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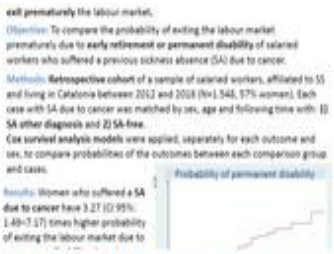

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The Southern European Atlantic Diet and all-cause...

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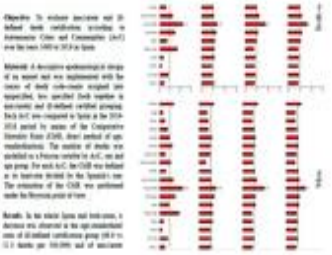

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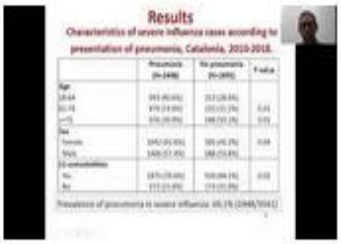
COVID-19 SEROPREVALENCE AMONG WORKERS OF THE CATA...

Towards sustainable plastic management of municip...



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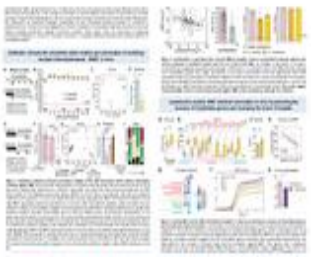

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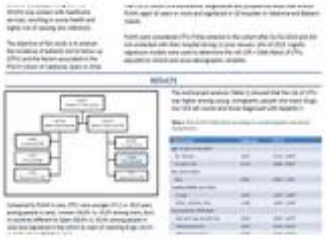
COVID SUSPECTED PATIENTS IN PRIMARY CARE IN MADRI...

SARS-CoV-2 pneumonia in primary care: observation...



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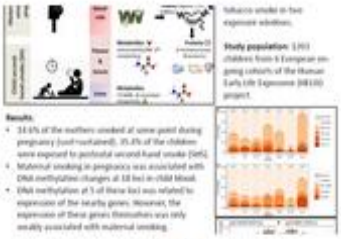

In utero and childhood exposure to tobacco smoke ...

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Concentrations of bisphenol-A in adults from the ...

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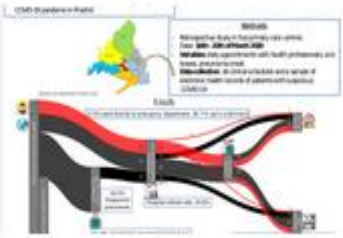

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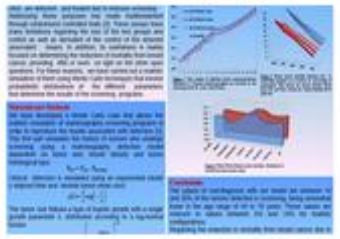
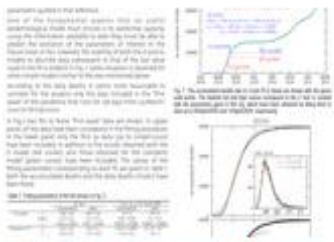
RAPID, SCALING UP OF HIGH THROUGHPUT SARS-COV-2 E...



Montecarlo simulation applied to breast cancer pr...



What are they really for? Analysis of the predic...

Qualitative study of needs assessment and concept...

Anticipated help-seeking for cancer symptoms and perceived barriers before and after the coronavirus pandemic: Results from a national survey

Dafina Petrova[1,2,3], Marina Pollán[1,4], Miguel Rodriguez-Barranco[1,2,3], Josep Maria Borrás[5,6], Maria-José Sánchez[1,2,3,7]

Affiliations: (1) CIBER de Epidemiología y Salud Pública (CIBERESP), (2) Escuela Andaluza de Salud Pública, (3) Instituto de Investigación Biosanitaria ibs.GRANADA, (4) Centro Nacional de Epidemiología, Instituto Carlos III, (5) IDIBELL, Universidad de Barcelona, (6) Catalonian Cancer Strategy, (7) Universidad de Granada. Contact: Dafina.Petrova.easp@juntadeandalucia.es

Background

- The SARS-CoV-2 pandemic has led, among other things, to the temporary suspension of cancer screening programs and the reallocation of economic and human resources from oncology to the health care of patients with COVID-19 (1).
- According to several studies from Spain and other countries, these circumstances have led to significant delays in the diagnosis and treatment of cancer (2). In addition to the changes in the functioning of the healthcare system, delays in diagnosis could also occur because people are taking longer to consult for their symptoms during the pandemic.

Aim

- To compare anticipated help-seeking times for cancer symptoms and the associated perceived barriers in the Spanish population before and after the first wave of the pandemic.

Method

- Data source: The Oncobarometer of the Spanish Association against Cancer is a periodic representative population survey that covers the entire territory of Spain and that in 2020 was administered in two waves: “Pre-coronavirus” with 3269 respondents in February/March of 2020 and “Post-coronavirus” with 1500 respondents in August/September 2020.
- Questionnaire: The international ABC (Awareness and Beliefs about Cancer) questionnaire (3) measures how long respondents would wait to consult their physician from the moment they first detect each of 13 potential cancer symptoms (time to help-seeking, 13 items) and the reasons that would make them delay the consultation (barriers, 4 items + 1 open-ended question about an additional barrier).
- Outcomes: Delayed response (waiting > 1 week) for each symptom (yes vs. no); perceiving each barrier (yes vs. no); number of symptoms with delayed response and number of perceived barriers.
- Sociodemographic variables: Age, sex, socioeconomic position, marital status, personal and family history of cancer.
- Statistical analysis: Pre-post wave comparisons using multiple logistic and Poisson regressions.

Results

Figure 1. Percentage of respondents reporting anticipated help-seeking times within the different time categories for 13 possible cancer symptoms as a function of wave.

- There was a consistent and significant increase in help-seeking times from Pre to Post for 12 of 13 cancer symptoms: *p*s<.05, ORs (adjusted for sociodemographics) between 1.20-1.54.
- Large increases for breast and colorectal cancer symptoms, the cancers with the highest incidence in the Spanish population.

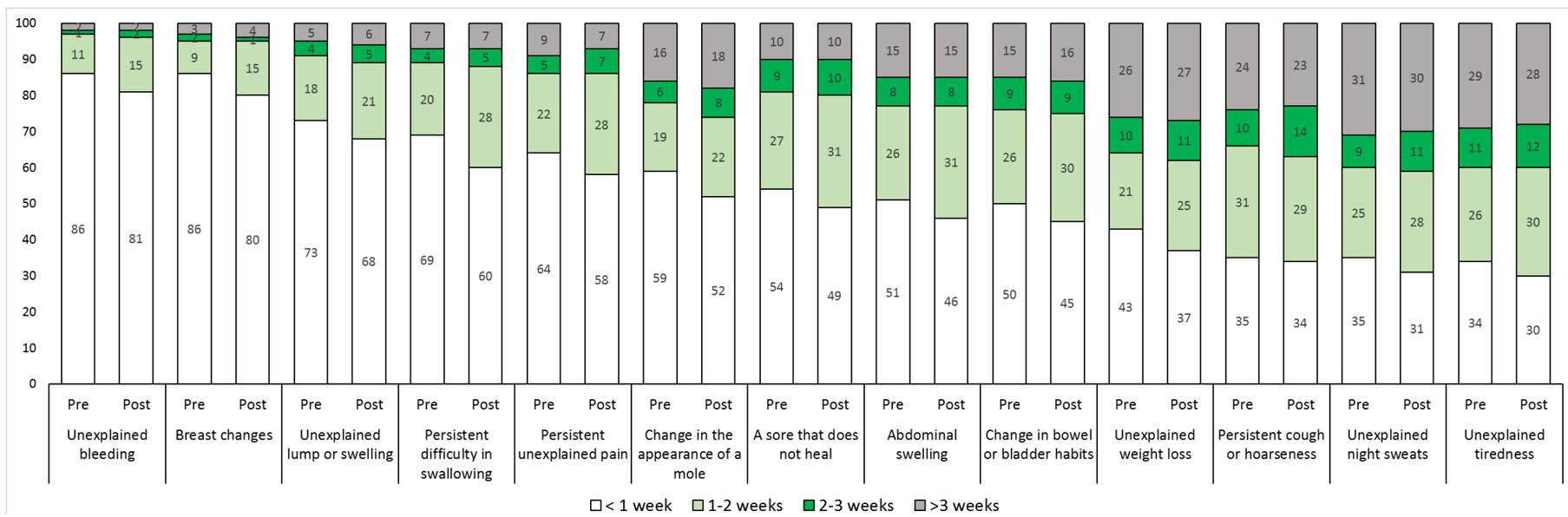
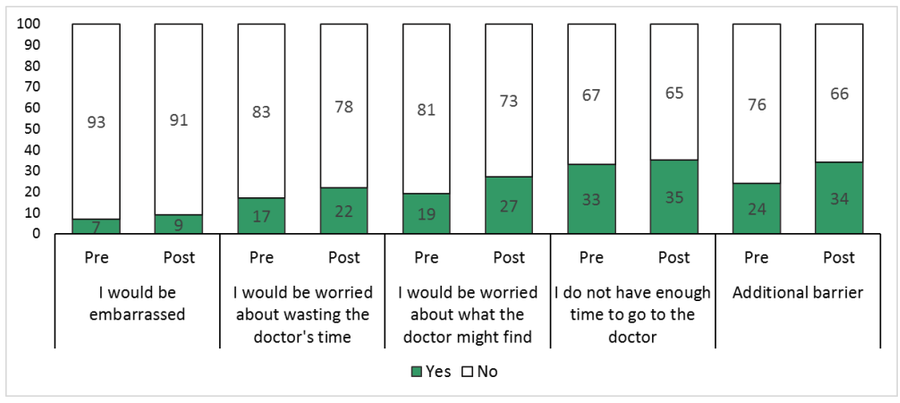


Figure 2. Percentage of respondents reporting different barriers to help-seeking for symptoms as a function of wave.

- There was a significant increase in the number of barriers reported, although the coronavirus did not emerge as a barrier in the Post wave, mentioned only by 2% of respondents.



Vulnerable sociodemographic groups

- Women: Both help-seeking times and perceived barriers increased more strongly among women than among men.
- Older persons (+65): although this group still reports the shortest waiting times and the fewest barriers, they suffered the largest Pre-Post increases.
- Detailed statistical results can be found here: https://tinyurl.com/Covid19OncoB

Discussion

- We observe an increase in waiting times and worry about health or wasting the doctor’s time (perceptions that one should consult only if it is absolutely necessary?).
- There is urgent need for campaigns and outreach activities encouraging people to consult their physicians with symptoms suggestive of cancer and counteracting the main barriers perceived during the pandemic situation.

Descarga este póster en español aquí: https://tinyurl.com/Covid19OncoBESP

References

(1) Petrova D, Pérez-Gómez B, Pollán M, Sánchez MJ. Implicaciones de la pandemia por COVID-19 sobre el cáncer en España. Medicina Clínica. 2020;155(6):263-6. **(2)** COVID-19 y cáncer. Resultados del estudio elaborado por AECC, SEAP, SEEO, SEHH, SEOM y SEOR. El número de pacientes de cáncer nuevos bajó un 21% durante el confinamiento. 2020. **(3)** Simon AE, Forbes LJ, Boniface D, Warburton F, Brain KE, Dessaix A, et al. An international measure of awareness and beliefs about cancer: development and testing of the ABC. BMJ Open 2012 Dec 18;2(6).

Funding: Cancer Observatory of AECC (www.aecc.es)

At Risk of Poverty and/or Social Exclusion: family environment and mental health problems in children aged 7-11 years

Llúcia González Safont[a,b], Marisa Estarlich Estarlich[a,b,c], Mario Murcia Hinarejos[a,b,d], Florencia Belén Barreto-Zarza[e,f], Loreto Santa-Marina[b,e,g], Sandra Simó Teufel[h], María Isabel Larrañaga Padilla[e,g], Estefanía Ruiz Palomino[i], Jesús Ibarluzea Maurolagoitia[b,c,e], Marisa Rebagliato Ruso [a,b,j]

[a]Epidemiology, Environmental Health Joint Research Unit, FISABIO-UJI-UV .[b]CIBERESP, [c]Department of Infirmary and Chiropody, UV. [d]Health Information Systems Analysis Service, Conselleria de Sanitat. [e]BIODONOSTIA. [f]UPV/EHU. [g]Public Health Division of Gipuzkoa. [h]Department of Basic Psychology, UV. [i]Department of Basic and Clinical Psychology and Psychobiology, UJI. [j]Predepartamental Unit of MedicineUJI.

OBJECTIVES

Assessing the impact of **Risk of Poverty and/or Social Exclusion (AROPE)** on **internalizing** and **externalizing problems** in children.

Consider if family context plays a **moderator** or a **mediator** role.

METHODS

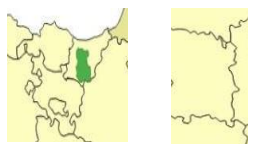
- **AROPE**: exposure.
- **Internalizing and externalizing** problems (CBCL): outcome.
- **HEFAS-7-11:** three dimensions of family context
  - Subscale 3. Organization of the Physical Environment and Social Context
  - Subscale 4. Parental Stress and Conflict
  - Subscale 5. Parental Profile Fostering Development

STATISTICAL ANALYSES

Adjusted Negative binomial regression for sociodemographic, lifestyle and child's characteristics variables.

Moderation models with Subscale 3.

Structural Equation Modelling with Subscale 4 and 5.



SAMPLE

Gipuzkoa N=395
Valencia N=382

RESULTS

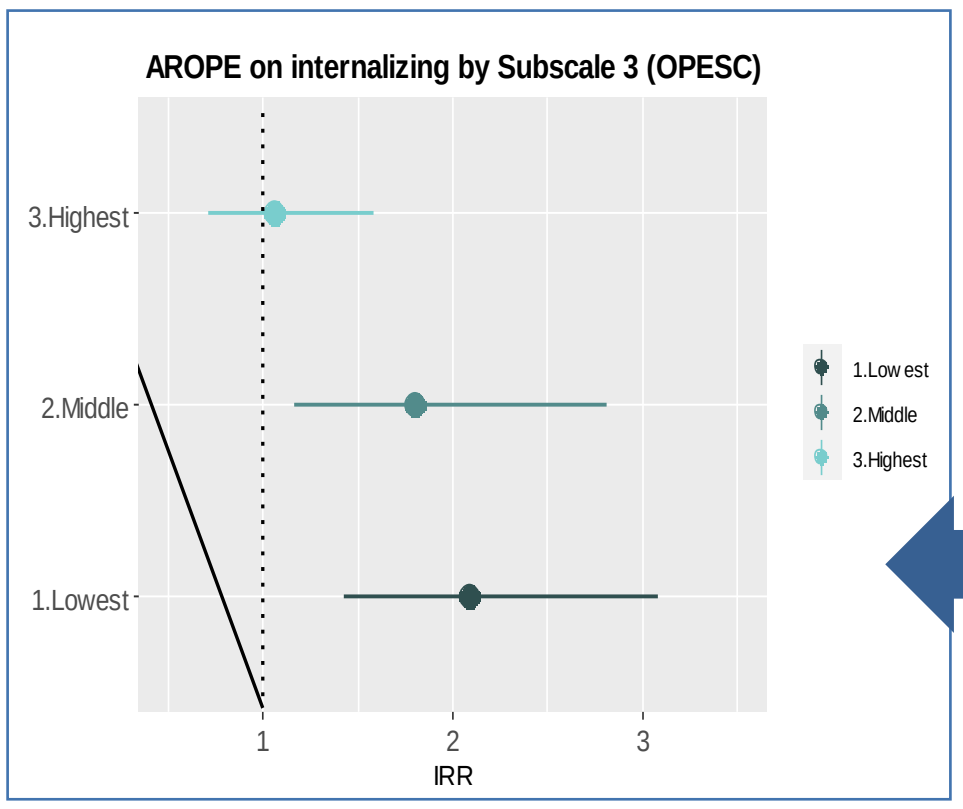
MAIN MODELS

Valencia presented higher risks than Gipuzkoa in AROPE (median, P25-P75, p: 0.31, 0.10-0.60 vs 0.11, 0.03-0.23, p<0.001) and internalizing (6, 3-11 vs 5, 2-9, p<0.001) and externalizing problems (6, 2-10 vs 5, 2-8, p=0.007)

Minimally adjusted models (Model 0) showed **risks close to 2**, and fully adjusted models (Model 1) showed **decreased ratios which did not affect signification.**

	Internalizing				Externalizing			
	IRR	CI 95% lower	CI 95% upper	p	IRR	CI 95% lower	CI 95% upper	p
Model 0: Unadjusted [a]	1.81	1.44	2.27	<0.001	1.98	1.51	2.61	<0.001
Model 1: Ajusted [b]	1.60	1.26	2.03	<0.001	1.80	1.35	2.39	<0.001

Core models:
Internalizing adjusted for: Small for Gestational Age (SGA), maternal and paternal tobacco in pregnancy, maternal alcohol in pregnancy and maternal age.
Externalizing adjusted for: SGA, family type, paternal tobacco in pregnancy, maternal alcohol in pregnancy.
[a]Model 0:Adjusted for age, sex and cohort
[b]Model 1: Model 0 + core models

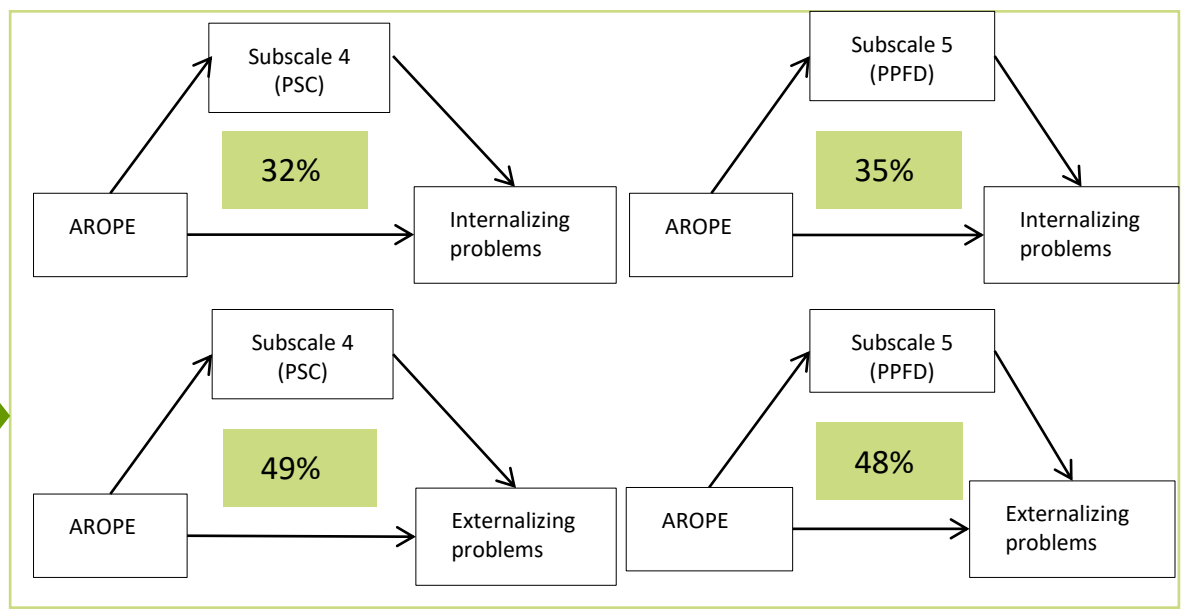


MODERATION ANALYSIS

Moderation of AROPE with Organization of Physical Environment and Social Context was only found in **Internalizing problems**. Families with the highest quality of context did not present association for AROPE, while for those with middle and low quality, s**ignificant gradients** were found.

MEDIATION ANALYSES

- **AROPE → Outcomes:** betas around 0.10
- **Subscales → Outcomes:**
  - **Internalizing:** betas were -0.25 to -0.23
  - **Externalizing:** betas were -0.41 to -0.37



CONCLUSIONS

- **Higher risks** of AROPE and Internalizing and Externalizing problems were presented in **Valencia in comparison to Gipuzkoa**.
- **AROPE increased risk of Internalizing and Externalizing problems** after adjusting for related variables.
- **Organization of the Physical Environment and Social Context moderated Internalizing problems**.
- **Parental Stress and Conflict and Parental Profile Fostering Development** mediated **32-49%** and **35-48%** of the relation between AROPE and Internalizing and Externalizing problems.

Concentrations of bisphenol-A in adults from the general population: A systematic review and meta-analysis

Sandra Colorado-Yohar[1,2,3,14], Ana Castillo-González[1], Julio Sánchez-Meca[4], María Rubio-Aparicio[5], Diego Sánchez-Rodríguez[6], Elena Salamanca-Fernández[7,8], Eva Ardanaz[2,9], Pilar Amiano[2,10,11], Mariana F. Fernández[2,8,12], Jaime Mendiola[2,13,14], Fernando Navarro-Mateu[2,4,14,15], María Dolores Chirlaque[1,2,13,14]

1 Department of Epidemiology, Murcia Regional Health Council. Murcia, Spain. 2 CIBER Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III (ISCIII), Madrid, Spain. 3 Research Group on Demography and Health, National Faculty of Public Health, University of Antioquia, Medellín, Colombia. 4 Department of Basic Psychology and Methodology. University of Murcia. Murcia, Spain. 5 Department of Health Psychology, University of Alicante. Alicante, Spain. 6 Teaching Unit of preventive medicine and public health, Murcia, Spain. 7 Andalusian School of Public Health (EASP). Granada, Spain. 8 Instituto de Investigación Biosanitaria de Granada. ibs. GRANADA, Spain. 9 Navarra Public Health Institute, IdiSNA, Pamplona, Spain. 10 Ministry of Health of the Basque Government, Sub-Directorate for Public Health and Addictions of Gipuzkoa, San Sebastián, Spain. 11 Biodonostia Health Research Institute, Epidemiology and Public Health Area, San Sebastián, Spain. 12 University of Granada, Center for Biomedical Research (CIBM), Spain. 13 Department of Health and Social Sciences, Universidad de Murcia, Murcia, Spain. 14 Murcia Biomedical Research Institute (IMIB-Arrixaca), Murcia Spain. 15 Unidad de Docencia, Investigación y Formación en Salud Mental, Servicio Murciano de Salud, Murcia, Spain.

Science of The Total Environment. *Volume 775, 25 June 2021, 145755.* https://doi.org/10.1016/j.scitotenv.2021.145755

Background

Human bisphenol-A (BPA) exposure has been linked to adverse health effects even at low doses, which may be of potential public health concern.

Objective

To summarize BPA concentrations in general human population and their variability according to sex, geographic area, and analytical method.

Methods

Systematic review and meta-analysis of studies reporting BPA concentrations in adult human populations. Separate meta-analyses of median values were carried out for BPA in serum, creatinine-adjusted urinary BPA, and unadjusted urinary BPA concentrations using a random-effects model. Cochran's Q-statistic, I2 index, 95% prediction intervals (PIs), between-studies standard deviation (τ), and forest plots were applied to verify study heterogeneity. Sensitivity and subgroup analyses and weighted ANOVAs and meta-regressions were conducted. Funnel plots and Egger's tests were used to examine publication bias.

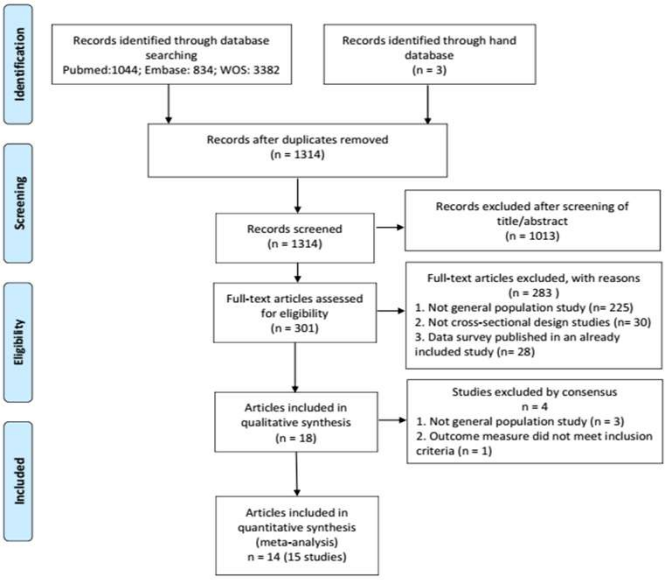


Figure 1. PRISMA 2009 flow diagram

Results

Fifteen studies were included in the meta-analysis, totaling 28,353 participants. BPA was detected in over 90% of participants. The pooled creatinine-adjusted urinary BPA concentration was 1.76 μg/g (95% PI: 0.79-2.73), with individual estimates ranging between 1.20 and 2.41. The pooled estimate for unadjusted urinary BPA was 1.91 μg/l (95% PI: 0-3.97), ranging between 0.81 and 3.50, while the pooled estimate for serum BPA was 1.75 μg/l (95% PI: 0-10.58), ranging between 0.34 and 3.76. No differences were found by sex, geographic area or analytical technique. Larger sample sizes were associated with lower BPA concentrations. There was large heterogeneity across studies, whereas data for urinary BPA levels suggested a publication bias affecting research in low exposed populations.

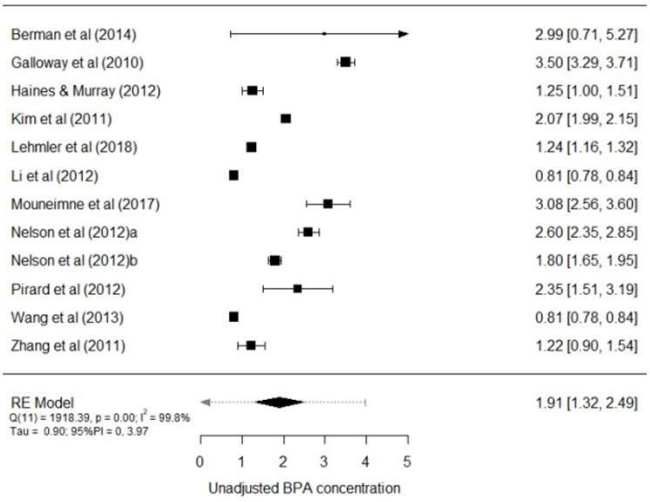


Figure 2. Forest plot of the median unadjusted urinary BPA concentrations (μg/l) of 12 studies from urine biological samples. 'Nelson et al (a)' and 'Nelson et al (b)' corresponded to the '2003-04' and '2005-06' NHANES samples, respectively. Black squares represent median BPA concentrations extracted from each study, whereas lines represent the 95% confidence limits around them. Black diamond represents the average of the median BPA concentrations. Dotted lines from the black diamond represent the 95% prediction interval limits (95%PI). Tau = between-studies standard deviation. RE model = random-effects model. Data in brackets are the lower and upper 95% confidence limits for the median BPA concentration and for its average.

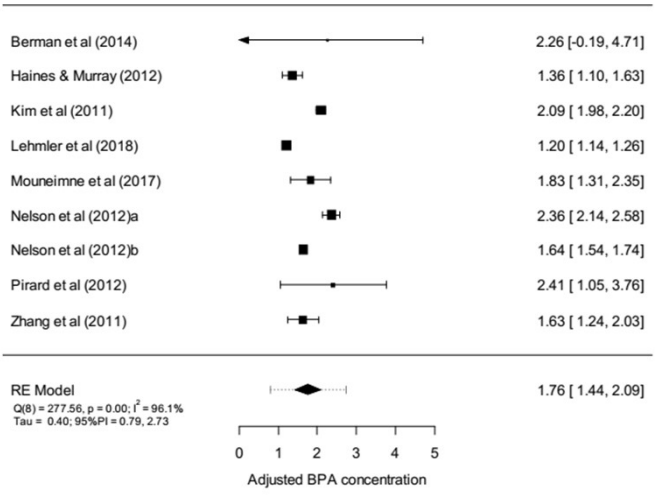


Figure 3. Forest plot of the median urinary BPA concentrations adjusted by creatinine (μg/g) of 9 studies. 'Nelson et al (2012)a' and 'Nelson et al (2012)b' corresponded to the '2003-04' and'2005-06' NHANES samples, respectively. Black squares represent median BPA concentrations extracted from each study, whereas lines represent the 95% confidence limits around them. The black diamond represents the average of the median BPA concentrations. Dotted lines from the black diamond represent the 95% prediction interval limits (95%PI). Tau = between-studies standard deviation. RE model = random-effects model. Data in brackets are the lower and upper 95% confidence limits for the median BPA concentration and for its average.

Conclusions

This first meta-analysis of human BPA concentrations highlights a widespread population exposure to BPA. Although there was high heterogeneity across studies, the expected range of estimated human BPA concentrations suggests that potential health risks are unlikely.

Funding: AECC-Junta Provincial de Murcia (FFIS-2006). IMIB-FFIS, CIBER (BOE-A-2020-6018).

COVID SUSPECTED PATIENTS IN PRIMARY CARE IN MADRID AT THE BEGINNING OF FIRST WAVE (I): CLINICAL CHARACTERISTICS AND PNEUMONIA ONSET

Authors: Miguel Menendez Orenga (1, 2), Miriam Arribas Mayordomo (3), Paula Gasser (3), Ileana Gefaell larrondo, Brenda Giusto Laureano (3), Carolina Sardi (3), Carolina Trovina (3), Sara Ares-Blanco (4). 1 - Investigador independiente. 2 - Instituto de investigacion i+12 (CIBERESP), Hospital 12 de Octubre. Madrid. 3 - Centro de salud Villa de Vallecas. Madrid. 4 - Centro de salud Federica Montseny. Madrid

INTRODUCTION

COVID-19 is a disease with a broad clinical spectrum. **Primary care** should care and follow-up patients with mild and moderate cases but also identify those who are severely ill. Little information about the COVID-19 has been published in this clinical setting. OBJECTIVE: to **describe** the **characteristics** of patients **attended at Primary Care** with a COVID-19 suspicion including **pneumonia onset**.

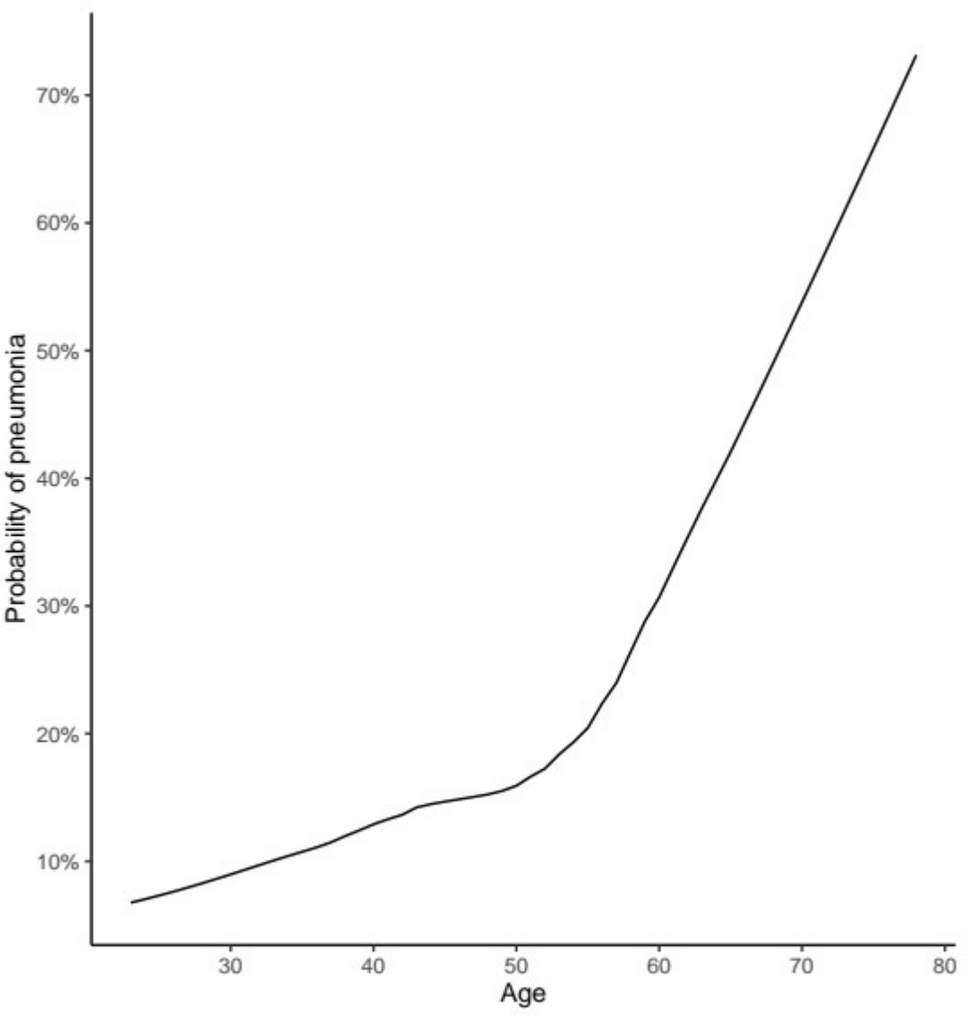
METHODS

Retrospective longitudinal observational study of clinical records. Probabilistic sampling of patients attended in the circuit of suspicion of COVID-19 in 5 Primary Health Care centers in Madrid, from March 16th to 20th. Basal characteristics of patients, symptoms, respiratory rate and oxygen saturation were collected; X-ray results and hospital assistance. **Descriptive analysis and time-to-event** (pneumonia) analysis was performed.

RESULTS

240 medical stories were reviewed. Mean age was 48 years, 60% were women. Most prevalent diseases were high blood pressure (28%), chronic respiratory disease (19%) and Diabetes Mellitus (8%). Most common symptoms were **cough (80%)** and high temperature (63%). Most patients had a short self-limiting process. **Pneumonia** was diagnosed in **23%**, **73%** of whom had **bilateral** pneumonia. Median time to diagnosis was 8 days. **20%** of patients were **admitted to the hospital,** whose mean age was 64 years. Age was related to pneumonia diagnosis. 7 patients died, all male, with a mean age of 79 years, their median day of death was day 13.

