Epidemiology of Multiple Myeloma in the Czech Republic

Epidemiologie mnohočetného myelomu v České republice

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Summary

Background: Multiple myeloma (MM) is a cancer of plasma cells with an incidence of 4.8 cases per 100,000 population in the Czech Republic in 2014; the burden of MM in the Czech Republic is moderate when compared to other European countries. This work brings the latest information on MM epidemiology in the Czech population. ***Material and Methods:*** The Czech National Cancer Registry is the basic source of data for the population-based evaluation of MM epidemiology. This database also makes it possible to assess patient survival and to predict probable short-term as well as long-term trends in the treatment burden of the entire population. ***Results:*** According to the latest Czech National Cancer Registry data, there were 504 new cases of MM and 376 deaths from MM in 2014. Since 2004, there has been a 26.9% increase in MM incidence and an 8.3% increase in MM mortality. In 2014, there were 1,982 persons living with MM or a history of MM, corresponding to a 74.4% increase when compared to MM prevalence in 2004. The 5-year survival of patients treated in the period 2010–2014 was nearly 40%. ***Conclusion:*** The available data make it possible to analyse long-term trends in MM epidemiology and to predict the future treatment burden as well as treatment results.

Key words

multiple myeloma – epidemiology – Czech National Cancer Registry – Registry of Monoclonal Gammopathies – Czech Republic

Souhrn

Východiska: Mnohočetný myelom (MM) je maligní nádorové onemocnění plazmatických buněk s incidencí 4,8 případů na 100 000 obyvatel v České republice v roce 2014; Česká republika patří mezi země se středním výskytem tohoto onemocnění v Evropě. Práce přináší aktuální informace v oblasti epidemiologie MM v české populaci. ***Materiál a metody:*** Základním zdrojem údajů pro populační hodnocení epidemiologie MM je Národní onkologický registr ČR. Tato databáze rovněž umožňuje hodnotit přežití dosahované u pacientů a predikovat pravděpodobné krátkodobé a dlouhodobé trendy v léčebné zátěži celé populace. ***Výsledky:*** Dle posledních dostupných dat Národního onkologického registru ČR bylo v roce 2014 nově diagnostikováno 504 nádorů MM a 376 pacientů na toto onemocnění zemřelo. Incidence stoupla od roku 2004 o +26,9 %, u mortality došlo ve stejném období k vzrůstu o +8,3 %. Prevalence dosáhla v roce 2014 hodnoty 1 982 osob a ve srovnání s rokem 2004 tak vzrostl počet žijících osob s tímto onemocněním o 74,4 %. Pětileté relativní přežití u léčených pacientů z období 2010–2014 bylo necelých 40 %. ***Závěr:*** Dostupná data umožňují analyzovat dlouhodobé trendy v epidemiologii MM, predikovat budoucí léčebnou zátěž i výsledky péče o pacienty.

Klíčová slova

mnohočetný myelom – epidemiologie – Národní onkologický registr – Registr monoklonálních gamapatií – Česká republika

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Introduction

The importance of cancer epidemiology has been growing steadily, partly as a result of a high cancer incidence worldwide. The Czech Republic is no exception in this regard; on the contrary, it is one of the countries with the highest burden in several cancer types. Tens of thousands of cancer patients are newly diagnosed in the Czech Republic each year, and hundreds of thousands of them are followed-up due to a history of cancer in the past. This work aims to describe epidemiological trends of multiple myeloma (MM) in the Czech population, to assess patient survival and to predict probable short-term as well as long-term trends in the treatment burden of the entire population.

Material and methods

High-quality data play a key role in the evaluation of cancer epidemiology; in particular, the following data sources [1] are used for this purpose in the Czech Republic:

