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Reaching Therapeutic Goals Impacts on Estimated Cost of Illness for Patients with Type 2 Diabetes in Poland

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ABSTRACT

Objective: To estimate savings for public payer and for society generated by reduction of diabetes mellitus complications through maintaining therapeutic goals set by Polish Diabetes Association (PDA).

Methods: Diabetes progress in lifetime horizon was simulated in a Polish cohort of newly diagnosed adults with type 2 diabetes mellitus (T2DM) using the IMS Core Diabetes Model. The natural course of disease (Uncontrolled patients) was compared to situation where patients meet therapeutic goals in the first year and keep it in following years (Controlled patients). Direct medical costs from public payer and patients perspective were complemented with indirect costs estimated using friction costs approach (FCA) and human capital approach (HCA).

Results: Mean life expectancy was higher for the Controlled vs Uncontrolled patients (11.3 vs 10.7 LYs). The average QALY was also higher for Controlled vs Uncontrolled patients (8.33 vs 7.87 QALYs).

Uncontrolled patients generated during lifetime total costs respectively 2053 PLN, 2826 PLN and 4417 PLN higher than Controlled patients, depending whether direct costs only or direct costs and indirect costs (FCA or HCA) were considered. Adopting the estimated mean annual savings per patient to 1.1 million of Polish patients with uncontrolled T2DM (HbA1c>7%) would result in 192 million PLN of total annual savings, if only direct costs were considered and 264 or 412 million PLN, if indirect costs (FCA or HCA) were also included.

Conclusion: Maintaining therapeutic goals in T2DM results in higher life expectancy and, through reduction of T2DM complications, reduces both direct and indirect costs per T2DM patient.

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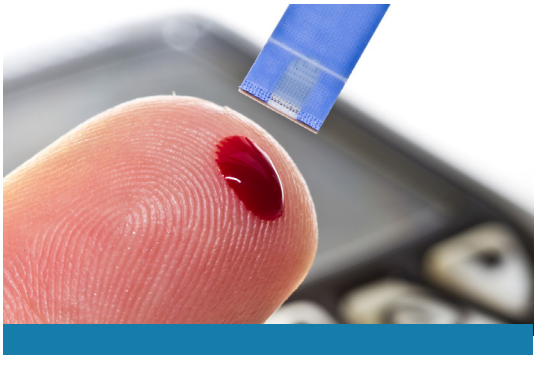


BACKGROUND

Type 2 diabetes (T2DM) is a social disease generating high costs for the patient, health care system and society. It is estimated that the 1.7 million of adult T2DM patients in Poland generated an annual cost of 4.3 billion Polish zloty (PLN) from the public payer and patients perspective in 2013, where 2.2 billion PLN was the direct cost of diabetes treatment (both drugs and medical care) and 2.1 billion PLN was the cost of specialist care related to diabetes complications. The cost of work productivity loss due to diabetes and its complications was estimated at 302 or 1779 million PLN depending if friction costs approach (FCA) or human capital approach (HCA) was used [1]. Keeping control of the disease reduces the risk of diabetes long term complications, such as heart disease, peripheral vascular disease or renal function impairment. The aim of the analysis was to estimate the savings generated by maintaining diabetes treatment goals set by Polish Diabetes Association (PDA) by the patients.

MATERIALS AND METHODS

Diabetes progress in lifetime horizon was simulated in a cohort of adult patients with newly diagnosed T2DM using the IMS Core Diabetes Model (8.0 version) [2], an extensively validated Markov's model replicating DM Type 1 and Type 2 course in one year cycles based on the data from clinical trials, including development paths of over a dozen of diabetes complications (each complication is simulated in a separate sub-model with an event-specific cycle length). The following complications and complication-related events were included in the model: myocardial infarction, coronary artery disease, heart failure, kidney transplant, hemodialysis, peritoneal dialysis, stroke, peripheral vascular disease, neuropathy, foot amputation, gangrene, foot ulcers, significant loss of vision, laser therapy, cataract surgery, severe hypoglycemia, depression and others.

Patient characteristics at the diagnosis of diabetes (Table 1) were drawn from Polish study ARETAEUS and were complemented with data from UK Prospective Diabetes Study (UKPDS).

ARETAEUS was a cross-sectional questionnaire-based study conducted in 2009 in Poland. It involved patients with T2DM diagnosed within 2 years before the study. The aim of the study was to describe the baseline characteristics of patients with newly diagnosed T2DM and to assess to what degree diabetic control criteria recommended by the PDA clinical practice guidelines were met. 1714 patients recruited by randomly selected physicians were included in the analysis [3].