Pneumonia probability related to age



Locally Weighted Scatterplot Smoothing(LoWeSS)

CONCLUSIONS

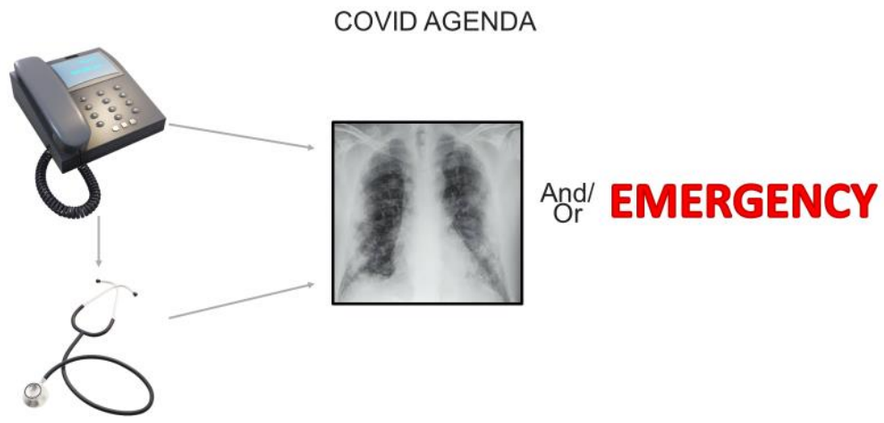
Most patients attended in Primary Care had a **short self-limiting process**, but a relevant number of them presented pneumonia or required hospital admission. **Age was strongly related to pneumonia development.**

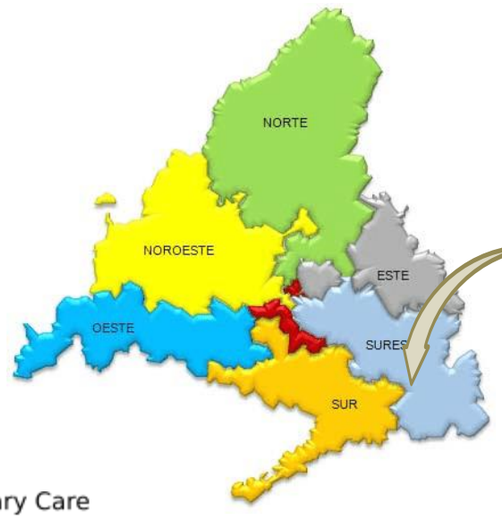
Authors: Miguel Menéndez Orenga (1, 2), Miriam Arribas Mayordomo (3), Paula Gasser (3), Ileana Gefaell Larrondo (3), Brenda Laureano (3), Carolina Sardi (3), Carolina Trovina (3), Sara Ares Blanco (3). 1 – Investigador Independiente. 2- Instituto de Investigación i+12 (CIBERESP), Hospital 12 de Octubre, Madrid. 3 - Servicio Madrileño de Salud.

COVID suspected patients in Primary Care in Madrid at the beginning of first wave (II): Healthcare assistance and patient flow

Introduction

- Health systems have adapted to COVID-19.
- In Spain, Health Care response was hospital centered despite primary care is the central pillar.
- In **Primary Care non-severe patients were followed** both **by phone and in-person appointments.**
- We **studied the role of primary care** at the beginning of COVID-19 pandemic in Madrid

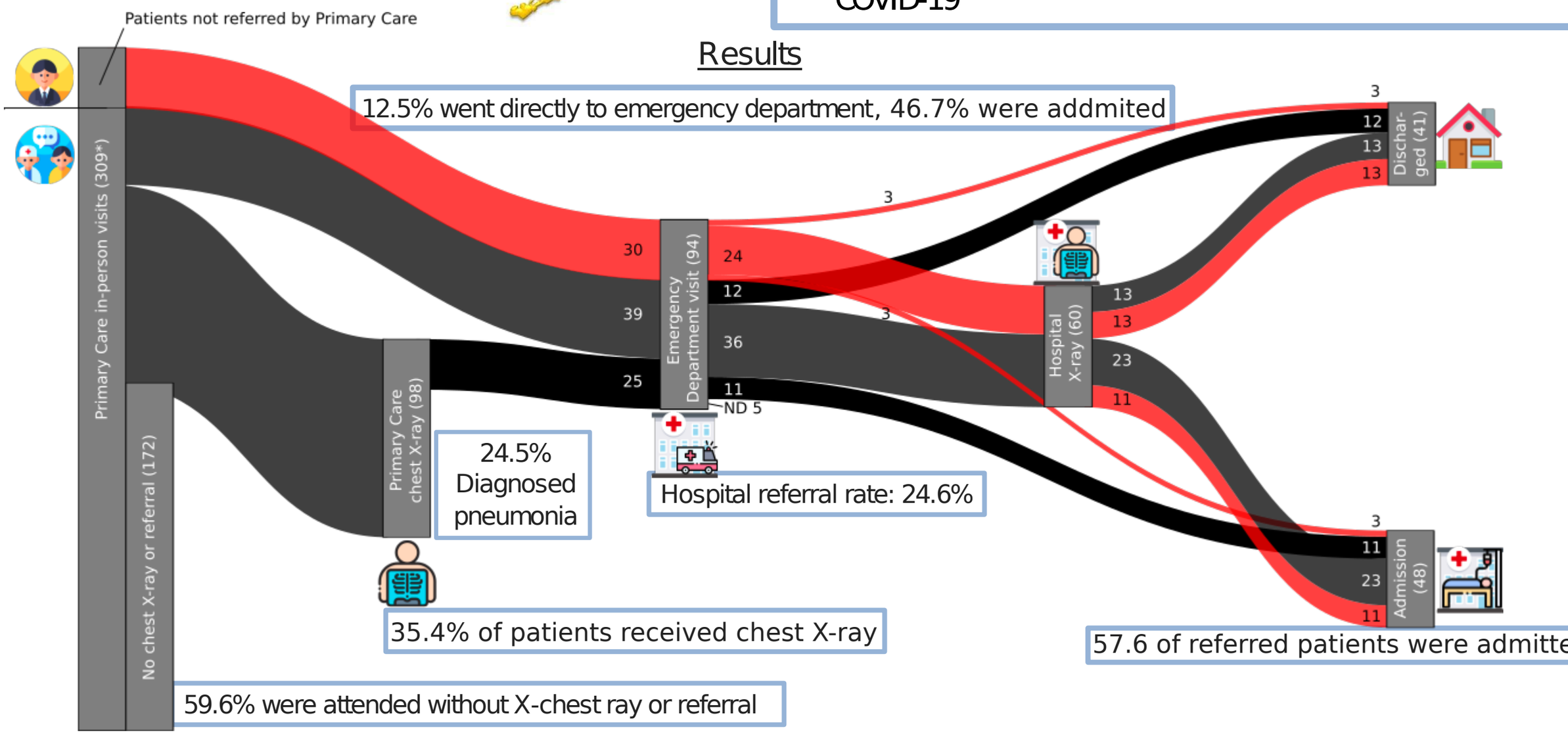




Methods

- Retrospective study in five primary care centres
- Date: **16th - 20th of March 2020**
- **Variables:** daily appointments with health professionals, sick leaves, pneumonia onset.
  Data collection: all clinical schedules and a sample of electronic health records of patients with suspicious COVID-19

Results



12.5% went directly to emergency department, 46.7% were addmited

24.5% Diagnosed pneumonia

Hospital referral rate: 24.6%

35.4% of patients received chest X-ray

59.6% were attended without X-chest ray or referral

57.6 of referred patients were admitted

Sankey Diagram: 240 Patients with COVID-19 suspicion, who received 260 in-person visits.
49 phone appointments have been included as a chest X-ray or Emergency referral was asked

All appointments from clinical shedules: 19,027

Sample of 240 COVID-19 suspicious patients: 1,384 appointments: 80.3% by phone, 18.8% in-person visits and 0.5% home visits

sick leaves

22.4% of family physician's sick leave

Unequal sick leaves among centres:
- Least affected centre → 9.3% working days
- Most affected one → 41.3%

Conclusions

1. Primary Care managed a relevant workload during the pandemic
2. Most patients **only needed family´s physician care**
3. Severe cases were identified and referred to ED
4. **Sick leave were intense**, this could have **diminished the quality of care**

COVID-19 PANDEMIC'S IMPACT ON LABORATORY CONFIRMED INFECTIOUS DISEASES IN CATALONIA

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INTRODUCTION AND OBJECTIVES

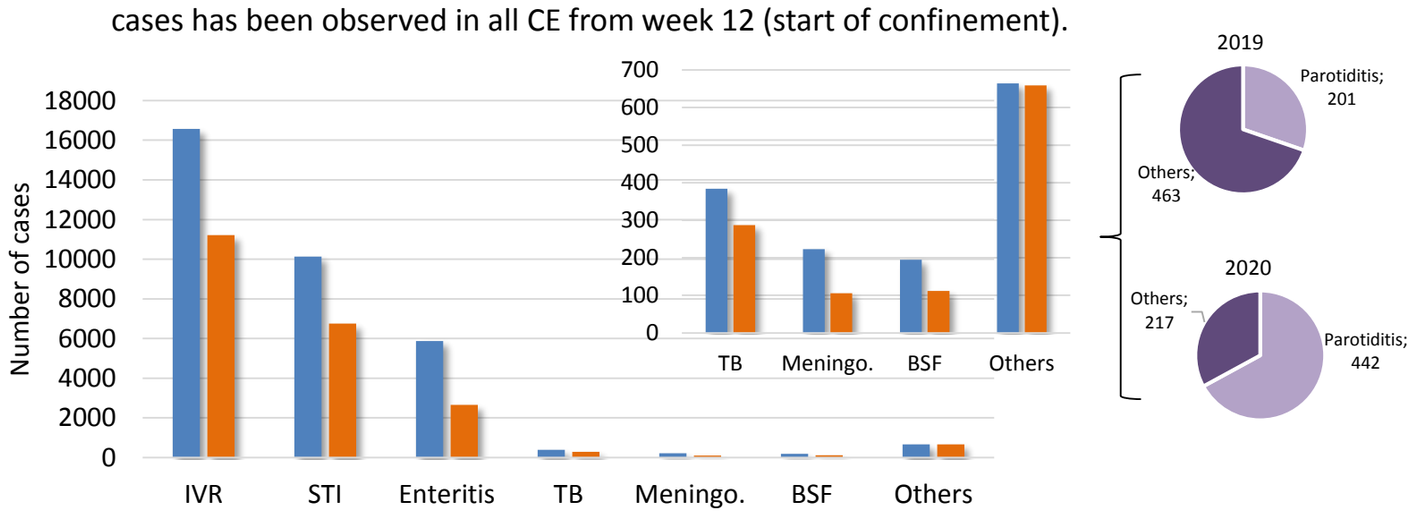
During the COVID-19 pandemic, different hygiene measures have been incorporated into everyday life. With all of them and the confinement, from March 15 to April 26, 2020, it is possible to think that there has been a reduction in the incidence of other common infectious diseases in this period of the year.
The objective of the study was to describe the impact of the COVID-19 pandemic on the declarations of microbiologically confirmed infectious diseases in Catalonia.

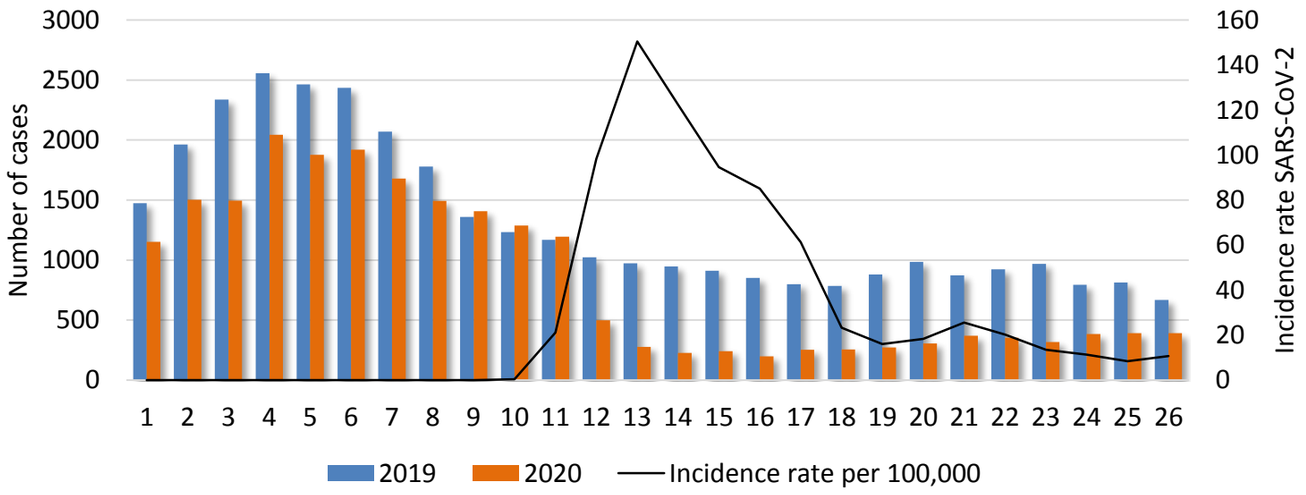
METHODS

All laboratory-confirmed cases (of the 75 microorganisms that cause infectious diseases) were declared to the Microbiological Notification System of Catalonia (SNMC) (Decree 203/2015). Infectious disease cases for weeks 1-26 of 2019 and 2020 have been analyzed. Weeks 1-11 (1st period, before confinement) and weeks 12-26 (2nd period, during confinement and de-escalation phase) of 2019 and 2020 have been compared. Diseases were grouped according to clinical entities (CE): infections respiratory infections (IVR), tuberculosis (TB), sexually transmitted infections (STI), enteritis, meningoencephalitis (Meningo.), bacteremia without apparent focus (BSF) and other infectious diseases (Others) (bacterial, viral and parasitic). In addition, a survey has been carried out to the centers to know the impact of SARS-CoV-2 on their notifications, considering the notification of cases to SNMC and the samples received in the laboratories. The p value <0.05 has been considered statistically significant.

RESULTS

- 21,792 cases were reported in 2020, 36.0% less than in 2019 (34,034 cases).
- The most frequent CE have been:
  - ✓ IVR (2019: 16,569 cases and 2020: 11,217 cases; reduction 32.3%)
  - ✓ STI (2019: 10,125 cases and 2020: 6,761 cases; reduction 33.2%).
  - ✓ Enteritis (2019: 5,874 cases and 2020: 2,650 cases; reduction 54.9%).
- All clinical entities have reduced cases in 2020 between 25% (TB) and 54.9% (enteritis) except for the group Others which have remained stable.
- In the comparison of the 1st and 2nd period between 2019 and 2020, a sharp decrease in cases has been observed in all CE from week 12 (start of confinement).

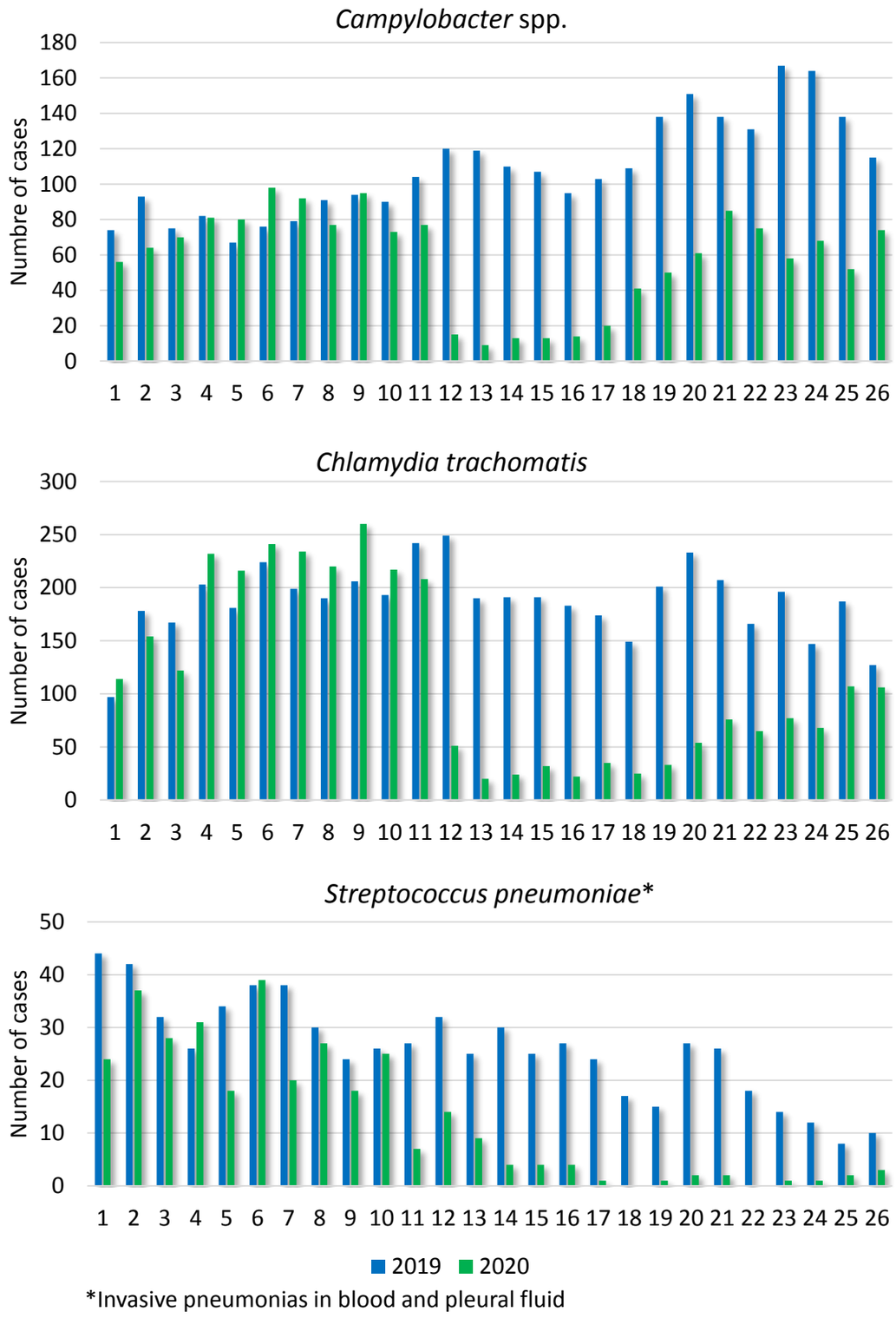




- Reduction in the incidence of confirmed cases in the 1st and 2nd period according to microorganism .

Microorganism	WEEK 1-11 2019 N (%)	WEEK 1-11 2020 N (%)	% change	p value	WEEK 12-26 2019 N (%)	WEEK 12-26 2020 N (%)	% change	p value
Campylobacter	925 (4.44)	863 (5.06)	-6.7	0.005	1,905 (14.43)	648 (13.68)	-66.0	0.211
Rotavirus	264 (1.27)	139 (0.82)	-47.3	0.005	847 (6.42)	40 (0.84)	-95.3	<0.001
Cryptosporidium spp.	37 (0.18)	6 (0.04)	-83.8	<0.001	75 (0.57)	2 (0.04)	-97.3	<0.001
C. trachomatis	2,080 (9.98)	2,218 (1.,00)	+6.6	0.005	2,791 (21.15)	795 (16.78)	-71.5	<0.001
T. vaginalis	630 (3.02)	388 (2.27)	-38.4	<0.001	567 (4.30)	161 (3.40)	-71.6	0.008
Herpes simplex	292 (1.40)	114 (0.67)	-61.0	<0.001	241 (1.83)	154 (3.25)	-36.1	<0.001
Influenza	9,385 (45.04)	5,942 (34.84)	-36.7	<0.001	259 (1.96)	158 (3.34)	-39.0	<0.001
*S. pneumoniae**	361 (1.73)	274 (1.61)	-24.1	0.363	310 (2.35)	48 (1.01)	-84.5	<0.001
Adenovirus	350 (1.68)	194 (1.14)	-44.6	<0.001	284 (2.15)	18 (0.38)	-93.7	<0.001
Virus parainfluenzae	87 (0.42)	62 (0.36)	-28.7	0.451	231 (1.75)	15 (0.32)	-93.5	<0.001
Total	**20,836 (100)**	**17,055 (100)**	**-18.1**		**13,198 (100)**	**4,737 (100)**	**-64.1**	

- The high incidence of cases in 2020 in the group Others was due to an outbreak of mumps at the beginning of the year, which ended abruptly in the first period.
- Of the 3 most frequent CE, the reduction in the number of cases in the second period of *Campylobacter*, *C. trachomatis* and *S. pneumonia** stands out.



*Invasive pneumonias in blood and pleural fluid

- Of the centers that responded to the survey (15/25), 66.7% observed a reduction in the number of samples received from basic areas or external consultations. All the centers verified the notification to SNMC.

CONCLUSIONS

Due to all the hygiene measures, the confinement and the fact that many centers did not receive samples from either basic areas or external consultations, it can be clearly seen how SARS-CoV-2 has caused a decrease in the incidence of other infectious diseases, especially from IVR, STI and enteritis.

Jornada Científica CIBERESP 23 y 25 Marzo 2021

COVID-19 SEROPREVALENCE AMONG WORKERS OF THE CATALAN INSTITUTE OF ONCOLOGY (ICO) IN CATALONIA, SPAIN

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OBJECTIVES

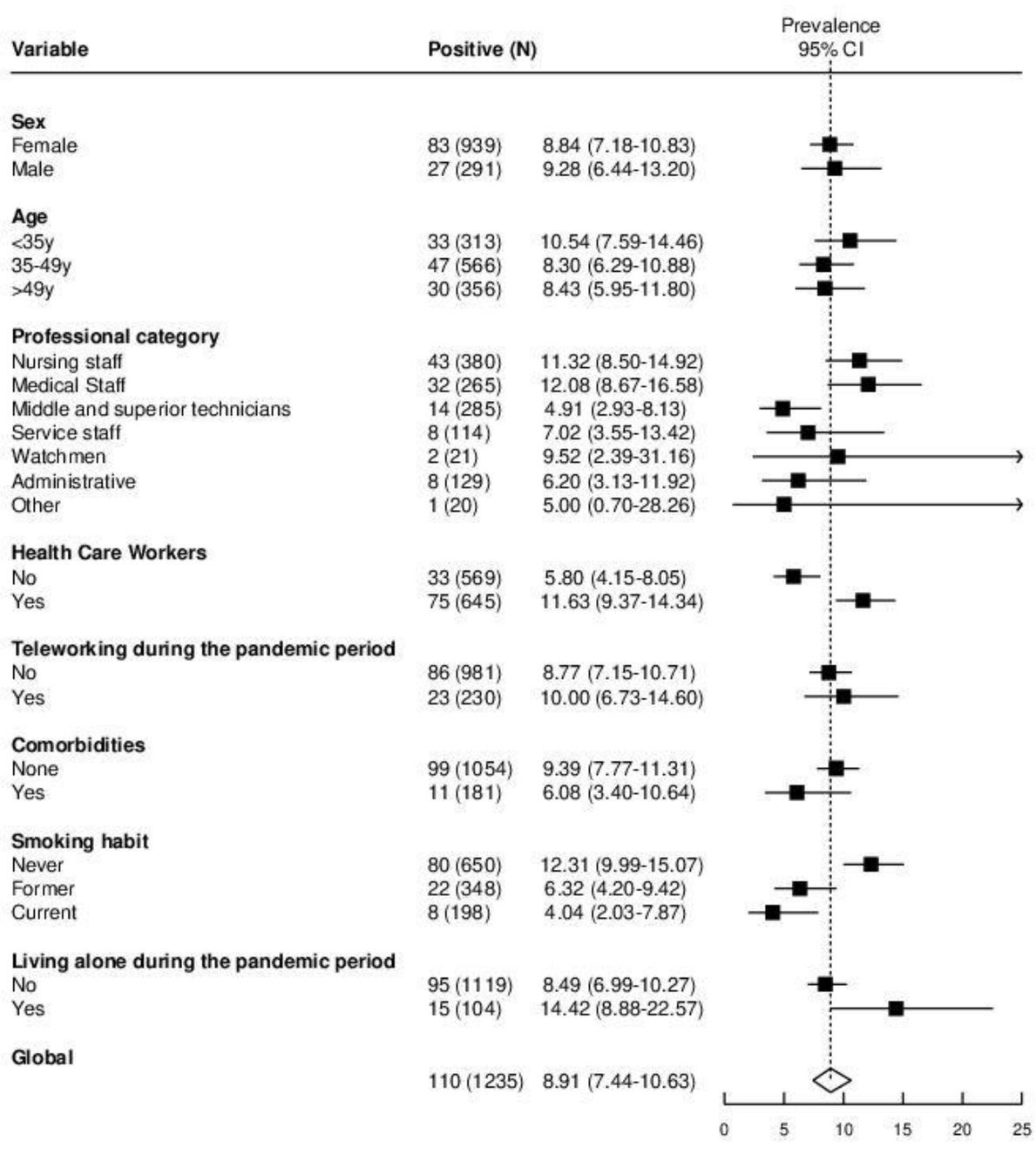
1. To estimate the SARS-CoV-2 seroprevalence among the Catalan Institute of Oncology (ICO) workers, a comprehensive cancer center (four hospitals in Catalonia, Spain)
2. To analyze its association with sociodemographic characteristics, exposure factors and behaviors

METHODS

In a cross-sectional study (21st May-26th June 2020) all ICO workers (n=1,969) were invited to complete an online self-administered epidemiological survey (sociodemographics, lifestyle, occupation, exposures at work and home and protection measures) and to provide a blood sample to test serum IgM and IgG antibody responses to SARS-CoV-2. Seroprevalences and prevalence ratios (PR) with 95% confident intervals (CI) were estimated using Poisson regression models with robust variance. Models were adjusted for sex, age, ICO center, professional category, teleworking and living alone.

RESULTS

Figure 1. SARS-CoV-2 seroprevalence (95%CI) by sociodemographic characteristics



Nursing staff includes: nursing and nursing assistants
Medical staff includes: resident physicians and specialists
Health staff workers includes: nursing and medical staff
Comorbidities include hypertension, obesity (BMI>=30), heart disease, liver disease, diabetes, chronic respiratory disease, renal disease, cancer, autoimmune disorders and other immunological disorders.

Among the 1,235 final participants included, 76.0% were female, the median age was 44 years (p25-p75: 34.8-51.0 years), 52.2% were health care workers, and 79.4% worked on-site during the pandemic period. Up to 28.7% reported presenting ≥1 comorbidities.

The global SARS-CoV-2 seroprevalence was 8.9% (95%CI:7.44-10.63). Statistically significant differences were found by professional category, smoking habits and living alone (Figure 1).

Workers who lived in the same household as someone with COVID-19 were more than 3 times likely to be seropositive. Among on-site workers, to be health care workers and having worked on COVID-19 zone increased twice the probability of seropositivity. Workers reporting to be exposed to SARS-CoV-2 by interacting with colleagues at work had a PR of 3.26 (95%CI: 1.49-7.15) (Table 1).

No statistical significant differences in PR were found for protective measures and hand hygiene (*data not shown*). Most of the participants performed the protective measures at the workplace. At the end of the work day and after utensils manipulation were the moment with less adherence to protective measures *(Figure 2)*.

CONCLUSIONS

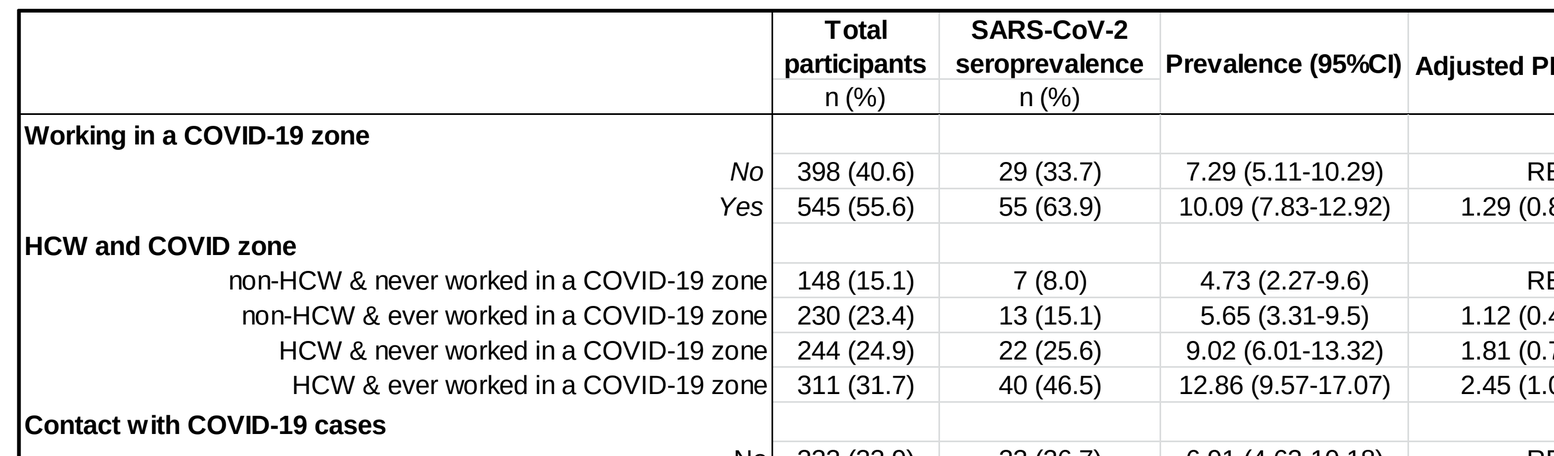
SARS-CoV-2 seroprevalence among ICO workers was lower than in other Catalan hospitals. Whereas among all the workers the main associated factors with seroprevalence was living in the same household as someone with COVID-19; among all on-site employees, working as medical health worker in COVID-19 zone and having contact with other colleagues stood out as the main associated factors of nosocomial infection. Strengthening preventive measures and health education among health-care workers is fundamental, especially in an oncological hospital.

Table 1. Occupational exposure among those working on-site (always/sometimes)

	Total participants n (%)	SARS-CoV-2 seroprevalence n (%)	Prevalence (95%CI)	Adjusted PR (95% CI) [3]
Working in a COVID-19 zone				
No	398 (40.6)	29 (33.7)	7.29 (5.11-10.29)	REF
Yes	545 (55.6)	55 (63.9)	10.09 (7.83-12.92)	1.29 (0.81-2.06)
HCW and COVID zone				
non-HCW & never worked in a COVID-19 zone	148 (15.1)	7 (8.0)	4.73 (2.27-9.6)	REF
non-HCW & ever worked in a COVID-19 zone	230 (23.4)	13 (15.1)	5.65 (3.31-9.5)	1.12 (0.44-2.82)
HCW & never worked in a COVID-19 zone	244 (24.9)	22 (25.6)	9.02 (6.01-13.32)	1.81 (0.77-4.26)
HCW & ever worked in a COVID-19 zone	311 (31.7)	40 (46.5)	12.86 (9.57-17.07)	2.45 (1.08-5.52)
Contact with COVID-19 cases				
No	333 (33.9)	23 (26.7)	6.91 (4.63-10.18)	REF
Yes	536 (54.6)	57 (66.3)	10.63 (8.29-13.54)	1.30 (0.77-2.20)
Contact with COVID-19 biological samples				
No	646 (65.9)	51 (59.3)	7.89 (6.05-10.24)	REF
Yes	282 (28.7)	30 (34.9)	10.64 (7.54-14.81)	1.09 (0.66-1.79)
Reporting to be exposed to SARS-CoV-2 by interacting with colleagues at work				
No	242 (24.7)	66 (76.7)	2.89 (1.38-5.95)	REF
Yes	608 (62.0)	7 (8.1)	10.86 (8.62-13.59)	3.26 (1.49-7.15)

PR: Prevalence Ratio, HCW: Health Care Workers
PR adjusted by sex, ICO center, age (continuous), HCW (No/Yes), telework (No/Yes), living with someone (No/Yes)

Figure 2. Adherence of occupational protective measures and hand hygiene (on-site workers)



PPE: personal protective equipment

No sources of funding nor potential conflicts of interest to declare

Dietary patterns and nutritional quality of the Spanish households during the COVID-19 pandemic

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Introduction

The approval of the state of alarm in Spain, during the health crisis situation caused by COVID-19 pandemic, led to a lockdown of the population, in 2020. Food consumption during those months was almost exclusively limited to households food purchases.

Objective

The aim of this study was to describe the diet and its nutritional quality in the Spanish population during the lockdown and to assess the changes in diet compared to the same months in 2019.