- Data on demographic structure of the Czech Republic population are processed by the Czech Statistical Office (CZSO) as part of its monitoring of the Czech population. These data cover demographic characteristics of the population, such as the total number of population, age structure, life expectancy etc. [2,3]. Population-based cancer mortality data are stored in a database of causes of death which is also processed by CZSO, in accordance with international methodology and based on data from death certificates (ICD-10 classification).
- The Czech National Cancer Registry (CNCR) is the main source of data on cancer epidemiology. CNCR is nowadays an integral part of comprehensive cancer care, covering 100% of the Czech population and containing more than 2.2 million records from the period 1977–2014. MM accounts for 0.6% of these records. The registration of malignant tumours is enshrined in the Czech legislation and is obligatory. CNCR is also the source of data for the assessment of basic performance indicators of cancer care, particularly for the assessment of patient survival. This work uses the estimate of 5-year relative survival [4] for this purpose. The Czech Society for Oncology has used CNCR data to develop an information system that predicts both the population burden of cancer as well as treatment burden for future periods. These predictions resulted from modelling of the development of demographic structure and cancer incidence in the population; survival models leading to predictions of prevalence of cancer patients to be treated in near future are another important component. The methodology and applied prediction scenarios are described in a publication by Dušek et al. [5].

The Registry of Monoclonal Gammopathies (RMG), established in 2007 by the Czech Myeloma Group, is another source of data. RMG represents an international database designed for the collection of data on patients with MM and other types of monoclonal gammopathies. Nineteen Czech centres and four Slovak centres currently contribute to the registry. The registry already contains data on more than 5,000 patients with MM (visit https://rmg.healthregistry.org to find more information). RMG not only contains data on MM incidence, but also makes it possible to monitor the use of individual treatment modalities, the occurrence of adverse events and drug toxicity [6]. RMG is therefore one of the largest and most comprehensive registries with regular monitoring in Europe. Treatment with all available therapies is recorded into the registry, thus making RMG a valuable source of data from real clinical practice. RMG represents a data basis that makes it possible to monitor the disease course on the population level. Data from RMG are utilised in the preparation of national guidelines for treatment of monoclonal gammopathies, serve as a basis for negotiations with the State Institute for Drug Control, and are also used for subsequent negotiations on reimbursements of new drugs with healthcare payers.

The database GLOBOCAN 2012, which is available at http://globocan.iarc.fr/, is the international source of data on cancer epidemiology. In view of the fact that these data are always available with a certain delay, this work presents estimated values for the year 2012, based on the most recent data available at the time of processing [7,8].

Results

International comparison of MM epidemiology

The estimated incidence of MM in 2012 was 114,251 new cases globally (23rd most common cancer, accounting for 0.8% of all cancers excluding non-melanoma skin cancer) and 38,956 new cases in Europe (21st most common cancer, accounting for 1.1% of all cancers excluding non-melanoma skin cancer). The cumulative risk of developing MM before the age of 74 is 0.17% globally (0.20% in men, 0.15% in women) and 0.31% in Europe (0.38% in men, 0.26% in women). The estimated mortality of MM in 2012 was 80,019 deaths globally (20th most common cause of cancer deaths, accounting for 1.0% of all cancer deaths excluding non-melanoma skin cancer) and 24,300 deaths in Europe (16th most common cause of cancer deaths, accounting for 1.4% of all cancer deaths excluding non-melanoma skin cancer). The estimated 5-year prevalence of MM in 2012 (i.e. the number of persons diagnosed within 5 previous years and still alive in 2012) was 229,468 globally (4.4 per 100,000 population) and 89,187 in Europe (14.3 per 100,000 population). Table 1 provides the basic overview of epidemiological characteristics of MM in Europe. Recent statistics have also clearly shown that the burden of MM in the Czech Republic – in terms of both incidence and mortality – is moderate when compared to other European countries [7,8].

Epidemiology of MM in the Czech Republic

For the purpose of analysis of data from CNCR, neoplasms with diagnosis C90.0 (according to the International Statistical Classification of Diseases and Related Health Problems – 10th Revision, ICD-10) and neoplasms with morphology code 9732/3 (according to the International Classification of Diseases for Oncology – 3rd edition, ICD-O-3) were included in the group of MM.

Trends in MM incidence and mortality in the Czech Republic over more

Tab. 1. Epidemiology of MM and immunoproliferative diseases (C90 + C88) in Europe (source: GLOBOCAN 2012).

