Ratios between gut bacteria as potential markers for colorectal cancer screening

Joan Mas-Lloret, Mireia Obón-Santacana, Gemma Ibáñez-Sanz, Robert Carreras-Torres, Elisabet Guinó, Ville N Pimenoff, Victor Moreno

Institut d'Investigació Biomèdica de Bellvitge // Institut Català d'Oncologia // CIBER Epidemiología y Salud Pública // Universitat de Barcelona

Background

The gut microbiome is very diverse, and its composition is related to diseases, including colorectal cancer (CRC). Certain bacteria, like *Fusobacterium nucleatum*, have been proposed as potential CRC drivers, as they can cause inflammation in the gut. Others, like *Roseburia spp* or *Faecalibacterium prausnitzii*, have been proposed as CRC protectors, mediated by processes such as butyrate production.
However, there are no screening programs that benefit from potential microbial markers to detect the presence or development of CRC.

Design and methods

We shotgun sequenced stool samples from 156 participants. We also obtained publically available shotgun sequencing data from five additional studies and analysed them using the same pipelines.
We classified sequencing reads taxonomically against the GTDB database using Kraken2 and performed statistical analyses to find patterns that differentiate between colorectal cancer patients and controls.

Software

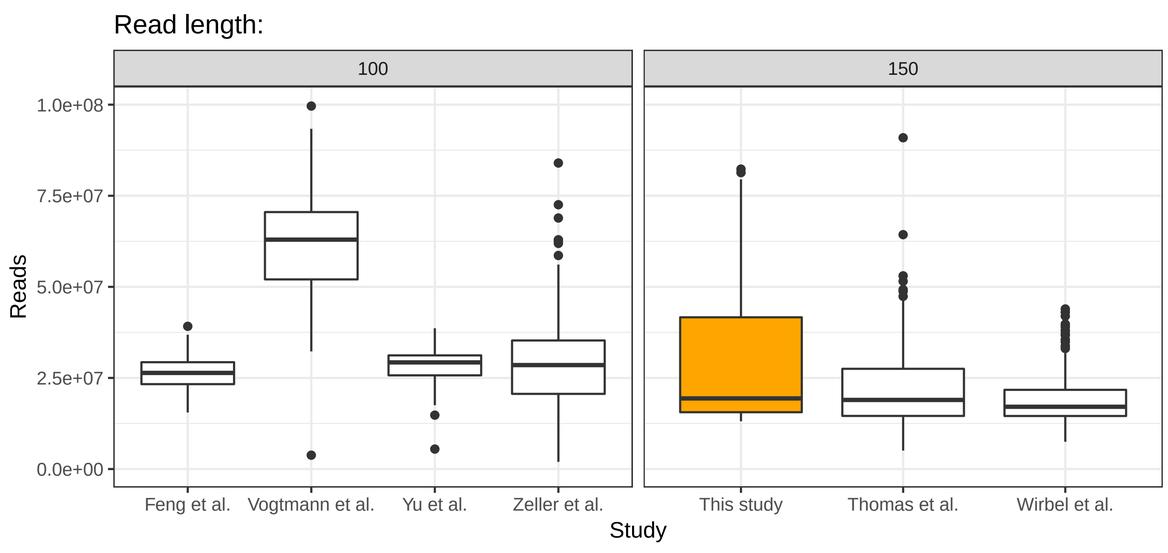
Quality control: `FASTQC`
Deduplication: `Clumpify`
Cleaning: `BBDuk`
Human reads removal: `Bowtie2`
Taxonomic classification: `Kraken2`
Statistics: `R` and `R` packages
ILR transform: `PhilR (R)`
Machine learning: `mlr (R)`

Data for meta-analysis

We collected sequencing reads from six datasets besides our own (sample sizes shown below)

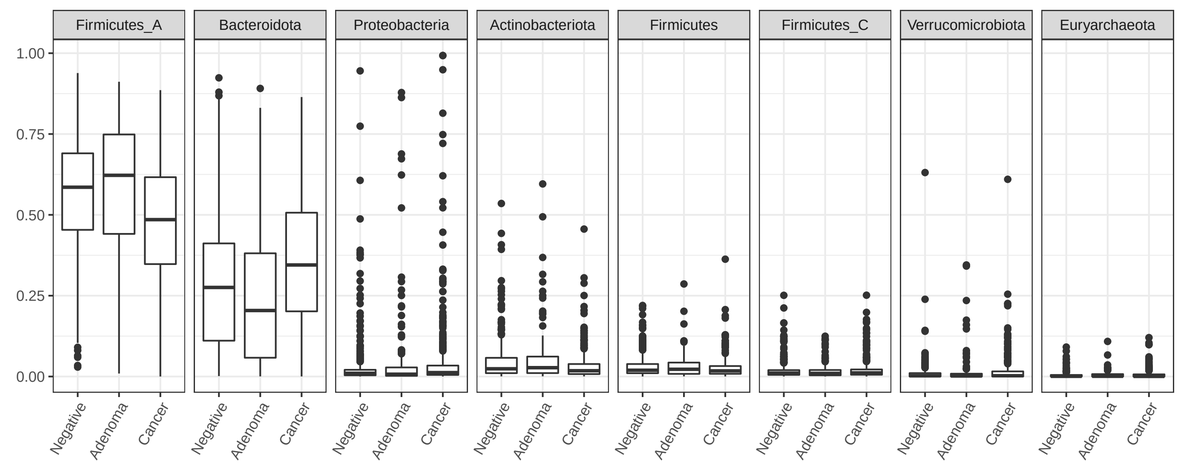
Study	Feng et al.	This study	Thomas et al.	Vogtmann et al.	Wirbel et al.	Yu et al.	Zeller et al.	Total
Cancer	46	51	61	52	22	75	91	398
Adenoma	47	54	27	0	0	0	42	170
Control	63	51	52	52	60	53	66	397

Our dataset was sequenced at a high coverage, matching previous datasets:



Phylum-level bacterial abundance

Under the GTDB taxonomy, the most common bacterial phylums are Firmicutes_A and Bacteroidota (Bacteroidetes). Genus in the Firmicutes_A phylum include *Blautia*, *Faecalibacterium* and *Roseburia*. Genus in the Bacteroidota phylum include *Bacteroides* and *Prevotella*.
Species belonging to other phylums, such as *Methanobrevibacter smithii*, *Bifidobacterium spp.* and *Lactobacillus spp.* are less abundant.



Though simple, phylum-level profiles group different types of bacteria and are not very informative of the bacterial composition. For this reason, statistical analyses are performed at species level, taking advantage of shotgun sequencing.

Why compositional methods?

Compositional data analysis is a branch of statistics which deals with datasets in proportions. This means that the increase of one feature implies a dicrease in all others. Microbiome sequencing data fits this description, because sequencing machines output a fixed amount of reads independent of the original amount of DNA present in the sample. In order to apply statistical methods to compositional data, it needs to be transform using a log-ratio transformation. The detected amount of sequencing counts of each bacteria cannot be used directly (if one grows, the rest have to decrease), but the ratios between one bacteria and another are mainained in the sequencing process!
Here, we used the isometric log-ratio (ilr) transform, exemplified here:

	Bacteria 1	Bacteria 2	Bacteria 3
Sample 1	10	5	2
Sample 2	3	10	3
Sample 3	20	10	4

→

	Bac 1 & 2 / Bac 3	Bac 1 / Bac 2
Sample 1	Positive	Positive
Sample 2	Positive	Negative
Sample 3	Same as sample 1	Same as sample 1

To define the partition, we used the phylogenetic tree in the GTDB taxonomy as implemented in the PhilR package.

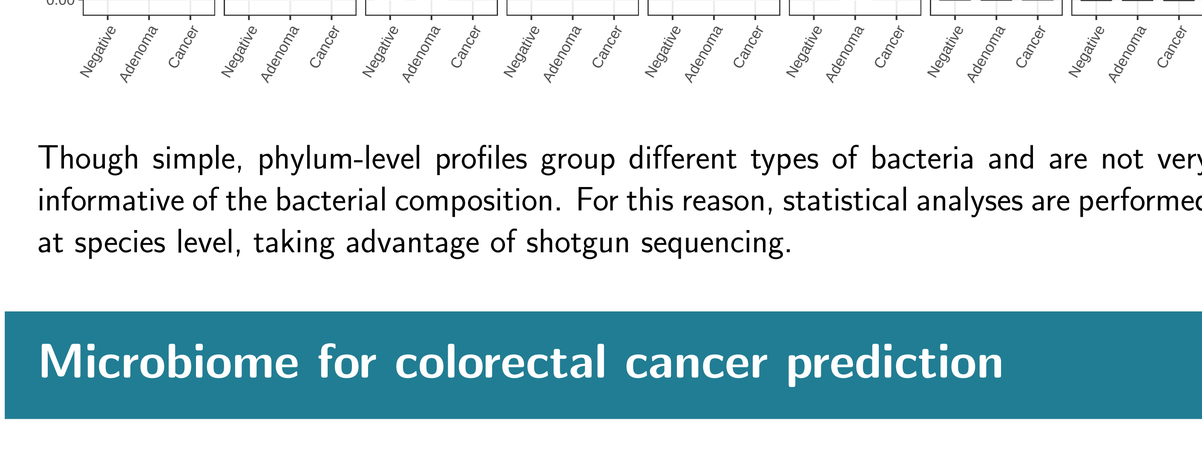
[1] Parks, D. H. *et al.* A standardized bacterial taxonomy based on genome phylogeny substantially revises the tree of life. *Nature Biotechnology* **36**, 996 (2018).

[2] Silverman, J. D., Washburne, A. D., Mukherjee, S. & David, L. A. A phylogenetic transform enhances analysis of compositional microbiota data. *eLife* **6**, 1–20 (2017).

[3] Gloor, G. B., Macklaim, J. M., Pawlowsky-Glahn, V. & Egozcue, J. J. Microbiome Datasets Are Compositional: And This Is Not Optional. *Frontiers in Microbiology* **8** (2017).

Microbiome for colorectal cancer prediction

In order to test the predictive potential of the gut microbiome for colorectal cancer, we built logistic regression models with LASSO correction excluding the adenoma samples. For each dataset, ROC curves were built by training a model on all other datasets, using the remaining one as the test dataset.
When building these models, the ratios between species were used as variables.



Colonbiome project is funded by Instituto de Salud Carlos III through the project PI17/00092 (co-funded by European Regional Development Fund. ERDF: a way to build Europe) and Ministry of Health, Government of Catalonia (grant SLT002/16/00496). Joan Mas Lloret is funded by Ministerio de Ciencia, Innovación y Universidades through the grant FPU17/05474. We thank CERCA Programme / Generalitat de Catalunya for institutional support.

Contact me!
e-mail: jmas@idibell.cat
Twitter: @JoanMasLloret
GitLab: JoanML

Incidence of dementia in the European Prospective Investigation into Cancer and nutrition (EPIC)-Spain study.

José María Huerta (1,2,3), María Encarnación Andreu-Reinón (2), Carmen Navarro (2), Fernando Navarro-Mateu (2,3,4,5), Pilar Amiano (3,6), Mikel Tainta (7), Eva Ardanaz (3,8), María Dolores Chirlaque (1,2,3,9).

(1) Department of Epidemiology, Murcia Regional Health Council, (2) Instituto Murciano de Investigación Biosanitaria (IMIB)-Arrixaca, Murcia, Spain. (3) CIBER Epidemiología y Salud Pública (CIBERESP), Spain. (4) Unidad de Docencia, Investigación y Formación en Salud Mental (UDIF-SM). Servicio Murciano de Salud. Murcia, Spain. (5) Departamento de Psicología Básica y Metodología, Universidad de Murcia, Spain. (6) Public Health Division of Gipuzkoa, Instituto BIO-Donostia, Basque Government, Donostia-San Sebastián, Spain. (7) Center for Research and Advanced Therapies, Fundación CITA-Alzheimer Fundazioa, San Sebastian, Spain. (8) Public Health Institute of Navarra, IDISNA, Pamplona, Spain. (9) Department of Health and Social Sciences, Universidad de Murcia, Spain.

Background

Dementia is a Public Health priority worldwide, but incidence data is scarce in countries like Spain. Our aim was to estimate incidence rates of dementia and Alzheimer disease for different populations participating in the EPIC-Spain study.

Methods

Prospective cohort study which recruited adult volunteers (30-70 years) between 1992 and 1996 in five Spanish regions. The incidence of dementia was ascertained in 25,015 subjects (57% women) from Gipuzkoa, Navarra, and Murcia, using a two-step identification and validation protocol. Potential cases were identified by record linkage with health databases (primary care, hospital records and mortality registers) using a combination of ICD-9 and -10, ICPC2 and ATC codes, who were further validated through the expert revision of all available medical records. Follow-up was complete until 2015-2017, depending on the center. Baseline data on sociodemographic, lifestyle, and health-related variables was obtained for all participants.

Results

After 21.5 (±3.6) years of follow-up, a total of 774 cases of dementia (67% Alzheimer) were validated. Age-standardised incidence rates (and 95% confidence intervals) for the age band of 65+ years were 4.6 (3.3-5.9) cases per 1000 person-years (py) for men, and 6.2 (4.8-7.6) per 1000 py for women (2013 European standard population), and 3.8 (2.9-4.6) and 5.0 (4.2-5.9) cases per 1000 py for men and women (world population standard). The estimated 20-years cumulative risk of dementia for the 60-65 years old group was 9% (7.4-11.1%) among men and 12.5% (10.6-14.6%) among women. Incidence was higher among participants of low educational level, obese, and not drinking alcohol, and in patients with chronic co-morbidities.

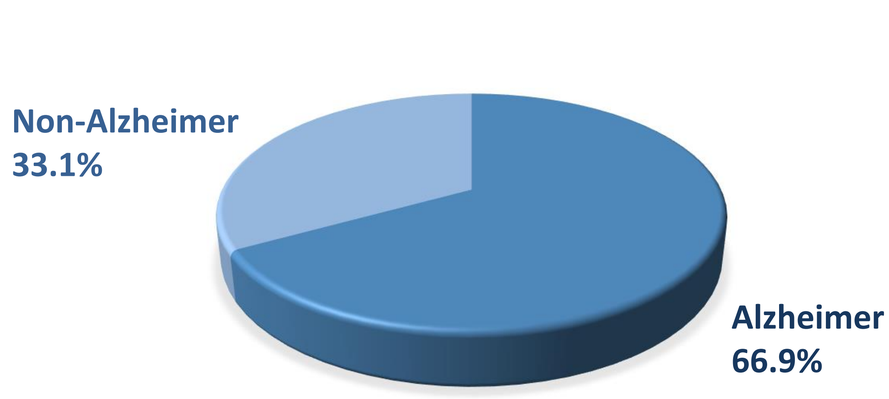


Figure 1 | Sub-types of incident dementia cases in the EPIC-Spain cohort.

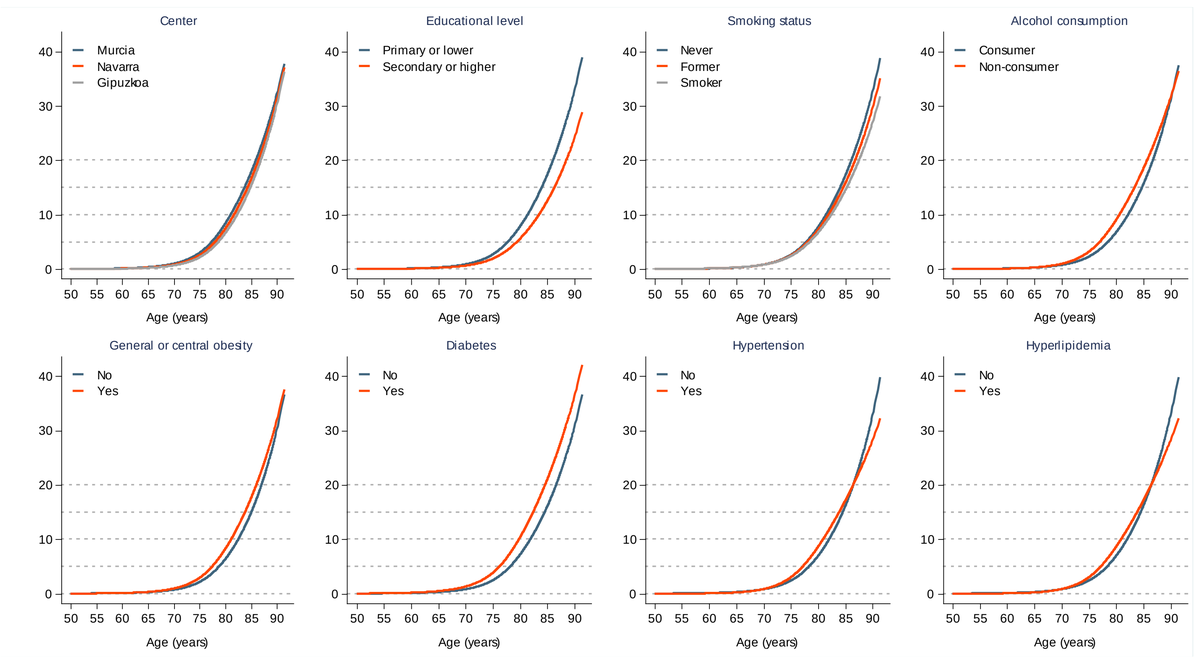


Figure 3 | Estimated cumulative incidence of dementia by selected variables in the EPIC-Spain cohort, by age.

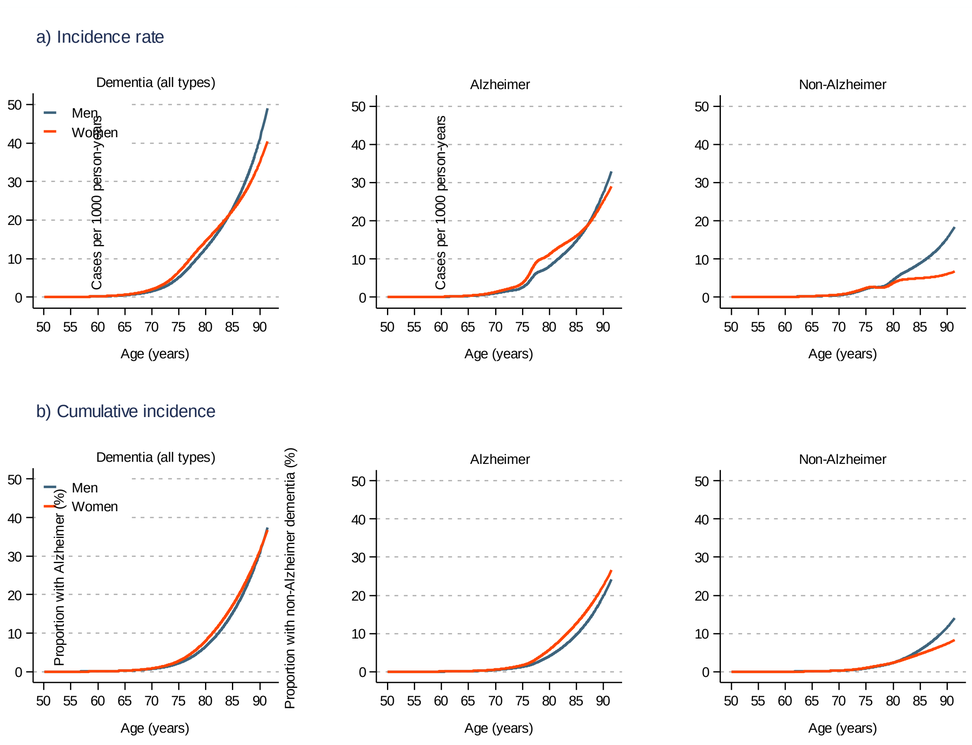


Figure 2 | Estimated incidence rates of dementia and sub-types in the EPIC-Spain cohort, by age and sex.

Sex	Age at enrolment	10-y cumulative hazard	15-y cumulative hazard	20-y cumulative hazard
		Proportion with dementia (%)		
Women	55-59.9 y	0.21 (0.08-0.56)	1.25 (0.83-1.87)	4.86 (3.94-6.01)
	60-64.9 y	1.36 (0.87-2.13)	4.11 (3.15-5.35)	12.45 (10.62-14.61)
	65-69.9 y	-	6.48 (2.43-17.27)	17.81 (9.56-33.19)
Men	55-59.9 y	0.18 (0.06-0.54)	0.92 (0.55-1.52)	4.01 (3.11-5.17)
	60-64.9 y	0.48 (0.21-1.07)	2.96 (2.11-4.14)	9.05 (7.36-11.12)
	65-69.9 y	-	5.73 (1.84-17.85)	13.00 (5.80-29.13)
Sex	**Age at enrolment**	**Proportion with Alzheimer's disease (%)**		
Women	55-59.9 y	0.16 (0.05-0.49)	0.87 (0.53-1.41)	3.40 (2.64-4.37)
	60-64.9 y	0.64 (0.34-1.24)	2.32 (1.63-3.30)	8.84 (7.31-10.68)
	65-69.9 y	-	6.48 (2.43-17.27)	16.06 (8.33-30.95)
Men	55-59.9 y	0.12 (0.03-0.47)	0.74 (0.42-1.30)	2.73 (2.01-3.71)
	60-64.9 y	0.32 (0.12-0.86)	1.84 (1.20-2.82)	6.03 (4.67-7.78)
	65-69.9 y	-	3.61 (0.90-14.43)	8.43 (3.13-22.71)

Table 1 | Nelson-Aalen cumulative hazard estimates (with 95% confidence invervals) of dementia and Alzheimer's disease at 10, 15 and 20 years from enrolment in 25 015 participants from the EPIC-Spain cohort, by sex.

Conclusions

The incidence of dementia was higher in women than men participating in the EPIC-Spain cohort, and lower than neighboring countries. 12% of women and 9% of men between 60-65 years would develop dementia in a 20-year period. This has important implications for dementia prevention.

Funding: The EPIC-Dem study received partial funding from the Fundación SÉNECA (19487/PI/14). The EPIC study received financial support from the International Agency for Research on Cancer (AEP/93/06), the European Commission (SO-97-200302-05F02, SP23-CT-2005-006438), the Health Research Fund (FIS) of the Spanish Ministry of Health, the Red Temática de Investigación Cooperativa de Centros de Cáncer (RTICCC C03/10, RD06/0020), the CIBER de Epidemiología y Salud Pública (CIBERESP), the participating Regional Governments of Andalusia, Asturias, Basque Country, Murcia (no. 6236), and Navarra, and the Catalan Institute of Oncology (ICO).

Recent trends in cancer survival in adult patients in Spain

Results from thirteen population-based cancer registries

M. Guevara (1)*, A. Molinuevo (2), D. Salmerón (3), R. Marcos-Gragera (4), M. J. Sánchez (5), M. D. Chirlaque (6), A. Lopez de Munain (7), J. R. Quirós (8), F. Almela (9), M. Chico (10), R. Jiménez (11), J. Perucha (12), M. C. Sánchez-Contador (13), D. Rojas (14), A. Alemán (15), J. Galceran (16), E. Ardanaz (1) and N. Larrañaga (17)

(1) Registro de Cáncer de Navarra, CIBERESP. (2) Biodonostia Research Institute. (3) Universidad de Murcia, CIBERESP. (4) Registro de Cáncer de Girona, CIBERESP. (5) Registro de Cáncer de Granada, CIBERESP. (6) Registro de Cáncer de Murcia, CIBERESP. (7) Registro de Cáncer de Euskadi. (8) Registro de Cáncer de Asturias. (9) Registro de Cáncer de Castellón. (10) Registro de Cáncer de Ciudad Real. (11) Registro de Cáncer de Cuenca. (12) Registro de Cáncer de La Rioja. (13) Registro de Cáncer de Mallorca. (14) Registro de Cáncer de Canarias (Gran Canaria). (15) Registro de Cáncer de Canarias (Tenerife). (16) Registro de Cáncer de Tarragona. (17) Registro de Cáncer de Euskadi, CIBERESP.

*Contact: mguevare@navarra.es

Background

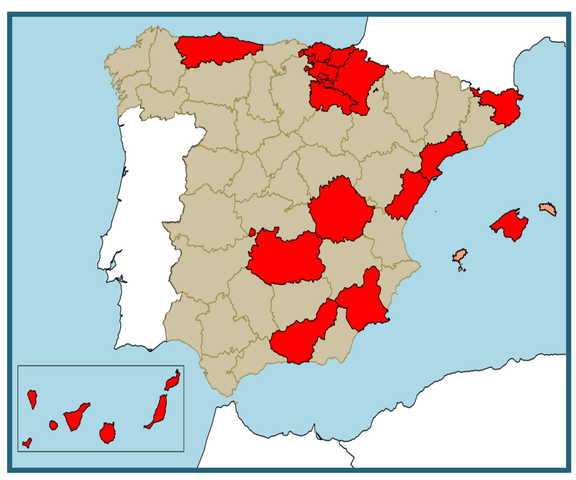
Cancer survival is a key indicator of the effectiveness of a health system in management of cancer. We aimed to examine recent trends in cancer survival in Spain.

Methods

Population-based data from thirteen REDECAN cancer registries, covering 27% of the Spanish population, were provided for ~600,000 adult patients diagnosed with primary cancer over two periods, 2002–2007 and 2008–2013, and followed up to 2015.