Methodology

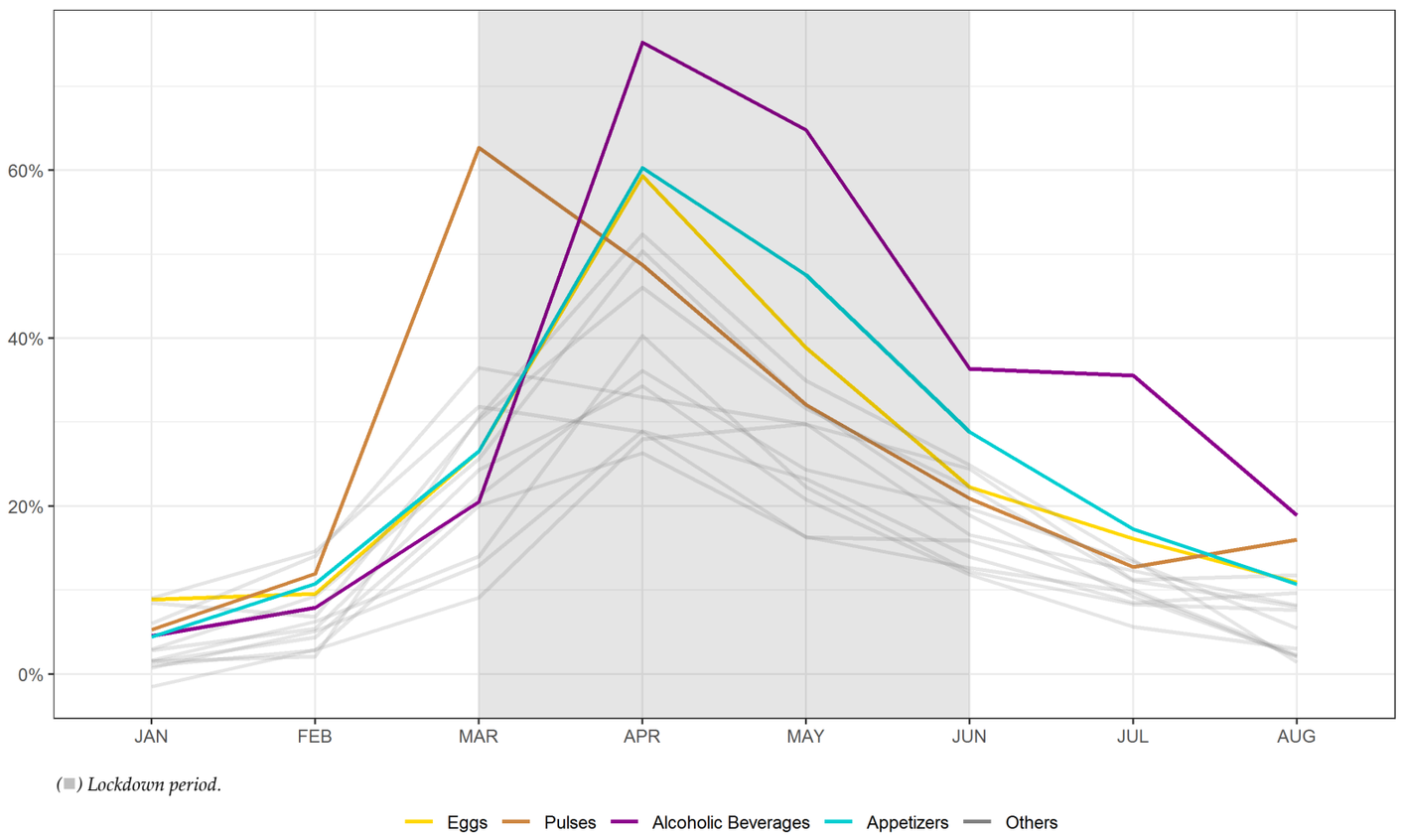
The data on food consumption and distribution in the household were obtained from the nationwide representative Food Consumption Survey (FCS) of the Ministry of Agriculture, Fisheries and Food (MAPA). For this task, the detailed data for the months from January to August 2019 and 2020 have been used (two months before and after state of alarm - from the 14th March and until the 21st June).

Food and beverages data were grouped in big categories of food according to their typology and composition. To calculate the energy and nutrient content, the amounts to food was converted into grams, person and per day, and transformed using the Food Composition Tables of Moreiras et al. 19th Ed.

Results

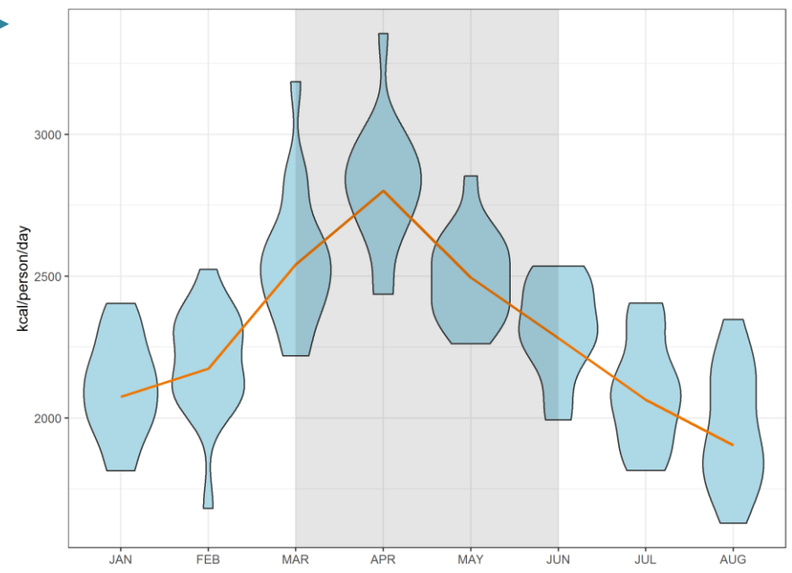
In 2020 there was an expected increase in consumption of all food groups in households, especially during the months of March to June, compared with 2019 (**figure 1**). This increase begins before the state of alarm, in February, and continues after the end of the lockdown. In April, there was an average increase of more than 40% for all food groups, with significant consumption peaks: 62% pulses in March, 75% alcoholic beverages and 60% appetizers and eggs in April. These changes began to decline in May, but they continued over time.

Figure 1. Food groups consumption in Spanish households (% change 2020 vs 2019).



(▒) Lockdown period.

Figure 2. Violin plot of regional variations in energy intake (kcal/person/day) in households and evolution of the national mean (orange curve), 2020.



(--) National mean. (▒) Regions distribution. (▒) Lockdown period.

Figure 3. Some of the changes in nutrient density in Spanish households (unit/1000 kcal), % change 2020 vs 2019.

MARCH	APRIL	MAY	JUNE
Sodium (+2%) **Vitamin E** (+2%)	**Fibre** (+3%) **Sodium** (+3%) **Folates** (+4%) **Carotenes** (+8%) **Alcohol** (+30%)	**Vitamin E** (+2%) **Carotenes** (+7%) **Alcohol** (+30%)	**Alcohol** (+20%)
Calcium (-4%) **Zinc** (-4%) **Riboflavin** (-5%) **Vitamin B_{12}** (-6%) **Vitamin A** (-7%) **Retinol** (-11%) **Alcohol** (-8%)	**Selenium** (-4%) **Vitamin B_{12}** (-6%) **Iodine** (-7%) **Vitamin D** (-9%) **Retinol** (-13%)	**Retinol** (-3%) **Iodine** (-6%)	**Selenium** (-3%) **Vitamin D** (-3%)

The mean energy consumption (**figure 2**) was 2801 kcal/person/day in April 2020, which represents an increase of 771 kcal/person/day (+ 38%) compared to the same month of 2019 households. In March and May the increase was + 528 kcal (+26.2%) and + 520 kcal (+26.3%), respectively, and in June was +343 kcal (+17.7%). In relation to nutrient density (nutrient/1000 kcal) (**figure 3**), a reduction has been seen for calcium, iodine, zinc, selenium, riboflavin, vitamin B_{12}, D, and A -especially retinol-. Conversely, there was an increase in fibre, sodium, folates, carotenes and vitamin E. Alcohol appeared to decline in the first month of lockdown, but then increased by more than 30% in April and May, and remains high.

Conclusions

Dietary patterns of Spanish households have been changed greatly during the months of lockdown and after, but these changes do not seem to have led to an improvement in the quality of the Spanish diet.

Effect biomarkers to improve the evaluation of environmental exposures on human health: BDNF as a case-study

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BACKGROUND & OBJECTIVE

Effect biomarkers (EfB) are measurable biological changes in an individual, that may indicate a health deterioration or disease. Depending on the level of biological organization, EfB can be classified as: molecular (e.g., epigenetic marks), biochemical (e.g., glucose or insulin), or physiological (e.g., blood pressure, fetal ultrasound measures). Despite their heterogeneity, EfB provide valuable information helping to: i) investigate potential modes of action between exposure-outcome associations; ii) identify subclinical effects without the need to wait years until the onset of a particular disease; iii) evaluate novel chemical families or substitutes of regulated chemicals in a timely manner.

EfB can be conceptualized as intermediate steps between the exposure-disease continuum (**Figure 1**). In the Human Biomonitoring for Europe (HBM4EU) Initiative, a general inventory of EfB, including both clinical and novel, was created based on wide literature searches, analyzing their advantages and limitations. Before implementing those novel effect biomarkers in aligned studies representing populations from the North, South, East and West Europe, their technical and physiological validity should be explored.

Bisphenol A (BPA) exposure has been linked to altered behavior in children. Within HBM4EU, an adverse outcome pathway (AOP) network was also constructed supporting the mechanistic link between BPA exposure and brain-derived neurotrophic factor (BDNF) (Mustieles et al., 2020).

Objective: we aimed to perform a case-study to test this toxicologically-based hypothesis in the prospective INMA-Granada birth cohort (Spain).

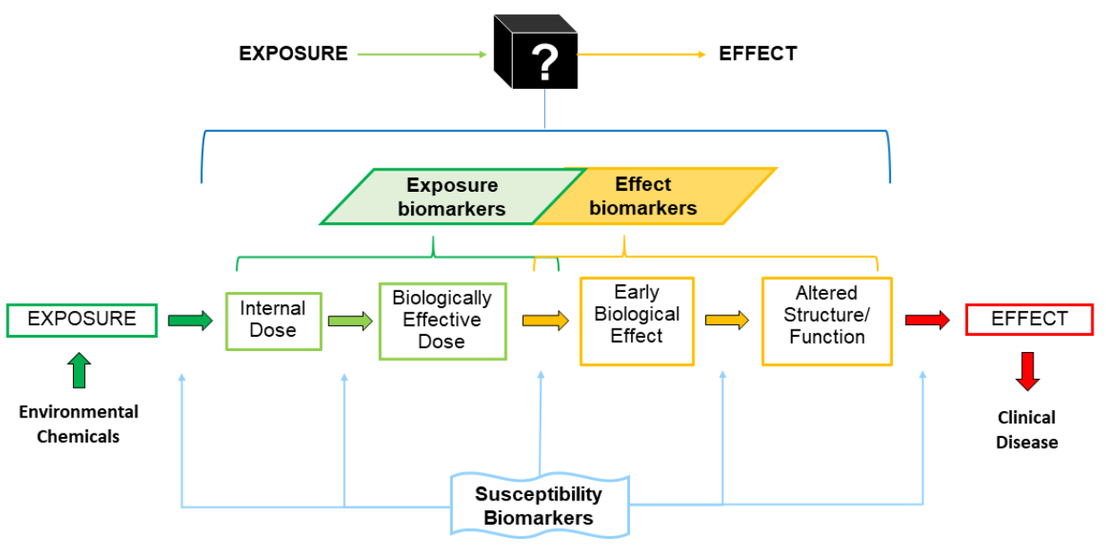


Figure 1. Exposure-disease continuum (Mustieles et al., 2020)

METHODS

- BPA was measured in one spot urine sample **at 9-11 years (n=130)** using HPLC-MS/MS and normalized by urinary creatinine.
- BDNF (serum and urinary) biomarkers assessed in the same boys at age **15-17 years,** by ELISA kits (total BDNF levels). DNA methylation of 6 CpG islands in Exon IV of the BDNF gene quantified in peripheral blood (bisulfite-pyrosequencing).
- Adolescents' behavior parent-reported with Child Behavior Check List (CBCL) and T-scores calculated.
- Linear regression analyses (with independent variables log2- transformed). All models adjusted by age (months) and BMI (Kg/m^2) at behavioral assessment, maternal education (primary, secondary or higher), and urinary cotinine at 9-11 years.

RESULTS

- Median urinary BPA, and urinary and serum BDNF concentrations were 5.20 µg/g, 2.14 µg/g and 32.0 ng/ml, respectively (data not shown).
- BPA was longitudinally and positively associated with several CBCL scales, especially with the "Thought Problems" subscale: 0.75 (0.02, 1.49) (Table 1).
- BPA was longitudinally and positively associated with the percentage of DNA methylation of CpG 3, 5, 6 and the mean methylation of all CpGs investigated (Table 2). The magnitude of the association was especially relevant for CpG6: 0.22 (0.06, 0.37).
- A potential mediation of CpG6 DNA methylation between BPA exposure and the "Thought problems" subscale of the CBCL test at adolescence was observed (Figure 2).

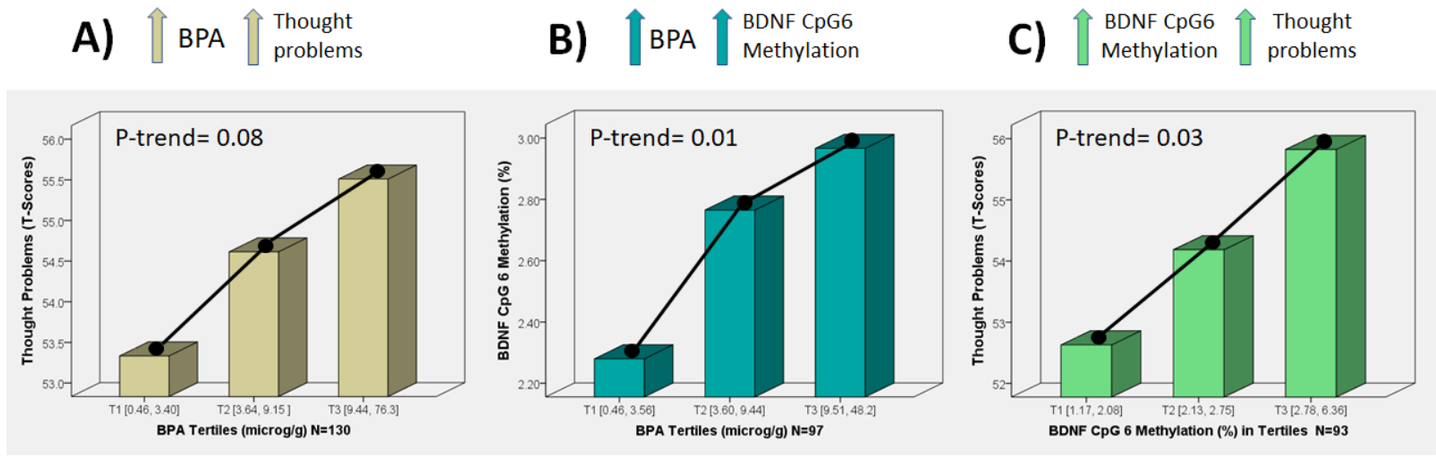
Table 1. Longitudinal BPA-behavior associations

Behavioral functions (CBCL)	BPA (µg/g of creatinine)	
Syndrome scores	β (95% CI)	p-value
Anxious/Depressed	0.34 (-0.43, 1.11)	0.390
Withdrawn	0.17 (-0.66, 0.99)	0.686
Somatic complaints	0.79 (-0.16, 1.75)	0.103
Social problems	-0.11 (-0.87, 0.66)	0.784
Thought problems	**0.75 (0.02, 1.49)**	**0.045**
Attention problems	-0.35 (-1.16, 0.46)	0.394
Rule-breaking problems	0.42 (-0.31, 1.14)	0.258
Aggressive behavior	0.01 (-0.76, 0.77)	0.998
Composite scores		
Internalizing problems	0.39 (-0.49, 1.28)	0.382
Externalizing problems	0.23 (-0.35, 0.81)	0.429
Total problems	0.80 (-0.14, 1.73)	0.093

Table 2. Longitudinal BPA-BDNF associations

BDNF measurements	BPA (µg/g of creatinine)		
BDNF protein levels	β (95% CI)	P-value	n
Serum BDNF (ng/ml)	-0.20 (-1.49, 1.08)	0.754	120
Urinary BDNF (µg/g)	0.12 (-0.11, 0.35)	0.303	116
Blood BDNF DNA methylation			
CpG1 (%)	0.03 (-0.09, 0.15)	0.623	104
CpG2 (%)	0.06 (-0.02, 0.13)	0.139	106
CpG3 (%)	**0.09 (-0.00, 0.17)**	**0.055**	107
CpG4 (%)	0.08 (-0.09, 0.26)	0.341	99
CpG5 (%)	**0.11 (0.00, 0.22)**	**0.047**	103
CpG6 (%)	**0.22 (0.06, 0.37)**	**0.007**	97
CpG mean (%)	**0.10 (0.02, 0.19)**	**0.022**	106

Figure 2. CpG6 DNA methylation as a potential link between BPA exposure and the "Thought problems" CBCL subscale



CONCLUSIONS

BDNF DNA methylation constitutes a promising effect biomarker of brain function that may improve the inference of causal relationships in observational studies, and consequently should be further investigated and replicated under different settings and in relation to other chemical exposures. A more systematic and toxicologically-supported implementation of EfB in HBM surveys and birth cohorts is needed.

Mustieles et al., 2020. Bisphenol A and its analogues: A comprehensive review to identify and prioritize effect biomarkers for human biomonitoring. Environ Int. doi: 10.1016/j.envint.2020.105811.

EPIDEMIOLOGICAL CHARACTERISTICS IN THE CONTENTION PHASE OF COVID-19 PANDEMIC IN CATALONIA

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1. Agencia Salut Pública de Cataluña
2. CIBER Epidemiologia y Salud Pública-CIBERESP (groups 01 and 12)

Introduction

In Catalonia, the first case of SARS-CoV-2 infection was reported on February 25, 2020. A descriptive study about COVID-19 cases confirmed by PCR and notified to the Epidemiological Surveillance Network of Catalonia in the contention phase (25/2/2020 to 15/03/2020) was carried out.

Methods

The variables studied were: age, sex, date of sample collection, date of onset of symptoms, hospitalization, ICU, evolution, and chain distribution of the cases.

Results

A total of 2,014 cases were reported, 33.7% required hospital admission, 5% presenting severity criteria. The cases increased progressively, ranging daily from 1 case on February 25 to 479 cases reported on March 15, with a median of 29 cases (Figure 1). The fatality rate was 1.6%. The territorial distribution was not homogeneous; the highest percentage of cases was reported in the city of Barcelona (32.7%) and the lowest in Terres de l'Ebre region (0.7%) (Figure 2).

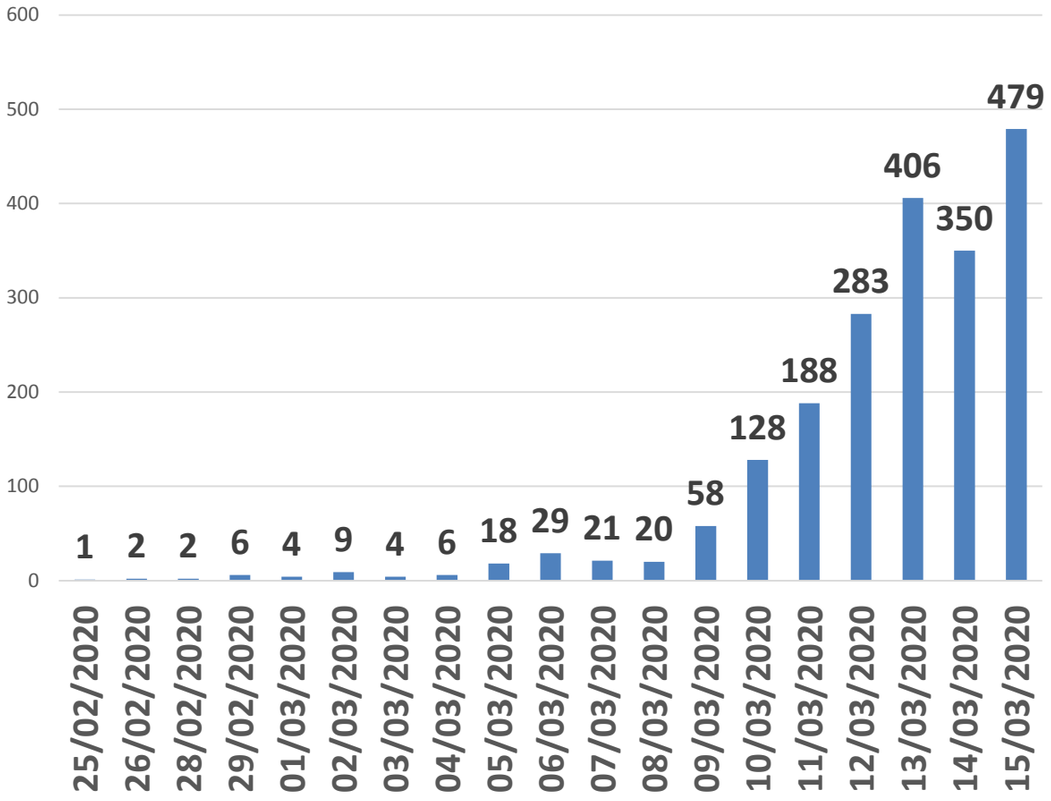

Figure 1. Confirmed cases evolution

Region	Frequency	%
Barcelona city	305	32,7%
Barcelonès Zona Sud	239	25,6%
Barcelonès Zona Nord-Maresme	88	9,4%
Vallès Oriental-Occidental	158	16,9%
Catalunya Central	71	7,6%
Girona	33	3,5%
Lleida	19	2,0%
Tarragona	14	1,5%
Terres de l'Ebre	7	0,7%
Total	934	100,0%

Figure 2. Confirmed cases regional distribution

The age distribution was: 0.22% of 0-4 years; 0.90% of 5-14 years; 9.88% of 15-29 years; 14.26% of 30-39 years; 14.37% of 40-49 years; 16.90% of 50-59 years; 14.04% of 60-69 years; 15.16% of 70-79 years; 10.89% of 80-89 years; 3.37% of 90 or more years. The gender distribution was: 51.1% of the cases were women and 48.9% men.

23 chains of cases were detected, 7 had their origin in trips to Italy, 3 were related to Germany (1 by trip and 2 by meetings in Catalonia with people from Germany), a chain started after a trip to Belgium (contact with people who came from Italy), one chain had its origin in the CA of Madrid and another in CA Valenciana. Ten of the chains had an unknown beginning, one of them led to a major nosocomial outbreak. The length of the chains ranged between 2 and 16 cases with a median of 3 cases. Those affected who were part of the chains ranged in age from 7 months to 88 years; 17 of those affected were health personnel.

Conclusions

The chains of transmission were identified during most of the contention phase. Subsequent community transmission led to the application of mitigation measures. The monitoring of confirmed cases and their contacts is decisive to direct the public health measures to be applied at each moment in the pandemic.

HCV cascade of care of people admitted to drug treatment (2015-2019) in Catalonia

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INTRODUCTION

People who use drugs (PWUD) have high rates of hepatitis C virus (HCV) infection.

This study aims to characterize the HCV cascade of care of people admitted to drug treatment in Catalonia, Spain, by main drug of consumption.

METHODS

Data from PWUD admitted to the 61 drug treatment centers (**01/2015–12/2019)** were derived and linked from three databases: The drug information System; The basic minimum data set of health centers; and HCV treatment registry. Results are based on main drug of consumption. The cascade was defined in four steps: diagnosis of HCV; initiation of treatment; cure and reinfection. Predictors of HCV treatment access were identified using a multivariable regression model.

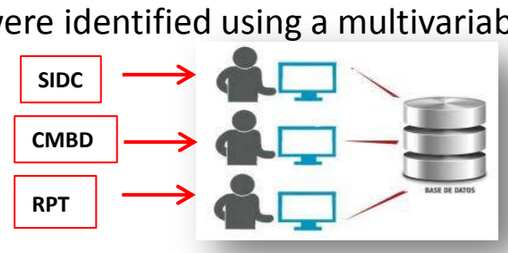

Figure 1. Sources of information linked them back to tract people. Drug information system of people under drug dependecy treatment (**SIDC**); Morbidity registry (**CMDB**); HCV treatment registry (RPT).

RESULTS

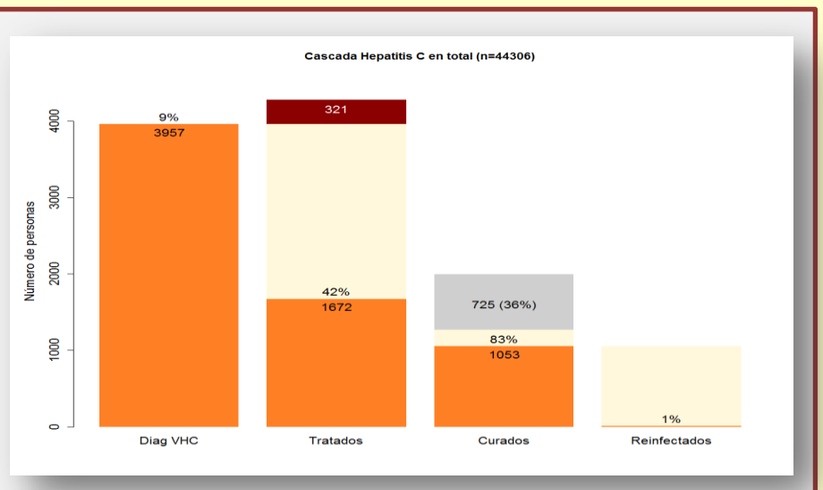

Figure 2. HCV cascade of care of people admitted to drug treatment in Catalonia, Spain

44,306 PWUD were admitted to treatment: **9.6%** (4,265) for heroine, **45.8%** (20,282) alcohol; **14.3%** (6,323) cannabis; **21.2%** (9,384) cocaine and **4.3%** (1,889) tobacco.

Overall, **9.7%** (4,278) had a diagnosis of HCV, **42%** (1,672) had started HCV treatment, **83%** (1,053) were cured and 1% (8) were reinfected.

In the multivariable analyses, human immunodeficiency virus seropositivity, imprisonment and tobacco users were independently and positively associated with HVC treatment access (P< .001), whereas being a woman was independently and negatively associated with HCV treatment access (P<.001).

HCV cascade by main drug of consumption

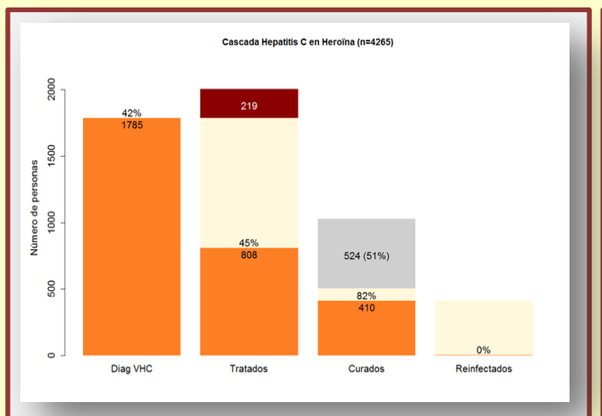

Figure 3. HCV cascade of care of people admitted to drug treatment due to heroin consumption

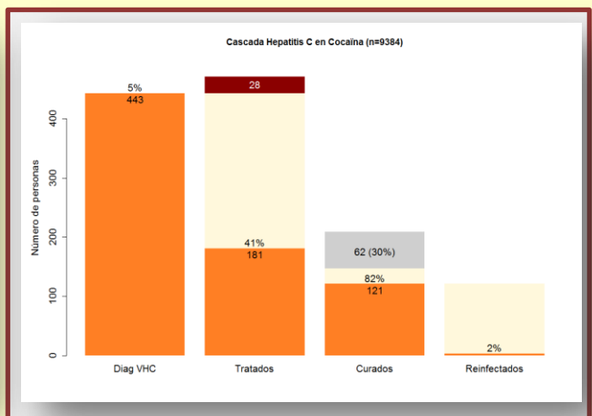

Figure 4. HCV cascade of care of people admitted to drug treatment due to cocaine consumption

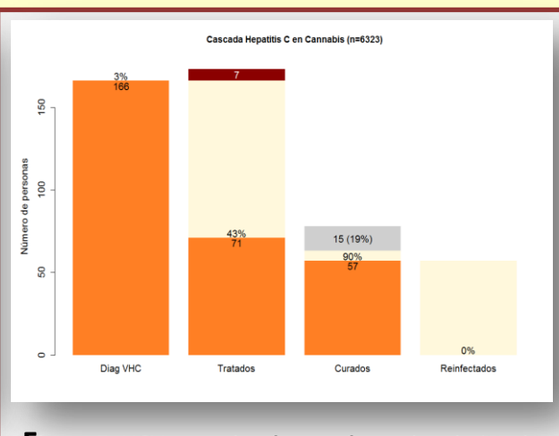

Figure 5. HCV cascade of care of people admitted to drug treatment due to cannabis consumption

	HVC n=3.960		No HVC n=40.488		Total n=44.448		OR	P valor
	N	%	N	%	N	%		
Sex								0,014
Dona	773	19.54	9603	23.8	10376	23.42	1,16	
Home	3184	80.46	30746	76.2	33930	76.58	Ref.	
Edat a l'inici de tractament (mitjana, 95%)	41.16	17-67	45.85	29-61	40.7	17-68	0,71	<0,001
Pais naixement								<0,001
Migrante	401	10.14	3891	13.55	5871	13.25	0,71	
España	3340	84.41	33619	83.32	36959	83.42	Ref.	
Missing	216	5.46	1260	3.12	1476	3.33		
Nivell d'instrucció								
Estudis primaris/sense estudis	2878	72.73	25720	63.74	28598	64.55	Ref.	
Estudis secundaris	594	15.01	9019	22.35	9613	21.7	0,84	0,006
Estudis superiors/universitaris	157	3.97	3556	8.81	3713	8.38	0,59	<0,001
Missing	328	8.29	2054	5.09	2382	5.38		
Situació laboral								
Treballa	621	15.69	15722	38.97	16343	36.89	Ref.	
Aturat/da	1520	38.41	13970	34.62	15490	34.96	1,7	<0,001
Incapacitat/pensionista	1052	26.59	5053	12.52	6105	13.78	1,86	<0,001
Altes situacions	463	11.7	3914	9.7	4377	9.88	0,92	0,483
Missing	301	7.61	1690	4.19	1991	4.49		
Presó								0,85
No	3495	88.32	38948	96.53	42443	95.8	0,221	
Sí	462	11.68	1401	3.47	1863	4.2	Ref.	
Edat al primer cosum (mitjana, 95%)	20.34	10-47	21.32	10-47	20.25	10-47	0,98	<0,000
Injector								<0,001
No	1887	47.69	37681	93.39	39568	89.31	Ref.	
Sí	1812	45.79	1081	2.68	2893	6.53	10,67	
Misisng	258	6.52	1587	3.93	1845	4.16		
Estat d'injector								
No injector	1887	47.69	37681	93.39	39568	89.31	Ref.	
Injector actual	995	25.15	688	1.71	1683	3.8	8,85	<0,001
Injector alguna vegada (fa més de 2 anys)	817	20.65	393	0.97	1210	2.73	12,9	<0,001
Missing	258	6.52	1587	3.93	1845	4.16		
Realització prèvia d'algun tractament								<0,001
No	631	15.95	20500	50.81	21131	47.69	Ref.	
Sí	3030	76.57	15952	39.54	18982	42.84	2,53	
Missing	296	7.48	3897	9.66	4193	9.46		
Droga per la que inicia el tractament								
Alcohol	1053	26.61	19229	47.66	20282	45.78	Ref.	
Alteres substàncies	420	10.61	1743	4.32	2163	4.88	2,79	<0,001
Cànnabis	166	4.2	6157	15.26	6323	14.27	1,1	0,438
Cocaïna	443	11.2	8941	22.16	9384	21.18	1,21	0,019
Heroïna	1785	45.11	2480	6.15	4265	9.63	4,72	<0,001
Tabac	90	2.27	1799	4.46	1889	4.26	0,87	0,296
Diagnòstic de HIV								<0,001
No	2745	69.37	39759	98.54	42504	95.93	Ref.	
Sí	1212	30.63	590	1.46	1802	4.07	12,57	

Table 1. Multivariable analysis to assess determinants of HCV seropositivty

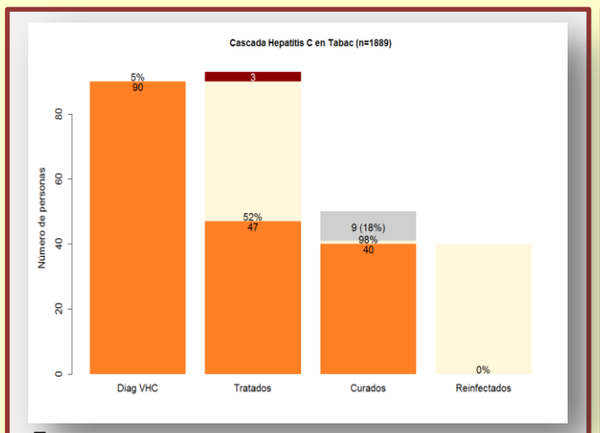

Figure 6. HCV cascade of care of people admitted to drug treatment due to tobacco consumption

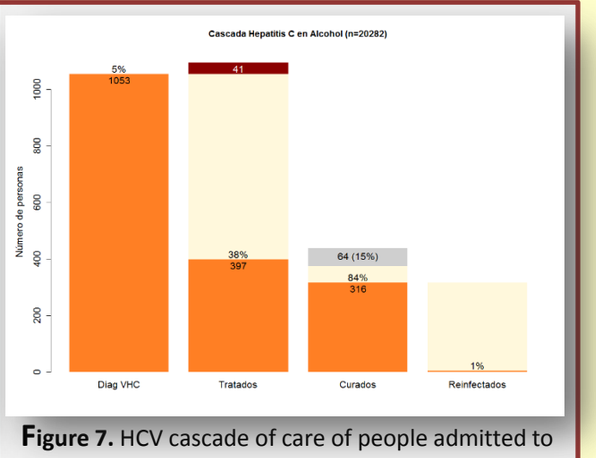

Figure 7. HCV cascade of care of people admitted to drug treatment due to alcohol consumption

	Tratados N=1.994		No tratados N=2.288		Diagnosticats y tratados pero no diagnosticados N=4.282		OR	Pvalor
	N	%	N	%	N	%		
Sexe								<0,001
Dona	305	15.3	494	21.62	799	18.68	Ref.	
Home	1688	84.7	1791	78.38	3479	81.32	0,68	
Edat a l'inici de tractament (mitjana, 95%)	45.47	28-61	45.12	28-59	45.78	29-62	0,99	0,226
Pais naixement								<0,001
Migrant	249	12,1	250	10,6	499	11,65	0,71	
España	1647	82.64	1903	83.28	3550	82.98	Ref.	
Missing	97	4.87	132	5.78	229	5.35		
Nivell d'instrucció								
Estudis primaris/sense estudis	1467	73.61	1648	72.12	3115	72.81	Ref.	
Estudis secundaris	273	13.7	363	15.89	636	14.87	0,84	0,006
Estudis superiors/universitaris	80	4.01	95	4.16	175	4.09	0,59	<0,001
Missing	173	8.68	179	7.83	352	8.23		
Situació laboral								
Treballa	285	14.3	381	16.67	666	15.57	Ref.	
Aturat/da	732	36.73	898	39.3	1630	38.1	1,7	<0,001
Incapacitat/pensionista	487	24.44	590	25.82	1077	25.18	1,86	<0,001
Altes situacions	342	17.16	244	10.68	586	13.7	0,92	0,483
Missing	147	7.38	172	7.53	319	7.46		
Presó								0,221
No	1620	81.28	2065	90.37	3685	86.14	Ref.	
Sí	373	18.72	220	9.63	593	13.86	0,85	
Edat al primer cosum (mitjana, 95%)	21.27	10-47	21.04	11-46	21.48	10-48	0,98	<0,001
Injector								<0,001
No	847	42.5	1147	50.2	1994	46.61	Ref.	
Sí	1020	51.18	987	43.19	2007	46.91	8,85	
Missing	126	6.32	151	6.61	277	6.47		
Estat d'injector								
No injector	847	42.5	1147	50.2	1994	46.61	Ref.	
Injector actual	588	29.5	542	23.72	1130	26.41	8,85	<0,001
Injector alguna vegada (fa més de 2 anys)	432	21.68	445	19.47	877	20.5	12,9	<0,001
Missing	126	6.32	151	6.61	277	6.47		
Realització prèvia d'algun tractament								<0,001
No	299	15	390	17.07	689	16.11	Ref.	
Sí	1537	77.12	1732	75.8	3269	76.41	2,55	
Missing	157	7.88	163	7.13	320	7.48		
Droga per la que inicia el tractament								
Alcohol	438	21.98	656	28.71	1094	25.57	Ref.	
Alteres substàncies	191	9.58	252	11.03	443	10.36	2,79	<0,001
Cànnabis	78	3.91	95	4.16	173	4.04	1,1	0,438
Cocaïna	209	10.49	262	11.47	471	11.01	1,21	0,019
Heroïna	1027	51.53	977	42.76	2004	46.84	4,72	<0,001
Tabac	50	2.51	43	1.88	93	2.17	0,87	0,296
Diagnòstic de VIH								<0,001
No	1286	64.53	1727	75.58	3013	70.43	Ref.	
Sí	707	35.47	558	24.42	1265	29.57	12,57	

Table 2. Multivariable analysis to assess determinants of HCV treatment access

DISCUSSION

Less than a half of those aware of their HCV infection had engaged in treatment, the lowest percentage was found among patients with alcohol dependence.