The UKPDS was a multicenter trial of glycaemic therapies among 5102 patients with newly diagnosed T2DM. It ran from 1977 to 1997. The study assessed impact of blood glucose and/or blood pressure control improvement on reduction of diabetes complications [4,5].

Table 1.
Characteristics of basal cohort of patients with T2DM

Parameter	Value	Source
Demographic data		
Age	59.7 years	ARETAEUS
Male %	49.83%	ARETAEUS
Time from diagnosis	0.8 years	ARETAEUS
Risk factors		
HbA1c	7.08%	UKPDS
Systolic blood pressure (SBP)	137 mmHg	ARETAEUS
Total cholesterol (TC)	209 mg/dl	UKPDS
High-density lipoprotein(HDL)	41 mg/dl	UKPDS
Low-density lipoprotein (LDL)	135 mg/dl	UKPDS
Triglicerides(TRIG)	208 mg/dl	UKPDS
Body Mass Index (BMI)	30.6 kg/m2	ARETAEUS
Smoking %	31.00%	UKPDS
Other		
Caucasian race %	100%	ARETAEUS
History of myocardial infarction %	10.40%	ARETAEUS
History of stroke %	4.03%	ARETAEUS
Microalbuminuria %	7.00%	ARETAEUS
Retinopathy %	17.59%	ARETAEUS
Uninfected foot ulcer %	1.70%	ARETAEUS

Two alternative scenarios were compared: one in which patients followed the natural course of the disease (Uncontrolled) and one in which they maintained disease control defined as keeping therapeutic goals set by PDA throughout the lifetime horizon (Controlled).

The natural course of disease was modeled using epidemiologic data from two large observational studies: UKPDS and Framingham Heart Study [4,6].

The therapeutic goals for the diabetic population set by PDA included maintaining certain levels of HbA1c, SBP, TC, HDL, LDL and TRIG as well as avoiding hypoglycaemia episodes [7]. The PDA recommendations that were used as Controlled patients treatment goals were presented in Table 2.

Table 2.
PDA goals for T2DM

Parameter	Value
HbA1c	7.00%
SBP	130 mmHg
TC	175 mg/dl
HDL	45 mg/dl
LDL	100 mg/dl
TRIG	150 mg/dl
Hypoglycaemic episodes	0

The assumption for the Controlled patients was that they would reach all the therapeutic goals in the first year of treatment and keep them during the whole analyzed period.

The direct costs were estimated from the public payer and patients perspective. The indirect costs were assessed from the societal perspective.

The direct cost comprised of the cost of drugs (diabetes treatment and prevention of diabetic complications) and cost of treatment related to particular diabetes complications (the state in particular sub-model).

The distribution of diabetes treatment type was taken from the Polish observational study [8] and included such active substances as acarbose, metformin, sulphonylurea and insulin (Table 3).

Table 3.
Distribution of diabetes treatment across newly diagnosed patients with T2DM in Poland

Active ingredient	Percentage
Acarbose	9.2%
Metformin	70.6%
Sulphynourea	62.1%
Insulin	37.1%

Patients were assigned frequency of prevention treatment of cardiovascular diseases (acetylsalicylic acid, ACE inhibitors, statins and alternatives to ACE inhibitors for patients who do not tolerate them) according to the frequency of its use observed in ARETAEUS [3] and POLKARD [9] studies.

The annual cost of drugs was assessed using the average price of the substances on Polish pharmaceutical market in 2014 [10].

The mean cost of treatment of diabetes-related complications such as angina pectoris, myocardial infarction, heart failure, peripheral vascular disease, stroke, renal failure, foot amputation, foot ulcer, gangrene, neuropathy, vision loss and hypoglycaemia was estimated using National Health Fund (NHF) statistical data [11]. The incidence of those events was based on results of UKPDS [4,5]. Parameters used in the model were presented in Table 4.

The indirect costs comprised of productivity loss (short-term absenteeism and work disability) due to angina pectoris, myocardial infarction, heart failure, peripheral vascular disease, stroke, haemodialysis, peritoneal dialysis, renal transplant, foot amputation, foot ulcer and its infection, gangrene, neuropathy, significant vision loss, cataract, depression and hypoglycaemia and its repercussions (see Table 5). No loss of productivity (absenteeism or work ability) was attributed to patients with T2DM without complications. The indirect cost of the event parameter comprised two categories: onset of event cost (productivity loss attributable directly to complication occurrence) and annual cost (absenteeism and work ability associated with the history of the event) accrued in first and following years after the event.

