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ABSTRACTS

RESEARCH PODIUM PRESENTATIONS

PODIUM SESSION I: CANCER OUTCOMES RESEARCH STUDIES

CA1

BREAST CANCER PATIENTS RECEIVING GUIDELINE-CONCORDANT ADJUVANT THERAPY REGIMENS HAVE BETTER ALL-CAUSE AND DISEASE-SPECIFIC SURVIVAL: NEW FINDINGS FROM RURAL GEORGIA

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OBJECTIVES: To examine whether receipt of chemo-, radiation, and hormonal therapy regimens that are jointly guideline concordant improve survival outcomes among women diagnosed with breast cancer in a rural region of the United States. **METHODS:** All women identified by the state cancer registry residing in rural southwest Georgia diagnosed with early stage breast cancer during 2001-2003 were included. Medical chart abstraction and state registry data were used to determine treatment concordance with guidelines established by the 2000 NIH consensus development conference on breast cancer treatment. Patients were Concordant versus Non-Concordant according to whether their receipt (or non-receipt) of each adjuvant therapy type was according to guidelines. To examine the effects of concordance on all-cause and breast cancer-specific survival, Cox models were developed that used both propensity score (PS) weighting and 2-stage residual inclusion (2SRI) instrumental variable techniques to adjust for patient selection effects. **RESULTS:** In all-cause analyses, Concordance versus Non-Concordance was associated with significantly better survival (hazard ratios (HRs) 0.41 (95% CI: 0.24-0.72) to 0.54 (95% CI: 0.33-0.87). Similar findings emerged in breast cancer-specific survival analyses, with HRs significantly less than 1.0 in most cases. Diagnosis at older age or later disease stage strongly predicted poorer survival outcome; being not married was significant in all-cause but not breast cancer-specific models. Survival was not generally associated with surgical treatment delay, insurance status, socioeconomic status, rural/urban status, comorbidities, tumor grade, or hormonal status. HR for black women versus white was greater than 1.0 across models but never significant (p=0.05). **CONCLUSIONS:** Breast cancer patients in rural Georgia who received guideline-concordant adjuvant therapy had significantly better all-cause and breast cancer-specific survival, based on Cox model analyses that attempted to control for multiple clinical and demographic factors, as well as selection effects. These findings extend the evidence that guideline bundles of care improve outcomes.

CA2

EVALUATION OF SURVIVAL OUTCOMES IN SELECT FIRST-LINE TREATMENT REGIMENS FOR ADVANCED NONSQUAMOUS NON-SMALL CELL LUNG CANCER PATIENTS

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OBJECTIVES: Evidence from clinical trials supports the use of platinum agents in combination with pemetrexed or paclitaxel plus bevacizumab as first-line treatments of nonsquamous non-small cell lung cancer (NSCLC). This retrospective study was performed to evaluate survival outcomes of these select first-line treatments in a real-world clinical setting. **METHODS:** Patients with advanced (Stage IIIB/IV) nonsquamous NSCLC who initiated treatment with pemetrexed/platinum (Pem/Plat [n=122]), carboplatin/paclitaxel+bevacizumab (C/Pac+Bev [n=440]), or carboplatin/paclitaxel (C/Pac [n=989]) from July 2006 to January 2010 were identified in the McKesson Specialty Health iKnowMed electronic health record database of US Oncology community practices. Patients were followed for at least one year or last available data stream to assess progression or death. Overall survival (OS) and progression-free survival (PFS) were calculated from treatment initiation to earliest of the following: progression (as defined by escalation in line of therapy), death, or end of study. Association between treatment and OS/PFS was assessed by using Kaplan-Meier and Cox regression analyses adjusting for age, gender, stage at diagnosis, Eastern Cooperative Oncology Group performance status, and comorbidity index. **RESULTS:** Patients treated with Pem/Plat had a median OS of 476 days compared to 348 days for C/Pac+Bev patients (adjusted hazard ratio [adj HR]: 0.81, p=0.156) and 280 days for C/Pac patients (adj HR: 0.70, p=0.012). Pem/Plat patients had a median PFS of 187 days compared to 225 days for C/Pac+Bev patients (adj HR: 0.86, p=0.224) and 170 days for C/Pac patients (adj HR: 0.78, p=0.038). **CONCLUSIONS:** HRs for OS and PFS, which controlled for possible confounding factors, were significantly improved for patients treated with Pem/Plat compared to C/Pac. For Pem/Plat compared to C/Pac+Bev, the HRs for both OS and PFS were not statistically significant at this sample size.