CONCLUSIONS

Targeted interventions to increase access to treatment among PWUD are essential to reach the WHO target of elimination by 2030.

High acceptability and effectiveness of an online self-sampling intervention for HIV in gay, bisexual and other men who have sex with men and trans women in Spain (TESTATE VIH).

Cristina Agustí[1,2], Héctor Martínez[1], Victoria González[1,2], Sergio Moreno[1], Esteve Muntada[1], Pol Romano[1], Laia Egea[1], Rafael Muñoz[1], Juan Hoyos[2] and Jordi Casabona[1,2,3].

[1]Centre of epidemiological studies on sexually transmitted infections and AIDS of Catalonia (CEEISCAT). Department of Health. Generalitat of Catalonia. Badalona. Spain.
[2]Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain
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Background:
Although HIV infection is preventable through effective public health measures, significant transmission continues in Spain. In 2019, 2,698 new HIV diagnoses were reported, representing a rate of 5,94 per 10 0,000 inhabitants. Transmission among gay, bisexual and other men who have sex with men (GBMSM) was the most frequent (56.4%). About half of new diagnoses (45,9%) were late presenters (CD4 cell cou nt <350 cells/mm at diagnosis) [1] .
It's necessary to design innovative approaches that promote greater access to HIV testing and reach hid den populations, which have not been accessed with the current strategies. Digital technologies are inc reasingly utilized to deliver sexual health interventions (e-sexual health) [2], including internet-accessed STI testing (e-STI testing). It enables users to order a test kit from a website or app, collect their own sa mples, return samples to a laboratory, and be notified of their results by text message, phone or e-mail [3] .

Objectives:
1.To design and implement an online self-sampling intervention for HIV testing and online results consultation (TESTATE Intervention).
2.**To evaluate the acceptability** of TESTATE intervention in GBMSM living in Spain, users of dating apps and websites.
3.**To analyze the capacity of TESTATE intervention to access** subpopulations that have never been tested or that do not test at the recommended frequency.
4.**To evaluate the proportion of participants with reactive results that are linked to the health system** for result confirmation and to initiate follow-up in an HIV unit.
5.To determine the cost-effectiveness of the TESTATE intervention **and the budgetary impact** that would include the TESTATE intervention as a complementary strategy for HIV screening addressed to GBMSM population in Spain

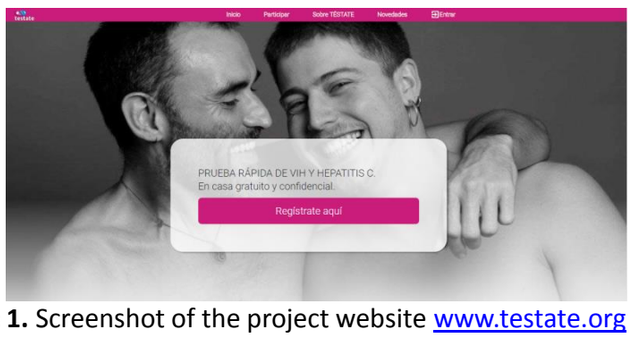

Figure 1. Screenshot of the project website www.testate.org

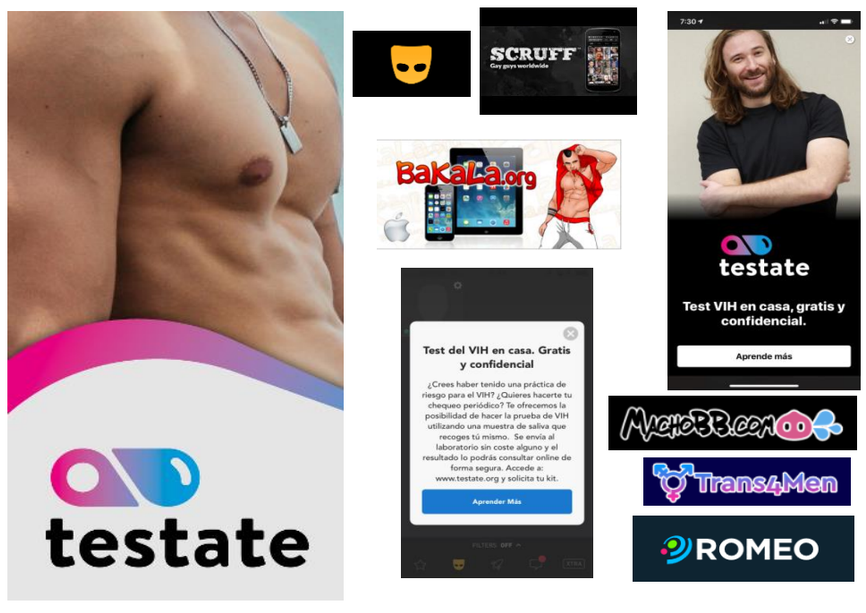

Figure 2. Banner and messages advertised in the main dating apps operating in Spain.

Methods:
The website www.testate.org was designed to offer the self sampling kits, consult the results and collect sociodemographic and behavioral information. It was advertised in th e most popular dating apps/websites in Spain: Grindr, Scruff, Wapo, PlanetRomeo, Bakala, MachoBB and Trans4men.
After signing the informed consent online, the participants requested the delivery of a saliva self-sampling kit by mail and a postage-paid envelope to send the sample to the r eference laboratory.
Lab analysis: The samples were analyzed in the reference lab (Hospital Germans Trias i Pujol, Badalona, Spain) with the Genscreen HIV1 + 2 enzyme immunoassay (Biorad Lab oratories) for the detection of antibodies against HIV1 + 2.
D**elivery of the results and follow up:** Once the results were uploaded to the project website the participants received an SMS with the link to consult them. Reminders by email and text message were sent to participants who have not consulted their results. Participants with reactive results were asked to attend clinic for treatment. There was an active follow-up of participants with a reactive result to confirm linkage to care. Participants were invited to repeat the process after 3/6/12 months based on their risk behavior. An anonymous **acceptability survey** was conducted on all participants.

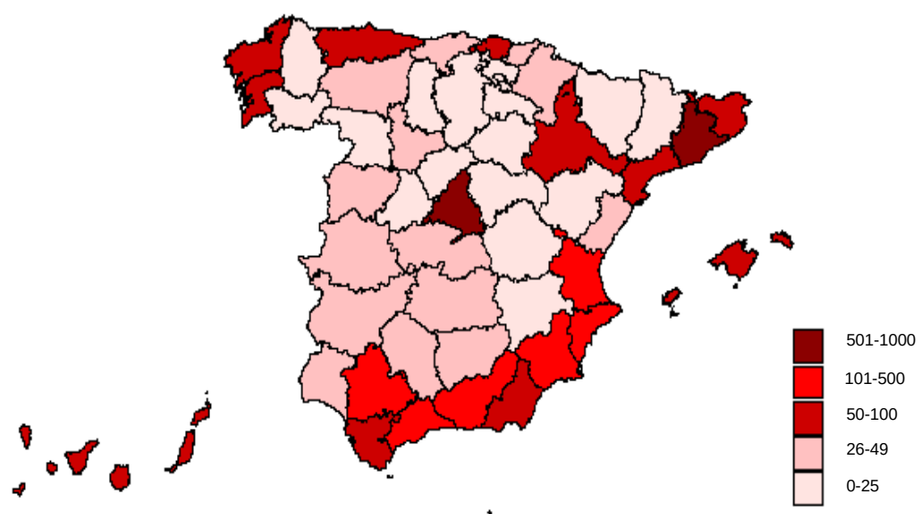

Figure 3. TESTATE project participants by provinces. N: 2,668, Spain. Nov 2019 – Dec 2020.

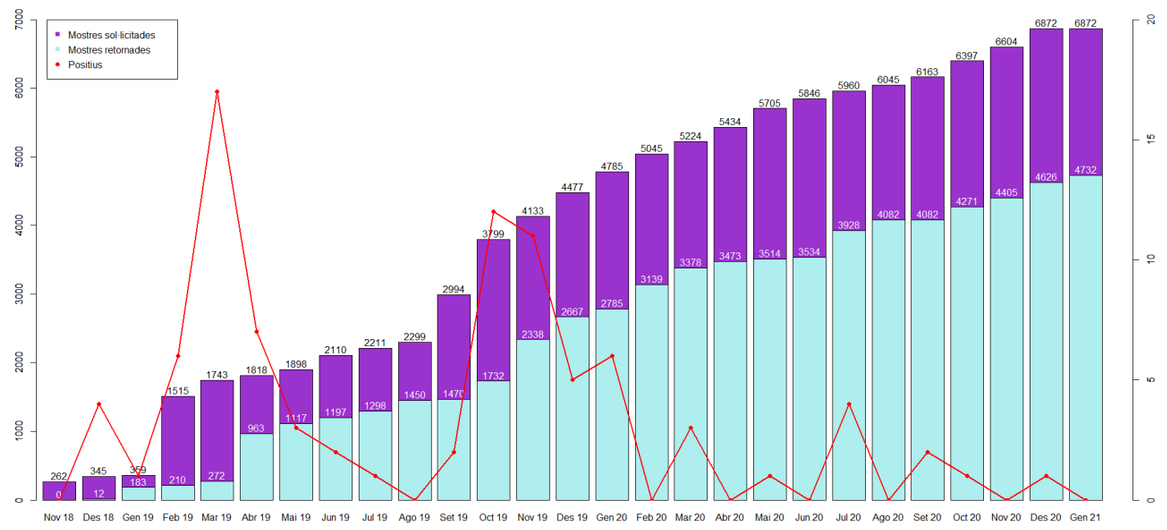

Figure 4. . Kits sent, samples received and number of reactive tests. TÉSTATE project. Samples analyzed: 4,626, Spain. Nov 2019 – Dec 2020.

Results:
From November 2018 to December 2020, 6,872 self-sampling kits were sent to 4,007 participants (69.5 % return rate). 2,668 individuals participated with at least one sample, 1,235 participants (46.24%) had a single test, 705 (23.39%) had two, 357 (13.37%) had three, 197 had four (7.38%) and 177 (6.62%) participants took more than four tests. 99.64% of participants were men, the median age was 32 (IQR: 25-40), 16.88% had not previously been tested for HIV. 47.25% had not used a condom in their last anal intercourse. 37.15% had had an STI in the last 5 years. 89 reactive results were detected (3.3%, 95% CI, 2.65%-4.01%). The proportion of reactive result among participants with a single test was 5.75%. The estimated incidence was 56 reactive cases per 1,000 individuals-year. Of 89 participants with a reactive result, 18 were already known positive, three were false positive, 62 confirmed their result and 54 were linked to care and started treatment. 97.8% would recommend it to a friend. The most identified advantages were comfort and privacy.

Conclusions:
•The **online offer of self-sampling kits for HIV** detection through dating Apps/websites and reporting results online **is feasible**.
•The intervention counted with a **high acceptability** on the part of the GBMSM users of the dating Apps/websites and was considered **novel, appropriate and practical.**
•The intervention was considered **effective** given the **high reactivity, confirmation and linkage to care rates** obtained.
•The intervention **allowed access** to a significant number of people who had **not previously tested for HIV** (16,9% of the participants).
•TESTATE was showed to be an **adequate periodic screening tool** for those who consider themselves at risk of infection. 53,8% of the participants participated more than once in the project. 16 incident cases were detected.
•It can be **useful as a source of information** about the GBMSM users of dating Apps/websites.

P40 High drug resistance levels could compromise the control of HIV infection in paediatric and adolescent population in Kinshasa, the Democratic Republic of Congo

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BACKGROUND

- Despite advances in antiretroviral treatment (ART) against HIV, the control and monitoring of infection still remains a challenge in some countries, due to suboptimal ART, poor adherence to ART, limited access to treatment, and absence of viral load (VL) quantification and resistance testing during clinical routine.
- In the Democratic Republic of the Congo (DRC), only 53% of people living with HIV received ART in 2019 and 28% of children.
- In the DRC, surveillance of VL and resistance to antiretroviral drugs (ARVs) is very limited in the clinical routine. Therefore, patients can spend months or years on inadequate ART, which benefits the development and transmission of ARV resistance.
- This study describes the drug resistance mutations (DRM) prevalence and its therapeutic impact in HIV-infected children and adolescents from Kinshasa, DRC.

METHODS

- From 2016-2019, dried blood specimens (DBS) were collected from 71 HIV-infected children and adolescents under ART in two hospitals in Kinshasa (Monkole and Kalembelembe) in the DRC and with clinical suspicion of therapeutic failure. Neither of the two hospitals had sufficient infrastructure or technology to perform antiretroviral resistance tests during clinical routine.
- The genetic regions encoding the HIV-1 *pol* gene proteins: protease (PR), reverse transcriptase (RT) and integrase (IN) were amplified by RT-PCR and nested PCR with primers designed by WHO and ANRS.
- DRM to protease inhibitors (PI), nucleoside RT analogs (NRTI) and non-analogs (NNRTI) inhibitors and integrase inhibitors (INI), as well as ARV susceptibility were tested using Stanford-HIVdb-v8.8.
- The HIV-1 variants were characterized by phylogenetical analysis of HIV-1 *pol* sequences.
- Statistical analyzes were performed with GraphPad v8.0.1.

RESULTS

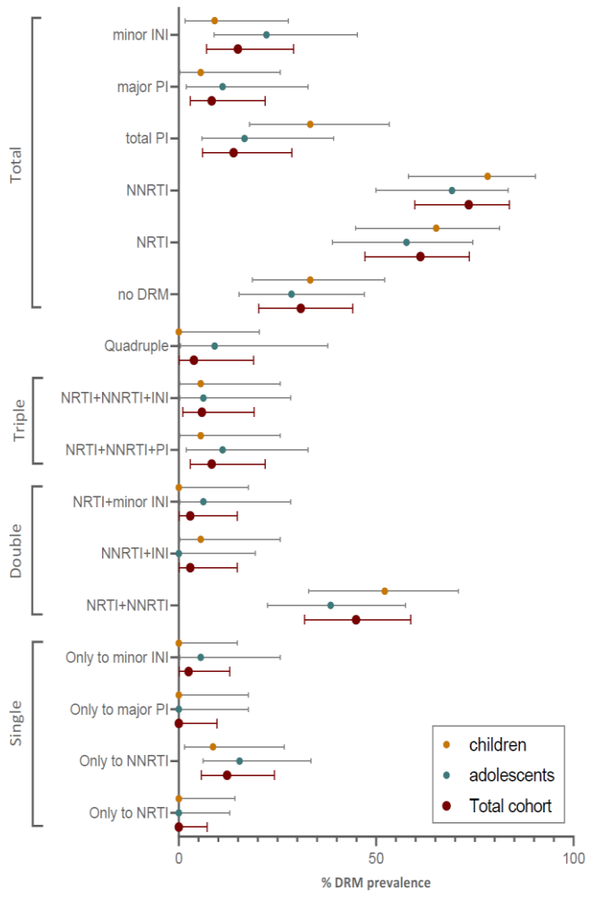
- HIV-1 sequences were recovered from 55 children/adolescents with 14 years of median-age (**Table 1**).
- All had received nucleoside and non-nucleoside reverse transcriptase inhibitors (NRTI, NNRTI), 9.1% protease inhibitors (PI) and only one integrase inhibitor (INI). Despite the use of ART, 89.1% showed virological failure (>1,000 HIV-1 RNA copies/ml) (**Table 1**).
- The 67.3% carried viruses with major-DRM to one (12.7%), two (47.3%), or three (5.5%) ARV-families (**Figure 1**).
- Most children/adolescents harbored DRM to NNRTI (73.5%) or NRTI (61.2 %). Major-DRM to PI was present in 8.3% and minor-DRM to INI in 15% (**Figure 2**). Dual-class-NRTI+NNRTI resistance appeared in 53.1% of patients.
- One third of the HIV-infected children and adolescents under study in Kinshasa had non-suppressed VL in the absence of resistant viruses.
- Viruses presented high/intermediate resistance to nevirapine (72.9% patients), efavirenz (70.9%), emtricitabine/lamivudine (47.9%), rilpivirine (41,7%), etravirine (39.6%), doravidine (33.3%), zidovudine (22.9%), among others. Most participants were susceptible to INI and PI (**Figure 3**).
- Great diversity of variants was found, with a high rate (40%) of unique recombinants (**Table 1**).
- Regarding HIV-1 variants, 52.8% children/adolescents carried pure subtypes at *pol* (13A, 1A2, 1B, 3C, 1D, 1F1, 6G, 2H, 1J) and 43.6% recombinants, being mainly URF (40%). CRF included 1 CRF27_cpx and 1 CRF47_BF. The remaining variants were unclassified (U) variants.
- All generated results were transferred to the clinicians responsible for the patients in Kinshasa to improve their clinical follow-up.

Table 1 Demographic and virological characteristics of children and adolescents of the study cohort with available HIV sequence.

	Children [0-14] (%)	Adolescents [15-21] (%)	P value	Total cohort (%)
Total available sequences	27 (100)	28 (100)		55 (100)
Female	12 (44.4)	17 (60.7)		29 (52.7)
Median age (years)				
At HIV diagnosis in the DRC [IQR]	4 [1-8]	10.5 [5.3-13]	**	6 [2-12]
At first ART experience[IQR]	4 [0.8-8]	12 [7-13]	**	7 [3.5-12]
At DBS collection [IQR]	11 [9-12]	16 [15-17]	**	14 [11-16]
HIV status in mothers				
HIV+	12 (44.4)	7 (25)		19 (34.6)
HIV-	2 (7.4)	5 (17.9)		7 (12.7)
unknown	13 (48.2)	16 (57.1)		29 (52.7)
HIV-1 viraemia				
>1,000c/ml by Roche VL	25 (92.6)	24 (85.7)		49 (89.1)
ART exposure at sampling				
ART	27 (100)	28 (100)		55 (100)
Median time under ART [IQR]	6 [1-8]	6 [1.3-10]		6 [1-8.5]
Mean ARV exposure time (years)				
To NRTI	5.2 (0-12.2)	6.2 (0-13.3)		5.8 (0-13.3)
To NNRTI	4.6 (0-11.2)	6.2 (0-13.3)		5.4 (0-13.3)
To PI	0.9 (0-12.2)	0.26 (0-3.4)		0.6 (0-12.2)
To INI	0	0.09 (0-2.7)		0.05 (0-2.7)
Number of different ART regimens until sampling				
1	13 (48.1)	6 (21.4)	*	19 (34.5)
2	7 (25.9)	10 (35.7)		17 (30.9)
3	5 (18.5)	8 (28.6)		13 (23.6)
4	1 (3.7)	1 (3.6)		2 (3.6)
5	1 (3.7)	2 (7.1)		3 (5.5)
7	0	1 (3.6)		1 (1.8)
NRTI experience				
3TC	27 (100)	28 (100)		55 (100)
AZT	21 (77.8)	26 (92.9)		47 (85.5)
TDF	13 (48.1)	23 (82.1)	*	36 (65.5)
DDI	1 (3.7)	0		1 (1.8)
ABC	5 (18.5)	2 (7.1)		7 (12.7)
D4T	0	4 (14.3)	*	4 (7.3)
NNRTI experience				
NVP	21 (77.8)	25 (89.3)		46 (83.6)
EFV	13 (48.1)	23 (82.1)	*	36 (65.5)
PI experience				
LPV/r	3 (11.1)	2 (7.1)		5 (9.1)
INI experience				
DTG	0	1 (3.4)		1 (1.8)
HIV+ subjects with available pol HIV-1 sequences				
PR	18 (66.7)	18 (64.3)		36 (65.5)
RT	23 (85.2)	26 (92.9)		49 (89.1)
INT	22 (81.5)	18 (64.3)		40 (72.7)
HIV-1 variants				
Non-B pure subtypes	15 (55.6)	14 (50)		29 (52.8)
CRF	1 (3.7)	1 (3.6)		2 (3.6)
URF	9 (33.3)	13 (46.4)		22 (40)
U	2 (7.4)	0		2 (3.6)

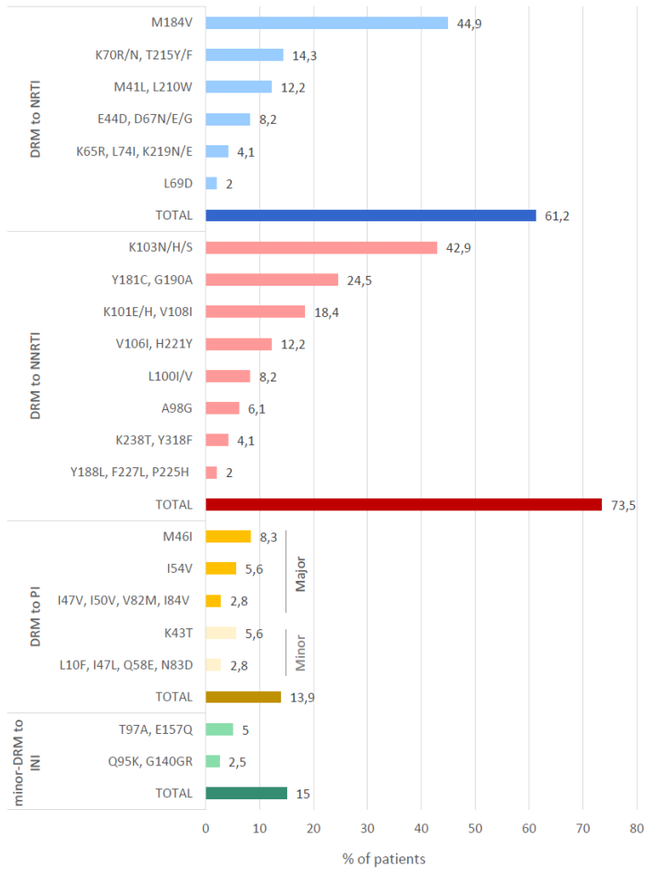
Legend Table 1. Data according to clinical reports. IQR; *interquartile range*; c/ml, copies of HIV-1 RNA per milliliter; 3TC, lamivudine; AZT, Zidovudine; TDF, Tenofovir; DDI, Didanosine; ABC, Abacavir; D4T, Stavudine; NVP, Nevirapine; EFV, Efavirez; LVP/r, Lopinavir/Ritonavir; DTG, Dolutegravir; PR, protease; RT, reverse transcriptase; IN, integrase; CRF, circular recombinants forms; URF, unique recombinants forms; U, unknown.***, p<0.001; *, p<0.05.* Viral load quantified by Roche Cobas v2.0.

Figure 1 Rate of patients carrying DRM to the main ARV families at study population.



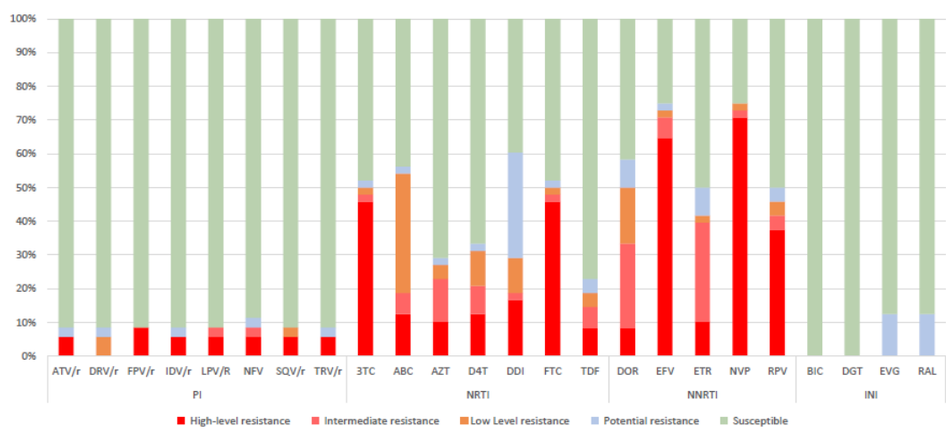
Legend Fig 1. Mean DRM prevalence (colored dots) and 95% confidence intervals on the study cohort with available sequence by age. Single resistance, to one ARV family; double, triple, or quadruple resistance and total DRM ARV families. DRM to PI are always major unless otherwise indicated. DRM to INI are always minor. ARV, antiretroviral drugs; NRTI, nucleoside transcriptase reverse inhibitor; NNRTI, non-nucleoside transcriptase reverse inhibitor; PI, Protease inhibitor; INI, integrase inhibitors. . Rates calculated considering available sequences (55) reported in **Table 1**.

Figure 2 Drug resistance mutations to the main antiretroviral families in the study population.



Legend Fig 2. DRM, drug resistance mutation; NRTI, nucleoside transcriptase reverse inhibitor; NNRTI, non-NRTI; PI, Protease inhibitor; INI, integrase inhibitor; Sec., Secondary. Available sequences of the 55 study patients: 38PR, 49RT and 40 IN. No DRM at primary INIs were found in the cohort analyzed.

Figure 3 Predicted ARV susceptibility by Stanford in patients with available sequence.



Legend Fig 3. Predicted ARV susceptibility in 38PR/49RT/40IN available sequences from 55 children/adolescents under study. NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INI, integrase inhibitor; ATV/r, Atazanavir/Ritonavir; DRV, Darunavir; FPV, Fosamprenavir; IDV/r, Indinavir/Ritonavir; LVP/r, Lopinavir/Ritonavir; NFV, Nelfinavir; SQW, Saquinavir; TPV/r Tipranavir/Ritonavir; ABC, Abacavir; AZT, Zidobudine; D4T, Estavudine; DDI, Didanosine; FCT, Emtricitabine; 3TC, Lamivudine; TDF, Tenofovir; DOR: Doravirine; EFV, Enfavirez; ERT, Etravirine; NVP, Nevirapine; RPV, Rilpivirine; DGT, Dolutegravir; EVG, Elvitegravir; RAL, Raltegravir.

CONCLUSIONS

- We present the first ARV resistance analysis study in HIV-infected children and adolescents in the DRC, the most recent data on resistance in the country, and the first data on INI resistance before the implementation of dolutegravir.
- Seven out of 10 HIV-positive children and adolescents on ART in Kinshasa with clinical suspicion of treatment failure were infected with resistant viruses, mainly to NNRTI and NRTI. The high prevalence of DRM found could compromise UNAIDS 95-95-95 targets to control infection in the DRC. Therefore, future periodic resistance monitoring will be very important to control the spread of resistant strains in the country and for the most optimal choice of rescue ART for each patient.
- Our data also provide relevant information to improve the ART offered to pediatric patients infected with HIV under study, by showing that PIs and INIs can be a good therapeutic alternative in the country, replacing NRTIs and NNRTIs, with high degree of resistance.
- The presence of virus without resistance in children and adolescents with non-suppressed VL suggests that this group requires reinforcement in adherence to ART.
- The high DRM prevalence observed among HIV-infected children and adolescents in Kinshasa could compromise the 95-95-95-UNAIDS targets in the DRC. It also reinforces the need for routine resistance monitoring for optimal rescue therapy election in this vulnerable population to control the spread of resistant HIV in the country.

This study was funded by fundraising activities and donations (mainly from Bomberos Ayudan Association), and by Instituto de Salud Carlos III through the Projects PI16/01908 and PI18/00904" (Co-funded by European Regional Development Fund "A way to make Europe"/"Investing in your future") and the Government of Navarra (grant 045-2015).

Identification of urinary metabolite quantitative trait loci in children and their interaction with dietary factors

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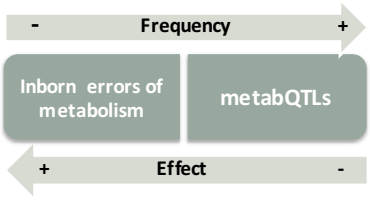
1. INTRODUCTION

- Metabolite Quantitative Trait Loci (metabQTLs) are genetic variants associated with metabolite levels.
- **Urine metabQTLs** have been reported in **adults**, but there is little information on whether these metabQTLs also affect metabolism in early life.
- Loci with an **age-dependent effect** have been described in children for some traits.

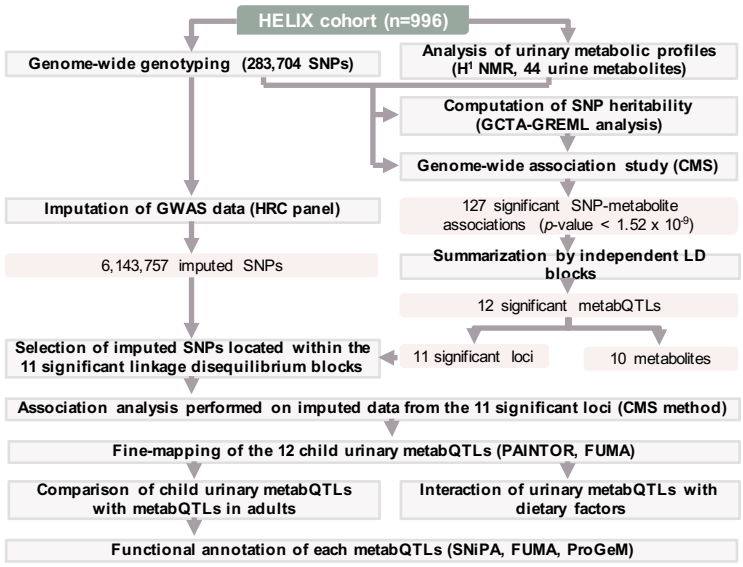


OBJECTIVES

1. Identification of urinary metabQTLs in children
2. Functional annotation of metabQTLs and comparison with findings in adults
3. Study of their interaction with dietary factors.

2. METHODS

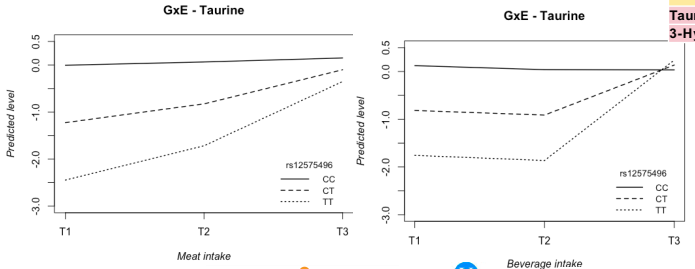
- **Human Early Life Exposome** (**HELIX**) project cohort:
  - 6 to 11 years old
  - From 6 European countries
- The **Covariates for Multi-phenotype Studies** (**CMS**) method was used to find associations between metabolite levels and SNPs.
  - CMS **increases statistical power** by including in the model other covariates (metabolite levels) that correlate with the outcome (metabolite under study).



3. RESULTS

- **12 metabQTLs** identified in **children**, involving 11 unique loci and 10 different metabolites.
- **6** are also described in adults (green), **1** has been described in serum in adults (orange), **2** involve the same locus as in adults but associated to different urinary metabolites (yellow) and **2** represent novel urine metabolite-locus associations (red).
- SNP **rs12575496** (chr. 11) **interacts** with **meat** (p-value = 2.50×10^{-4}) and **beverage** (p-value = 2.84×10^{-4}) frequency intake to determine urinary **taurine** levels.

