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Prevalence of Multiple Myeloma

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1. Rationale and background

In the European Union (EU), a disease is defined as rare if it affects fewer than 5 in 10,000 people across the EU.

Multiple Myeloma has, so far, been considered a rare disease. However, with the increasing number of medicines being authorised for this disease, and better management of the disease, the prevalence of Multiple Myeloma is likely to rise, as more and more patients benefit from an increased survival, living longer with the disease and leading to it becoming more and more chronic.

2. Research question and objectives

The objective of this study was to determine the prevalence of Multiple Myeloma in electronic health records of three European countries.

3. Research methods

3.1. Study design

This was a descriptive study to determine the complete prevalence of Multiple Myeloma in electronic health records of three European countries (France, Germany, United Kingdom).

3.2. Setting and study population

All observable patients, i.e. with at least one encounter (consultation, prescription), between 2015 and 2020, in the three databases from France, Germany and United Kingdom, were included in the analysis.

3.3. Variables

3.3.1. Multiple myeloma

Multiple myeloma is a type of blood cancer that affects plasma cells. Malignant white blood cells develop in bone marrow, suppressing healthy plasma cells that produce antibodies against infection. According to Dynamed (www.dynamed.com), Multiple Myeloma can also be called plasma cell myeloma or plasma cell leukemia.

There are two medical ontologies used in the three databases, ICD-10 and Read. Multiple Myeloma was defined respectively as:

For ICD-10 codes:

ICD-10 Code	Term
Included terms	

ICD-10 Code	Term
C90.0	Multiple myeloma
C90.1	Plasma cell leukaemia
Excluded terms	
C90.2	Extramedullary plasmacytoma
C90.3	Solitary plasmacytoma

For Read codes:

Read Code	Term
Included terms	
B630	Multiple myeloma
BBn0-2	[M]Myeloma NOS
B6303	Lambda light chain myeloma
BBn0	[M]Plasma cell myeloma
B63	Multiple myeloma and immunoproliferative neoplasms
BBn0-1	[M]Multiple myeloma
^ESCTPL340846	Plasma cell myeloma
B630-2	Myelomatosis
HNG0184	[RFC] Multiple myeloma
B630-1	Kahler's disease
^ESCTMU340844	Multiple myeloma
N3309	Osteoporosis in multiple myelomatosis
B63-99	Multiple myeloma etc.
B631	Plasma cell leukaemia
BBr3z	Plasma cell leukaemia
BBr30	[M]Plasma cell leukaemia
Excluded terms	
B6302	Plasmacytoma
B6301	Solitary myeloma
B63z	Immunoproliferative neoplasm or myeloma NOS
B6300	Malignant plasma cell neoplasm, extramedullary plasmacytoma
B6300-1	Extramedullary plasmacytoma

Read Code	Term
B6304	Plasmacytoma - disorder
B63y	Other immunoproliferative neoplasms

3.4. Data sources

The databases used were the IQVIA™ Disease Analyser Germany, IQVIA™ Disease Analyser France and IQVIA™ Medical Research Data (IMRD) EMIS UK.

For IQVIA™ Disease Analyser France and IMRD EMIS UK, only data from General Practice is available and was used.

For IQVIA™ Disease Analyser Germany, General Practice and Paediatric specialties were used. In Germany the choice of physician is free, and it is common that caretakers of children choose to consult with paediatricians instead of general practices and thus, use of these two specialties provides a more accurate depiction of prevalence.

3.5. Statistical analysis

3.5.1. Main statistical methods

Prevalence was determined using the any-time method. The denominator was calculated as the count of patients of all ages who are eligible, i.e., had at least one observation (consultation or prescription), during the period of interest. The numerator was computed as the count of patients that had at least one code for Multiple Myeloma, as listed above, during the period starting from the start of data collection for the patient to the end of the period of interest (i.e., complete prevalence). Results were not stratified by age or gender.

The report includes, in appendix, published prevalence data of Multiple Myeloma from Nordic cancer registries. They were not included in the main report as these stem from a different data collection and statistical analysis methodology.

Forecasts of prevalence of multiple myeloma using an autoregressive integrated moving average (ARIMA) model without seasonality are presented as annex to this study.

Analyses were completed by EMA researchers using SAS and IHD platform.

3.5.2. Sensitivity analyses

None.

3.6. Quality control

The study was conducted according to the ENCePP code of conduct (European Medicines Agency 2018).

Standard operating procedures or internal process guidance were adhered to for the conduct of the study. These procedures include rules for secure and confidential data storage, quality-control procedures for all aspects of the study from protocol development to the reporting of the results.

All documents underwent at least one round a review by an experienced reviewer, while the results from the statistical analysis were either reviewed or checked via double coding.