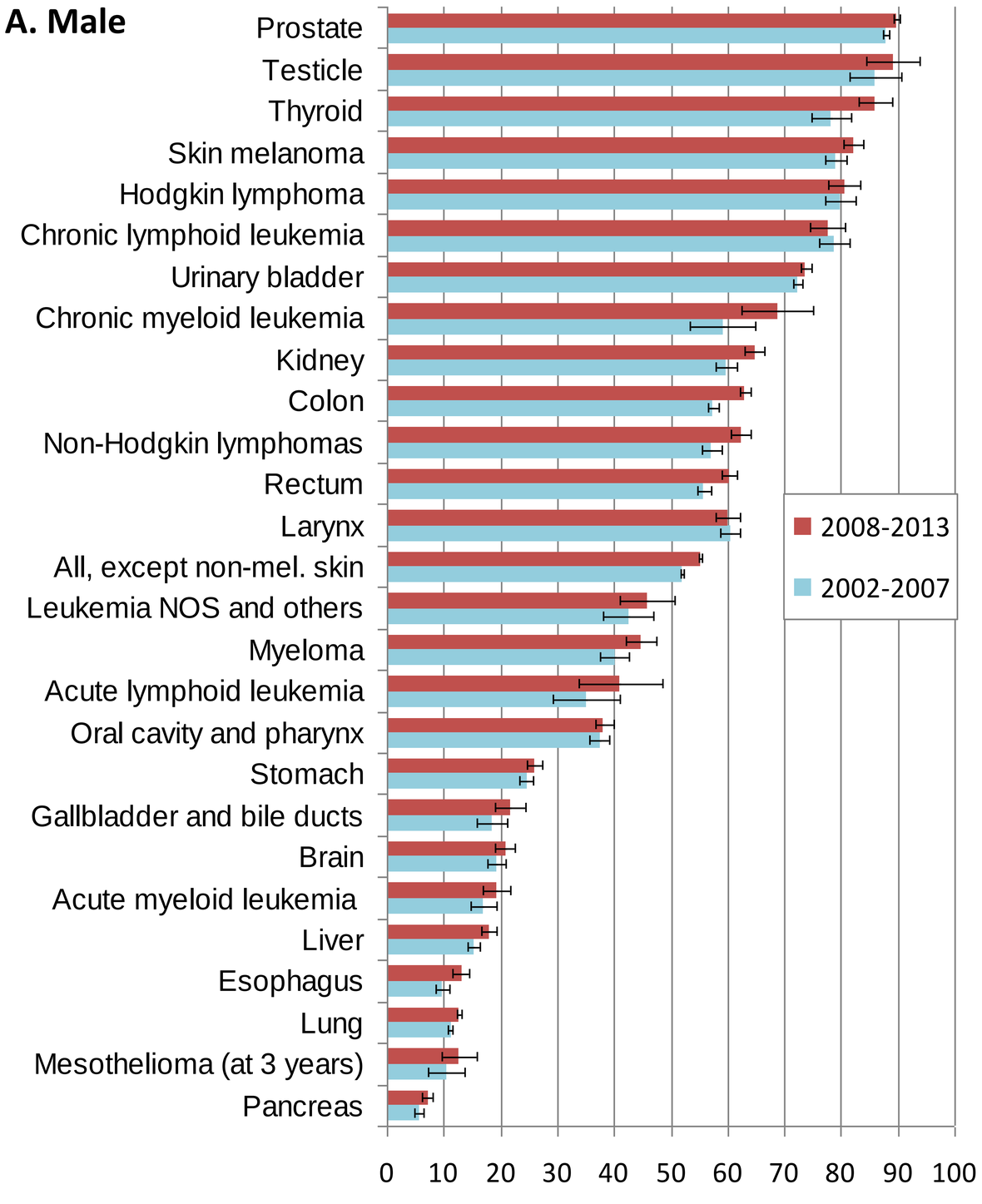
For thirty groups of cancers, 5-year net survival (NS) was estimated through the Pohar-Perme method, by sex, age and period. We used the international cancer survival standard weights to calculate age-standardized estimates.

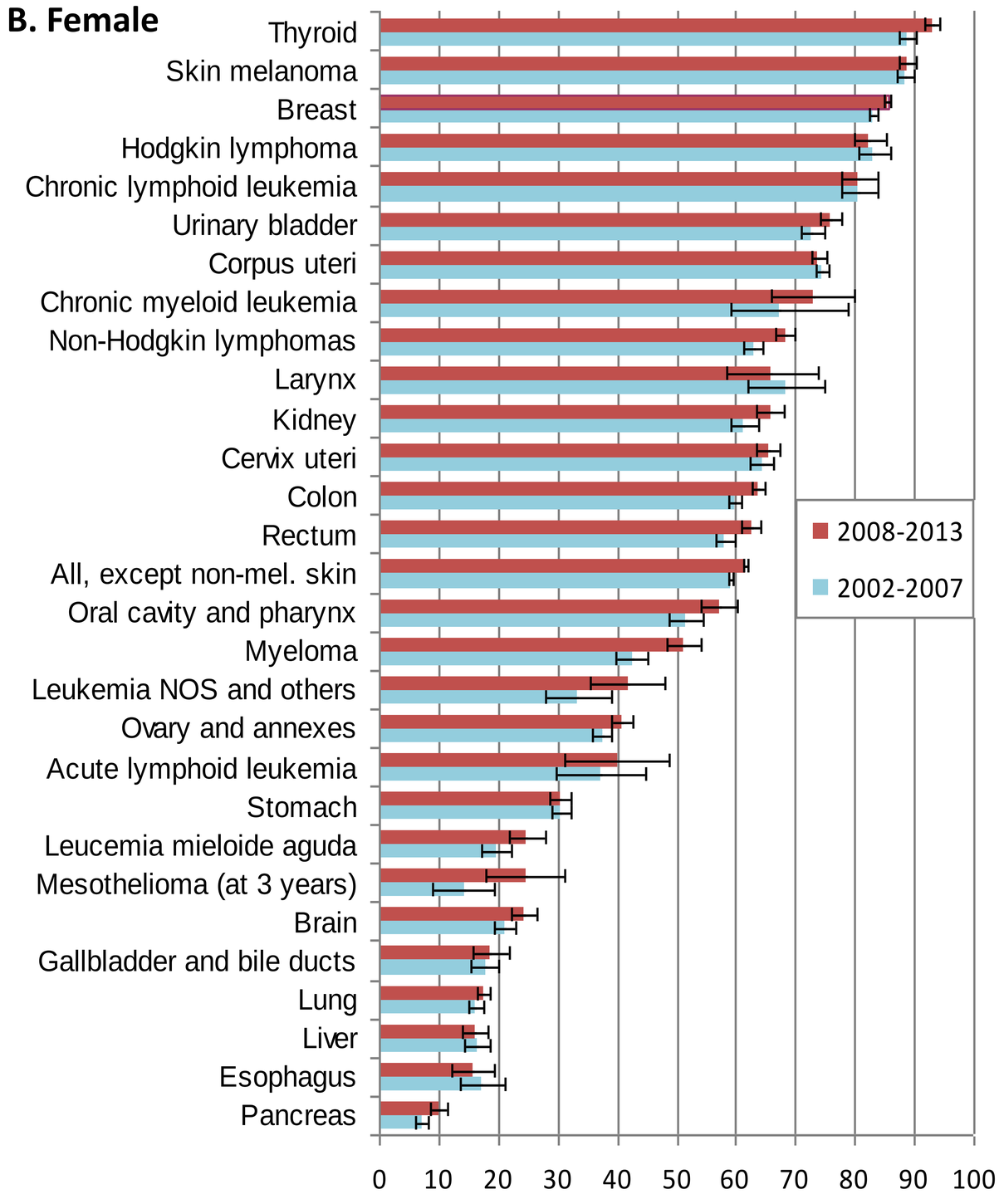
Fig 1. Cancer registries participating



Results

Fig 2. Five-year age-standardized net survival (%) by tumor type and period in male (A) and female (B). REDECAN, Spain.





Conclusions

Short-term survival improved for most common cancers over 2002–2013, especially the survival of colon and rectum cancers (increase of >4% points). These improvements are probably due to advances in cancer management, i.e. earlier diagnosis and better treatment. Poor prognosis still found in some tobacco-related cancers highlights the continuing need for prevention efforts.

Acknowledgments: Cancer registries from Euskadi, Navarra, Murcia, Granada and Girona acknowledge support from CIBERESP/ISCIII

GEO_CIBER: a geocoding tool for the cancer surveillance program (VICA)

Pablo Fernández Navarro (AEAC, CNE, ISCIII, CIBERESP), Javier González Palacios (AEAC, CNE, ISCIII, CIBERESP), Mario González Sánchez (AEAC, CNE, ISCIII, CIBERESP), Daniel Redondo Sánchez (ibs.GRANADA, CIBERESP), Miguel Rodríguez Barranco (EASP, ibs.GRANADA,CIBERESP), Olivier Nuñez (AEAC, CNE, ISCIII, CIBERESP), Miguel Ángel Luque Fernández (CIBERESP, ibs.Granada), Rafa Marcos Gragera (Girona; CIBERESP), Jaume Galcerán (Tarragona), Eva Ardanaz (Navarra, CIBERESP), Nerea Larrañaga (Guipúzcoa, CIBERESP), Antonio Mateos (Albacete), Rosario Jiménez (Cuenca), Fernando Almela (Castellón), Marina Pollán (AEAC, CNE, ISCIII, CIBERESP), María José Sánchez (EASP, CIBERESP, ibs:GRANADA, UGR)

Introduction

- Address geocoding can be very useful in the context of cancer surveillance developed by population-based cancer registries in Spain (REDECAN).
- There are numerous geocoding systems, with different capacities, limitations and complexities of use.
- The objective of this work as part of the VICA cancer surveillance subprogram is to develop a free and easy to use application of geocoding based on reliable results.

Methods

Pilot study to develop the geocoding tool:

Phase 1. Geocoder selection

a. Sample of **214 addresses** randomly selected from the databases of the cancer registries participating in VICA.
b. Implementation and feature evaluation of several free geocoding software (probability of success, easy to use, time,…)
c. **Geocoding software selected:**

bing CartoCiudad

Phase 2. App Development

Software: Java R

Outputs: **Latitude, longitude and geo_ciber_score (1=High predicted probability to 6= Low predicted probability to be correctly geocoded),** kml file.

Phase 3. Validation

Geocoded and validated database of **2722 addresses** from Granada Cancer Registry

Results

Phase 1

geo_ciber_score	Number of addresses	Accumulated % of sample	Accumulated % of addesses geocoded correctly	% of addresses geocoded correctly
1	108	50	49	97
2	31	65	63	97
3	38	83	79	92
4	10	87	84	90
5	13	93	88	77
6	14	100	91	36

Phase 3

geo_ciber_score	Number of addresses	Accumulated % of sample	Accumulated % of addesses geocoded correctly	% of addresses geocoded correctly
1	275	10	10	97
2	0	10	10	0
3	1853	78	71	90
4	53	80	73	91
5	40	82	74	95
6	501	100	82	40

Phase 2

Conclusion

- The application provides enough information and reliable geocoding results to be useful in cancer surveillance.
- The quality of the information on the addresses is important in order to obtain a better performance.

The study was supported by CIBERESP/ISCIII

Pilot study about the chemical pollution of drinking water sources in rural Mozambique.

Cristina M Villanueva[1,2,3,4], Iro Evlampidou[1], Fernando Goñi[2,5,6], Jochen Kuckelkorn[7], Lourdes Arjona[1,2,3,4], Berta Grau[1,8,9], Jose Muñoz[1]

(1) Barcelona Institute for Global Health, ISGlobal, Barcelona, Spain; (2) CIBERESP, Madrid, Spain; (3) Universitat Pompeu Fabra, Barcelona, Spain; (4) IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain; (5) Public Health Laboratory in Gipuzkoa, Basque Government, San Sebastian, Spain; (6) Biodonostia Health Research Institute, San Sebastian, Spain; (7) German Environment Agency, Toxicology of Drinking Water and Swimming Pool Water, Bad Elster, Germany; (8) Centro de Investigaçao em Saúde de Manhiça-CISM, Manhiça, Mozambique Fundación Mundo Sano, Madrid, Spain

Most chemicals were far below the maximum regulatory levels in the EU except manganese, with ≈50% samples exceeding the EU regulations.

Background and objective

- Limited knowledge of the chemical quality of drinking water in low and middle-income countries.
- Manhiça is a rural village in southern Mozambique where pesticides including DDT are widely used for malaria control, and with sugar cane fields and a factory where pesticides and chemicals are used.
- We measured a wide range of chemicals and toxicity in drinking water sources in Manhiça.

Methods

- Drinking water samples collected in 20 locations (Fig 1).
- Chemicals analysed: nitrate, fluoride, 20 elements including metals, 84 pesticides (21 organochlorines, 26 organophosphates, 11 triazines , 9 phenoxy acids, 17 other), 19 disinfection by-products, and 2 industrial organochlorinated chemicals.
- In-vitro bioassays of mutagenicity, genotoxicity and endocrine disruption.

Results

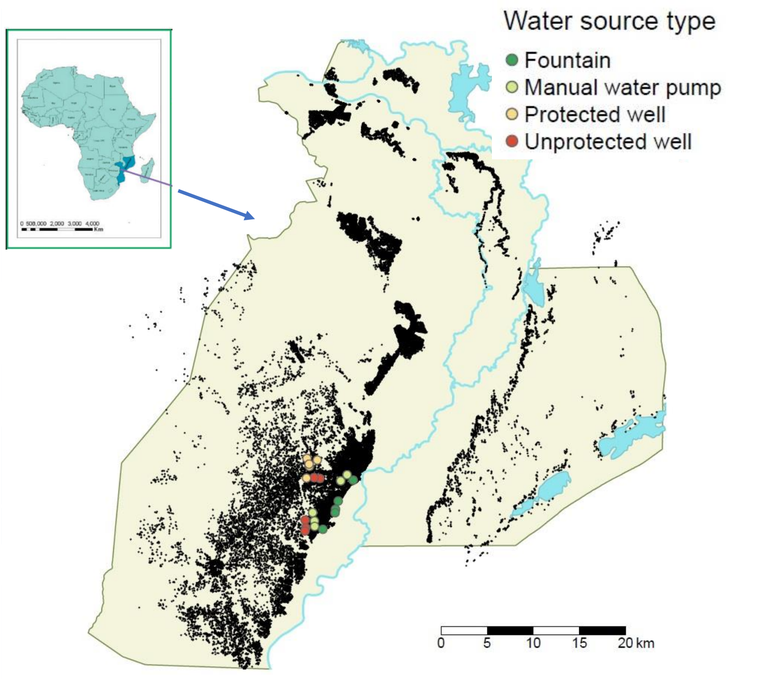
Elements, µg/L	N (%) >QL	Median	Max.	Regulatory limit EU[1]
Antimonium (Sb)	0 (0%)	<1.0	<1.0	5.0
Cadmium (Cd)	0 (0%)	<1.0	<1.0	5.0
Copper (Cu)	0 (0%)	<50	<50	2.0
Mercury (Hg)	0 (0%)	<0.2	<0.5	1.0
Zinc (Zn)	0 (0%)	<50	<50	-
Silver (Ag)	0 (0%)	<1.0	<1.0	-
Arsenic (As)	2 (10%)	<1.0	2.8	10
Lead (Pb)	3 (15%)	<1.0	4.0	10
Selenium (Se)	8 (40%)	<1.0	2.1	10
Iron (Fe)	9 (45%)	<25	3190	200
Nickel (Ni)	13 (65%)	<1.0	5.0	20
Cobalt (Co)	18 (90%)	0.6	8	-
Manganese (Mn)	18 (90%)	32	196	50
Aluminium (Al)	20 (100%)	61	376	200
Barium (Ba)	20 (100%)	250	1830	-
Calcium (Ca)	20 (100%)	7.5	34.3	-
Chromium (Cr)	20 (100%)	2.0	17.0	50
Magnesium (Mg)	20 (100%)	5.8	15.7	-
Potassium (K)	20 (100%)	5.5	8.3	-
Sodium (Na)	20 (100%)	54	72	200

Other				
Nitrate (mg/L)	20 (100%)	7.5	33	50
Fluoride (mg/L)	1 (5%)	<0.10	0.11	1.5
Hardness (mg/L)	20 (100%)	39	121	-

Pesticide, ng/L	QL	N <QL, >DL	N>QL	Max	Regulatory limit EU[1]
Imidachloprid	20	3	0	(13)	100
Diuron	20	1	3	60	100
Dieldrin	10	0	3	44	100
op'-DDT	10	0	1	12	100
pp'-DDT	10	0	1	13	100
Pirimiphos methyil	25	1	1	29	100
Total				171	500

	N (%) >QL	Median	Max.	Regulatory limit EU[1]
Disinfection by-products (µg/l)				
Trihalomethanes				
Chloroform	5 (28%)	<0.4	0.4	100[4]
Dibromochloro-methane	3 (17%)	<0.4	<0.4	
Bromoform	3 (17%)	<0.4	<0.4	
Haloacetic acids				
Dichloroacetic ac.	1 (5%)	<0.1	0.3	-
Bromoacetic ac.	2 (10%)	<0.1	0.2	-
Dibromoacetic ac.	4 (21%)	<0.05	3.8	-
Bromochloroac. ac.	3 (16%)	<0.1	0.18	-
Chlorethenes				
Trichloroethene	0 (0%)	<0.40	<0.40	10[5]
Tetrachloroethene	0 (0%)	<0.40	<0.40	

Figure 1. Sampling locations in Manhiça district, Mozambique.



In vitro Assay	Endpoint	Results
Ames test TA98	Mutagenicity	Negative
Ames t. TA98 + S9	Mutagenicity	Negative
Ames t. TA100	Mutagenicity	Negative
Ames t. TA100 + S9	Mutagenicity	Negative
MN-FACS	Micronuclei, genotoxicity	Negative
ER-CALUX	Endocrine disruption, estrogenic	Negative
ER-CALUX + S9		Negative
AntiAR-CALUX	Endocrine disruption, anti androgenic	Negative
AntiAR-CALUX + S9		Negative

QL - quantification limit.

[1]Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption

Discussion

- Representativeness of results? – Few samples, and type of water sources covered (not at homes),
- Pesticide analysis was partial. Pyrethroids and pesticides used in the sugar can industry not covered.

cristina.villanueva@isglobal.org

ciberesp Centro de Investigación Biomédica en Red Epidemiología y Salud Pública
MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
Instituto de Salud Carlos III
Unión Europea
FONDO EUROPEO DE DESARROLLO REGIONAL Una manera de hacer Europa
FONDO SOCIAL EUROPEO El FSE invierte en tu futuro
ISGlobal Barcelona Institute for Global Health
www.isglobal.org

Jornada Científica CIBERESP 2019

Efectividad de la vacuna antigripal en embarazadas para prevenir infección grave de gripe en niños menores de 6 meses en España, 2017-2019

C Mazagatos[1,6], Pere Godoy[2,6], Carmen Muñoz Almagro[3,4,6], Francisco Pozo[5,6], A Larrauri[1,6] y el Grupo de trabajo de la EV antigripal en embarazadas

(1) Centro Nacional de Epidemiología, ISCIII; (2) Agencia de Salud Pública de Cataluña; (3) Instituto de Recerca Pediátrica, Hospital Sant Joan de Déu; (4) Dpto de Medicina, Universitat Internacional de Catalunya; (5) Centro Nacional de Microbiología, ISCIII; (6) CIBER Epidemiología y Salud Pública (CIBERESP)

ANTECEDENTES Y OBJETIVO

- La vacunación antigripal se recomienda a mujeres embarazadas en cualquier trimestre, y en niños a partir de 6 meses de edad si existe algún factor de riesgo.
- Los niños menores de 6 meses pueden recibir protección a través de la vacunación materna durante el embarazo.

Objetivo: Estimar la efectividad de la vacuna antigripal durante el embarazo para prevenir casos graves hospitalizados confirmados de gripe en niños menores de 6 meses

RESULTADOS

Fig. 1. Diagrama de inclusión de casos

Casos notificados en niños hospitalizados con gripe grave en 2017-18 y 2018-19 **N=94**

Criterios de inclusión:

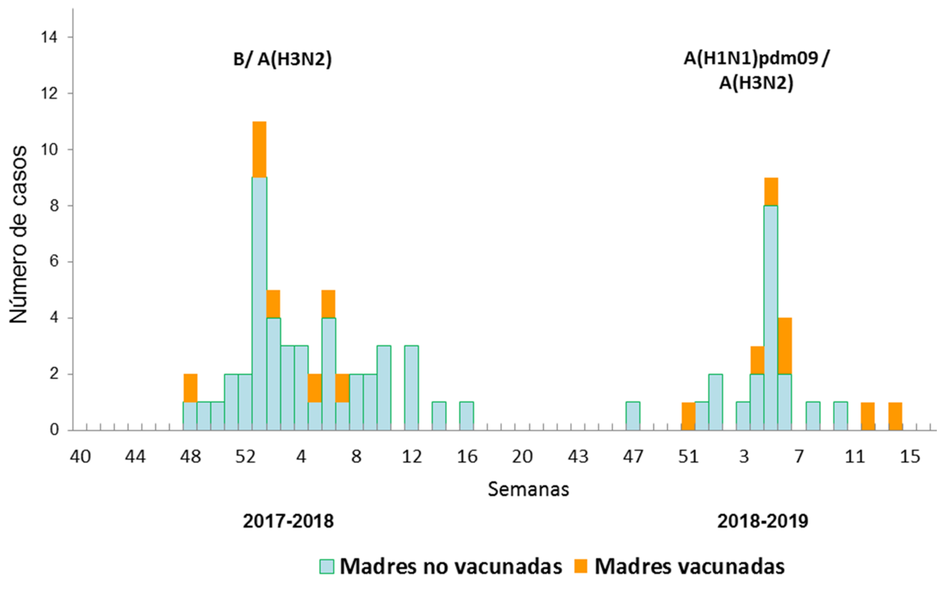
- Periodo de estudio (2017/18 y 2018/19) **N=93**
- Edad menor o igual a 6 meses **N=80**
- Información sobre vacunación de la madre **N=77**

Casos incluidos (n=77)

Madre vacunada (n=14) **18,2%**

Madre no vacunada (n=63) **81,8%**

Fig. 3. Número semanal de casos en niños ≤6 meses hospitalizados con gripe confirmada y estado de vacunación de sus madres. España, temporadas 2017-18 y 2018-19



MÉTODOS

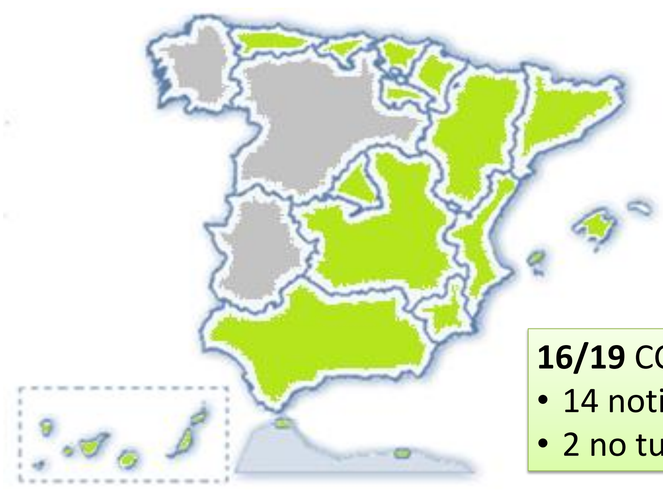
- **Diseño del estudio:** Estudio retrospectivo, usando datos de vigilancia de Casos Graves Hospitalizados Confirmados de Gripe (CGHCG) en España, en las temporadas 2017/18 y 2018/19.
- **Estimación de la efectividad de la vacuna antigripal (EV):** Método de screening (ref Farrington)

$$Logit\{PCV\} = Logit\{PPV\} + a + b_1 x_{i1} + \ldots + b_k x_{ik}$$

PCV: proporción de casos vacunados — Proporción de casos con madres vacunadas

PPV: proporción de población vacunada — Proporción de mujeres embarazadas vacunadas en España (Fuente: MSCBS)

Fig. 2. Comunidades Autónomas que participaron en el estudio



16/19 CCAA participaron:
- 14 notificaron casos
- 2 no tuvieron ningún caso

Tabla 1. Vacunación materna según características de los casos graves hospitalizados confirmados de gripe en niños de hasta 6 meses

	Total casos	Madre vacunada
Enfermedades crónicas		
No	57	7 (12%) *
Sí	15	6 (40%) *
Complicaciones		
No	19	5 (26%)
Sí	51	8 (16%)
Admisión a UCI		
No	35	5 (14%)
Sí	42	9 (21%)
Defunción		
No	70	12 (17%)
Sí	2	1 (50%)
Tratamiento antiviral		
No	34	11 (32%) *
Sí	39	3 (8%)

Tabla 2. Efectividad de la vacuna antigripal en embarazadas para prevenir casos graves hospitalizados con gripe confirmada en niños ≤6 meses

	Casos vacunados	Casos totales	PCV (%)	PPV (%)	**EV % (IC 95%)**
2017/18	7	51	13,7	29,9	**63 (18; 84)**
2018/19	7	26	26,9	38,5	**44 (-34; 77)**
Total	14	77	18,2	34,2	**56 (21; 75)**

CONCLUSIONES

- La vacunación antigripal durante el embarazo es efectiva previniendo la hospitalización con infección grave de gripe en niños hasta 6 meses.
- Estos resultados refuerzan la recomendación de vacunación en embarazadas.
- Son necesarios más estudios en esta línea para contribuir a aumentar la cobertura de vacunación antigripal durante el embarazo, dado su doble efecto protector sobre la madre y el niño

No hay conflicto de intereses por parte de los autores

ciberesp Centro de Investigación Biomédica en Red Epidemiología y Salud Pública
MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
Instituto de Salud Carlos III
Unión Europea
FONDO EUROPEO DE DESARROLLO REGIONAL Una manera de hacer Europa
FONDO SOCIAL EUROPEO El FSE invierte en tu futuro

SJD Sant Joan de Déu Barcelona · Hospital

Outbreak of brainstem encephalitis associated with enterovirus-A71 in Catalonia, Spain (2016): a clinical observational study in a children's reference centre in Catalonia

Launes C[1,2,3], Casas-Alba D[1] , de Sevilla MF[1,2], Barrabeig I[4], González-Sanz R[5], Cabrerizo M[5], Muñoz-Almagro C[1,2,6].

1 Hospital Sant Joan de Deu (University of Barcelona), Spain.
2 Paediatric Infectious Diseases Research Group, Institut de Recerca Sant Joan de Déu, Esplugues de Llobregat, Spain; CIBER en Epidemiología y Salud Pública, Spain.
3 Universitat de Barcelona, Barcelona, Spain.
4 Epidemiological Surveillance Unit of Health Region, Barcelona-South, Public Health Agency of Catalonia, Hospitalet de Llobregat, Spain.
5 Enterovirus Unit, National Centre for Microbiology, Institute of Public Health "Carlos III", Madrid, Spain.
6 Universitat Internacional de Catalunya, Barcelona, Spain.

