

# CLINICAL AND ECONOMIC BENEFITS OF EXTENDED-RELEASE METFORMIN IN PREDIABETES MANAGEMENT

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## BACKGROUND

- Prediabetes, defined by elevated blood glucose levels below diabetes thresholds, significantly increases the risk of progression to type 2 diabetes (T2D) and cardiovascular diseases (CVD)<sup>1</sup>

## OBJECTIVES

- This study evaluates the clinical and economic impact of extended-release (XR) metformin treatment compared to no pharmacological intervention for patients aged 40–59 with prediabetes (fasting plasma glucose 6.1–6.9 mmol/L<sup>2</sup>), focusing on healthcare resource utilization and clinical outcomes.

## METHODS

- The target population comprised patients aged 40–59 years with prediabetes inadequately controlled by lifestyle modification; this age range was selected due to the increased T2D risk after 40 and recommendations to consider metformin in individuals under 60<sup>3</sup>
- Data sources and diagnostic criteria were based on ESSE-RF studies applying national definitions (fasting plasma glucose 6.1–6.9 mmol/L)<sup>4,5</sup>; broader HbA1c 5.7–6.4% screening criteria from the NATION study were acknowledged but not used for the base case.
- A Markov model compared two scenarios over a 10-year horizon: XR metformin treatment in all eligible patients, versus no pharmacological intervention. Patients transitioned among four health states: prediabetes, normoglycemia, T2D, and death.
- Transition probabilities between health states, as well as event probabilities, were derived from literature and statistical data<sup>6,7,8</sup>. Cardiovascular risk estimates were informed by hazard ratios for individuals with prediabetes<sup>9</sup> (see Table 1).

Glycemic state	NG	PD	DM	NG	PD	DM	NG	PD	DM
Major cardiovascular disease	Ischemic heart disease (I21, I22)			Ischemic stroke (I63)			Hemorrhagic stroke (I61, I64)		
HR*	1.00	1.3	1.95	1.00	1.38	2.14	1.00	1.21	1.53

Note: The reference category for relative risk estimation is normoglycemia (NG). All differences are statistically significant. NG – normoglycemia; PD – prediabetes (FPG 110–125 mg/dL (6.1–6.9 mmol/L)); DM – diabetes mellitus (FPG  $\geq$ 126 mg/dL ( $\geq$ 7.0 mmol/L)); HR – hazard ratio. \*Age-standardized estimates. ICD-10 codes for respective diagnoses are indicated in parentheses.

Table 1. Relative Risks of Selected Major Cardiovascular Conditions Across Glycemic Status Groups

- Mortality probabilities in the model were derived from Russian population life tables (age 40–59)<sup>10</sup> and adjusted using state-specific mortality HRs for normoglycemia, prediabetes, and type 2 diabetes (Table 2), considering the average duration of type 2 diabetes from diagnosis to death<sup>11</sup>, life expectancy in the age-matched general population, differences in cardiovascular risks<sup>9</sup>, and the rates of cardiovascular mortality in the overall population versus patients with T2D<sup>12</sup>.

Glycemic state	Males	Females	Combined
T2D	2.70	2.35	2.47
Prediabetes	1.12	1.12	1.12
Normoglycemia	0.99	0.99	0.99

Table 2. Mortality HRs by Glycemic State (vs. General Population)

- Outcomes assessed included:
  - progression rates to diabetes;
  - incidence of cardiovascular events;
  - overall mortality;
  - out-of-pocket expenditures for metformin;
  - public healthcare system costs for managing and monitoring prediabetes and its complications.
- The analysis included several types of costs:
  - drug therapy for prediabetes and T2D;
  - outpatient monitoring;
  - inpatient care for cardiovascular complications;
  - public procurement of glucometers and test strips.

## RESULTS

- Use of metformin (including XR) in prediabetes reduces progression to T2D and cardiovascular complications, resulting in fewer patients in the “T2D” and “Death” states compared with no pharmacological intervention (Figure 1).

