**Durvalumab versus placebo with chemoradiotherapy for locally advanced cervical cancer (CALLA): a randomised, double-blind, phase 3 trial**

**Abstract**

**Background:**Concurrent chemoradiotherapy has been the standard of care for locally advanced cervical cancer for over 20 years; however, 30-40% of treated patients have recurrence or progression within 5 years. Immune checkpoint inhibition has improved outcomes for patients with PD-L1 positive metastatic or recurrent cervical cancer. We assessed the benefit of adding durvalumab, a PD-L1 antibody, with and following chemoradiotherapy for locally advanced cervical cancer.

**Methods:**The CALLA randomised, double-blind, phase 3 trial included 105 hospitals across 15 countries. Patients aged at least 18 years with previously untreated locally advanced cervical cancer (adenocarcinoma, squamous, or adenosquamous; International Federation of Gynaecology and Obstetrics [FIGO] 2009 stage IB2-IIB lymph node positive, stage ≥III any lymph node status) and WHO or Eastern Cooperative Oncology Group performance status of 0 or 1 were randomly assigned (1:1) through an interactive web response system using a permuted block size of 4 to receive durvalumab (1500 mg intravenously once every 4 weeks) or placebo with and following chemoradiotherapy, for up to 24 cycles. Chemoradiotherapy included 45 Gy external beam radiotherapy at 5 fractions per week concurrent with intravenous cisplatin (40 mg/m2) or carboplatin (area under the concentration-time curve 2) once weekly for 5 weeks, followed by image-guided brachytherapy (high-dose rate, 27·5-30 Gy or low-dose/pulse-dose rate, 35-40 Gy). Randomisation was stratified by disease stage status (FIGO stage and node status) and geographical region. Chemoradiotherapy quality was continuously reviewed. The primary endpoint was progression-free survival, assessed by the investigator using Response Evaluation Criteria in Solid Tumors, version 1.1, in the intention-to-treat population. Safety was assessed in patients who received at least one dose of study treatment. This study is registered with ClinicalTrials.gov.

**Findings:**Between Feb 15, 2019, and Dec 10, 2020, 770 women were randomly assigned (385 to durvalumab and 385 to placebo; median age 49 years [IQR 41-57]). Median follow-up was 18·5 months (IQR 13·2-21·5) in the durvalumab group and 18·4 months (13·2-23·7) in the placebo group. At data cutoff, median progression-free survival had not been reached (95% CI not reached-not reached) for either group (HR 0·84; 95% CI 0·65-1·08; p=0·17); 12-month progression-free survival was 76·0% (71·3-80·0) with durvalumab and 73·3% (68·4-77·5) with placebo. The most frequently reported grade 3-4 adverse events in both groups were anaemia (76 [20%] of 385 in the durvalumab group vs 56 [15%] of 384 in the placebo group) and decreased white blood cells (39 [10%] vs 49 [13%]). Serious adverse events occurred for 106 (28%) patients who received durvalumab and 89 (23%) patients who received placebo. There were five treatment-related deaths in the durvalumab group (one case each of urinary tract infection, blood loss anaemia, and pulmonary embolism related to chemoradiotherapy only; one case of endocrine disorder related to durvalumab only; and one case of sepsis related to both durvalumab and chemoradiotherapy). There was one treatment-related death in the placebo group (pneumonia related to chemoradiotherapy).

**Interpretation:**Durvalumab concurrent with chemoradiotherapy was well tolerated in participants with locally advanced cervical cancer, however it did not significantly improve progression-free survival in a biomarker unselected, all-comers population. Concurrent durvalumab plus chemoradiotherapy warrants further exploration in patients with high tumoral PD-L1 expression. Rigorous monitoring ensured high chemoradiotherapy compliance with advanced technology and allowed patients to receive optimal care.

**Funding:**AstraZeneca.

**Pandrug-resistant *Acinetobacter baumannii* from different clones and regions in Mexico have a similar plasmid carrying the *bla*OXA-72 gene**

**Abstract**

**Background:**Multidrug-resistant *Acinetobacter baumannii* is a common hospital-acquired pathogen. The increase in antibiotic resistance is commonly due to the acquisition of mobile genetic elements carrying antibiotic resistance genes. To comprehend this, we analyzed the resistome and virulome of Mexican *A. baumannii* multidrug-resistant isolates.

**Methods:**Six clinical strains of *A. baumannii* from three Mexican hospitals were sequenced using the Illumina platform, the genomes were assembled with SPAdes and annotated with Prokka. Plasmid SPAdes and MobRecon were used to identify the potential plasmid sequences. Sequence Type (ST) assignation under the MLST Oxford scheme was performed using the PubMLST database. Homologous gene search for known virulent factors was performed using the virulence factor database VFDB and an *in silico* prediction of the resistome was conducted via the ResFinder databases.

