

# BMJ Open Estimation of long-term costs of postacute care in survivors of the methanol poisoning outbreak

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## ABSTRACT

**Objectives** To fill the existing research gap related to long-term costs of postacute care in methanol poisoning survivors, healthcare cost for 6 years after the outbreak has been modelled and estimated.

**Design** In a prospective longitudinal cohort study, data collected from 55 survivors of the Czech methanol mass poisoning outbreak in 2012 were collected in four rounds (5 months, then 2, 4 and 6 years after the discharge) in the General University Hospital in Prague according to the same predefined study protocol. The collected data were used to inform the cost model.

**Setting and participants** All 83 patients discharged from a hospital poisoning treatment after the 2012 methanol outbreak were informed about the study and invited to participate. Fifty-five patients (66%) gave their written informed consent and were followed until their death or the last follow-up 6 years later. The costs were modelled from the Czech healthcare service (general health insurance) perspective.

**Main outcome measures** Long-term national budget impact of the methanol poisoning outbreak, frequencies of sequelae and their average costs.

**Results** The postacute cost analysis concentrated on visual and neurological sequelae that were shown to be dominant. Collected data were used to create process maps portraying gradual changes in long-term sequelae over time. Individual process maps were created for the central nervous system, peripheral nervous system, sequelae detected during eye examinations and sequelae concerning the visual evoked potentials. Based on the process maps the costs of the postacute outpatient care were estimated.

**Conclusions** In 2013–2019 the highest costs per patient related to postacute care were found in the first year; the average costs decreased afterwards, and remained almost constant for the rest of the studied period of time. These costs per patient ranged from CZK4142 in 2013 to CZK1845 in 2018, when they raised to CZK2519 in 2019 again.

## INTRODUCTION

Mass methanol poisoning due to consumption of illicit alcohol containing a high proportion of methanol has been described in many countries since the 19th century, and they have always posed a challenge for

## Strengths and limitations of this study

- The study estimates costs of postacute care in methanol poisoning survivors.
- The model is based on data collected over 6 years after the outbreak.
- Process maps were created to visualise the development of health problems related to poisoning and their respective costs of outpatient care in the survivors.
- The health insurance records have not been provided for this research (although they exist); thus, this research is based on independently collected data and expert opinions.
- Fifty-five survivors (out of the total of 83 discharged from hospital care and invited to the study) agreed to participate in the research; the results may be affected by this non-random selection. No information is available related to the survivors not included in this study.

the respective healthcare system.<sup>1–3</sup> The methanol poisoning outbreak in the Czech Republic in 2012, together with the outbreaks in Norway<sup>4</sup> and Estonia,<sup>5</sup> belongs to the largest methanol mass poisonings in Europe and the most visible ones worldwide in the last two decades.<sup>2</sup>

High fatality rates of poisoned, brain damage and severe visual impairment in survivors are the main sequelae of methyl alcohol intoxication.<sup>6–10</sup> Recent studies estimate hospital mortality during methanol ‘epidemics’ above 20% and the prevalence of toxic long-term visual and brain damage at 40%–50% in survivors.<sup>4 5 8 9 11–13</sup> Since these brain and visual damages have been directly related to methyl alcohol intoxication,<sup>9 13 14</sup> also the costs of their treatment can be fully assigned to the poisoning episode. Central nervous system sequelae of methyl alcohol poisoning can be identified with MRI of the brain as haemorrhagic or non-haemorrhagic necrotic lesions of the putamen, pale globe or subcortical white matter.<sup>8 12 15 16</sup> Although

visual impairments typically recover 1–2 weeks after exposure,<sup>7 17</sup> visual loss up to complete blindness may be permanent, leading to disability and substantial decrease in quality of life of the survivors.<sup>7 9 18 19</sup>

The toxic concentration of methyl alcohol in blood is 200 mg/L and over. Thus, a patient exposure can be considered low if he shows methyl alcohol concentration lower than 200 mg/L unless the patient shows metabolic acidosis (ie, arterial blood pH lower than 7.35) or visual impairment at the hospital admission.<sup>3 10</sup>

