) of deceased patients with non-T2DM was determined using a similar method (subtraction of death among people with T2DM from national data). Rates were expressed as standardized rate per 100,000 non-T2DM patients per year and crude per cent (%) in non-T2DM population.

2.4. Standardization

During direct standardization, all crude incidence, prevalence and mortality data were adjusted to age by using the 2013 European Standard Population in order to facilitate comparison with other population [6].

2.5. Data evaluation and statistical analysis

At first, we extracted data from the central database. We identified incidence, prevalence and mortality cases and rates (crude numbers, crude rates without standardization) and then, we performed the standardization in order to establish standardized rates of incidence, prevalence and all-cause mortality. We considered standardized rates for evaluating changes over time. For analyzing the changes in standardized rates over time we used the Poisson regression model. We determined mean annual changes in incidence (prevalence, all-cause mortality) rates with 95% confidence interval (95% CI) using Poisson regression model for this calculation. The target variable was the age-standardized incidence (mortality) per 100,000 person-years and age-standardized prevalence per 100,000 persons rounded to whole number, the explanatory variable was the year as a continuous variable. Comparing the mortality rate of T2DM patients and non-T2DM subjects, the group and the interaction of group and time were also included. Men and women were included into different models. Generalized linear models, like Poisson regression need independent data. Otherwise the estimation of the standard errors, and in conclusion, the p-values may be biased. This problem can be fixed with random resampling. We were using bootstrap method with a fixed block size of 3 and 10,000 bootstrap replicates. A $p < 0.05$ value was considered statistically significant. All calculations were performed with R version 3.5.2 (2018-12-20) with package boot version 1.3-20.

We estimated all changes using annual data. Figures depict annual observed data (mean values with 95% CI); however, Supplementary Tables report triennial data with the mean annual changes in standardized rates.

3. Results

3.1. Trends in incidence

From 2001 to 2016 we identified a continuous and significant decrease in incident cases and in standardized rates of incidence of pharmacologically treated T2DM. In 2001, 76,645 new cases were registered (931.6/100,000 person-years; 95% CI: 925.0–938.2/100,000 person-years) while in 2016 we found only 29,122 new cases (350.7/100.000 person-years; 95% CI: 346.7–354.7/100,000 person-years) resulting in a −62.4% change (annual average change −6.46% [95% CI: −7.64%; −5,67%]; $p < 0.0001$). Although the incidence cases were numerically higher among women in each year, the incidence rate expressed as per 100,000 person-years proved to be higher among men due to female predominance in the total population (Fig. 1, Table S2). At registration, the mean age of patients was around 59 years (male patients: 57–58 years, female patients 60–61 years) with no significant changes over time. During the entire period, the incidence rates were the highest, irrespective of its decrease over time, in the age-group of 61–70 years, followed by age-group of 51–60 years and ≥71 years. The annual decrease in incidence rates were nearly similar around 6–7% in all age groups over 30 years, however we found no significant change over time in patients with age 18–30 years (Fig. S1, Table S2).

3.2. Trends in prevalence

From 2001 to 2016 we documented a significant increase in annual numbers and in standardized prevalence rates of pharmacologically treated T2DM. The crude prevalence increased from 5.29% in 2001 to 9.30% in 2016, whereas the annual number of patients with pharmacologically treated T2DM increased from 422,707 in 2001 to 743,797 in 2016. The standardized rate of prevalence increased from 4949.9/100,000 persons (95% CI 4935.0–4964.9/100,000 persons) in 2001 to the highest number of 8135.3/100,000 persons (95% CI: 8116.7–8153.8/100,000 persons) in 2011, which plateaued during the next 3 years and slightly decreased thereafter to

