The EpiChron Cohort Proven Useful for Pharmacoepidemiological Studies

Alexandra Prados Torres,[1] Beatriz Poblador Plou,[1] Francisca González Rubio,[1] Antonio Gimeno Miguel,[1] Jordi Castellsagué,[2] Susana Pérez-Gutthann,[2] Alejandro Arana[2]

[1]EpiChron Research Group on Chronic Diseases, Aragón Health Sciences Institute (IACS), IIS Aragón, REDISSEC ISCIII, Zaragoza, Spain; [2]RTI Health Solutions, Barcelona, Spain

CONFLICT OF INTEREST

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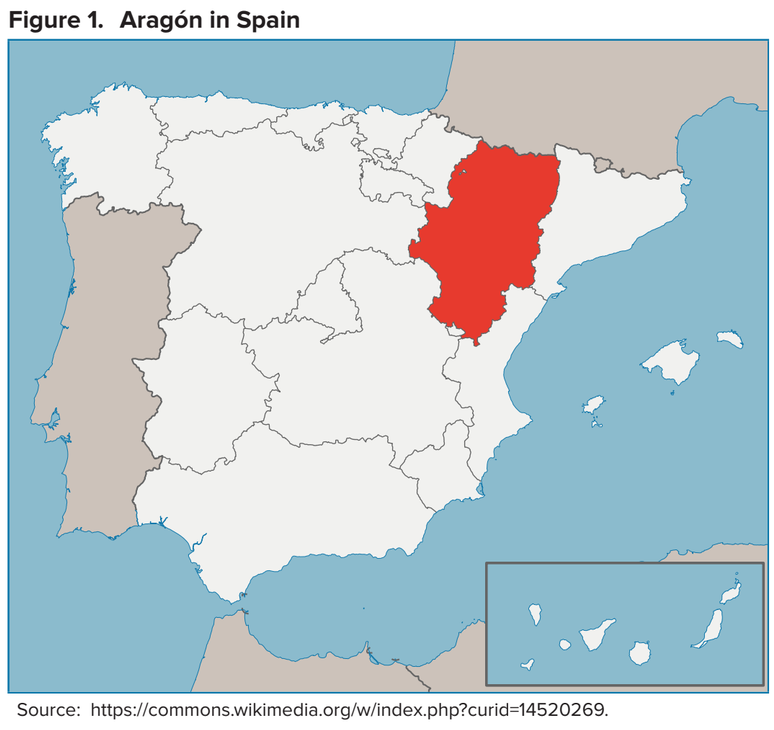
A. Prados Torres, B. Poblador Plou, F. González Rubio, and A. Gimeno Miguel are members of the EpiChron Research Group on Chronic Diseases of the Aragón Health Sciences Institute (IACS), ascribed to IIS Aragón, and do not have any conflict of interest with this project.

A. Arana, J. Castellsagué, and S. Pérez-Gutthann are employees of RTI, an independent nonprofit research organization that does work for government agencies and pharmaceutical companies.

BACKGROUND

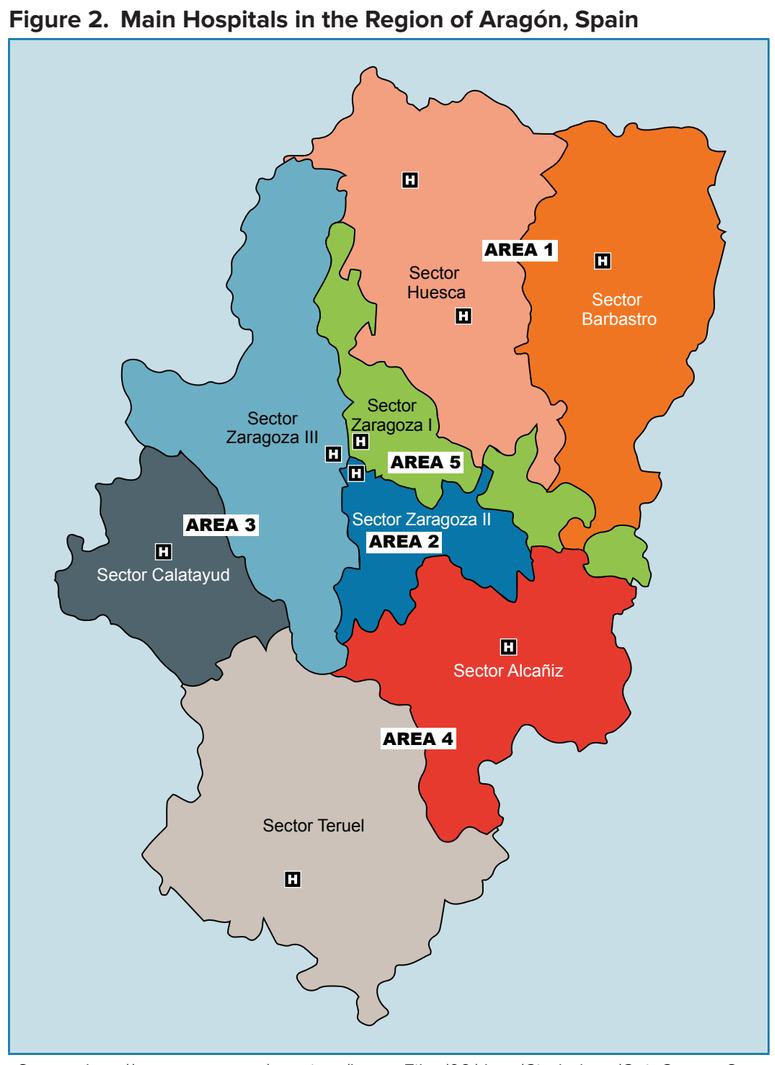
- New sources of reliable data for pharmacoepidemiological research are needed.
- In Aragón, Spain, the EpiChron Research Group on Chronic Diseases (pictured below) has developed a cohort that links the most relevant clinical, services utilization, and administrative information contained in Aragón's health registries.
- The EpiChron cohort[1] covers all individuals enrolled in the public health system of Aragón.
- As of 2015, the estimated population of Aragón was 1,317,847, and an estimated half of Aragón's population (50.45%) lived in the capital city of Zaragoza.