Phenotype	SNP	Chr.	Pos.	AF	CMS beta	CMS p-val	N. covs.	% Var. Explained	N. SNPs credible set / N. SNPs locus	Potential causal gene
Glycine	rs12655635	5	150693906	0.162	-0.266	3.18E-11	29	2.49	7 / 7	*SLC36A2*
Lysine	rs12459052	19	33346341	0.471	0.363	3.76E-18	29	7.4	2 / 318	*SLC7A9*
Trimethylamine	rs942814	10	100151305	0.363	-0.972	3.34E-146	28	48.28	2 / 228	*PYROXD2*
2-Hydroxyisobutyrate	rs2596144	12	122297738	0.139	-0.632	3.36E-34	24	10.01	6 / 88	*HPD*
3-Hydroxybutyrate+3-Aminoisobutyrate	rs11613331	12	351467	0.466	-0.340	5.13E-17	30	4.82	5 / 10	*SLC6A13*
3-Hydroxybutyrate+3-Aminoisobutyrate	rs37370	5	35039486	0.100	0.782	4.29E-28	28	10.26	2 / 62	*AGXT2*
3-Hydroxyisovalerate	rs2270967	3	182757084	0.307	0.296	7.31E-13	30	2.88	13 / 31	*MCCC1*
N-Acetylneuraminic acid	rs550057	9	136146597	0.269	0.341	2.00E-14	30	4.7	2 / 12	*ABO*
N-Acetylneuraminic acid	rs10206899	2	73900900	0.219	-0.507	8.66E-25	27	8.13	5 / 471	*ALMS1* or *NAT8*
3-Aminoisobutyrate	rs17008991	2	73610116	0.091	-0.490	2.09E-12	28	4.03	2 / 192	*ALMS1* or *NAT8*
Taurine	rs12575496	11	80936097	0.054	-0.643	1.54E-11	30	4.96	8 / 24	-
3-Hydroxyisobutyrate	rs2274870	9	107515214	0.365	0.277	7.85E-14	30	4.02	2 / 12	*NIPSNAP3A*



4. CONCLUSIONS

- **12 urinary metabQTLs** (11 loci and 10 metabolites) have been identified in children.
- A substantial fraction of SNP – metabolite associations are **common** in **children** and **adults**
- Urinary **taurine** levels result from the combined effect of **genetic variation** and **dietary patterns**

In utero and childhood exposure to tobacco smoke and multi-layer molecular signatures in children

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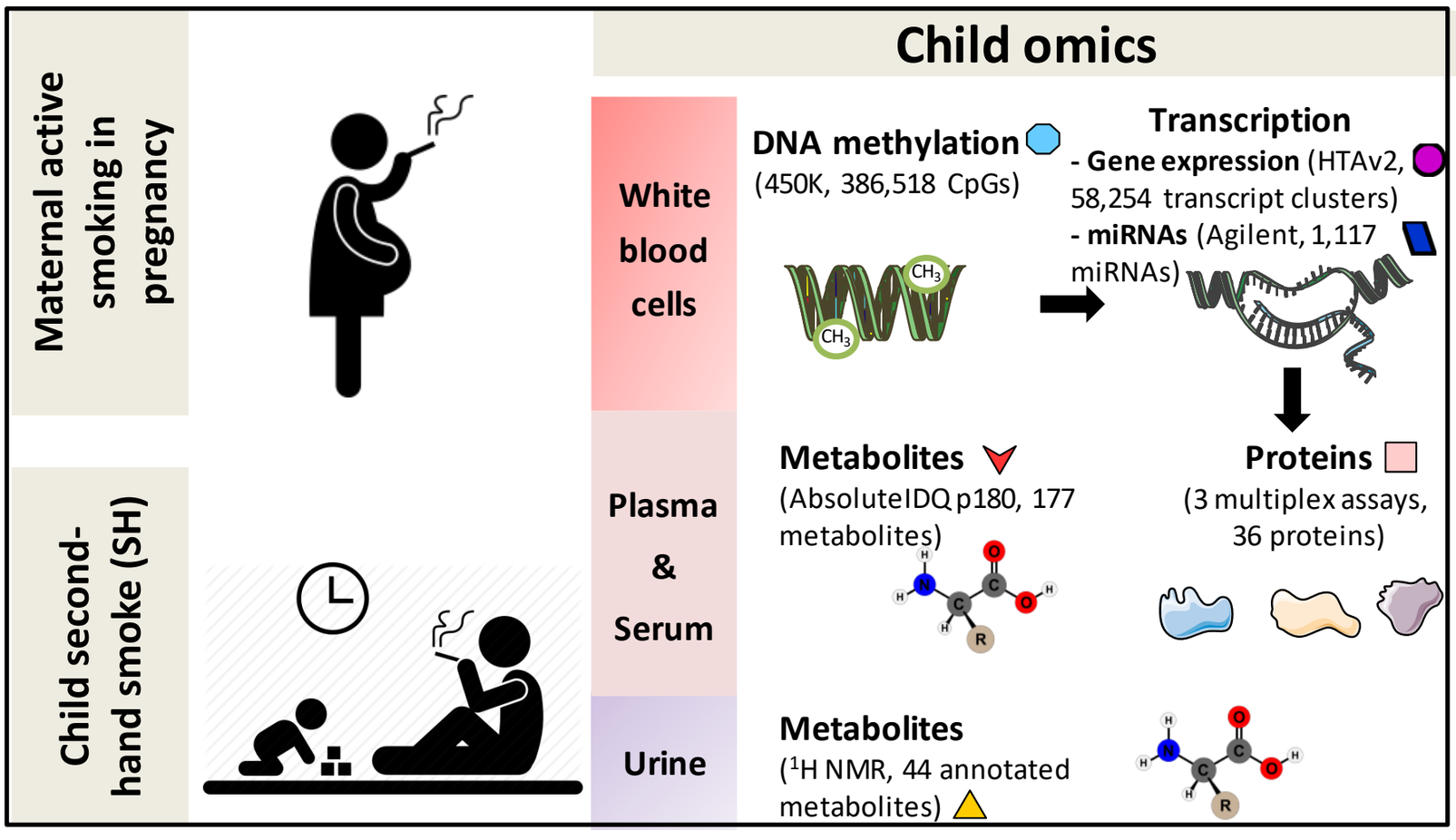
[1] ISGlobal; [2] Universitat Pompeu Fabra (UPF); [3] CIBERESP; [4] Centro Nacional de Análisis Genómico (CNAG-CRG), Center for Genomic Regulation, Barcelona Institute of Science and Technology (BIST); [5] CIBERER; [6] Departament de Biomedicina, Institut de Neurociències, Universitat de Barcelona (UB)

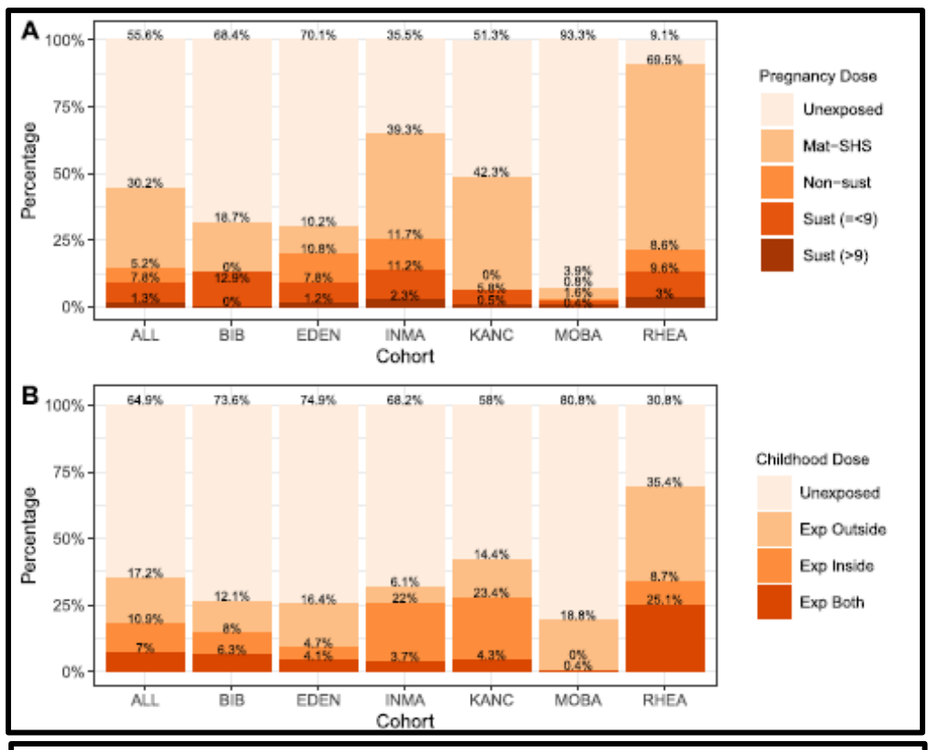


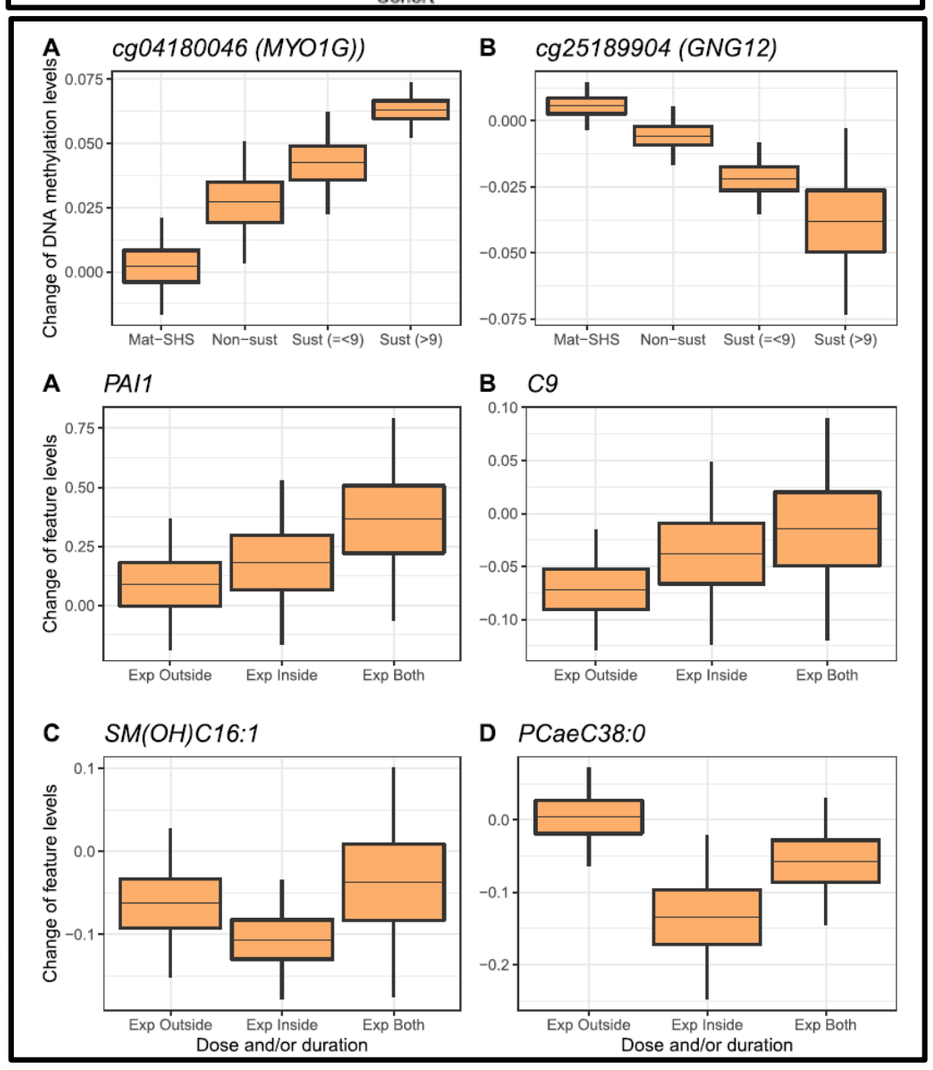
Aim: To identify multi-layer molecular signatures associated with exposure to tobacco smoke in two exposure windows.

Study population: 1203 children from 6 European on-going cohorts of the Human Early Life Exposome (HELIX) project.

Results:

- 14.6% of the mothers smoked at some point during pregnancy (sust=sustained). 35.4% of the children were exposed to postnatal second-hand smoke (SHS).
- Maternal smoking in pregnancy was associated with DNA methylation changes at 18 loci in child blood.
- DNA methylation at 5 of these loci was related to expression of the nearby genes. However, the expression of these genes themselves was only weakly associated with maternal smoking.
- Childhood SHS was not associated with blood DNA methylation or transcription patterns, but with reduced levels of several serum metabolites (C9, SM(OH)C16:1, and PCaeC28:0) and with increased plasma PAI1 (a protein that inhibits fibrinolysis).
- Some of the molecular marks showed dose-response trends, with stronger effects with higher dose or longer duration of the exposure.





Interplay between *Lactobacillus* and Clostridiales restricts gut colonization by multidrug-resistant Enterobacteriaceae.

Djukovic A[1], Garzón MJ[1], Canlet C[2,&], Cabral V[3,&], Lalaoui R[4,&], García-Garcerá M[5,&], Rechenberger J[6,&], Tremblay-Franco M[2], Peñaranda I[1], Puchades-Carrasco L[7], Pineda-Lucena A[7,8], González-Barberá E[9], Salavert M[9], López-Hontangas JL[9], Sanz MA[9,10], Sanz J[9,10,#], Kuster B[6,#], Rolain J[4,#], Debrauwer L[2,#], Xavier KB[3,#], Xavier JB[11,12,#], Ubeda C[1,13*].

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Abstract

Infections by multidrug-resistant Enterobacteriaceae (MRE) are life-threatening to patients. The commensal microbiome of a healthy individual protects its host against MRE colonization, but antibiotic treatment causes collateral damage to commensals, opening the way to colonization and subsequent infection. Despite the significance of this problem, the commensals that confer protection and the mechanisms they use to restrict MRE colonization remain largely unknown. Here, we integrate multiple omics techniques (metagenomics, metabolomics and metaproteomics) to study the microbiome in hospitalized patients, a mouse model that mimics the conditions in which these patients are colonized with MRE, and gnotobiotic mice, to determine how the commensal microbes impair MRE gut colonization. We find that *Lactobacillus* sp. is key, though not sufficient, to restrict MRE gut colonization: *Lactobacillus* sp. increases the levels of several Clostridiales genera, which increase intestinal levels of butyrate and ultimately impair MRE growth. This mechanism—an interaction between *Lactobacillus* sp. and commensal butyrate producers—is conserved in patients and mice. To best of our knowledge this is the first mechanism of colonization resistance common to mice and patients involving cooperation between microbiota members. These results stress the importance of exploiting microbiome interactions—not just its members in isolation—to develop effective probiotics that prevent infections in hospitalized patients.

Antibiotics disrupts the microbiota which enables gut colonization of multidrug-resistant Enterobacteriaceae (MRE) in mice.

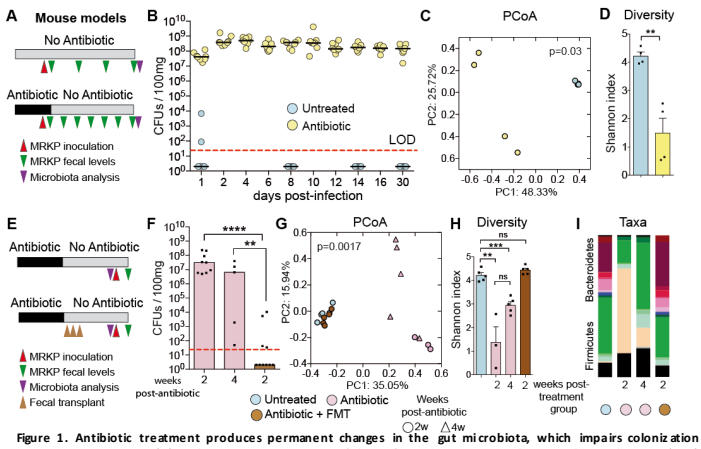

Figure 1. Antibiotic treatment produces permanent changes in the gut microbiota, which impairs colonization resistance against MRE. (A) A schematic representation of the performed experiment whose results are shown in (B-D). Mice were treated with antibiotics (i.e. ampicillin, vancomycin and neomycin). Mice were inoculated with an MRE clinical isolate of *the Klebsiella pneumoniae* species (MRKP) on the 6th day of the treatment. The next day, antibiotic treatment was stopped. As a control, untreated animals were also gavaged with MRKP. (B) Antibiotic-treated mice had high MRKP colonization levels that persisted for one month after the antibiotic cessation, while untreated mice are resistant to MRKP. (C, D) Persistent changes in the microbiota were detected in antibiotic treated mice, 4 weeks after antibiotic cessation through PCoA analysis and the Shannon diversity index. (E) Schematic representation of the experiment whose results are shown in (F-I). Mice were treated with antibiotics. After cessation of the treatment one group received a fecal transplant (FMT) from untreated mice. Another group was left to recover spontaneously. After 2 or 4 weeks post antibiotic cessation, fecal samples were collected for microbiota analysis and subsequently mice were orally gavaged with MRKP. (F) MRKP colonization levels on the first day post-inoculation were significantly lower in mice that received FMT compared to animals that were left to recover spontaneously. (G-I) Mice that received the FMT recovered a microbiota similar to untreated mice, while those that did not received the FMT had permanent changes. The results indicate that permanent changes in the microbiota after antibiotic cessation allow MRKP persistence in the gut.

Lactobacillus restricts MRE gut colonization in antibiotic-treated mice.

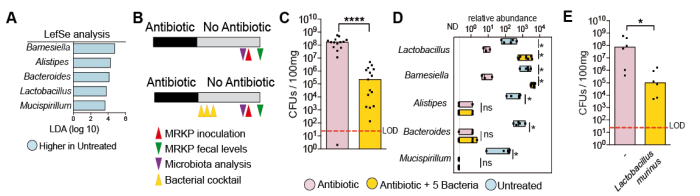

Figure 2. *Lactobacillus murinus* restricts MRE gut colonization in antibiotic-treated mice. (A) LEfSe analysis was performed to identify microbiota members associated with protection against MRKP (i.e. those with higher abundances in untreated mice: resistant to MRKP colonization, as compare to mice allowed to recover for 2 or 4 weeks after stopping antibiotic treatment: highly susceptible to MRKP colonization). In blue are represented potential protective bacteria (i.e. higher abundance in untreated animals). (B) Schematic representation of the experiment in which we tested the role of the 5 bacterial genera detected by LEfSe in providing colonization resistance against MRKP. Mice were treated with antibiotics for a week. After cessation of the treatment, one group was orally gavaged with the mix of 5 strains (*Barnesiella, Alistipes, Bacteroides, Lactobacillus, Mucispirillum*). Two weeks after, mice were inoculated with MRKP. (C) MRKP colonization levels on the first day post MRKP inoculation were significantly lower in the group of mice that received the bacterial mix. (D) 16S rRNA analysis revealed that only *Lactobacillus* and *Barnesiella* were able to colonize the gut of antibiotic-treated animals. (E) Administration of *Lactobacillus* alone restricts MRKP colonization to similar levels observed when the mix of 5 bacterial strains was given. The results suggest that *Lactobacillus* is key for conferring protection against MRKP in mice.

Lactobacillus is associated with reduced MRE colonization levels in hospitalized leukemia patients.

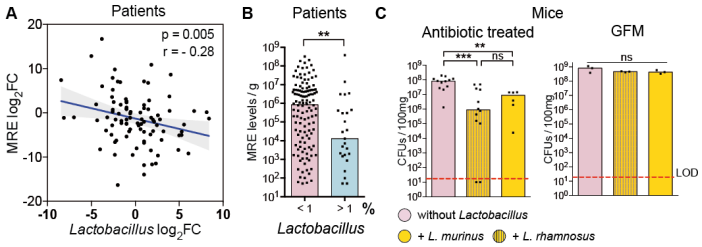

Figure 3. *Lactobacillus* is associated with reduced MRE colonization levels in hospitalized leukemia patients and confers protection in antibiotic-treated mice but not in Germ Free Mice. (A) Changes in abundance of the genus *Lactobacillus* are negatively associated with changes in MRE levels in our patient's cohort. (B) MRE-colonized samples from hospitalized patients with higher abundances of the genus *Lactobacillus* (>1%) had significantly lower MRE colonization levels. (C) Colonization of antibiotic-treated mice with the isolate of *L. rhamnosus* obtained from a patient's sample restricted MRKP colonization to the levels observed in the group of mice that were colonized with *L. murinus*. (D) No differences in MRKP levels were detected in GFM monocolonized with the *Lactobacillus* strains. **The results suggest that *Lactobacillus* is key for conferring protection against MRE in mice and patients, although not sufficient.**

Lactobacillus restricts MRE intestinal colonization in mice by promoting the recovery of Clostridiales genera and increasing the levels of butyrate.

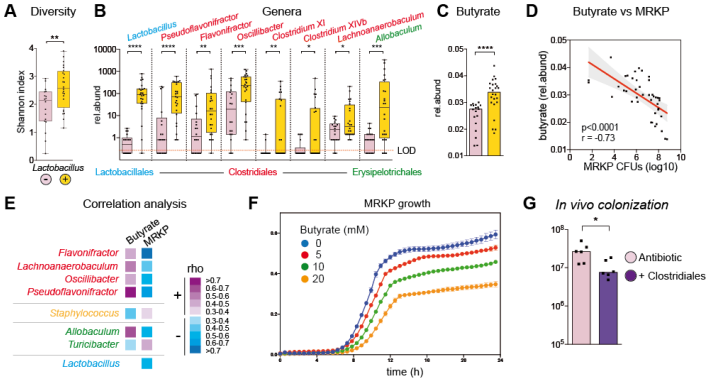

Figure 4. *Lactobacillus* restricts MRE intestinal colonization in mice by promoting the recovery of Clostridiales genera and increasing the levels of butyrate. *Lactobacillus* promotes (A) the recovery of the microbiota diversity after antibiotic treatment in mice, (B) the recovery of the abundance of multiple Clostridiales genera, which is associated with (C) an increase in the levels of butyrate, which (D) negatively correlate with the capacity of MRKP to colonize the intestine. (E) Spearman correlation analysis suggest that the Clostridiales genera recovered after *Lactobacillus* administration are responsible for the increase in butyrate levels and the protection against MRKP. Only genera with a significant association are shown. (F) Butyrate inhibits MRKP growth in a dose dependent manner suggesting a key role for the butyrate increase after *Lactobacillus* administration in MRKP inhibition. (G) Administration of Clostridiales strains to antibiotic treated mice significantly impairs MRKP gut colonization.

High levels of Clostridiales and butyrate correlate with lower MRE levels in hospitalized leukemia patients.

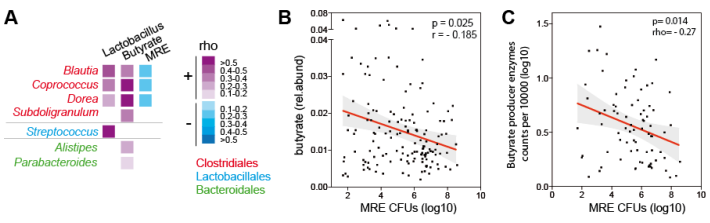

Figure 5. Similar interactions between *Lactobacillus*, Clostridiales genera, butyrate and MRE levels are detected in hospitalized leukemia patients. (A) Spearman correlation between (i) the changes in the abundance of most abundant genera and the changes in abundance of the genus *Lactobacillus*, (ii) the abundance of the most abundant genera and the levels of butyrate or (iii) the butyrate levels and MRE in acute leukemia hospitalized patients. Only genera with a significant association are shown. The results indicate that also in patients an increase in *Lactobacillus* is associated with the expansion of Clostridiales genera which are positively associated with butyrate and negatively with the levels of MRE. (B,C) The fecal levels of butyrate (B) or butyrate producer enzymes (C, proteomic data) are negatively associated with MRE fecal levels in patients suggesting a role for butyrate in protection against MRE in patients.

INVOLVENENT OF WORKERS IN CLOSED AND SEMICLOSED INSTITUTIONS IN OUTBRETAKS OF ACUTE GASTROENTERITIS DUE TO NOROVIRUS

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INTRODUCTION

Norovirus is a major cause of outbreaks of acute gastroenteritis (AGE). AGE outbreaks due to Norovirus (NoV) frequently occur in closed or semiclosed institutions. **The objective of the study was to investigate the involvement of workers in outbreaks due to norovirus in closed and semiclosed instutions according to type of center, mode of transmission, genogroups involved and viral load.**

METHODS

Prospective study of AGE outbreaks due to norovirus in 2017-2019 to the Notifiable Diseases System of Catalonia. All laboratory-confirmed AGE outbreaks due to norovirus were included. In all reported outbreaks, the type of institution, the number of users, the number of workers, clinical data and type of occupation of workers were recorded. As well as the transmission mechanism of the outbreak: person-to-person or common vehicle. Sample of feces were collected from workers and users to identify NoV genogroups I, II and IV by RTqPCR.

The attack rates (TA) and the rate ratios (RRs) and their 95% CIs were calculated for global and for the mode of transmission, type of institutions and type of work activity. The means of cycle of quantification (Cq) were compared using the Student's test.

RESULTS

During the study period, 99 AGE outbreaks due to NoV were detected in these institutions that involved 451 workers. In 74 outbreaks (74.8%), the mode of transmission was person-to-person and in remaining 25 (25.2%), it was due to a common vehicle.

The attack rate in workers was 43.9% in person-to-person outbreaks and 32.6% in outbreaks with a common vehicle (Table 1). The risk of workers being symptomatic was higher in person-to-person outbreaks than in those with a common vehicle (RR 1.35; 95% CI 1.05-1.74). Analysis by type of institution showed the RR of attack rates was only significant for schools (RR 1.93; 95% CI 1.07-3.49) (Table 1).

Table 1. Attack rates and rate ratios in workers according to type of institutions and mode of transmission.

Type of Institution	Symptomatic	Exposed	Attack Rate	RR (95% CI)
Summer camp				
Person-to-person	1	11	*9.09%*	0.17 (0.02 - 1.30)
Common vehicle	12	32	*37.5%*	1
Mixed transmission	0	8	*0.0%*	Not calculable
School				
Person-to-person	15	56	*26.79%*	1.93 (1.07 - 3.49)
Common vehicle	11	69	*15.94%*	1
Daycare center				
Person-to-person	6	14	*42.86%*	Not calculable
Common vehicle	0	0	*0.00%*	
Hotel				
Person-to-person	9	40	*22.50%*	0.93 (0.44 - 1.95)
Common vehicle	5	21	*23.81%*	1
Nursing home				
Person-to-person	77	133	*57.89%*	1.03 (0.78 - 1.38)
Common vehicle	28	50	*56.00%*	1
Long-term care facility				
Person-to-person	11	17	*64.70%*	Not calculable
Common vehicle	0	0	*0.00%*	
Total				
Person-to-person	119	271	*43.91%*	1.35 (1.05 - 1.74)
Common vehicle	56	172	*32.56%*	1
Mixed transmission	0	8	*0.00%*	Not calculable
Total	175	451	*38.80%*	

With respect to the type of occupation, caregivers in nursing homes and healthcare workers had an increased risk of becoming ill (Table 2).

Table 2. Attack rates and rate ratios in workers according to type of occupation

Type of Occupation	Attack Rate	RR (95% CI)
Cook	*9.8%*	0.26 (0.12-0.56)
Kitchen assistant	*15.0%*	0.36 (0.23-0.59)
Waiter	*37.5%*	1.13 (0.45-2.79)
Dining monitor	*27.8%*	0.79 (0.54-1.14)
Caregiver or healthcare worker	*71.6%*	3.18 (2.32-4.35)
Global attack rate	*38.8%*	

NoV was detected by RTqPCR in 143 workers (102 symptomatic and 41 asymptomatic). NoV GI was detected in 39 workers (30 symptomatic and 9 asymptomatic) and NoV GII workers in 104 workers (72 symptomatic and 32 asymptomatic).

Mean Cq was lower in symptomatic workers than in asymptomatic infected workers, with a higher viral load in symptomatic workers, for genogroups GI and GII (Table 3).

Table 3. Difference in viral load between symptomatic and infected asymptomatic workers according to genogroup

Genogroup	Symptomatic	N	Mean Cq	SD	p-Value
GI	Yes	30	30.01	5.51	0.002
	No	9	36.97	5.13	
GII	Yes	72	27.01	5.84	0.07
	No	32	29.19	5.26	

CONCLUSIONS

The attack rate in workers in these institutions was high and was related to the type of activity, being higher in workers with closer contact with users. The frequency of asymptomatic infected workers suggests that in an AGE outbreaks due to NoV, personal hygiene measures should be followed by all workers in the institution where the outbreak occurred, as these asymptomatic workers can be the source of infection.

MEDITERRANEAN DIET AND RISK OF DEMENTIA AND ALZHEIMER'S DISEASE IN THE EUROPEAN PROSPECTIVE INVESTIGATION INTO CANCER AND NUTRITION-SPAIN DEMENTIA COHORT STUDY.

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Nutrients **2021**, *13*(2): 700; **https://doi.org/10.3390/nu13020700.**

BACKGROUND | The Mediterranean diet (MD) has shown to prevent the occurrence of several chronic diseases. Its potential protective role on cognition is attracting growing interest in recent years.

OBJECTIVE | To evaluate the relationship between adherence to a MD pattern and the risk of dementia and dementia sub-types in the EPIC-Spain Dementia Cohort.

DESIGN | Prospective cohort study of 16,160 healthy participants recruited from three Spanish regions (Murcia, Navarra, Gipuzkoa) between 1992-1996 and followed-up for a mean (±sd) of 21.6 (±3.39) years. A total of 459 incident cases of dementia were ascertained through expert revision of medical records. Data on habitual diet was collected through a validated diet history method and adherence to the relative Mediterranean Diet (rMED) score was assessed. Hazard ratios (HR) of dementia by rMED levels were estimated using multivariate proportional hazards Cox models. Time-dependent effects were evaluated using flexible parametric Royston-Parmar (RP) multivariate models. Participants with major chronic pathologies, and energy mis-reporters were excluded from the analyses.

RESULTS | High versus low adherence to the rMED score was associated with a 20% reduced risk of dementia overall (*P* for trend = 0.021). Dementia risk decreased by 8% (95%CI: 1-15%) for each 2-point increment of the rMED score. A protective effect was found in women for non-AD ($HR_{continuous,\ per\ 2\text{-}points}$ = 0.74, 95%CI: 0.62-0.89) and in men for AD ($HR_{continuous,\ per\ 2\text{-}points}$ = 0.88, 95%CI: 0.76-1.01). The association was stronger in participants with lower education (*P* = 0.039).

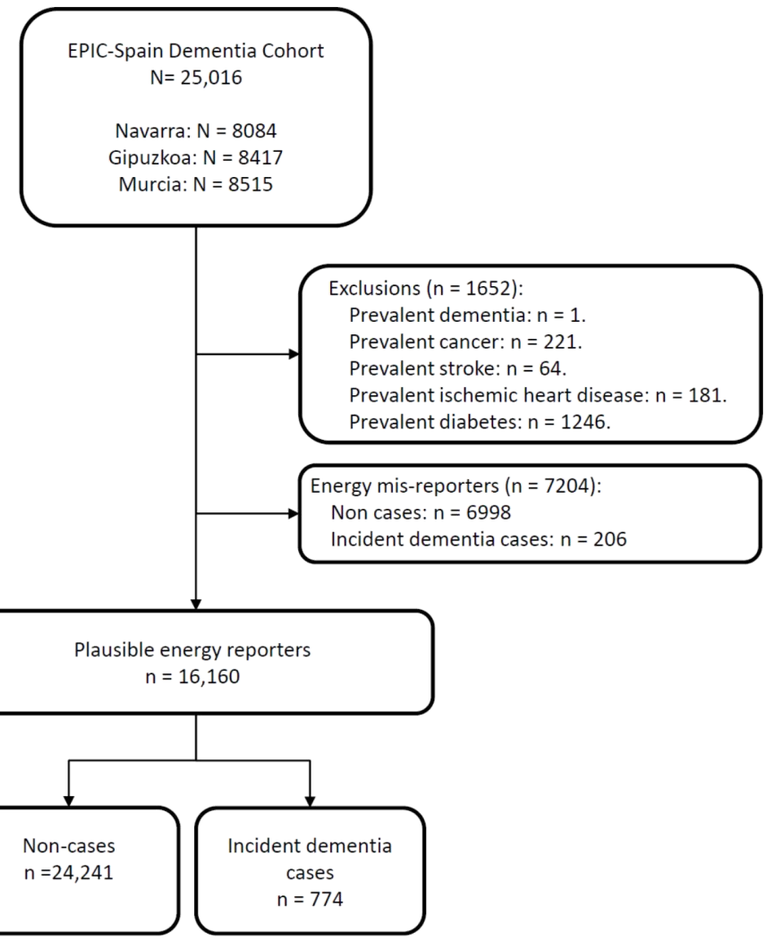

Figure 1.. Flowchart of study participants.

Table 1. Hazard ratio of dementia by levels of the Mediterranean Diet score (rMED) in participants from the EPIC-Spain Dementia Cohort study (N = 16,160).

			Model 1	Model 2
Adherence to the rMED	**Person-Years**	**Cases**	**HR (95% CI)**	**HR (95% CI)**
All				
rMED categorical Low	68,876	85	1	1
Medium	181,469	235	0.85 (0.66, 1.09)	0.85 (0.66, 1.09)
High	98,957	139	0.79 (0.59, 1.04)	0.80 (0.60, 1.06)
rMED Continuous (per 2-point increment)			0.91 (0.85, 0.98)	0.92 (0.85, 0.99)
p for linear trend *			0.012	0.021
p for non-linear trend *			0.063	0.094
Women				
rMED categorical Low	47,718	59	1	1
Medium	106,420	137	0.85 (0.63, 1.16)	0.84 (0.61, 1.15)
High	47,884	69	0.88 (0.61, 1.25)	0.87 (0.60, 1.26)
rMED Continuous (per 2-point increment)			0.91 (0.83, 1.00)	0.90 (0.82, 1.00)
p for linear trend *			0.042	0.040
p for non-linear trend *			0.077	0.086
Men				
rMED categorical Low	21,158	26	1	1
Medium	75,049	98	0.80 (0.52, 1.24)	0.81 (0.52, 1.26)
High	51,073	70	0.65 (0.41, 1.03)	0.69 (0.43, 1.09)
rMED Continuous (per 2-point increment)			0.91 (0.82, 1.02)	0.93 (0.83, 1.03)
p for linear trend *			0.092	0.174
p for non-linear trend *			0.400	0.579

* *p*-values for linear and non-linear trend on the continuous variable. HR, hazard ratio; CI, confidence interval. *p*-values <0.05 or 95% CI that did not include the null value (i.e., 1) were considered statistically significant. Model 1: Cox regression adjusted by sex, education, and energy intake, and stratified by center and age. Model 2: As model 1, plus smoking, BMI category, elevated waist circumference, household and recreational physical activities, hypertension (self-reported), hyperlipidemia (self-reported), coffee and tea consumption (combined), and intake (in g/day per 2000 kcal) of potatoes, eggs, and cakes and biscuits. Women-specific model further adjusted by menopausal status, use of oral contraceptives (ever) and hormone replacement therapy (ever). MD adherence levels defined as low: 0–6 points, medium: 7–10 points, and high: 11–18 rMED score points.