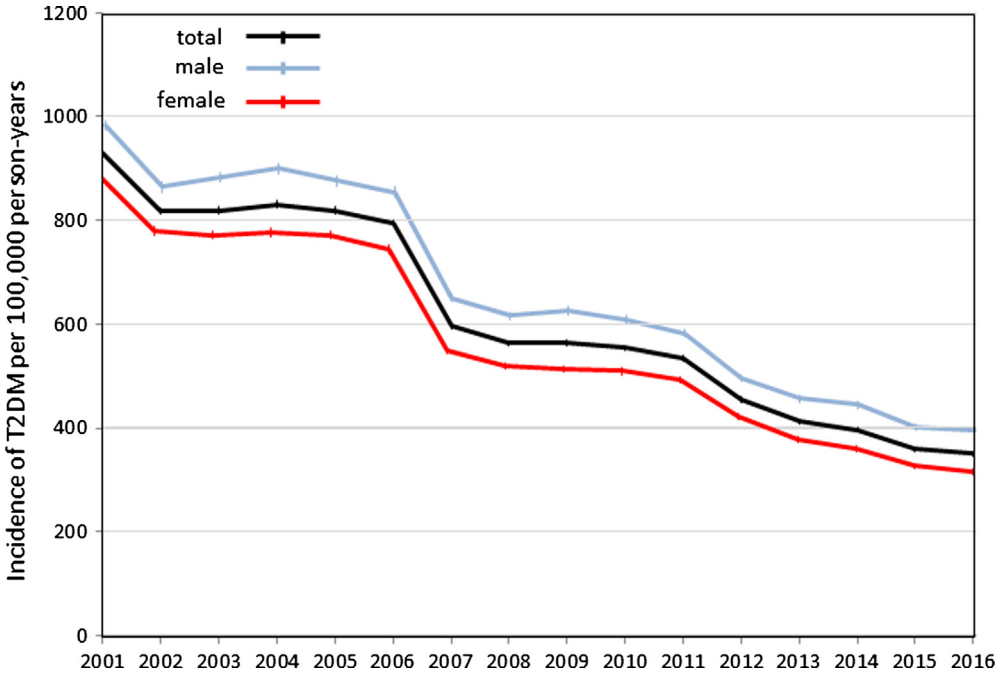

Fig. 1 – Changes in standardized incidence rates of newly registered subjects with pharmacologically treated Type 2 diabetes mellitus (T2DM) between 2001 and 2016 in Hungary (mean values ± 95% confidence interval).

7942.6/100,000 persons (95% CI: 7924.5–7960.6/100,000 persons) in 2016. (Fig. 2, Table S3). The standardized prevalence rate of T2DM changed by + 60.45% in the entire investigation period (annual average change + 2.68% [95% CI: 1.08%; 4.27%]; p = 0.0006). Although T2DM cases were numerically higher among women in each year, the prevalence rates expressed as per 100,000 persons proved to be higher among men. The prevalence rate of T2DM increased with increasing age; from 2010 it was ≥ 20% in patients with age-groups of 61–70 and ≥71 years (Fig. S2, Table S3). The mean age of T2DM cases was around 63 years (female 65 years, male 61 years) at the beginning and around 65–66 years (female 68 years, male 64 years) at the end of the study. During the entire period, the increase in standardized prevalence rate was most pronounced in age-group of 18–30 years, whereas no change was observed in patients with age 41–50 years.