Introduction and aims

Enteroviruses (EV) are small RNA viruses that infect > 95% of children before 5 y-old. Most of them, causing mild symptomatic infections. Between April and June 2016, an outbreak of EV infection affected more than 100 children mainly in Catalonia (Spain).
The purpose of this study was to describe and analyse the characteristics and clinical management of this outbreak of brainstem encephalitis and encephalomyelitis related to EV infection.

Patients and methods

Data were **prospectively** collected from all children with **clinical diagnosis of Brainstem Encephalitis (BE) or Encephalomyelitis (EM)** (WHO Guide to HFMD), **EV detection** in any sample and no other cause associated, admitted to a reference children's hospital in Catalonia (Spain) between April and June 2016.
Etiologic diagnosis: blood and CSF analysis, bacterial cultures, **PAN-EV real time-PCR** in plasma, CSF, nasopharyngeal aspirate and stools. RT-PCR for HSV was tested in CSF. **FilmArray-M/E** panel in the CSF of the first 20 patients. EV-positive samples were **genotyped** at the National Centre for Microbiology. **Brain and spine MRI**.

Results

52 patients with BE or EM → **44** with informed consent → **41** BE and **3** EM. Median age was **27.8 months** (p25-p75:19.1-37.3), 25/44 (56,8%) were males.

Non-NRL manifestations

	< 24 h	Total
Fever	44 (100%)	**44 (100%)**
Vomits	26 (59%)	31 (71%)
Enanthem	24 (55%)	26 (59%)
Exanthema	12 (27%)	14 (32%)
URI	12 (27%)	12 (27%)
Diahorrea	2 (5%)	5 (11%)
Bronchitis	1 (2%)	3 (7%)

• HFMD vesicular exanthema: 8 (18%).

NRL manifestations

	< 24 h	Total
Ataxia	7 (16%)	**37 (84%)**
Lethargy	**8 (18%)**	**34 (76%)**
Tremor	5 (11%)	**25 (57%)**
Myoclonic jerks	4 (9%)	**22 (50%)**
Irritability	**7 (16%)**	15 (34%)
Meningeal signs	6 (14%)	11 (25%)
CCPP alt.	2 (5%)	9 (20%)
Headache	6 (14%)	6 (14%)
Paresia	0	3 (7%)
ANS dysfunction	0	2 (5%)

• Admitted in ICU: 8 cases (14%).

Virological findings in CSF (20 first cases)

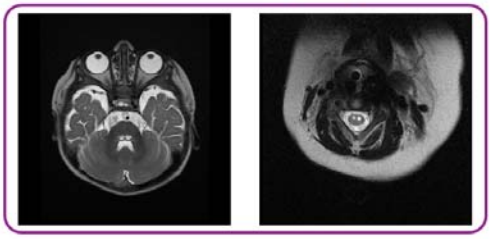
Frequency of cases (n)	Cerebrospinal Fluid: Real-time PCR-HSV 1 and 2	PAN-EV Real-time PCR	FA-M/E
7	Negative	Negative	No detection
4	Negative	Negative	No detection
2	Negative	Negative	ENTEROVIRUS
2	Negative	Negative	ENTEROVIRUS
2	Negative	Negative	HUMAN HERPESVIRUS 6
1	Negative	Negative	No detection
1	Negative	Negative	No detection
1	Negative	Negative	HUMAN HERPESVIRUS 6

Virological findings:

• **EV detection**: stools 32/40 patients, nasopharyngeal aspirate 31/43 patients, CSF 5/40 patients, plasma 1/31 patients.

Brain and spine MRI:

• 41 MRI → 25 with typical alterations.
• 15 with bulbar involvement and 18 with medullar involvement.



Management:

• 33 patients (58%) received **IVIG** depending on the severity of the disease and 26 patients (46%) subsequently received **steroids**.
• All the most severe patients received treatment, so **no conclusions can be drawn** concerning its effectiveness.
• **No patients receiving IVIG ± steroids developed paresis/ANS dysfunction**.

Outcomes and variables associated with a more severe disease:

•All the patients but **3 with EM** had a **good clinical course** and had **no significant sequelae at day 30**. **No deaths occurred**.

Conclusions

• **EV-A71** was the only type found in all the patients with BE or EM. It affected children of around **2 year-old**.
• The new clinical manifestations (non-previously seen in EV infections in our setting) were caused by a **new German recombinant strain (2015)** .
• **Clinical and microbiological surveillance systems** provide valuable data to monitor the emergence of new EV subgenotypes/types .

PROMOCIÓN DE LA PRUEBA DE VIH Y OTRAS INFECCIONES DE TRANSMISIÓN SEXUAL EN HOMBRES QUE TIENEN SEXO CON HOMBRES A TRAVÉS DE APLICACIONES PARA MÓVILES

Alarcón-Gutiérrez, M[1,2]; Fernández-Quevedo, M[1]; Martín-Valle, S[1]; García de Olalla, P[1,3]; Rius, C[1,3]

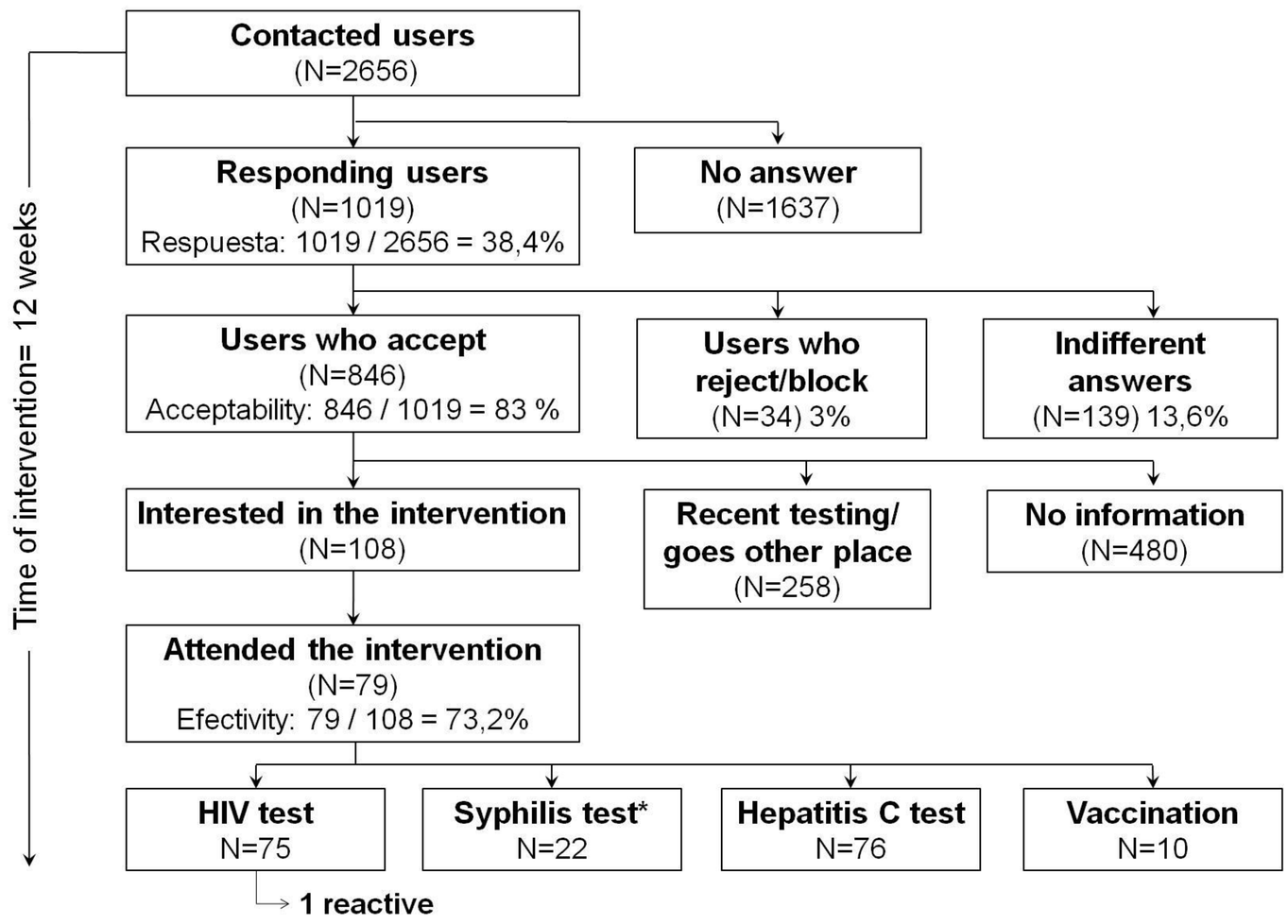
1. Agència de Salut Pública de Barcelona (ASPB)
2. Máster de Salud Pública, Universitat Autònoma de Barcelona/Universitat Pompeu Fabra
3. Consorcio de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP)

Introducción

El diagnóstico tardío del VIH es una pérdida de oportunidad para el control de la epidemia. El diseño de nuevas estrategias que promuevan la realización de la prueba del VIH y de otras infecciones de transmisión sexual (ITS) representa un reto para los programas de prevención y control.

Objetivo

Conocer la tasa de respuesta, aceptabilidad y efectividad de un programa piloto que ofrece la prueba rápida del VIH y otras ITS a través de aplicaciones móviles (Apps) para contactos sexo-sociales entre hombres que tienen sexo con hombres (HSH) en Barcelona, entre diciembre 2015 y marzo 2016.



Metodología

Mediante un mensaje a través de las Apps se ofrecieron las pruebas rápidas. Se recogió información sobre el perfil de los usuarios, así como características sociodemográficas, conductas sexuales y uso de apps. Se calculó la tasa de respuesta, la aceptabilidad y la efectividad del programa. Se realizó un análisis descriptivo de las características de los perfiles y de usuarios que se realizaron las pruebas, y se determinaron las variables asociadas a la respuesta mediante regresión logística.

Resultados

Se enviaron 2656 mensajes. La tasa de respuesta fue del 38,4%, la aceptabilidad del 83% y la efectividad del 73,2%. De los 77 encuestados un 45,5% se había realizado la prueba del VIH hacía más de un año. El 24,7% reportó alguna ITS anterior, hubo penetración anal sin condón en el 51,4% y el 52% utilizaba alcohol y otras drogas para el sexo.

Conclusiones

La elevada respuesta, aceptabilidad y efectividad de esta estrategia la hace una herramienta útil para la promoción de las pruebas rápidas de VIH y otras ITS en HSH. El programa alcanza a usuarios de Apps con una alta proporción de prácticas sexuales de riesgo, consumo de drogas y que no se habían realizado las pruebas del VIH en el tiempo recomendado.

Temporal evolution of lymphogranuloma venereum cases in Madrid during 7 years

Martínez-García L[(1)], Puerta T[(2)], González-Alba JM[(1)], Rodríguez C[(2)], Rodríguez-Domínguez M[(1)], del Romero J[(2)], and Galán JC[(1)].

[(1)]Grupo 33 CIBERESP. Servicio de Microbiología. Hospital Ramón y Cajal [(2)] Centro Sanitario Sandoval. Madrid

Background

The current lymphogranuloma venereum (LGV) epidemic in Europe began 15 years ago, but the epidemic situation is far from being controlled. The last ECDC report suggested that four countries, including Spain, are responsible for 86% of all European cases. Between 2003-2009, the LGV cases were related to L2b variant, but from 2009, in Spain and other European countries, a co-circulation of two variants (L2b and L2) was described. The aims of this study were to analyze the temporal evolution of LGV epidemic in Spain.

Materials/methods

During the 2012-2018 period, all clinical samples in which *C. trachomatis* (CT) DNA was detected, were subsequently genotyped for detecting the presence of LGV based on a *pmpH* internal deletion. The *ompA* and *pmpH* genes were sequenced in those positive samples for LGV genotypes. Finally, a phylogenetic analysis using PhyML 3.0 allowed us to infer potential transmission nodes. In those patients were LGV genotypes were detected, other sexually transmitted infections were also screened.

Results

- The LGV cases were increasing 25% every year of the study, until to reach 4-fold more number of cases in 2018 compared to 2012 **(Figure 1)**. Moreover, the proportion LGV-positive/CT-positive evolved from 10.6% to 18% **(Figure 2).**
- During this period, the percentage of HIV+/LGV+ was constant (74% vs 76%), but practically all patients had undetectable viral load in 2018 compared to patients in 2012 (20%). We did not observe a global increasing in the percentages of concomitant STIs (~50%); while the number of cases of HCV and syphilis decreased significantly, gonococcal infection increased (15% to 25%).
- The phylogenetic analysis of *pmpH* and *ompA* sequences (442 samples) revealed the sequential appearance of up to four transmission related to L2b (L2b *sensu-stricto*, L2 and SPA112 and nSPA). The dynamic of partial replacement among these variants is also described) (**Figures 3 and 4**).

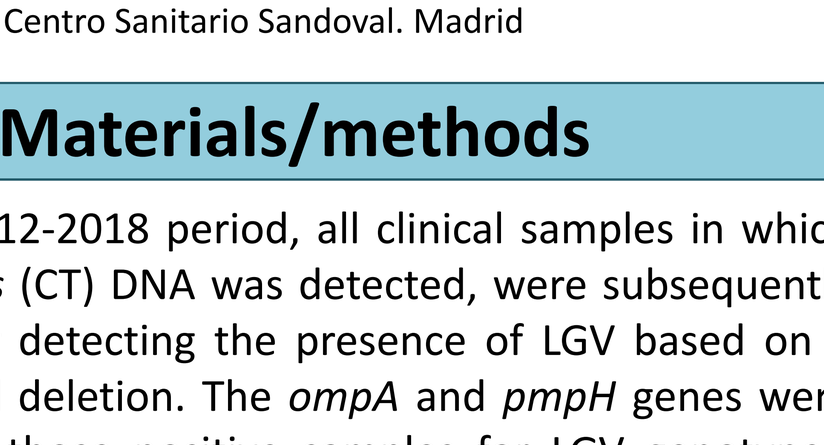


Figure 1: Number of LGV cases (2009-2018)

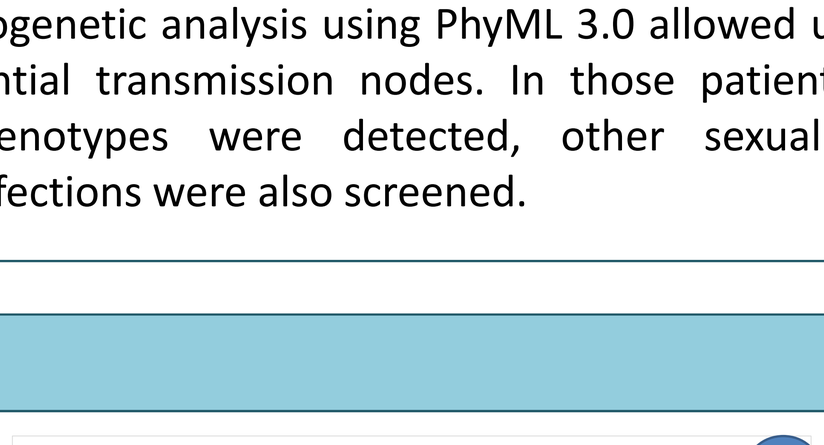


Figure 2: Proportion of LGV and non-LGV cases in 2009-2018 period

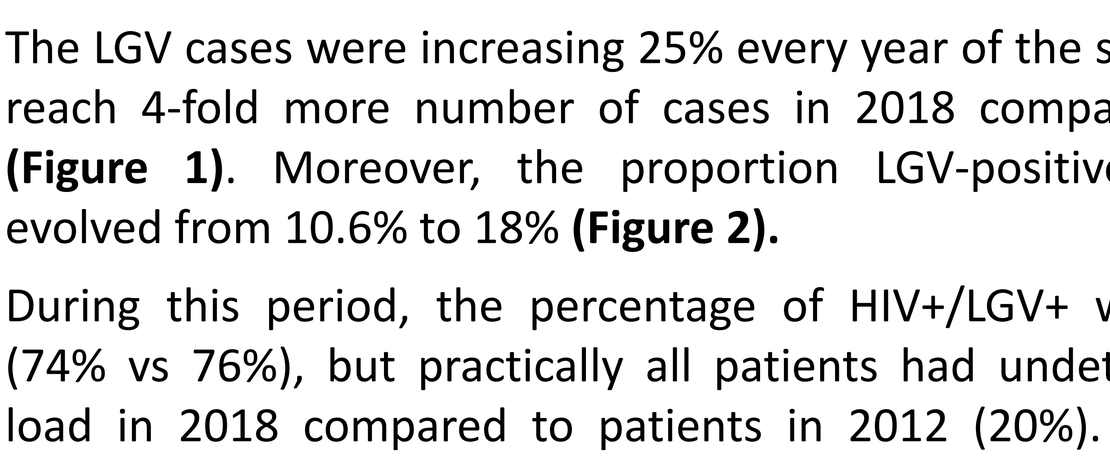


Figure 3: Network of *OmpA* sequences (2012 and 2018)

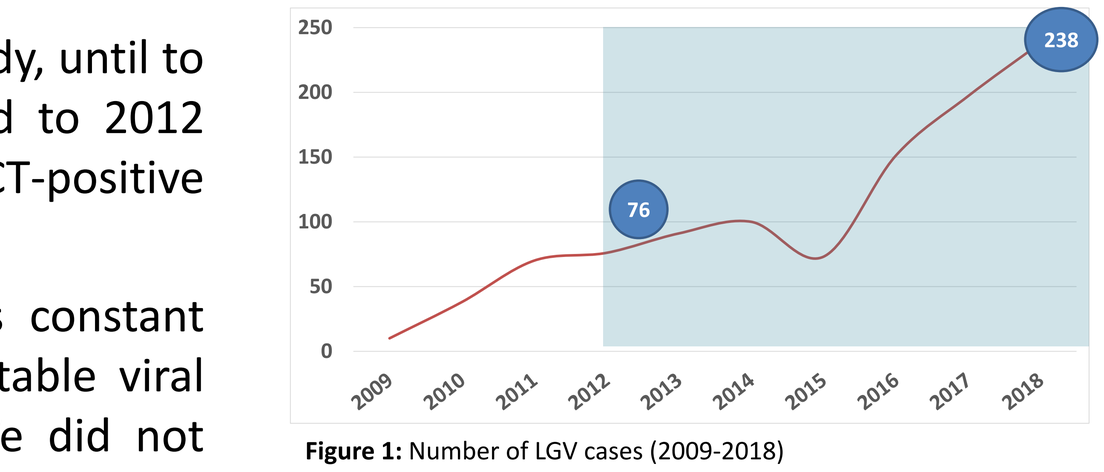


Figure 4: Temporal evolution of each LGV variant during the last period (2016-2018)

Conclusions

- The Spanish epidemiological situation now seems more complex due to an increase in the number of cases but also because of the spreading of new variants.
- These data suggest that it will be increasingly difficult to eradicate LGV infections in the population.

Funded by: PI16/01242

Inconsistencies between HCV testing coverage and seroprevalence in primary care, Catalonia 2011-2016

Juliana Reyes-Urueña[1,2,3], Ana Celly[1,3,4], Sergio Moreno[1,3], Jordi Casabona[1,2,3,4]

1 Centre Estudis Epidemiologics sobre les Infeccions de Transmissió Sexual i Sida de Catalunya (CEEISCAT), Dept Salut, Generalitat de Catalunya, Spain. 2 CIBER Epidemiologia y Salud Pública (CIBERESP), Spain. 3 Institut d'Investigació Germans Trias i Pujol (IGTP), Spain. 4 Departament de Pediatria, d'Obstetrícia i Ginecologia i de Medicina Preventiva, Universitat Autònoma de Barcelona, Bellaterra

Objectives

In an era of effective, safe, all-oral HCV medications, it is not adequate to have less than half of newly identified, chronically infected patients referred for HCV specialized care. Therefore, the purpose of this study was:

1). To gain insights into (primary care provider) PCP HCV testing coverage and the prevalence of anti-HCV in Catalonia, from 2011 to 2016, by examining their epidemiological characteristics and their geographic distribution and coincidence over time.

2). The secondary objectives were to identify the undiagnosed rate and to determine the socio-demographic factors related to anti-HCV diagnosis and undiagnosed.

Methods

Population 274 PCP centres (3,414 GPs)→ (SIDIAP) → anonymized data.

Definitions:

- **HCV testing coverage** was defined as the percentage distribution of women and men eligible for HCV testing, who were tested during the study period. The denominator used was the number of women and men assigned to ABS.
- **Positive HCV test** was defined as the first positive anti-HCV assay recorded in the medical history, based on all HCV testing codes employed by the laboratory database.
- **HCV uninfected or negative** was defined as those without these positive tests, those who did not have a valid serum sample or with an intermediate test result.
- **HCV diagnosed** was defined as those with a positive anti-HCV and with an assigned diagnosis.
- **Denominators:** Number of assigned people to a PCP per year and per period.

Mapping: 6-year maps (2011-2016) → ABS were aggregated in providences using QGIS.

Cluster Detection: Geographic clusters of significantly elevated HCV testing coverage and prevalence of HCV seroprevalence were identified using SaTScan. We ran a retrospective space discrete Poisson model to scan for areas with high testing coverage and seroprevalence, the mean RR of each cluster (including one or more ABS) was also computed.

Statistical analysis: In order to determine the probability to have an positive anti-HCV diagnosis and be undiagnosed it was used the log-binomial model – a generalized linear model where the link function is the logarithm of the proportion of socio-demographic factors related to positive anti-HCV and be undiagnosed by year, adjusted by sex, age category, region of origin and DI. Results obtained using R.

Results

Table 1. Rate of HCV testing coverage in primary care per 1,000 population assigned to the basic health area, by year, sex, age category, region of origin and deprivation index, Catalonia - Spain, 2011-2016.

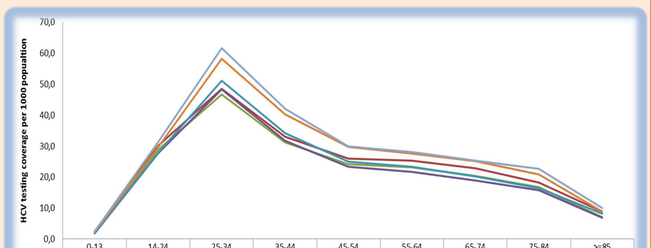
	2011-2016 Period Rate (CI 95%)
Sex	
Men	113.97 (113.63, 114.32)
Women	142.36 (141.99, 142.74)
Age category	
0-13	10.37 (10.15, 10.59)
14-24	146.94 (146.04, 147.84)
25-34	284.11 (283.10, 285.12)
35-44	194.84 (194.08, 195.61)
45-54	143.00 (142.25, 143.74)
55-64	136.37 (135.54, 137.20)
65-74	118.34 (117.47, 119.21)
75-84	103.33 (102.35, 104.31)
>=85	48.07 (47.22, 48.92)
Region of Origin	
Spain	128.86 (128.49, 129.23)
Europe and North America	134.19 (132.93, 135.45)
Africa	208.60 (206.92, 210.29)
Asia	108.48 (107.34, 109.63)
Latin America and The Caribbean	304.10 (301.77, 306.43)
Unknown	111.21 (110.81, 111.60)
Deprivation index	
Rural	99.15 (98.61, 99.69)
Urban 1	120.29 (119.84, 120.74)
Urban 2	134.14 (133.47, 134.82)
Urban 3	154.11 (153.60, 154.61)
Total	**128.26 (128.01, 128.52)**

Table 2. Seroprevalence of HCV in primary care per 1,000 population assigned to the basic health area, by year and entire study period, by sex, age category, region of origin and deprivation index, Catalonia - Spain, 2011-2016.

	2011-2016 Period Seroprevalence (CI 95%)
Sex	
Men	3.74 (3.67, 3.80)
Women	2.74 (2.68, 2.80)
Age category	
0-13	0.14 (0.11, 0.16)
14-24	0.66 (0.59, 0.72)
25-34	2.08 (1.97, 2.18)
35-44	3.81 (3.69, 3.93)
45-54	7.19 (7.01, 7.37)
55-64	4.36 (4.20, 4.52)
65-74	5.11 (4.91, 5.30)
75-84	7.26 (6.99, 7.53)
>=85	3.02 (2.81, 3.24)
Region of Origin	
Spain	3.40 (3.33, 3.46)
Europe and North America	4.41 (4.17, 4.65)
Africa	1.75 (1.58, 1.92)
Asia	3.97 (3.74, 4.20)
Latin America and The Caribbean	1.44 (1.25, 1.64)
Unknown	3.05 (2.98, 3.12)
Deprivation Index	
Rural	4.65 (4.53, 4.77)
Urban 1	1.53 (1.48, 1.58)
Urban 2	8.06 (7.88, 8.24)
Urban 3	1.65 (1.59, 1.71)
Total	**3.23 (3.19, 3.28)**

Urban 1 (urban area with none material deprivation), Urban 2 (urban area with low material deprivation) and Urban 3 (urban area with high material deprivation).

Figure 1. Over-time trend of HCV testing coverage acording to age category in Primary Care, Catalonia- Spain, 2011-2016



	0-13	14-24	25-34	35-44	45-54	55-64	65-74	75-84	>=85
2011	2,4	30,1	48,5	33,0	25,9	25,3	22,8	18,3	8,8
2012	2,1	28,8	46,6	31,2	24,2	23,2	20,4	16,7	7,0
2013	1,8	27,7	48,3	31,7	23,4	21,7	18,9	15,7	6,9
2014	1,9	27,7	51,1	34,2	25,0	23,3	20,2	16,3	8,1
2015	2,3	29,5	58,2	40,3	29,7	27,6	25,1	20,9	8,9
2016	2,4	31,2	61,6	42,1	29,9	28,1	25,3	22,7	10,1

Between, 2011-2016 there were **839,072** people tested for HCV infection, **21156 anti-HCV** tests were identified as the first positive test, and **22356 anti-HCV** were performed in people who already were identified as a seroprevalent, the average of repeated tests performed in one person was of **13.5** (min-max; 2-25). The period rate of HCV testing coverage was **of 128.26/10³ pop (95% CI; 128.01-128.52)**

Figure 3. Geographic clusters of significantly elevated HCV testing coverage Catalonia-Spain, 2011-2016.