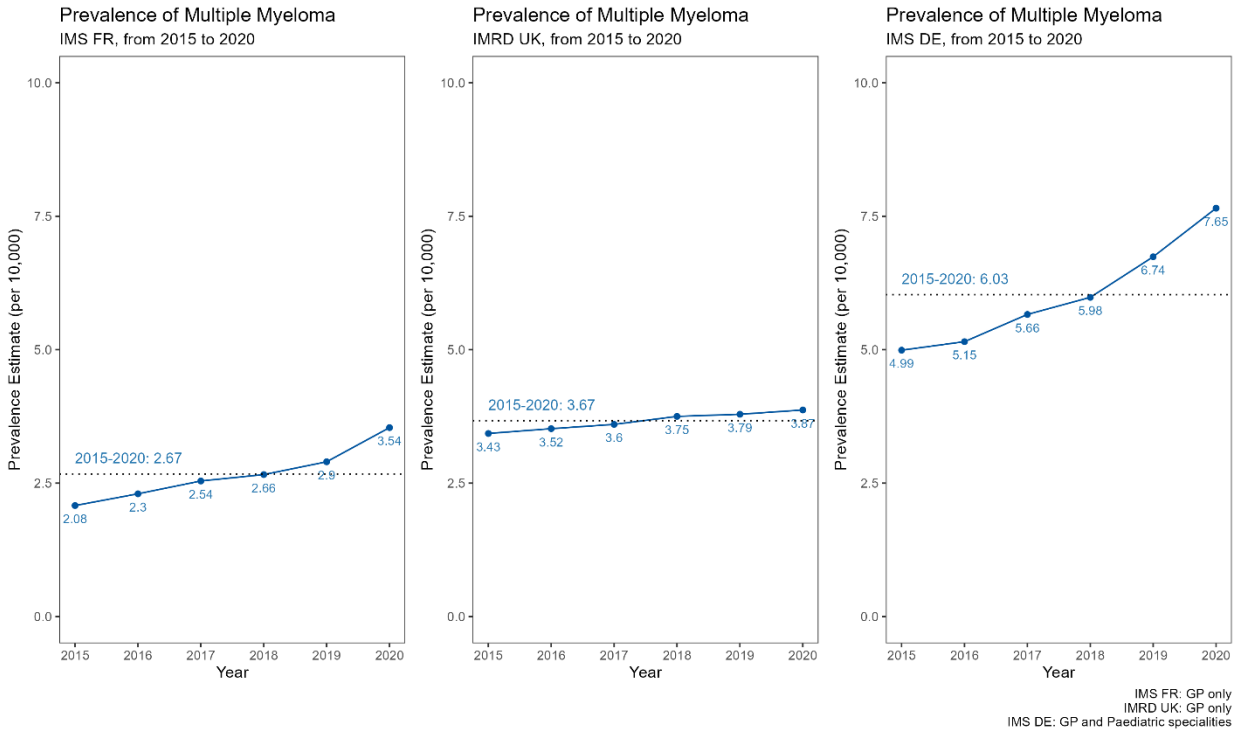
The quality control of the data is the responsibility of the data holder.

4. Results

The six-year prevalence, between 2015 and 2020, of Multiple Myeloma was 2.67 per 10,000 in the IQVIA™ Disease Analyser France database, 3.67 per 10,000 in the IMRD UK database, and 6.03 per 10,000 in the IQVIA™ Disease Analyser Germany (Figure 1).

Only the prevalence estimated using the IQVIA™ Disease Analyser Germany database was above the threshold of 5 per 10,000, both annually from 2016 onwards and for the total period 2015 to 2020. The prevalence for IQVIA™ Disease Analyser France and IMRD UK databases was always below 5 per 10,000 (Figure 1).

Figure 1: Prevalence of multiple myeloma across the three databases* between 2015 and 2020



* IMS FR = IQVIA™ Disease Analyser France, IMS GE = IQVIA™ Disease Analyser Germany

The prevalence of Multiple Myeloma in the Nordic countries, Denmark, Finland, Iceland, Norway, Sweden, presented in Annex I, shows that for the year 2019, the prevalence was, respectively, 5.29, 3.67, 4.91, 4.90, 4.54 per 10,000 patients.

5. Discussion

5.1. Key results

The six-year prevalence, between 2015 and 2020, of Multiple Myeloma was 2.67 per 10,000 in the IQVIA™ Disease Analyser France database, 3.67 per 10,000 in the IMRD UK database, and 6.03 per 10,000 in the IQVIA™ Disease Analyser Germany. For the data stemming from the Nordic cancer registries, the prevalence per 10,000 was 5.29 for Denmark, 3.67 for Finland, 4.91 for Iceland, 4.90 for Norway and 4.54 for Sweden.

From the electronic health record data, only IQVIA™ Disease Analyser Germany indicated a prevalence above the 5 per 10,000 threshold. However, a limitation of IQVIA™ Disease Analyser Germany is that there may be duplicate recording of events leading to a slightly over-estimated prevalence – see 7.2 Limitations of the research methods. The registry data also suggested that in only one of the five countries the prevalence was above the rare disease prevalence threshold.

