EE585

MODELING THE CLINICAL AND ECONOMIC IMPACT OF DPP-4 INHIBITORS IN UNCONTROLLED T2D

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BACKGROUND

- Type 2 diabetes (T2D) remains a major contributor to population mortality, driven by poor glycemic control and cardiovascular complications in Russia.
- In 2023, 4.8 million people in Russia were living with T2D, its prevalence has grown by 60% since 2010, and 113,373 deaths were associated with the disease.
- T2D treatment in Russia is largely centered on metformin (about 66% of regimens) or sulfonylureas (around 35%). At the same time, newer drug classes, including DPP-4 and SGLT-2 inhibitors, offer opportunities to enhance disease control and clinical outcomes[1,2].

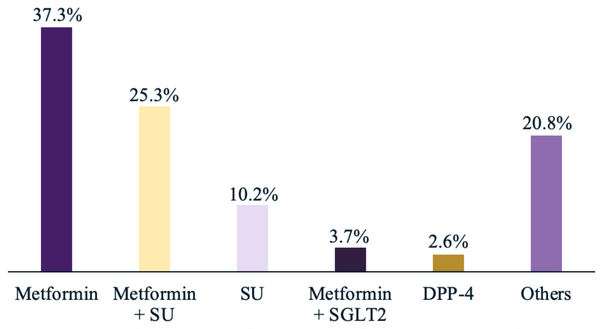

Figure 1. Treatment Structure of Patients with T2D in 2023.

- Although HbA_{1c} <7.0% is a key treatment target, many patients on MET and/or SU do not achieve it. Since 2023, the Federal Project "Combatting Diabetes" aims to raise the share of patients with HbA_{1c} ≤7% to 42.39%.

OBJECTIVES

This study assesses the clinical and economic impact of expanding the use of dipeptidyl-peptidase 4 (DPP-4) inhibitors in patients with uncontrolled T2D despite current oral therapy.

METHODS

- The study's target population included adult patients with type 2 diabetes mellitus (T2DM) whose HbA_{1c} is 7.1–9.0% while receiving glucose-lowering therapy:
  1. Metformin, sulfonylurea, or their combination, in the absence of clinically significant comorbidities (ischemic heart disease, cerebrovascular disease, prior myocardial infarction, or diabetic nephropathy);
  2. Metformin in combination with a sodium–glucose cotransporter-2 (SGLT2) inhibitor.
- Expert consultations with Russian endocrinologists identified recommended switching pathways to DPP-4 inhibitor–based regimens (table 1).

From (current) → To (DPP-4i escalation in eligible patient)	MET + DPP-4i	SU + DPP-4i	MET + SU + DPP-4i	MET + SGLT-2i + DPP-4i
MET	100%			
SU		5%	95%	
MET + SU	15%		85%	
MET + SGLT-2i				100%

Notes: MET – metformin, SU – sulfonylurea, SGLT-2i – sodium-glucose co-transporter type 2 inhibitor

Table 1. Rate of patient transition from current regimens to iDPP-4 containing regimens in the "DPP-4i escalation in eligible patients" scenario

- A mathematical model was developed to evaluate two scenarios over a 5-year horizon: continuation of current treatment patterns versus adding a DPP-4 inhibitor in eligible patients.
- We used HbA_{1c} distribution data from the Federal Diabetes Registry (2023) for T2D patients with recorded measurements (2.21M of 4.81M registered; see Figure 2). We assumed that this distribution is representative of the overall registered T2D population and can be applied across treatment subgroups.

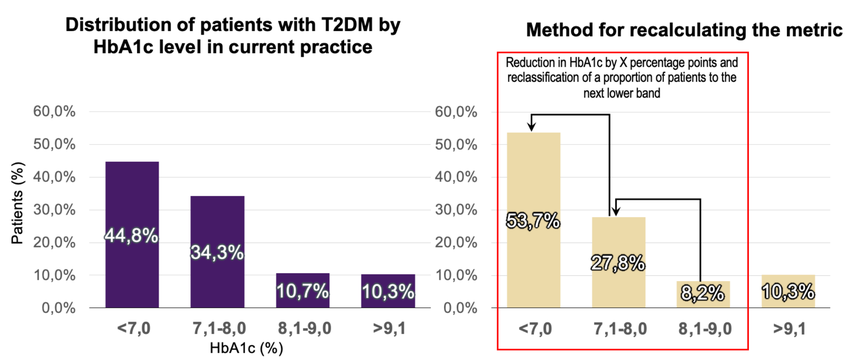

Figure 2. Conceptual representation of the methodology for recalculating the distribution of patients by HbA_{1c} levels under the "DPP-4i escalation in eligible patients" scenario.

