Is Social Media Information Useful to Understand Patient Experiences and the Burden of Disease?

P33
PATIENT EXPERIENCES AND INSIGHTS ON CHRONIC OCULAR PAIN FROM A SOCIAL MEDIA LISTENING STUDY

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Objective: To identify the perceived causes for chronic ocular pain (COP) (≥3 months pain duration), its impact on quality of life (QoL) and understand the patient journey from social media posts.
Methods: In this retrospective study, publicly available social media conversations were identified from searches triaged by a combination of automated relevancy keyword algorithm and manual review, and subsequently analyzed post anonymizing for COP content. Twitter, forums, and other (Facebook, Blogs, etc.) platforms were leveraged for the time period February 2020 to February 2021. ***Results:*** A total of 464 (UK=208, US=175, Canada=65 and Australia=16) patient/caregiver conversations on COP were identified. Top discussion points were symptoms (62%) and causes of COP (58%). Ocular factors (including dry eye disease, thyroid/Graves' disease, and ocular surgeries) contributed to ~46% of causes identified, while non-ocular factors (including migraine, COVID, and side-effects/withdrawal of medications) contributed to ~54%. The most commonly mentioned symptoms (555) were headache/head pressures (96), dry/gritty eyes (67), light sensitivity (34), insomnia (29), and redness/pink eyes (28). Symptoms impacted all aspects of patients' QoL: physical day-to-day activities such as reading, driving, and sleeping; emotional wellbeing such as depression/hopelessness, frustration/anger, fear, and suicidal thoughts; functional wellbeing such as difficulty at work/study place, reduced productivity or having to quit their job; social impacts such as being irritated around people, and having a less active social life. Eye drops (58/140 mentions) are the most commonly mentioned treatment option. Common coping strategies mentioned were blue-light filter glasses/eyeglasses (17), and hot compresses (11). Key unmet needs mentioned by patients were failed, improper, delayed diagnosis (62), and lack of effective treatments or appropriate management (30). ***Conclusion:*** Insights from this study reported patients' experiences, concerns, and the adverse impact on overall QoL. The results can help in better understanding the patients' perspective, which can be considered during drug development.

P34
USE OF SOCIAL MEDIA LISTENING (SML) METHODS FOR UNDERSTANDING THE PATIENT EXPERIENCE OF CHRONIC DISEASE: A SCOPING REVIEW

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Objectives: To conduct a scoping review of the literature related to the use of social media listening (SML) methods for understanding patients' experiences of chronic disease. ***Methods:*** Methodological guidance for conducting scoping reviews was followed. PubMed, Medline and EMBASE databases were searched using terms for social media listening, patient experience and quality of life. Primary research studies and systematic reviews that investigated the use of SML for understanding the patient experience of health or healthcare were included. Titles and abstracts were reviewed by two reviewers. One reviewer extracted data from full text articles. Quality of data extraction was assessed and verified by a second reviewer. A descriptive synthesis was performed with a focus on summarizing information related to the type of social media platforms, methods, data extraction tools and outcomes reported. ***Results:*** The literature search identified 53 studies; 14 met the inclusion criteria and were included in the full-text review and data extraction. Social media platforms included Twitter, Facebook, HealthUnlocked, and disease-specific online communities. methods used by researchers conducting SML included keyword frequency analysis, identification of patient reported terms for functional status, qualitative content analysis, identification of frequently asked questions and modelling of the patient experience. Outcomes included identification of symptoms experienced by and of importance to patients (including physical, psychological and cognitive symptoms), experience of medical treatment and procedures, social relationships and support, financial difficulties, information on the temporal patterns of symptoms experienced by patients and identification of racial and ethnic disparities in patient experience of disease. ***Conclusions:*** The findings highlight the potential value of SML as a method for capturing the patient voice and understanding patient experiences of chronic disease. SML has the potential to complement traditional methods, reduce patient burden and include the experience of people who may not take part in formal research studies.