	Men	Women	Both sexes
Incidence			
number of new cases	20,513	18,443	38,956
number of new cases per 100,000 population	5.7	4.8	5.3
ASR(W)	3.2	2.1	2.6
proportion of all newly diagnosed cancers (apart from non-melanoma skin cancer)	1.1%	1.1%	1.1%
Mortality			
number of deaths	12,220	12,080	24,300
number of deaths per 100,000 population	3.4	3.1	3.3
ASR(W)	1.7	1.2	1.4
proportion of all cancer deaths (apart from non-melanoma skin cancer)	1.3%	1.5%	1.4%
Prevalence rates (patients alive 5 years after diagnosis)			
absolute number of patients	47,507	41,680	89,187
rate per 100,000 population	15.9	12.7	14.3
Cumulative risk			
from birth until the age of 74	0.38%	0.26%	0.31%

ASR(W) – age-standardised rate (world standard population)

than three decades are shown in Fig. 1A. There has been a significant and consistent increase not only in incidence rates, but also in mortality rates (however, European age-standardised mortality rate is stabilised). Between 1980 and 2014, MM incidence increased from 2.3 to 4.8 new cases per 100,000 population and MM mortality increased from 1.4 to 3.6 deaths per 100,000 population. In absolute numbers in 2014, MM incidence was 504 new cases, MM mortality was 376 deaths and MM prevalence (i.e. all cases diagnosed in the past and still alive in 2014) was 1,982 persons (corresponding to 18.8 per 100,000 population). Although the incidence of MM in the Czech Republic is low when compared to other cancer types, its prevalence has been growing over the years (Fig. 1B) and the absolute number of persons with a history of MM, who need to be followed-up, is certainly not negligible. The overall epidemiological situation of MM in the Czech Republic in the period 2010–2014 is summarised in Tab. 2.

MM is mostly diagnosed in older people – the median age is 68 years in men and 70 years in women. Incidence rates are highest between the age of 61 and 75 years in men and between the age of 62 and 78 years in women (Fig. 2A). At the time of diagnosis, less than 1% of all MM patients are under the age of 40, and 18.6% of all MM patients are under the age of 60. Age-specific incidence rates, shown in Fig. 2B, demonstrate the growing risk of developing MM in older age. Age-specific incidence rates rise sharply from around age 45.

MM as a subsequent primary cancer in the same patient

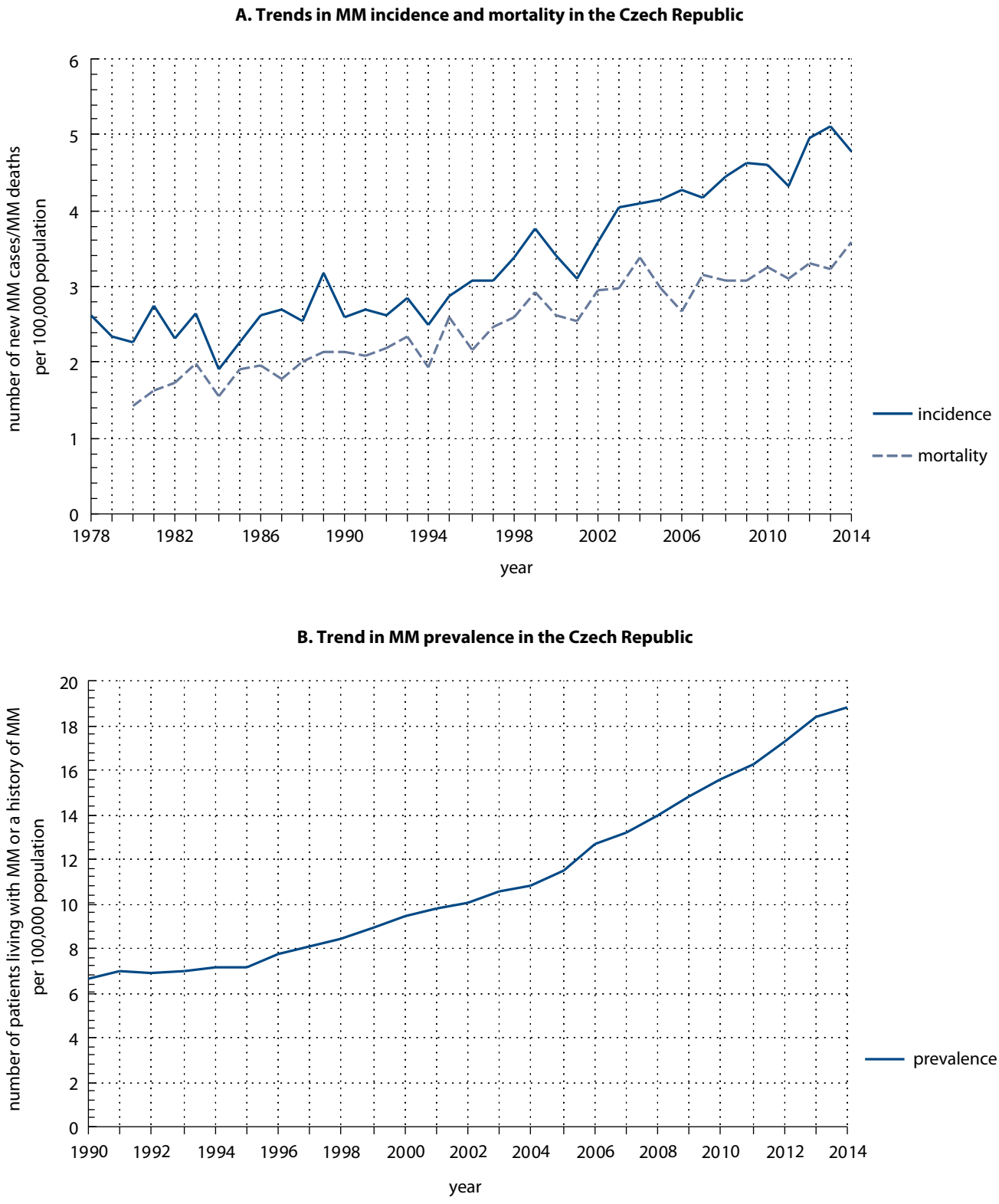
The occurrence of subsequent primary cancers in the same patient significantly contributes to the overall epidemiological burden of the Czech population. A detailed analysis of historical data from CNCR has revealed a significant increase in the number of cases of MM as subsequent primary cancers over time (Tab. 3). Until 1994, these cases accounted for less than 5% of the overall number of new cases of MM. This proportion grew to almost 9% in the period 1995–2004, and available data from 2014 have shown that as much as 17% of all newly diagnosed cases of MM were subsequent primary cancers. Nowadays, MM is expected to be diagnosed as a subsequent primary cancer in about 80 persons each year.

