

Supplemental material

Description of the health databases

The database of regional potential healthcare beneficiaries includes demographic information and the residential history of all the subjects living in the region. The hospital discharge database, the ambulatory care database and the Emergency Department (ED) database include records from all the regional hospitals (either public or private accredited to the public health system). The pharmaceutical prescription database contains information on all the prescriptions made by physicians working in the public health system, except prescriptions paid out-of-pocket. The mortality database includes data on all deaths of the subjects living in the region. The anatomic pathology database includes information on all the cytological and histological examinations performed in the Region to inpatients and outpatients. The database of exemptions from medical charges includes records on all the potential health care beneficiaries who are entitled, because of low income, age, or chronic diseases, to receive free medications and outpatient specialist care. The Italian Ministry of Health assigned codes to all the diseases which entitle patients to exemptions. Currently, they include approximately 100 chronic and disabling diseases [1] and groups of rare diseases, including GCA (exemption code G0080) [2]. We started our analysis from year 2001 when the Italian Ministry of Health established a national network of rare diseases and dictated the rules for exempting patients with rare diseases from medical charges [3].

The regional rare disease registry, on the other hand, has been implemented since 2009: patients with rare diseases having contacts with the regional hospitals either for diagnosis or treatment are actively flagged by the attending doctor and enter the registry.

To identify patients with GCA living in the Italian Region of Friuli Venezia Giulia (FVG), we used a combination of two data sources: the exemption database and the rare disease registry. In fact, none of the two databases is complete: the exemption database may not identify patients with GCA if they have other stronger reasons for being exempted from medical charges, such as low income,

older age, or disability. On the other hand, the rare disease registry was established only in 2009 and patients with an earlier diagnosis may not have been recorded. In addition, since active registration is needed, it is likely that, particularly in the first years of the registry, not all cases were properly flagged. To cope with the initial low compliance of attending doctors with the registry, in 2013 the Regional Rare Disease Coordinating Center put special efforts into encouraging and monitoring registration. Thus, in FVG, some patients with GCA are expected to be found on both data sources, whereas others are identifiable in just one of the two databases. The combined analysis of both data sources maximizes completeness of the assessment.

In all subjects with GCA, identified either from the rare disease registry or from the exemption database, we assessed access to medical care since the earliest date when the disease was recorded. In particular, we assessed ED visits because of headache, vision loss, or non-traumatic pain, ambulatory specialist visits, hospitalizations, prescriptions of drugs in selected categories, commonly used in this Region for the management of GCA, as below. Subjects were observed from the date of first registration as GCA patients to the date of death or change of residency outside of the Region or 31st December 2017, whichever came first. The absolute frequency of each health-related event was divided by the total person-years of observation.

List of medications and codes

1. glucocorticoids (ATC codes H02AB07 – prednisone, H02AB04 – methylprednisolone, H02AB13 – deflazacort, H02AB02– dexamethasone)
2. immunomodulating agents (L04AX03 – methotrexate, L01AA01 – cyclophosphamide, L04AX01 – azathioprine, L04AC07 – tocilizumab)
3. calcium homeostatis agents (H05AA02 – teriparatide)
4. drugs affecting bone structure and mineralization (M05BX04 – denosumab, M05BAxx and M05BBxx – bisphosphonates)

5. antithrombotic agents (B01AC06 – acetylsalicylic acid, B01AA03 – warfarin, B01AA07 – acenocoumarol, B01ABxx – heparin group, B01AE07 – dabigatran etexilate, B01AFxx – direct factor Xa inhibitors).

Table 1. Incidence rate in 2017 and prevalence of GCA as of December 31st, 2017 among the population ≥ 45 years of age in the Italian Region of Friuli Venezia Giulia.