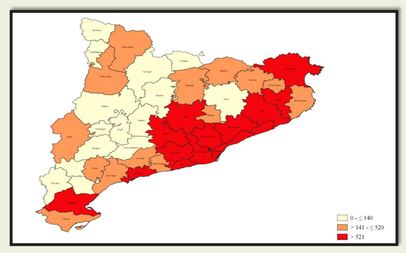


Figure 4. Geographic clusters of significantly elevated HCV seroprevalence Catalonia-Spain, 2011-2016.

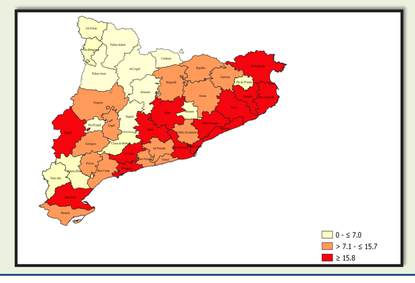


Table 3. Baseline characteristics of people tested for HCV in primary care comparing by test result, and socio-demographic determinants of having a positive anti-HCV, Catalonia, 2011-2016.

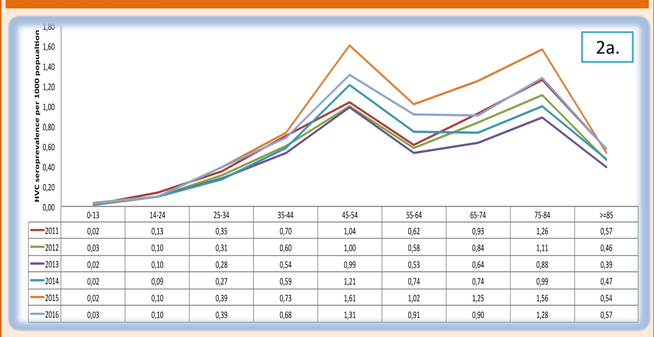
	Anti-HVC (+) n (%) N=21156	Anti-HVC (-) n (%) N=817916	Total N= 839072	Adjusted OR (95% CI)
Sex				
Women	9020 (42.63)	459734 (56.20)	468754 (55.86)	Ref.
Men	12136 (57.36)	358182 (43.79)	370318 (44.13)	1.52 (1.46-1.57)
Age [median-(IQR)]	52 (25)	39 (23)	45 (24)	
Age category				
<13	91 (0.43)	8148 (0.99)	8239 (0.98)	2.07 (1.58-2.71)
14-24	350 (1.65)	87119 (10.65)	87469 (10.42)	Ref.
25-34	1519 (7.17)	215341 (26.32)	216860 (25.84)	1.76 (1.53-2.02)
35-44	3823 (18.07)	199018 (24.33)	202841 (24.17)	4.36 (3.82-4.97)
45-54	6120 (28.92)	115266 (14.09)	121386 (14.46)	10.88 (9.56-12.39)
55-64	2986 (14.11)	86354 (10.55)	89340 (10.64)	7.19 (6.28-8.22)
65-74	2699 (12.75)	60069 (7.34)	62768 (7.48)	9.26 (8.08-10.62)
75-84	2742 (12,96)	35634 (4.35)	38376 (4.57)	15.52 (13.52-17.81)
>85	826 (3.90)	10967 (1.34)	11793 (1.41)	14.33 (12.16-16.89)
Region of Origin				
Spain	16521 (78.09)	585480 (71.58)	602001 (71.75)	Ref.
Europe and North America	1957 (9.25)	53556 (6.55)	55513 (6.62)	1.90 (1.78-2.03)
Africa	608 (2.88)	68581(8.38)	69190 (8.25)	0.56 (0.51-0.62)
Asia	1738 (8.22)	67180 (5.27)	44857 (5.35)	2.15 (2.01-2.30)
Latin America and The Caribbean	331 (1.57)	67180 (8.21)	67512 (8.05)	0.28 (0.25-0.33)
Deprivation index				
Rural	3036 (15.50)	113193 (14.66)	116229 (14.7)	1.14 (1.08-1.21)
Urban 1	5451 (27.83)	233255 (30.22)	238706 (30.2)	Ref.
Urban 2	3276 (16.72)	126949 (16.44)	130225 (16.5)	1.13 (1.07-1.19)
Urban 3	7822 (39.93)	298348 (38.65)	306170 (38.7)	1.16 (1.11-1.22)

Table 4. Baseline characteristics of HCV diagnosed and undiagnosed people in primary care and socio-demographic determinants of being undiagnosed, Catalonia, 2011-2016.

	HCV diagnosed people n (%) N=10628 (50.2)	HCV undiagnosed people n (%) N=10528 (49.8)	Total n (%) 21156	Adjusted OR (95% CI)
Sex				
Women	6352 (52,34)	5784 (47,66)	12136 (57.36)	Ref.
Men	4276 (47,41)	4744 (52,59)	9020 (42.64)	1.10 (1.02-1.18)
Age [median-(IQR)]				
Age category				
<13	30 (27,27)	80 (72,73)	110 (0.52)	0.66 (0.38-1.16)
14-24	158 (40,41)	233 (59,59)	391 (1.85)	Ref.
25-34	919 (58,02)	665 (41,98)	1584 (7.49)	1.89 (1.44-2.49)
35-44	2251 (56,77)	1714 (43,23)	3965 (18.85)	2.29 (1.76-2.97)
45-54	3285 (53,81)	2820 (46,19)	6105 (28.86)	2.18 (1.68-2.82)
55-64	1382 (48,41)	1473 (51,59)	2855 (13.49)	1.66 (1.27-2.18)
65-74	1171 (43,24)	1537 (56,76)	2708 (12.80)	1.47 (1.12-1.93)
75-84	1122 (41,62)	1574 (58,38)	2696 (12.74)	1.45 (1.10-1.92)
>85	310 (41,78)	432 (58,22)	742 (3.51)	1.60 (1.15-2.23)
Region of Origin				
Spain	5150 (48,5)	5468 (51,5)	10618 (50.19)	Ref.
Europe and North America	824 (66,13)	422 (33,87)	1246 (5.89)	1.93 (1.68-2.21)
Africa	183 (46,56)	210 (53,44)	393 (1.86)	0.95 (0.76-1.18)
Asia	838 (74,82)	282 (25,18)	1120 (5.29)	3.01 (2.58-3.51)
Latin America and The Caribbean	95 (43,98)	121 (56,02)	216 (1.02)	0.83 (0.62-1.10)
Unknown	3538 (46,78)	4025 (53,22)	7563 (35.75)	-
Deprivation index				
Rural	1464 (48,22)	1572 (51,78)	3036 (14.35)	0.94 (0.84-1.06)
Urban 1	2742 (50,3)	2709 (49,7)	5451 (25.77)	Ref.
Urban 2	4005 (51,2)	3817 (48,8)	7822 (36.97)	0.97 (0.87-1.09)
Urban 3	1628 (49,69)	1648 (50,31)	3276 (15.48)	0.95 (0.87-1.04)
Unknown	789 (50,22)	782 (49,78)	1571 (7.43)	-

Urban 1 (urban area with none material deprivation), Urban 2 (urban area with low material deprivation) and Urban 3 (urban area with high material deprivation). CI: Confidence Intervals; OR: Odds Ratio; IQR: Interquartile range. Log-binomial model was adjusted by sex, age category, region of origin, and depravation index.

Figure 2. Over-time trend of HCV testing coverage acording to age category in Primary Care, Catalonia- Spain, 2011-2016 2a. Total 2b. Men 2c Women



	0-13	14-24	25-34	35-44	45-54	55-64	65-74	75-84	>=85
2011	0,02	0,13	0,35	0,70	1,04	0,62	0,93	1,26	0,57
2012	0,03	0,10	0,31	0,60	1,00	0,58	0,84	1,11	0,46
2013	0,02	0,10	0,28	0,54	0,99	0,53	0,64	0,88	0,39
2014	0,02	0,09	0,27	0,59	1,21	0,74	0,74	0,99	0,47
2015	0,02	0,10	0,39	0,73	1,61	1,02	1,25	1,56	0,54
2016	0,03	0,10	0,39	0,68	1,31	0,91	0,90	1,28	0,57

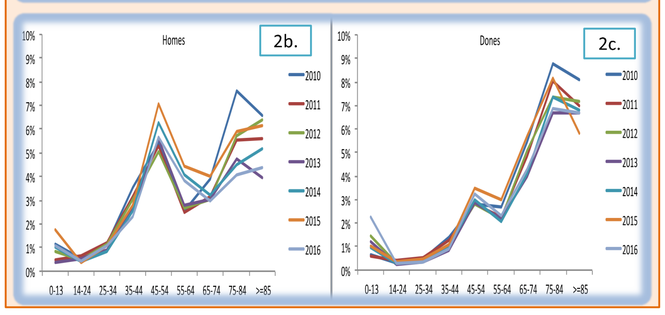
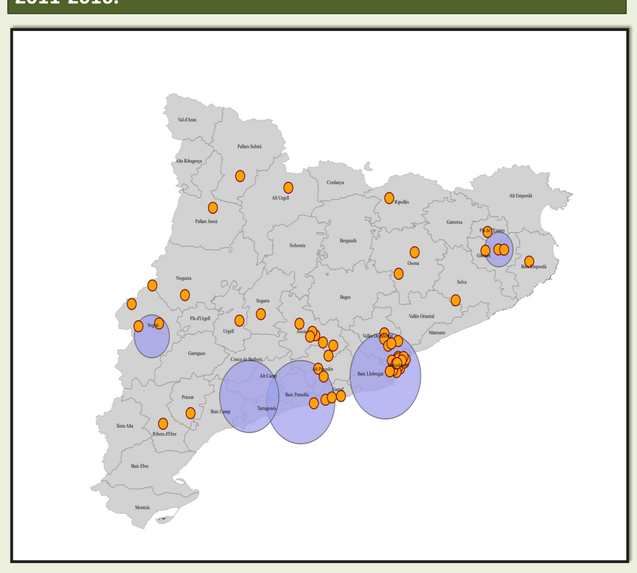


Figure 5. Geographic clusters of significantly elevated HCV testing coverage and high HCV seroprevalence Catalonia-Spain, 2011-2016.



Clusters of significantly elevated HCV seroprevalence

Clusters of significantly elevated HCV testing coverage

Conclusions

- HCV testing coverage was found higher among women, between 25-34 years old and from Latin America, whereas, seroprevalence was higher among men, between 45 and 54 years and over 75 years of age, and from Spain, Northern Europe and Asia. This means that we found a discrepancy between the population tested and the HCV seroprevalent population.
- Determinants of being Anti-HCV positive were being male, between 45 and 54 years and older than 75 years and Asian.
- One of the striking finding was that **49.8%** of people with **positive anti-HCV** did not have an associated diagnosis, and its determinants were being male, between 25 and 54 years of age and from Asia.
- We also found a geographic discrepancy between testing coverage and HCV seroprevalence.

Sweetie project: prevalence and determinants of sexually transmitted infections in a high risk population

Proyecto Sweetie: prevalencia y determinantes de infecciones de transmisión sexual en una población de alto riesgo

L. Alemany[1,2º], L. Ferrer[2,3º], V. Rodriguez[1] , V. González[2,3], E. Martró[2,4], R. Muñoz[3], V. Saludes[2,4], MA. Pavón[1,5], S. Paytubi[1], M. Torres[1], S.Tous[1,5], C. Folch[2,3], F. Pérez[6], M. Cebrián[7], C. Fons[6,7], M. Villar[6], L. Villegas[6], M. Meroño[7], S. de Sanjose[1,2,8*], J. Casabona[1,2*] y Grupo Sweetie

[1] Programa d'Investigació d'Epidemiologia del Càncer, Institut Català d'Oncologia (ICO), L'Hospitalet de Llobregat (Barcelona); [2] Consorcio de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Instituto de Salud Carlos III, Madrid; [3] Centre d'Estudis. Epidemiològics sobre les ITS i la Sida de Catalunya (CEEISCAT), Agència de Salut Pública de Catalunya (ASPCAT); [4] Servicio de Microbiología, Laboratorio Clínico Metropolitana Norte, Hospital Universitario Germans Trias i Pujol, Instituto de Investigación Germans Trias i Pujol (IGTP), Badalona (Barcelona); [5] Consorcio de Investigación Biomédica en Red de ONCología (CIBERONC), Instituto de Salud Carlos III, Madrid; [6] STOP SIDA, Barcelona; [7] Fundació AMBIT Prevenció, Barcelona; [8] PATH, Seattle. (º) Co-main autors; (*) Co-Seniors

Antecedentes y objetivos

Los hombres *cisgénero* y mujeres transgénero trabajadores sexuales (HTS y TTS, respectivamente) son poblaciones de difícil acceso en programas de prevención y detección de infecciones de transmisión sexual (ITS).

Los objetivos del estudio son describir la prevalencia y determinantes de ITS (Virus del Papiloma Humano-VPH, *Chlamydia trachomatis*-CT, *Neisseria gonorrhoeae*-NG, Virus de la hepatitis B y C-VHB/C) en población de HTS y TTS, de Barcelona y área metropolitana.

Materiales y métodos

- Estudio tranversal
- Criterios inclusión: ≥ 18 años, ejercer trabajo sexual, firmar consentimiento informado
- Periodo reclutamiento: 2017-2018
- Recogida de datos:
  - Epidemiológicos
  - Muestras biológicas: oral, faringe, anal, perianal, pene, orina, sangre
- Análisis moleculares:
  - VPH: ADN-Anyplex II HPV28
  - CT/NG: ADN-BD Max CT/NG
  - VHB/C: Anticuerpos-Vitros, ARN-Abbott

Resultados

Descripción del perfil sociodemográfico y conductual de los/las participantes

Características socio-demográfica según el género

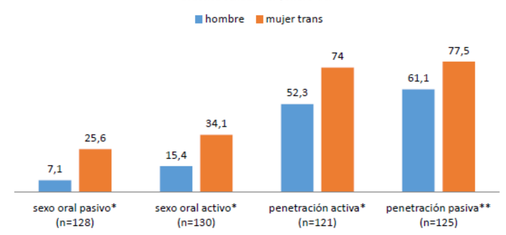
	Hombres (N=47)	Mujeres trans (N=100)	p-valor
edad media (Desviación Estándard, DE)	33 (8,1)	36 (10)	(Anova) <0,1
Nivel educativo (%)			<0,05
primario	**2,1**	**21,7**	
secundario	**61,7**	**68,5**	
universitario completo	21,3	1,1	
universitario incompleto	14,9	8,7	
Origen (%)			<0,1
España	14,9	6	
Otro	**85,1**	**94**	

9% de los/las participantes iniciaron las relaciones sexuales antes de los 10 años

Trabajo sexual y conducta sexual con los clientes

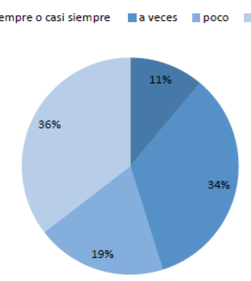
	Hombres	Mujeres trans	Anova
media de años dedicados al trabajo sexual (DE)	4,5 (5,1)	12,5 (10,9)	<0,05
Media de clientes/ semana (DE)	5,9 (5,8)	9,5 (7,8)	<0,05

Uso consistente del preservativo el último mes con los clientes según la práctica sexual y el género (%)



*p<0,05; **p<0,1

Frecuencia de consumo de drogas recreativas de los/las participantes antes o durante las relaciones con un cliente el último mes (N=144)



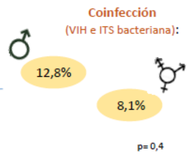
2,8% de los/las participantes se han inyectado drogas

Prevalencia de VIH e ITS

	Hombre (n=47)	Mujer trans (n=100)	Total (n=147)	p-valor
VIH	25,5	25,3	25,3	ns
CT	10,6	10,1	10,3	ns
orina	6,4	0	2	0,01
faringe	0	7	4,8	0,1
anal	6,4	4	4,8	0,7
NG	19,1	19,2	19,2	ns
orina	0	0,1	0,7	1,0
faringe	14,9	14	14,3	0,9
anal	12,8	8,1	9,6	0,6
VPH	93,3	95,9	95,1	ns
orina	22,5	10	13,8	0,06
oral	15,6	16,1	15,9	0,9
anal	82,6	91,8	88,8	0,1
pene	47,8	38,1	40,7	0,4
perianal	94,4	92,1	92,9	0,4

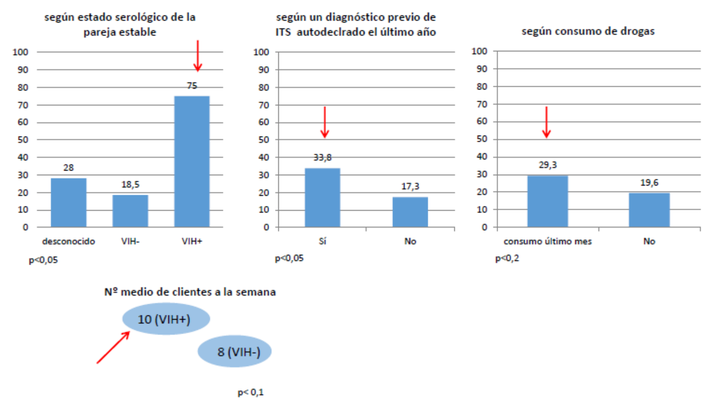
	Hombre (n=39)	Mujer trans (n=84)	Total (n=123)	p-valor
VHC activa	0	0	0	ns
VHC exposición previa	5,1	1,2	2,4	0,3
VHB activa	0	1,2	0,8	ns
VHB exposición previa	28,2	36,9	34,1	0,3

Coinfección (VIH e ITS bacteriana):



Prevalencia del VIH según variables epidemiológicas

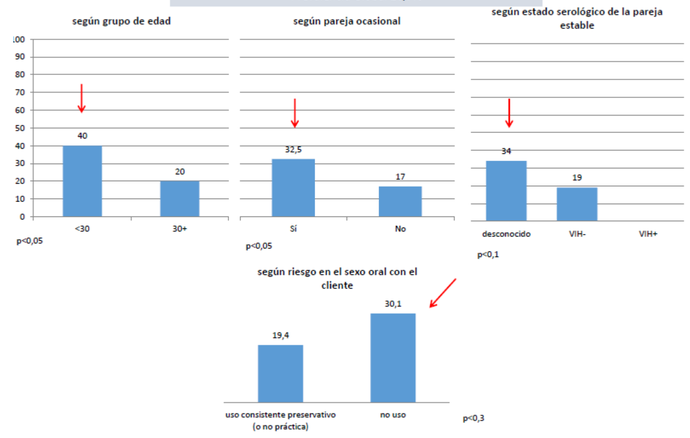
Prevalencia Global 25,3%



Nº medio de clientes a la semana

Prevalencia de ITS bacterianas según variables epidemiológicas

Prevalencia Global 26,7%



Conclusiones

- Los HTS y TTS presentan elevadas prevalencias de VIH/ITS y de exposición de riesgo
- Existen diferencias entre algunos determinantes socio-económicos, y las condiciones y prácticas sexuales entre HTS y TTS
- El proyecto ha visibilizado a los HTS y TTS en nuestro contexto
- La colaboración entre centros de investigación y centros comunitarios ha hecho posible la implementación del estudio y podernos acercar a estas poblaciones clave

Assessing the role of dietary patterns in the etiology of lymphoid neoplasms

Marta Solans[1,2,3], Yolanda Benavente[1,4], Adela Castelló[1,5,6], Marina Pollán[1,5], Rafael Marcos-Gragera[1,2,3], Marc Saez[1,2], Delphine Casabonne[1,4] on behalf of the EPIC and MCC-Spain groups.

1. Centro de Investigación Biomédica en Red: Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
2. Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Girona, Spain **contact: marta.solans@udg.edu**
3. Epidemiology Unit and Girona Cancer Registry, Catalan Institute of Oncology, Girona, Spain
4. Unit of molecular epidemiology and genetic in infections and cancer (UNIC-Molecular), Cancer Epidemiology Research Program, IDIBELL, Catalan Institute of Oncology, L'Hospitalet De Llobregat, Spain
5. Environmental and Cancer Epidemiology Unit, National Center of 6. Epidemiology, Instituto de Salud Carlos III, Madrid, Spain,
7. Faculty of Medicine, University of Alcalá, Alcalá de Henares, Madrid, Spain

Background

Previous studies examining the association between diet and lymphoid neoplasms have focused on nutrients or single-food items, yielding inconclusive results.

Objective

This study aimed to evaluate the association between several dietary patterns and lymphoid malignancies, using data from the European prospective investigation into cancer and nutrition (EPIC) and the multicase-control Spanish (MCC-Spain) studies.

Methods

- **EPIC study**: 476,160 subjects and 3136 lymphoma cases (after 13.9 average follow-up).
- **MCC-Spain study**: 369 chronic lymphocytic leukemia (CLL) cases and 1,605 controls.
- The adapted relative Mediterranean diet index (arMED), ii) the inflammatory score of diet (ISD), iii) a Western, Prudent, and Mediterranean *a posteriori* dietary patterns, and iv) the 2018 Word Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) score were reconstructed in the EPIC (i., ii., and iii.– only Western) and MCC-Spain (iii. and iv.) studies.

Results

- EPIC study -

Table 1. Association between adherence to the arMED, the ISD, and a Western dietary pattern and risk of lymphoma and its subtypes in the EPIC study.

	Lymphoma		HL		NHL		Mature T/NK-cell		Mature B-cell	
	N	HR[1] (95% CI)	N	HR[1] (95% CI)	N	HR[1] (95% CI)	N	HR[1] (95% CI)	N	HR[1] (95% CI)
arMED										
Low	**1,016**	Ref	**39**	Ref	**835**	Ref	**47**	Ref	**766**	Ref
Medium	**1,371**	0.93 (0.85; 1.02)	**65**	0.97 (0.61; 1.53)	**1,128**	0.90 (0.82; 1.00)	**54**	0.72 (0.47; 1.14)	**1,043**	0.91 (0.82; 1.01)
High	**749**	0.91 (0.80; 1.03)	**31**	0.64 (0.34; 1.19)	**643**	0.94 (0.82; 1.08)	**29**	0.78 (0.42; 1.44)	**593**	0.95 (0.82; 1.10)
P-trend[2]		0.12		0.16		0.31		0.35		0.4
1-unit increase		**0.98 (0.97; 1.00)**		0.93 (0.86; 1.01)		0.98 (0.97; 1.00)		0.99 (0.91; 1.07)		0.98 (0.97; 1.00)
ISD										
Q1	**784**	Ref	**25**	Ref	**658**	Ref	**34**	Ref	**603**	Ref
Q2	**783**	1.01 (0.91; 1.13)	**35**	1.48 (0.86; 2.57)	**659**	1.03 (0.91; 1.15)	**35**	0.86 (0.51; 1.43)	**608**	1.05 (0.93; 1.19)
Q3	**786**	1.04 (0.92; 1.16)	**35**	1.60 (0.88; 2.90)	**647**	1.04 (0.92; 1.19)	**31**	0.70 (0.39; 1.25)	**596**	1.08 (0.94; 1.23)
Q4	**783**	1.07 (0.93; 1.22)	**40**	1.90 (0.97; 3.71)	**642**	1.10 (0.94; 1.27)	**30**	0.61 (0.31; 1.19)	**595**	1.15 (0.99; 1.35)
P-trend[2]		0.34		0.08		0.24		0.12		0.08
1-SD increase		1.05 (1.00; 1.11)		1.22 (0.94; 1.57)		**1.06 (1.00; 1.13)**		0.99 (0.76; 1.29)		**1.07 (1.01; 1.14)**
Western										
Q1	**781**	Ref	**26**	Ref	**660**	Ref	**41**	Ref	**604**	Ref
Q2	**818**	1.06 (0.96; 1.18)	**39**	1.51 (0.91; 2.50)	**672**	1.03 (0.93; 1.15)	**25**	0.62 (0.38; 1.03)	**621**	1.05 (0.93; 1.17)
Q3	**724**	0.96 (0.86; 1.06)	**30**	1.19 (0.68; 2.06)	**599**	0.93 (0.83; 1.05)	**35**	0.84 (0.52; 1.35)	**547**	0.94 (0.83; 1.06)
Q4	**813**	1.03 (0.92; 1.16)	**40**	1.49 (0.84; 2.63)	**675**	1.01 (0.90; 1.15)	29	0.66 (0.38; 1.14)	630	1.05 (0.92; 1.19)
P-trend[2]		0.948		0.318		0.771		0.237		0.907
1-SD increase		1.02 (0.98; 1.06)		1.02 (0.86; 1.21)		1.02 (0.98; 1.07)		0.89 (0.72; 1.11)		1.04 (0.99; 1.08)

N, number of cases; HR, hazard ratio; CI, confidence interval; SD, standard deviation; Q, quartile; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; [1]Multivariate model: Cox proportional hazard model stratified by age (in 1-year categories), center and sex, and further adjusted for body mass index, total energy intake, educational level, height, physical activity, smoking status, and alcohol intake. [2]P value of Cox proportional model fitted with the dietary pattern ordinal variable as continuous to test for lineal trend.

For the three dietary patterns, null associations were reported for all mature B-cell subtypes: diffuse large B-cell lymphoma, follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, and multiple myeloma/plasma cell neoplasms (*data not shown*).

Conclusions

- Overall, our results suggest that dietary patterns may have, at best, a modest role in lymphoma etiology.
- Further large prospective studies with lymphoma subtype-specific data are warranted to confirm these findings.