**Results:**The six strains studied belong to different STs and clonal complexes (CC): two strains were ST208 and one was ST369; these two STs belong to the same lineage CC92, which is part of the international clone (IC) 2. Another two strains were ST758 and one was ST1054, both STs belonging to the same lineage CC636, which is within IC5. The resistome analysis of the six strains identified between 7 to 14 antibiotic resistance genes to different families of drugs, including beta-lactams, aminoglycosides, fluoroquinolones and carbapenems. We detected between 1 to 4 plasmids per strain with sizes from 1,800 bp to 111,044 bp. Two strains from hospitals in Mexico City and Guadalajara had a plasmid each of 10,012 bp pAba78r and pAba79f, respectively, which contained the *bla* OXA-72 gene. The structure of this plasmid showed the same 13 genes in both strains, but 4 of them were inverted in one of the strains. Finally, the six strains contain 49 identical virulence genes related to immune response evasion, quorum-sensing, and secretion systems, among others.

**Conclusion:**Resistance to carbapenems due to pAba78r and pAba79f plasmids in Aba pandrug-resistant strains from different geographic areas of Mexico and different clones was detected. Our results provide further evidence that plasmids are highly relevant for the horizontal transfer of antibiotic resistance genes between different clones of *A. baumannii.*

**Keywords:**Acinetobacter baumannii; Mexico; blaOXA-72 gene; pandrug-resistant; plasmid.

**External urology consultation quality at a third-level public hospital in Mexico**

[Article in English, Spanish]

**Abstract**

**Introduction:**Patient satisfaction is the degree of conformity with the healthcare they receive. It is real evidence and one of the most important factors in determining the effectiveness and quality of healthcare systems.

**Objective:**To identify the quality of care in the Urology outpatient department of a third-level hospital.

**Materials and methods:**The NHS (National Health Service) 2018 quality of care questionnaire with 11 sections, 133 items, and duration of approximately 25 min was randomly administered to 250 patients attending Urology outpatients at a third-level public hospital in Mexico.

**Results:**According to responses, 92% (n = 230) knew the reason for the consultation. 64.8% (n = 162) had a consultation with the same physician by whom they were initially seen. The longest reported hospital wait time before being seen was more than 2 h in 29.6% (n = 74). As for consultation time, 212 patients responded and the duration was 11-20 min in 52.8% (n = 112). Finally, 33.2% (n = 83) considered the quality of service to be good.

**Conclusions:**The use of the NHS 2018 survey in the Urology service at a third-level public hospital in Mexico is feasible, since we managed to obtain a significant and continuous improvement in all its indicators which is satisfactory for all.

**Keywords:**Calidad asistencial; Clinical research; Consulta externa hospital; Hospital outpatient clinic; Investigación clínica; National Health Service (NHP); National Health Service (NHS); Quality of care; Urologia; Urology.

**Quality of sexual life in Mexican men after spinal cord injury**

**Abstract**

**Objective:**To evaluate the quality of sexual life in men with spinal cord injury.

**Design:**Cross-sectional analytical study.

**Patients:**Males with a history of spinal cord injury who attended an outpatient rehabilitation service.

**Methods:**An analytical study examined adult male patients with complete spinal cord injury in rehabilitation. A modified Sexual Life Quality Questionnaire (SLQQ) examined quality of sexual life, with scores below 50 suggesting significant sexual dysfunction and dissatisfaction. The assessment evaluated age, occupation, marital status, comorbidities, and treatment methods.

**Results:**A total of 80 patients were included; 33 (41%) had a thoracic spinal cord injury, and 47 (59%) had a lumbar spinal cord injury. Thirty-seven patients (46%) were dissatisfied with the quality of their sexual life; 29 patients (88%) with thoracic spinal cord injury and 8 patients (17%) with lumbar spinal cord injury were dissatisfied with the quality of their sexual life (p = 0.001). Patients with higher education level experienced less sexual dissatisfaction (p = 0.03).

**Conclusion:**Human sexuality involves numerous interconnected elements that impact on general health. Sexual pleasure, self-esteem, and personal relationships are crucial for patients with spinal cord injury to identify rehabilitation needs. These results indicate the importance of supporting sexual well-being in recovery. Further studies of sexual enjoyment and quality of life for patients with spinal cord injury are needed, using larger and more diverse populations.

**Obstetric pulmonary embolism and long-term cardiovascular symptoms: a cross-sectional study in Western Mexico**

**Abstract**

**Objectives:**Pulmonary embolism (PE) is an important cause of maternal mortality. There are several guidelines for its diagnosis and management, but there is little information regarding follow-up and frequency of long-term complications. The aim of the study was to determine the frequency of long-term cardiovascular symptoms in patients who had obstetric PE.

