reviewers. To determine the association between biases related to attrition, missing data, and the use of intention to treat and effect sizes, a two-level analysis was conducted using a meta-meta-analytic approach.

Results. Three-hundred and ninety-three trials included in 43 meta-analyses, analyzing 44,622 patients contributed to this study. From these, 134 trials (34.1%) used ITT and 218 (55.5%) did not use ITT. Trials which did not use the ITT principle, or which were assessed as having an inappropriate control of incomplete outcome data (based on the Cochrane risk of bias tool) tended to underestimate the treatment effect when compared with trials with adequate use of ITT (ES= -0.13; 95%CI -0.26, -0.01) or trials which were assessed as having an appropriate control of incomplete outcome (ES= -0.18; 95%CI -0.29, -0.08).

Conclusions. Our results suggest that when evaluating risk of bias of primary RCTs, systematic reviewers should pay attention to these biases since they could underestimate treatment effects. Systematic reviewers should perform sensitivity analysis including trials with low risk of bias in these domains.

OP53 Health Technology Assessment Acceptability Of Innovative Survival Metrics In Oncology

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Introduction. Most new oncology therapies are studied in the advanced/metastatic setting. However, there is an increasing focus on earlier stage disease. Nevertheless, measuring Overall Survival (OS) in neo-/adjuvant therapy trials can be very challenging due to the increased life expectancy and the confounding effects of subsequent treatments. Thus, their primary endpoints tend to be surrogate survival metrics (e.g. metastases-free survival). This research aims evaluates the health technology assessment (HTA) acceptability of such endpoints through recent neo-/adjuvant HTA assessments.

Methods. The European Medicines Agency (EMA) website was screened for any neo-/adjuvant oncology therapies approved (1 January 2013-22 October 2018) and any corresponding publicly-available assessments by HTA bodies (NICE, SMC, IQWiG, G-BA, CADTH, PBAC, HAS) were identified and key data extracted.

Results. Six neo-/adjuvant therapies have received marketing authorization by the European Commission (EC). These six have been on the market for an average of 8.9 months (range: 0.9-39.3 months, median: 3.3 months). In four of the six, the pivotal trial primary endpoints were measures of relapse-/disease-free survival, (others: pathological complete response and PFS/OS co-primary). Only one had mature OS data available at EC-approval. Four of the six therapies had received at least draft guidance by an HTA body, encompassing 11 HTA assessments in total (4: NICE, 2: IQWiG, HAS; 1: SMC, CADTH, G-BA). Only two of 11 (18%) were positive outcomes (both NICE), the remaining nine were negative.

Conclusions. Oncology therapies are increasingly receiving regulatory approval in the neo-/adjuvant setting. However, their pivotal trials are frequently powered to show benefits in disease-/metastases-free survival. Whilst sufficient for regulatory approval, translating this to favorable HTA decisions has been more challenging. Clearly establishing linkages between surrogate survival metrics and OS alongside measuring metrics that clearly portray patient benefits (e.g. time to symptomatic progression) could improve HTA-acceptability. Further, some payers allow for temporary reimbursement whilst additional evidence is generated (e.g. Cancer Drugs Fund in England).

OP54 Monitoring Evidence On Overall Survival Benefits Of Anti-Cancer Drugs

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Introduction. The introduction of fast-track licensing strategies increases the approval of anti-cancer drugs with ambiguous benefit-risk profiles. Thus, in many instances there is lacking evidence about overall survival (OS) at the time of marketing authorisation. Our objective was to monitor and characterise therapies with ambiguous benefit-risk profiles and identify any post-approval updates on median OS after at least three years of approval by the European Medicines Agency (EMA).

Methods. We included all originator anti-cancer drugs with initially ambiguous benefit-risk profiles that received marketing authorization from the EMA between 1 Jan 2009 and 31 May 2015. Our monitoring timeframe was at least three years after EMA-approval. To identify study updates, the following three sources were included: clinicaltrials.gov, European Public Assessment Reports (EPARs), and PubMed.

Results. In total, we identified 102 eligible approval studies. Out of these, a negative difference in median OS or no information was available in forty-three (42.2%) instances. During monitoring, eleven updates with accessible information on median OS could be identified. Including monitoring results, there are still thirty-two remaining therapies (31.4%) where no or negative information (n = 27 [26.5%] and n = 5 [4.9%], respectively) regarding median OS was present at least three years after EMA approval.

Conclusions. One-third of oncology drugs with ambiguous benefit-risk profiles failed to demonstrate a survival benefit even several years following marketing authorization. Systematic and transparent post-approval monitoring mechanisms will be of high relevance to assure a clinically relevant patient benefit, since the trend towards faster access to medicines with uncertain benefit is increasing rather than declining.

OP56 Are Therapeutic Positioning Reports Driving Pharmaceutical Reimbursement Outcomes In Spain?