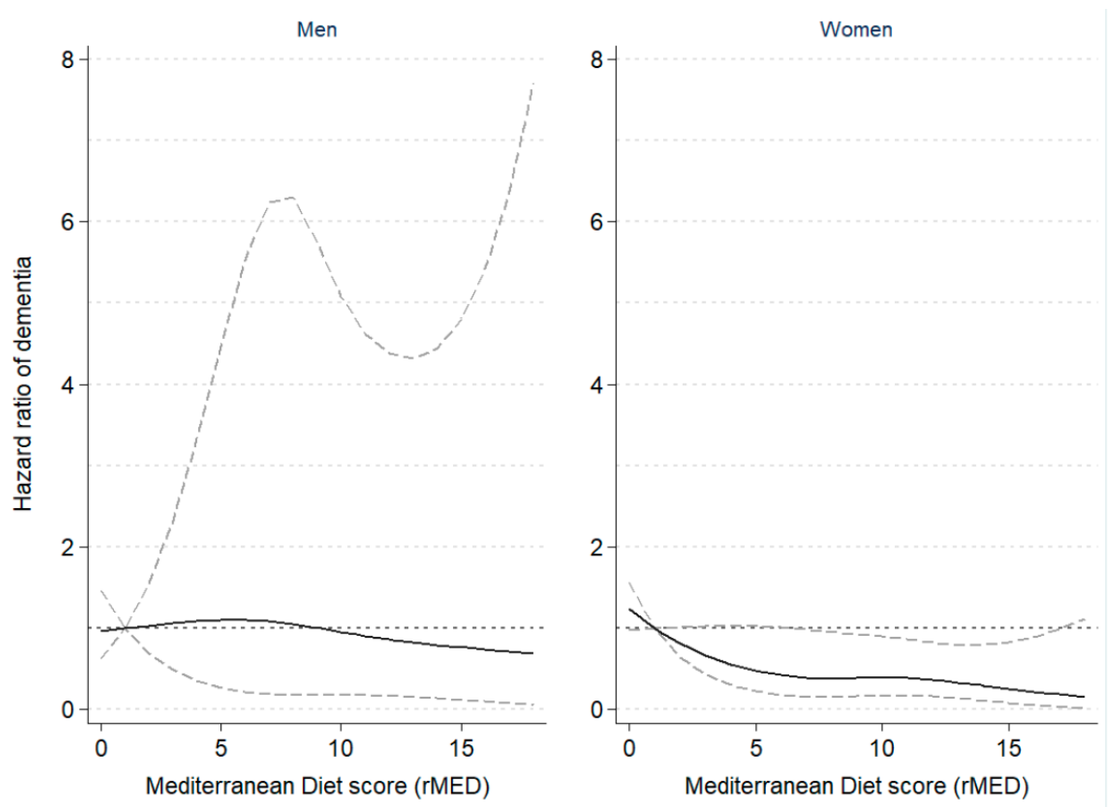

Figure 2.. Hazard ratio of dementia according to Mediterranean Diet scores in the EPIC-Spain Dementia Cohort study (N = 16,160), by sex. The dashed lines represent the upper and lower 95% confidence interval limits of the estimates. A non-linear inverse association between risk of dementia and rMED scores was observed among women, but not among men. Hazard ratios of dementia were estimated using Cox proportional hazards regression models, with age as the time scale, stratified by center and age (in 5-year categories), and adjusted by sex, education, energy intake, smoking, BMI category, elevated waist circumference, household and recreational physical activities, hypertension (self-reported), hyperlipidemia (self-reported), coffee and tea consumption (combined), and intake (in g/day per 2,000 kcal) of potatoes, eggs, and cakes and biscuits. In women, models were further adjusted by menopausal status, oral contraceptive use, and hormone replacement therapy. Dementia risk was modelled following a restricted cubic spline transformation of the rMED variable with 3 degrees of freedom (knots were placed at the 33rd and 67th percentiles).

CONCLUSION | MD had a protective effect on dementia incidence in the Mediterranean EPIC-Spain Dementia cohort in multivariate models accounting for major cardiovascular risk factors, but the strength of the association differed by dementia sub-type, sex, and education. Significant associations were revealed only after excluding mis-reporters of energy intake. Further studies are needed to elucidate the mechanisms underlying this association.

FUNDING | 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 CIBER de Epidemiología y Salud Pública (CIBERESP), and the participating Regional Governments of Basque Country, Murcia (no. 6236), and Navarra. The present project received partial funding from the Fundación Séneca (19487/PI/14), The EPIC-Murcia study received partial funding from the Fundación Séneca (19487/PI/14), the Murcia Biomedical Research Institute (IMIB)-FFIS and the Spanish Biomedical Research Network Center (CIBER) (BOE-A-2020-6018).

MICROBIOLOGICAL VARIABLES ASSOCIATED WITH SEVERITY IN PEDIATRIC INFECTION BY RHINOVIRUS

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Introduction

Clinical spectrum of **rhinovirus/enterovirus (RV/EV) infection** is wide, ranging from asymptomatic or mild symptomatic infection to be often the only etiological agent in patients requiring advanced life support in paediatric intensive care units (PICU).

In literature evaluating variables associated with a more severe disease, the role of **viral coinfection** remains controversial and the diagnosis of **bacterial superinfection** is often missed. Moreover, data about species and severity is scarce. The aim of this study is to determine the **impact of viral and bacterial coinfection** in RV/EV severity.

Patients and methods

Patients **<5 year-old** admitted to the PICU of a tertiary paediatric hospital in Barcelona with a severe lower-respiratory tract infection and RV/EV detection. The study period spans **2018-2019**. Patients with comorbidities were excluded, as well as bacterial results of patients receiving antibiotics for more than 48 hours at the time of respiratory sampling.

Nasopharyngeal-aspirate (NPA) samples were collected during the first 48 hours of hospital admission and a **PCR for multiple-respiratory-pathogens** (Filmarray-RP) and **bacterial cultures** were performed. Characterization of RV / EV was carried out at the National Center for Microbiology (ISCIII).

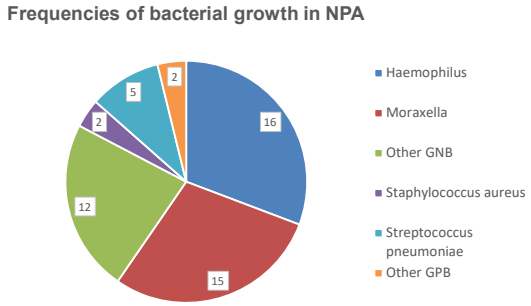
Results

71 patients were included. Median age was 2 month-old.

RV / EV was detected as the unique viral infection in 31 (44%) patients. **The main viral co-detection was RSV (42%),** followed by adenovirus (14%), parainfluenza virus (12%) and metapneumovirus (9%).

The characterization of the RV / EV indicated that **25 (45%) were RV of species A (RV-A), 6 (11%) RV-B, 22 (40%) RV-C and 2 (4%) EV -B**. All RV-B cases were detected in the RV / EV + RSV group (p = 0.028). Only two EV-B were detected (1 in RV+RSV group and 1 in the multiple viral co-infection group). No EV-A, EV-C or EV-D68 were detected.

Bacterial cultures were performed in 49 and 42 were positive (86%). ***Haemophilus influenzae*** was the most frequent bacterial co-detection (42%) followed by *Moraxella spp* (32%) and other gram-negative bacteria (16.1%).



Variables	Univariate analysis			Multivariable analysis	
	PICU stay > 5 d (n=33)	PICU stay < 5 d (n=38)	P-value	Adjusted Odds-ratio	P-value
Sex (male), n (%)	20 (61%)	20 (53%)	0.499		
Age (months), median (IQR)	2.2 (1.2-5.6)	2.1 (0.9-14.8)	0.836		
Viral infection: RV/EV, n (%) RV/EV+RSV, n (%) Multiple viral coinfections, n (%)*	 16 (48%) 14 (42%) 3 (9%)	 15 (39%) 8 (21%) 15 (40%)	 0.445 0.052 0.003	 - 1.04 (0.25-4.29) 0.06 (0.01-0.59)	 - 0.95 0.16
Bacterial detection in NPA (total n=49) GN bacteria, n (%) GP bacteria, n (%)	 22 (84%) 3 (11%)	 12 (52%) 8 (35%)	 0.014 0.052	 5.65 (1.3-24.5) -	 0.02 -
HRV/EV species HRV A, n (%) HRV B, n (%) HRV C, n (%) EV B, n (%) Unknown, n (%)	 14 (42%) 4 (12%) 8 (24%) 1 (3%) 6 (18%)	 14 (37%) 3 (8%) 15 (39%) 1 (3%) 5 (13%)	0.688		
C-RP (mg/L), median (IQR)	38 (21-64)	30 (11-72)	0.302		
PCT (ng/mL), median (IQR)	0.35 (0.19-1.49)	0.20 (0.08 – 2.08)	0.328		

Conclusions

In RV infection, **co-infection with other respiratory viruses and bacteria such as H influenza and Moraxella spp**, can determine the severity of the clinical disease. The analysis of the nasopharyngeal bacterial and viral microbiota may help to identify the most susceptible patients and to select specific treatments for them and preventive strategies.

This project is supported by de Spanish National Health Institute Carlos III (Grant id. PI17/349), "Rinovirus humano (HRV) en niños menores de 5 años, del resfriado común a la unidad de intensivos: rol de la microbiota"

MONTE CARLO SIMULATION APPLIED TO BREAST CANCER PROGRAMS AND RANDOMIZED CONTROLLED TRIALS

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Introduction

Massive mammography screening programs are currently widespread throughout the developed world and are considered a powerful public health tool to reduce mortality from one of the most common tumors in the female population: breast cancer. However, many questions remain open in relation to these programs [1]:

•Does early really decrease mortality.

•What are the most suitable target groups for these programs.

•What percentage of tumors that would never appear in the clinic, are detected and treated due to massive screening.

Addressing these purposes has made traditionalment through randomized controlled trials [2]. These assays have many limitations regarding the size of the test groups and control as well as derivated of the control of the inherent associated biases. In addition, its usefulness is mainly focused on determining the reduction of mortality from breast cancer, providing little or even no light on the other open questions. For these reasons, we have carried out a realistic simulation of them using Monte Carlo techniques that involve probabilistic distributions of the different parameters that determine the results of the screening programs.

Material and Methods

We have developed a Monte Carlo code that allows the realistic simulation of mammography screening programs in order to reproduce the results associated with detection [3]. This first part simulates the history of women who undergo screening using a mammography detection model dependent on tumor size, breast density and tumor histological type:

$$P_{det} = P_{size} \cdot P_{hist,dens}$$

Clinical detection is simulated using an exponential model (t elapsed time and lambda tumor mean size):

$$p(t) = \frac{1}{\lambda}\exp\left(-\frac{t}{\lambda}\right)$$

The tumor size follows a type of logistic growth with a single growth parameter b, distributed according to a log-normal fuction:

$$V_{tum}(t) = 1.1\cdot 10^{6}\left[1+\frac{1023}{\exp\left(\frac{bt}{4}\right)}\right]^{-4}$$

The simulations take into account the evolution of histological types from *in situ* to invasive carcinomas as well as the evolution of the density of the breast in women with age.

We have studied overdiagnosis [4], understood as the excess of tumors detected by screening with respect to clinical detection in the absence of the program.

In a second iteration [5], we introduce the concepts of lead time and global sensitivity to model the global effect of mammographic screening on the detection of tumors, as well as survival after detection and treatment, in order to simulate the reduction in mortality that the screening mammographic programs regarding the absence of them.

Finally, we reproduce the main randomized controlled trials on mammographic screening carried out to date in order to evaluate their internal and external validity [6].

Results

The results of our model applied to overdiagnosis are shown in Figure 1. In this figure, overdiagnosis appears as the excess of tumors detected in the screening programs with respect to the absence of these, once the program has ceased.

Regarding the reduction in mortality that screening supposes compared to clinical detection, the results are shown in Figure 2, depending on the age configuration of the women, time interval between mammograms and percentage of participation.

Finally, the compared results of the main randomized trials are shown in Figure 3.

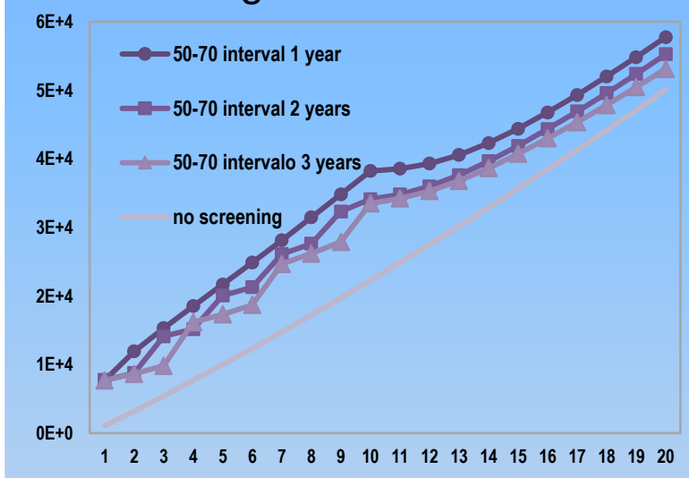

Figure 1. Total number of detected tumors (screening+clinical detection) in a 10-years screening program as a function of the screening round for usual interval times.

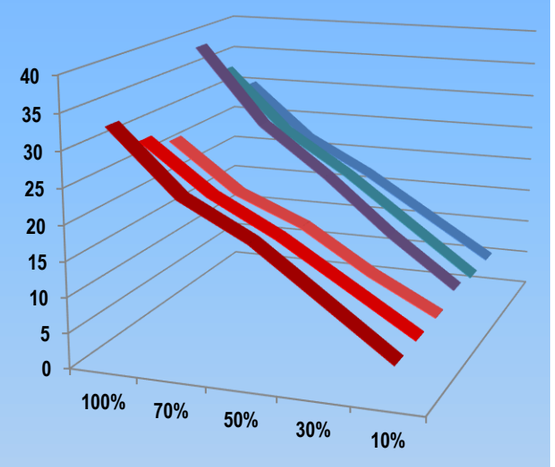

Figure 2. Breast cancer mortality reduction due to screenings programs as a function of percentage of participation. Red colorus for women between 50-70 years old and blue colours for women between 40-70 years old.

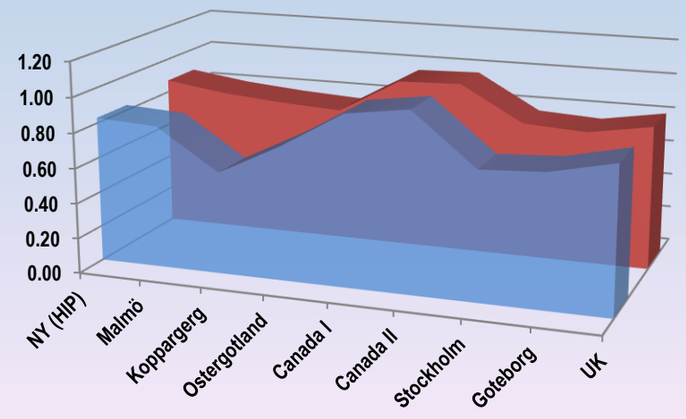

Figure 3. Relativ Risk of breast cancer mortality. Simulations in red and real trials results in blue.

Conclusions

The values of overdiagnosis with our model are between 10 and 20% of the tumors detected in screening, being somewhat lower in the age range of 40 to 70 years. These values are reduced to values between 6% and 14% for realistic configurations.

Regarding the reduction in mortality from breast cancer due to screening, it would be between 23% and 33%. This is reduced to an interval between 16% and 23% for typical participation in screening programs (80%).

Finally, our simulations of the randomized controlled trials show that the Malmö, Östergötland, Stockholm, Göteborg and UK Age trials show good methodological quality and their results are more general. The Kopparberg and NY HIP trials have major methodological flaws.

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Qualitative study of needs assessment and conceptualization of a new healthcare indicator library, BiblioINDICA.

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BiblioINDICA

Virtual library of healthcare quality indicators and methodological support tools

Figure 1. Conceptualization of BiblioINDICA (beta phase)

Aims

- To gather key informants' opinions on needs not covered in the quality of care assessment field and their views on the potential of a new virtual library of indicators and methodological support tools (BiblioINDICA, **figure 1**).

Results

- Most informants were women (72.7%). Three levels of decision-making: micro (centre), meso (provider/scientific society) and macro (region) levels were equitably represented.
- When respondents were asked for the role for a new virtual library of indicators, they called for a platform that unifies, with a global view as well as a glimpse of the care process (not fragmented). The opinion on the added value of BiblioINDICA is shown in **figure 2**.

Methodology

Design and type: A qualitative study using semi-structured interviews with key informants was carried out based on a phenomenological perspective.

Data collection: the fieldwork took place from January to May 2019. Information from the interviews was triangulated with a previous literature review and other information sources.

Sampling: a theoretical sample of 22 informants representing the views of clinical and quality of healthcare management, strategic health planning or purchasing process, and related scientific societies was defined (Catalonia).

Analysis: each interview was audiotaped and transcribed. Content and discourse analysis was applied.

Knowledge transfer project	Tools available in the system	Source for inspiration and exchange	Evaluation culture
✓ BiblioINDICA could be a unifying and homogenizing platform.	✓ Visibility of methodological tools to support indicators that guarantee validity, robustness and reliability.	✓ Facilitate access to new indicators and good practices that serve as benchmarks.	✓ Foster a culture of evaluation to improve the quality of healthcare in the whole system.

Figure 2. Main categories expressing the opinion of informants on the added value of BiblioINDICA (n=22)

Conclusions

- A new library like BiblioINDICA could help users share and collaborate on good practice initiatives by making them more visible and useful, while aiding in assessing their robustness and reliability. Potential users could benefit from this type of library as a knowledge transfer project.

Funding: this project was partially funded by CIBERESP.

RAPID, SCALING UP OF HIGH THROUGHPUT SARS-COV-2 EMERGENCY DIAGNOSTIC TESTING IN PUBLIC HEALTH LABORATORIES.

Laura Cano (1), Susana Ortolá (2), Martín Llácer (2), Sandra García-Esteban (1), Blanca Navarro Cubells (3), Mª Piedad Olmos (2), Marisa Camaró (2), Pedro Martí Requena (2*), F. Xavier López-Labrador (1,4*)

(1) Laboratorio de Virología, Área de Genómica y salud, FISABIO-Salud Pública (Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunidad Valenciana), Generalitat Valenciana.
(2) Laboratorio de Salud Pública de Valencia, Dirección General de Salud Pública, Generalitat Valenciana.
(3) Blanca Navarro Cubells, Dirección General de Salud Pública, Generalitat Valenciana.
(4) CIBER-ESP, Instituto de Salud Carlos III.
(*) On behalf the FISABIO-LSPV-DGSP covid-19 team

Introduction

On April 14th, 2020 the Laboratory of Virology of the Area of Genomics and Health of FISABIO-Public Health and the Laboratory of Public Health of Valencia (General Directorate of Public Health, DGSP) were jointly accredited by the Instituto de Salud Carlos III for molecular diagnostics testing of SARS-CoV-2, to improve the Covid-19 diagnostic capacity.

Aims

1) Validation of alternative automated viral RNA extraction methods and 2) alternative SARS-COV-2 amplification tests. 3) Transfer to the Laboratory of Public Health, as alternative diagnostic scheme for emergency use and preparation for the second wave.

Methodology

In a first step, alternative commercial methods for viral RNA extraction and "in-house" RTPCR tests for SARS-CoV-2 according to WHO protocols (Charité and CDC) were validated and adapted to automation in open systems, to avoid shortages of reagents (i.e. Biomerieux, Roche).

In a second step, we scaled-up the most reliable methods to high throughput, including commercial kits and reagents when available, by means of automation of viral RNA extraction and RTPCR in 96-sample format using open robotic platforms (Hamilton Robotics and Eppendorf Epmotion).

Results and discussion

- We rapidly validated our own methods for the diagnostic of SARS-CoV-2, with similar performance to CE-IVD marked commercial kits. The immediate impact was to provide a diagnostics alternative for emergency use to face reagent shortages.

- In a second phase, once high throughput protocols were automated, we transferred the diagnostic procedures to the Laboratory of Public Health and adapted the automated platforms to commercial reagents, once again available.

- In May-June we had already developed a platform with a capacity for processing 800 samples/day (two shifts). To date we have tested more than 30.000 samples of different origins: nursing homes, educational centres, outbreaks, etc.; also giving support to tertiary-care hospitals; primary care, and centres dedicated to vulnerable populations.

- **Public Health Laboratories have a significant added value to support pandemic/emergency situations.**

EasyMag / eMAG
Extracction of 24 / 48 samples: 1,5 h

Epmotion 5070
96 sample RTPCR set-up:
15 - 20 min

April

May-June

Epmotion 5070-Con
96 Sample trasfer to DWP inside a BSC in BSL2+ lab
15 min

Hamilton STARlet Hi-thoughput platform
Extraction of 96 samples in DWP: 1 hr. 20 min.

Epmotion 5075 Hi-thoughput platform
Extraction of 96 samples in DWP: 1.5 hr.
96 sample RTPCR set-up: 10 min.

Contact: F.Xavier.Lopez@uv.es or marti_ped@gva.es

Relationship between sickness absence due to cancer and risk of early exit from labour market in Catalonia (Spain) (2012- 2018)

Amaya Ayala-García [1,2,3], Laura Serra [1,2,3,4], Fernando G. Benavides [1,2,3]

(1) Center for Research in Occupational Health (CiSAL), University Pompeu Fabra, Barcelona, Spain; (2) CIBER of Epidemiology and Public Health (CIBERESP), Spain; (3) IMIM – Parc Salut Mar, Barcelona, Spain; (4) Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Spain.

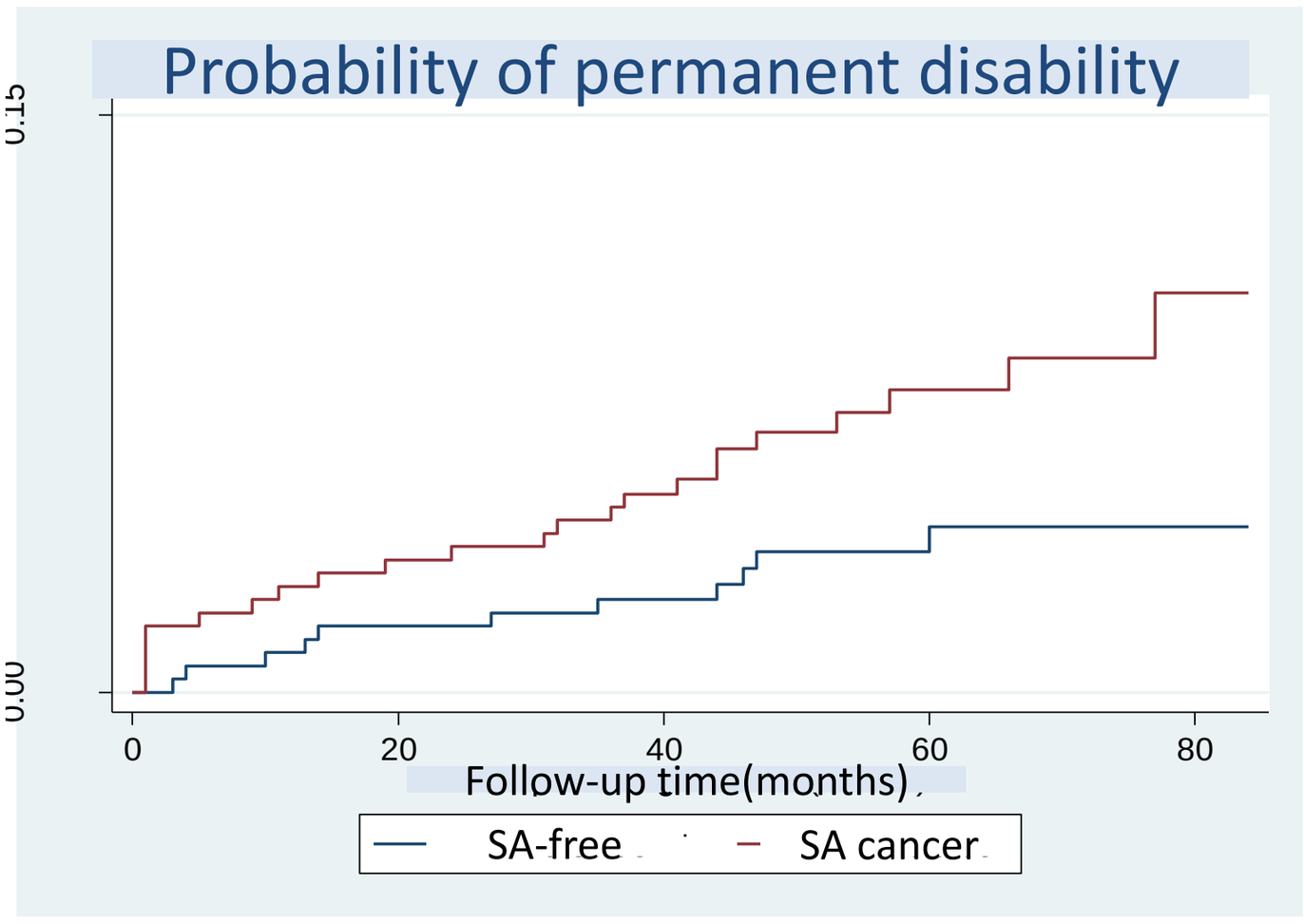
Background: **Incidence and survival rates** of cancer have increased in Spain. Half of the diagnosis are made throughout **working life**. Cancer survivors find big difficulties in the transition after ending treatment due to **long-term impairments** that affect their **work capacity**. It has been estimated that **40% exit prematurely** the labour market**.**

Objective: To compare the probability of exiting the labour market prematurely due to **early retirement or permanent disability** of salaried workers who suffered a previous sickness absence (SA) due to cancer.

Methods: **Retrospective cohort** of a sample of salaried workers, affiliated to SS and living in Catalonia between 2012 and 2018 (N=1.548, 57% women). Each case with SA due to cancer was matched by sex, age and following time with: **1) SA other diagnosis** and **2) SA-free**.

Cox survival analysis models were applied, separately for each outcome and sex, to compare probabilities of the outcomes between each comparison group and cases.

Results: Women who suffered a **SA due to cancer** have 3.27 (CI 95%: 1.49–7.17) times higher probability of exiting the labour market due to **permanent disability** than those who were **free of SA**. No differences were found in the probability of early retirement.



Discussion and conclusions: Agreement with literature. Permanent disability could be a reasonable outcome depending on cancer severity. **Workplace adaptations and return to work interventions** could help cancer survivors (occupational risk prevention services).

Jornada Científica CIBERESP 23 y 25 Marzo 2021

SARS-CoV-2 ANTIBODIES AND UTILITY OF POINT OF CARE TESTING IN HEALTH CARE WORKERS FROM A SPANISH UNIVERSITY HOSPITAL IN MADRID.

Rodríguez-Domínguez M*, Romero-Hernández B, Marcos-Mencía D, Sánchez-López J, del Campo Albendea L, Abreu M, **Martínez-García L**, Muedra M, Fernández-Escribano M, Ferrer-Masferrer M, Cantón R y **Galán JC**

*(mariojose.rodriguez@salud.madrid.org). Hospital Ramón y Cajal. [1]Bold names: members of Group 33 CIBERESP

BACKGROUND

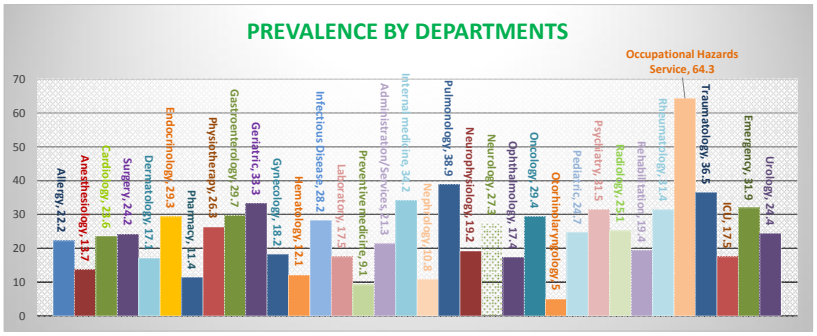
People working in essential services, such as health care workers (HCW), have an increased risk of exposure to SARS-CoV-2. It has been proposed, with limited evidence, that household settings and the socialization between HCW could have played a role in this rate. Access to testing should be available to everyone who needs it. The use of lateral-flow immunoassays (LFIA), could be useful for wide testing in particular groups or in settings with limited access to references techniques

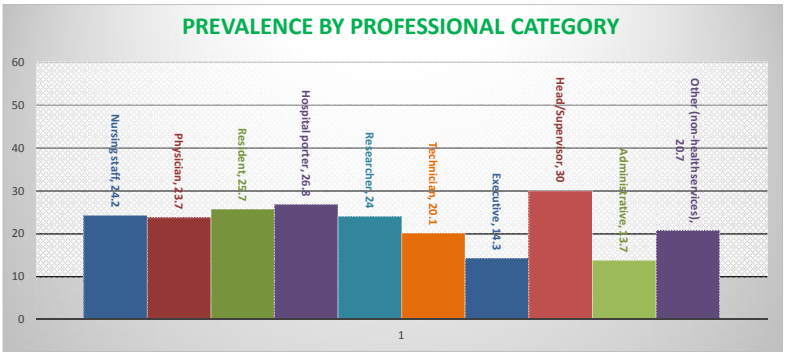
METHODS

The present study was carried out in May-June 2020, during the slowdown phase of the first epidemic wave. Serological studies were offered to all staff working in the Ramon y Cajal Hospital, and inclusion in the study was voluntary. Each participant provided whole blood and serum samples. Information about sex, age, professional category, work in COVID areas and history of previous RT-PCR for SARS-Cov-2. A two-step protocol was applied, first a LFIA (Hangzhou ALLTEST Biotech Co., Ltd., China) in whole blood for fast identification of IgG and IgM antibodies against SARS-CoV-2, and in a second serum samples were tested by Vircell COVID-19 ELISA IgG test (Vircell Spain S.L.U., Granada, Spain). Those participants with a positive IgM result were tested for SARS-CoV-2 RT-PCR, which was performed using the TaqMan 2019-nCoV Assay kit v1 (ThermoFisher Scientific, Inc. Massachusetts, USA). In this group of professionals a second serum sample was obtained two weeks after the first one for IgG seroconversion analysis.

RESULTS

A total of 5,875 HCW (87.0% of the total) accepted to participate in the study (women 80.3%, men 19.7%). **IgG antibodies were detected in 23.1% subjects, being significantly more prevalent in men than in women** (25.5% vs 22.3%; p=0.01). Association with any age interval was not detected.





By professional category, most affected sanitary personal were hospital porters (26.8%) followed by residents (25.7%) nursing staff (24.2%) and physicians (23.7%). Prevalence among professionals not directly related to patient care was 16.8% including executive, administrative and other non-health services. **The highest prevalence were detected in the Heads of the Departments and Nursing Supervisors (30.0%)**

Correlation between results of serology and previous results of PCR

	Positive PCR N (%)	Mean days (range) between PCR+ and serology	Negative PCR N (%)	Mean days (range) between PCR- and serology	NO PCR
Positive IgG	386 (6.5)	29 (2-78)	301 (5.1)	22 (3-63)	675 (11.5)
Negative IgG	25 (0.4)	28 (13-47)	667 (11.3)	26 (2-81)	3821 (65.1)

11.5% of IgG positive HCW did not have history of PCR testing which may correspond to undiagnosed infections. Conversely, IgG was not detected in 6.1% of 411 HCW that did not have history of previous positive PCR result. Considering only HCW with positive IgM together with positive PCR post-serology and those with positive seroconversion, **we demonstrated current asymptomatic infections in 1.1% HCW.**

Considering ELISA as the reference technique, the global agreement between both tests for IgG was 96.9% . LFIA sensitivity and specificity were 93.5% and 98.0%, respectively. On the other hand, global agreement for IgM was 86.9%, with a specificity of 98.2%, but the sensitivity was extremely low (33.1%), which made it unreliable for diagnosis of acute or asymptomatic cases.

CONCLUSIONS

- We found high impact of SARS-CoV-2 in sanitary and non-sanitary Health Care Workers. Our results suggest that infections are not only related to patient care in a Hospital setting
- Asymptomatic and undiagnosed infections could have contributed to high transmission rates during this first epidemic wave
- Lateral flow immunoassay demonstrates good performance for IgG detection respect to reference method, which could be useful in some settings with difficult access to high throughput platforms or sanitary systems

Authors: V Aguilar Ruiz (1), I Gefaell Iarrondo (1), M Guisado-Clavero (1), M Pérez Álvarez (1), A Herrero Gil (1), M Castelo Jurado (1), A Herrera Marinas (1), S Ares-Blanco (1), M Menéndez (2, 3). (1) Servicio Madrileño de Salud, (2) Investigador independiente, (3) Instituto de investigacion i+12 (CIBERESP), Hospital 12 de Octubre. Madrid.

SARS-CoV-2 pneumonia in primary care: observational study in a practice in Madrid city.

