OP45 Biological Drugs And Rheumatoid Arthritis In Brazil: An Overview

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Introduction. The Brazilian Unified Health System (SUS) is known worldwide for ensuring universal assistance to citizens, which includes the supply of medicines free of charge. Biological drugs consume about 40 percent of the public budget for pharmaceutical services in the SUS and Rheumatoid Arthritis (RA) is the largest consumer of these resources, serving about 110,000 patients. Since 2002 there has been a clinical guideline for the care of patients with rheumatoid arthritis in Brazil, currently providing 10 biological drugs for treatment of RA. The objective of this study is to present data about the provision, expenditure and profile of users of biological drugs for rheumatoid arthritis in SUS.

Methods. Retrospective and exploratory study, using administrative data regarding the purchase and consumption of biological drugs Infliximab, Etanercept, Adalimumab, Rituximab, Abatacept (intravenous and subcutaneous), Tocilizumab, Golimumab and Certolizumab pegol for the treatment of RA between 2012 and 2017 in SUS.

Results. There was an expenditure of approximately USD 421.7 million from the Brazilian Ministry of Health with the supply of about 2 million pharmaceutical units of biological drugs for treatment of rheumatoid arthritis, 79 percent of them destined for female users and 89.2 percent for the 40-69 age group. The M05.8 and M.06.0 codes of the International Classification of Diseases (ICD-10) were the most prevalent among the arthritic population served. Adalimumab and Etanercept accounted for 68.3 percent of total expenditure. A reduction in the use of these medicines were observed after the availability of new drugs for the treatment of the disease between 2014 and 2017.

Conclusions. Brazil is one of the largest consumers of biological medicines in the world. The use of real-life data allows monitoring trends and costs of the use of these drugs as well as changes with the entry of new therapies and biosimilar medicines.

OP47 Need For New Thrombectomy Centers? A Practical Decision Framework

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Introduction. Stroke is a major contributor to mortality, disability and long-term use of healthcare services. As for all chrono-dependant conditions, clinical results are associated with timely access to appropriate care. Thrombectomy (EVT) is an effective treatment for large vessel occlusions, but can only be provided in highly-specialized centers by experienced personnel. We sought to develop a framework to aid decision-making on the appropriateness of opening new EVT centers in Québec, Canada.

Methods. Data sources included provincial administrative healthcare databases, population density statistics, field evaluation of Québec's four existing EVT care networks, and literature review concerning structural and performance criteria for EVT centers. We consulted EVT clinical teams, interdisciplinary stroke experts, patients, professional association representatives, healthcare managers and decision-makers.

Results. Access to EVT is suboptimal in all 17 regions of Québec, with virtually no access in remote areas. Results of key performance indicators indicated favorable treatment delays after arrival at the EVT center. However, door-to-needle and door-in-door-out times were long for patients transferred from non-EVT centers. High use of ambulances indicated the potential to transport patients to the most appropriate center. In light of 'real world' results and other sources of information, the need for a new EVT center should consider the following criteria: sub-optimal EVT access within the region; transport time to an existing EVT center >1 hour; expected patient volume within 2 hours of transport; impact on volume of existing programs; availability of long-term financial support; availability of a critical mass of neurointerventionists, vascular neurologists, and neurosurgeons; demonstrated quality of stroke care; and, presence of a stroke unit.

Conclusions. The triangulation of literature, clinician experience and the Québec context enriched the evaluation process. Furthermore, this facilitated the development of a framework that was broadly applicable across regions to the real-world setting of decision-making in a complex system of care.

OP48 Nursing Requirements In Long-Term Care: A Health Technology Assessment

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Introduction. The objectives of this study were to systematically review published research on the relationship between nursing staff coverage, care hours, and quality of care (QoC) in long-term care (LTC) facilities; and to conduct a real world evidence (RWE) analysis using Alberta real world data (RWD) to inform policy makers on whether any amendments could be made to current regulations.

Methods. A systematic review (SR) of research evidence published between January 2000 and May 2018 on the relationship between nursing staff coverage, care hours, and QoC in LTC facilities was conducted. Panel data regressions using available RWD from Alberta, Canada, were performed to assess associations between nursing care hours and LTC outcomes. Outcomes of interest included quality indicators related to resident outcomes, hospital admissions, emergency room visits and family satisfaction. Nursing care hours considered in SR and RWE analysis included those provided by registered nurses (RNs) and licensed practical nurses (LPNs).

Results. The SR found inconsistent and poor quality evidence relevant to the questions of interest, indicating a great uncertainty about the association between nursing staff time and type of coverage and QoC. Although some positive indications were suggested, major weaknesses of reviewed studies limited interpretation of SR results. RWE analysis found that impact of care hours on LTC outcomes was heterogeneous, dependent on outcome measurements.