- For each patient switched to a DPP-4i–containing regimen in "DPP-4i escalation in eligible patients" scenario, HbA_{1c} level was reduced by X pp. Effect sizes used in the model (ΔHbA_{1c}) were based on the results of systematic literature review:
  - MET vs. MET + DPP-4i: −0.64 (12–52 weeks)[3]
  - SU vs. SU + DPP-4i: −0.68 (24–52 weeks)[3]
  - MET + SU vs. MET + SU + DPP-4i: −0.89 (24 weeks)[5]
  - MET + SGLT2i vs. MET + SGLT2i + DPP-4i: −0.55 (52 weeks)[6]
  - MET + SU vs. MET + DPP-4i: no difference reported
- Patients were then reassigned to lower HbA_{1c} bands; crossing >1 band was allowed if ΔHbA_{1c} exceeded the gap between the patient's current HbA_{1c} and the lower band boundary. The procedure is illustrated in Fig. 2.
- To model survival, we used the established relationship between HbA_{1c} levels and all-cause mortality in T2DM. We assumed a J-shaped relationship between HbA_{1c} and Hazard Ration (HR) of all-cause death (Fig. 3)[7].
- To convert HRs into mortality rates, we calibrated the model so that the total predicted deaths matched the registry-reported T2DM deaths in 2023. These rates were adjusted for cohort aging and used across the 5-year modeling horizon.

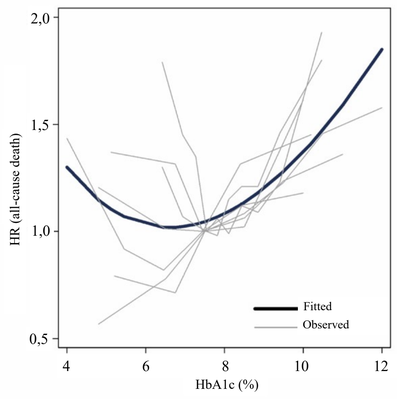

Figure 3. J-shaped relationship between HbA_{1c} and all-cause mortality risk in T2DM: observed study-specific hazard ratios (grey) and the regression-based fitted curve (black).

- Number of prevented deaths was defined as the difference in cohort size between scenarios, summed across all modeled years.
- We also estimated total treatment costs and the cost per death prevented, using evogliptin as a representative DPP-4 inhibitor, assuming no meaningful efficacy differences within the class.

RESULTS

- Patient counts by treatment regimen under each scenario are shown in Figure 4. Under current practice, about half of target population were on metformin monotherapy (372,266; 47.9%), 30.5% (236,913) on MET+SU, 11.2% (86,896) on SU, and 10.5% (81,782) on MET+SGLT2i. In the "DPP-4i escalation in eligible patients" scenario, all patients receive DPP-4i–containing regimens: 52.4% (407,803) on MET+DPP-4i, 36.5% (283,927) on MET+SU+DPP-4i, 10.5% (81,782) on MET+SGLT2i+DPP-4i, and 0.6% (4,345) on SU+DPP-4i.

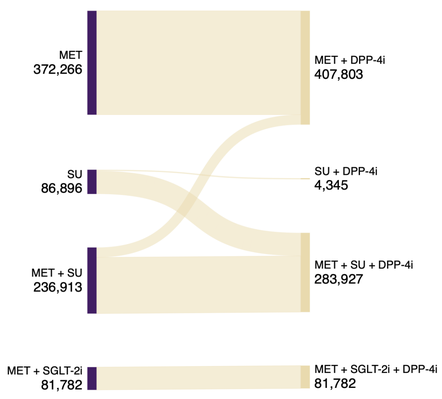

Figure 4. Patient flow from **current regimens** to **DPP-4 inhibitor–containing regimens**.