- MCC-Spain study -

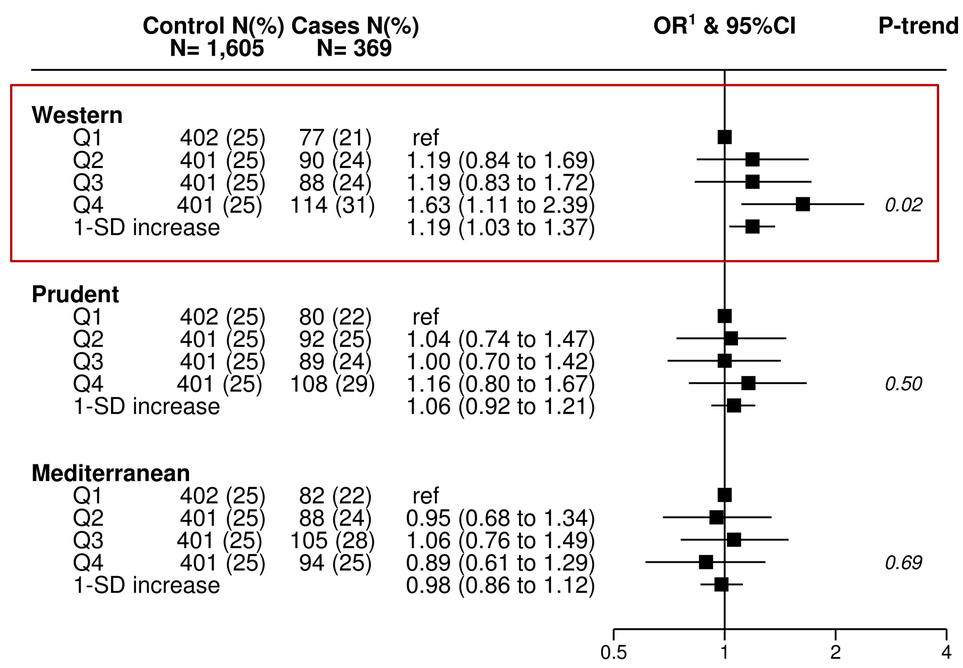


Figure 1. Association between adherence to dietary patterns and chronic lymphocytic leukemia in the MCC-Spain study. OR, Odds Ratio; 95%CI, 95% confidence interval; Q: quartile; SD: standard deviation. Black squares indicate OR and horizontal lines represent 95%CI. [1]Logistic regression models adjusted for age, sex, education, energy intake (kcal/day) with province of residence as random effect.

Table 3. Association between adherence to the 2018 WCRF/AICR score and chronic lymphocytic leukemia in the MCC-Spain study.

	CLL		
	N cases	N controls	HR[1] (95% CI)
WCRF/AICR 2018			
T1	124	558	Ref
T2	93	371	1.08 (0.78; 1.48)
T3	101	374	1.25 (0.91; 1.73)
P-trend[2]			0.172
1-unit increase			1.06 (0.91; 1.23)

N, number; OR, odds ratio; 95% CI, 95% confidence interval; T, tertile. [1]Logistic regression analyses adjusted for age, sex, educational level, province, family history of hematological neoplasms, ever worked in farming or agriculture, total energy intake, and smoking. [2]P value of Cox proportional model fitted with the score variable as continuous to test for lineal trend.

Acknowledgments

EPIC/MCC-Spain collaborators and CIBERESP

Energy poverty and health: trends in the European Union before and during the economic crisis, 2007-2016

Oliveras L[1,2,3], Peralta A[1,3], Palència L[1,2,4], Gotsens M[1,2], López MJ[1,2,3,4], Artazcoz L[1,2,3,4], Borrell C[1,2,3,4], Marí-Dell'Olmo M[1,2,4]

[1]Agència de Salut Pública de Barcelona; [2]Institut d'Investigació Biomèdica Sant Pau, [3]Department of Experimental and Health Science, Universitat Pompeu Fabra; [4]CIBER Epidemiología y Salud Pública (CIBERESP)

Funding: CIBERESP/ISCIII (PI15/02006)

Introduction

Energy poverty (EP) can be understood as the inability of a household to secure a socially and materially required level of energy services in the home.[1] Several studies have shown how EP negatively affects people's health and well-being.[2] The economic crisis that started in 2008 in Europe has directly affected the structural determinants of EP, which may have further worsened the effects on health.

Objective 1

To create an index of structural EP vulnerability for 27 countries of the European Union (EU) and to define country typologies according to the value of the index.

Objective 2

To analyse the time trend in the EU by country typology before and during the economic crisis in 1) the EP prevalence; 2) the association between EP and health; and 3) the impact of EP on health.

Methods 1

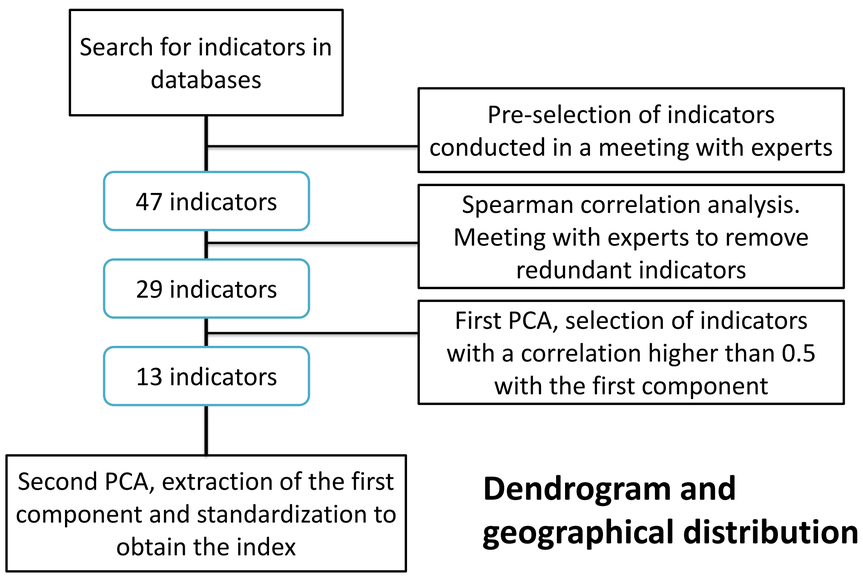
- Ecological cross-sectional study; analysis units were EU-27 countries.
- Collection of indicators on the three structural dimensions of EP: 1) Labor Market and Welfare State; 2) Housing Market and Policies and 3) Energy Market and Policies. Taken mainly from the Eurostat database and for the period 2010-2017.
- Pre-selection of indicators through a meeting with experts.
- Creation of a composite index through principal component analyses.
- Hierarchical cluster analysis to group countries according to their index value.

Methods 2

- Individual-based trends study which analyses three cross-sectional waves (2007, 2012, 2016) of the European Quality of Life Survey.
- The dependent variables studied were poor self-reported health, reduced well-being and poor mental health. The main independent variable was EP, defined as the inability to afford to keep the home adequately warm during the cold months.
- Calculation through age adjusted Poisson regression models with robust variance of 1) prevalence ratios (PR) as an association measure and 2) population attributable risk percent (PAR%) as an impact measure.
- Analyses were stratified by sex and country typologies.

Results 1

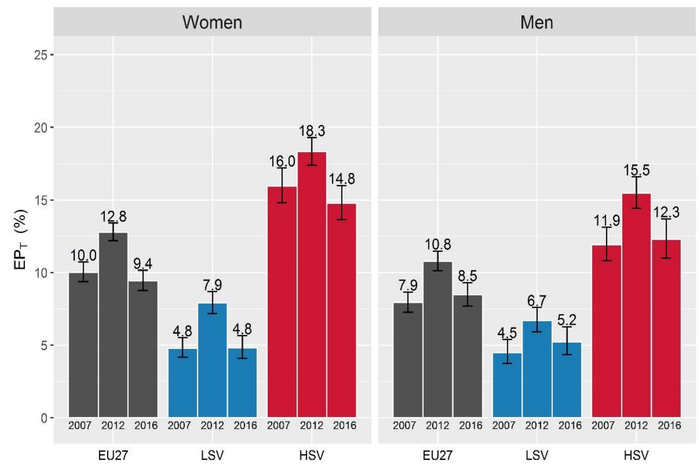
Flowchart representing the steps taken to obtain the index



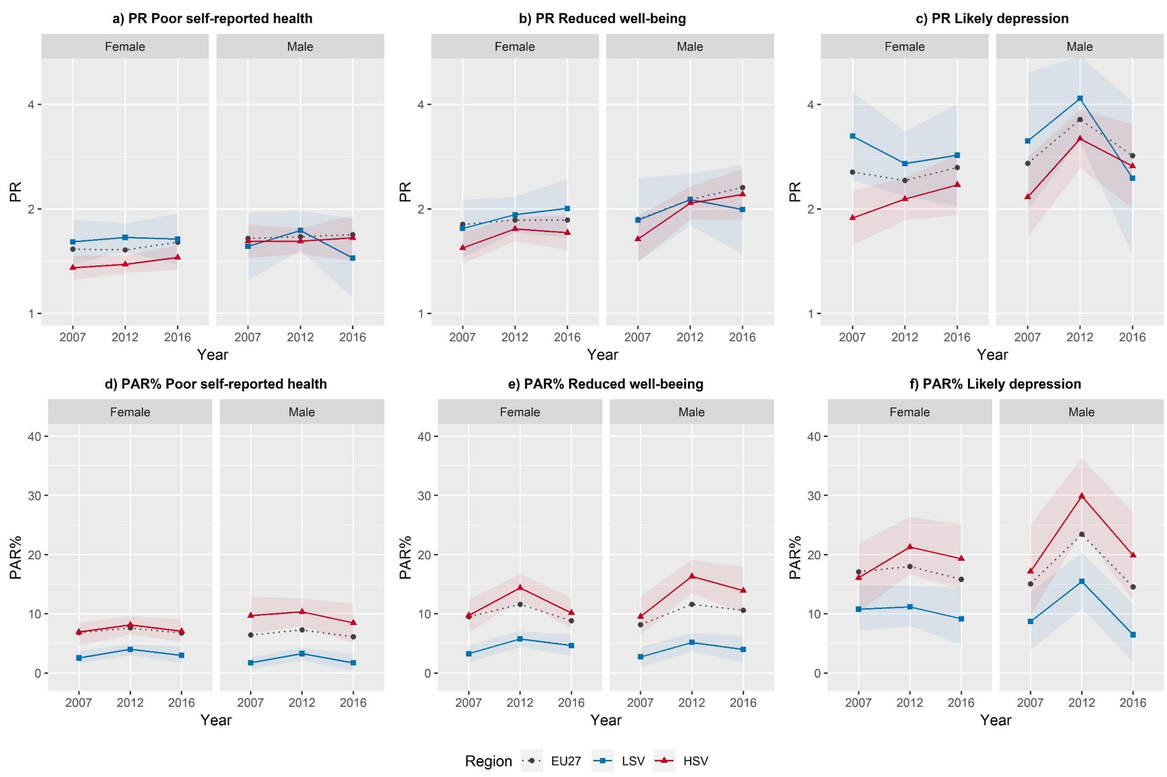
Dendrogram and geographical distribution

Results 2

Trend in EP over time in countries with Low Structural Vulnerability (LSV) and High Structural Vulnerability (HSV) to EP.



Trend in the association (PR) and impact (PAR%) of EP on health outcomes.



Conclusion

- There are geographical patterns in the distribution of structural energy poverty vulnerability in the EU, with the countries of southern and eastern Europe being most affected.
- Energy poverty and its impact on health worsened in the EU during the economic crisis, most of all for women and in countries with higher structural vulnerability to energy poverty.

[1]Bouzarovski S. Energy poverty in the European Union: Landscapes of vulnerability. *Wiley Interdiscip Rev Energy Environ*. 2014; [2]Marmot Review Team. The Health Impacts of Cold Homes and Fuel Poverty.

La violencia contra la mujer en la pareja en las distintas etapas de la vida. Factores de riesgo e impacto en salud

Belén Sanz-Barbero [1,2], Natalia Barón[3] , Carmen Vives-Cases[2,3]

1. Instituto de Salud Carlos III. España.; 2. CIBER de Epidemiología y Salud Pública (CIBERESP).; 3. Universidad de Alicante. España.

Objetivo

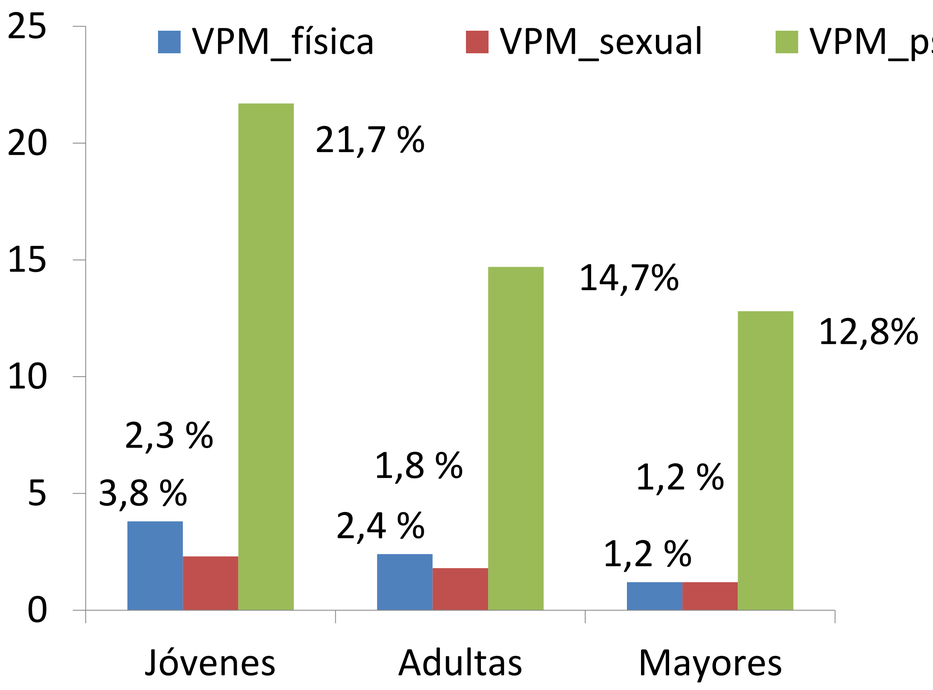
Analizar, en el contexto español, la prevalencia, los factores de riesgo y el impacto en salud de la Violencia de Pareja contra la Mujer (VPM) en distintas etapas de la vida.

Metodología

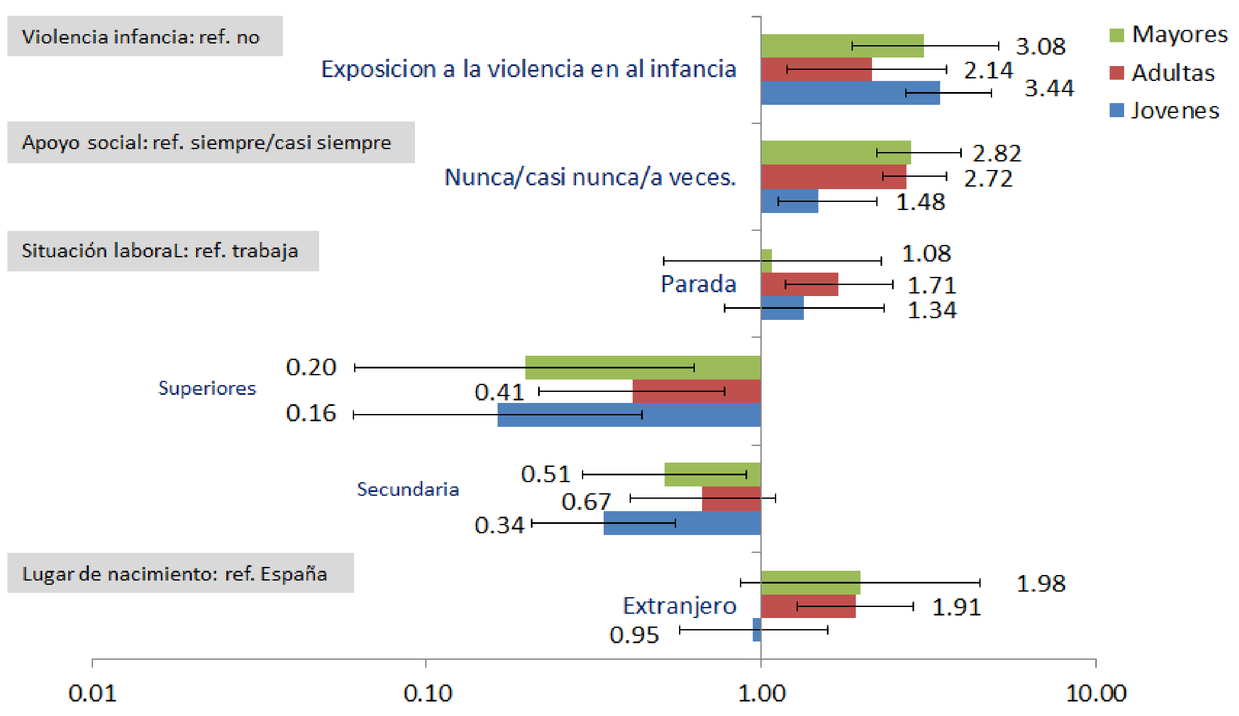
Estudio transversal de Macroencuesta de Violencia contra la Mujer, 2015. Incluye una sub-muestra de 9805 mujeres residentes en España de 16 y más años de edad, que tenían o habían tenido pareja. Variables dependiente: VPM física y/o sexual últimos 12 meses; VPM psicológica últimos 12 meses; limitación de actividad, mala salud percibida, mala salud mental. Covariables: País de nacimiento, estudios, situación laboral, apoyo social, exposición a la violencia. Análisis estratificado en grupos de edad: jóvenes (16-29 años), adultas (30-49 años) y mayores (mayor de 50 años). El análisis se realizó mediante la estimación de razones de prevalencia (RP), obtenidas por regresiones de Poisson robusta.

Resultados

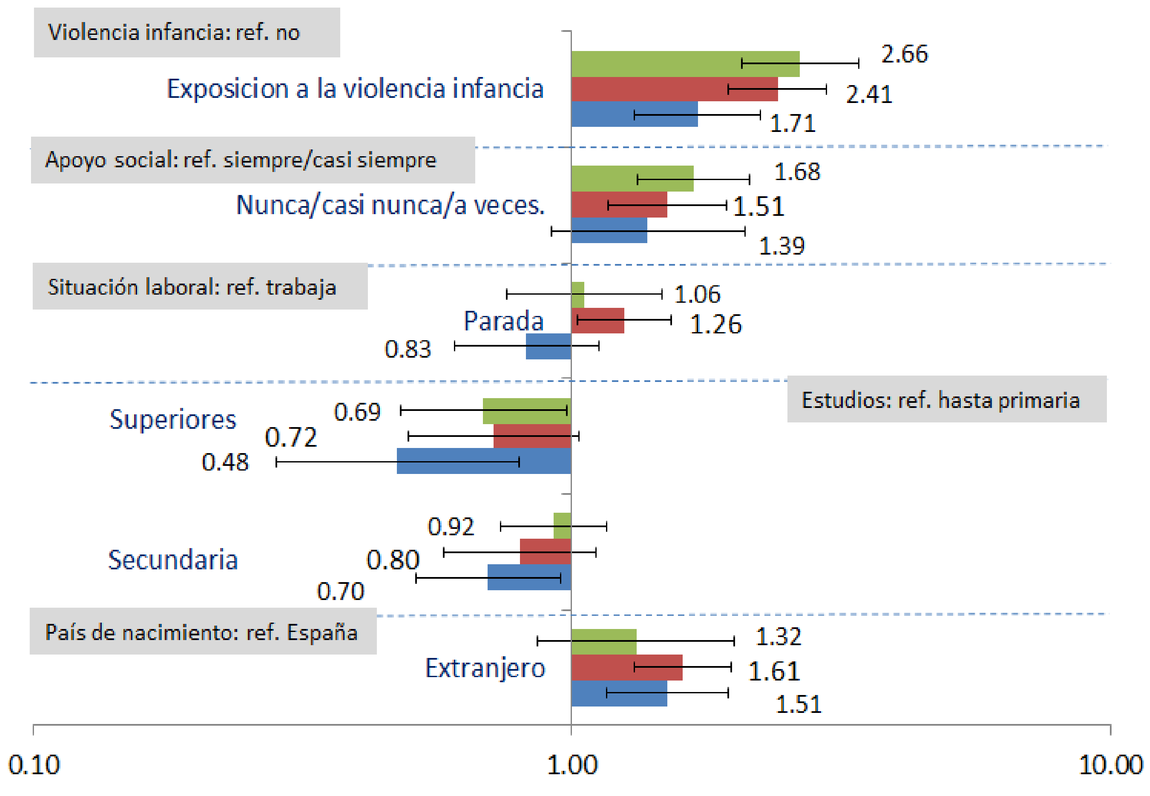
Prevalencia de la VPM física, sexual y psicológica por grupos de edad. Últimos 12 meses.



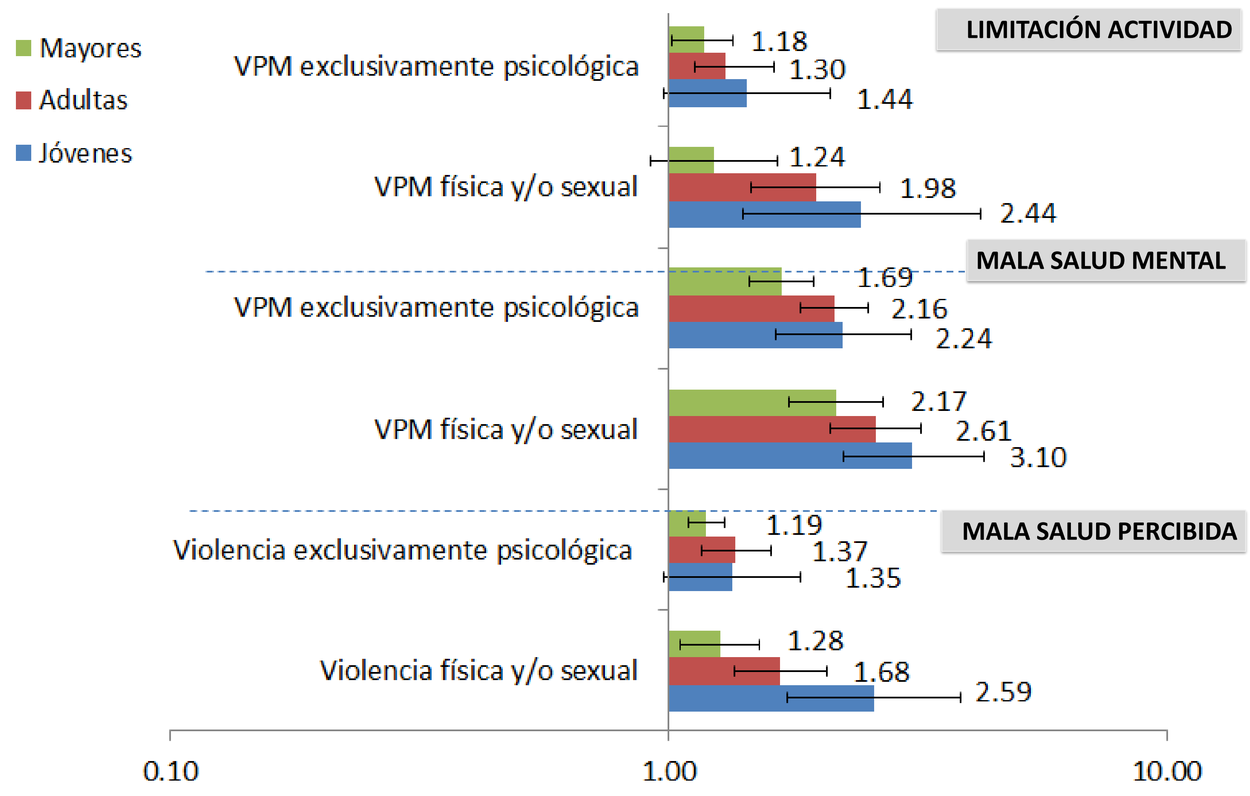
Variables asociadas a la prevalencia de la VPM física y/o sexual, últimos 12 meses por grupos de edad.



Variables asociadas a la prevalencia de la VPM exclusivamente psicológica últimos 12 m. por grupos de edad.



Asociación entre el estado de salud y la VPM, últimos 12 m, por grupos de edad .Macroencuesta de Violencia de Género, 2015



Conclusiones

La variable que incrementa en mayor medida el riesgo de cualquier tipo de VPM, es la exposición a abusos en la infancia. Estar en situación de desempleo incrementa la probabilidad e sufrir cualquier tipo de VPM en las mujeres adultas. Tener un nivel de estudio alto protege mayoritariamente a la población joven de sufrir VPM. La VPM física y/o sexual es más prevalente en las mujeres inmigrantes adultas que en las mujeres españolas. La VPM psicológica es más prevalente las mujeres inmigrantes jóvenes y adultas. Las salud de las mujeres se ve fuertemente deteriorada por la exposición de a la VPM, tanto si esta violencia de física/sexual como si es exclusivamente psicológica.

Financiación: Proyecto AESI expediente número PI17CIII/0002

Long-term physical activity induces brain resilience in middle-aged adults

Rubén Corpas[1], Elisabeth Solana[2], Adrian De la Rosa[3], Sara Sarroca[1], Christian Griñán-Ferré[4], Mireia Oriol[5], Emili Corbella[6], Eduard Rodríguez-Farré[1], Jose Viña[3], Mercè Pallàs[4], David Bartrés-Faz[2], Mari Carmen Gomez-Cabrera[3], Coral Sanfeliu[1]

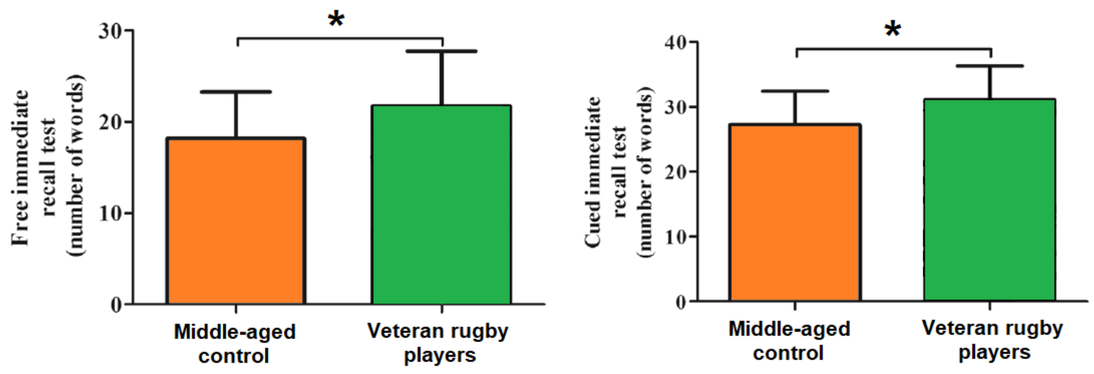
[1]CIBERESP, IIBB-CSIC and IDIBAPS, Barcelona. [2]Facultat de Medicina, Universitat de Barcelona and IDIBAPS, Barcelona. [3]Faculty of Medicine, University of Valencia, CIBERFES, and INCLIVA, Valencia. [4]Facultat de Farmàcia i Ciències de l'Alimentació, Universitat de Barcelona, and CIBERNED, Barcelona. [5]Hospital Clínic, Barcelona. [6] Hospital de Bellvitge, Barcelona.