The Czech 2012 outbreak is documented, including its epidemiological and clinical,<sup>3 8 10 13 20</sup> public health,<sup>2</sup> addiction,<sup>21</sup> quality of life,<sup>14</sup> as well as economic<sup>22</sup> perspectives. According to our best knowledge, with four rounds of follow-up check-ups during 6 years following the outbreak, they probably represent the most comprehensive national set of studies on the topic. A couple of wide-scope retrospective and/or follow-up studies have appeared also on the international scene. However, these studies do not cover the issue of cost of treatment, when they go into details about other features of poisoning and its consequences.<sup>7 18 23</sup>

The costs of methanol poisoning treatment, including hospital care costs and their effectiveness, have been mentioned in papers by Anseeuw *et al.*<sup>24</sup> and by Rulisek *et al.*<sup>22</sup> The main question in the published studies is that of costs and cost-effectiveness of fomepizole treatment as compared with haemodialysis and/or ethanol treatment. In the Czech environment, the evidence of Rulisek *et al.*<sup>22</sup> suggests that the total hospital costs in patients with acute methanol poisoning were more than three times higher in the patients treated with fomepizole than in those treated with ethanol (after an adjustment for the poisoning severity). No papers have dealt with the costs of long-term postacute healthcare in a similar way as other hospital cost-related studies do; hence, the question of the costs of outpatient care in the long-term perspective has not been answered yet. We can presume that the cost will be driven by both perceived health needs and results of medical examinations. We are aware of the fact that some of the methanol poisoning consequences and related complications can take effect in even more than 6 years covered by the currently available data. Nonetheless, the collected data allow for preliminary conclusions.

The aim of the study is to fill the existing research gap related to long-term costs of postacute care related to methanol poisoning in survivors, modelling and estimating the cost of the care for 6 years after the outbreak.

## METHODS

### Study design and the participants

For this prospective longitudinal cohort study, we analysed data from the Czech methanol mass poisoning outbreak that took place in September to December 2012.<sup>2 3</sup> All 106 patients hospitalised with confirmed acute methanol poisoning during this outbreak were included in the study.<sup>22</sup> The other 31 patients (of the

total 137 poisoned—see the detailed decomposition of this number in online supplemental figure S1) who died before admission to the hospital were excluded. The clinical, toxicological and biochemical data, including data on personal and family history, comorbidities and chronic alcohol abuse, were obtained from treatment providers by applying a standardised data collection form. Information on prehospital and hospital therapeutic interventions, as well as on the outcome, was obtained from hospital discharge summaries. These outbreak data were analysed and published earlier.<sup>3 8–13 20 22</sup> The diagnosis was established when (1) a history of recent ingestion of illicit spirits was available and serum methyl alcohol was higher than 200 mg/L, or (2) there was a history or clinical suspicion of methyl alcohol poisoning and serum methyl alcohol was above the limit of detection with at least two of the following: pH <7.3, serum bicarbonate <20 mmol/L or anion gap ≥20 mmol/L.<sup>3 8</sup>

All 83 patients who survived and were discharged from the hospital were informed about the prospective study and invited to participate. Fifty-five (66%) of them gave their written informed consent and were followed in a prospective and systematic study until their death or the last follow-up 6 years later (31 December 2018). These patients were examined in four rounds (5 months, then 2, 4 and 6 years after discharge) in the General University Hospital in Prague according to the same predefined study protocol described in detail in previous publications.<sup>13 22 25–27</sup>