Note: Left: patient counts under current practice; right: counts under the "DPP-4i escalation in eligible patients" scenario. Flow width is proportional to the number of patients switched (expert-elicited rates).

- Among an estimated 777,857 eligible patients, adding a DPP-4 inhibitor to existing regimens increased the proportion of patients achieving HbA_{1c} <7.0% from 44.8% to 53.7% (Fig. 5).

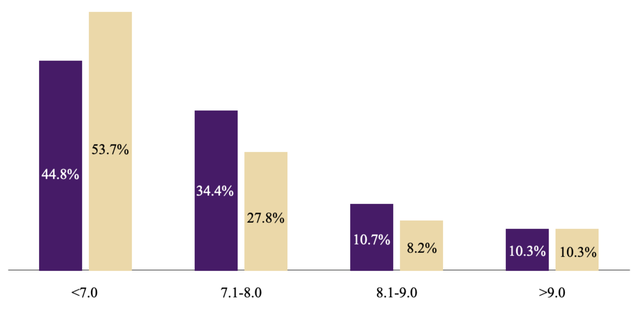

Figure 5. Distribution of patients by HbA_{1c} levels in **current** and **"DPP-4i escalation in eligible patients" scenario**

- With the federal project target of 42.39% of patients achieving HbA_{1c} < 7%, DPP-4 inhibitor use not only enables rapid attainment of this goal but also allows it to be exceeded.
- Figure 6 shows how the number of patients in the cohort changes over time in both scenarios. Each scenario start with 777,587 eligible patients and decline over time due to mortality. Under current practice, the cohort falls to 680,428, while under the "DPP-4i escalation in eligible patients" scenario, the decline is slower and resulting in higher cohort population: 690,168 patients by the end of year 5.

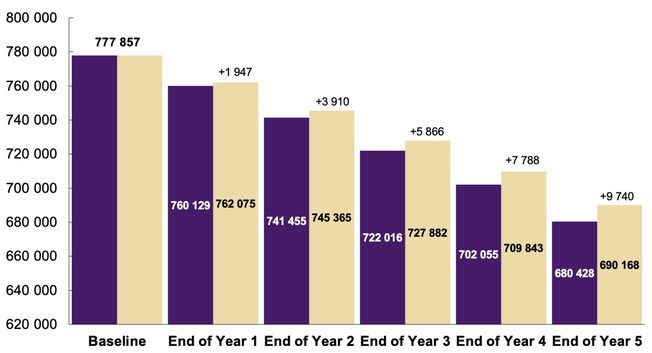

Figure 6. Size of the target cohort over time under **current practice** versus the **"DPP-4i escalation in eligible patients scenario"** (5-year horizon).

Note: labels above bars show incremental survivors under the "DPP-4i escalation in eligible patients" scenario.

- Over five years, approximately 9,740 deaths could be avoided (Table 2).
- The incremental annual cost of implementing DPP-4 inhibitors across the entire eligible population was projected at USD 105 million.
- Based on modeled mortality outcomes, the estimated cost per death prevented was USD 53,928 (Table 2). While direct drug expenditures increased with introduction of DDP-4 inhibitor, these could be partly offset by the potential long-term benefits of reduced disease progression and fewer diabetes-related complications.

Period	Additional full-year DPP-4i treatment courses required (patient-years)	Budget impact, USD million	Change in mortality, cases	Cost per death prevented, USD per case
1st year	769,966	109.7	-1,947	56,369
2nd year	753,720	107.5	-1,963	54,756
3rd year	736,624	105.2	-1,956	53,769
4th year	718,863	102.7	-1,922	53,446
5th year	700,006	100.1	-1,952	51,296
Total		525.3	-9,740	53,928

Table 2. Estimating the cost of death prevented

CONCLUSIONS

Expanding access to DPP-4 inhibitors for patients with uncontrolled T2D can substantially increase the share of patients reaching glycemic targets and prevent premature deaths.

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ISPOR Europe 2025, Glasgow, Scotland, 9-12 November 2025