

## 1. Impact of cancer awareness campaigns in Peru: a 5-year Google Trends analysis

Impacto de las campañas de concientización sobre el cáncer en Perú: un análisis de Google Trends de 5 años

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**TIPO DE CÁNCER:** Especialidades Médicas

**ABSTRACTO:** Background: The aim of this research was to characterise the interest on the most frequent cancers in Peru through Google Trends, its geographic and temporal relationship with massive awareness campaigns. Methods: A temporal trends analysis for the last 5 years was carried out, comparing the Relative Search Volume (RSV) with the dates of mass cancer awareness campaigns in Peru. Google Trends application was used to evaluate the interest in the topics: breast, prostate, cervical stomach and colorectal cancer between 1 January 2016 and 31 December 2020, expressed in RSV. The annual RSV for each neoplasm was compared, as well as its annual variation using the Kruskal-Wallis test. The correlation between the RSV and the estimated incidence for each province was measured using the Spearman test. Results: The topics with the highest RSV were breast (median: 20, range: 6-100) and prostate cancer (median: 28, range: 9-48). The topic 'breast cancer' showed a cyclical punctual increase in October, its awareness month. Searches for cervical, stomach and colorectal cancer were smaller and did not show peaks of interest. It was observed that the RSV was variable when compared with previous years ( $p < 0.05$  for all the evaluated topics). Geographically, different provincial configurations of interest were observed according to neoplasia. When correlating the RSV with the incidence by province, a non-significant positive correlation ( $p > 0.05$ ) was found for breast, cervical and colorectal cancer. Conclusions: This study suggests a positive temporal correlation between RSV and awareness cancer campaigns in Peru specially to breast cancer and, to a lesser extent, prostate cancer. Significant variations of interest were demonstrated for each neoplasm among the evaluated years. No significant correlation was found between the incidence rate and the average RSV among Peruvian provinces.

## 2. On the risk of further excluding outcast patient populations in South America

Sobre el riesgo de excluir aún más a las poblaciones de pacientes marginados en América del Sur

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**ABSTRACTO:** It is with great interest that we read the article by Farah and colleagues on the epidemiological transition at work regarding risk factors for hepatocellular carcinoma (HCC) in South America [1]. In this study, the authors compiled data from 339 patients seen between 2019 and 2021 in six countries of the region, with Peruvian patients accounting for the most significant proportion, i.e., 125 HCC cases (37%) collected at one general services hospital. The results suggest a rise in HCCs associated with non-alcoholic fatty liver disease (37%) at the regional level, whereas infection with the hepatitis B virus (HBV) tends to decrease as an associated risk factor for HCC in South America (12%). However, our experience at the National Cancer Institute of Peru (INEN), the country's main specialist cancer hospital, gives a contrasting picture of HCC epidemiology in Peru and may provide deeper insights into the real socio- epidemiological situation at the regional level. Due to the multi-tiered health systems in Peru and South America,

it is unlikely that data from a single center per country can provide an accurate picture of HCC epidemiology and its risk factors. For example, INEN treats more socially marginalized people (ca. 120 HCC patients/year) while representing a larger fraction of the country's population [2], many of whom are of Native ancestry, in comparison to the gentrifying population living in metropolises and having the benefit of health insurance [3]. Our team has published a series of articles that shed light on the elevated ratio of HBV-related HCC (81.5%) in the patient population treated at INEN [4,5]. Intriguingly, HBV infection in these patients is associated with a very low viral DNA burden, disclosing a significant rate of occult infections (33.8%) with HBV sub-genotype F1b, only detectable by ultra-sensitive molecular tests [4]. Furthermore, we identified through integrative genomic analysis a distinct molecular subtype of HBV-associated HCC with ancestry-related molecular traits [6,7]. Such higher prevalence rates of occult infection with autochthonous HBV clades (F, G, H) have been documented to a great extent in Latin American patients [8], [9], [10], [11], [12], stressing the need for precautions when identifying risk factors for HCC in the region [13]. Another issue concerning the study by Farah and colleagues is the data collection period between 2019 and 2021 amid the COVID-19 pandemic. Indeed, cancer patients originating from remote and underserved regions, which correspond in Peru with areas where HBV is highly endemic [14], could not reach metropolitan health centers during the COVID-19 lockdowns [15], creating thereby the possibility of recruitment bias in the collection of data. We understand that the article by Farah and colleagues has particular relevance for health policymakers in South America, who could then be deterred from persisting in their efforts to combat hepatitis B. Therefore, it appears of the utmost importance for decision-making to provide a truly comprehensive overview of the HCC epidemiology in the region by considering all published literature, in order to prevent further exclusion from cancer control programs of populations already among the most deprived in South America.