### Estimation of the needed care and its cost

Information on the long-term poisoning health sequelae was obtained from searching in the documentation of follow-up clinical examinations during the 6-year period of patient observation, when visual and neurological sequelae were expected to manifest themselves. Visual sequelae of poisoning were diagnosed by complete ocular examination and standard ophthalmic tests, including visual acuity measurement, slit lamp examination, intraocular pressure measurement, fundus examination, colour vision, visual fields, optical coherence tomography with retinal nerve fibre layer measurements and visual evoked potentials.<sup>9 26</sup> Central nervous system sequelae (methanol-induced brain lesions, mainly bilateral necrosis of the putamen) were diagnosed using brain MRI or native computer tomography, single-photon emission CT and neurological and neuropsychological examinations.<sup>12 16 28</sup> Peripheral nervous system sequelae were studied above all by electromyography and functional tests.<sup>14 27</sup>

Data collected in the study were used to create process maps portraying gradual changes in long-term sequelae in the cohort over time. These process maps were later used as the basis for modelling the costs. Individual process maps were created for the central nervous system, peripheral nervous system, sequelae detected during eye examinations and sequelae according to the visual evoked potentials. All process maps contain states detected in patients in the four rounds of examinations. In the first

round, basic states describe existence or non-existence of sequelae (in the case of a diagnosed threshold value, the sequelae were recorded as present). Following rounds made it possible to record also improvement or worsening of the state. Two states ‘non-participation’ and ‘death’ were added to complete the picture.

Standard needed care was attached to each state (box) included in the process maps. This was done by expert clinicians in the fields of neurology and ophthalmology that collaborate with Czech Technical University, Faculty of Biomedical Engineering, on a long-term basis. Consultations with physicians were preceded by an analysis of health condition of the respective patients according to their discharge summaries and the conclusions of medical examinations within individual research rounds.

In the Czech Republic there is the Bismarck model of the healthcare system. Most healthcare is reimbursed by health insurance companies from obligatory health insurance according to the decrees issued annually by the Ministry of Health of the Czech Republic that always fix the reimbursement for delivered healthcare for the following year (the values are never changed during the current year, for example, due to unexpected outbreaks or other events). Thus, the amounts of this reimbursement can be considered as the costs determined from the perspective of health insurance companies, that is, healthcare payers. In many diagnosis-related groups, the reimbursement differs, sometimes substantially, in a positive or negative way, from real costs borne by individual healthcare providers, that is, costs from the perspective of healthcare payers.<sup>29</sup> In this study, the needed care was valued by its reimbursement values. Due to biannual follow-up checks, the needed care determined for the year of an examination was considered also for the following year. In each year, pricing was done according to the decree in effect for that year.

Thus, anticipated cost of healthcare of the whole examined sample of patients was determined independently for each year from 2013 to 2019. Average costs of healthcare of one patient were then calculated.

### Calculations and statistical analysis

Statistical analysis was performed using MS Excel and R applications. Next to basic statistical characteristics, most calculations consisted of calculating frequencies, sums of costs of individual medical interventions and their weighted averaging and consolidations. All cost data are given in Czech crowns (CZK). The exchange rate fluctuated between CZK25.643 and CZK27.533 for €1 (Czech National Bank average exchange rates). No discounting was applied.

### Patient and public involvement

The studied patients were not involved in the preparation of the research directly; however, they got a benefit in the form of above-standard and regular diagnosing and recommendations for health regime as well as referral to further treatment if needed. The reasonable costs related

**Table 1** Age distribution and sex data of the participants

Age group	Participants (n)
0–29	6
30–39	14
40–49	10
50–59	14
60–69	10
70+	1
Age characteristics	Age
Average	46.7
Minimum	23
Maximum	73
Sex	Participants (n)
Men	46
Women	9

to the participation in the research were covered. All 83 patients got an invitation to participate in the study. The analysis described in this paper only used retrospective data collected in the previous examination rounds. The results will be published in an open-access source, and thus available to public, patient organisations and patients. The public administration bodies and patient associations will be actively involved in disseminating the results of the research.