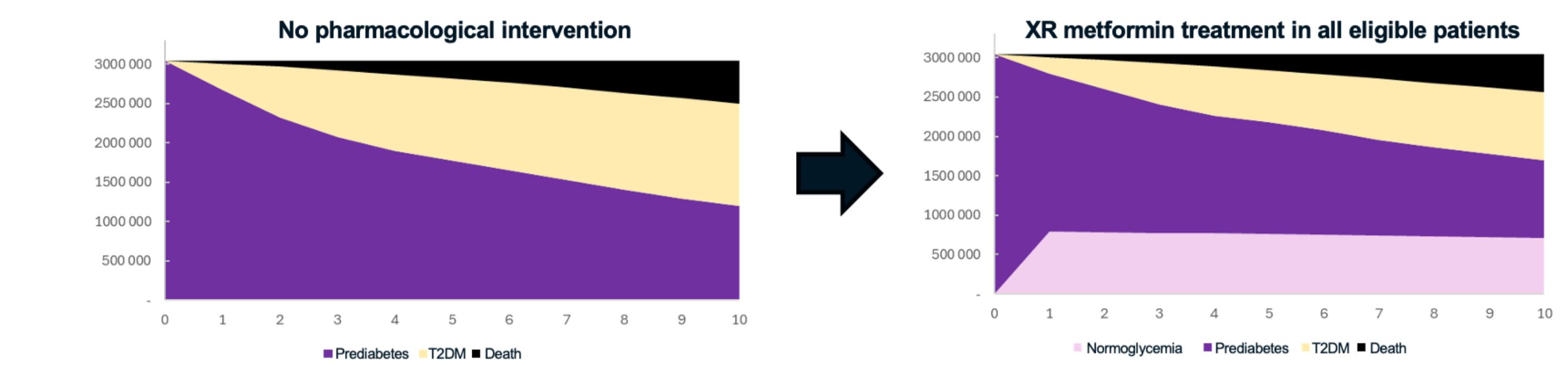


Figure 1. Distribution of patients across model health states by scenario.

- In a cohort of approximately 3 million individuals with prediabetes over the 3-, 5-, and 10-year horizons, treatment maintained a larger share of the cohort in normoglycemia or prediabetes, while the number of patients progressing to T2D was 326,553, 380,944, and 440,162 lower, respectively, compared with no pharmacological intervention.
- Over a 10-year period 63,524 deaths were prevented, including 41,561 from cardiovascular causes, 2,984 due to myocardial infarction, and 8,884 due to stroke, thus leading to a dramatic decline in cardiovascular mortality (Figure 1).
- The estimated annual cost of metformin extended-release therapy for 100% of prediabetic individuals aged 40–59 years was 50.2 million US\$; however, the prevention of diabetes progression and cardiovascular complications resulted in average annual savings of up to 30.2 million US\$ for diabetes treatment, 11.5 million US\$ for outpatient care, 2.4 million US\$ for cardiovascular therapy, and 10.9 million US\$ for medical devices, with the total savings estimated at an average of 4.8 million US\$ per year (Table 3).

Year	For 3 years	For 5 years	For 10 years	Average per year
No pharmacological intervention	561.5	1,114.7	2,638.0	263.8
Drug therapy, including:	155.4	345.9	843.8	84.4
for T2DM	155.4	345.9	843.8	84.4
for prediabetes	-	-	-	-
Outpatient medical care	306.6	558.8	1,243.3	124.3
Inpatient medical care	50.9	96.6	243.0	24.3
Medical devices purchase	48.6	113.4	307.8	30.8
XR metformin treatment in all eligible patients	668.1	1,203.6	2,589.8	259.0
Drug therapy, including:	304.3	529.8	1,044.3	104.4
for T2DM	93.5	214.5	542.1	54.2
for prediabetes	210.8	315.3	502.2	50.2
Outpatient medical care	287.8	515.6	1,128.5	112.9
Inpatient medical care	46.8	87.8	218.6	21.9
Medical devices purchase	29.3	70.4	198.4	19.8
Cost difference	106.6	88.9	-48.2	-4.8
Drug therapy, including:	148.9	183.9	200.5	20.0
for T2DM	-61.9	-131.4	-301.7	-30.2
for prediabetes	210.8	315.3	502.2	50.2
Outpatient medical care	-18.8	-43.2	-114.8	-11.5
Inpatient medical care	-4.1	-8.8	-24.4	-2.4
Medical devices purchase	-19.4	-43.0	-109.5	-10.9

Table 3. Costs (by type of medical care provided), million US\$.

- Figure 2 presents the composition of government and out-of-pocket payments under both scenarios at 3-, 5-, and 10-year time points.