Sex	Age category	Prevalent cases	Prevalence per 100,000	95%CI	Incident cases	Incidence rate per 100,000 person-years	95%CI
F	45-49	0	0.0	.	0	0.0	-
F	50-54	0	0.0	.	0	0.0	-
F	55-59	6	13.7	5.5-28.5	2	4.6	0.8-15.1
F	60-64	7	17.4	7.6-34.5	1	2.5	0.1-12.3
F	65-69	21	49.9	31.7-75-0	3	7.1	1.8-19.4
F	70-74	25	65.8	43.5-95-8	4	10.5	3.3-25.4
F	75-79	27	73.0	49.1-104.8	4	10.8	3.4-26.1
F	80-84	22	80.1	51.5-119.3	3	10.9	2.8-29.7
F	85-89	16	79.1	46.8-125.6	0	0.0	-
F	≥ 90	6	39.7	16.1-82.6	0	0.0	-
M	45-49	0	0.0	.	0	0.0	-
M	50-54	0	0.0	.	0	0.0	-
M	55-59	5	11.7	4.3-25.9	2	4.7	0.8-15.4
M	60-64	2	5.3	0.9-17.6	0	0.0	-
M	65-69	15	39.5	23.0-63.7	2	5.3	0.9-17.4
M	70-74	7	20.9	9.1-41.4	3	9.0	2.3-24.4
M	75-79	10	33.5	17.0-59.7	0	0.0	-
M	80-84	8	44.3	20.6-84.0	0	0.0	-
M	85-89	7	70.6	30.9-139.6	1	10.1	0.5-49.7
M	≥ 90	1	22.6	1.1-111.4	1	22.6	1.1-111.4

Total		185	27.2	23-5-31.4	26	3.8	2.5-5.5
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Table 2. Frequency of prescription of glucocorticoids, immunomodulating agents, calcium hemostatis agents, drugs affecting bone structure and mineralization, and antithrombotic agents among a cohort of patients with giant cell arteritis in the Italian Region of Friuli Venezia Giulia, 2001-2017.

Drug ATC code	Drug active principle	N prescriptions	% of patients with prescriptions
glucocorticoids			
H02AB02	dexamethasone	25	3.37
H02AB04	methylprednisolone	1412	41.35
H02AB07	prednisone	2602	61.06
immunomodulating agents			
L01AA01	cyclophosphamide	57	8.65
L04AC07	tocilizumab	74	1.92
L04AX01	azathioprine	150	4.81
L04AX03	methothrexate	480	39.42
antithrombotic agents			
B01AA03	warfarin	195	8.17
B01AA07	acenocoumarol	9	0.96
B01AB04	dalteparin	1	0.48
B01AB05	enoxaparin	81	15.38
B01AB06	nadroparin	76	7.21
B01AB08	reviparin	4	1.44
B01AB12	bemiparin	1	0.48
B01AC06	acetylsalicylic acid	2527	67.79
B01AE07	dabigatranetexilate	27	1.44
B01AF01	rivaroxaban	13	1.44
B01AF02	apixaban	35	1.92
calcium hemostatis agents			
H05AA02	teriparatide	33	1.44
drugs affecting bone structure and mineralization			
M05BA02	clodronic acid	9	0.48
M05BA04	alendronic acid	865	38.46
M05BA06	ibandronic acid	118	4.81

M05BA07	risendronic acid	418	14.42
M05BB03	alendronic acid and colecalciferol	362	9.18
M05BX04	denosumab	14	1.92
statins			
C10AA01	simvastatin	1229	24.13
C10AA02	lovastatin	8	1.51
C10AA03	pravastatin	377	4.52
C10AA04	fluvastatin	7	1.51
C10AA05	atorvastatin	1266	26.63
C10AA06	cerivastatin	14	3.02
C10AA07	rosuvastatin	490	11.56
C10BA02	simvastatin plus ezetimibe	64	2.01

References

1. Ministry of Health. Elenco malattie e condizioni croniche e invalidanti. Allegato 8 DPCM 12 gennaio 2017.
<http://www.trovanorme.salute.gov.it/norme/renderPdf.spring?seriegu=SG&datagu=18/03/2017&redaz=17A02015&artp=13&art=1&subart=1&subart1=10&vers=1&prog=001>.
Accessed 24 April 2018
2. Ministry of Health. Elenco malattie rare esentate dalla partecipazione al costo. Allegato 7 DPCM 12 gennaio 2017.
<http://www.trovanorme.salute.gov.it/norme/renderPdf.spring?seriegu=SG&datagu=18/03/2017&redaz=17A02015&artp=12&art=1&subart=1&subart1=10&vers=1&prog=001>.
Accessed 24 April 2018
3. Ministry of Health. Decreto 18 maggio 2001, n. 279. Regolamento di istituzione della rete nazionale delle malattie rare e di esenzione dalla partecipazione al costo delle relative prestazioni sanitarie, ai sensi dell'articolo 5, comma 1, lettera b), del decreto legislativo 29 aprile 1998, n. 124.
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