ECONOMIC BURDEN OF ATHEROTROMBOTIC DISEASE IN THE CZECH REPUBLIC

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Background

Atherothrombotic diseases impose a large burden on Czech society, mainly because of the high prevalence of risk factors compared to other countries. The Czech Republic has some of the worst mortality figures for heart disease and stroke. Death rates from heart disease are 260.4 per 100 000 population – **more than double the OECD average** of 115.2. For stroke, the rate is 106.4 per 100 000 population, compared to an OECD average of 69.1, i.e. **more than third** (1).

Although secondary prevention strategies, such as aspirin treatment, are available, up to 10% of patients with cardiovascular disease experience recurrent events each year. When used for secondary prevention, aspirin results in 19% lower risk of major adverse cardiovascular events and 9% lower risk of cardiovascular death compared to placebo (2).

However, innovative treatment alternatives, such as selective direct factor Xa inhibitors (e.g. rivaroxaban) combined with aspirin, proved to be more effective in preventing cardiovascular events in patients with coronary artery disease (CAD) and peripheral artery disease (PAD). According to the COMPASS trial (3) rivaroxaban (2.5 mg twice daily) plus aspirin significantly reduced the incidence of cardiovascular death, stroke, or myocardial infarction compared to aspirin alone (4.1% vs. 5.4%; HR 0.76; P<0.001).

To acquire reimbursement from public health insurance in this new indication and assure these potential benefits, it was necessary to also **evaluate the economic burden of the indicated population** (currently using only aspirin as a secondary prevention) in order to critically assess the economic impact of the prospective new intervention.

Objectives

- To evaluate both direct and indirect costs associated with CAD and PAD in the Czech Republic where only aspirin is used in secondary prevention.
- To create evidence supporting future health policy decisions concerning possible reimbursement of innovative treatment (e.g. rivaroxaban 2.5 mg).

Methods

- The prevalence of CAD combined with PAD was estimated based on health insurance claims for years 2015-2017 provided by the fifth largest health insurance fund (700 000 insured, i.e. 7 % of the population) and expert opinion from KOLs.
- A global **Markov model** was adopted to **predict the number of subsequent cardiovascular events** in the indicated population treated with aspirin in secondary prevention (i.e. current standard of care).
  - Lifetime Markov model with 3-months cycle length was developed in Microsoft Excel. Model settings are shown in **Table 1**.
  - The health states considered in the model included event-free health state, myocardial infarction (MI), ischemic stroke (IS), intracranial haemorrhage (ICH) and death. Each of these main events were implemented as acute and post-acute states. Moreover, patients may also experience a second main event. **Figure 1** illustrates the structure of the Markov model.
  - The co-occurrence of other health events within each health state was also simulated, i.e. extracranial haemorrhage, acute limb ischaemia, amputations and venous thromboembolism.
  - Each health state and health events were defined by their probability and related costs.
    - **Table 2** presents transition probabilities for main events, **Table 3** second main events and **Table 4** other health events. These are derived from the results of the COMPASS trial for aspirin arm (3).
    - Healthcare costs were provided by corresponding reimbursement tariffs and approved previous pharmacoeconomic analyses (4–6). The costs presented in **Table 5** and **Table 6** correspond to one cycle length, i.e. 3 months.
- **Indirect costs** of atherothrombotic disease were calculated based on **claims from the Czech Social Security Administration database**.
  - Costs of invalidity pensions were derived directly from the database.
  - The productivity losses were calculated a product of the average Czech salary in 2018 (i.e. € 85 per day) and the incidence which was derived from the database.

Table 1. Summary of the model settings used to estimate health-care costs

Analysis type and model type	Cost-effectiveness analysis, Markov model
Software	Microsoft Excel 2013
Perspective	Healthcare payer's (public health insurance)
Time horizon	Life-time
Discount rate	3% for costs and outcomes
Intervention	Aspirin 100mg (i.e. current standard of care)
Patient population	Patients corresponding to COMPASS inclusion/exclusion criteria (3)
Efficacy data	COMPASS trial (3)
Outcomes	Health events (myocardial infarctions, ischaemic strokes, cardiovascular death, extra- and intracranial haemorrhage, acute limb ischaemia, amputations, venous thromboembolism)
Half cycle correction	Yes (for costs and outcomes)
Mortality	General Czech population mortality (2017) (7)