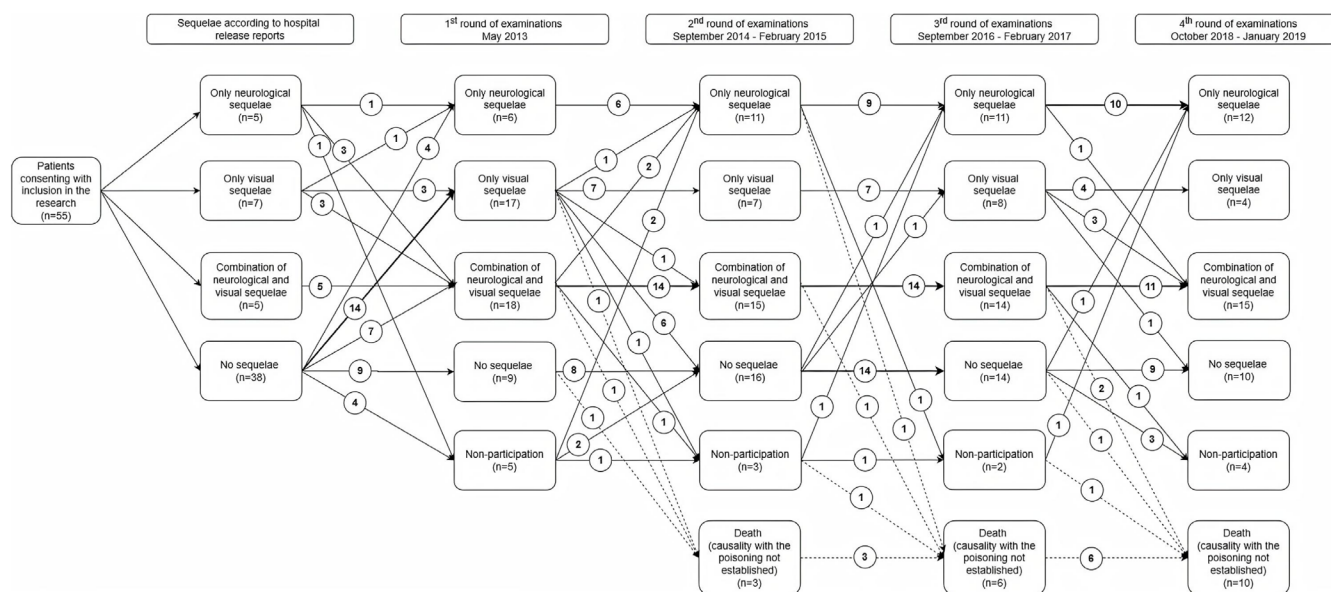
### RESULTS

The study is based on four examination rounds of 55 survivors of the poisoning. Their age and sex distributions are shown in [table 1](#), and participation in each round of examinations is summarised in [table 2](#). Only 37 patients took part in all rounds of examination, while each round missed some participants.

The postacute cost analysis concentrated on visual and neurological sequelae that were shown to be dominant (see the Introduction section). Basic overview of the results is depicted in [figure 1](#). Online supplemental

**Table 2** Follow-up round participation data of the participants

Time of examination	Participants (n)
5-month check	50
2-year check	49
4-year check	47
6-year check	41
Frequency of participation	Participants (n)
4 times (always)	37
3 times	7
Twice	7
Once	4



**Figure 1** Methanol intoxication sequelae development. (The number (n) in each box is the number of patients going through that particular state; the circled number on the arrow is the number of patients who moved between the boxes (states) connected with the arrow.)

figures S2–S5 show detailed process maps with sequelae development in individual areas (central nervous system, peripheral nervous system, visual system). If a patient death occurred during the study, it was not possible to prove any causality with the poisoning.

Based on online supplemental figures S2–S5, neurologists and ophthalmologists determined the necessary healthcare. Their recommendations are represented schematically in online supplemental figures S6–S8. The goal of these figures (flow charts) was to describe the process leading to the determination of the necessary healthcare in individual patients involved in the study. The indicated care (for all patients over 6 years) was summarised in [table 3](#) (healthcare performances) and [table 4](#) (pharmaceuticals). (This care need not correspond to the actual care of the participants, since they were only diagnosed within this trial, and then they were referred to their attending physicians in the place of their residence. The researchers did not have access to the participants' medical records describing the actual therapy that followed after the patients were discharged from the acute hospital care, as this took place in their places of residence.)