Background:

- Most of SARS-CoV-2 pneumonia data is published from hospitalized patients.
- Possible cases of SARS-CoV-2 infection were diagnosed in primary care in Madrid, some of these cases had pneumonia.
- **Objective: The present study describes clinical characteristics of patients with SARS-CoV-2 pneumonia diagnosed in primary care across age groups and type of pneumonia.**

Methods:

- Observational retrospective study .
- Clinical health records were collected by in-person or remote consultation during the 10th March to the 7th of April.
- Diagnosis of SARS-CoV-2 pneumonia by **chest X-ray ordered by the General Physician .**

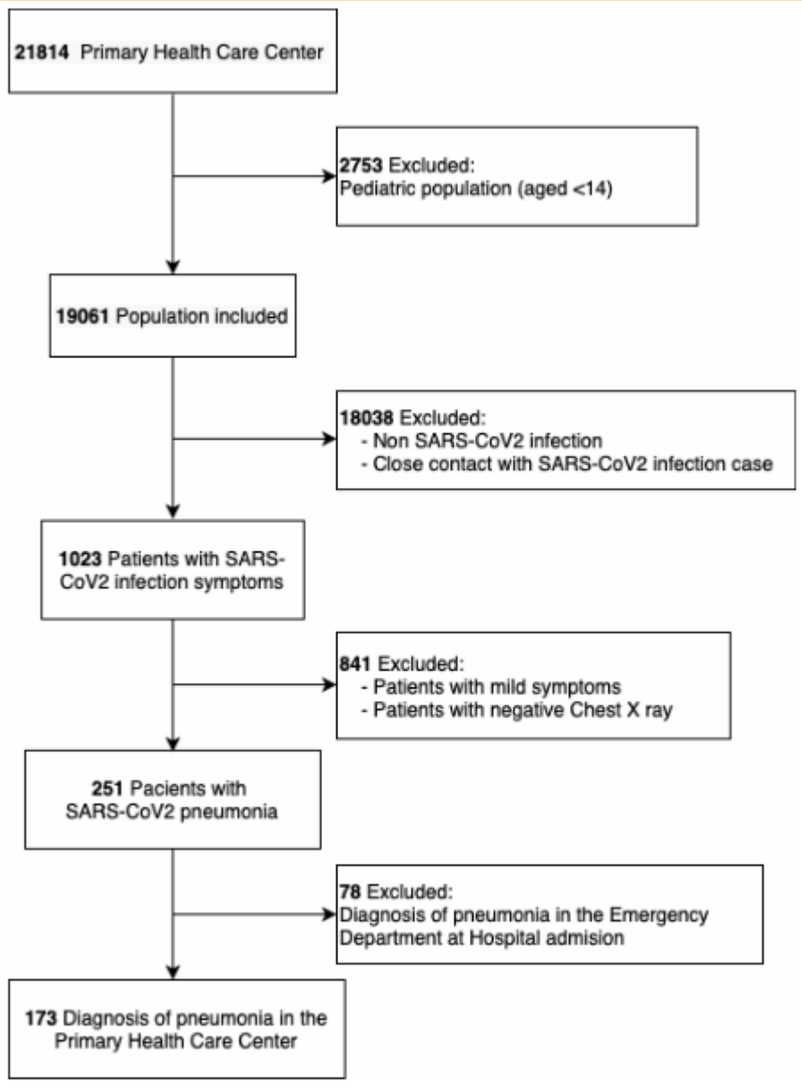


Figure 1: Flowchart

Results:

- Comorbidities were body **mass index ≥25 kg/m2** (52.3%), **hypertension** [48.3%]), **dyslipidaemia** (39.5%) and **diabetes** [19.2%]).
- The sample was stratified by age groups **(<50 years, 50-75 years and ≥75 years),** showing fewer symptoms in the elderly.
- Clinical manifestations at onset were **fever** (83.7%), **cough** (140 [81.4%]), **dyspnoea** (103 [59.9%]) **and gastrointestinal disturbances** (41.9%).
- **Day 7.8** (SD:4.1) from clinical onset was the **mean day of pneumonia diagnosis.**
- Bilateral pneumonia was more prevalent than unilateral (73.3%).

UNILATERAL PNEUMONIA:

- Higher pulse oximetry (96% vs 94%, p <0.001).
- **Unilateral cases obtained better results** in C-reactive protein (29.6 vs 81.5mg/L, p <0.001), and lymphocytes (1400.0 vs 1000.0E3/ml, p<0.001).
- ***Complications:***
  - **Pulmonary embolism was only present at bilateral pneumonia** (5.6%).
  - Death occurred in 1 patient with unilateral pneumonia (2.2%) vs 10 patients (7.9%) with bilateral pneumonia (p 0.170).
  - **Only the 43.5% of unilateral cases required hospital admission** compared to 95.2% of bilateral pneumonias.

Conclusion:

- Clinical manifestations of SARS-CoV-2 pneumonia were fever, cough and dyspnoea; this was especially clear in the elderly.
- **Primary care can manage unilateral pneumonia without red flags, relying on a correct exploration and the use of appropiate medical testing.**

Socioeconomic Inequalities in Colorectal, Lung, and Breast Cancer Incidence in Spain: A multilevel Population-based Study

Daniel Redondo-Sánchez[1,2,3], Rafael Marcos-Gragera[2,4,5], Marià Carulla[6,7], Arantza Lopez de Munain[8], Consol Sabater Gregori[9], Rosario Jimenez Chillarón[10], Marcela Guevara[2,11,12], Olivier Nuñez[2,13], Pablo Fernández-Navarro[2,13], María-José Sánchez[1,2,3,14]*, Miguel Angel Luque-Fernandez[1,2,3]*

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** These authors contributed equally*

INTRODUCTION

Social inequalities in cancer incidence and cancer outcomes have an economic impact on health care costs. Identifying and characterizing socioeconomic and geographic disparities in cancer outcomes helps optimize and redistribute healthcare services in a more equitable fashion. Socioeconomic inequalities in cancer incidence are not well documented in Spain. We aim to study the association between socioeconomic status (SES) and incidence for colorectal, lung, and breast cancers in Spain.

METHODS

SES was measured using the Spanish Deprivation Index, a standardized measure that uses national census data from 2011. We conducted a multilevel study using data from population-based cancer registries. We included incident cancer cases diagnosed for the period 2010-2013 in nine Spanish provinces. We used Poisson mixed-effects models, including the census tract as a random intercept, to derive cancer incidence rate ratios by deprivation adjusted for age and calendar year. We produced and mapped the age and SES standardized cancer incidence smoothed rates by census tracts.

RESULTS

Male adults with the lowest SES compared to those with the highest SES showed weak evidence of being at increased risk of lung cancer (risk ratio -RR-: 1.18 95%CI: 0.94–1.46) but showed moderate evidence of being at reduced risk of colorectal cancer (RR: 0.84, 95% CI: 0.74 –0.97). Female adults with the lowest SES compared to those with the highest SES showed strong evidence of lower breast cancer incidence with 24% decreased risk (RR: 0.76, 95% CI: 0.68–0.85). Among women, we did not find evidence of an association between SES and lung or colorectal cancer.

Figures: Colorectal (**Figure 1**), lung (**Figure 2**) and breast (**Figure 3**) smoothed cancer incidence rates adjusted for deprivation and age by census tract in seven Spanish provinces during 2010-2013.

Figure 1

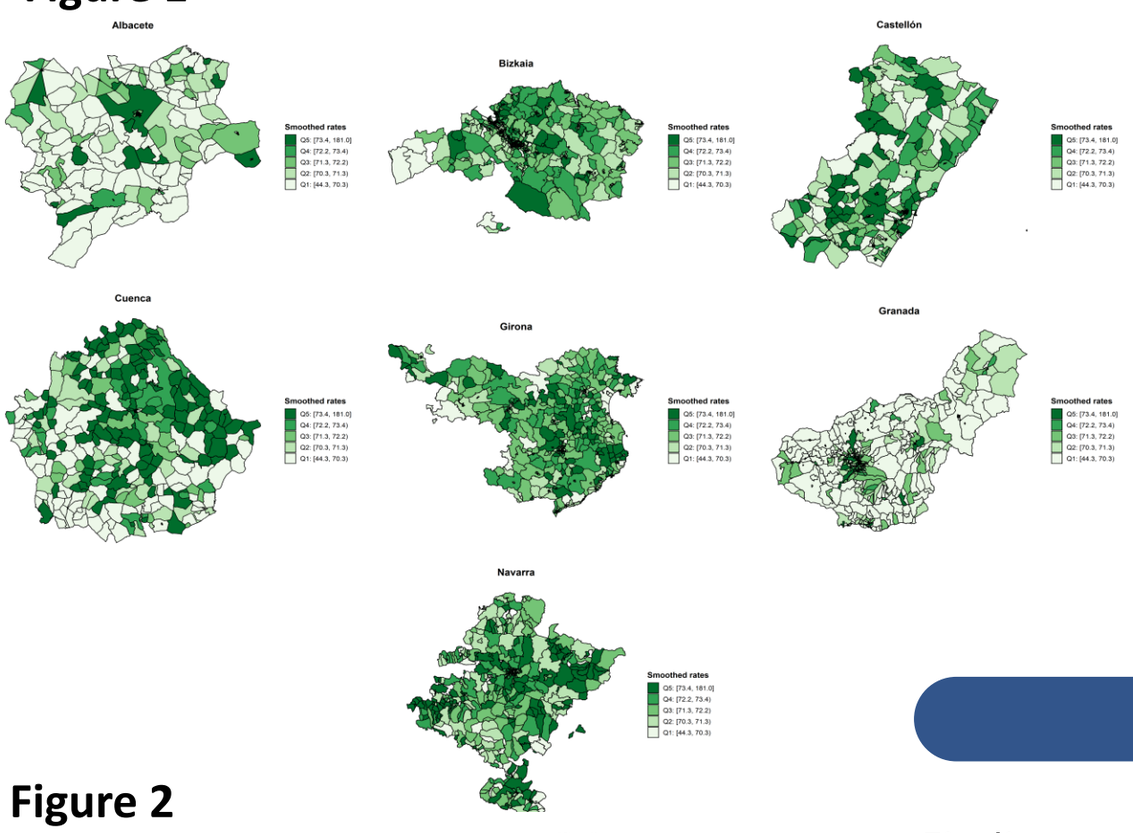


Figure 2

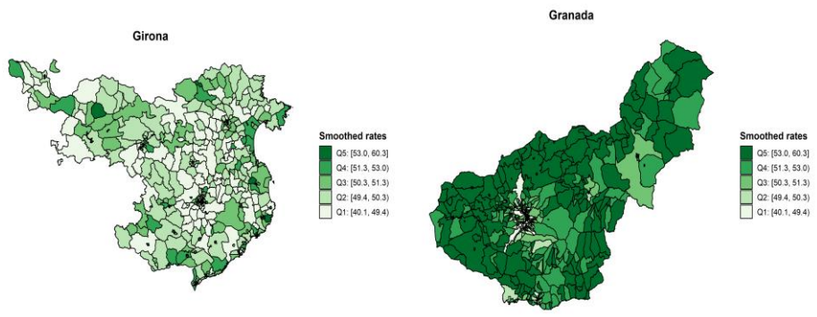
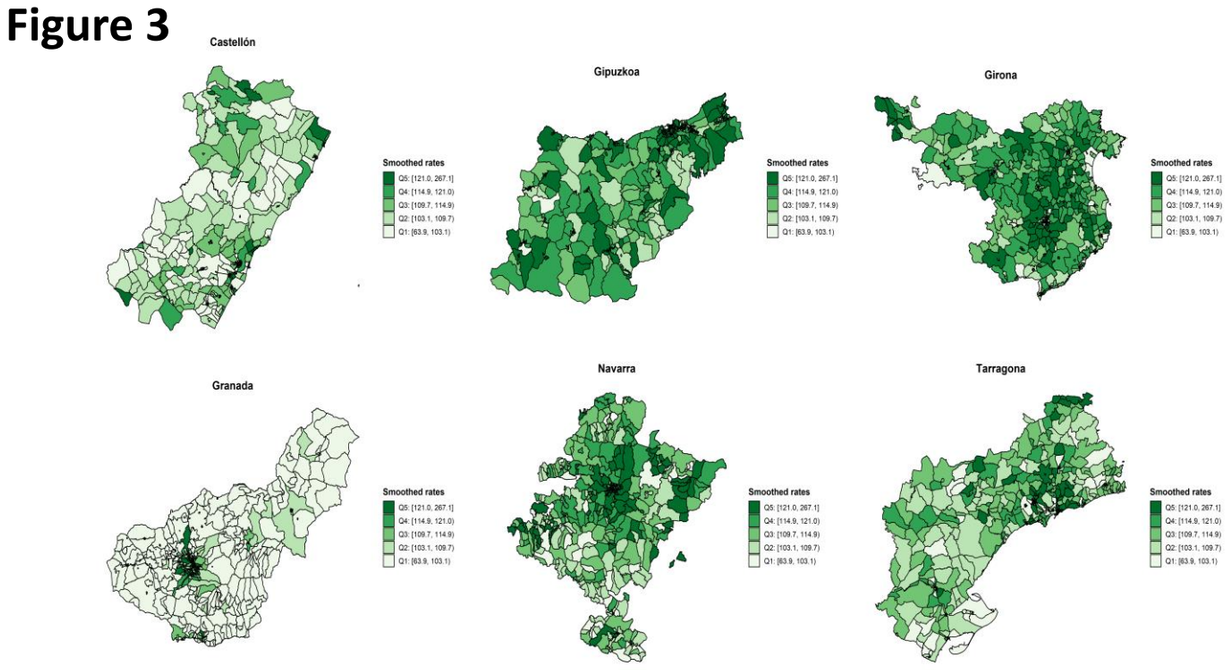


Figure 3



DISCUSSION

Findings are consistent with other European countries showing the association between socioeconomic inequalities and lung cancer among men and reduced breast incidence risk among women with lower SES. Understanding the reasons behind these associations could help develop appropriate public health programs to promote health and reduce socioeconomic inequalities in cancer incidence in Spain.

TEMPORAL DYNAMICS AND STABILITY ANALYSIS OF INTESTINAL MICROBIOTA IN A MEDITERRANEAN COHORT

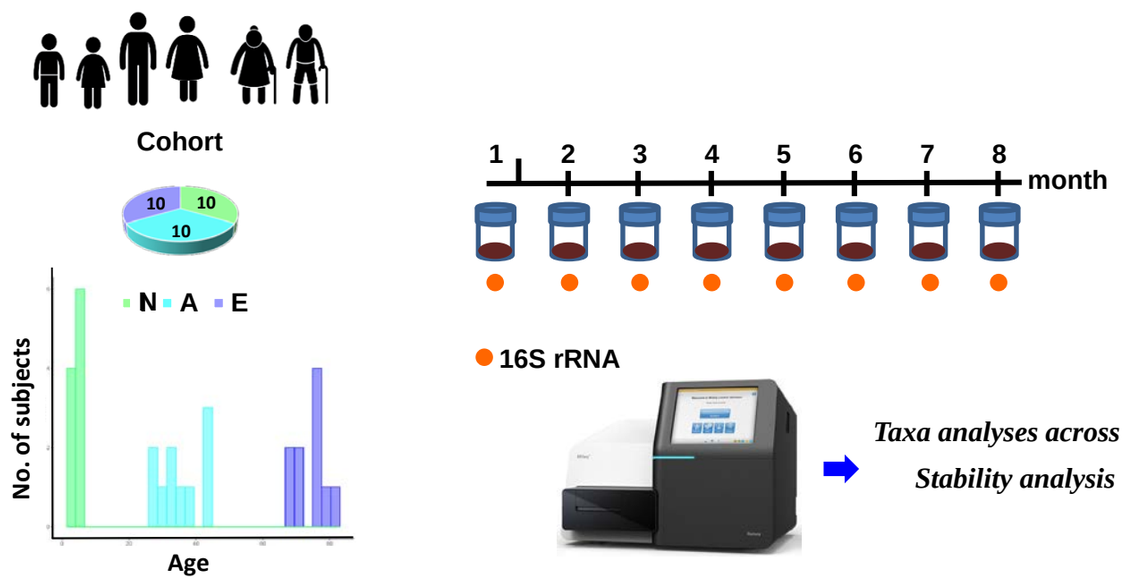
Susana Ruiz-Ruiz[1,2,*], Benjamí Pérez-Rocher[3], Javier Pons-Tamarit[1], Alejandro Artacho[1] and Andrés Moya[1,2,3]

[1]Foundation for the Promotion of Sanitary and Biomedical Research of the Valencian Community (FISABIO), València
[2]CIBER in Epidemiology and Public Health (CIBEResp), Madrid.
[3]Institute of Integrative Systems Biology, Universitat de València and CSIC, València

INTRODUCTION

A Mediterranean cohort with three age groups was established with 10 children between 2 and 5 years (3.9 ± 1.5), 10 adults between 25 and 45 years (35.4 ± 6.6) and 10 elderly between 65 and 85 years (74.5 ± 4.3). With monthly collections for eight months of feces from these individuals (240 samples in total), we determined the composition of the microbiota by means of the 16S gene analysis (Illumina platform). The objective of the study was to differentially evaluate the stability of the microbiota in the three groups by applying the model developed in the group (Marti *et al*. 2017, *mSytems* 2:e00144-16) which is based on Taylor's power law. We found that children had statistically significant differences compared to adults and the elderly, with a clear indication that the intestinal microbiota, for different reasons, evolves from infancy to the adult/old age period until reaching stability. The condition of poorer health in the infant microbiota must be interpreted as a process of gradual establishment and incorporation of new taxa that will finally make up the adult microbiota.

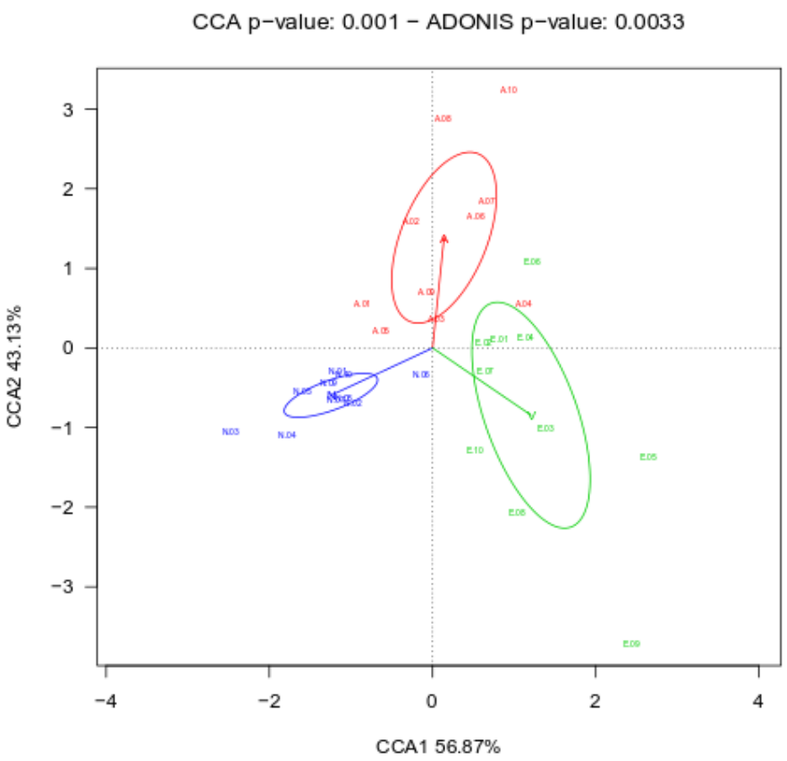
MATERIAL AND METHODS



RESULTS AND DISCUSSION

Taxa analyses across life

The distribution of relative abundances of phyla showed that the faecal microbiota in the three groups of age was dominated by two phyla, Firmicutes and Bacteroidetes, which increased with age (infants, 82.0%; adults, 85.5% and elderly 88.7%), followed by phyla Actinobacteria, Proteobacteria, Fusobacteria, Verrucomicrobia and Lentisphaera (<1-18%), which collectively decreased with age (infants, 17.8%; adults, 13.8% and elderly, 10.7%). At genus level, the 15 most abundant taxa contributed 67.5% to infants, 69.4% to adults and 61% to elderly, respectively. Eight of those genera belonged to class Clostridia, two to phylum Actinobacteria and one more, *Streptococcus* to class Bacilli. On the other hand, Chao 1 richness estimator and Shannon diversity index between groups of age, either at genus and species levels, increased with age.



A first analysis carried out of the distribution of taxa of individuals samples at different times and at genus level showed statistically significant differences (CCA analysis and Adonis test) pointing towards an age effect (Figure 1).

Figure 1. Canonical correspondence analysis (CCA) plots of bacterial microbiome at genus level, according to the three groups of age.

Analyses carried out on particular genus showed significant differences between ages (Wilcoxon test). Among infants and adults 8 genera showed significant differences (p value < 0.05) highlighting the genera Tyzzerella, Veillonella and Intestinibacter that were more abundant in infants while Dorea, Paraprevotella, Blautia, Butyricicoccus and Butyricimonas were more abundant in adults.

Among infants and elderlies 10 genera showed significant differences (p value < 0.05) highlighting genera Tyzzerella, Flavonifractor, Intestinibacter, Bifidobacterium and Erysipelatoclostridium that were more abundant in infants while Butyricimonas, Ruminococcaceae, Desulfovibrio, Lachnospiraceae and Coprococcus more abundant in elderlies

Among adults and elderlies 10 genera showed significant differences (p value < 0.05) highlighting the genera Blautia, Paraprevotella, Flavonifractor and Collinsella were more abundant in adults while Veillonella, Escherichia/Shigella, Ruminococcaceae, Christensenellaceae, Haemophilus and Odoribacter were more abundant in elderlies.

Stability analysis

We have applied the stability analyses developed by Martí et al. (2017) that allowed us to determine and to compare the microbiota stability of the three groups of age based on the relative composition of genus over, normally, the eight time points of the different individuals of our cohort. The main parameters of the model are *V*, the amplitude of the fluctuation of taxa over time and β, the index of the power law.

In our study, the fit to the power law was always robust. β was always less than 1 for all the individuals, no matter the group of age, which indicates that the most abundant genus in the microbial community were less susceptible to perturbations than the less abundant. Interestingly, however, *V* appears to vary between groups of age, it being higher in infants (0.351 +/- error) than in adults (0.277 +/- error) and elder people (0.267 +/- error) (Figure 2). High values of the *V* parameter are associated with greater instability (lower health) than lower values.

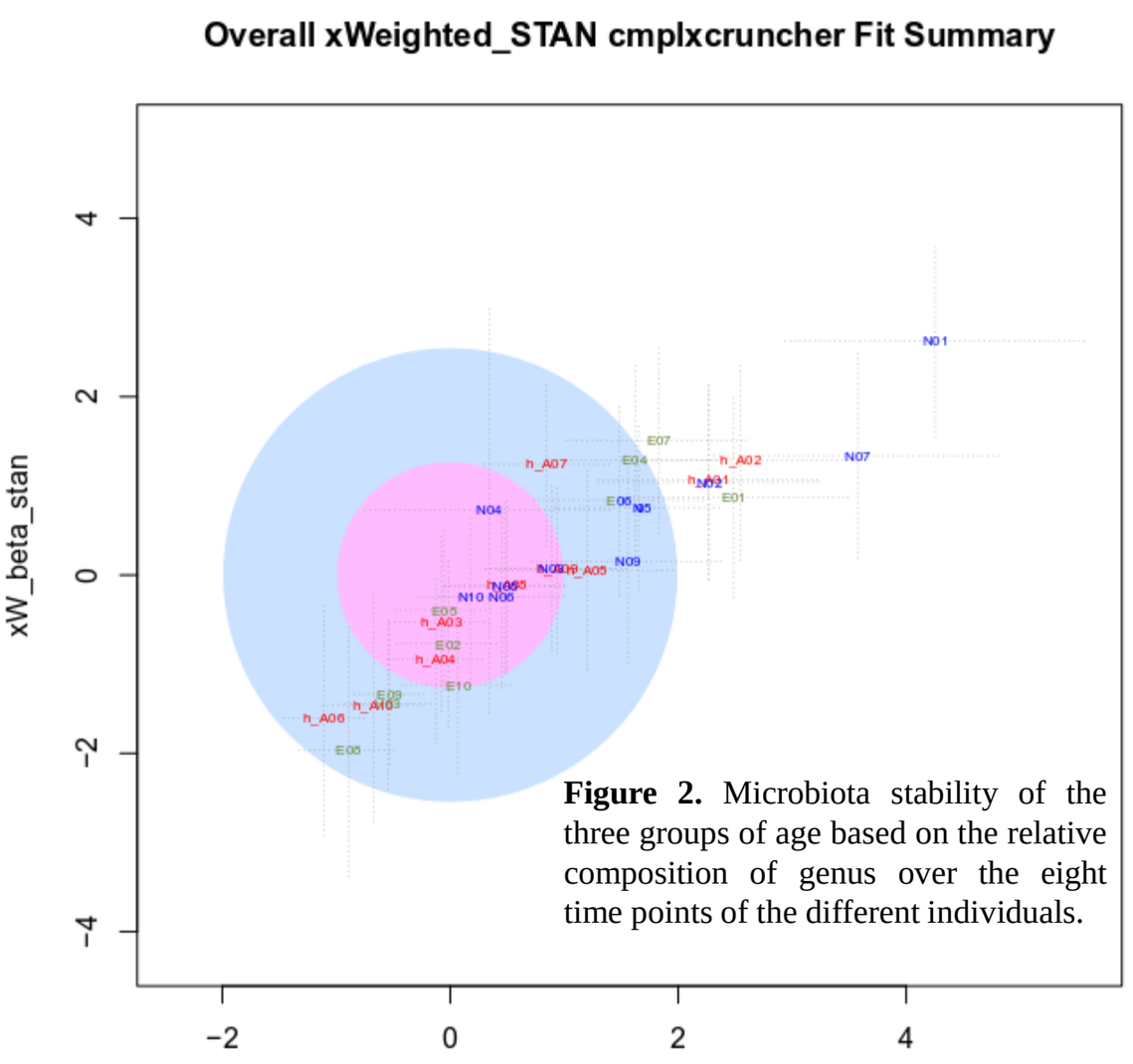


Figure 2. Microbiota stability of the three groups of age based on the relative composition of genus over the eight time points of the different individuals.

CONCLUSIONS

- These first results seem to indicate that the gut microbiota of adults and elderly is more stable than children's microbiota.

The Initial Medication Adherence intervention trial (IMA-cRCT): *study protocol*

European Research Council 948973

Authors: *Corral-Partearroyo C [(1)]*, Sanchez-Viñas A[(1)]*, Peñarrubia-María M[(2,3)], Gil-Girbau M[(1,4)], Aznar-Lou I[(1,5)], Rubio-Valera M[(1,5)]*

BACKGROUND:

10%

of prescriptions for chronic treatments are not initiated

Associated with

- Poorer clinical outcomes
- More days of sick leave
- Higher costs for the healthcare system

Aims to improve:

- Medication initiation, implementation & persistence
- CVD and diabetes clinical symptoms & reduce risks

Based on the **Theoretical Model of Medication Non-Initiation**

THE IMA INTERVENTION

Promotes:

- Health literacy
- Shared decision making

AIMS & METHODS:

Aim 1 To evaluate effectiveness and cost-effectiveness of the IMA intervention.

1. **CLUSTER RANDOMISED CONTROL TRIAL (cRCT)** – January'22 to June'22 with one-year follow-up

SETTING:

Institut Català de la Salut

34 Urban and Rural PC Centres

Cluster Randomisation

CG

IG

4000 patients

Usual care

IMA intervention

Patients prescribed with a new treatment for:

CVD

Diabetes

Aim 2 To understand the effect of the intervention and the generalisability of its effectiveness.

2. **PROCESS EVALUATION** of the:
   - IMA implementation
   - Mechanisms of impact of IMA
   - Context

Aim 3 To assess long-term cost-effectiveness and cost-utility of the IMA intervention.

3. **ECONOMIC MODELLING**

Aim 4 To disseminate the results to stakeholders & promote change in clinical practice.

4. **DISSEMINATION OF RESULTS**
   - *Publications in high-impact journals & professional networks.*
   - *Presentation of results to decision-makers.*
   - *Web and mass media news.*

ANALYSIS:

1. Real World Data (RWD)

- ☐ No additional data registry
- ☐ **Effectiveness** GLM: Initiation, implementation, persistence & clinical outcomes
- ☐ **Short-term CEA** ≠ costs & probability of initiation. ICER

2. Process Data

- ☐ Descriptive analysis of **quantitative data** on implementation
- ☐ **Qualitative data** to understand professionals & patients' perception

3. Markov Models

- ☐ **Long-term CEA & CUA** Costs, LYG, REGICOR & QALY

EXPECTED RESULTS:

Provide **evidence** on:
- The IMA intervention
- Novel methodology for developing & evaluating complex interventions

RESULTS WILL

Be **Disseminated** to:
- Facilitate its transferability to clinical practice

Have **implications** for:
- Practice
- Policy
- Research

CEA: Cost-Effectiveness Analysis; CUA: Cost-Utility Analysis; CG: Control Group; CVD: Cardiovascular disease; GLM: generalized linear model; IG: Intervention Group; IMA: Initial Medication Adherence; LYG: Life-Years Gained; QALY: Quality-Adjusted Life-Years; PC: Primary Care

The quality of causes of death on mortality statistic in Spain by land

Lluís Cirera and Diego Salmerón on the behalf of the Mortality Working Group of the Spanish Epidemiological Association. *Dept of Epidemiology, Murcia Regional Health Council - IMIB-Arrixaca, Murcia. CIBER de Epidemiología y Salud Pública, Madrid. Dept of Health and Social Sciences, University of Murcia, Murcia.*

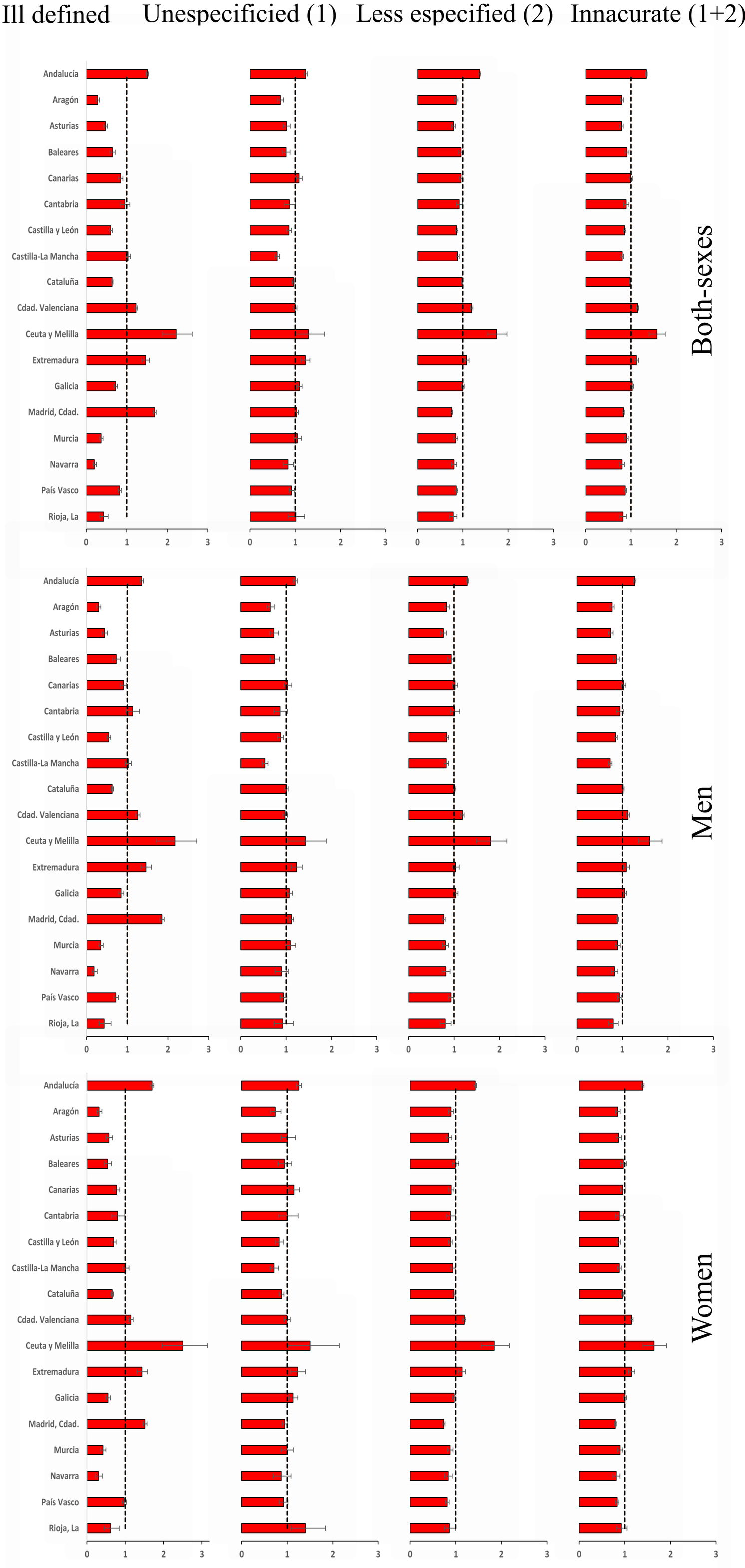
Introduction. The Spain's return to democracy in 1978 has decentralized into Autonomous Communities the generation of cause of death statistics. The internationalization by the European Union and the statistical scope of EuroStat, has been essential for the automation process of codification of death causes, and provisional statistical mortality outcomes.

Objective. To evaluate inaccurate and ill-defined death certification according to Autonomous Cities and Communities (AcC) over the years 1980 to 2018 in Spain.

Material. A descriptive epidemiological design of an annual unit was implemented with the causes of death code-counts assigned into unspecified, less specified (both together in inaccurate) and ill-defined certified grouping. Each AcC was compared to Spain in the 2016-2018 period by means of the Comparative Mortality Ratio (CMR, direct method of age-standardization). The number of deaths was modelled as a Poisson variable by AcC, sex and age group. For each AcC, the CMR was defined as its land-rate divided by the Spanish's one. The estimation of the CMR was performed under the Bayesian point of view.

Results. In the whole Spain and both-sexes, a decrease was observed in the age-standardized rates of ill-defined certification group (48.6 vs 11.3 deaths per 100,000) and of inaccurate certifications (116.4 to 31.8). This decreasing trend was also found in AcC. In the last period (2016-2018), the maximun range in rates differences between AcC for both-sexes has achieved 17 percentage points in ill-defined and inaccurate medical certification. Moreover, there was a significant excess of ill-defined certification in died women and men over the Spanish average, in Andalusia, Valencia, Ceuta+Melilla, Extremadura, and Madrid lands. This datum was land-recurrent for inaccurate certification with the Madrid exception.

Discussion. The observed differences are suggestive of a medical mistraining in causes of death certification.