CA3

TREATMENT PATTERNS AFTER CASTRATION RESISTANT PROSTATE CANCER (CRPC) DIAGNOSIS: A EUROPEAN PHYSICIAN SURVEY

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OBJECTIVES: Treatment for CRPC has evolved rapidly with new drug approvals. However, few studies have evaluated recent treatment patterns. Our objective was to describe treatment sequences after CRPC diagnosis in EU-5 countries (UK, Germany, Spain, Italy, France). **METHODS:** This study used IMS Oncology Analyzer, a proprietary database of patient chart abstractions, collected through a quarterly physician panel survey. The data includes the history of the patient's cancer from diagnosis and treatment choices.. The most recent panels of data (July 2011 - June 2012) were used to identify patients with physician-defined CRPC and to describe treatments initiated after CRPC diagnosis. **RESULTS:** Of 4479 prostate cancer patients, 624 patients had CRPC defined by the physicians (32% UK, 21% Germany, 18% Spain, 15% Italy, 14% France). A total of 76.4% of patients were >65y. A total of 57.7% were diagnosed with CRPC within the past year; 90.1% had metastases, mostly bone (80.4%). After CRPC diagnosis, 50.5% of patients (n=280) had docetaxel-alone specified as first therapy, of which 34.6% had a second treatment specified [52.5% chemotherapy, 40.2% androgen deprivation therapy (ADT) only]. Median time on first docetaxel therapy was 181 days; median number of cycles was five. A total of 24.5% of CRPC patients (n=136) continued with only single-agent ADT as first therapy, of which 53.7% had a second treatment specified [56.2% chemotherapy; 39.7% ADT; 2.7% combined chemo-ADT]. A total of 16.0% of CRPC patients had multiple-agent ADT specified as first therapy after CRPC diagnosis, and 3.4% had combined chemo-ADT. Of the 502 CRPC patients with bone metastases, 34.1% received zoledronic acid and 16.5% radiotherapy after their diagnosis of CRPC. **CONCLUSIONS:** Docetaxel was the most common first treatment after CRPC diagnosis, followed by continued ADT. Few physicians specified combined chemotherapy with ADT. Low rates of initiation of zoledronic acid in patients with bone metastases warrants study on alternative timing and choices.

CA4

THE USE OF TRANSARTERIAL CHEMOEMBOLIZATION FOR TREATING HEPATOCELLULAR CARCINOMA IN THE SEER-MEDICARE POPULATION

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OBJECTIVES: Transarterial chemoembolization (TACE) is a first-line therapy to treat hepatocellular carcinoma (HCC). Repeated TACE treatments are common. TACE is often used as a bridge-therapy to surgery or to treat tumor recurrence, and TACE-Sorafenib combination therapy is a promising new therapeutic approach based on synergistic properties. We explore historical patterns of TACE use to inform future evaluations of the effectiveness of TACE as it is utilized in a transformative therapeutic landscape for HCC. **METHODS:** Medicare enrollees with an initial diagnosis of primary HCC between 2000-2007, followed through 2009. Data are from the SEER and linked Medicare databases, with claims generated from Parts A and B. We describe rates of TACE use before and after transplant, resection, and ablation in the follow-up period. Among non-transplant/non-resection patients, we describe rates of multiple TACE treatments and use Kaplan-Meier analysis to examine mean weeks between HCC diagnosis, first TACE, repeated TACE, and death. **RESULTS:** There were 11,047 HCC patients. Among 411 transplants, 29%/3% received TACE before/after transplant. Among 851 resections, 2%/11% received TACE before/after resection. Among 1116 ablations, 17%/19% received TACE before/after ablation. Among 1228 non-transplant/non-resection patients who received TACE, 57%, 24%, 11%, and 8% received 1, 2, 3, and 4+ TACE treatments, respectively; on average, TACE was discontinued after 35, 53, 95, and 125 weeks, and mean weeks survived post-discontinuation was 64, 61, 59, and 50 weeks, respectively. **CONCLUSIONS:** With transplantation, TACE has been more often used as a bridge-therapy; with resection, more often to treat non-optimal tumor response. TACE is frequently used concomitantly with ablation. Intent to treat first-line TACE patients with

multiple courses of TACE is difficult to ascertain since additional courses may be prescribed under a patient-specific treatment protocol or due to non-optimal tumor response. Nonetheless, mean survival after discontinuing TACE was relatively similar regardless of number of treatments received.