Considering the heterogeneity in the databases and the small number of data sources, a meta-analyses of the pooled results would have been difficult to interpret and thus an Europe-wide prevalence is difficult to extrapolate.

Nonetheless, it seems clear that the prevalence of Multiple Myeloma is close to 5 per 10,000 patients. For IQVIA™ Disease Analyser France and IMRD UK the prevalence is likely to be above this number between 2025 (for IQVIA™ Disease Analyser France) and 2030 (for IMRD UK) assuming the deterministic trend identified by the ARIMA models does not change (Annex II). It could even be that this prevalence is reached earlier should effective new treatments appear in the meanwhile.

5.2. Limitations of the research methods

A limitation of this study was related to number as well as the type of data sources available for the analysis. Only three different databases from the UK, Germany and France were available for this analysis, which gives only a partial image of the prevalence of multiple Myeloma in Europe. In addition, there was the possibility that Multiple Myeloma was not adequately recorded in general practices, which is the care setting mainly captured by the three databases, as this is a malignancy most likely to be treated by specialist oncology care. However, the number of multiple myeloma related diagnoses reported per patient seemed to vary between 2 and 4, with some patients having tens of codes reported for Multiple Myeloma, which suggested that it was fairly well represented in these databases.

Another limitation was specific to the IQVIA™ Disease Analyser Germany data. As there is a free choice of physician in the German system, it is possible that the same patient is reported in more than one practice. This may lead to a slightly over-estimated prevalence.

Finally, it was not possible to stratify prevalence by stage of disease for several reasons, but in particular because that granular information is not available in the vocabulary used to code the diseases in the databases used.

6. Conclusion

One of the three databases used – IQVIA™ Disease Analyser Germany – showed a prevalence above 5 per 10,000 patients. Furthermore, one of the five countries in the Nordic countries registries for cancer also showed a prevalence above 5 per 10,000 patients. In general, the prevalence of Multiple Myeloma across the European Union seemed to be below 5 per 10,000 patients but only marginally.

Forecasts suggested that as early as 2025, the prevalence of multiple myeloma might go above the threshold to classify the disease as rare. While these are merely forecasts, they help plan for when a new estimate of prevalence should be conducted.

Annexes

Annex I – Prevalence of Multiple Myeloma in Nordic Countries

The information below was extracted from NORDCAN – the Association of the Nordic Cancer Registries (Nordcan 2.0 (iarc.fr)).

Based on the total number of cases per year and the total population size the yearly prevalence between 2017 and 2019 is shown in the table below.

*Table: Prevalence of multiple myeloma in Nordic countries between 2017 and 2019 (*Nordcan 2.0 (iarc.fr))

	2017		2018		2019	
	Total no. of cases	Prevalence per 10,000	Total no. of cases	Prevalence per 10,000	Total no. of cases	Prevalence per 10,000
Denmark	2664	4,62	2851	4,92	3074	5,29
Finland	2050	3,72	2044	3,71	2028	3,67
Iceland	148	4,31	172	4,88	177	4,91
Norway	2314	4,39	2453	4,62	2618	4,90
Sweden	4188	4,16	4425	4,35	4663	4,54
Total	**11,364**	**4,22**	**11,945**	**4,40**	**12,560**	**4,60**

The data on prevalence has been calculated from the total number of male and female cases per year and the total size of the population during the year, which is also provided in the database.

In Sweden, data could also be found in the yearly report for the quality registry for myeloma in 2021, please see https://cancercentrum.se/globalassets/cancerdiagnoser/blod-lymfom-myelom/myelom/myelomrapport8_20210906.pdf. In this report it was stated that the total number of patients living with multiple myeloma on 31 December 2018 in Sweden was 4344; 2484 men (prevalence 4,83 per 10,000) and 1860 women (prevalence 3,66 per 10,000).

Also in Denmark, data could be found in the yearly report for the quality registry for myeloma in 2020, please see https://myeloma.hematology.dk/index.php/dmsg/arsrapporter-myeloma/431-dmsg-2020/file. In this report it was stated that the number of patients in Denmark that were alive with a diagnosis of myeloma on 1 January 2021 was 1916. This is based on an estimated completeness of patients in the database of 98%. This number is lower than the number reported by NORDCAN in 2016, and the prevalence was not specifically provided.

In Norway, information about the prevalence of multiple myeloma in 2020 was published in the yearly report from the cancer registry, please see https://www.kreftregisteret.no/globalassets/cancer-in-norway/2020/cin-2020.pdf. The number of patients alive with multiple myeloma was 2821. The population in Norway was 5,383,300 in November 2020, which would give a prevalence per 10,000 of 5.24.

Annex II – Forecast of Prevalence for IQVIA™ Disease Analyser France and IMRD UK