**Methods:**Cross-sectional study including patients who had PE during pregnancy or the puerperium. A telephone interview was conducted at least one year after PE, to determine the frequency of cardiovascular symptoms, general health, and COVID-19 infection, considering the study was conducted during the 2020 pandemic.

**Results:**In five years (2015-2019) there were eleven patients with PE, two died during the acute phase, and the rest (nine) were alive and able to answer our interview. Cardiovascular symptoms were common (6, 67 %), the most frequent were fatigue, edema, and mild dyspnea. Four patients (44 %) had slight limitation of physical activity and one (11 %) had PE recurrence. Of the six symptomatic patients four had obesity and one was overweight.

**Conclusions:**There is a high frequency of long-term cardiovascular symptoms in patients who had PE during pregnancy or the puerperium. Stronger evidence is needed to design a long-term care pathway after obstetric PE.

**Keywords:**cardiovascular; obstetric; pregnancy; pulmonary embolism.

**Aberrant B-cell activation and B-cell subpopulations in rheumatoid arthritis: analysis by clinical activity, autoantibody seropositivity, and treatment**

**Abstract**

Few studies analyze the role of B-cell subpopulations in rheumatoid arthritis (RA) pathophysiology. Therefore, this study aimed to analyze the differences in B-cell subpopulations and B-cell activation according to disease activity, RA subtype, and absence of disease-modifying antirheumatic drugs (DMARDs) therapy. These subgroups were compared with control subjects (CS). One hundred and thirty-nine subjects were included, of which 114 were RA patients, and 25 were controls. Patients were divided into 99 with seropositive RA, 6 with seronegative RA, and 9 without DMARDs. The patients with seropositive RA were subclassified based on the DAS28 index. A seven-color multicolor flow cytometry panel was used to identify B-cell immunophenotypes and cell activation markers. There were no changes in total B-cell frequencies between RA patients and controls. However, a lower frequency of memory B cells and pre-plasmablasts was observed in seropositive RA compared to controls (P < 0.0001; P = 0.0043, respectively). In contrast, a higher frequency of mature B cells was observed in RA than in controls (P = 0.0002). Among patients with RA, those with moderate activity had a higher percentage of B cells (P = 0.0021). The CD69+ marker was increased (P < 0.0001) in RA compared to controls, while the CD40+ frequency was decreased in patients (P < 0.0001). Transitional, naïve, and double-negative B-cell subpopulations were higher in seronegative RA than in seropositive (P < 0.01). In conclusion, in seropositive and seronegative RA patients, there are alterations in B-cell activation and B-cell subpopulations, independently of clinical activity and DMARDs therapy.

**Keywords:**B-cell subpopulations; CD40; CD69; DAS-28; rheumatoid arthritis.

**Relationship between lipid profile, anthropometric indicators, and appetite-regulating hormones in infants according to type of feeding**

**Free article**

**Abstract**

in [English,](https://pubmed.ncbi.nlm.nih.gov/37522456/#eng-abstract)[Spanish](https://pubmed.ncbi.nlm.nih.gov/37522456/#spa-abstract)

Background: infants receiving full breastfeeding (FBF) regulate their appetites differently from those receiving human milk substitutes (HMS). In addition, early exposure to the dietary cholesterol in human milk could lead to better cholesterol regulation in later stages of life. Therefore, the purpose was to compare lipid profiles in 4-month-old infants and to correlate lipid profile with anthropometric indicators and appetite-regulating hormones according to the type of feeding. Methods: this was a cross-sectional and correlational study, which included 145 mother-infant dyads according to the type of feeding; 64 received FBF, 47 partial breastfeeding (PBF), and 34 HMS. The complete lipid profile, total ghrelin, leptin, peptide YY, and glucagon-like peptide type 1 were measured. Z-scores for weight/age, length/age, weight/length, triceps (TSF) and subscapular folds (SSF) and body mass index for age were also obtained. Results: there were significant differences in triglycerides and LDL cholesterol according to the type of feeding. In the HMS group, an inverse relationship was observed between ghrelin and triglycerides (p = 0.038), ghrelin and total cholesterol (TC) (p = 0.026), and peptide YY and HDL cholesterol (p = 0.017). In the PBF group, a direct relationship was observed between length/age (z) and triglycerides (p = 0.001) and between subscapular folds and TC (p = 0.049). In infants receiving HMS, a direct correlation was observed between weight/age (z) and TC (p = 0.045) and between length/age (z) and LDL cholesterol (p = 0.010). Conclusion: these findings show a relationship between growth, energy reserve, lipid profile, and modulation of appetite-regulating hormones according to the type of feeding they received.

**Keywords:**Lactantes. Perfil lipídico. Regulación del apetito. Indicadores de crecimiento..

Online ahead of print.