PODIUM SESSION I: CONCEPTUAL PAPERS

CP1

ADJUSTING FOR INFLATION IN ECONOMIC EVALUATIONS OF HEALTH TECHNOLOGIES: ARE WE DOING IT WRONG?

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OBJECTIVES: Economic evaluations of health technologies typically require consideration of costs incurred in future years. Conventionally, all costs are represented in 'real terms' by adjusting for inflation. Future costs are then discounted to account for time preference. Although much has been written on the practice of discounting, health economists have paid surprisingly little attention to the issue of appropriately adjusting for inflation. This paper argues that the conventional approach to adjusting for inflation in economic evaluations of health technologies is inappropriate. **METHODS** & **RESULTS:** The conventional approach follows the recommendations of the Washington Panel: costs must be converted to "constant dollars" using a single inflation rate representing the rate of "general price inflation". However, "if the prices of the goods in question change at a rate different from general price levels, this variation should be reflected in the adjustment used". Some analyses therefore use the 'Medical Component' of the Consumer Price Index (CPI), or an equivalent measure, rather than the headline rate. Critically, for the conventional approach to be appropriate requires that all costs change at the same rate over time. This is generally not the case – some costs may rise (e.g. pharmaceuticals) at the same time as other costs fall (e.g. personal computers). In particular, products losing patent protection may experience a sudden fall in price out-of-line with general price inflation. A solution is to assign each cost a unique time profile subject to specific market conditions. Rather than applying an inflation rate, future costs are instead estimated using a unique projection model for each cost. **CONCLUSIONS:** The conventional approach to adjusting for inflation is inappropriate. A solution is to estimate a unique time profile for each cost component. Models routinely used by financial analysts may provide an example for how this projection can be done in practice.

CP2

THE NOTION OF REPRESENTATIVE LANGUAGES IN THE CONTEXT OF TRANSLATABILITY ASSESSMENT

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BACKGROUND: While current best-practices in PRO development include evaluation of the relative ease of translation for global trial use prior to instrument finalization, methodologies for this translatability assessment (TA) vary greatly. In the proposed approach, representative languages (RLs) are selected to assess the translation difficulty of PRO concepts without the time and cost of evaluating multiple languages with shared characteristics. **METHODS:** In the genealogical approach employed by linguists, languages sharing a common ancestor that become separated by geographical or socio-political boundaries will evolve in distinct ways, resulting in sets of languages (families) with common linguistic features (e.g. word order, phrasal structure, morphology, lexical items, etc.). Because of this relative similarity within language groups, efficiency can be gained by assessing translatability with sets of appropriately-selected representative languages, which can in turn predict translation problems likely to affect others in their linguistic families. As such, use of appropriate criteria for the selection the RLs is of key importance. **RESULTS:** Selection of RLs should be based both on linguistic properties and other features salient to outcomes research. A family or group of languages may also be defined by shared characteristics that are not purely linguistic in nature. Features such as geographic and cultural (religious/dietary/social) aspects, number and distribution of speakers worldwide, and criteria related to health care utilization or study implementation should be considered in the definition of language families/groups and in the selection of RLs. **CONCLUSIONS:** Despite differences that undeniably exist between individual languages, limited information can be gained by the repetitive assessment of prospective translation difficulty within groups of languages having similar characteristics. Instead, the use of a representative language to assess translation difficulty for a related group of languages provides greater resource efficiency and more effective application of TA in providing important feedback prior to finalization of newly developed measures.

