PRM11

TRENDS OF RESEARCH RELATED BRAZIL PUBLISHED IN ISPOR MEETINGS: A BIBLIOMETRIC ANALYSIS FROM 1998 TO 2014

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OBJECTIVES: Health economics and outcomes evaluations has become an indispensable tool to guide decision-making processes regarding incorporation of new technologies. Since 2009, with the publication of methodological guidelines by REBRATS, followed by creation of the National Committee for Health Technology Incorporation (CONITEC), in 2011, health economics research are emerging in Brazil. Therefore, the aim of this study is to evaluate temporal trends and main areas of interest in scientific production in these fields by a bibliometric analysis. **METHODS:** A search in the ISPOR Scientific Presentations Database was performed, using the term "Brazil" as keyword search in "Abstract" field, evaluating all results between 1998 and 2014. Abstracts were classified according to study characteristics (topic and subtopic), sponsorship and disease area. **RESULTS:** Among the total of 29,759 abstracts available in ISPOR presentation database, only 716 (2.4%) mentioned the term "Brazil" in the abstract, of which 169 (23.6%) the first author was not from Brazil and 325 studies (45%) were sponsored by pharmaceutical companies. Up to 2006, scarce publications were found. The majority of the studies (62.6%) was published from 2012 to 2014. The most studied diseases were cancer (16.9%), infection (5.9%), GI disorders (3.9%) and diabetes (3.1%) and 14.5% classified as "no specific disease". In addition, 57.3% of the analyses were classified as "cost studies" and 24.1% as "Health care use & policy studies". According to the subtopic, 140 (19.6%) were cost-effectiveness analysis and 73 (10.2%) budget impact analysis. **CONCLUSIONS:** This analysis showed a low rate of publication related to Brazil. On the other hand, the increasing number of published studies from 2012 may be related to CONITEC foundation. Thus, the rising number of studies observed over this period indicates an increase in importance of health economics as a support for health polices development and decision making process

PRM12

TABAGISMO EM UNIVERSITÁRIOS: UMA REVISÃO SISTEMÁTICA DA LITERATURA

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OBJETIVOS: caracterizar a prevalência e o consumo de tabaco em universitários a partir de uma revisão sistemática da literatura, no período de 2003 a 2013. **MÉTODOS:** A busca de artigos publicados foi feita nas bases de dados eletrônicas LILACS; MEDLINE e SCIELO com os descritores tabagismo e universitários. A metodologia PRISMA -Preferred Reporting Items for Systematic Reviews and Meta-Analyses- para trabalhos de revisão sistemática foi usada na pesquisa. Na análise quantitativa dos dados coletados aplicou-se a distribuição de frequência simples, relativa e cálculo de média e na qualitativa, o critério de categorização. **RESULTADOS:** De 316 artigos encontrados, 62 foram incluídos por preencherem os critérios de inclusão. Deste total, a maioria foi publicada em espanhol (46,77%) e português (41,94%). Houve forte concentração de publicações nos anos de 2009 (19,35%), 2011 (22,58%) e 2012 (17,74%). A distribuição das publicações quanto áreas das revistas, em termos nacionais, mostrou que a saúde geral e a medicina tiveram maior número de publicações (19,35% para cada uma), seguida da enfermagem (14,51%). Para as revistas internacionais, a área de medicina se destacou em 19,35%, ficando a saúde geral com 12,90%. Sete eixos temáticos principais foram identificados, os quais foram distintos em termos de metodologia, mas estavam inter-relacionados sobre os aspectos: tabagismo e universitários da área da saúde (9); tabagismo e universitários de diversos cursos superiores (7); universitários, tabaco e outras drogas ilícitas (10); fatores que influenciavam o consumo tabágico em universitários (20); tabagismo e atividade física em universitários (6); universitários e medidas educativas sobre tabagismo (6) e malefícios do tabagismo em universitários (4). **CONCLUSÕES:** o tabagismo é um tema atual e relevante, pois apresentou um alto número de artigos publicados nos últimos anos; entretanto, estas publicações relatam divergências entre a prevalência e o consumo de produtos derivados do tabaco por universitários.