MM incidence according to data from CNCR vs. RMG

Comparison of the number of patients according to the CNCR with the number of patients according to the RMG shows that RMG covers approximately 80% of data contained in CNCR for the period 2007–2014.

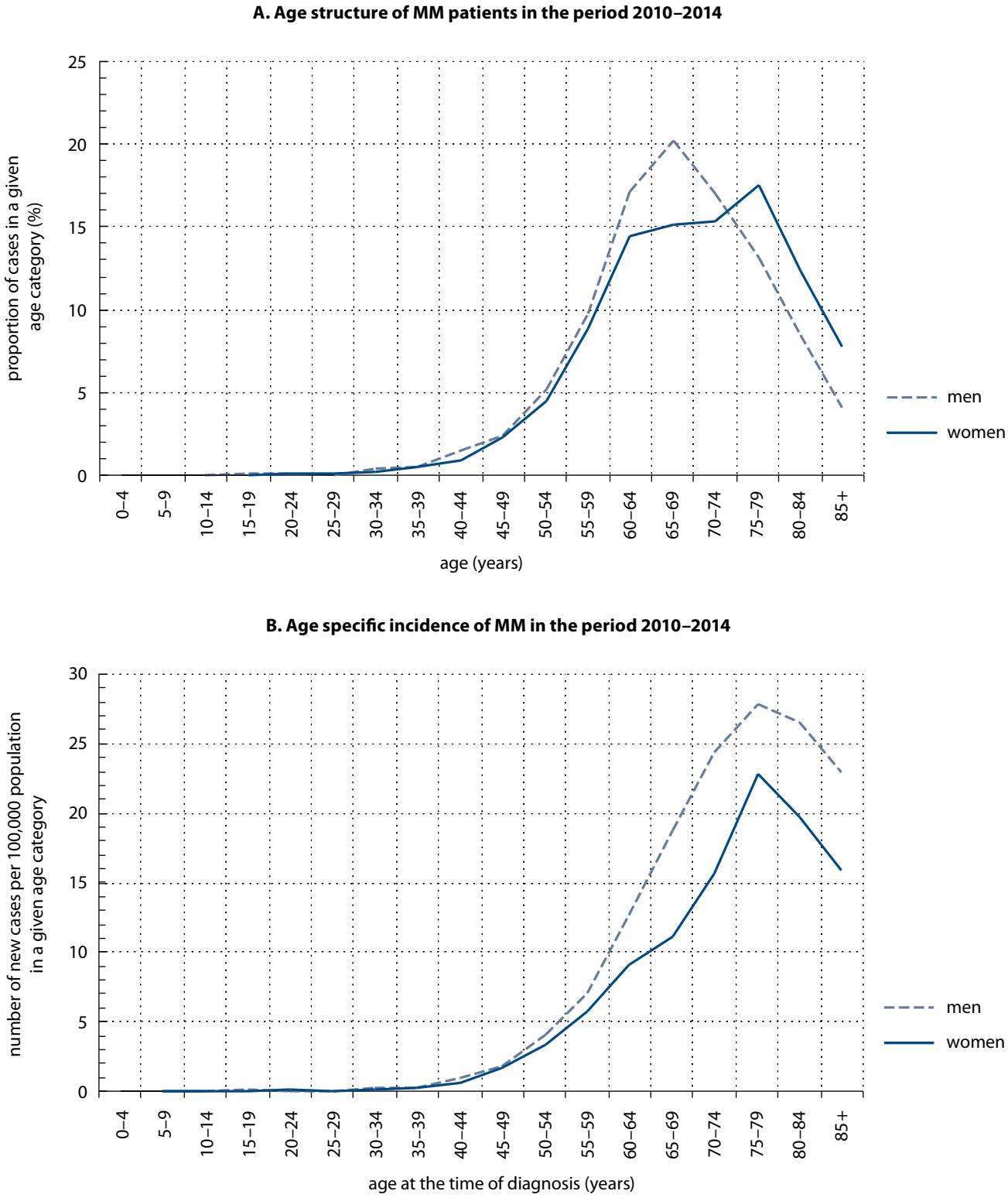
Predicted numbers of MM patients to be treated