Data on work productivity loss due to complications were collected in a cross-sectional study of 920 patients with diabetes complications performed in various specialist ambulatory centers in Poland in 2014 [12] complemented by data from a wide-ranged survey among specialist treating such conditions and Central Statistical Office [13] and NHF data (DRG statistics) [11].

Two methods of indirect cost assessment were used: friction costs approach (FCA) and human capital approach (HCA). The first one assumed that productivity loss was produced only for a transitional period in which the workers substitute is found (3 months) and the latter estimated productivity loss in a broader time horizon (until reaching post-productive age of 67).

The unit cost of productivity loss was estimated using the average gross wages in Poland in 2013 [14]. The assumptions regarding the characteristics of labor market in Poland were based on Central Statistical Office methodology of economic activity estimation and were presented in Table 6.

The costs were not discounted, as the objective of the analysis was to represent the average annual cost of T2DM in Polish population of uncontrolled patients on various stages of the disease and at various points from its onset, which was approximated by averaging the annual costs in the analyzed cohort throughout the lifetime simulation.

All costs were presented for 2014 in PLN (1EUR=4.26PLN). The incremental results were presented with 95% confidence intervals.

RESULTS

Mean life expectancy was higher for the Controlled vs Uncontrolled patients (11.27 vs 10.72 LYs, difference: 0.52, 95% CI: 0.05; 0.98). The average quality-adjusted life expectancy was also higher for Controlled vs Uncontrolled patients (8.33 vs 7.87 QALYs, difference: 0.45, 95% CI: 0.10; 0.79).

The difference in the average lifetime costs of disease between Uncontrolled and Controlled group amounted to 2053 PLN (95% CI: 266; 3935 PLN), 2826 PLN (95% CI: 496; 5295) and 4417 PLN (95% CI: -349; 9088) depending on type of costs taken in consideration: direct costs only, direct costs and indirect costs (FCA) or direct costs and indirect costs (HCA). The average lifetime cost of disease from the three perspectives were shown in Figure 1. Differences between the groups by cost categories were presented in Table 7.

Table 4.
Parameters – direct costs

Cost category	Costs [PLN]
Treatment of diabetes	
Treatment (annual)	814.76
Prevention of cardiovascular disease	
Statins	201.87
Angiotensin converting enzyme inhibitors	204.09
Stopping angiotensin converting enzymes due to side effects	119.26
Monitoring	
Screening for microalbuminuria	35.00
Screening for gastrin-releasing peptide	70.00
Eye screening	30.38
Foot screening program	35.00
Treatment of diabetes complications	
Myocardial infarction - 1st year	13363.54
Myocardial infarction – 2nd and following years	2942.84
Angina - 1st year	844.58
Angina - 2nd and following years	844.58
Congestive heart failure - 1st year	6709.70
Congestive heart failure - 2nd and following years	6709.70
Stroke - 1st year	12866.29
Stroke - 2nd and following years	437.86
Stroke - death within 30 days	3953.88
Peripheral vascular disease - 1st year	574.61
Peripheral vascular disease - 2nd and following years	574.61
Hemodialysis - 1st year	72194.55
Hemodialysis - 2nd and following years	69471.47
Peritoneal dialysis - 1st year	87537.72
Peritoneal dialysis - 2nd and following years	84814.64
Renal transplantation -1st year	60680.84
Renal transplantation - 2nd and following years	14447.91
Major hypoglycemia	117.18
Diabetic ketoacidosis event	2518.25
Lactic acid event	2518.25
Laser treatment	1692.86
Cataract operation	2423.03
Following cataract operation	60.77
Blindness - year of onset	2814.46
Blindness - 2nd and following years	260.77
Neuropathy - 1st year	724.94
Neuropathy - 2nd and following years	439.64

Cost category	Costs [PLN]
Amputation (event based)	8863.19
Amputation and costs of prosthesis (event based)	13110.06
Gangrene treatment	4803.70
Observation after healed ulcer	31.44
Infected ulcer	864.14
Standard uninfected ulcer	31.44
Healed ulcer history of amputation	144.29