RESEARCH ON METHODS – Modeling Methods

PRM13

PERFIL DEL GASTO DE BOLSILLO EN MEDICAMENTOS ESENCIALES EN PANAMÁ, 2014

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OBJETIVOS: Obtener los perfiles socioeconómicos que caracterizan el acceso a los medicamentos, con base en el poder adquisitivo, disponibilidad y uso racional. **METODOLOGÍAS:** Diseño muestral estratificado, con selección aleatoria en 6 dominios en el ámbito nacional, cubriendo zonas urbanas, rurales e indígenas. Encuesta multipropósito de línea de base. La muestra fue de 2,696 individuos de 15 años y más. El instrumento recogió información sobre las características socioeconómicas, condiciones de salud, gasto, financiación, acceso, disponibilidad y uso racional de los medicamentos. El análisis estadístico, se realizó con el software SPSS 20.0. **RESULTADOS:** Las comarcas indígenas son las más pobres según la distribución del ingreso en el primer quintil, 41.9% en la Ngäbe Buglé y 62.7% en Madugandí. Las enfermedades crónicas (circulatorias y diabetes) y las infecciosas (diarrea, infecciones generales y malestar estomacal), son las principales morbilidades. El gasto promedio general fue USD 83.25, siendo en diabetes USD 96.81 en las diarreas, infecciones y malestar estomacal con USD 96.80. El 43.3% financia parcialmente la compra con sus ingresos y 13.0% no cuenta con los mismos, 50% de los medicamentos estuvieron disponibles y 61% declaró que el precio es inaccesible. Mientras tanto, 29% consume medicamentos sin receta, siendo mayor en las comarcas Ngäbe Buglé con 59% y Madugandí con 35%. La elasticidad ingreso resultó de 0.20 (t=2.577, p=0.01) indicando que los medicamentos son productos necesarios, con relación a la edad, por cada año adicional, el gasto en medicamentos

se incrementa en 2%(t=3.779, p=0.000). Respecto a la tenencia de seguro social la probabilidad de comprar medicamentos se reduce en -0.201 o un riesgo relativo de compra de 0.818 (Wald=4.241, p=0.039). **CONCLUSIONES:** Existe una mayor vulnerabilidad de la población indígena, respecto al acceso a medicamentos. Se hace necesario desarrollar estrategias e intervenciones sanitarias para mejorar el acceso, disponibilidad y costo de medicamentos en Panamá.

PRM14

CALIBRATION OF PIECEWISE MARKOV MODELS USING A CHANGE-POINT ANALYSIS THROUGH AN ITERATIVE CONVEX OPTIMIZATION ALGORITHM

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OBJECTIVES: Relative survival represents cancer survival in the absence of other causes of death. Cancer Markov models often have a distant metastasis state, a state not directly observed, from which cancer deaths are presumed to occur. The aim of this research is to use a novel approach to calibrate the transition probabilities to and from an unobserved state of a Markov model to fit a relative survival curve. **METHODS:** We modeled relative survival for newly diagnosed cancer patients through a piecewise Markov model. For each segment we used a constant transition matrix with three cancer states: 1) no evidence of disease, 2) metastatic recurrence and 3) cancer death. We estimated the optimal time points at which the slope of the cumulative hazard changes using a free-knot spline model. We calibrated the transition probabilities using a two-step iterative convex optimization (TICO) algorithm. The dynamics of the disease can be defined as $x_{t+1} = x_t A$, where x_{t+1} is the state vector that results from the transformation given by the monthly transition matrix A. A is a piecewise block-diagonal matrix that includes a block-diagonal matrix (i.e. A1, A2, A3) in each segment. **RESULTS:** We applied our method to model relative survival for stage 3 colorectal cancer patients 75 years old and younger. The estimated change points were at months 9 and 37. We compared our piecewise calibration method to a single-segment Markov model. While the single-segment converged faster, the piecewise method improved the goodness of fit by 50%. **CONCLUSIONS:** By estimating the change points in the relative survival we were able to find the optimal transition probabilities for a piecewise Markov model. This model allowed us to impose a particular structure defined by the progression of the disease. We propose a piecewise calibration method that produces more accurate solutions compared to a single-segment approach.