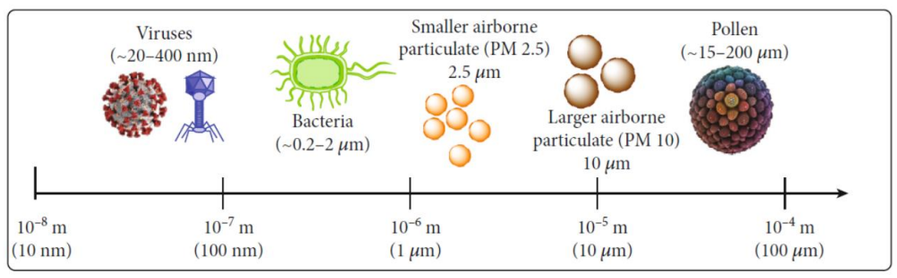


Towards sustainable plastic management of municipal residue waste (MRW): Lessons learned in the COVID19 crisis and proposals for action

***Olea N**, Peula F, Sánchez-Rios M, Iribarne-Durán L, Calero de Hoces M, Martín-Lara, MA, Fernández MF*

Grupo CIBERESP-19/ibs.GRANADA, Dptos Radiología e Ingeniería Química/Univ. Granada, Serv Prov Trato. Residuos, Diputación de Granada

Background: Emergency measures established under the COVID-19 pandemic have highlighted the contribution and benefits of plastics used in protection, prophylaxis, medical materials and devices and food packaging. However, the sudden **increase in plastics demand and poor waste management** points out the unsustainability of the plastics economy and the failures in environmental pollution containment measures. The EU has defined that plastic pollution is, together with climate change and biodiversity loss, one of the most pressing challenges. Production, disposal and management of plastic waste is responsible for **greenhouse gas emissions** due to outdoor burning, inadequate residues treatment at recycling plants, and intensive incineration for energy production and **animal and human exposure** to plastic residues.

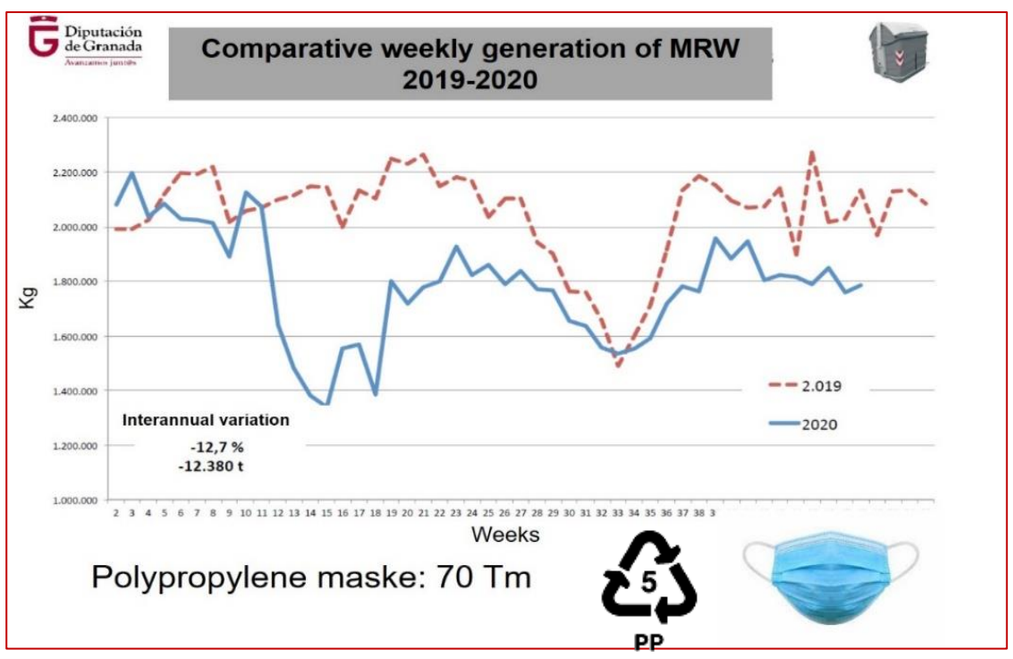


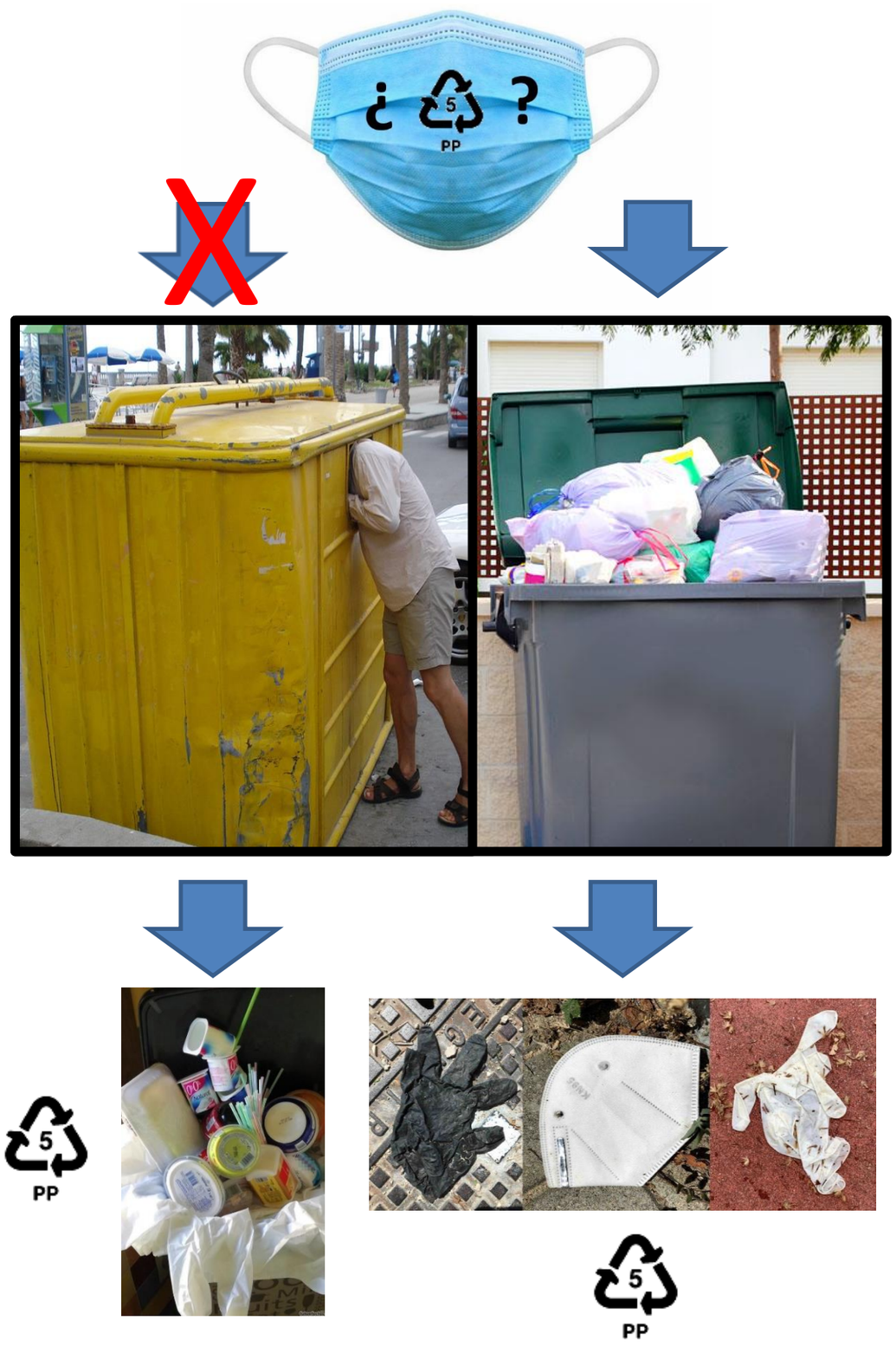
Relative size chart of common airborne contaminants and pathogens.

Objectives:

1. To explore, after the first nine months of COVID-19 crisis, how measures taken to protect against the virus have changed the **qualitative and quantitative composition of MRW**
2. To propose **measures to reduce the impact** of MRW management

Results: In a MRW plant serving a million people, nine moths of COVID19 alert resulted in a reduction in 12.7% (approximately 12.000 Tm) of the total residues generated but an increase of 70 Tm of polypropylene products (mainly masks and gloves). These amounts of plastic-based personal protective equipment waste threatens the existing MRW management streams. Moreover, plastic-based personal protective equipment waste in the environment will deteriorate and fragment, originating plastic particles of micro- and nano-size and impose severe risks to both environmental and human health.





Proposal: A plan to improve MRW management has been developed which is summarized in the following points:

1) **Better management of personal protective equipment (PPE) made of plastic materials**: i) Implementation of sustainable/rational use of personal protective equipment in sanitary and non-sanitary facilities, in particular in hotspot areas of the pandemic; ii) Promotion of the use of dressing gowns and other reusable PPE to prevent the generation of plastic waste; iii) Promotion of energy recovery with recovery of disposable PPE material.
2) **Management of plastic materials derived from the packaging of food and consumer goods**: i) Implementation of sustainable security measures to ensure the safety of consumer goods packaging and ensure the provision of services; ii) Promotion of sustainable and safe consumption and production patterns for plastics; iii) Promotion of attitudes of citizen collaboration at all stages of reducing plastic consumption, reuse and recycling.
3) **Remediation measures to mitigate potential adverse effects of plastic pollution due to pandemic scenarios**: i) Establishing stricter protocols for the treatment of plastic waste with selective separation at source; ii) Increasing professional protection measures against potentially hazardous waste from a biological point of view; iii) Extending the selective recovery of plastics to groups of materials that by their composition or size are not routinely recovered

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Acknowledgements: ISCIII-CIBERESP; ibs.GRANADA; Universidad de Granada (Dptos Ingeniería Química y Radiología y Medicina Física); Servicio Provincial Tratamiento Residuos, Diputación de Granada; FEDER

Ultra-processed food intake and all-cause mortality in Spain

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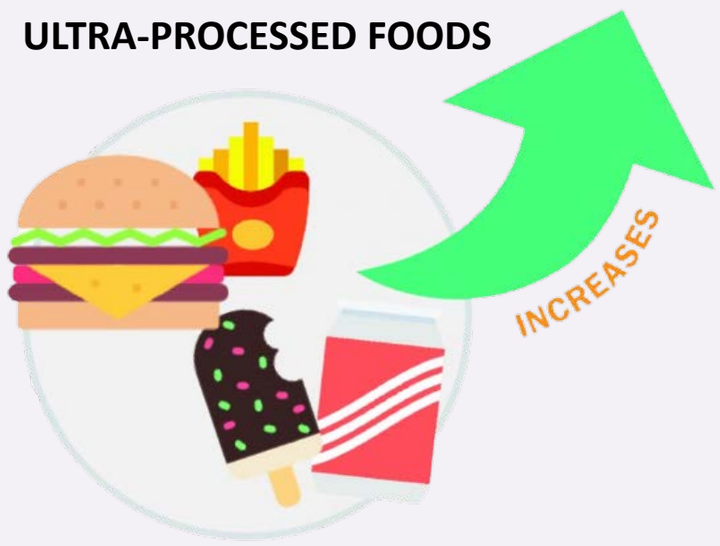
INTRODUCTION

ULTRA-PROCESSED FOODS



Dietary habits have changed in recent decades. One of the most important changes is the increase in the **ultra-processed foods (UPFs)** consumption around the world. UPFs are industrial formulations made from substances derived from food or synthesized in laboratories (dyes, flavourings, and other additives) usually containing little or no whole food. The beneficial effects of fresh or minimally processed foods on mortality are well known [1], but few studies have described the detrimental effects of high consumption of UPFs.

OBJECTIVE

To determine the association between ultra-processed food intake and **all-cause mortality** and to compare the effects of the different NOVA groups in vital status using isocaloric substitution.

METHODS

Prospective cohort of 4679 subjects from the multicenter study Diet and Risk of Cardiovascular Diseases in Spain **(DRECE)** [2].
Follow-up ≈ **27 years** ⟶ Baseline (1991) to mortality date or December 31st, 2017, whichever was first (**INE** agreement).
Validated food frequency questionnaire categorized according to the **NOVA** classification [3].
Cox regression models to evaluate the association between consumption of ultra-processed food and mortality.
Comparison of the health effects of the different NOVA groups by **isocaloric substitution**.

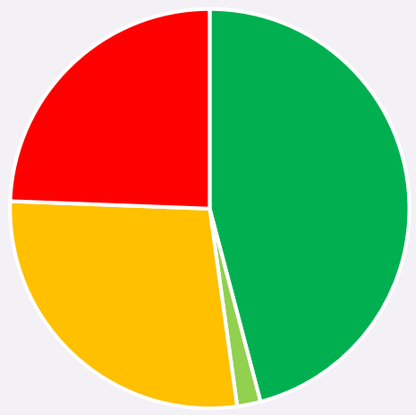
RESULTS

Cox model was adjusted for age, sex, lifestyle and clinical factors. Those who consumed the highest amount of ultra-processed foods had higher risk of mortality. After performing the isocaloric substitution in the model, an inverse response was observed when ultra-processed foods were substituted by unprocessed or minimally processed foods. A reduction of 14% in all-cause mortality was estimated (**Table 1**).

Cox model: all-cause mortality	HR (95% CI)	p-value
Overall, For every 10% of energy from UPFs	1.15 (1.03 to 1.27)	**0.012**
Replace % energy of UPFs with % energy of:		
Processed foods (Group 3 + Group 2)	0.88 (0.78 to 1.01)	0.051
Unprocessed or minimally processed foods (Group 1)	0.86 (0.77 to 0.98)	**0.018**

UPFs consumption in Spain according to the NOVA classification

UPFs ⟶ 24.4% of the total energy intake



NOVA classification
Group 1 Unprocessed processed foods
Group 2 Processed culinary ingredients
Group 3 Processed products
Group 4 Ultra-processed foods (UPFs)

Table 1. Hazard ratios (HR) from Cox multiple regression. Overall and Isocaloric substitution.

CONCLUSIONS

An increase in ultra-processed foods consumption was associated with higher risk of all-cause mortality in a representative sample of the Spanish population. Furthermore, the theoretical substitution ultra-processed food by unprocessed or minimally processed foods would suppose a reduction of the mortality risk.

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Urinary concentrations of non-persistent pesticide metabolites and association with hormone levels in adolescent males from the INMA-Granada cohort

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Background and objective

Experimental data show that numerous modern non-persistent pesticides, including insecticides, fungicides and herbicides, interfere with estrogen, androgen, and/or thyroid signaling pathways; however, epidemiological studies on the potential endocrine effects of pesticide exposure in children and adolescents remain scarce.

Objective: To describe the concentrations of urinary metabolites of **organophosphate (OP)**, **pyrethroid (PYR)** and **carbaryl** insecticides, and **dithiocarbamate fungicides**, and examine their association with serum levels of reproductive, thyroid, and adrenal hormones in adolescent males from the **"Infancia y Medio Ambiente" (INMA) Project.**

Methods

668 INMA-Granada cohort (boys) recruited at birth (2000-2002)

↓

155 Follow-up visit age 15-17 years → **Cross-sectional study, N=134**

Pesticide metabolites in urine

- TCPy (chlorpyrifos)
- IMPy (diazinon)
- MDA (malathion)
- DETP (several OPs)
- 3-PBA (several PYR)
- DCCA (several PYR)
- 1-naphthol (carbaryl)
- ETU (dithiocarbamates)

X

Serum hormones

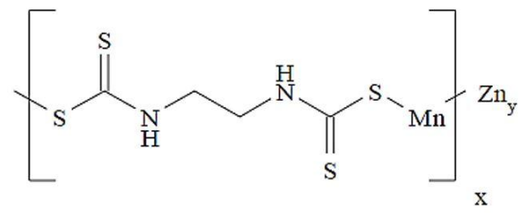
- Reproductive: TT, E_2, DHEAS, SHBG, LH, FSH, AMH, IGF-1, prolactin
- Thyroid: free T4, total T3, TSH
- Adrenal: ACTH, cortisol

Linear regression models adjusted for urinary creatinine, age, BMI, season, and time of day.

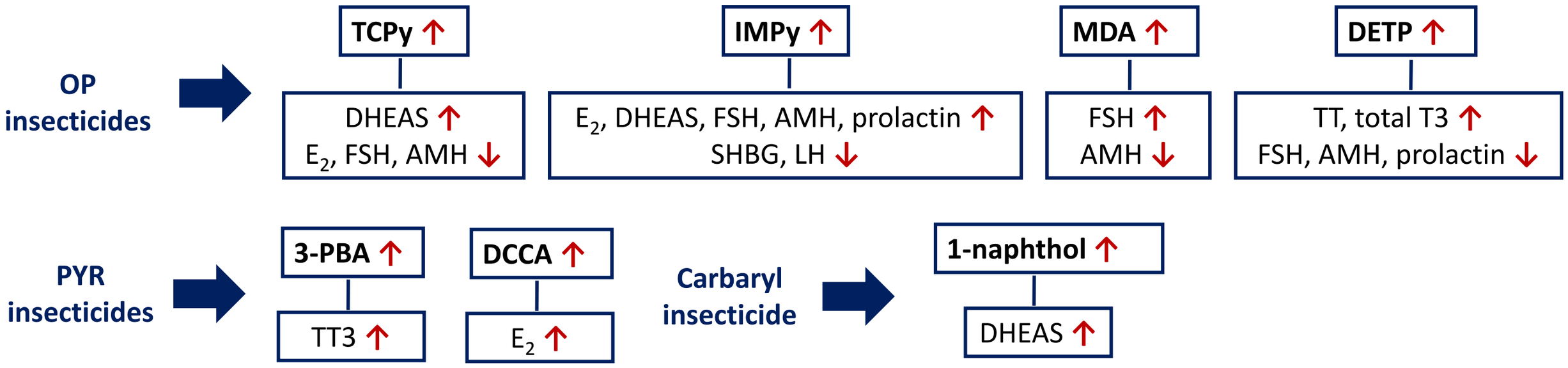
Results

Urinary concentrations of pesticide metabolites (µg/L)

	DF (%)	25th percentile	Median	75th percentile	Max.
TCPy	32.4	<0.039	<0.039	0.084	1.213
IMPy	76.3	<0.117	0.254	0.807	27.11
MDA	84.0	0.131	0.297	0.466	1.501
DETP	54.7	<0.116	0.2515	0.694	40.35
3-PBA	19.3	<0.117	<0.117	<0.117	0.720
DCCA (*cis+trans)*	65.0	<0.172	1.031	3.428	8.256
1-naphthol	37.8	<0.156	<0.156	0.341	2.878
ETU	74.8	<0.072	0.256	0.703	19.37



Adjusted associations of urinary pesticide metabolite concentrations and hormone levels:



Data suggest that pesticide exposure may lead to altered hormone levels in male adolescents. Some of the observed associations could be explained by the potential **interference of pesticides on aromatase and deiodinase activity**, and **oxidative stress at the pituitary level.** Nonetheless, further studies with larger sample size are warranted to confirm our findings.

WHAT ARE THEY REALLY FOR?
ANALYSIS OF THE PREDICTIVE CAPACITY OF SOME SIMPLE EPIDEMIOLOGICAL MODELS

Antonio M. Lallena[1], Marta Anguiano[1], Damián Guirado[2,3], Manuel Vilvhes[4]

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The pandemic generated by the appearance of COVID-19 has developed a widespread interest in epidemiology. The lock-down imposed in order to stop the runaway spread of the disease has led many scientists, with some knowledge of basic statistics, to venture into describing the evolution of the pandemic by using very simple models. Curiously these authors have a scarce, if not nil, knowledge on epidemiology. The consequence of this situation has been an unprecedented proliferation of manuscripts sent to different journals in the field. Although some of these journals have seriously asked these new epidemiology "experts" to limit such activity, quite a few articles have been published with such contents [1,2].

In Fig. 1 the accumulated deaths in Spain due to COVID-19 are shown as a function of the date (green points). Two of the models fitted in Ref. [2] to data are shown by using the fitting parameters quoted in that reference.

One of the fundamental aspects that an useful epidemiological model must ensure is its predictive capacity: using the information available to date they must be able to predict the evolution of the parameters of interest in the future (near or far). However, the inability of both the D and D_2 models to describe data subsequent to that of the last value used in the fit is evident in Fig. 1. Same situation is observed for other simple models similar to the two mentioned above.

According to the daily deaths, it seems more reasonable to consider for the analysis only the data included in the "first wave" of the pandemia that runs for 138 days from 03/March/2020 to 18/July/2020.

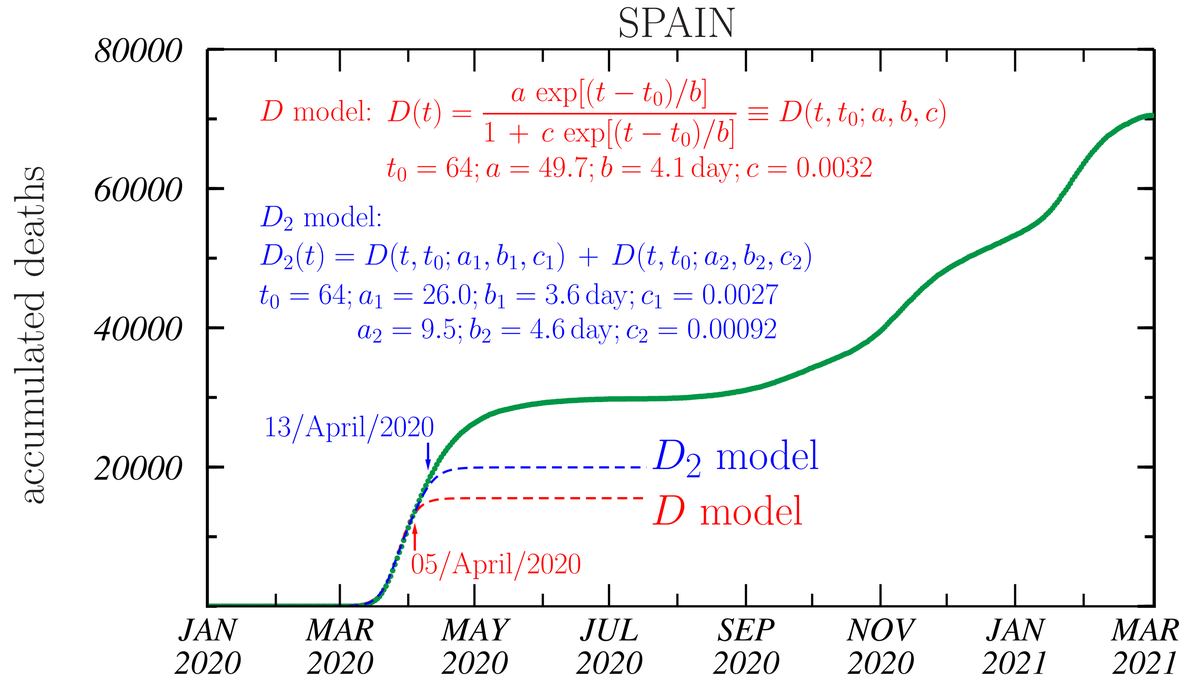

Fig. 1. The accumulated deaths due to Covid-19 in Spain are shown with the green solid points. The dashed red and blue curves correspond to the D and D_2 models with the parameters given in Ref. [2], which have been obtained by fitting them to data up to 05/April/2020 and 13/April/2020, respectively.

In Fig.2 two fits to these "first wave" data are shown. In upper panel, all the data have been considered in the fitting procedure. In the lower panel only the first 30 data (up to 01/Apri/2020) have been included. In addition to the results obtained with the D model (red curves), also those obtained for the Gompertz model (green curves) have been included. The values of the fitting parameters corresponding to each fit are given in Table 1. Both the accumulated deaths and the daily deaths (insets) have been fitted.

Table 1. Fitting parameters of the fits shown in Fig. 2.

		all data		data up to 01/April/2020	
		accumulated	daily	accumulated	daily
D model	a	530 ± 46	601 ± 82	18 ± 2	39 ± 9
	b (day)	8.9 ± 0.2	8.4 ± 0.2	3.80 ± 0.06	4.4 ± 0.2
	c	0.018 ± 0.002	0.021 ± 0.003	0.0013 ± 0.0001	0.0024 ± 0.0005
Gompertz (*)	u	2.0 ± 0.3	0.3 ± 0.1	0.013 ± 0.007	$(5 \pm 7) \cdot 10^{-4}$
	v	9.6 ± 0.2	11.5 ± 0.3	14.5 ± 0.5	18 ± 1
	w (day^{-1})	0.0753 ± 0.0005	0.082 ± 0.001	0.095 ± 0.002	0.104 ± 0.004

* The Gompertz model fitted to accumulated deaths data is $D(t) = u \exp\{v[1 - \exp(-w\,t)]\}$

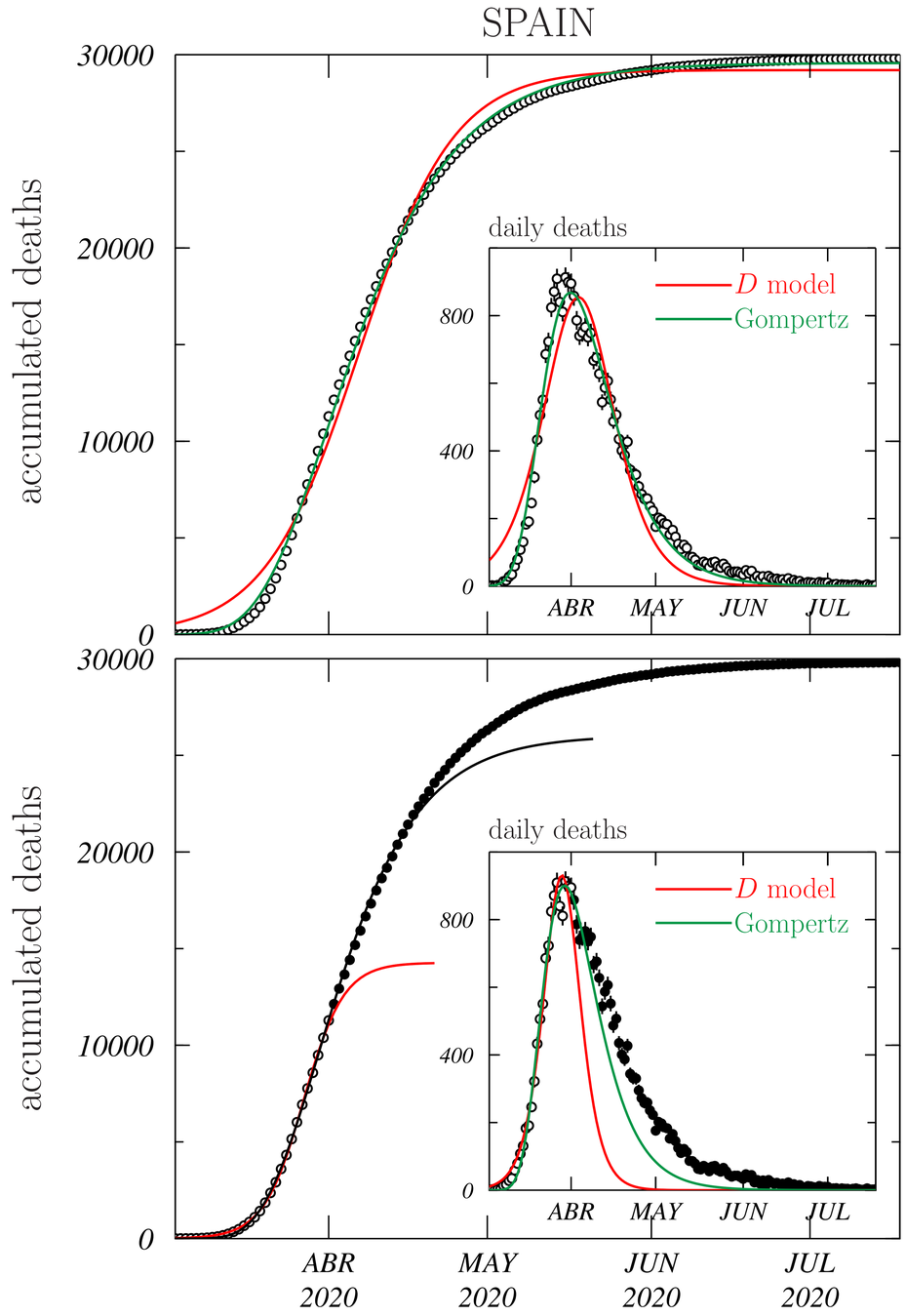

Fig. 2. Fits to "first wave" data (both accumulated and daily deaths) of the D (red curves) and Gompertz (green curves) models. In the upper panel the fit has been done to all data. In the lower panel the fit has been done to the first 30 data, up to 01/April/2020.

The results obtained indicate:

1. Fits to accumulated deaths or to daily deaths produce different models with different fitting parameters.
2. Simple models are unable to give a good description of the whole data sample.
3. The predictive capabilities of these models are extremely limited, accounting only for a few data successive to those considered in the fit. This has been already shown in Ref. [1]

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Who is lost in the last steps of the cascade of HIV services in Catalonia? Results of the PISCIS Cohort

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INTRODUCTION

Some of the people living with HIV (PLWH) lose contact with healthcare services, resulting in worse health and higher risk of causing new infections.

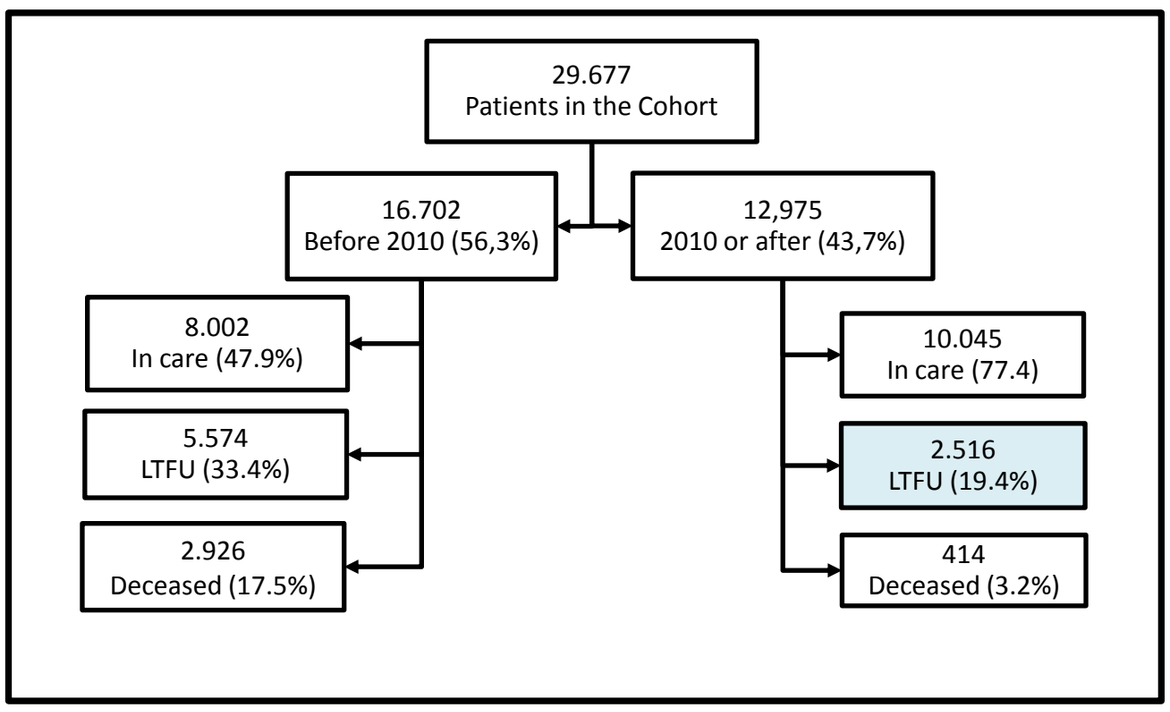
The objective of this study is to analyse the incidence of patients lost to follow up (LTFU) and the factors associated in the PISCIS Cohort of Catalonia, Spain in 2018.

METHODS

The PISCIS Cohort is a multicentre, longitudinal and prospective study that follows PLWH, aged 16 years or more and registered in 18 hospitals in Catalonia and Balearic Islands.

PLWH were considered LTFU if they entered in the cohort after 01/01/2010 and did not contacted with their hospital during 12 prior January 1ths of 2019. Logistic regression models were used to determine the risk (OR = Odds Ratio) of LTFU, adjusted by clinical and socio-demographic variables.

RESULTS



Compared to PLWH in care, LTFU were younger (37,2 vs. 38,6 years among people in care), women (16,8% vs. 15,0% among men), born in countries different to Spain (56,9% vs. 55,6% among people in care) and registered in the cohort as users of injecting drugs (16,3% vs. 8,4% among PLWH in care).

Clinical characteristics were also different among PLWH in care and LTFU. The proportion of people diagnosed with AIDS were higher among LTFU (9,1% vs. 8,0% among PLWH in care), this group had lower CD4 cells counts (22,6% vs. 29,7% among PLWH in care) and their prevalence of Hepatitis C coinfection was higher (8,4% vs. 4,8% among PLWH in care).

The multivariant analysis (Table 1) showed that the risk of LTFU was higher among young, immigrants, people who inject drugs, low CD4 cell counts and those diagnosed with hepatitis C.

Table 1. Risk of LTFU (Odds Ratio) according to sociodemographic and clinical characteristics

Characteristic	Odds ratio	95% IC
Age, 32 years or less (Ref.)		
33 – 40 anys	0,827	0,712 – 0,962*
41 anys o mes	0,776	0,668 – 0,901*
Sex, women (Ref.)		
Men	0,901	0,661 – 1,229
Country of birth, Spain (Ref.)		
Europe	1,556	1,287 – 1,881*
Africa _ America_ Asia	1,186	1,043 – 1,348*
Key population, PWID (Ref.)		
Men who have sex with men	0,359	0,283 – 0,457*
Heterosexual men	0,413	0,315 – 0,541*
Heterosexual women	0,380	0,261 – 0,522*
Years in treatment	0,780	0,761 – 0,798*
AIDS Diagnosis, No (Ref.)		
Yes	1,170	0,942 – 1,454
HCV diagnostic, positive (Ref.)		
Negative	0,763	0,576 – 0,942*

* p-valor<0,05

CONCLUSSIONS

The results of this study can be used to design and implement reengagement strategies in the HIV care units participating in the PISCIS Cohort. Taking into consideration socio-demographic and clinical determinants is key to avoid losses of and have to be considered in the design and evaluation of HIV care services. Other healthcare and social services, such as harm reduction or HCV prevention and control can be used to support of HIV care.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