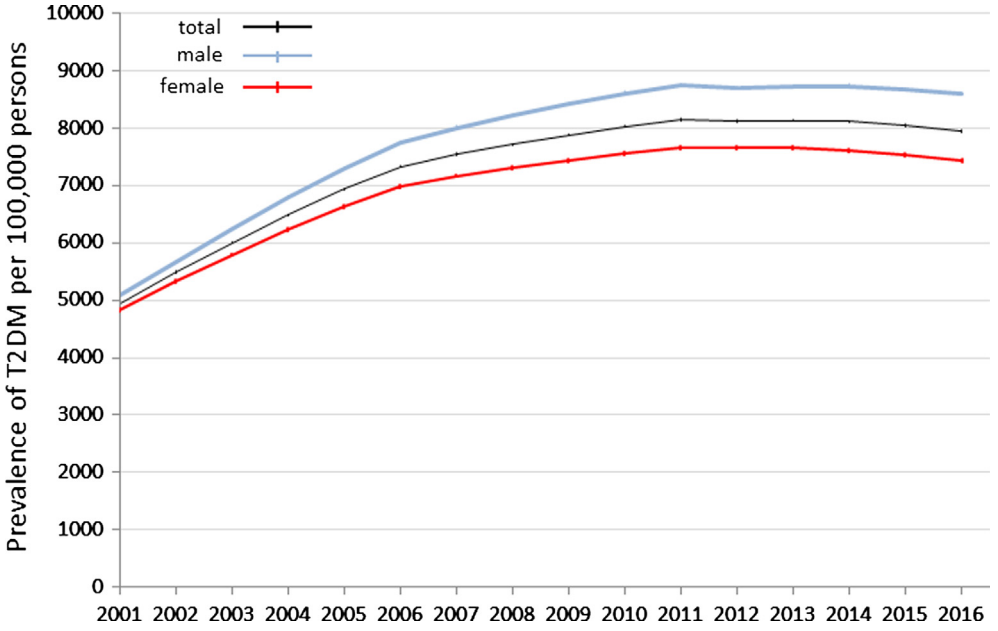

Fig. 2 – Changes in standardized prevalence rates of patients with pharmacologically treated Type 2 diabetes mellitus (T2DM) between 2001 and 2016 in Hungary (mean values ± 95% confidence interval).

3.3. *Trends in all-cause mortality in patients with T2DM*

Standardized all-cause mortality rate decreased from 2186.1/100,000 T2DM patients (95% CI 2154.0–2218.2/100,000 T2DM patients) in 2001 to 1928.8/100,000 T2DM patients (95% CI 1907.9–1949.7/100,000 T2DM patients) in 2016 resulting in a −11.9% change (annual average change −0.84% [95% CI: −1.22%; −0.39%] p = 0.0034). Although mortality cases were numerically higher among women in each year, the standardized mortality rate expressed as per 100,000 T2DM patients proved to be higher among men. All-cause mortality rates were higher in upper than in lower age-groups during the entire period (Fig. 3, Table S4). The decrease in mortality rates over time was observed in all but one (51–60 years) age-groups (Fig. S3, Table S4).

3.4. *All-cause mortality rates of T2DM patients compared to non-T2DM subjects*

Comparing standardized all-cause mortality rates of T2DM patients to those of non-T2DM subjects, higher mortality rates of T2DM patients were observed every year. Overall, the standardized mortality rates decreased over time both in T2DM and non-T2DM populations (total change: −11.9% and −17.6%; annual average change: −0.84%, 95% CI: −1.22%; −0.39%; p = 0.0034 and −1.28%, 95% CI: −1.41%; −1.16%, p < 0.0001, respectively). T2DM patients compared to non-T2DM populations did not differ significantly (p = 0.0618) regarding annual average changes in standardized all-cause mortality rates, and a gap remained. Although this gap tended to diminish over time, however it widened in later years of the observational period. This feature was due to a continuous decrease in standardized all-cause mortality rate of non-T2DM subjects which was slightly slower in T2DM patients where an initial decrease was followed by nearly unchanged rates (Fig. 4).

4. Discussion

In our 16-year-long analysis, the incidence rate of pharmacologically treated T2DM patients decreased, whereas the prevalence rate increased from 2001 to 2011 followed by a plateau and slight decrease thereafter. In addition, we observed a continuous decrease in all-cause mortality rate in T2DM patients, however mortality rate of T2DM patients remained higher during the entire period than that of non-T2DM subjects.

We performed our analysis using data from a central registry in Hungary. Diabetes registers are valuable sources of data for description of the trends in occurrence, development, and mortality of diabetes [7]. Nevertheless, the inevitable characteristics of database-analysis have to be taken account and results should be evaluated accordingly. Using the Hungarian central database, we performed a retrospective, 16-year-long study in a nationwide cohort for assessing the basic epidemiological data of pharmacologically treated T2DM patients. This is the first nationwide, long-term study from Hungary with simultaneous evaluation of incidence, prevalence and all-cause mortality in patients with T2DM. Using the 2013 European Standard Population for standardization, our results are comparable with other population.