Table 5.
Parameters – productivity loss

Category	Productivity loss (days)
Myocardial infarction - event	25.36
Myocardial infarction - annual	22.36
Angina - onset	16.92
Angina - annual	18.81
Congestive heart failure - annual	30.46
Stroke - event	56.85
Stroke - annual	25.46
Peripheral vascular disease - annual	5.58
Hemodialysis - onset	21.14
Hemodialysis - annual	15.32
Peritoneal dialysis - onset	11.27
Peritoneal dialysis - annual	10.08
Renal transplantation - onset	37.79
Renal transplantation - annual	12.32
Significant visual loss - onset	10.77
Significant visual loss - annual	30.08
Cataract - onset	14.98
Cataract - annual	8.99
Neuropathy - onset	0.15
Neuropathy - annual	27.49
Ulcer - onset	11.49
Ulcer - annual	50.16
Infected ulcer - onset	24.73
Infected ulcer - annual	59.08
Healed ulcer - annual	46.33
Gangrene - onset	26.89
Gangrene - annual	85.51
Amputation - event	31.52
Amputation - annual	14.26
Major hypoglycemia	2.62
Cataract - annual	44.70

Table 6.
Parameters regarding labor market in Poland

Category	Value
Retirement age	67 years
Age at first income	18 years
Mean annual salary	43800.72 PLN
No. work days/year	224
Months until substitution of productivity loss (FCA)	3

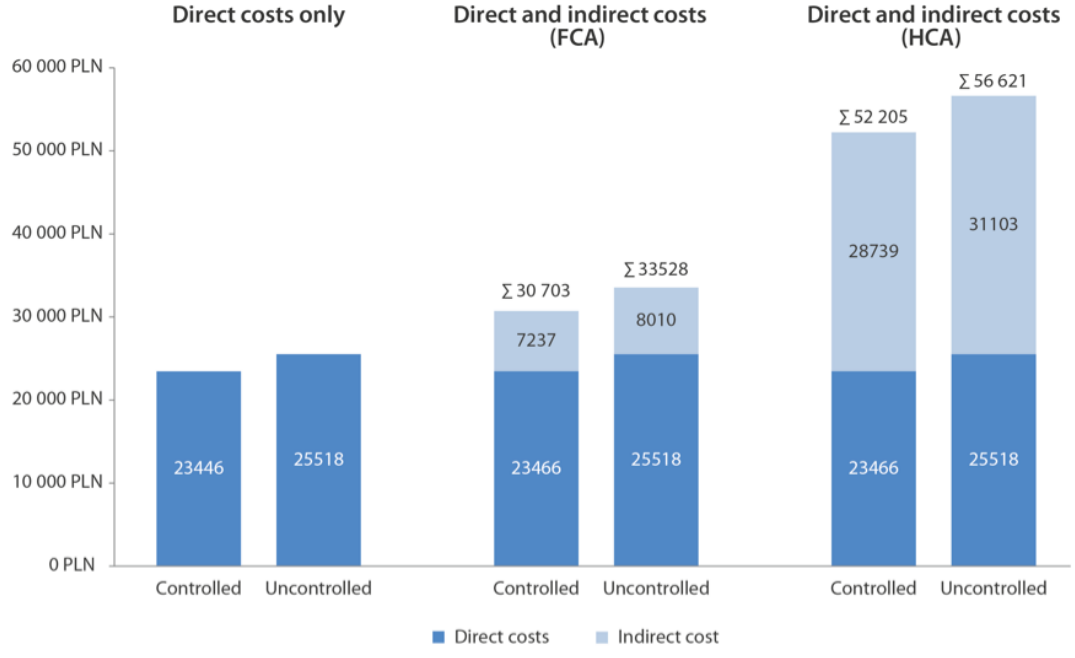


Figure 1.
Mean total lifetime cost of T2DM per Controlled and Uncontrolled patient [PLN]

Table 7.
The difference in average lifetime costs of T2DM between Uncontrolled and Controlled patients by cost categories [PLN]