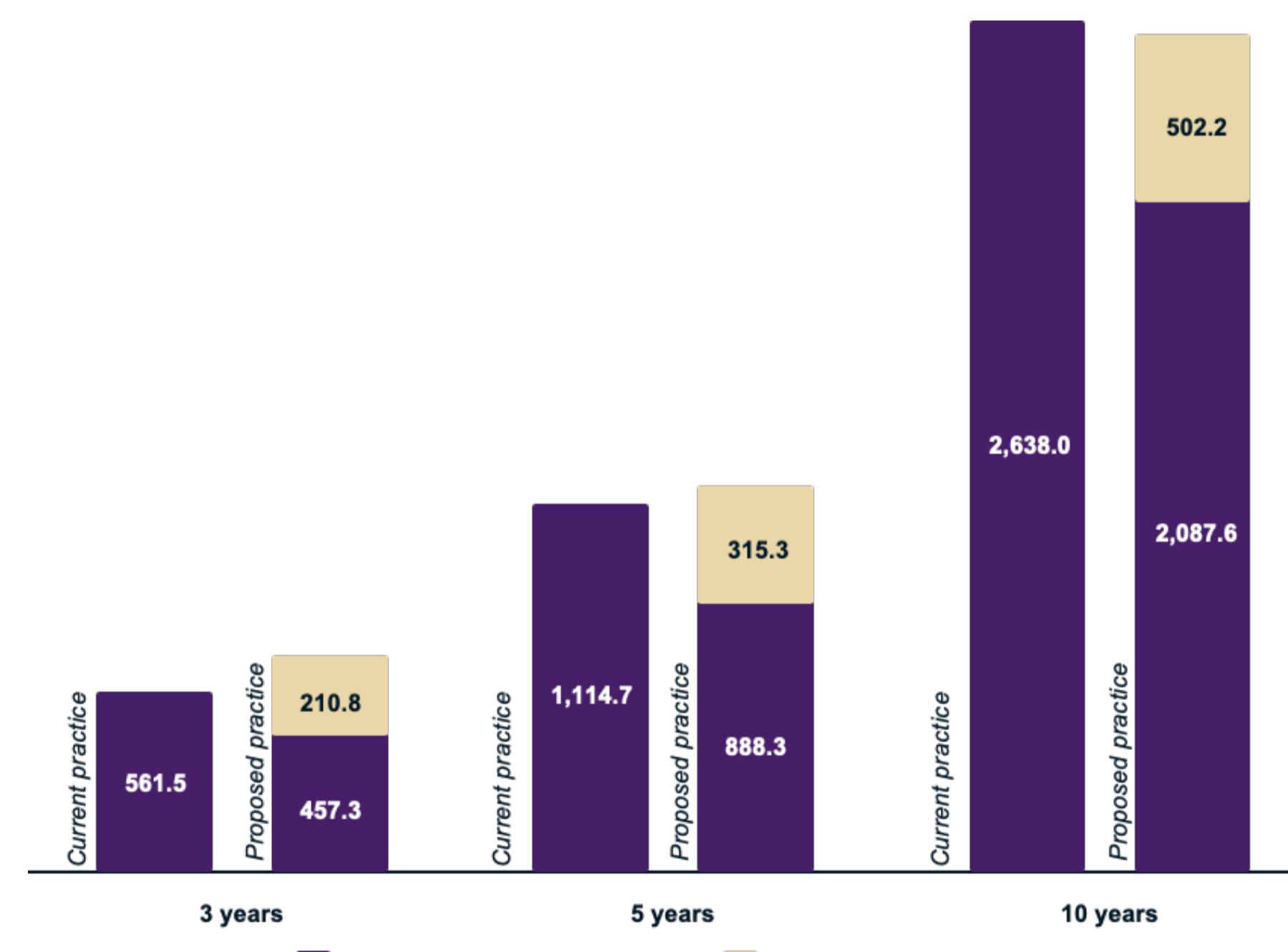


Figure 2. Breakdown of government and out-of-pocket healthcare expenditures under “No pharmacological intervention” scenario and “XR metformin treatment in all eligible patients” scenario, showing cumulative budget impact, million US\$.

## CONCLUSIONS

- Routine XR metformin use in prediabetes lowers risks of T2D, CVD, and death, while reducing overall public healthcare costs despite modest individual spending.

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