### 3. **Epidemiological Features and Outcomes of HTLV-1 Carriers Diagnosed With Cancer: A Retrospective Cohort Study in an Endemic Country**

Características epidemiológicas y resultados de los portadores de HTLV-1 diagnosticados con cáncer: un estudio de cohorte retrospectivo en un país endémico

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**ABSTRACTO:** **PURPOSE:** Human T-lymphotropic virus type 1 (HTLV-1) is an endemic virus in Latin America that is directly linked to adult T-cell leukemia/lymphoma (ATL). Previous studies have suggested an oncogenic role of HTLV-1 in non-ATL neoplasms and have found higher mortality in HTLV-1 carriers without ATL. **METHODS:** In this retrospective cohort study, HTLV-1 carriers were identified through screening at a tertiary cancer center between 2006 and 2019. We compared the overall survival (OS) outcomes of patients with ATL with those with other solid or hematologic malignancies by sex stratification. **RESULTS:** We identified 1,934 HTLV-1 carriers diagnosed with cancer. The median age at diagnosis was 62 (range 20-114) years, 76% were female, 60% had no or elementary school education, and 50% were born in the Andean highlands. The most common non-ATL neoplasm was cervical cancer (50%) among females and non-ATL non-Hodgkin lymphoma (26%) among males. With a median follow-up of 66 months, the 5-year OS of HTLV-1 carriers with non-ATL neoplasms (26%- 47% for females and 22%-34% for males) was inferior to those reported in the general population. As expected, patients with ATL had a worse prognosis (5-year OS: 10% for females and 8% for males). **CONCLUSION:** HTLV-1 carriers with cancer were middle age and from underprivileged settings, suggesting an undetected transmission among vulnerable populations, especially females. Survival estimates of HTLV-1 carriers with

non-ATL neoplasms were lower than the regional outcomes. Future research should ascertain how the biology of HTLV-1 and health care disparities affect the outcomes of HTLV-1 carriers, as well as determine the burden of HTLV-1 infection in the cancer population to recommend screening in the outpatient setting of endemic regions.

#### 4. Femicides and Victim's age-Associated Factors in Peru

Femicidios y factores asociados a la edad de las víctimas en el Perú

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**TIPO DE CÁNCER:** Especialidades médicas

**ABSTRACTO:** Background. Femicides are an increasing social problem worldwide. In this study, we aim to describe the trend of femicides in the prepandemic decade and characterize the femicide victims and their perpetrators. Methods. We assessed the trend of femicides in Peru during 2010-2019 and performed a cross-sectional study to analyze the femicides reported in 2019 using open data. Results. We analyzed 166 femicides reported in 24/25 regions of Peru in 2019 and calculated a yearly incidence of 1.01 femicides per 100,000 women. This incidence level represents an increase of 38% compared to the mean annual incidence from 2010 to 2018 (0.74 femicides per 100,000 women). Most femicides occurred in urban areas (64%), through strangling/asphyxiation (25.9%), stabbing (23%), and shooting (16%). Most victims were mothers (61%) 30 years old or over (51%). Most perpetrators have had a partner history with their victims (69%), 30 years old or over (62%), employed (57%), and consumed enablers (51%). Our regression analysis observed that the victim's age was associated with the perpetrator's age and partner history. Conclusions. Femicides are endemic in Peru, and the main characteristics of the victims and their perpetrators offer opportunities for tackling this social problem in Peru and similar low-to middle-income countries.

#### 5. Metastatic pheochromocytoma and paraganglioma: a retrospective multicentre analysis on prognostic and predictive factors to chemotherapy

Feocromocitoma y paraganglioma metastásico: un análisis multicéntrico retrospectivo sobre los factores pronósticos y predictivos de la quimioterapia

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**ABSTRACTO:** Background: Prognostic and predictive markers in metastatic pheochromocytoma and paraganglioma (mPPGL) are unknown. We aimed to evaluate epidemiology of mPPGL, and prognostic factors of overall survival (OS) and predictive markers of treatment duration with first-line chemotherapy (TD1L). Patients and methods: Retrospective multicentre study of adult patients with mPPGL treated in Latin American centres between 1982 and 2021. Results: Fifty-eight patients were included: 53.4% were female, median age at diagnosis of mPPGL was 36 years and 12.1% had a family history of PPGL. The primary site was adrenal, non-adrenal infradiaphragmatic and supradiaphragmatic in 37.9%, 34.5% and 27.6%, respectively. 65.5% had a functioning tumour and 62.1% had metachronous metastases. Positive uptakes were found in 32 (55.2%) 68Gallium positron emission tomography (PET/CT), 27 (46.6%) 2-deoxy-2-[fluorine-18]fluoro-D-glucose PET/CT and 37 (63.8%) of 131Iodine- metaiodobenzylguanidine (MIBG) tests.