Neurontin was recommended for the sequelae to the peripheral nervous system—300 mg in the case of medium severity polyneuropathy, 600 mg in the case of allodynia and/or burning dysesthesia (online supplemental figure S7); Nakom was indicated for patients with signs of Parkinson's syndrome, that is, for the sequelae to the peripheral nervous system (online supplemental figure S6).

The indicated care ([tables 3 and 4](#)) was transformed to costs estimated for individual years (both for the whole cohort and the average per patient). Partial calculations

are included in online supplemental table S1 (neurological disorders), online supplemental table S2 (visual disorders) and online supplemental table S3 (pharmaceuticals). The resulting costs are summarised in [table 5](#).

## DISCUSSION

In this study, the postacute cost analysis concentrated on visual and neurological sequelae that were shown to be dominant.<sup>6–10</sup> In the period 2013–2019 the highest costs related to postacute care were found in 2013; the average costs decreased afterwards, and remained almost constant for the rest of the studied period of time.

This paper analyses a 6-year time series commencing with patient discharge from the acute hospital care, and covering four regular comprehensive follow-up checks. Although further medical problems and related costs may (and likely will) appear even later than 6 years from the outbreak, this medium-term study probably covers the principal health hazards caused by the intoxication. We created process maps to visualise the development of health problems related to the poisoning and their costs in survivor postacute care.

The main finding is that the estimated average costs per patient associated with postacute treatment of survivors are relatively low, ranging annually from CZK1845 to CZK4143. Compare, for example, the following facts about the Czech Republic<sup>30 31</sup>: the 2019 gross domestic product per capita was CZK538 803, the 2019 average monthly salary was CZK32 923, the average 2018 healthcare reimbursement from Czech public health insurance was CZK27 788 per one inhabitant, the 2019 expenditure on social security benefits (without old-age pension insurance benefits) was CZK11 409 per one inhabitant.



**Table 3** Overview of healthcare performances indicated in 2013–2019 (see online supplemental figure S6 for indications according to the model (figure 1 and online supplemental figures S2–S8))

Performance	n (per patient in the years when indicated)	Number of patients indicated for the respective performance in the year						
		2013	2014	2015	2016	2017	2018	2019
Complex neurological examination	1	24	0	4	0	1	0	4
Targeted neurological examination	1	0	24	22	26	21	22	20
Specialised neurological tests	1	7	7	7	7	1	1	8
EMG examination of nerve conduction velocity	6	7	7	7	7	1	1	8
EMG examination of reflexes, neuromuscular transmission and tetany	2	7	7	7	7	1	1	8
EMG muscle examination using an electrode needle	2	7	7	7	7	1	1	8
MRI of the head, limbs, one spinal section	1	22	0	1	0	3	0	0
Complex kinesiology examination	1	0	0	1	1	1	1	2
Therapeutic physical education on neurophysiological basis	10	0	0	1	1	1	1	2
Kinesiological check-up	1	0	0	1	1	1	1	2
Complex ophthalmology examination	1	24	0	0	0	0	0	0
Targeted ophthalmology examination	1	0	24	21	21	20	20	17
Static perimetry (1 eye)	2	24	24	21	21	20	20	17
Fundus biomicroscopy with mydriasis (1 eye)	2	24	24	21	21	20	20	17
Non-contact tonometry (1 eye)	2	24	24	21	21	20	20	17

EMG, electromyography.

Since the postacute treatment costs are covered by the public health insurance, they do not create any particular burden for the patients. However, the estimation character of the cost calculations and non-availability of health insurance (real world) data might cause an underestimation of the assessed costs. In a wider context, we also need to take into consideration the lower subjective quality of life related to the methanol poisoning and its consequences.<sup>14</sup> The study is important also for national policymakers who need to be aware of medium-term and

long-term costs originated in relation with the methanol poisoning taking place several years ago.