Figure 1. Aragón in Spain



Source: https://commons.wikimedia.org/w/index.php?curid=14520269.

Figure 2. Main Hospitals in the Region of Aragón, Spain



Source: http://www.aragon.es/estaticos/ImportFiles/09/docs/Ciudadano/GuiaCentrosServiciosSanitarios/OrdenacionSanitaria/MapaSanitario/MAPA_SANITARIO_ARAGON.pdf.

OBJECTIVE

- To describe the EpiChron cohort as a data source for pharmacoepidemiology studies in the context of a European regulatory multidatabase study of characteristics of new users of cilostazol.

METHODS

- New users of cilostazol between 2002 and 2013 were identified in five health databases from four different countries: the United Kingdom (THIN), Spain (EpiChron cohort and SIDIAP), Sweden (National Registers), and Germany (GePaRD).
- New users were characterized according to the prevalence of cardiovascular disease and other comorbidities, concurrent use of interacting medications, new contraindications, duration of use, and potential off-label prescribing.
- A subcohort of new users of cilostazol between 2009 and 2012 was identified and described in the EpiChron cohort.
- The study and its protocol were registered in the European Union Postauthorization Study (EU PAS) register prior to the start of data collection.[2]

RESULTS

Table 1. The EpiChron Cohort

User Database (BDU)[a]	Primary Care (OMI-AP)[a]	Minimum Basic Data Set (CMBD)[b]	Hospital Emergency (PCH)[c]	Specialist Care (CEX)[a]	Pharmacy Billing (FARMASALUD)[a]	Prescriptions Primary Care[a]
• Patient ID • Primary health care center ID • Type of user • Sex • Date of birth • Nationality • Country of birth • Record date • Postal code • City	• Patient ID • Diagnostics – Opening date – Closing date – ICPC code • Visits – Date of visit – Type of visit – Specialty • Referrals – Date – Specialty • Diagnostic tests – Date – Type of test • Clinical parameters – Date – Value • Adverse drug reactions – Start date – Ending date – Name of medication – Route of administration – Dose – Adverse reactions – Hospital admission – Outcome	• Patient ID • Hospital ID • Type of admission • Date of admission • Reasons for discharge (ICD-9 code) • Date of discharge • Hospital transfer • Diagnostics (ICD-9 code) • Procedures • Treatments • Diagnosis-related groups (DRG) • Death • Readmission • Days in intensive care • Length of stay	• Patient ID • Hospital ID • Support date • First evaluation length • Service • Priority • Clinical group • Reason for visit • Diagnostics (ICD-9 code) • Type of consultation • Discharge date • Type of discharge • Diagnostic tests (Rx) • Ambulance • Number of prescriptions	• Patient ID • Specialist health care center ID • Date • Source of referral • First or subsequent visit • Specialty	• Patient ID • Billing date • Prescription date • ATC code • Number of packages • Price • Level of care that prescribes	• Patient ID • ATC code • Dosage • Code • Packages • Prescription date

ATC = Anatomical Therapeutic Chemical classification system; ICD-9 = International Classification of Diseases, Ninth Edition; ICPC = International Classification of Primary Care; ID = identification.

[a] Records for all individuals registered within the public regional health service (= 1,300,000 individuals).

[b] Records from all public hospitals within Aragón (provincial hospitals, CASAR, MAZ, and military hospitals) and San Juan de Dios Hospital.

[c] Records from all acute hospitals within Aragón (Barbastro, Calatayud, Clínico, Huesca, HUMS, and Teruel).