AIM: **Physical activity** practiced regularly is known to improve the well-being and to reduce the risk of age-related diseases. We aimed to determine the impact of long-term physical activity on **memory maintenance** and search for **peripheral blood markers** related to cognitive function that may be detectable at middle-age.

METHODS: We performed neuropsychological analyses to veteran **amateur rugby players** (n = 24, age: 46–68 y) and **middle-aged sedentary controls** (n = 25, age: 47–67 y). We analyzed the expression of selected genes in whole blood mRNA of player and control groups and **young sedentary controls** (n = 21, age: 17–25 y). A young trained group (n = 16, age: 18–25 y) was added to analyze age-related response in circulating neurotrophins induced by chronic exercise.

RESULTS:

NEUROPSYCHOLOGICAL TESTING

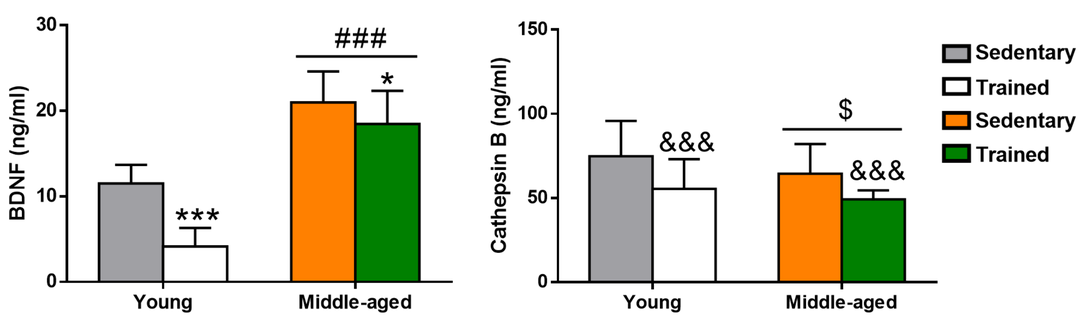


Bars represent mean ±SEM.
Two-tailed *t* test; **P*<0.05 vs Control.

Long-term physical exercise ⇨ **Memory at middle-age**

Physical activity increased memory score in immediate recall test.

NEUROTROPHIC FACTORS IN BLOOD SERUM

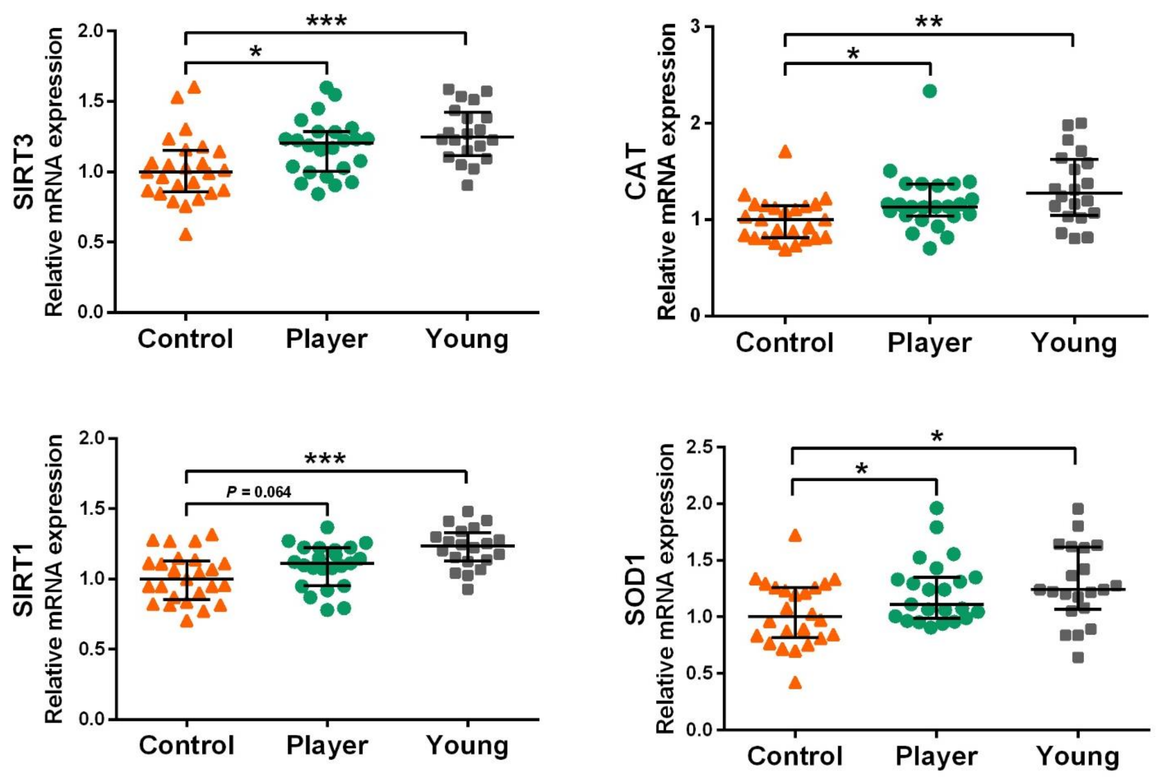


Bars represent mean ± SD. Two-way ANOVA test, Bonferroni's: *p < 0.05, ***p < 0.001 vs sedentary group; ###p < 0.001 vs young group; $p < 0.05 factor age; &&&p < 0.001 factor exercise training.

Physical exercise ⇨ **Neurotrophic factors**

Resting levels of the neurotrophic factors BDNF and Cathepsin B were lowered by physical exercise at both middle-aged and young trained group.

GENE EXPRESSION IN WHOLE BLOOD

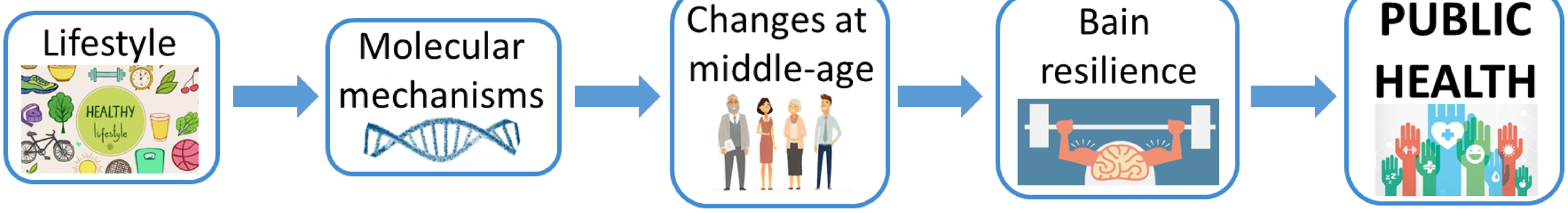


Data and statistics: median [IQR], Kruskal-Wallis followed by Dunn's test, **P*<0.05, ***P*<0.01, ****P*<0.001.

Control vs Young	Players vs Control/Young
↓ Sirtuins	↑ / =
↓ Antioxidants	↑ / =
= Inflammatory	↓ / ↓

Middle-aged amateur rugby players with a long-term practice [35 y; range: 7-59] showed maintained peripheral expression of key genes of the SIRT1-SIRT3 axis of resilience at a young-like level.

CONCLUSIONS:



Our results suggest that **long-term physical exercise** induces a rejuvenating effect in middle-aged adults, indicative of **brain resilience** against age-related cognitive loss. Interestingly **SIRT1, SIRT3, CAT and SOD** genes can be detected as peripheral blood **biomarkers** of resilience. This confirms the value of physical exercise to improve **public health.**

Funding: Ajut Mario Sàlvia i Ferret 2014, Institut d'Estudis Catalans; SAF2016-77703, MINECO and ERDF; 2017-SGR-106, AGAUR.

ruben.corpas@iibb.csic.es

The INMA-Valencia cohort:

A new health survey after 15 years of follow-up

MJ Lopez-Espinosa[1,2,3], A Ferrero[1,3], S Llop[1,3], T Oltra[4,5], R Soler-Blasco[1], L Gonzalez[1,3], A Beneito[1], A Esplugues[1,2,3], O Costa[1], M Murcia[1,3], M Lozano[4], P Carrasco[1], M Estarlich[1,2,3], L Margaix[6,1,2], J Vindel[5], R Roldán[5], A Farga[7], J Ferrando[8], A Saa[4], C Carrizosa[4], A Garay[4], M Salvador[4], R Bermúdez[4], M Rebagliato[1,3], F Ballester[1,2,3], C Iñiguez[1,3,9]

[1]Epidemiology and Environmental Health Joint Research Unit, FISABIO−Universitat Jaume I−Universitat de València, Valencia, Spain; [2]Department of Nursing, University of Valencia, Valencia, Spain; [3]Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), ISCIII, Madrid, Spain; [4]FISABIO-Public Health, Valencia, Spain; [5]Health Center of Paterna, Valencia, Spain; [6]Health Center of Puçol, Valencia, Spain; [7]Department of Microbiology, Hospital Arnau de Vilanova, Valencia, Spain; [8]Department of Pathological anatomy, Hospital Arnau de Vilanova, Valencia, Spain; [9]Department of Statistics and Computational Research, University of Valencia, Valencia, Spain

INTRODUCTION AND OBJECTIVES

The **INMA Project –Childhood and Environment-**is a multi-center study of 7 prospective Spanish cohorts (Ribera D´Ebre, Menorca, Granada, Valencia, Asturias, Gipuzkoa, and Sabadell) with the following specific objectives[1,2]:

1. To evaluate environmental exposure to contaminants and their related factors in adolescents and their mothers.
2. To study the health effects of biological, socioeconomic, dietary and environmental factors, and lifestyle throughout the life cycle.
3. To evaluate how these factors can modify the effects of contaminants on health.

METHODOLOGY

The INMA-Valencia cohort is undertaking its 11th follow-up, starting in 2019 (Figure 1). The participants (n≈400) are adolescents and their mothers from a specific Valencian region (Figure 2) with a range age between: 14–16 and 31–58 years old, respectively.

Data are being collected through questionnaires, physical examination (anthropometric measurements, lung function, blood pressure and pubertal development), neuropsychological development tests, and collection of biological samples (blood, urine, hair, fecal microbiota, and cervicovaginal mucosa, the latter only in the INMA mothers).

EXPECTED RESULTS

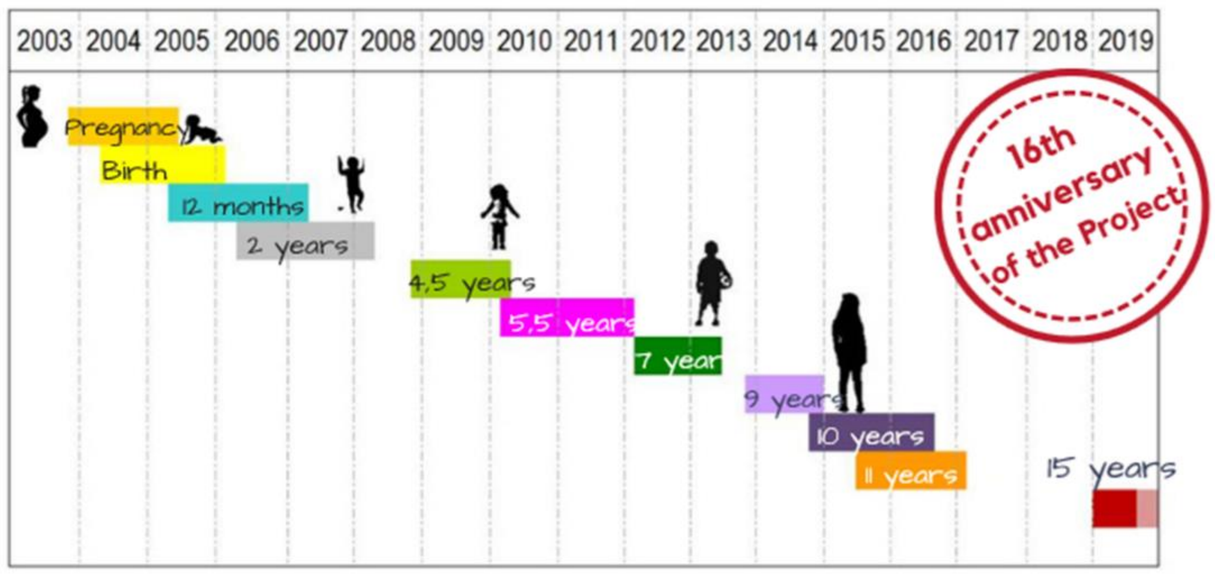


Fig. 1: Surveys INMA-Valencia

Fig .2: Study Area INMA-Valencia

The survey of 14–16-year-olds will consider: i) Socioeconomic level, diet quality, living environment, physical activity, sleep patterns, and habits of use of technologies regarding participants‘ health status; ii) Exposure to pollutants and biomarker levels of effect concerning health; and iii) Health role of gut microbiota (Figure 3).

In the mothers, cervicovaginal microbiota composition will be correlated with i) Infections by oncogenic human papillomavirus (HPVs), HPV-related dysplasias and other cervical lesions (e.g. cancer of cervix) during perimenopause; and ii) Quality of life during the climacteric period (Figure 3).

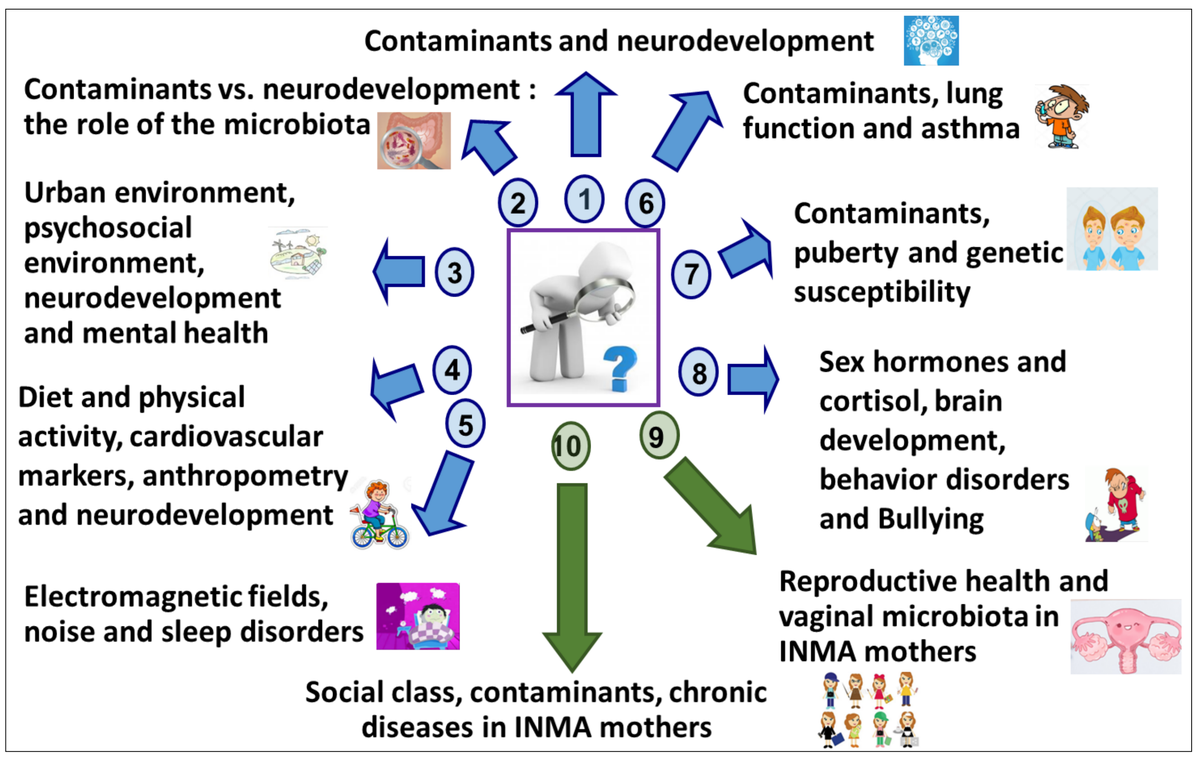


Fig. 3: Research priorities within the new survey (blue and green arrows: lines of research in INMA children and mothers, respectively)

CONCLUSIONS

The relevance of the INMA Project lies in its longitudinal design with health information on toxic exposure, diet, and socioeconomic context collected since the beginning of life.

Additionally, it is a multicenter study of cohorts in different Spanish regions and participates in many international projects and networks.

INMA contributes to knowledge about the health effects of environmental, socioeconomic and lifestyles factors throughout life. This information could be of special relevance for the preparation of Public Health guidelines and policies aimed at protecting health in Spain and Europe.

REFERENCES AND FUNDING

1.http://www.proyectoinma.org/
2. Guxens M, Ballester F, Espada M et al. Cohort Profile: the INMA--INfancia y Medio Ambiente--(Environment and Childhood) Project. Int J Epidemiol. 2012;41(4):930-940.

FUNDING: Health Institute Carlos III (FIS-FEDER:PI14/00891, PI16/1288, PI17/00663, and PI19/1338; Miguel Servet-FSE MS15/0025 and MSII16/00051; Rio Hortega CM18/00098; and FIS-FSE:FI17/00260); Koplowitz Foundation 2017; Spanish Association Against Cancer (AECC)-”Seed Ideas” 2019; Euroepan Union (Horizon 2020: 874583 –ATHLETE).

CONTACT: *E-mail: MJ Lopez-Espinosa (lopez_josesp@gva.es)*
www.ciberesp.es
www.proyectoinma.org

Association of urinary metal concentrations with blood pressure and serum hormones among male adolescents in the INMA-Granada cohort

F. Castiello, F. Gil, P. Olmedo, M. Molina, A. Mundo, R.R. Romero, C. Ruíz, J. Gómez-Vida, M.F. Fernández, C. Freire

Instituto de Investigación Biosanitaria de Granada (ibs.GRANADA); Universidad de Granada; Hospital Universitario San Cecilio de Granada; Consorcio de Investigación Biomédica de Epidemiología y Salud Pública (CIBERESP).

OBJECTIVE

To examine the association of urinary concentrations of arsenic (As), cadmium (Cd), mercury (Hg), nickel (Ni), lead (Pb), manganese (Mn), and chromium (Cr) with **blood pressure** (BP) and **serum hormone levels** in a sub-sample of **male adolescents** belonging to the INMA (Environment and Childhood)-Granada cohort .

METHODS

Participants were selected from the **INMA-Granada cohort** of boys at their follow-up visit when aged **15-17 years**. Metal concentrations were measured in urine samples using inductively coupled plasma mass spectrometry. Outcomes were BP measurements (systolic, diastolic, and pulse pressure) and concurrent serum levels of hormones, including thyroid hormones (FT4, TT3, TSH), sex steroids (testosterone, 17β-estradiol, DHEA), non-steroidal sex hormones (LH, FSH, SHBG, anti-Müllerian hormone, prolactin), adrenal hormones (ACTH, cortisol), human growth hormone (hGH), and insulin-like growth factor-1 (IGF-1). Associations were assessed by regression analysis in **133 boys** with available data on urinary metals, outcomes, and relevant covariates.

RESULTS

Table 1. Urinary metal concentrations among study participants

Metals	% detection	Non-adjusted (µg/L) GM	Non-adjusted (µg/L) Percentiles 25th	50th	75th	Non-adjusted (µg/L) Range	Creatinine-adjusted (µg/g) GM	Creatinine-adjusted (µg/g) Percentiles 25th	50th	75th	Creatinine-adjusted (µg/g) Range
As	100	21.3	7.75	21.0	40.3	1.04-942	12.1	5.02	10.4	25.7	0.58-465
Cd	98.5	0.08	0.05	0.08	0.12	<0.01-0.33	0.04	0.03	0.04	0.06	0.01-0.55
Hg	97.0	0.52	0.32	0.63	0.99	<0.05-4.57	0.30	0.17	0.36	0.57	0.01-3.24
Ni	36.8	-	<1.03	<1.03	1.67	<1.03-350	-	<0.55	<0.55	3.03	<0.55-188
Pb	89.5	0.42	0.29	0.43	0.71	<0.16-4.44	0.24	0.16	0.26	0.34	<0.09-2.64
Cr	14.3	-	<0.83	<0.83	<0.83	<0.83-819	-	<0.44	<0.44	1.22	<0.44-440
Mn	33.8	-	<0.03	<0.03	0.09	<0.03-84.2	-	<0.02	<0.02	0.82	<0.02-45.3

GM: geometric mean.

For **hormones**, significant associations were also found between:

- ✓ Hg and ↑ testosterone by 5% (95%CI=2-10) for each 50% increase in Hg.
- ✓ Hg and ↑ LH by 8% (95%CI=4-14) for each 50% increase in Hg.
- ✓ Hg and ↓ TSH by 4% (95%CI=1-8) for each 50% increase in Hg.
- ✓ Cr and ↓ TSH by 24% (95%CI=1-42) for detected *vs* undetected Cr.
- ✓ Cd and ↑ ACTH by 8% (95%CI=0-16) for each 50% increase in Cd.

Table 2. Change (95%CI) of diastolic and systolic BP and pulse levels, and odds ratios (95%CI) of elevated BP associated with urinary metals.

Exposure variables	Change (95%CI) Systolic BP (mmHg)	Change (95%CI) Diastolic BP (mmHg)	Change (95%CI) Pulse (bpm)	OR (95%CI) Elevated systolic BP (≥120 mmHg) N=100	OR (95%CI) Elevated diastolic BP (≥80 mmHg) N=5	OR (95%CI) Elevated BP (120-129/<80 mmHg) N=54
Urinary metal levels†						
As[a]	0.70 (0.11; 1.29)**	0.27 (-0.24; 0.77)	0.08 (-0.74; 0.91)	1.28 (1.04; 1.56)**	1.04 (0.97; 1.12)	1.00 (0.96; 1.02)
Cd[a]	1.47 (0.30; 2.63)**	0.54 (-0.45; 1.53)	0.41 (-1.22; 2.03)	1.10 (0.78; 1.55)	1.07 (0.82; 1.07)	0.98 (0.94; 1.01)
Hg[a]	0.15 (-0.61; 0.92)	0.36 (-0.31; 1.02)	0.43 (-0.66; 1.52)	0.91 (0.72; 1.14)	1.15 (0.95; 1.38)	1.00 (0.98; 1.02)
Ni[b]	0.76 (-2.92; 4.43)	-0.08 (-3.27; 3.10)	3.25 (-1.97; 8.46)	0.80 (0.28; 2.27)	0.19 (0.01; 4.98)	0.55 (0.23; 1.35)
Pb[a]	-0.70 (-1.58; 0.18)	-0.17 (-0.93; 0.60)	0.33 (-0.92; 1.59)	0.84 (0.65; 1.10)	1.03 (0.91; 1.16)	1.00 (0.97; 1.02)
Cr[b]	0.56 (-4.93; 6.05)	-1.67 (-6.34; 3.09)	-5.58 (-13.4; 2.22)	0.94 (0.18; 4.80)	-	1.12 (0.30; 4.24)
Mn[b]	1.05 (-3.07; 5.17)	1.06 (-2.52; 4.63)	2.91 (-2.94; 8.76)	1.67 (0.49; 5.69)	-	1.14 (0.42; 3.09)
Number of detected metals per subject: Mn and Cr included (ref: 2-3)‡						
4	6.54 (0.80; 12.3)**	4.58 (-0.20; 9.37)*	2.87 (-4.90; 10.6)	1.46 (0.34; 6.21)	-	0.45 (0.13; 1.57)
5	6.66 (0.42; 12.9)**	4.58 (-0.63; 9.80)*	3.23 (-5.23; 11.7)	2.01 (0.41; 9.80)	-	0.45 (0.11; 1.74)
6-7	6.58 (0.14; 13.0)**	3.89 (-1.49; 9.27)	5.56 (-3.17; 14.3)	1.47 (0.29; 7.39)	-	0.35 (0.08; 1.43)
p for trend	0.25	0.44	0.22	0.94	-	0.20
Number of detected metals per subject: Mn and Cr excluded (ref: 2-3) ‡						
4	5.84 (0.40; 11.3)**	3.65 (-0.91; 8.21)	3.37 (-3.94; 10.7)	1.51 (0.37; 6.10)	-	0.43 (0.13; 1.42)
5	7.01 (1.01; 13.0)**	3.77 (-1.26; 8.80)	6.95 (-2.12; 15.0)	1.22 (0.27; 5.51)	-	0.48 (0.06; 1.09)
p for trend	0.05	0.26	0.08	0.99	-	0.07

†Models adjusted for urinary creatinine, age (15-16 *vs* 17 yrs), serum triglycerides, HDL and LDL, BMI, and for all metals simultaneously.

‡Models adjusted for urinary creatinine, age (15-16 *vs* 17 yrs), serum triglycerides, HDL and LDL, and BMI.

[a]Change or OR of outcome for each 50% increase in urinary metal level; [b]Change or OR in outcome for detected (*vs* undetected) urinary level.

BP: blood pressure; *p<0.10; **p<0.05.

CONCLUSIONS

These findings suggest that environmental exposure to toxic metals, especially As and Cd, may contribute to BP elevation in male adolescents and that exposure to Hg, Cd, and Cr may affect their hormone levels.

Financiación: Instituto de Salud Carlos III / Fondo Europeo de Desarrollo Regional (ISCIII/FEDER) (MS16/00085)

A new online system for the standardized appraisal of PRO instruments: the EMPRO platform

Yolanda Pardo, Olatz Garin, Gemma Vilagut, Itxaso Alayo, Victor Zamora, Cristina Oriol, José María Valderas, Carlos García-Forero, Jordi Alonso, Montse Ferrer, and the EMPRO Group.