Table 4 shows the estimates of incidence, prevalence and number of MM patients who will probably be treated in 2017. The estimate of overall prevalence



MM – multiple myeloma
Source: Czech National Cancer Registry (CNCR), Institute of Health Information and Statistics of the Czech Republic (IHIS).

Fig. 1. Epidemiological trends of MM in the Czech Republic.



MM – multiple myeloma
Source: Czech National Cancer Registry (CNCR), Institute of Health Information and Statistics of the Czech Republic (IHIS).

Fig. 2. Age of MM patients.

Tab. 2. Basic epidemiological characteristics of MM in the Czech Republic.

	Men	Women	Both sexes
Incidence			
absolute number of new cases (period 2010–2014, annual average)	257	242	500
rate per 100,000 population (period 2010–2014)	5.0	4.5	4.8
proportion of all newly diagnosed cancers apart from non-melanoma skin cancer (period 2010–2014)	0.84%	0.91%	0.87%
proportion of all newly diagnosed hemato-oncological malignancies (period 2010–2014)	11.4%	12.0%	11.7%
trend in the period 2004–2014	+33.0%	+20.8%	+26.9%
typical age of patients – median (25th to 75th percentile) (period 2010–2014)	68 (61–75) years	70 (62–78) years	69 (62–77) years
occurrence men : women (period 2010–2014)			1.1 : 1
Mortality			
absolute number of deaths (period 2010–2014, annual average)	175	171	346
deaths per 100,000 population (period 2010–2014)	3.4	3.2	3.3
proportion of the overall mortality (period 2010–2014)	0.32%	0.32%	0.32%
trend in the period 2004–2014	+13.9%	+3.3%	+8.3%
Prevalence			
absolute number of living patients (year 2014)	979	1,003	1,982
living patients per 100,000 population (year 2014)	18.9	18.7	18.8
trend in the period 2004–2014	+80.4%	+69.0%	+74.4%

Tab. 3. MM as a subsequent primary cancer in the same patient according to CNCR data.