4.1. *Incidence over time*

We observed a clear and continuous decline in standardized incidence rates of pharmacologically treated T2DM from 2001 to 2016, the net change was −62.4% (annual average change −6.46%). Our results are in line with a recent publica-

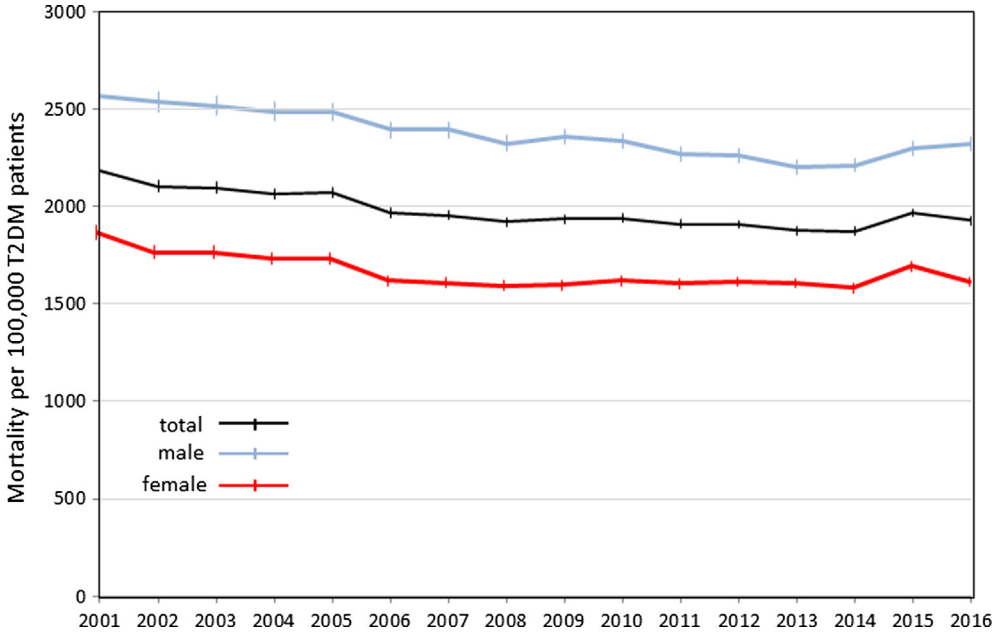

Fig. 3 – Changes in standardized all-cause mortality rates of patients with pharmacologically treated Type 2 diabetes mellitus (T2DM) between 2001 and 2016 in Hungary (mean values ± 95% confidence interval).