**Decreasing central line-associated bloodstream infections rates in intensive care units in 30 low- and middle-income countries: An INICC approach**

**Abstract**

**Background:**Central line (CL)-associated bloodstream infections (CLABSIs) occurring in the intensive care unit (ICU) are common and associated with a high burden.

**Methods:**We implemented a multidimensional approach, incorporating an 11-element bundle, education, surveillance of CLABSI rates and clinical outcomes, monitoring compliance with bundle components, feedback of CLABSI rates and clinical outcomes, and performance feedback in 316 ICUs across 30 low- and middle-income countries. Our dependent variables were CLABSI per 1,000-CL-days and in-ICU all-cause mortality rates. These variables were measured at baseline and during the intervention, specifically during the second month, third month, 4 to 16 months, and 17 to 29 months. Comparisons were conducted using a two-sample t test. To explore the exposure-outcome relationship, we used a generalized linear mixed model with a Poisson distribution to model the number of CLABSIs.

**Results:**During 1,837,750 patient-days, 283,087 patients, used 1,218,882 CL-days. CLABSI per 1,000 CL-days rates decreased from 15.34 at the baseline period to 7.97 in the 2nd month (relative risk (RR) = 0.52; 95% confidence interval [CI] = 0.48-0.56; P < .001), 5.34 in the 3rd month (RR = 0.35; 95% CI = 0.32-0.38; P < .001), and 2.23 in the 17 to 29 months (RR = 0.15; 95% CI = 0.13-0.17; P < .001). In-ICU all-cause mortality rate decreased from 16.17% at baseline to 13.68% (RR = 0.84; P = .0013) at 17 to 29 months.

**Conclusions:**The implemented approach was effective, and a similar intervention could be applied in other ICUs of low- and middle-income countries to reduce CLABSI and in-ICU all-cause mortality rates.

**Keywords:**Antibiotic resistance; Developing countries; Device-associated infection; Health care–associated infection; Hospital infection; Limited resources countries; Low income countries; Network; Nosocomial infection.

**Role of Silver Nitrate Spray for Skin Wound Care in Patients with Toxic Epidermal Necrolysis: Our Experience in 4 Patients**

**Free PMC article**

**Abstract**

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are examples of severe cutaneous adverse reactions to drugs (SCARs) with several international recommendations for global medical management, ranging from pharmacological systemic therapy to skin wound care. There is no defined best management of the skin wounds in SJS/TEN. The care of wounds is essential to initiate re-epithelialization. Our objective is to improve the cicatrization process, avoiding scarring due to deepening of the wounds, as well as prevent infections, achieve pain control, and avoid loss of serum proteins, fluids, and electrolytes. In this retrospective case series, we highlight the value of systemic therapy and the use of silver nitrate for wound management in four patients with TEN.

**Keywords:**Stevens–Johnson syndrome; silver nitrate; toxic epidermal necrolysis; wound care.

**Assessing the impact of a multidimensional approach and an 8-component bundle in reducing incidences of ventilator-associated pneumonia across 35 countries in Latin America, Asia, the Middle East, and Eastern Europe**

**Abstract**

**Background:**Ventilator associated pneumonia (VAP) occurring in the intensive care unit (ICU) are common, costly, and potentially lethal.

**Methods:**We implemented a multidimensional approach and an 8-component bundle in 374 ICUs across 35 low and middle-income countries (LMICs) from Latin-America, Asia, Eastern-Europe, and the Middle-East, to reduce VAP rates in ICUs. The VAP rate per 1000 mechanical ventilator (MV)-days was measured at baseline and during intervention at the 2nd month, 3rd month, 4-15 month, 16-27 month, and 28-39 month periods.

**Results:**174,987 patients, during 1,201,592 patient-days, used 463,592 MV-days. VAP per 1000 MV-days rates decreased from 28.46 at baseline to 17.58 at the 2nd month (RR = 0.61; 95% CI = 0.58-0.65; P < 0.001); 13.97 at the 3rd month (RR = 0.49; 95% CI = 0.46-0.52; P < 0.001); 14.44 at the 4-15 month (RR = 0.51; 95% CI = 0.48-0.53; P < 0.001); 11.40 at the 16-27 month (RR = 0.41; 95% CI = 0.38-0.42; P < 0.001), and to 9.68 at the 28-39 month (RR = 0.34; 95% CI = 0.32-0.36; P < 0.001). The multilevel Poisson regression model showed a continuous significant decrease in incidence rate ratios, reaching 0.39 (p < 0.0001) during the 28th to 39th months after implementation of the intervention.

**Conclusions:**This intervention resulted in a significant VAP rate reduction by 66% that was maintained throughout the 39-month period.

**Keywords:**Developing countries; Device-associated infection; Healthcare-associated infection; Hospital infection; Limited resources countries; Low-income countries; Network; Nosocomial infection; Ventilator-associated pneumonia.