CP3

PIECEWISE MODELING OF TIME-TO-EVENT DATA WITH FLEXIBLE PARAMETERIZATION OF COVARIATES AND EFFECTS

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Projection of time-to-event distributions is necessary to obtain accurate estimation of life expectancy, or prediction of event times for economic models. Parametric survival analysis techniques are typically used, and can represent a broad range of shapes. In some cases, however, the best distributional fit fails to capture the variation in hazards over the entire time span, or it provides acceptable fit to the data but yields clinically implausible projections (e.g., constant hazard of death). More flexible techniques, like piecewise exponential models, can overcome these issues but remain generally underused. In piecewise models, the time axis is divided into contiguous segments with a common parametric distribution assumed within each segment, but values of the parameters are allowed to vary. In addition to greater flexibility, this framework allows inclusion of time-dependent predictors and/or time-dependent effects. Two important considerations are the number and placement of divisions on the time axis, and the choice of the common distribution. Examination of the cumulative and log-cumulative hazards plots can assist with these issues. For instance, the number/placement of divisions for a piecewise-exponential model could be determined visually such that the points within each division of the cumulative hazard plot follow a linear pattern. The same can be done with log-cumulative hazard function for a piecewise-Weibull model. Although piecewise-exponential models can be made progressively more flexible by increasing the number of segments to capture even very complex patterns, the assumption of a constant hazard for the last segment can be limiting for projection. Thus, models based on Weibull distributions may be more appropriate, and possibly achieve similar fit with fewer segments. The subjectivity involved in these decisions can be minimized by using numeric optimizing strategies (e.g., grid search for placement of divisions) and use of fit statistics to select distributions.

CP4

MEASURING HEALTH OUTCOMES IN THE ABSENCE OF RIGOUR: WILLFUL IGNORANCE OR DELIBERATE MALPRACTICE?

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The evaluation of cost-effectiveness plays a central role in appraisal of new technologies undertaken by regulatory agencies across the world. As a consequence, health economists now play a critical part in generating the evidence base used to determine both access to and the price of treatment. No matter the complexity of any economic evaluation there is an inescapable need to describe and value the benefits of health care interventions. The computation of an ICER depends totally on the capacity to quantify marginal changes in health status. The orthodoxy adopted by most HTA agencies relies on the notion of capturing such outcomes via the use of generic health status measurement systems (for example HUI or EQ-5D) together with their corresponding social preference weights. The requirement that the values of the general population constitute the "correct" perspective is one element of the health economics credo. A second dictates that the "worth" of a health outcome shall be expressed in terms of utility – a concept that lacks a defined unit of measure or any agreed standard elicitation method. It is a regrettable fact that although health economists privately recognise the non-commensurability of Standard Gamble (SG) and Time Trade-Off (TTO) methods their public posture generally belies this contradiction. The status of the QALY as a useful metric of health benefit/loss has been fatally compromised by the failure of the scientific community to agree on a single method for determining the quality-adjustment factor. The preparedness of health economists to ignore this gap in their armamentarium runs counter to the rational practice of science. This paper challenges the intellectual deadweight of traditional health economics, specifically in regards to the measurement of health outcomes. Examples of defective practice drawn from Canadian and UK HTA reports will be used to illustrate the conceptual issues raised in this paper.

PODIUM SESSION I: HEALTH CARE STUDIES – EXPENDITURE OR REIMBURSEMENT STUDIES

HC1

ORPHAN DISEASE DRUG COSTS IN THE UNITED STATES: ASSESSMENT OF LAUNCH PRICING TRENDS IN NON-CANCER ORPHAN DISEASES AND THE FUTURE IMPLICATIONS ON HEALTH SYSTEM ACCESS

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OBJECTIVES: With an increasing number of orphan disease (OD) drugs in development, the objective of the current study is to assess launch pricing trends of orphan drugs in the U.S. From this pricing assessment, implications and effects of increasing orphan drug prices on US managed care payer access is discussed. **METHODS:** Non-cancer OD approvals between 2003 and 2012 were extracted from the FDA Orphan Products database. Oncology and acute indications were excluded due to the confounders of acute and chronic treatments. Wholesale acquisition cost drug prices were collected from Medispan-PriceRx for product launch year. Annualized drug costs were calculated using the product label and consistent assumptions on weight-based dosing. Drug costs were adjusted to 2012 dollars using the CPI. **RESULTS:** From 2003-2012, 33 ODs gaining U.S. market approval were included in the present analysis, with 30% of the drugs approved in 2011 and 2012. Launch pricing trends indicate that average launch price of ODs has increased 107% to $276,471/year during the examined time period. In 2012, 4 of 6 new ODs were priced between $294,000 and $295,000. **CONCLUSIONS:** The OD approvals and prices have grown substantially since 2003, accelerating in the last two years. The historically open US payer policy towards ODs must be reconsidered for sustainability. Expansion of the covered population will increase the traditionally modest payer OD economic burden, accelerated by new treatments. Payers must prepare by creating OD policy that identifies the most appropriate patients through collaboration with thought leaders and manufacturers. Payer investment should be made in patient management programs to ensure clinical benefit is delivered. The OD regulatory mechanism encourages manufacturers to invest modestly in clinical development and assign ultra-premium prices. Manufacturers may be