RESEARCH ON METHODS – Statistical Methods

PRM15

APPLIED COMPARISON OF META-ANALYSIS TECHNIQUES

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OBJECTIVES: Meta-analysis is an approach that combines findings from similar studies. The aggregation of study level data can provide precise estimates for outcomes of interest, allow for unique treatment comparisons, and explain the differences arising from conflicting study results. Proper meta-analysis includes five basic steps: identify relevant studies; extract summary data from each paper; compute study effect sizes, perform statistical analysis; and interpret and report the results. This study aimed to review meta-analysis methods and their assumptions, apply various meta-techniques to empirical data, and compare the results from each method. **METHODS:** Three different meta-analysis techniques were applied to a dataset looking at the effects of the bacille Calmette-Guerin (BCG) vaccine on tuberculosis (TB). First, a fixed-effects model was applied; then a random-effects model; and third meta-regression with study-level covariates were added to the model. Overall and stratified results, by geographic latitude were reported. **RESULTS:** All three techniques showed statistically significant effects from the vaccination. However, once covariates were added, efficacy diminished. Independent variables, such as the latitude of the location in which the study was performed, appeared to be partially driving the results. **CONCLUSIONS:** Meta-analysis is useful for drawing general conclusions from a variety of studies. However, proper study and model selection are important to ensure the correct interpretation of results. Basic meta-analysis models are fixed-effects, random-effects and meta-regression.

RESEARCH ON METHODS – Study Design

PRM16

CHOLIC ACID DECREASES THE DISTRIBUTION COEFFICIENT OF SIMVASTASTIN: A POTENTIAL FOR INCREASING SIMVASTATIN BIOAVAILABILITY

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OBJECTIVES: Distribution coefficient is used as a quantitative measure for assessing a drug molecule affinity for the biological membranes. Since bile acids are known for their function as modifiers of drug penetration across biological membranes, the aim of this study was to estimate the influence of cholic acid (CA) on the distribution coefficient of simvastatin (SV) which is a highly lipophilic compound with extremely low water-solubility and bioavailability. **METHODS:** Distribution coefficients and logD of SV with or without CA were measured by shake-flask method in n-octanol/buffer systems at pH 5 and pH 7.4. SV concentrations in aqueous phase were determined by HPLC-DAD. In order to analyse theoretically complexation of SV with CA, semi-empirical PM3 method implemented in MOPAC software package in the Chem3D Ultra program has been applied. **RESULTS:** Upon addition of CA, statistically significant decrease of SV logD was observed at both selected pH values (from 4.70±0.01 to 4.41±0.13 at pH 5, and from 4.59±0.06 to 4.40±0.04 at pH 7.4). Analysing the molecular aggregates of SV with CA, it was observed that CA is

bonded to SV by hydrophobic interactions, while OH groups are oriented towards the outer side of the aggregate. Hence, the formed aggregate is more hydrophilic than SV molecule alone. **CONCLUSIONS:** Our data indicate that CA decreases the values of SV distribution coefficient. This may be the result of the formation of hydrophilic complexes increasing the solubility of SV that could consequently lead to the increase of SV bioavailability. In order to confirm these results, further in vivo investigations of their interactions at molecular level need to be undertaken. Acknowledgement: This work is supported by Ministry of Education, Science and Technological Development of Serbia, Project III41012.

PRM17
COMPARISON OF CHRONIC HEPATITIS C TREATMENT EFFICACY IN RANDOMIZED CONTROLLED TRIALS AND REAL-LIFE STUDIES - INFLUENCE OF STUDY DESIGN IN THE SUSTAINED VIROLOGICAL RESPONSE: A SYSTEMATIC REVIEW OF PUBLISHED LITERATURE

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OBJECTIVES: To assess whether hepatitis C treatment outcome was similar among different study designs. **METHODS:** Two independent reviewers conducted a double-screened systematic review on hepatitis C treatment. Studies were categorized under study design: randomized controled trials (RCT), pragmatic trials (PRG) and registries; and treatment course: pegylated interferon and ribavirin (IR), IR and boceprevir (BCP), IR and telaprevir (TLP). 3,713 abstracts were retrieved, and 253 studies were included according to previously selected criteria, comprising 77,042 patients. Sustained virological response (SVR) was stablished as treatment end-point. Mann-Whitney-U and Kruskall-Wallis tests were used with a 95% CI. **RESULTS:** In the IR group, registries had a lower SVR than PRG (P=0.039) and than RCT (P=0,3368). RCT had a worse outcome than PRG (P=0.283). Statistical difference was seen among the three BCP groups (P=0.040), and RCT had a higher SVR than registries (P=0.028). BCP PRG group couldn't be analysed in comparison to other study designs due to a very small group. PRG (SVR=80.13%) had a better outcome than RCT (SVR=75.00%) and than registries (SVR=62.00%), but tests have shown no statistical significance among study designs (P>0.05). **CONCLUSIONS:** It's possible to design close to the real-life settings RCT. Though it's not a rule, each drug should be studied separately and its clinical scenario considered. PRG might be not as pragmatic as they claim to be, as their results were more similar to RCT than to registries. Further analysis should assess whether PRG are fully bridging RCT's gap to the real-life settings, as they are intent to be the main guide to drug's embodiment to the clinical practice. Also, boceprevir was less studied than telaprevir, and whether remains unclear which drug is more effective, new data could answer that, specially a large proportions head-to-head RCT comparing both drugs. Although, as of new and better treatment courses are approved, this RCT most probably will not be done.