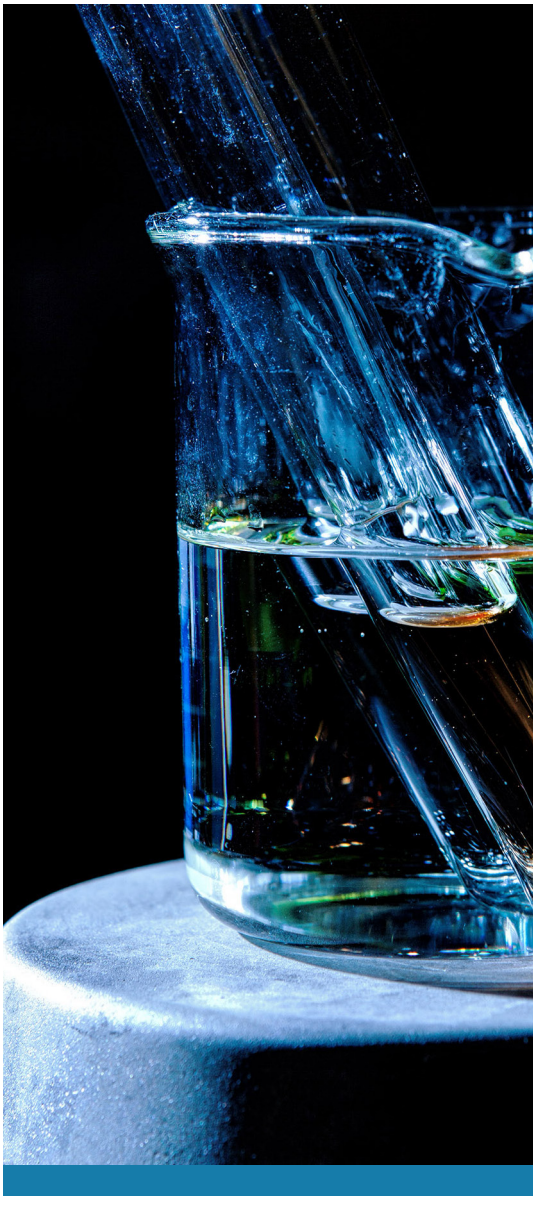
Category	Controlled patients	Uncontrolled patients	Savings due to diabetic control
Diabetes treatment	8468	8140	-328
Prevention of CVD and diag-nostics	2716	2638	-78
Complications -medical costs	12282	14739	2457
Total medical costs	23466	25518	2053
Complications - productivity loss (FCA)	7237	8010	774
Complications - productivity loss (HCA)	28739	31103	2364

Using lifetime costs per patient divided by average survival length obtained from the model mean annual costs of T2DM per patient were calculated for both cohorts to determine the value of annual savings for an average patient related to maintaining good diabetes control (HbA1c ≤ 7%). The results were then applied to the Polish population of patients with Type 2 diabetes who do not keep the sufficient disease control to simulate a hypothetical situation in which all the presently uncontrolled patients gain control in the first year of observation. The estimated mean annual savings per patient resulting from lowering the risk of diabetic complications by keeping PDA therapeutic goals by the whole uncontrolled population, estimated at 62.7% of 1.7 million Polish Type 2 diabetics, translated into significant amounts.

The average annual savings resulting from keeping the therapeutic goals summed up to 192 million PLN, in case where only direct costs were considered, 264 million PLN, if direct and indirect costs (FCA) were included, and 412 million PLN, if the analysis included direct costs and indirect costs (HCA).

DISCUSSION AND CONCLUSIONS

Type 2 diabetes and its complications generate a significant cost for the society in the long-term horizon. Many studies show that presence of diabetic complications is the most significant cost moderator which leads to the conclusion that preventing their development by maintaining control of the HbA1c levels, which influences strongly complications' incidence, would



result in significant cost reduction for the public payer and for the society. Our study confirmed that prolonged maintenance of the therapeutic goals reduced both direct and indirect costs per DM patient in lifetime horizon and affected both life expectancy and quality-adjusted life expectancy of T2DM patients by reducing the number of diabetes complications. It leads us to conclude that increasing the budget for education and treatment of the Polish population of diabetic patients, which would help them keep the therapeutic goals and improve their quality of life, in long term can also result in costs savings for the public payer and society. It is also important to note that the paper did not aim at presenting methods for reaching diabetic control in the presumed period of time nor did it include the costs of said process, which undoubtedly could be significant. Its objective was to estimate the savings generated by controlling diabetes in the Polish T2DM population.

One of the limitations of the analysis may be the fact, that in both groups, the same cost of treatment, based on Polish observational study for whole T2DM population, was assumed. In practice, uncontrolled patients are probably treated with different regimens than patients that are controlled what can influence results of treatment. Moreover, patient's adherence was not taken into consideration which can also affect the results. However, assumptions concerning treatment regimens used in Polish population were based on best available data so influence of above restrictions on final results of the study seems to be negligible.