P36
UNMET NEEDS OF CAREGIVERS IN LOCALLY ADVANCED OR METASTATIC BLADDER CANCER FROM SOCIAL MEDIA IN THE US

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Objectives: Bladder cancer (BC) is the sixth most common cancer in the US; the prognosis for patients with locally advanced or metastatic BC is very poor. Few studies have assessed its burden on caregivers. This study aimed to characterize difficulties and unmet needs of caregivers for patients with locally advanced or metastatic BC as reported on social media. ***Methods:*** US caregiver testimonials were collected from social media posts between January 2015 and April 2021 using specific terms for locally advanced or metastatic BC. These were qualitatively analyzed to identify caregiver difficulties and unmet need until saturation. ***Results:*** Of 1214 testimonials from 679 caregivers on 72 social media sources, 423 were randomly selected and analyzed until saturation. From those that reported age-related data (<15% of testimonials), most caregivers were women (83.2%) with a mean age of 35.4 years, whereas the reported mean age of patients was 67.2 years. A total of 177 testimonials that expressed ≥1 caregiver- or patient-centered difficulty were identified and classified into a list of 36 types of challenges. The main difficulties related to the caregivers' psychological impact throughout the patient journey (26%), the desire to share experiences among peers/support groups (15.8%), and the fear and management of patients' adverse events (12.4%). Other major difficulties expressed included the specific psychological burden of end-of-life support or grief work (10.2%), the daily impact of being a caregiver (relocation, time consumption; 9.6%), stress due to screening and diagnostic delay (7.3%), and the change in relationships between patients and caregivers (5.1%). ***Conclusions:*** Qualitative analysis of social media testimonials from caregivers of patients with BC in the US provided insights on the substantial psychological impact and burden of care on them. Future research may explore BC caregiver well-being and quality of life as outcomes in quantitative studies.

Issues with Health Technology Assessment of Specialised Technologies

P37
THE CURE MYTH: EXPERIENCE FROM RECENT HEALTH TECHNOLOGY ASSESSMENT (HTA) SUBMISSIONS IN RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA (R/R DLBCL)

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Objectives: Recent clinical trials testing novel cancer therapies such as CAR-Ts are detecting a plateau in the survival curves, conveying a potential opportunity for cure. Long-term survival data are limited, and clinicians are often cautious to make conclusions on the basis of the trial outcomes. Nevertheless, cure assumptions have appeared in oncology HTA submissions such as those in R/R DLBCL. This study aims to investigate how cure assumptions are applied across different HTA submissions for therapies in R/R DLBCL. ***Methods:*** Publicly available HTA dossiers in R/R DLBCL submitted to NICE, SMC, CADTH, ICER, PBAC and HAS in the past five years were reviewed. Information related to cure assumptions (methodology, cure time point, cure proportion) and the critiques received by the HTA bodies were reviewed and extracted. ***Results:*** Of the twelve HTA documents identified, ten submissions applied cure assumption in overall survival extrapolation. These submissions focused on two CAR-T agents (axicabtagene and tisagenlecleucel) and polatuzumab vedotin. From the ten submissions that reported cure assumptions, six used cure-mixture models and four used simple cure assumptions. Eight models set mortality of cured patients to that of the general population, while two considered an adjustment factor. Cure was considered only for the intervention arm in seven models, while the rest considered it for all treatments. The timepoint and proportion of cure varied across the submissions. Critiques were mainly around the issues caused by immaturity of survival data, such as uncertainty in cure assumptions and the choice of cure timepoint. ***Conclusions:*** While cure modelling is frequently used in R/R DLBCL and in oncology, there seems to be no consensus on the implication of cure and its implementation in the economic analyses. Clear guidance must be provided by health authorities on how to approach the cure concept in economic modelling and how to validate the assumptions.

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SUFFICIENT UPTAKE OF HIGHLY SPECIALISED TECHNOLOGIES?

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The National Institute for Health and Care Excellence (NICE) introduced a Highly Specialised Technology (HST) pathway in 2015 to provide more consistency in appraising high cost therapies for rare and neglected diseases. This research evaluates the number of HSTs appraised to date and the actual number of patients treated under this pathway. All HST guidance was identified and disease prevalence/incidence, and recommendations were extracted (to 25-Jun-2021). Actual uptake data was provided by NHS England in April 2021. NICE published 14 recommendations through the Highly Specialised Technology (HST) pathway (after an average of 19.6 months after EC-approval) compared to 357 recommendations through the technology appraisal pathway (single or multiple) since 2015. Approximately 1254 patients have been treated with an HST approved therapy. 5 of the 14 HSTs have exceeded the number of patients treated than the NICE-estimated eligible patient population. Notably, 373 patients had been treated with eculizumab (HST1) since