RESEARCH ON METHODS – Conceptual Papers

PRM18
ENGAGING HISPANIC CAREGIVERS IN RESEARCH: A FRAMEWORK TO DESIGN CULTURALLY SENSITIVE APPROACHES FOR ENGAGEMENT IN PATIENT-CENTERED OUTCOMES RESEARCH

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The Latin American perspective on caregivers' preferences is underrepresented in research largely due to lack of culturally sensitive approaches to enhance research literacy. Identification of the most effective engagement strategies is needed so that patient centered outcomes research (PCOR) can address the needs and priorities of caregivers of Latin American origin. Our objectives were to develop a methodological framework for engaging caregivers of Latin American origin in research and to improve PCOR literacy in this population. The 'pre-engagement' framework with hard-to-reach patients was used in a study designed to identify caregivers' priorities for treatment and outcomes in children of Hispanic origin living in the U.S. with complex mental health conditions. Based on the principles of community based participatory research, the pre-engagement implementation phases were: 1. Identify Hispanic community leaders with common goals; 2. Partner with leaders to select key topics of interest; 3. Design culturally appropriate strategies; 4. Implement pre-engagement strategies. During phase 1, academic partnerships were developed with community leaders to allow integration into the research process. Community needs and practical challenges to engage caregivers and the strategies to overcome barriers were identified during phase 2. In phase 3, a series of four workshops, delivered in Spanish, were designed as interactive activities each addressing a unique challenge: understanding the caregiver's perspective, understanding the child's perspective, providing behavior management strategies, and discussing community resources for families. Each workshop emphasized research literacy by linking the benefit of research in advancing the challenge being discussed. An outcome of this work will be a caregiver resource guide in Spanish, developed by Hispanic community leaders, for distribution in their communities. In the absence of culturally appropriate tools to address health and medical preferences of non-English speaking communities, this framework can be used to engage caregivers and communities in patient-centered research.

PRM19
O MÉTODO PARACONSISTENTE COMO SUPORTE ÀS TOMADAS DE DECISÃO EM SAÚDE

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INTRODUÇÃO: O presente estudo objetiva apresentar a Lógica Paraconsistente Anotada Evidencial (LPAE), que é a base teórica para o modelo proposto de suporte às tomadas de decisão em saúde. **DESENVOLVIMENTO:** A Lógica Paraconsistente é uma opção metodológica que permite manipular dados imprecisos, inconsistentes e paracompletos. A aplicação do método consiste basicamente de oito etapas: 1-fixar o nível de exigência da decisão que se pretende tomar; 2-selecionar os fatores mais importantes e de maior influência na decisão; 3-estabelecer as seções para cada um dos fatores; 4-construir a base de dados que é constituída pelos pesos atribuídos aos fatores e pelos valores de evidência favorável e de evidência contrária atribuídos a cada um dos fatores em cada uma das seções (os pesos e os valores das evidências são atribuídos por especialistas selecionados para o estudo); 5-fazer a pesquisa de campo para verificar, no caso em análise, em que seção (condição) cada um dos fatores se encontra; 6-obter o valor da evidência favorável e o valor da evidência contrária resultantes para cada um dos fatores escolhidos, por meio da aplicação das técnicas de maximização e minimização da LPAE; 7- obter o grau de evidência favorável e o grau de evidência contrária do baricentro dos pontos que representam os fatores escolhidos no reticulado paraconsistente; 8-tomar a decisão, aplicando-se a regra de decisão ou algoritmo para-analisador. **CONCLUSÃO:** Em situações em que a tomada de decisão precisa ser realizada em curto período de tempo, transferir e adaptar avaliações econômicas realizadas em outros contextos pode ser uma necessidade considerável. O método paraconsistente pode contribuir nesse processo, apoiando o trabalho das comissões hospitalares de avaliação e incorporação de tecnologias em saúde.