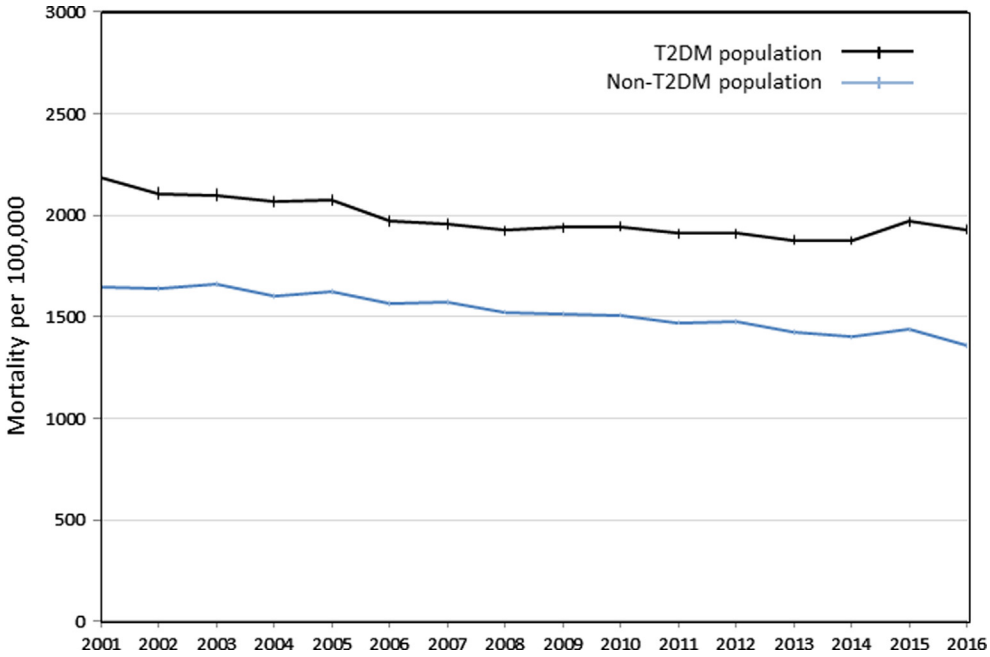

Fig. 4 – Changes in standardized all-cause mortality rates of patients with and without pharmacologically treated Type 2 diabetes mellitus (T2DM vs. non-T2DM populations) between 2001 and 2016 in Hungary (mean values ± 95% confidence interval).

tion from Norway documenting epidemiological data of both pharmacologically and non-pharmacologically treated T2DM patients from 2009 to 2014 [3]. The authors reported a 10.1% annual reduction of incidence in the entire diabetes population. Although the cohorts and the follow-up periods were different, the trends of changes are similar to our observations. Another publication from Norway reported also a decreasing trend in incidence of new users of glucose-lowering medication, particularly in patients aged ≥70 years, between 2006 and 2011 [8]. A modest decrease in incidence of pharmacologically treated T2DM was reported from Sweden between 2005 and 2013 [9]. From the United States, a study showed dramatic decrease in incidence from 2007 to 2012 [10] while another study reported only a modest decrease from 2008 to 2012 [11].

On the contrary, other studies reported stable or rising incidence of T2DM. For example, a study from UK primary care documented an increasing trend in incidence from 2000 to 2005 which stabilized later to 2013 [12]. In this study incidence increased with age peaking between 70 and 79 years and women had lower incidence than men. Another study from Scotland reported stable incidence rate between 2004 and 2013 [13]. Specifically, a decline in incidence was observed in older patients and incidence rate was higher in men than women in this particular study. A database-analysis from Sweden found a relatively stable incidence rate of pharmacologically treated T2DM patients between 2006 and 2013 (420 new cases per 100,000 inhabitants annually which are numerically close to our results in the respective years) [14].

In our study, incidence rates were higher among people aged over 50 years than those under 50 years, and they were highest for those aged 61–70 years. In addition, women had lower incidence rate than men. These results are very close to data from UK primary care [12] but dissimilar to others [13]. During the observation period the mean age of patients with incident T2DM did not change remarkably, similarly to data from Sweden [14]. Interestingly, a downward shift in age at diagnosis of T2DM was observed in a study from the United States [10].

It is noteworthy that we observed a significant decrease in changes of incidence rates in all age-groups over 30 years, however we found no significant change in patients with age 18–30 years. This result is in line with other observations indicating that appearance of T2DM has been nowadays shifted to younger population [10].

No clear explanation for the decreasing incidence rate can be derived from our data. Nevertheless, some factors should be considered. In 1999, the diagnostic criteria for diabetes were modified by the World Health Organization [15] and the lower diagnostic blood glucose values might contribute to the higher incidence rate in the subsequent years. Potentially, this might operate in earlier years of our study period. A larger fall in incidence rate was observed around 2007 when the former free of charge care was stopped and the government introduced an obligatory fee for visits in both primary and secondary care. This might reduce the number of appointments and, ultimately, decrease the prescriptions of antihyperglycaemic agents. It is of note, that although this regulation was withdrawn within a year, the decrease in incidence rates continued further on. Additionally, we cannot rule out that a small decrease in incidence rate in 2015 and 2016 was due to the fact that a single generic metformin lost its reimbursement and, consequently, patients treated initially only with this brand of metformin were not registered in the central database. Furthermore, incidence rate might