The main limitation of the study appears to be the assumption concerning PDA therapeutic targets which are constant over time of the analysis. In real life, goals of PDA are adapted to patient's age and condition. The aim of our study was to assess situation where patients reach general therapeutic goals apart from the fact that it is more difficult in older age. Therefore, the study presents savings in case of the best possible results of treatment.

This is the first Polish study assessing savings associated with effective treatment of diabetes not only in terms of direct but also indirect costs.

STUDY FUNDING AND CONFLICT OF INTERESTS

The study was financed by Sanofi-Aventis, Poland.

The authors declare that they have no competing interests.

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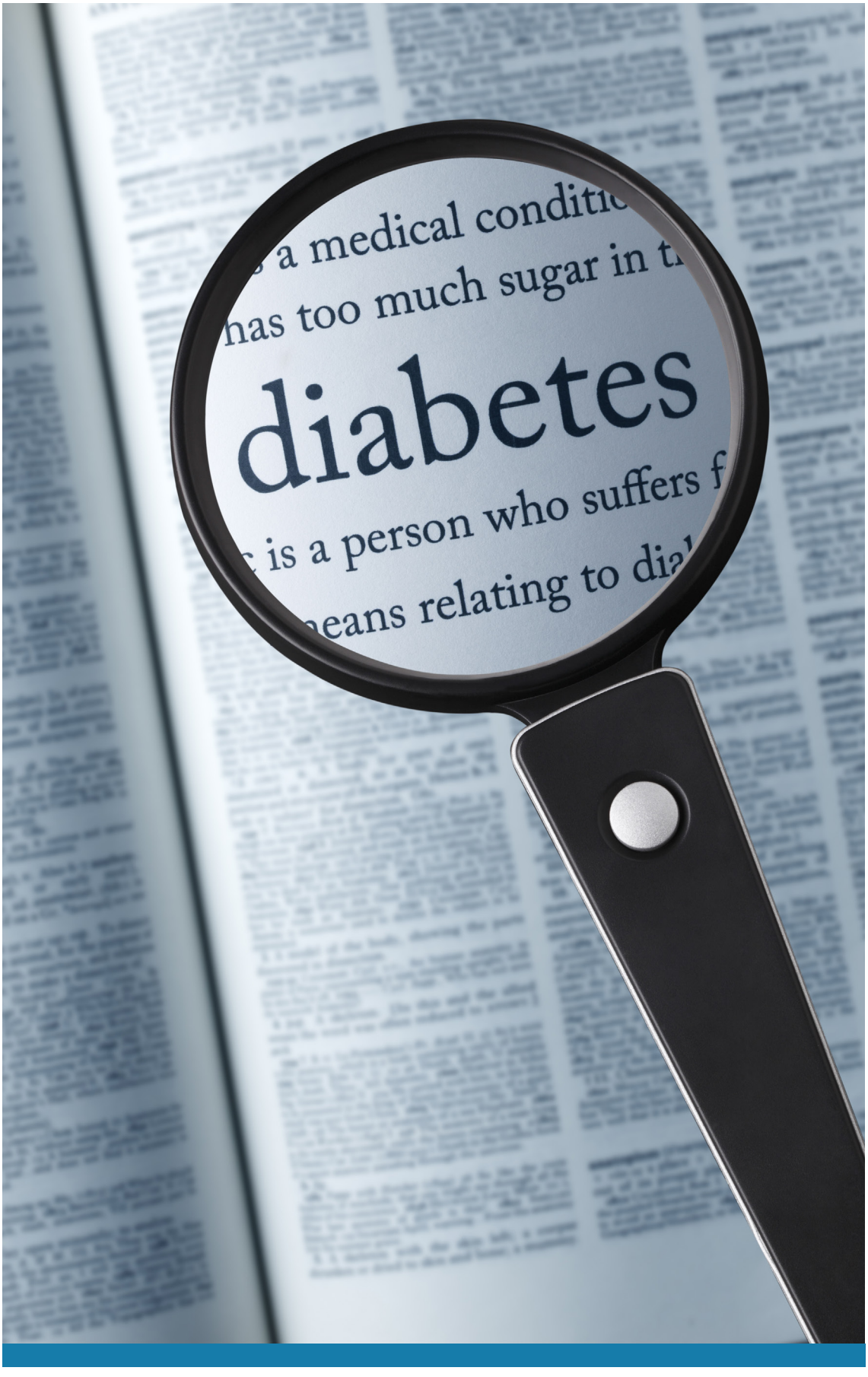
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