There was evidence that total staff, RN, and LPN hours had positive effects on some resident outcomes and magnitude of effect differed for different nursing staff.

Conclusions. No definitive conclusion could be drawn on whether changing nursing staff time or nursing staff coverage models would affect residents' outcomes based on the research evidence gathered in the SR. RWE analysis helped to fill a gap in the available published literature and allowed policy makers to better understand the impact of revising current regulations based on actual outcomes.

OP49 MAIC-ing Use Of Trials? Study Of Matching-Adjusted Indirect Comparisons

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Introduction. When conducting a Network Meta-Analysis (NMA) for a Health Technology Assessment (HTA), the submitting company typically will have access to Individual Patient Data (IPD) from their own trials, but only aggregate data (AgD) for the comparator. In this case, they can re-weight the IPD so that the covariate characteristics in the IPD trials match that of the AgD trials, using the increasingly popular method of Matching-Adjusted Indirect Comparison (MAIC).

Methods. We carried out a simulation study to investigate this method in a Bayesian setting. We simulated three IPD trials comparing treatments A and B (AB-IPD trials), and one aggregate data trial comparing treatments B and C (BC-AgD trial). We investigated two options of weighting covariates: 1. all three studies are weighted separately to match the BC-AgD trial (MAIC Separate Trials). 2. patients are weighted across all three IPD studies to match the BC-AgD trial, but the NMA still considers each trial separately (MAIC Pooled Trials). We compared the results of the MAIC to a standard NMA and a mixed IPD/AgD NMA. We applied these methods to a network of treatments for multiple myeloma.

Results. MAIC can provide more accurate estimates of the relative treatment effects than a standard NMA in the BC-AgD trial population. However, MAIC may decrease the accuracy of the relative treatment effects in the overall population. Treatment rankings were unchanged when applying MAIC to the multiple myeloma network.

Conclusions. MAIC is beneficial as a sensitivity analysis to demonstrate that results hold across patient populations. If there is a difference in relative treatment effects attributable to population imbalances, then it is useful to be able to quantify this difference. However, we recommend using either a standard NMA or a mixed IPD/AgD NMA for the base case analysis, given the potential bias that can arise in an MAIC.

OP50 IQWiG And GRADE – An Exemplary Comparison Of Methods

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Introduction. Efforts to harmonize health technology assessment (HTA) processes and methods across Europe are currently intensified. In this context, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach has been proposed as a "common ground" in joint HTAs. However, GRADE has been primarily developed to support authors of clinical guidelines. Therefore, it is unclear whether HTA reports based on GRADE are compatible with the methods currently applied by European HTA organizations.

Methods. We contrasted IQWiG's methods paper and publications by the GRADE Working Group with regard to the following domains: 1) risk of bias (RoB) assessment 2) prerequisites for "greater benefit" (assuming that IQWiG's "greater benefit" corresponds to a GRADE assessment of at least low certainty and a small important effect) and 3) consideration of non-randomized studies (NRS). We present illustrative differences and highlight similarities.

Results. Overall, RoB assessments are very similar under both approaches. However, we identified several important differences. In case of very severe publication bias, IQWiG methods preclude drawing a conclusion, whereas GRADE requires only downgrading the certainty of evidence while still allowing for a conclusion on effect sizes. Secondly, IQWiG generally requires a statistically significant effect for a "greater benefit", while GRADE does not (statistically non-significant effects would only necessitate downgrading the certainty of results for imprecision). Another difference is that in general, NRS are not included in IQWiG assessments when randomized studies (RS) are available and thus possible. In contrast, preliminary GRADE guidance recommends considering NRS in addition to RS when the RS evidence is of low or very low certainty.

Conclusions. While GRADE and IQWiG's method share some similarities, our exemplary analysis shows that there are some notable differences. Therefore, GRADE should not be used "out of the box" for European HTAs. To foster further discussion, more research (including a comprehensive comparison of methods and an analysis of resources for adaptation) is needed.

OP52 Use Of Intention To Treat And Magnitude Of Treatment Effects

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Introduction. Intention to treat (ITT) is a gold standard strategy to analyze the results of randomized controlled trials (RCTs). ITT analysis has been considered a methodological indicator of the quality of clinical trials. The extent to which the use of ITT is related to the treatment effects observed in RCTs has not been rigorously explored. Therefore, the main objective of this study was to determine the association between biases related to attrition and missing data and the use of intention to treat principle, and changes in effect size estimates in RCTs.

Methods. This was a meta-epidemiological study. A random sample of RCTs included in meta-analyses was identified. Data extraction including assessments of the use of intention to treat principle, missing data and drop-outs was conducted independently by two