decrease due to increasing health promotion activities with more intensive screening procedure for early diagnosis of T2DM [16]. While these actions have become more and more popular and effective in the entire society [17], the pool of subjects with undiagnosed diabetes might decrease resulting in a declining number of incident diabetes cases in subsequent years. Finally, T2DM should be considered preventable [18] and lifestyle modification may result in a decrease of diabetes manifestation in subjects with prediabetes [19,20]. If prevention is successful, no antihyperglycaemic medication is needed for treatment, this might be a partial explanation for the decreasing incidence of pharmacologically treated T2DM in our study.

Honestly, the continuous decrease of standardized incidence rate and particularly its magnitude was a surprise in our study. Obesity and sedentary life-style are predisposing factors for T2DM and the proportion of subjects with overweight and obesity increased in the last decades worldwide [21] and also in Hungary [22]. Consequently, an increasing trend in incidence of T2DM has been generally anticipated but this was not found in our study. For explanation, we should consider that obesity-related newly detected T2DM patients are usually treated with lifestyle-modification at first, but these cases were not captured in our survey because only patients with pharmacologically treated T2DM were registered in the database. It is noteworthy, that a decreased risk for diabetes and/or hypertension was found in both men and women with obesity (but not with overweight) compared to those with normal weight in a recent representative, cross-sectional national survey in Hungary [22].

Importantly, the international diabetes community has been working towards diabetes prevention since late 1990s and, obviously, some positive results may also be expected from this work. The results of our study meet these expectations indicating that substantial decrease in T2DM incidence may occur. While we acknowledged the results obtained, we suggest that all limiting factors mentioned above might moderately affect but did not considerably influence the decreasing trend in incidence of pharmacologically treated T2DM from 2001 to 2016 in Hungary. It remains open, however, that the decreasing trend in incidence will or will not change in the future.

4.2. *Prevalence over time*

We observed a marked increase in standardized prevalence rate of pharmacologically treated T2DM in our study from 2001 to 2011 that was followed by a plateau and a modest decline thereafter. The net change in prevalence rate was +60.45% in the entire period.

In our study we calculated the period prevalence. We acknowledge that the term of prevalence originally means the proportion of people in a defined population at a defined instant in time; that is often referred as point prevalence. Nevertheless, period prevalence is also used, especially in studies with chronic diseases. As period prevalence reflects the total annual number of people with pharmacologically treated T2DM in our study, we preferred this approach of data presentation, similarly to others [3]. We hope that availability of such data would be useful for health authorities as an indicator of burden of T2DM in the population.

The increase in prevalence of T2DM in adulthood is a global phenomenon although its magnitude varies [1] due to calendar years in which the study was performed, the definitions used, and the population investigated. In addition, subgroups of patients might be affected differently. In Europe, increasing prevalence rate of pharmacologically treated T2DM was published from Norway between 2009 and 2014 [3] as well as from Sweden between 2005 and 2013 [9]. In the UK, the prevalence rate of T2DM became more than double from 2000 to 2013 [12]. A report from Scotland documented an increasing prevalence rate from 2004 to 2013 [13]. From the United States, a stable overall prevalence of T2DM was reported from 2007 to 2012 [10] while another nationally representative study documented a doubling of the prevalence of diabetes during 1990–2008, and a plateauing between 2008 and 2012 [11].

Prevalence of T2DM is determined by several factors, among those ageing and access to modern treatment are of great importance. In Hungary, the life expectancy at birth increased in the last couple of decades and new treatment options and modern technologies delayed the progression of chronic diseases such as diabetes and postponed the time of death [23–25]. Accordingly, the proportion of elderly people among the entire society increased, the longevity became more prominent. We suggest that these factors with reduced mortality rates substantially contributed to the increasing prevalence of pharmacologically treated T2DM. The plateauing and a modest decrease in prevalence in the later phase of our observation might be due to the significant decrease in incidence rate.