Twenty-three (40%) patients received first-line chemotherapy, with cyclophosphamide, vincristine and dacarbazine used in 12 (52%) of patients. At a median follow-up of 62.8 months, median TD1L was 12.8 months. Either functional exams, tumour functionality, pathological characteristics or primary tumour location were significantly associated with response or survival. Yet, negative MIBG, Ki67 $\geq$  10%, infradiaphragmatic location and functional tumours were associated with numerically inferior OS. Conclusions: In patients with mPPGL, prognostic and predictive factors to chemotherapy are still unknown, but negative MIBG uptake, Ki67  $\geq$  10%, infradiaphragmatic location and functional tumours were numerically linked to worse OS. Our results should be further validated in larger and independent cohorts

## 6. First Report of OXA-181-Producing Enterobacterales Isolates in Latin America

Primer reporte de aislamientos de Enterobacterales productores de OXA-181 en América Latina

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**ABSTRACTO:** We characterized five carbapenemase-producing Enterobacterales (CPE) isolates from two health care institutions in Lima, Peru. The isolates were identified as *Klebsiella pneumoniae* (n = 3), *Citrobacter portucalensis* (n = 1), and *Escherichia coli* (n = 1). All were identified as blaOXA-48-like gene carriers using conventional PCR. Whole-genome sequencing found the presence of the blaOXA-181 gene as the only carbapenemase gene in all isolates. Genes associated with resistance to aminoglycosides, quinolones, amphenicols, fosfomycins, macrolides, tetracyclines, sulfonamides, and trimethoprim were also found. The plasmid incompatibility group IncX3 was identified in all genomes in a truncated Tn6361 transposon flanked by  $\Delta$ IS26 insertion sequences. The qnrS1 gene was also found downstream of blaOXA-181, conferring fluoroquinolone resistance to all isolates. CPE isolates harboring blaOXA-like genes are an increasing public health problem in health care settings worldwide. The IncX3 plasmid is involved in the worldwide dissemination of blaOXA-181, and its presence in these CPE isolates suggests the wide dissemination of blaOXA-181 in Peru. **IMPORTANCE** Reports of carbapenemase-producing Enterobacterales (CPE) isolates are increasing worldwide. Accurate detection of the  $\beta$ -lactamase OXA-181 (a variant of OXA-48) is important to initiate therapy and preventive measures in the clinic. OXA-181 has been described in CPE isolates in many countries, often associated with nosocomial outbreaks. However, the circulation of this carbapenemase has yet to be reported in Peru. Here, we report the detection of five multidrug-resistant CPE clinical isolates harboring blaOXA-181 in the IncX3-type plasmid, a potential driver of dissemination in Peru.

## 7. The STOP Program: a Hybrid Smoking Prevention and Cessation Training for Cancer Care Providers in Colombia and Peru

El programa STOP: una capacitación híbrida para la prevención y el abandono del hábito de fumar para proveedores de atención del cáncer en Colombia y Perú

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**ABSTRACTO :**We designed and tested the feasibility of the Smoking Cessation Training Program for Oncology Practice (STOP), a hybrid (face-to-face plus web-based) educational intervention to