Figure 1. Markov model structure

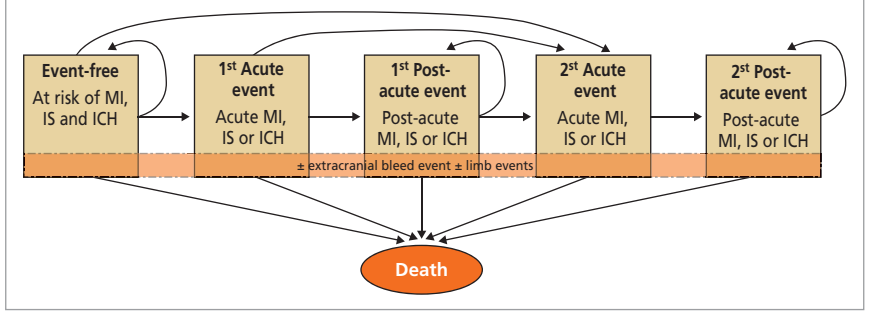


Table 2. Transition probabilities: first-event three-month risk of main events

	Risk of IM	Risk of IS	Risk of ICH
Event-free	0.00290	0.00176	0.00029
Acute MI	0.00641	0.00641	0
Post-acute MI	0.01852	0.00231	0
Acute IS	0	0.01042	0
Post-acute IS	0.00356	0.01779	0
Acute ICH	0	0	0.07143
Post-acute ICH	0	0.01754	0

Table 3. Transition probabilities: second-event three-month risk of main events

Post-acute MI + acute MI	0.00001
Post-acute MI + acute IS	0.00001
Post-acute MI + acute ICH	0
Post-acute IS + acute MI	0
Post-acute IS + acute IS	0.00004
Post-acute IS + acute ICH	0
Post-acute ICH + acute MI	0
Post-acute ICH + acute IS	0

Table 4. Health event three-month probabilities

	Three-month probability
Acute limb ischaemia	0.0006393
Major amputation	0.0004262
Minor amputation	0.0003694
Extracranial haemorrhage (major, non-fatal)	0.0021738
Venous thromboembolism	0.0006109

Table 5. Health state costs

Health states	Costs per 3 months
Event-free	€ 0
Acute MI	€ 2 596
Post MI	€ 104
Acute IS	€ 2 121
Post IS	€ 449
Acute ICH	€ 2 454
Post ICH	€ 87
Cardiovascular death	€ 850
Non-cardiovascular death	€ 0

Table 6. Health events costs

Other health events	Costs per 3 months
Acute limb ischaemia	€ 981
Post acute limb ischaemia	€ 0
Minor amputation	€ 7 507
Post minor amputation	€ 598
Major amputation	€ 9 318
Post major amputation	€ 532
Extracranial haemorrhage (major, non-fatal)	€ 2 622
Post extracranial haemorrhage (major, non-fatal)	€ 0
Venous thromboembolism	€ 981
Post venous thromboembolism	€ 0