Table 2. Characteristics of New Users of Cilostazol in the EpiChron Cohort

Characteristics	EpiChron Cohort, Aragón, Spain
Patient characteristics	
Base population (millions)	1.3
Study period	1 Jun 2009-31 Dec 2012
Number of users	4,024
Average annual prevalence of use (per 100,000)	162
Men (%)	72.2
Median age in years	
All users	70.1
Men	69.0
Women	73.9
Age in years (%)	
> 60	77.5
> 70 men	46.9
> 70 women	58.5
> 80 men	16.5
> 80 women	25.7
Drug use characteristics	
Total number of prescriptions	35,719
Total number of defined daily doses	1,133,944
Mean number of prescriptions per user	8.9
Total number of prescriptions per user (%)	
1	31.1
2-4	20.4
5+	48.5
Mean number of defined daily doses per user	281.8
Number of users of 100 mg strength (%)	100
Daily dose of 200 mg at start date (%)	77.3
Discontinuation of use (%)	
< 1 month	33.9
< 3 months	51.9
< 6 months	60.5
< 12 months	69.1
< 24 months	77.8
Contraindications (%)[a]	
Renal failure	NA
Liver disease	1.6
Heart failure	2.9
Risk factors for bleeding	1.7
Active peptic ulcer	0.1
Recent cerebral hemorrhage	NA
Proliferative diabetic retinopathy	1.7
Poorly controlled hypertension	NA
Arrhythmias	0.2
Ventricular tachycardia	0.2
Ventricular fibrillation or multifocal ventricular ectopics	NA
Prolongation of the QT interval	NA
Any contraindication	6.2

NA = not applicable.

[a] Contraindications were severe renal impairment, moderate to severe hepatic impairment, congestive heart failure, risk factors for bleeding (active peptic ulcer, hemorrhagic stroke within the prior 6 months, proliferative diabetic retinopathy, and poorly controlled hypertension), and history of arrhythmias.

Source: Aragón Health Sciences Institute, Aragón, Spain.

The EpiChron Cohort

- The database is based on information from health registries of primary and secondary care in Aragón, and it contains detailed data on all prescription medicines dispensed in the community pharmacies.
- The Healthcare System User Identification Code (permanent and unique) is used as the cross-database reference and tool for direct linkage. The following information sources form the EpiChron cohort:
  - User Database (BDU): contains administrative and demographic information of the individuals in Aragón
  - Minimum Basic Data Set (CMBD): contains information on hospital admission diagnoses and additional information during hospitalization
  - Specialist Care Database (CEX): contains information on outpatient specialty care
  - Database of the Electronic Medical Record of Primary Care (OMI-AP): contains information on diagnoses, prescriptions, referrals, investigations, clinical parameters, adverse drug events, and patient visits to primary care
  - Hospital Emergency Database (PCH): contains information on visits to hospital emergency departments
  - Pharmacy Billing Database (FARMASALUD): contains information on pharmacy-invoiced prescriptions
- Table 1 shows in detail the structure and information contained in the EpiChron cohort.
  - Primary care health information is coded based on the International Classification of Primary Care (ICPC-2), and specialized care information is coded based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Each prescription is included in the database by use of the Anatomical Therapeutic Chemical (ATC) coding system for medication.
  - In order to ensure the compliance of this project with both the Biomedical Research Act and the Data Protection Act, especially in regard to ensuring the confidentiality of patient-level information, all records will be made anonymous and encrypted.
  - Access to medical records by EpiChron researchers to validate potential cases or to complete additional clinical information is possible if stated by the research protocol and approved by the research ethical committee.

Cilostazol Project Findings

- A total of 4,024 patients had a recorded prescription for cilostazol, 72.2% were men, the median age was 70.1 years, and 74.5% had a history of cardiovascular diseases other than peripheral arterial disease (Table 2).
- Hypertension was the most frequent cardiovascular condition (54.9% of users). About 82% of users were concurrently treated with CYP3A4- or CYP2C19-interacting medications, and 10% with potent CYP3A4 or CYP2C19 inhibitors.

CONCLUSION

- The EpiChron cohort is a useful resource for population-based pharmacoepidemiological studies, contains primary and secondary care data and detailed information on prescriptions dispensed, and allows access to medical records for case validation.

REFERENCES

1. European Commission. Clinically consistent multimorbidity patterns from the EpiChron cohort database. November 1, 2015. Available at: https://ec.europa.eu/eip/ageing/library/clinically-consistent-multimorbidity-patterns-epichron-cohort-database_en. Accessed June 7, 2016.
2. European Network of Centres for Pharmacoepidemiology and Pharmacovigilance. Available at: http://www.encepp.eu/encepp/viewResource.htm?id=12303. Accessed June 7, 2016.

CONTACT INFORMATION

Alexandra Prados Torres MD, PhD
Grupo EpiChron de Investigación en Enfermedades Crónicas
Instituto Aragonés de Ciencias de la Salud (IACS)
Instituto de Investigación Sanitaria Aragón (IIS Aragón)

Hospital Universitario Miguel Servet
Hospital General, Pl +2
Paseo Isabel La Católica 1-3
50009 Zaragoza (Spain)
Tlfno. +34 976 76 5500 - Ext. 5370/5371

ABSTRACTS FROM THIS PROGRAM ALSO PRESENTED AT THIS CONFERENCE

Jordi Castellsagué et al. Characterization of new users of cilostazol in the United Kingdom, Spain, Sweden, and Germany.