IMIM (Hospital del Mar Research Institute); CIBER en Epidemiologia y Salud Pública CIBERESP, CIBER en Salud Mental CIBERSAM, CIBER en Enfermedades Neurodegenerativas CIBERNED, Health Services Research on Chronic Patients Network REDISSEC

AIMS

The **EMPRO** (Evaluating the Measurement of Patient-Reported Outcomes) was designed to perform a standardized assessment of the **quality of PROs**. It has demonstrated to have **good validity and reliability**[1] and has been applied on ten conditions (over 50 instruments)[2-4]. Our aim was to developed an **online platform** which enables the independent review by several appraisers, and the consensus process to achieve an **agreement**.

1. Valderas et al. Value Health 2008, 11:700-708.
2. Schmidt et al. Qual Life Res 2014, 23, 2169-2181.
3. Maratia et al. Qual Life Res 2016, 25.
4. Sinclair et al. Patient 2017, 10, 4.

METHODS

An **online platform** was developed considering administrator and appraiser profiles. The **administrator profile** allows to design each EMPRO evaluation, specifying: the PROs to be evaluated, the number of appraisers by PRO; the **EMPRO attributes selected** (out of 8 possible); and evaluated materials (articles, instrument itself and its manual,…). In the **appraiser profile** the appraisers can check the materials, complete the EMPRO items for the evaluated PRO, and participate in the consensus process until **agreement**.

Figure 1. List of the appraiser's EMPRO evaluations screen.

Figure 2. EMPRO item assessment screen.

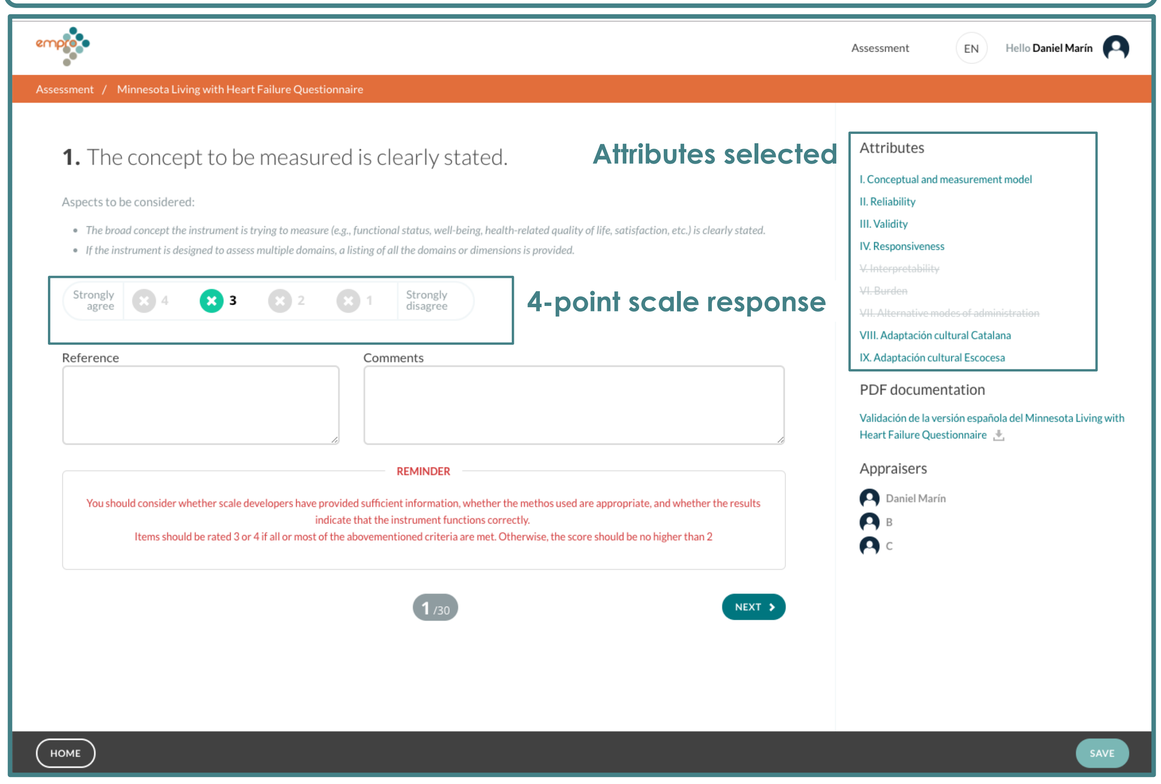


Figure 3. EMPRO item assessment split screen.

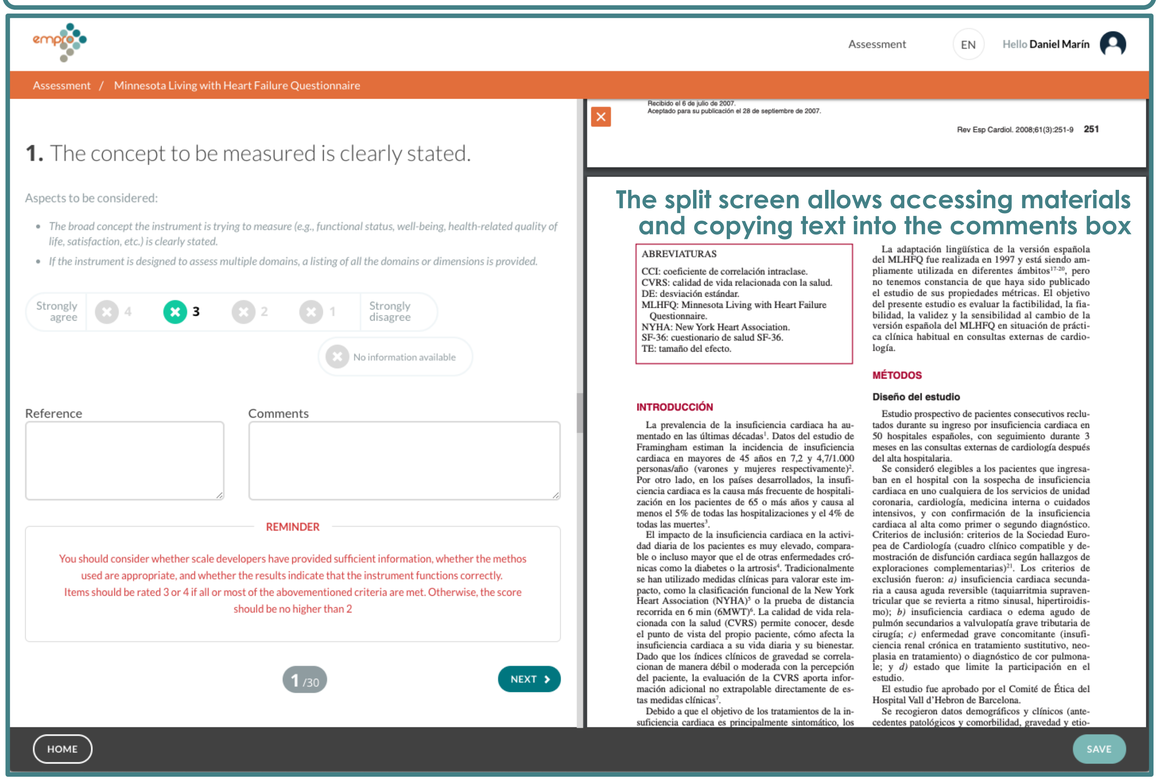
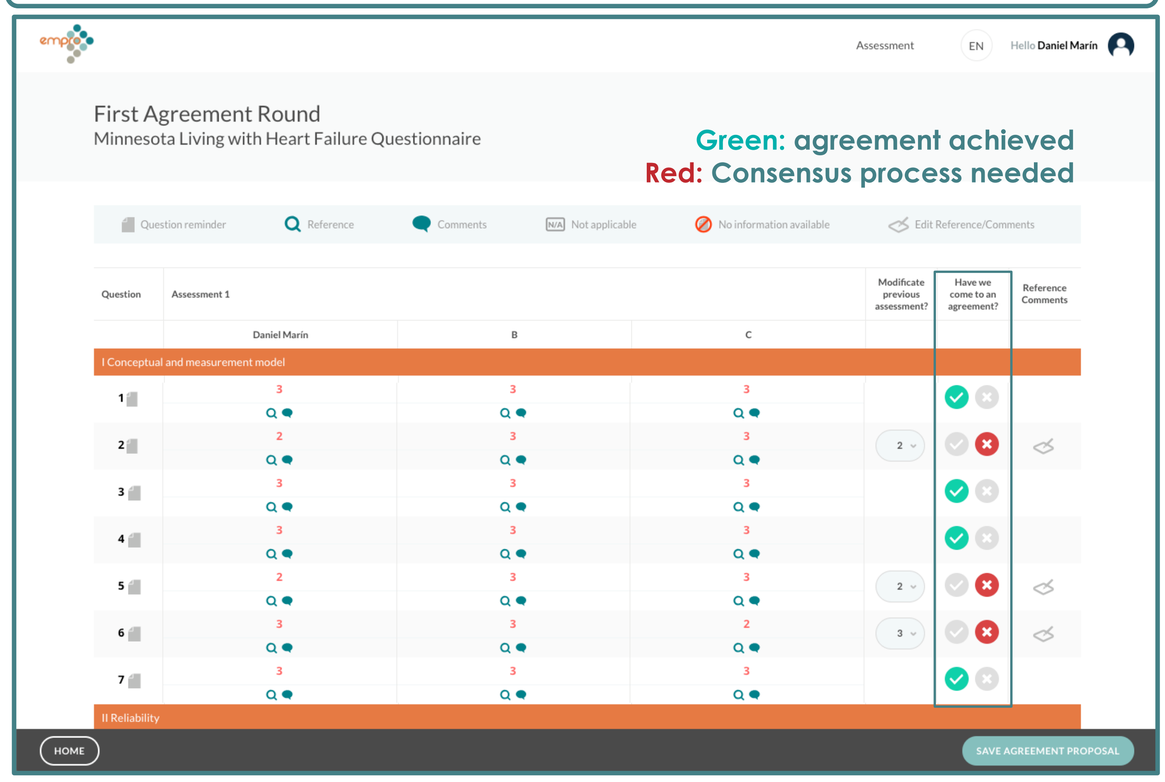


Figure 4. EMPRO consensus screen.



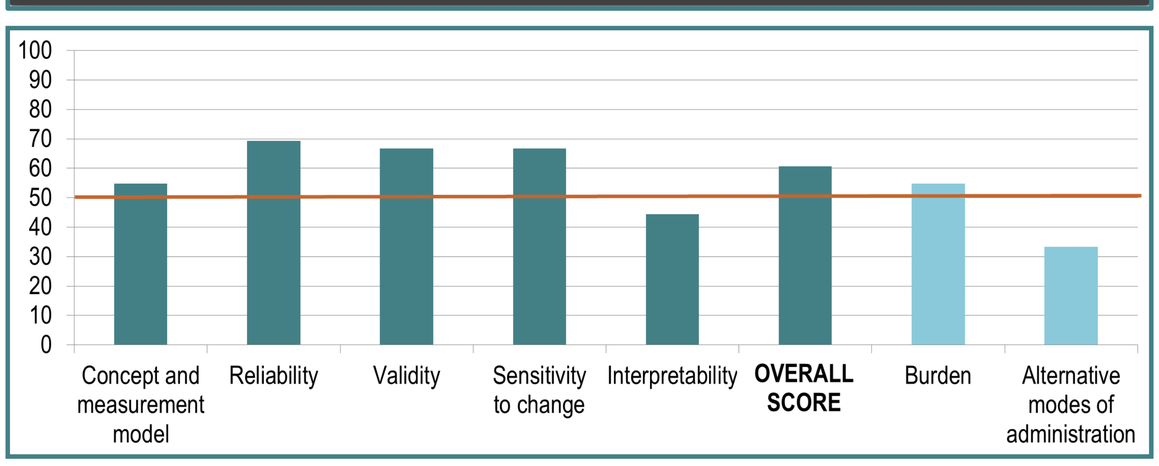


Figure 5. EMPRO scores for the Minnesota Living with Heart Failure questionnaire*.
*Garin et al. Heart Fail Rev 2014; 19(3): 359-367.

RESULTS

The new EMPRO online platform website is accessible with a user created for each appraiser. The application shows the **list of EMPRO evaluation projects** in which the user participates (**figure 1**). Each EMPRO item is shown on a screen (**figure 2**) with its evaluating criteria, scoring recommendations, and response options. **PRO materials can be consulted in parallel on a split screen** (**figure 3**). Once all appraisers of a specific PRO have finished their evaluation, they can access to the **consensus screen** (**figure 4**) displaying all the appraisers anonymized responses, so they can comment and modify their responses **to achieve an agreement**. Through these **consensus rounds** the experts achieve a **final agreement, which will become the EMPRO scores** (**figure 5**).

CONCLUSIONS

The new EMPRO online platform allows the standardized assessment of the quality of PRO instruments by expert consensus. It facilitates the exchange of information among appraisers, recording every step in the process, therefore simplifying collaborative and international studies.

Funding: This work was supported by grants from CIBER en Epidemiología y Salud Pública (CIBERESP), DIUE Generalitat de Catalunya (2017 SGR 452), and Instituto de Salud Carlos III FEDER PI16/00130-ISCIII/FEDER

Transitions from suicidal ideation to suicide plans and/or suicide attempts among incoming college students – results from the WMH-ICS Initiative

Mortier, P.[1,2,3], Auerbach, R.P.[4], Alonso, J.[1,2,5], Bantjes, J.[6], Benjet, C.[7], Cuijpers, P.[8], Ebert, D.D.[9], Green, J.G.[10], Hasking, P.[11], Nock, M.K.[12], O'Neill, S.[13], Pinder-Amaker, S.[14], Sampson, N.A.[15], Vilagut, G.[1,2], Zaslavsky, A.M.[15], Bruffaerts, R.[3], Kessler, R.C.[15]

1. Health Services Research Group, IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain
2. CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
3. Research Group Psychiatry, Department of Neurosciences, KU Leuven University, Leuven, Belgium
4. Department of Psychiatry, Columbia University, New York, NY, USA; Division of Clinical Developmental Neuroscience, Sackler Institute, New York, NY, USA.
5. Department of Health & Experimental Sciences, Pompeu Fabra University (UPF), Barcelona, Spain
6. Psychology Department, Stellenbosch University, South Africa
7. Division of Epidemiological and Psychosocial Research, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico City, Mexico.
8. Department of Clinical, Neuro- and Developmental Psychology, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands; Amsterdam Public Health Research Institute Amsterdam, Amsterdam, the Netherlands.
9. Department of Clinical, Neuro- and Developmental Psychology, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands; Department of Psychology, Chair for Clinical Psychology and Psychotherapy, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany
10. Wheelock College of Education & Human Development, Boston University, Boston, MA.
11. School of Psychology, Curtin University, Perth, Australia.
12. Department of Psychology, Harvard University.
13. School of Psychology, Ulster University, Coleraine, Northern Ireland.
14. Harvard Medical School, Boston, and McLean Hospital, Belmont, MA.
15. Department of Health Care Policy, Harvard Medical School, Boston, MA.

INTRODUCTION

Adolescence is a high-risk period for the onset of suicidal thoughts and behaviors (STB). About **21% to 50% of those with adolescent-onset STB continue to experience STB** when transitioning into young adulthood. This transition includes **college entrance** for about **two-thirds** of young people in developed countries. College entrance may therefore be a strategic "**point of capture**" for detecting STB.

Objectives:

- to obtain representative STB prevalence and transition rates among college students
- to investigate sociodemographic and college-specific correlates for college student STB
- to compare STB prevalence rates with groups of same-aged peers

MATERIALS AND METHODS

Recent data of three papers from the World Mental Health International College Student (WMH-ICS) Initiative:

- a **systematic review** of 36 all-year college student samples that were assessed for STB, representing a total of 634,662 students (median sample size = 2,082 [IQR 353–5,200]; median response rate=74% [IQR 37–89%]); random-effects meta-analyses to obtain pooled STB prevalence estimates were used (Mortier et al. 2018 [a])
- analyses of the **baseline data of the WMH-ICS surveys,** in which web-based self-report questionnaires were administered to representative samples of first-year students from 19 colleges and universities, located in 8 mostly high-income countries (n=14,371; response rate=45.5%; mean age=19.3 years) (Mortier et al. 2018 [b])
- analyses of data from the **WHO World Mental Health Surveys**, which include face-to-face interviews with 5,750 young adults (college students, college dropouts, secondary school graduates who never entered college, and secondary school non-graduates) aged 18–22 spanning 21 countries (response rate=71.4%) (Mortier et al. 2018 [c])

RESULTS

Figure 1 shows that

- lifetime and 12-month prevalence of **suicide attempts** was significantly **lower** among first-year college students (red) and all-year college students (green) compared to findings from a meta-analysis of adolescent samples worldwide (blue; Evans et al. 2005)
- a similar pattern was **not found** for **suicidal ideation**.

Figure 1. Lifetime and 12-month prevalence of suicidal ideation and suicide attempts among adolescents, incoming college students, and all-year college students.

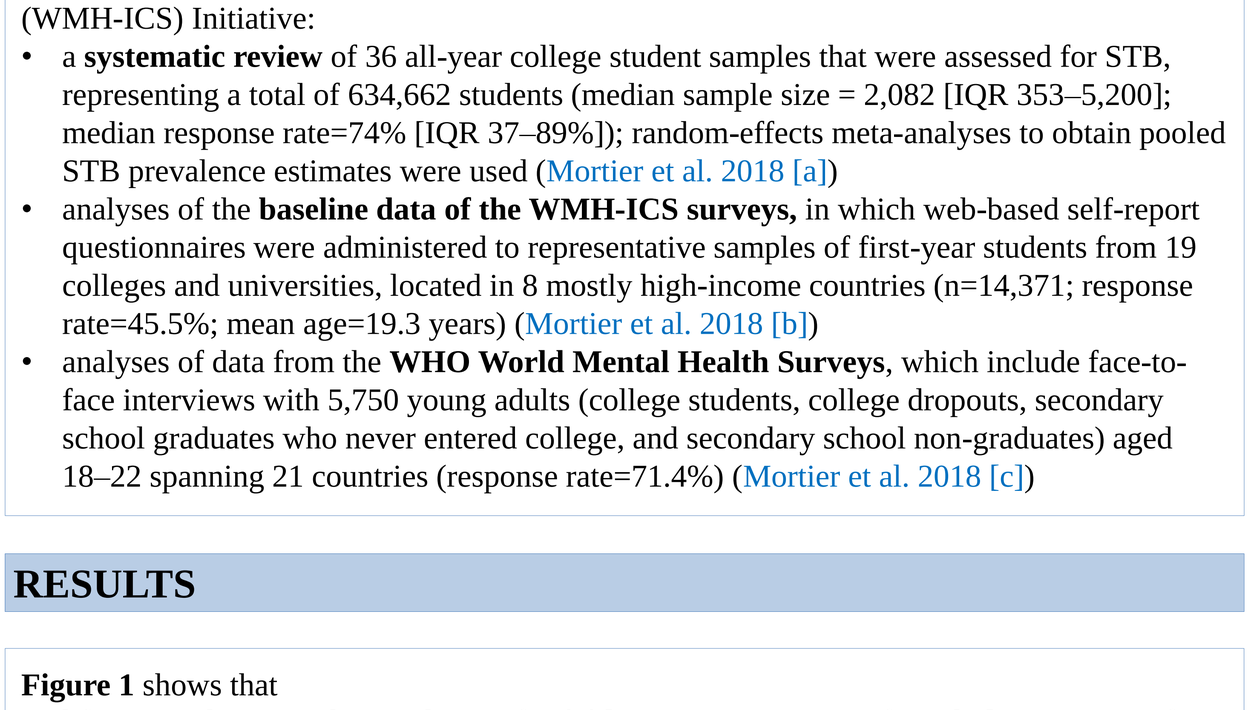
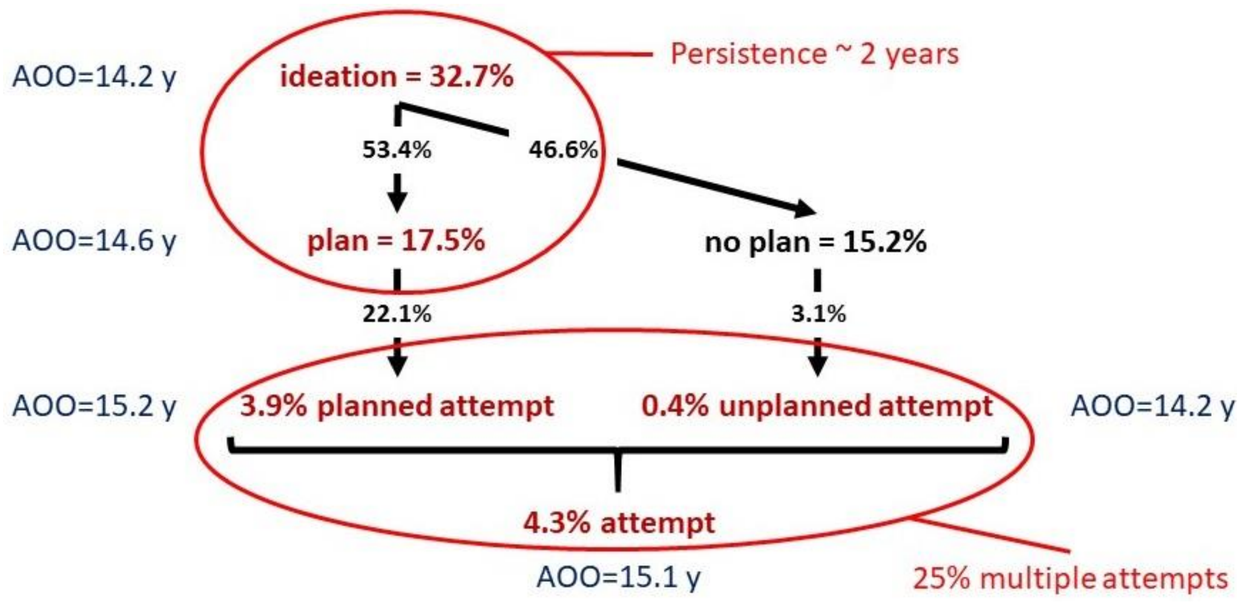


Figure 2 (Mortier et al. 2018 [b]) shows that

- the **majority** of lifetime suicide attempts were **planned attempts**
- **transitioning** from ideation to attempt occurred, on average, **within the year**
- students with lifetime ideation or planning experienced symptoms for **2 years** on average, and 25% of attempters attempted **2 times or more**.

Figure 2. Prevalence estimates, transition probabilities, median age-of-onset (AOO), and persistence of lifetime suicidal thoughts and behaviors among incoming college students.



Five out of 11 correlates (i.e., gender, age, parental education, parental marital status, urbanicity, religious background, sexual orientation, living situation, student job, ranking in high school, and reasons to go to college) were consistently positively associated with all three STB outcomes (Mortier et al. 2018 [b]):

- the strongest correlate was **sexual orientation**, i.e., non-heterosexual orientation with same-sex sexual intercourse (**aOR 4.2-7.9**), without same-sex sexual intercourse (**aOR 3.3-4.3**), and heterosexual orientation with some same-sex attraction (**aOR 1.9-2.3**).
- sexual orientation was also the strongest correlate of **transitioning** from ideation to plan (**aOR = 1.6-2.9**), unplanned attempts among ideators (**aOR = 6.1**), and planned attempts among ideators (**aOR = 1.1-4.0**).
- the correlates under study were quite **consistent across countries**, with only 32 of 192 correlate-by-country interactions (i.e., [24 correlates]*[8 countries]) being statistically significant.

Pre-matriculation onset STB (but not post-matriculation onset STB) was significantly associated with being a **college non-attender** versus a college entrant (aOR = 1.4-2.0), and with being a **college drop-out** versus being in college (aOR = 1.7-2.5; Mortier et al. 2018 [c]).

CONCLUSIONS

About **one third** of college entrants have a **lifetime history of STB**.

- lifetime and 12-month suicide attempts among (first-year) college students appear to be lower compared to same-aged peers not in college, which may be due to **selection effects**, i.e., the failure to matriculate into college as well as a higher rate of college drop-out, both related to pre-matriculation suicide attempts.
- **Sexual orientation** is a strong correlate of lifetime STB among college entrants, and is associated with an increased probability of transitioning from ideation or plans to suicide attempts.

Taken together, our findings point to the **need for implementing college STB prevention interventions in the pre-college period**, including targeted interventions for those adolescents experiencing issues in exploring their sexual orientation, and specific strategies to prevent suicide attempt-related academic failure.

References: **Evans**, E., Hawton, K., Rodham, K., & Deeks, J. (**2005**). The prevalence of suicidal phenomena in adolescents: a systematic review of population-based studies. Suicide & Life-Threatening Behavior. **Mortier**, P., Cuijpers, P., Kiekens, G., Auerbach, R. P., Demyttenaere, K., Green, J. G., … Bruffaerts, R. (**2018 [a]**). The prevalence of suicidal thoughts and behaviours among college students: A meta-analysis. Psychological Medicine. **Mortier**, P., Auerbach, R.P., Alonso, J., Bantjes, J., Benjet, C., Cuijpers, P., … Kessler, R. (**2018 [b]**). Suicidal Thoughts and Behaviors Among First-Year College Students: Results From the WMH-ICS Project. Journal of the American Academy of Child and Adolescent Psychiatry. **Mortier**, P., Auerbach, R. P., Alonso, J., Axinn, W. G., Cuijpers, P., Ebert, D. D., … Bruffaerts, R. (**2018 [c]**). Suicidal thoughts and behaviors among college students and same-aged peers: results from the World Health Organization World Mental Health Surveys. Social Psychiatry and Psychiatric Epidemiology.
Funding for this work includes funding from: ISCIII-FEDER (PI13/00343), Generalitat de Catalunya (2017 SGR 452), and ISCIII (Sara Borrell, CD18/00049).