Figure 2. Number of events experienced by Czech patients with CAD and PAD

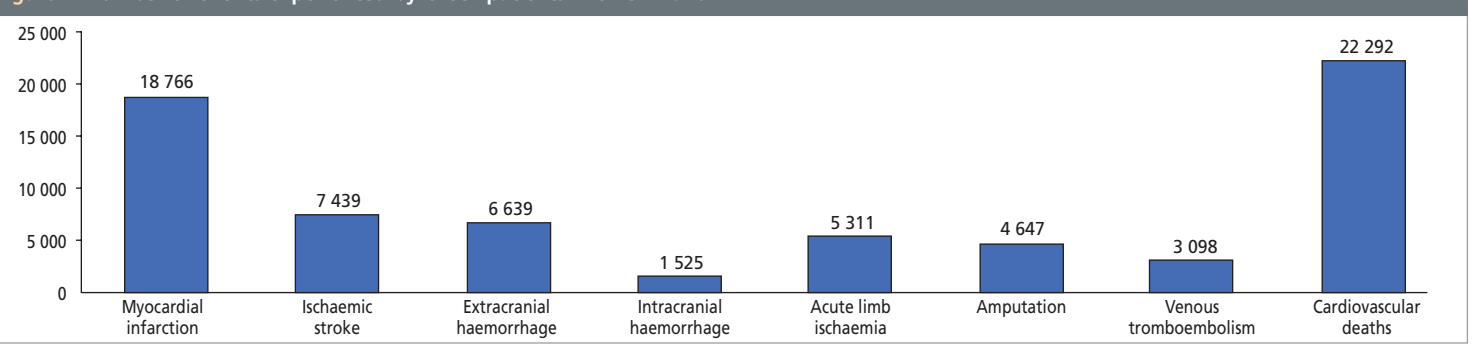


Figure 3. Indirect costs incurred by atherothrombotic diseases in Czech Republic

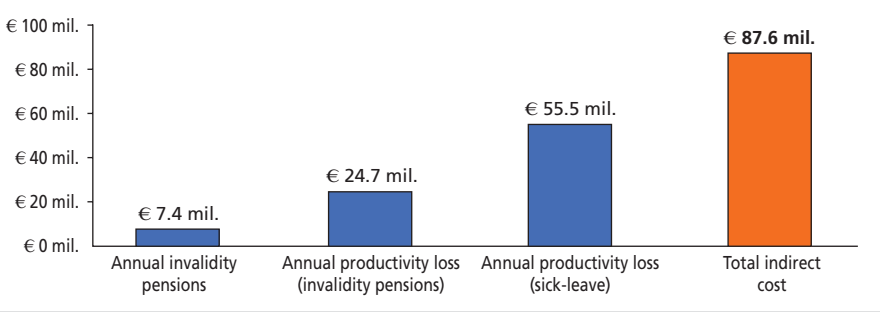
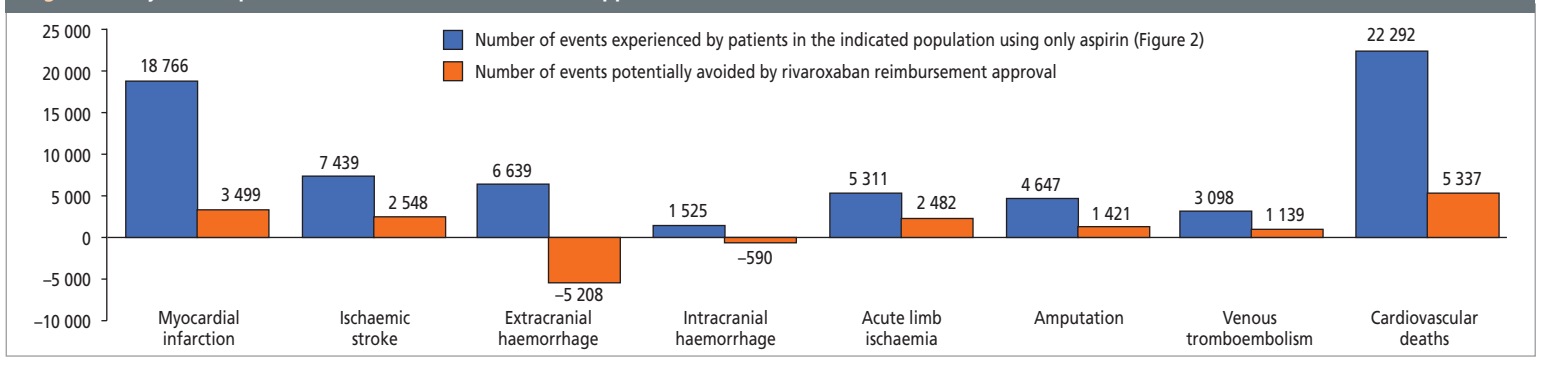


Figure 4. Projected impact of rivaroxaban reimbursement approval (current state without rivaroxaban vs. with rivaroxaban)



Results

- A total number of 49 215 patients suffering from both CAD and PAD was estimated in the Czech Republic.
- **Figure 2** presents the total number of events which will be developed by these patients in a lifetime horizon:
  - **18 766** myocardial infarctions,
  - **7 439** ischaemic strokes,
  - **6 639** cases of extracranial haemorrhage,
  - **1 525** cases of intracranial haemorrhage,
  - **5 311** cases of acute limb ischaemia,
  - **4 648** amputations,
  - **3 098** cases of venous thromboembolism,
  - **22 292** cardiovascular deaths.
- From a **healthcare payer perspective**, all these events will be associated with **total costs of €360.7 million** (in 4/2019 euros, i.e. 25.677 CZK per €).
- **Figure 3** shows indirect costs incurred by atherothrombotic diseases in Czech Republic:
  - According to Social Security Administration database, atherothrombotic diseases induce 1 946 cases of invalidity per year, corresponding to **€7.4 million of invalidity pensions** and **€24.7 million loss of productivity** per year.
  - Moreover, atherothrombotic diseases led to 4 802 sick-leaves each year, corresponding to annual productivity loss **of €55.5 million**.
  - In sum, these indirect costs equal to **€87.6 million per year**.

Conclusions

The costs associated with atherothrombotic diseases are substantial. Our analysis was designed to support future health policy decisions concerning various prevention and intervention programs. Indeed, it served as a valuable source of evidence for optimal decision-making strategy, more specifically in supporting the negotiation with local public health insurance companies. **As a result of these negotiations, rivaroxaban (Xarelto 2.5mg twice/day) combined with aspirin received reimbursement in this sub-population of patients**. The projected impact of this decision on health patients' outcomes is illustrated in **Figure 4**.

To our knowledge, this is the first Czech study evaluating the economic burden of atherothrombotic diseases from a societal perspective.

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