enhance Spanish-speaking cancer care professionals' (CCPs') ability to provide brief smoking prevention and cessation counseling to cancer patients and survivors. Changes in the CCPs' competencies (knowledge, attitude, self-efficacy, and practices toward smoking and smoking cessation services) were assessed post-training. Sixty CCPs from one major cancer center in Colombia (n = 30) and Peru (n = 30) were invited to participate in a 4-module hybrid training program on smoking prevention and cessation. Demographic and pre- and post-test evaluation data were collected. The training's acceptability was measured after each module. Bivariate analysis was conducted using Wilcoxon signed-rank test to compare the CCPs' competencies before and after the delivery of the STOP Program. Effect sizes were computed over time to assess the sustainability of the acquired competencies. Twenty-nine CCPs in Colombia and 24 CCPs in Peru completed the STOP Program (96.6% and 80.0% retention rates, respectively). In both countries, 98.2% of the CCPs reported that the overall structure and organization of the program provided an excellent learning experience. The pre-post-test evaluations indicated that the CCPs significantly improved their knowledge, attitude, self-efficacy, and practices toward smoking, smoking prevention, and cessation services. We found that the CCPs' self-efficacy and practices increased over time (1-, 3-, and 6-month assessments after completing the 4 educational modules). The STOP Program was effective and well-received, demonstrating remarkable changes in CCPs' competencies in providing smoking prevention and cessation services to cancer patients.

**8. Effect of Phenylalanine-Arginine Beta-Naphthylamide on the Values of Minimum Inhibitory Concentration of Quinolones and Aminoglycosides in Clinical Isolates of *Acinetobacter baumannii***

Efecto de la fenilalanina-arginina beta-naftilamida sobre los valores de concentración mínima inhibitoria de quinolonas y aminoglucósidos en aislados clínicos de *Acinetobacter baumannii*

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**ABSTRACTO:** Background: *Acinetobacter baumannii* has become the most important pathogen responsible for nosocomial infections in health systems. It expresses several resistance mechanisms, including the production of  $\beta$ -lactamases, changes in the cell membrane, and the expression of efflux pumps. (2) Methods: *A. baumannii* was detected by PCR amplification of the blaOXA-51-like gene. Antimicrobial susceptibility to fluoroquinolones and aminoglycosides was assessed using the broth microdilution technique according to 2018 CLSI guidelines. Efflux pump system activity was assessed by the addition of a phenylalanine-arginine beta-naphthylamide (PA $\beta$ N) inhibitor. (3) Results: A total of nineteen *A. baumannii* clinical isolates were included in the study. In an overall analysis, in the presence of PA $\beta$ N, amikacin susceptibility rates changed from 84.2% to 100%; regarding tobramycin, they changed from 68.4% to 84.2%; for nalidixic acid, they changed from 73.7% to 79.0%; as per ciprofloxacin, they changed from 68.4% to 73.7%; and, for levofloxacin, they stayed as 79.0% in both groups. (4) Conclusions: The addition of PA $\beta$ N demonstrated a decrease in the rates of resistance to antimicrobials from the family of quinolones and aminoglycosides. Efflux pumps play an important role in the emergence of multidrug-resistant *A. baumannii* strains, and their inhibition may be useful as adjunctive therapy against this pathogen.

9. **Deciphering anti-infectious compounds from Peruvian medicinal Cordoncillos extract library through multiplexed assays and chemical profiling**

Descifrando compuestos antiinfecciosos de la biblioteca de extractos de cordoncillos medicinales peruanos a través de ensayos multiplexados y perfiles químicos

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**ABSTRACTO:** High prevalence of parasitic or bacterial infectious diseases in some world areas is due to multiple reasons, including a lack of an appropriate health policy, challenging logistics and poverty. The support to research and development of new medicines to fight infectious diseases is one of the sustainable development goals promoted by World Health Organization (WHO). In this sense, the traditional medicinal knowledge substantiated by ethnopharmacology is a valuable starting point for drug discovery. This work aims at the scientific validation of the traditional use of Piper species ("Cordoncillos") as firsthand anti-infectious medicines. For this purpose, we adapted a computational statistical model to correlate the LCMS chemical profiles of 54 extracts from 19 Piper species to their corresponding anti-infectious assay results based on 37 microbial or parasites strains. We mainly identified two groups of bioactive compounds (called features as they are considered at the analytical level and are not formally isolated). Group 1 is composed of 11 features being highly correlated to an inhibiting activity on 21 bacteria (principally Gram-positive strains), one fungus (*C. albicans*), and one parasite (*Trypanosoma brucei gambiense*). The group 2 is composed of 9 features having a clear selectivity on *Leishmania* (all strains, both axenic and intramacrophagic). Bioactive features in group 1 were identified principally in the extracts of *Piper strigosum* and *P. xanthostachyum*. In group 2, bioactive features were distributed in the extracts of 14 Piper species. This multiplexed approach provided a broad picture of the metabolome as well as a map of compounds putatively associated to bioactivity. To our knowledge, the implementation of this type of metabolomics tools aimed at identifying bioactive compounds has not been used so far.