Jornada Científica CIBERESP 2019

Evaluación económica de una intervención compleja en atención primaria desarrollada en 7 CC.AA combinando Real World Data y cuestionarios a pacientes: Estudio EIRA

Ignacio Aznar-Lou[1,2], Antoni Serrano-Blanco[1,2], Marc Casajuana[3], Cristina Carbonell[1], Maria Rubio-Valera[1,2]

1 SJD Sant Joan de Déu Institut de Recerca
2 ciberesp Centro de Investigación Biomédica en Red Epidemiología y Salud Pública
Ministerio de Ciencia, Innovación y Universidades
Instituto de Salud Carlos III
Unión Europea
FONDO EUROPEO DE DESARROLLO REGIONAL Una manera de hacer Europa
FONDO SOCIAL EUROPEO El FSE invierte en tu futuro
3 IDIAP Jordi Gol

Objetivo

Presentar la metodología, las dificultades, retos y soluciones del estudio EIRA para la evaluación del Coste-Utilidad de la una intervención compleja dirigida a mejorar las conductas saludables desde la perspectiva social.

Flow Chart

Reclutamiento

26 Centros de Primaria Aleatorizados

Asignación Centros

Centros Intervención (13)
Centro sale (mot. admin.) (1)

Centros Control (13)

Reclutamiento Participantes

Se les ofrece participar (2262)
Acceden a participar (1857)
Cumplen criterios inclusión (1703)
No acuden v. eval. inicial (188)
Reclutados (**1515**)

Se les ofrece participar (2125)
Acceden a participar (2002)
Cumplen criterios inclusión (1829)
No acuden v. eval,. inicial (188)
Reclutados (**1626**)

Retención Participantes

Reclutados (1515)
Inician Intervención (1331)
Tienen ≥1 visita seguimiento (937)
Perdidos (405)
Visita evaluación final (**1110**)

Reclutados (1626)
Perdidos (360)
Visita evaluación (**1266**)

Análisis

Reclutados (1515)
Excluidos por falta datos bas. (31)
Datos Basales (1484)
Datos Finales (1098)

Reclutados (1626)
Excluidos por falta datos bas. (43)
Datos Basales (1583)
Datos Finales (1253)

Análisis de los datos

Se aplicarán **modelos multinivel** para la estimación de la diferencia en costes y AVAC para estimar la ratio coste-efectividad incremental.
Se aplicarán técnicas de **remuestreo** para estimar los planos coste-efectividad y las curvas de aceptabilidad coste-efectividad.

Metodología

Ensayo clínico aleatorizado por conglomerados en AP en Andalucía, Aragón, Castilla y León, I. Baleares, Galicia y País Vasco.
La intervención era compleja y trabajó 3 elementos:

Actividad física | Alimentación saludable | Hábito tabáquico

Efectos medidos: Años de vida ajustados por calidad (**AVAC**): **EQ-5D-5L**.

Fuentes de información de costes

Los costes para el paciente relacionados con la intervención se obtuvieron mediante cuestionario.

El uso de servicios en atención primaria (visitas en centro y domicilio a medicina, enfermería y trabajo social) y secundaria (visitas, pruebas y hospitalización), fármacos, bajas laborales y mortalidad, así sus costes unitarios, se obtuvo en cada CCAA de distintas fuentes.

Origen de la información de costes

Sistemas de información automatizados
Historias clínicas individuales
Cuestionario ad hoc

	Anda.	Arag.	C.León	Catal.	Balear.	Galicia	P.Vasc.
AP							
At. 2ria							
Fármacos							
Bajas			N.d.				
Muerte	N.d.		N.d.	N.d.			N.d.
Intervenc.							

Origen de la información de costes unitarios

Sanitarios	**Tarifas publicadas en cada CCAA: BOJA, BOA, BOA, BOYCL, DOGC, BOIB, DOG, Osakidetza**
Fármacos	**BOE**
Productividad	**Salario medio: BOE (interprofesional), INE (por CCAA)**
Intervención	**Participante**

Dato/Factor	Dificultad	Solución
Costes sanitarios	Heterogeneidad en fuentes de información: Disponibilidad, detalle y calidad de fuentes de CC.AA variable	Análisis de sensibilidad utilizando la mínima (más homogénea) y máxima (más heterogénea) información disponible en cada CCAA.
	Datos auto-reportados: sesgo de memoria y sobrecarga del cuestionario.	Estimación y corrección del sesgo de memoria a partir de CCAA con datos disponibles. Reducción del cuestionario al mínimo.
	Ausencia de información de mortalidad en algunas CCAA.	Imputación de datos de mortalidad y análisis sin mortalidad.
Costes unitarios	Heterogeneidad en el coste unitario del mismo servicio entre CCAA.	Análisis de sensibilidad: costes específicos por CCAA, coste medio en España y coste mínimo y máximo para cada servicio.
	Antigüedad de los datos de tarifas.	Actualización por IPC por CCAA.
Intervención	Estimación del coste del estilo de vida y el ejercicio físico.	Estimación a partir de información facilitada por el paciente.
Datos missing	Pérdidas de datos de seguimiento del 26% de los pacientes.	Utilización de técnicas de imputación múltiple.
Acceso a datos individuales	Barreras de los comités éticos y legales de los gestores de algunas bases de datos de práctica clínica real (RWD).	Acciones legales y administrativas para garantizar la seguridad y legalidad de la extracción de datos a partir de los CI.

Conclusión

El acceso a datos de uso de servicios sanitarios, pérdidas en productividad y costes de bolsillo a partir de bases de datos de práctica clínica (RWD) en distintas CCAA en España presenta dificultades derivadas de la variedad en los sistemas de registro y mecanismos de acceso. Hemos desarrollado aproximaciones y estrategias que nos permitirán determinar el impacto que tiene la heterogeneidad en el origen de los datos sobre las estimaciones de coste efectividad de una intervención compleja en atención primaria en 7 CCAA.

Impact of late neonatal sepsis by coagulase negative *staphylococci* in very low birthweight infants (NeoKissEs cohort)

Pijoan JI[1,2,3,7], Madrid M[2,4,7] , Pérez Lopez J[2,7], Roqué M[3,5], Fernández BM[3,6] , López Herrera MC[1,7,8] , Santiago P[1,7], Villate JI[1,7]

1 HU Cruces-Osakidetza; 2 Biocruces-Bizkaia; 3 CIBERESP; 4 Red SAMID; 5 HU Santa Creu i Sant Pau; 6 HU Ramón y Cajal; 7 Grupo NeoKissEs; 8 Grupo Cooperativo SEN-1500.

Background: coagulase-negative staphylococci (CNS) are the most common cause of late onset sepsis (LOS) in very-low-birth-weight-infants (VLBWI; ≤ 1,500 gr at birth). There is current controversy regarding its actual clinical impact in terms of mortality and short and long-term morbidity as compared with sepsis due to other germs (mainly Gram negative bacteria and fungi).

Methods: observational study of the NeoKissEs cohort (2014-2018). NeoKissEs collects standardized data on perinatal variables, use of antibiotics and medical devices and incidence of both overall and device-associated LOS in VLBWI from more than 40 Spanish Neonatal Intensive Care Units (NICUs). First LOS episodes from 45 NICU providing data for at least four years are assessed. Neonates transferred from other hospital are excluded.

Data from 2014-5 have been linked to the SEN-1500 dataset, which collects additional in-hospital morbidities.

Chi square, ANOVA and Kruskal-Wallis tests. Random-intercept logistic models to estimate adjusted Odds Ratios (**aOR**) between type of first LOS and short-term mortality and morbidity, accounting for intra-NICU correlation

Objective: to describe short-term mortality and morbidities in VLBWI with an episode of CNS related LOS and to compare them with those with sepsis caused by other germs, clinically suspected sepsis (negative cultures) and no LOS episodes.

Results:

-**8,150** VLBW infants
-**1,700** with 1 episode of LOS (20.9%)
-**822** CNS related sepsis (48.4%)

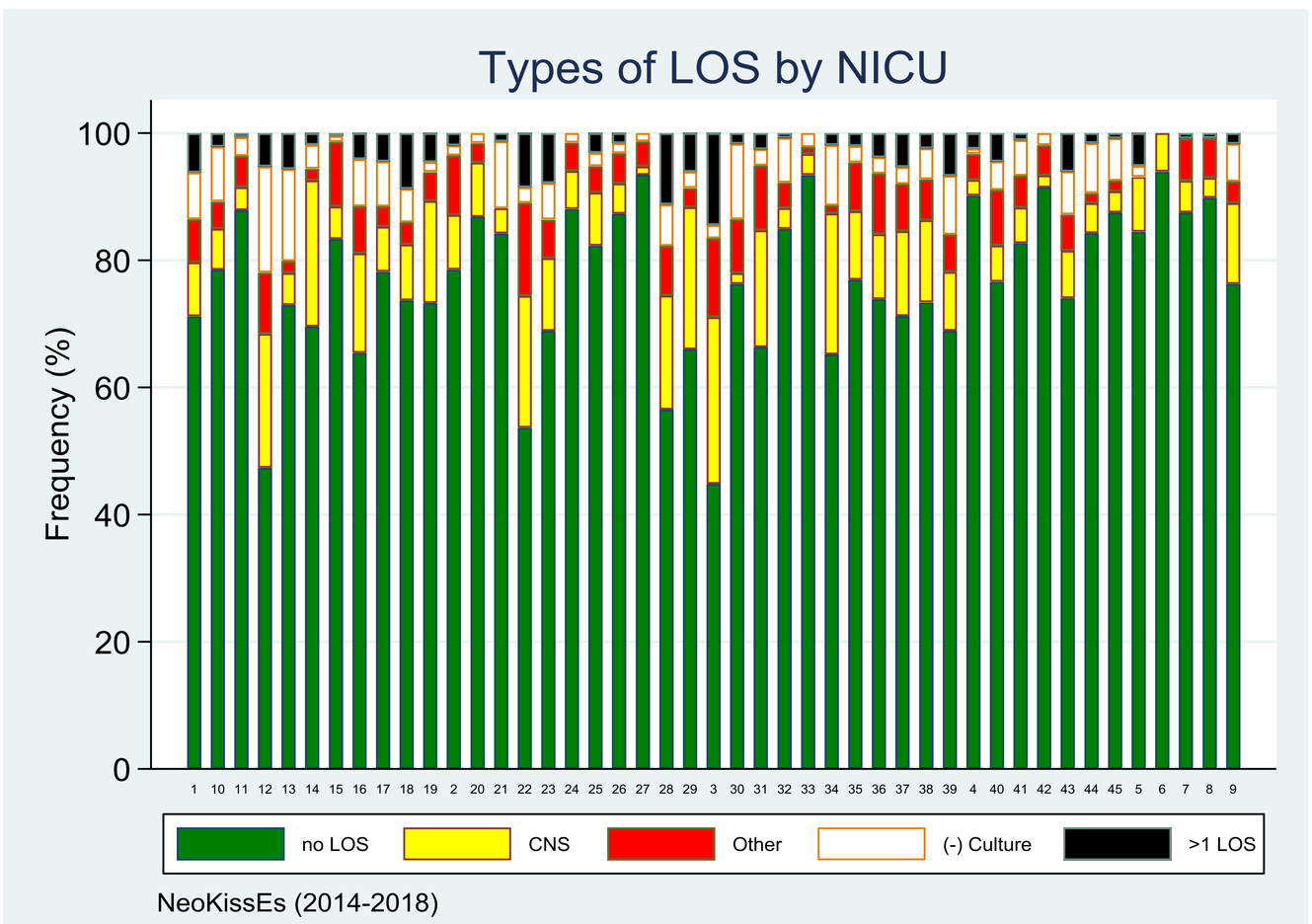
Patient characteristics	No LOS (n=6,117)	CNS LOS (n=822)	Other LOS (n=491)	(-) culture LOS (n=387)	p-value[1]	p-value[2]
Birthweight (grams)	1,179.7 (249.2)	1,005.6 (251.9)	964.8 (262.3)	991.1 (256.9)	<0.001	0.020
Gestational age (weeks)	29.8 (2.7)	28.2 (2.6)	27.5 (2.5)	27.9 (2.4)	<0.001	<0.001
Length of stay at NICU (days)	32.8 (16.0)	45.6 (19.0)	43.9 (22.5)	43.9 (20.8)	<0.001	0.250
Days with central lines	9.9 (9.1)	19.8 (11.4)	21.2 (14.0)	19.0 (12.3)	<0.001	0.027
Days with peripheral lines[3]	0 (0-3)	2 (0-8)	3 (0-11)	2 (0-8)	<0.001	0.064
Days with antibiotic[3]	4 (0-8)	15 (10-21)	17 (12-25)	14 (10-19)	<0.001	<0.001
Time to sepsis (days)		12.1 (7.6)	14.2 (10.4)	14.4 (10.4)		<0.001

Outcomes	No LOS (n=6,117)	CNS LOS (n=822)	Other LOS (n=491)	(-) culture LOS (n=387)	p-value[1]	p-value[2]
Short-time mortality n. (%)	367 (6.0)	41 (5.0)	96 (19.6)	52 (13.4)	<0.001	<0.001
NEC n (%)	73 (3.4)	28 (9.5)	19 (12.1)	22 (15.2)	<0.001	0.214
Severe IVH n(%)	120 (2.0)	20 (2.4)	18 (3.7)	14 (3.6)	0.016	0.349
Severe PVL n(%)	43 (0.7)	6 (0.7)	4 (0.8)	2 (0.5)	0.962	0.866
BPD n(%)	135 (8.1)	60 (23.7)	41 (34.8)	23 (21.9)	<0.001	0.043

[1] comparisons across all four groups; [2] comparisons across groups with one LOS episode; [3] median (Q1-Q3)

Outcomes	Other LOS	(-) culture LOS
Short-time mortality	4.2 (2.8-6.3)	3.2 (2.0-5.0)
NEC	1.1 (0.6-2.2)	1.6 (0.8-3.2)
Severe IVH	1.3 (0.6-2.5)	1.6 (0.8-3.3)
Severe PVL	1.0 (0.3-3.6)	0.6 (0.1-3.2)
BPD	1.5 (0.9-2.8)	0.9 (0.5-1.7)

aOR (Odds Ratios adjusted for gestational age, birthweigth, gender, delivery type, multiple delivery, level of NICU care); **Level of reference:** CNS related sepsis; **NEC:** Necrotizing Enterocholitis; **IVH:** Intraventricular Haemorrhage; **PVL:** Periventricular Leukomalacia; **BPD:** Bronchopulmonar Dysplasia



Conclusions: CNS related sepsis develop earlier and are associated with lower short-term mortality.

They do not seem to be associated with lower short-term morbidity as compared to sepsis caused by other germs or culture negative sepsis.

There are substantial variability across NICUs in the frequency of CNS related sepsis

A SCOPING REVIEW INDICATES THAT RAPID REVIEWS OF MEDICAL TESTS ARE MORE COMPREHENSIVE THAN EXPECTED

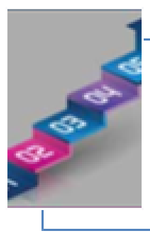
Arevalo-Rodriguez I [a], Moreno-Nunez P [b], Nussbaumer-Streit B [c], Steingart K [d], Gonzalez Peña L [e], Buitrago-Garcia D [e], Kaunelis D [f], Emparanza JI [g], Alonso-Coello P [h], Tricco AC [i], Zamora J [a]

a) Clinical Biostatistics Unit, Hospital Universitario Ramon y Cajal (IRYCIS), CIBER of Epidemiology and Public Health, Madrid, Spain; b) Department of Preventive Medicine, Hospital Universitario Ramon y Cajal (IRYCIS), Madrid, Spain; c) Department for Evidence-based Medicine and Clinical Epidemiology, Danube University Krems, Krems, Austria; d) Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK; e) Fundación Universitaria de Ciencias de la Salud, Bogotá, Colombia; f) Canadian Agency for Drugs and Technologies in Health, Ottawa, Canada; g) Clinical Epidemiology Unit, Hospital Universitario Donostia, BioDonostia, CIBER of Epidemiology and Public Health, San Sebastian, Spain; h) Centro Cochrane Iberoamericano, IIB Sant Pau, CIBER of Epidemiology and Public Health, Barcelona, Spain; i) Li Ka Shing Knowledge Institute, St. Michael's Hospital. Epidemiology Division, Dalla Lana School of Public Health, University of Toronto, Toronto, Canada.

AIM

We aimed to identify recently published rapid reviews of medical tests and to describe their characteristics and methods. This exploration may also help to identify shortcomings of current rapid reviews and needs for future research.

METHODS



Rapid reviews of medical tests (any purpose and setting) published between 2013-2018

Searching of institutional websites and repositories + electronic searches (MEDLINE, EMBASE, Cochrane Library, LILACS)

Selection of reports by at least two authors (independent)

Data extraction by one author, verified by a second author

RESULTS

We identified 191 rapid reviews. All reviews were developed within a short time (≤ 12 months) and were relatively concise (≤ 10 pages). The reviews involved multiple index tests (44%), multiple outcomes (88%), and several test applications (29%).

A. Narrowing the scope	• Limiting the number of populations, interventions and outcomes considered	Multiple index tests, multiple outcomes, multiple applications
B. Parallelisation of tasks	• Increasing the intensity of work on review processes where multiple reviewers simultaneously complete review steps	Insufficient information
C. Using review shortcuts	• One or more systematic review steps may be reduced or omitted	Comprehensive search strategies, no MA
D. Automating review steps	• Developing, adapting and using new technologies to fast-track the standard systematic review steps	Insufficient information

WHAT IS NEW?

KEY FINDINGS

- Most rapid reviews were broad in scope and assessed multiple index tests, outcomes, and test applications. In general, well-known methodological tailoring strategies, such as setting limits for literature searching by date or language or searching a single database, were rarely used.

- Information about parallelisation of tasks and the use of automated approaches was infrequently reported.

WHAT THIS ADDS TO WHAT WAS KNOWN?

Rapid reviews of medical tests have many of the same characteristics and use similar methods as those of standard systematic reviews. However, we found that several critical items for rapid reviews were infrequently reported.

WHAT IS THE IMPLICATION AND WHAT SHOULD CHANGE NOW?

- Standards for reporting of rapid reviews are needed. Those standards would cover the essential items that should be included in every rapid review.

- Further research should inform the most appropriate methods for performing rapid reviews of medical tests.

Full-text access on:

instituto ramón y cajal de investigación sanitaria irycis

ciberesp Centro de Investigación Biomédica en Red Epidemiología y Salud Pública

MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

Instituto de Salud Carlos III

Unión Europea

FONDO EUROPEO DE DESARROLLO REGIONAL
Una manera de hacer Europa

FONDO SOCIAL EUROPEO
El FSE invierte en tu futuro

Nuevo factor de riesgo de mortalidad en una cohorte poblacional: Consumo de ultraprocesados

Romero Ferreiro, Carmen[1,2];Martín−Arriscado Arroba, Cristina[2,3];Cancelas Navia, Pilar[2,3];Garcia Morales, Maria Teresa[2,3];Lora Pablos, David[1,2,3];Gomez de la Cámara, Agustín[1,2,3].

1. CIBER de epidemiología y salud pública (CIBEResp)
2. Unidad de Investigación y Soporte Científico (I+12), Hospital Universitario 12 de Octubre. Madrid, España
3. Plataforma de Unidades de Investigación Clínica y Ensayos Clínicos (SCReN)

INTRODUCCIÓN

El estudio DRECE (**Dieta y Riesgo de Enfermedades Cardiovasculares en España**) se inició en 1991 con el objetivo de conocer el perfil lipídico, la prevalencia de factores de riesgo cardiovasculares (FRCV) en la población española y su relación con hábitos dietéticos.

Las investigaciones actuales relacionadas con la dieta, la nutrición y la salud basan sus hallazgos y recomendaciones en el perfil nutricional y la composición química de los alimentos. Sin embargo, el tema del procesamiento de los alimentos se ignora o minimiza en gran medida. Los **alimentos ultraprocesados** son productos elaborados en su mayoría o en su totalidad a partir de sustancias extraídas o derivados de los alimentos. En 2016 Monteiro & Col. publican **NOVA**, un nuevo sistema de clasificación de alimentos que divide los alimentos en cuatro grupos según su grado de procesamiento.

Figura 1. Clasificación de alimentos según NOVA

OBJETIVO

Actualizar los factores de riesgo en la población española y consumo de alimentos ultraprocesados, de acuerdo a la clasificación NOVA

MÉTODOS

- ⇨ En este estudio se incluyó una cohorte de 4787 personas, estratificadas por sexo y edad, entre 5 y 59 años, seleccionadas de forma aleatoria en todo el territorio nacional. Anualmente, el Instituto Nacional de Estadística (INE) proporciona, por convenio, el listados de mortalidad por causas.
- ⇨ Las **tasas de mortalidad** se estimaron por regresión de Poisson, ajustando por edad, sexo y años de seguimiento
- ⇨ El consumo de ultraprocesados se determinó a través del **cuestionario de dieta validado** de la cohorte histórica DRECE, utilizando la clasificación NOVA para categorizar los alimentos y obtener las kcal consumidas de cada uno de los 4 grupos
- ⇨ Se utilizó la **regresión de riesgos proporcionales de Cox** para evaluar la relación entre la mortalidad general y los diferentes factores de riesgo. El modelo multivariante final fue construido considerando todos aquellos factores que habían tenido significación estadística en el análisis bivariable, y aquellos con especial relevancia clínica. Se excluyeron los factores de antecedentes personales o familiares en el modelo multivariante. Se calculó el **Hazard Ratio** (HR) junto con el intervalo de confianza de Wald.
- ⇨ Todos los análisis fueron llevados a cabo usando Software SAS, versión 9.4 para Windows (2017)

RESULTADOS

Tras la actualización de los datos en 2017, los sujetos tenían edades comprendidas entre 32 y 87 años. Fallecieron 462 sujetos, 301 varones y 161 mujeres. La tasa de mortalidad global fue de 3,68 por 1000 habitantes/año, para los hombres, la tasa de mortalidad de 4,96 por 1000 habitantes/año y para las mujeres una tasa de mortalidad de 2,48 por 1000 habitantes/año.
Según la clasificación NOVA, el consumo de ultraprocesados (Grupo 4) representaba el 23,01% de las Kcal totales ingeridas; mientras que el consumo de comida no procesada representaba el 36,73% del total (**Figura 2**).

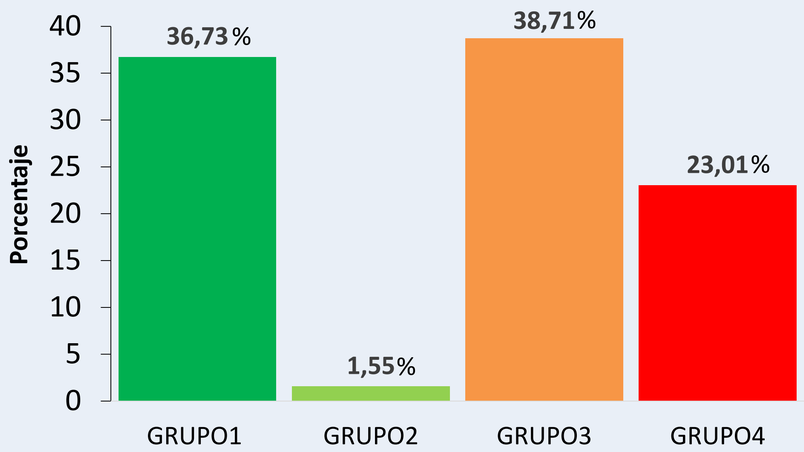


Figura 2. Consumo de ultraprocesados en España según NOVA

Factores de riesgo	HR (IC95%)
Edad	1,10 (1,09-1,11)
Sexo (Hombre)	1,89 (1,54-2,34)
Creatinina> 1,5 mg/dL	3,09 (1,64-5,85)
Diabetes	1,75 (1,34-2,66)
HTA	1,24 (1,01-1,53)
Tabaco	1,42 (1,16-1,75)
Ultraprocesados	1,53 (1,12-2,09)

Tabla 1. Factores de riesgo en la mortalidad

El análisis crudo con los principales factores de riesgo asociados a la mortalidad se observó una fuerte asociación en factores de antecedentes personales o familiares, la creatinina >1,5 mg/dl, sexo y diabetes. En el análisis final se hallaron 7 factores (**Tabla 1**). El índice C obtenido para el modelo fue 0,71.

CONCLUSIÓN

Los factores de riesgo asociados a mortalidad siguen siendo similares a los análisis previos de la cohorte realizados durante los 27 años de seguimiento, con la excepción de un nuevo componente: el consumo de los ultraprocesados, que representan una parte importante de las calorías consumidas en muchos países.
Los resultados obtenidos en el análisis de supervivencia sugieren que un **mayor consumo de alimentos ultraprocesados se asocia con un mayor riesgo de mortalidad** por cualquier causa, que concuerda con hallazgos previos.
Nuestros hallazgos refuerzan la evidencia existente sobre el **impacto negativo** de los alimentos ultraprocesados en la mortalidad global.

Referencias

1. *GÓMEZ DE LA CÁMARA, Agustín, et al. Seguimiento de 1991 a 2004 de la mortalidad y los factores de riesgo emergentes en una cohorte de población general española: estudio Drece III (Dieta y Riesgo de Enfermedades Cardiovasculares en España). Revista española de salud pública, 2008, vol. 82, p. 415-423.*
2. *BALLESTEROS-POMAR, M. D., et al. Dietary habits and cardiovascular risk in the Spanish population: the DRECE study (I). Annals of nutrition and metabolism, 2000, vol. 44, no 3, p. 108-114.*
3. *MONTEIRO, Carlos A., et al. NOVA. The star shines bright. World Nutrition, 2016, vol. 7, no 1-3, p. 28-38.*
4. *SCHNABEL, Laure, et al. Association between ultraprocessed food consumption and risk of mortality among middle-aged adults in France. JAMA internal medicine, 2019, vol. 179, no 4, p. 490-498.*

Unidad de Investigación y Soporte Científico — Instituto de Investigación. Hospital Universitario 12 de Octubre
i+12 Instituto de Investigación Hospital 12 de Octubre
Hospital Universitario 12 de Octubre — SaludMadrid — Comunidad de Madrid
ciberesp — Centro de Investigación Biomédica en Red — Epidemiología y Salud Pública
SCReN Spanish Clinical Research Network ISCIII
MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
Instituto de Salud Carlos III
Unión Europea
FONDO EUROPEO DE DESARROLLO REGIONAL — Una manera de hacer Europa
FONDO SOCIAL EUROPEO — El FSE invierte en tu futuro