DISEASE – SPECIFIC STUDIES

CANCER – Clinical Outcomes Studies

PCN1
PHARMACOVIGILANCE IN ONCOLOGY: KNOWLEDGE AND PERCEPTION ON ADVERSE EVENTS REPORTING IN BRAZIL

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OBJECTIVES: Pharmacovigilance represents an important tool to support the maintenance of drug safety through evaluation of spontaneous adverse events (AE) reporting. AEs represent one important cause of morbidity and mortality worldwide when not managed correctly, being very frequent, especially during oncology treatments. However, underreported phenomenon occurs often due inefficient spontaneous reporting by patients, physicians and caregivers. Therefore, the aim of this survey was to evaluate the knowledge and perception related to pharmacovigilance in Brazil. **METHODS:** From February to March 2015, 260 respondents answered an internet-based survey related to knowledge on pharmacovigilance from Oncoguia Institute, an independent nonprofit cancer advocacy institution. Descriptive analyses were performed according to answers frequency. **RESULTS:** Among the respondents, 70.8% were diagnosed with cancer, of which breast cancer was the most frequent (58%) followed by colorectal cancer (4%). Reported treatment included chemotherapy (96%), surgery (84%), 48% radiotherapy (48%). Of all, 46% and 44% were treated by public and private health insurance, respectively. Most of the respondents were not aware of the importance of a pharmacovigilance AE report (52%). In fact, 21% of the respondents were not aware of what AEs are. In 66% of the cases, physicians have described the main AE expected to the prescribed treatment. Respondents reported nausea (80%), hair loss (77%), weight gain (49%) and vomiting (45%) as the most common AEs. Only 7% and 4% of the respondents were aware that AEs could be reported to pharmaceutical industry and ANVISA, respectively. **CONCLUSIONS:** This survey demonstrates that knowledge and perception regarding AEs, such as definition, importance and how to proceed in case of having one, including the importance of pharmacovigilance system, are very reduced among common public, including cancer patients. Therefore, there is an enormous need for educational intervention regarding AEs reporting importance in general public, patients and physicians, especially in oncology.

PCN2
EFICACIA Y SEGURIDAD DEL USO DEL CETUXIMAB EN PACIENTES CON CANCER COLORRECTAL METASTÁSICO

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OBJECTIVOS: Determinar la eficacia y seguridad de Cetuximab solo o asociado a otros fármacos en el tratamiento del cáncer colo-rectal metastásico comparado a los tratamientos actualmente disponibles **METODOLOGÍAS:** Se realizó una búsqueda bibliográfica de revisiones sistemáticas y Ensayos Clínicos Aleatorizados (ECAS) en bases electrónicas Cochrane, Pubmed y Lilacs, que comparan ramas de tratamiento con y sin Cetuximab **RESULTADOS:** Se seleccionaron 2 revisiones sistemáticas y 8 ECAS. Los resultados para los puntos finales de eficacia y seguridad en la población general fueron: Sobrevida Global (SG) HR 0,97 [0,89-1,05], Sobrevida Libre de Progresión (SLP) HR 0,84 [0,70-0,98], eventos adversos (EA) grado 3-4 HR 2,15 [1,88-2,45] y reacciones de piel 44,5 [22,1-89,5]. En la población KRAS wild la SG fue HR 0,796 IC95% [0,670-0,946] en el estudio de Van Cutsem, HR, 0,855 IC95% [0,599-1,219] en el estudio de Bokemeyer, 1,04 IC95% [0,87-1,23] en el estudio de Maughan y HR 0,55 IC95% [0,41-0,74] en el estudio de Jonker. Para la SLP en población KRAS wild los resultados fueron HR 0,57 IC95% [0,38-0,86] en el estudio de Bokemeyer, HR 0,40 IC95% [0,30-0,53] en el estudio de Jonker, HR 0,96 IC96% [0,82-1,12] en el estudio de Maughan y HR 0,70 IC95% [0,56-0,87] en el estudio de Van Cutsem **CONCLUSIONES:** Los resultados analizados muestran un incremento en la SG en pacientes con KRAS wild y de la SLP. También se constata un incremento en la ocurrencia de EA graves. Considerando los resultados de eficacia y seguridad para Cetuximab, se recomienda realizar un estudio de costo-efectividad para decidir su posible inclusión en el FTM. En este sentido, no debe darse por concluida la evaluación hasta contar con dicha información.