January 2015, compared with an estimated 20-30 patients diagnosed-per-year (estimated total uptake of 120-180 from recommendation). However, in some instances the number of patients treated with an HST were very low: zero patients for Strimvelis® (HST7), ≤10 for eliglustat (HST5), and ≤10 for metreleptin (HST14); much lower than any reported estimates in their respective HST appraisals (Strimvelis®: 3 diagnosed/year; eliglustat: 50-100 eligible patients; metreleptin: <200 eligible patients). Relatively few therapies have been recommended under the NICE HST pathway since 2015 compared to the standard NICE process with STA/MTA. Further, these recommendations have been over 19-months from EC-approval. Even following a positive NICE recommendation, several of these have not achieved meaningful patient access, potentially due to the lack of awareness for rare diseases, and likelihood of underdiagnoses.

P39
BETTER OUTCOMES AND VALUE FOR MONEY WITH COST-EFFECTIVENESS MODELLING OF CASCADE SCREENING STRATEGIES FOR FAMILIAL HYPERCHOLESTEROLAEMIA

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Objectives: Cascade screening for familial hypercholesterolaemia (FH) refers to the systematic testing of relatives of people known to have FH (termed 'indexes'). Cascade screening is cost-effective compared to no screening, but alternative screening strategies have not been studied. Our objective was to identify the cost-effective strategy to select indexes to cascade, and to contacting and testing their relatives. ***Methods:*** We developed a new cost-effectiveness model informed with routinely collected UK data from indexes and their relatives. Our decision tree model takes the UK National Health Service perspective and calculates, per index assessed to the cascade, the relatives diagnosed, cascade costs, quality-adjusted life years (QALYs), healthcare costs and incremental cost-effectiveness ratios (ICERs). ***Results:*** We compared 1792 strategies. The cost-effectiveness frontier was mostly formed by strategies which contacted 1st and 2nd degree relatives of indexes with genetic FH simultaneously and directly. The cost-effective strategy diagnoses relatives according to whether they were on lipid lowering treatment, cholesterol, and age, with some having confirmatory genetic testing – it diagnoses 52% affected relatives, at a cascade cost of £536; ICER = £13,996/QALY. Sequential contact (i.e. contacting second degree relatives only when their first degree relative was diagnosed with FH), indirect contact via their index/relatives and genetically testing them diagnoses 36% of relatives, while direct and simultaneous contact with genetic testing diagnoses more relatives (56%); neither are in the cost-effectiveness frontier. If genetic testing is not available, cascade screening remains cost-effective, diagnosing 41% of relatives (ICER=£5,603 vs no cascade). Results are robust to alternative scenarios bar those affecting long-term benefits of diagnosis. ***Conclusions:*** Simultaneous and direct contact of relatives of indexes with genetic FH and a mixed approach to testing relatives is cost-effective and achieves better outcomes than sequential and indirect contact. Identifying this strategy required systematic comparison of multiple alternatives, which is only achievable with cost-effectiveness modelling.

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HTA AGENCIES PERSPECTIVE ON SURVIVAL MODELLING IN CELL OR GENE THERAPY APPRAISALS

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Objectives: The first cell- and gene therapies, so called advanced therapy medicinal products (ATMPs), have recently become available, making it possible to treat, and even potentially cure, very severe and sometimes previously untreatable conditions. These characteristics have led to a discussion among health economists about whether a specific methodological reference case is required for economic evaluation of gene therapies and the conclusion has been that a new methodological reference case is not required but that "the confluence of various characteristics can lead to specific methodological challenges...". Traditional survival modeling may underestimate outcomes by assuming the same mortality rate for all patients, in situations where the treatment could lead to the cure of a patients. Mixture cure models have been suggested as a supplementary analysis, alongside standard parametric models. The aim of this study was to review reimbursement appraisal reports of the 12 EMA approved ATMPs, to identify the differences in methods and assumptions in survival modelling of long-term treatment effects across different HTA agencies. ***Methods:*** Publicly available assessment reports were retrieved from each reimbursement agency's website in the Nordics, the Netherlands, England and Wales, Canada and Australia for the relevant drugs. ***Results:*** Across the HTA agencies different level of acceptance to non-standard survival modelling is seen. E.g. in appraisals of cell-therapies, mixture cure models have been accepted in the Nordic countries and in England and Wales but assumptions around the percentage of cured patients and the preferred source for the survival extrapolation post clinical trial follow-up differs. In appraisals of gene-therapies, the exploration of the impact of the main assumptions that drive model results have been recommended across the HTA agencies. ***Conclusions:*** There is yet not an established golden standard on how to apply survival modelling to ATPMs and the preferences on the methodology varies across HTA agencies.