Future research is desirable to prolong the exploration of the costs related to the postacute healthcare beyond 2019. The attention needs to be paid also to the estimation of the methanol poisoning fraction in these costs, as the survivors may have suffered also from conditions that cannot be directly linked with their methanol episode. On the other hand, during our research, we encountered evidence that many of the personal and/or societal costs

**Table 4** Overview of pharmaceuticals indicated in 2013–2019

Period of use	Pharmaceutical tradename	Number of pills/ capsules in one packaging	Dozing (pills/day)	Number of packagings (patient/ year)	Number of patients with indicated pharmaceutical
2013–2014	Neurontin 600 mg	50	3	22	1
	Nakom	100	3	11	7
2015–2016	Neurontin 300 mg	100	3	11	1
	Neurontin 600 mg	50	3	22	1
	Nakom	100	3	11	7
2017–2018	Neurontin 300 mg	100	3	11	1
	Nakom	100	3	11	7
2019	Neurontin 300 mg	100	3	11	2
	Nakom	100	3	11	7

**Table 5** Modelled cost of the indicated care of the patient sample in 2013–2019

Year	Patients monitored (n)	Share of patients with signs of damage (%)	Average cost per patient (CZK)
2013	50	66.0	4142.93
2014	50	66.0	2446.42
2015	49	67.3	2759.94
2016	49	67.3	2380.84
2017	47	61.7	2127.30
2018	47	61.7	1845.45
2019	41	70.7	2519.69

linked to the methanol poisoning outbreak are related to other sectors than healthcare, above all the social affairs; such costs have not been assessed yet.

Our study has certain limitations similar to our 6-year study of quality of life based on the same 6-year follow-up and four consecutive rounds of examinations according to the same standardised clinical protocol in the same medical facility.<sup>14</sup> The population of 55 survivors of acute methanol poisoning exposed during one short-time mass ‘epidemic’ and systematically followed at a single medical centre represents a sufficient sample size to inform model cost estimations; however, this size limitation must be taken into consideration in any interpretation of this longitudinal study. We did not estimate the effect of possible pre-existing ocular or neurological diseases on the cost of healthcare of methanol-exposed patients, although the included disorders have been previously proved to belong among direct consequences of the intoxication. The 6-year follow-up period provided sufficient time to study changes in diagnostic results and trends, and to model treatment cost estimates. Nevertheless, it is probable that further sequelae will appear in the following years.

## CONCLUSION

The average costs of postacute healthcare related to the 2012 Czech methanol outbreak as modelled for the period 2013–2019 started at CZK4.142 in 2013 and then fluctuated between CZK1.845 and CZK2.760 in the following 5 years showing that the poisoning health sequelae and the costs generated by them persist for a long time. The model is valid for averaged (statistical) results, while it is inappropriate for individual patient predictions. Thus, our results can serve only to population interpretations. Our estimation of the costs provides the basic overview that needs to be specified in future (continuing) research, as other complications related to the methanol poisoning (eg, the risk of development of parkinsonian syndromes<sup>27</sup>) will probably appear and will

influence the future needs of healthcare and related costs later than 6 years covered by this study.

**Contributors** MB, VR and JD conducted the health economic assessment including data analysis, data interpretation and writing. JŠ was involved in data collection and contributed to data interpretation. BP contributed to data interpretation and writing. MM initiated this interdisciplinary study, discussed the interpretation framework and managed the research team in the Department of Addictology. SZ is the principal investigator of the Czech methanol outbreak research involved also in data interpretation and writing.

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**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The study was approved by the General University Hospital Ethics Committee (approval number 31/15). All 83 patients who potentially qualified for the study were informed about the study and its design. Out of them, 55 agreed to participate, giving their informed consent.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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