4.3. *All-cause mortality over time*

Our study documented an improvement in standardized mortality rates (change −11.9%), however T2DM patients, compared to non-T2DM subjects, had higher annual mortality rates during the entire period.

Over the last couple of decades, a decreasing mortality trend in patients with T2DM was observed in several countries, as it was summarized in a current global overview [4]. In addition, researchers from the United States very recently analyzed 963,648 adults receiving care in the US Veterans Affairs Healthcare System from 2002 to 2014. The authors found that although diabetes mellitus-related excess mortality is lower in contemporary era than previously, diabetes remains significantly associated with all-cause and cardiovascular mortality [26,27]. A decrease in mortality of patients with diabetes mellitus was reported from Latvia during the period of 2000–2012, however, the type of diabetes was not mentioned [28]. Our data about all-cause mortality trends are close to those of the Swedish National Diabetes Register which documented a smaller reduction in fatal outcomes of T2DM patients compared to matched controls from 1998 to 2012 [29]. As for the somewhat slower changes in mortality rates over time in pharmacologically treated T2DM compared to non-T2DM people, we cannot provide any clear explanation due to lack of important co-variances, apart from age, with potential influence on mortality trends.

4.4. *Strengths and limitations*

The use of central database made available to perform a nationwide survey which could be considered as a strength of our investigation. The follow-up period (16 years) was long enough to evaluate trends in incidence, prevalence and mortality over time. We used the 2013 European Standard Population in order to adjust for confounding by age; owing to this method our results are easy to compare to other populations. We reported incidence rates with coexisting prevalence and all-cause mortality data which is another strength of our study.

Our results have to be interpreted within the context of their limitations. We analyzed epidemiological data of pharmacologically treated adult T2DM patients, and we had no data about T2DM patients treated with lifestyle modification only. Consequently, our data should not be extrapolated to the entire T2DM population. For classification of existing diabetes for T2DM, we used a hierarchical classification algorithm; although it was carefully designed, some non-differential misclassification could not be ruled out. Nonetheless, the impact of this potential misclassification should be considered minimal due to high total number of patients enrolled. New patients with a single generic metformin in monotherapy were not registered in the database in 2015 and 2016, and consequently, we could not capture them. Nevertheless, if this metformin was used in combination with other antidiabetic drugs or was changed to another form of metformin, patients became "visible" and were registered in the database. Taken together, it is unlikely that this concern had any major impact on the results. In the database we used, clinical information such as comorbidities, duration of diabetes, glycaemic control, smoking habits, treatment beyond antihyperglycaemic therapy, socioeconomic status, educational level and laboratory findings were not registered and, therefore, we could not involve important covariates into the analysis. Finally, we excluded women with gestational diabetes or polycystic ovary syndrome from the analysis and we were not able to follow the subsequent potential manifestation of T2DM in these patients. Despite limitations, we feel that our results are valuable and useful – as first report from Hungary – for national health authorities in designing different projects for prevention and treatment of T2DM in the future. In addition, we hope that our results are of importance for the scientific community as well, enriching the current knowledge about global trend of T2DM with data from Central-European region.

4.5. *Conclusions*

We observed a clearly decreasing incidence rate of pharmacologically treated T2DM among people aged over 18 years from 2001 to 2016 while the prevalence rate increased from 2001 to 2011 followed by a 3-year-long plateau and a slight decrease thereafter. These long-term trends were accompanied by a reduced all-cause mortality rate among people with pharmacologically treated T2DM over time. These changes may indicate favorable effects of health promotional activities for preventing and treating T2DM in Hungary.

5. Disclosures

All authors (G. Jermendy, Z. Kiss, G. Rokszin, Z. Abonyi-Tóth, I. Wittmann, P. Kempler) have nothing to disclose.

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Author contributions

All authors made a significant contribution to this manuscript, interpreted the results, revised the manuscript, approved the final version and agreed to its submission for publication in DRCP.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107788.

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