Methodological Developments in Network Meta-Analysis and Comparative Effectiveness Research

P41
CROSNMA: A NEW R PACKAGE TO SYNTHESIZE CROSS-DESIGN EVIDENCE AND CROSS-FORMAT DATA

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Objectives: In network meta-analysis, we synthesize all relevant available evidence about health outcomes from competing treatments. That evidence might come from different study designs and in different formats: from non-randomized studies (NRS) or randomized controlled trials (RCT) as individual participant data (IPD) or as aggregate data (AD). To utilize all available evidence, we need a software that allows us to combine these different pieces of information accounting for their differences, e.g. RCTs have typically lower risk of bias than NRS. ***Methods:*** We integrate the three-level hierarchical model that combine IPD and AD with the following four models that incorporate both RCT and NRS evidence by (a) ignoring their differences in risk of bias (b) using NRS to construct discounted treatment effect priors (c,d) adjusting for the risk of bias in each study and controlling the contribution of high risk of bias information in two different ways. ***Results:*** We have implemented these models in a new R package, crosnma. This software allows us for conducting Bayesian network meta-analysis and meta-regression. Up to three study- or patient-level covariates can be also included, which may help explaining some of the heterogeneity and inconsistency across trials. The package runs a range of models with JAGS by generating the code automatically from user's input. ***Conclusions:*** crosnma is a new R package to conduct Bayesian network meta-analysis and meta-regression to synthesise cross-design evidence and cross-format data. We believe that this package will encourage the investigators to not discard any relevant evidence on their analysis. Authors are supported by the HTx-project. The HTx project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement N° 825162

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COMPARISON OF ESTIMATION METHODS FOR SINGLE-ARM TRIALS IN RARE DISEASES WITH HISTORICAL CONTROL GROUPS

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Objectives: Randomized controlled trials are the gold standard for estimating treatment effects. However, in rare diseases with high unmet need, single-arm trials are used when randomization of patients to placebo or standard of care is infeasible or unethical. We evaluated various methods to control for confounding in estimating treatment effects in a small single-arm trial with a historical comparator group. ***Methods:*** We used simulation to evaluate different techniques to estimate the "true" treatment effect on overall survival (OS) and objective response rate (ORR) in a specific target population using an external comparator design. We varied effect size, sample size, confounders, and correlation between confounders. We assessed two broad categories of methods: i) requiring specification for treatment allocation [propensity score (PS)-based inverse probability of treatment weighting (IPTW), standardized mortality/morbidity ratio (SMR), stabilized IPTW (SIPTW), overlap weighting (OW), stratification, and matching], and ii) adding outcome information (g-computation). Their precisions and accuracies were evaluated by a combination of 95% confidence interval (CI) coverage, power, bias, and mean square error (MSE). ***Results:*** G-computation resulted in the most accurate and precise estimator of OS (95% CI coverage: 93.5%, power: 69.3%, bias: -0.001, MSE: 0.055) in a small sample size scenario of 30 treated subjects compared with 120 comparator subjects. Similar results were observed for ORR. In comparison, results for OS were: 95% CI coverage: 72.8%, 65.6%; power: 75.9%, 62.6%; bias: -0.026, 0.072; MSE: 0.114, 0.167 for SMR and IPTW, respectively. ***Conclusions:*** In our simulated example, the g-computation estimator performed best to control confounding in a small single-arm trial with an external comparator group. PS based methods (e.g., SMR & IPTW) may be suitable as an initial step in the creation of the comparator arm when researchers are blind to the outcome, while g-computation can be subsequently used to estimate the efficacy of treatment.

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A CASE STUDY AND SIMULATION TO COMPARE DIFFERENT INDIRECT TREATMENT COMPARISON METHODS UNDER VARYING ACCESS TO INDIVIDUAL PATIENT DATA

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