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Introduction. Following marketing authorization in Spain, new medicines are assessed by the Inter-Ministerial Pricing Commission for Pharmaceuticals (CIPM), which provides reimbursement recommendations with a maximum ex-factory price. However, there are 17 autonomous regions, which can make distinct reimbursement decisions. To drive consistency, the Spanish Agency for Medicines and Health Products has issued national Therapeutic Positioning Reports (TPRs) for new medicines since 2012. Since November 2017, CIPM recommendations have been published monthly, giving the opportunity to analyze the impact of TPRs on the speed and outcome of CIPM decisions, which this research evaluates.

Methods. Publicly-available CIPM and TRP decisions were identified from www.msssi.gob.es and www.aemps.gob.es, respectively. Marketing authorization dates were identified from www.ema.europa.eu or www.aemps.gob.es (10 March 2007-11 February 2018). Pearson's chi-squared and Mann-Whitney U statistical tests were performed using R.

Results. One hundred and ninety-three drug-indication pairings with an associated TPR were identified. The majority (62% [120/193]) were recommended as alternative treatment options with only 19 percent (36/193) deemed to be superior and 19 percent (37/193) not recommended. One hundred and eight CIPM recommendations were identified across seven monthly reports, issued a mean of 12.2 months after market approval, 59 percent (64/108) were positive and 41 percent (44/108) were negative recommendations. There were 34 drug-indication pairings with both CIPM and TPR recommendations available. Of these, 24 percent, 56 percent and 21 percent had TPR outcomes of 'superior', 'alternative' and 'not recommended', respectively and 71 percent and 29 percent had positive and negative CIPM outcomes. Drug-indication pairings with 'negative' TPRs were significantly more likely to have negative CIPMs than those with either 'alternative' or 'superior' TPRs (71% vs. 19%, respectively, $\chi 2 = 5.16$, $p = 0.02$) and were more likely to experience significantly longer delays to CIPM recommendation (23.9 vs. 13.5 months, respectively, $U = 50$, $p = 0.03$).

Conclusions. Drug-indication pairings with 'positive' and 'alterative' TPR outcomes are associated with significantly better and faster CIPM recommendations than those with 'not recommended' TPR outcomes

OP57 Threats And Opportunities To Digital Health In Primary Care

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Introduction. The use of digital technologies in healthcare systems (digital health)– such as electronic health records and telehealth – can improve primary care (PC). However, integration of digital health can be constrained/impaired and/or facilitated due to several factors. We propose an integrative framework for classifying the factors that could favour or limit digital health integration in PC in order to guide the identification of strategies that could be helpful for technology promoters, managers, clinicians and researchers.

Methods. Based on a systematic review, our framework includes seven categories to classify the main opportunities and threats to digital health integration in PC: technological; individual/interpersonal; professional; organisational/institutional; ethical/legal; sociopolitical; economical. We consulted a panel of researchers, managers, clinicians, and citizens/patients in a scientific meeting regarding the main opportunities and threats to the integration of digital health in PC. We performed a content analysis of the reported factors according to the framework.

Results. Technological factors such as maturity, interoperability and ease of use were often mentioned as key conditions for digital health integration. Individual and interpersonal factors such as depersonalisation and digital literacy were seen as threats. The impact on workload and shared responsibility were threats at the professional level, whereas silos and change management were noted as organisational threats. Current policies and social trends favored digital health. Threats regarding privacy and confidentiality were mentioned at the legal/ethical level. The possibility to reduce costs and sharing of benefits were noted as opportunities at the economic level.

Conclusions. Knowing these multidimensional conditions, perceived as either threats or opportunities depending on the context of each PC setting, is essential to inform decisions, from strategic planning to evaluation. Our integrative framework allows a simple classification of opportunities and threats that can guide the development and implementation of tailored strategies favouring the integration of digital health in PC.

OP58 Developing An Evaluation Based Taxonomy For mHealth Apps

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Introduction. Mobile Health (mHealth) apps offer potential to promote greater public engagement in health, improve efficiency and open up new care pathways and models of care. However, the volume and heterogeneity of apps has led to uncertainty and lack of standardization around app definitions. Some mobile apps carry minimal risks to consumers, but others can carry significant risks. Work has been carried out to develop a framework for assessment (for example, for the NHS app library [beta version]). We discuss work helping to inform a preliminary framework of categorizing mHealth apps for proportionate assessment and validation, and the challenges involved.

Methods. A literature review was carried out to identify different types of categorizations used to define health apps and the most important dimensions for their assessment. A taxonomy of apps and a process for routing them towards appropriate methods of evaluation was developed through iterative review, discussion and refinement.

Results. Fourteen types of mHealth apps were established which were categorized by app function and by the potential risk involved with use. Subsequently, this research suggested a method of routing apps towards the most appropriate and proportionate method of evaluation, by using four example dimensions of impact (population size, disease burden, priority of clinical condition, and innovation), and four levels of risk.

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