Assessed category	Period 1985–1994 n = 2,745	Period 1995–2004 n = 3,528	Period 2005–2014 n = 4,741
MM is the first cancer in a given patient	2,621 (95.5%)	3,214 (91.1%)	4,010 (84.6%)
MM is a subsequent primary cancer in a given patient	124 (4.5%)	314 (8.9%)	731 (15.4%)

MM – multiple myeloma

involves both the number of newly diagnosed patients in 2017 and the estimated number of living patients who were diagnosed and treated in previous years (calculated by population survival models). The overall sum for 2017 expects at least 2,079 newly treated patients (with a 90% CI ranging between 1,876 and 2,303); in case of optimally full reimbursements, the predicted number of newly treated patients is 2,680 (2,442; 2,936).

The predicted numbers of patients are updated each year and provided to healthcare payers as a background for their planning of treatment costs. Determination of the number of patients to be treated, which is based on the epidemiological situation, provides population-based reference data for a subsequent monitoring of clinical practice. In this way, the Czech Society for Oncology and healthcare payers are informed about the availability of therapy nationwide and in individual regions. It has been repeatedly shown that the numbers of actually treated patients do not substantially exceed the epidemiologically estimated burden.

Assessment of results of care provided to MM patients

The 5-year relative survival is the most common measure to describe the seriousness of a given cancer type on a population level, expressing the proportion of patients who have not died from that cancer type within 5 years of diagnosis. The relative survival is calculated as the ratio of the overall survi-

Tab. 4. MM – predicted epidemiological characteristics and numbers of patients to be treated in the Czech Republic in 2017.

MM	Predictions for the year 2017 (90% CI)
incidence	546[1] (508; 586)
prevalence	2,738 (2,653; 2,826)
clinically adjusted prediction of newly started treatments[2] with targeted therapies	2,079 (1,876; 2,303)

[1] The overall incidence of MM is provided, including new cases of MM diagnosed in cancer patients.

[2] Based on epidemiological models (incidence and prevalence of treated patients) corrected on the basis of clinical decision support models.

MM – multiple myeloma

Tab. 5. Reference values of 5-year relative survival of MM patients in the Czech Republic. The rates are age-standardised.

Type of record	5-year relative survival in different periods (95% CI)				
	Comparison of two periods further in the past[1]		Comparison of three recent periods with available data[2]		
	1990–1994	1995–1999	2000–2004	2005–2009	2010–2014
all CNCR records with non-zero survival values[3]	24.7 (21.9–27.7)	27.0 (24.4–29.7)	27.7 (25.2–30.3)	34.5 (29.8–39.2)	37.3 (35.0–39.5)
only patients treated with anticancer therapy	25.4 (22.0–28.8)	27.1 (24.0–30.3)	28.0 (25.0–31.1)	38.0 (32.3–43.7)	39.3 (36.6–42.0)

[1] Cohort analysis of patients diagnosed in a given time period.

[2] Period analysis – information on the survival of patients diagnosed in a recent period is involved in the calculation.

[3] Records on diagnosis based on autopsy or DCO (death certificate only) were left out from the overall population database. All other records were involved in the analysis.

CNRC – Czech National Cancer Registry

val (representing the overall observed mortality in a cohort of patients with a given cancer type) and the so-called expected survival (representing the mortality in a general population which corresponds in age and sex to the monitored group of patients). In other words, the relative survival describes the overall survival adjusted to mortality related to other diseases which the patient might die of. Furthermore, relative survival rates are age-standardised due to different age structures of patients in individual time periods; this means that the resulting survival is obtained as a weighted mean of relative survival rates in defined age categories [9,10].

In this regard, population-based data from CNCR provide the possibility of a very valuable assessment of the overall survival of cancer patients. Table 5 shows the assessment of relative survival of MM patients in the Czech Republic. Comparison of different time periods shows that there has been a significant increase in the 5-year survival of MM patients over time: the 5-year relative survival of MM patients who had been diagnosed before 2000 was 27.0%; by contrast, the 5-year relative survival of MM patients who were treated with anticancer therapy was almost 40% in the period 2010–2014.

Conclusion

The aim of this work was to describe epidemiological trends of MM in the Czech population, to assess patient survival and to predict probable short-term trends in the treatment burden of the entire population. This work proves that adequate data sources are available for the above-mentioned analyses. Each year in the Czech Republic, about 500 people are newly diagnosed with MM and about 350 people die of it. MM prevalence – i.e. the number of persons living with MM or a history of MM – was 1,982 in 2014, corresponding to a 74.4% increase when compared to MM prevalence in 2004. The probability of 5-year survival of MM patients has significantly increased over the last 20 years.

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