six assessments that resulted in conditional reimbursement were targeted therapies. Typically, with these targeted therapies, PFS or OS ranged from 3 months to 9 months with the cost per QALY > £45,000. Five of the six manufactures participated in a patient-access scheme which consisted of fixed-price discounts such as Cetuximab (CRC) or performance schemes like sunimab (GIST), Bortezomib (myeloma), and Lenalodome (myeloma). CONCLUSIONS: Based on the retrospective analysis, it is clear that the biggest challenge for targeted-cancer therapies is affordability with only one of the targeted therapies receiving unconditional reimbursement. However, nearly all the other targeted therapies evaluated that offered >5 months OS or PFS were recommended by NICE with a proviso to bring down the cost of treatment. Therefore, when companies develop their market access strategy, they should include a patient-access scheme in order to enter the UK market.

OBJECTIVES: Achieving market access for new products has become complex for pharmaceutical companies. Faced with growing expenditure, health-care authorities accept or propose various schemes (risk sharing/payment for performance commer- cial): UK’s Department of Health coined a term Patient Access Scheme (PAS) and published specific guidance for the industry. We performed an in-depth analysis of design of PASs in UK to revisit their typology and rationale. METHODS: We reviewed official and grey literature on the Web sites of UK’s HTA Agency—NICE, the Depart- ment of Health and the industry, in the Internet. We searched for documents containing all synonyms of PAS and different scheme types. We selected PASs launched after 2006. RESULTS: We identified 13 PASs, all of which were designed/implemented in consultation with NICE. Drug’s comparative effectiveness was central to the rationale behind the design of PASs. If effectiveness was acknowledged in the HTA, PAS was based on cost-containment (rituximab, erlotinib). If it was not recognized, this was for one of the two reasons: (1) the uncertainty about the long-term effect of the drug, or (2) the value of ICER was questioned in the HTA. In case of (1), the PAS consisted in free provision of the drug by manufacturer after a predefined period (lenalidomide, ranibizumab). In the case of (2), the PAS aimed at lowering the ICER either through cost containment (sunitinib, cetuximab, pemetrexed), through linking payment to outcomes (bortezomib, omalizumab), or by a mix of the two (cetrotuzumab, ustekinumab). CONCLUSIONS: Formalized Health Technology Assessment is both a prerequisite and reason for implementing Patient Access Schemes in the UK. If the comparative effectiveness of a drug is acknowledged, the agreement is based on cost containment. On the other hand, if it is questioned, the PAS may have a form of a risk-sharing scheme and may be linking the payment to health outcomes (performance-based scheme).

OBJECTIVES: Since its establishment, NICE has become increasingly explicit about the way it uses evidence on cost-effectiveness in decision-making—and, more recently, about what it considers. This, together with other ways in which NICE’s decision-making has evolved, suggests a number of testable hypotheses. We propose and empirically test alternative ways that NICE decision-making might be modeled, building on and extending Devlin and Parkin (2004) and Dakin et al. (2006). The large number of NICE decisions now observable facilitates the use of more sophisticated modeling techniques. METHODS: NICE’s decisions are characterized as binary choices: yes or no to a technology in a specifically defined patient group or indication. NICE Guidance often contains multiple such decisions. The probability of NICE recommending a technology is modeled as depending on evidence on effectiveness and cost-effectiveness; characteristics of the patients, disease, or treatment; and contextual factors. Data were obtained from HTAInsite (http://www.htaisite.com) on November 2009. RESULTS: Initial results, drawing on data for 262 decisions, suggest cost-effectiveness alone explains the vast majority of NICE’s decisions, correctly classifying 85%, with high sensitivity and specificity. The estimated threshold, around £45k, is higher than NICE’s stated threshold (£30k–£50k) but similar to that estimated by Devlin and Parkin (2004). Results across alternative model specifications showed that almost none of the other variables exert a statistically significant effect on decisions, with two exceptions. First, technologies for the treatment of cancer have a significantly higher probability of being accepted, ceteris paribus, implying a willingness to pay an additional >£150 per QALY gained by cancer patients. Second, analysis of the subset of decisions made after NICE’s second “social value judgment” document suggests an increase in positive recommendation. CONCLUSIONS: This work in progress further results will be available to report from additional data extraction and modeling.

OBJECTIVES: In the UK, Patient Access Schemes (PAS) have become more common in submissions to the National Institute for Health and Clinical Excellence (NICE). The increase in PAS is a result of the essential role such schemes play in enhancing the accessibility of high-cost treatments to payers. In published appraisals, minimal emphasis has been placed upon the administrative burden of PAS, which is typically described as “acceptable.” The aim of this study was to assess the impact of administering PAS in the UK, using both primary research and existing literature to identify key administrative challenges. METHODS: A literature search was conducted in PubMed and Google Scholar. Freedom of information requests were sent to NICE for data on PAS administration. A pilot questionnaire was distributed to all 19 contacts listed on the directory of NHS Chief Pharmacists in Wales, to assess the real-life burden of PAS administration. RESULTS: Limited literature is available on the administra- tion of PAS. However, the literature search uncovered evidence that the admin- istrative impact of PAS is being recognized. The creation of the Patient Access Scheme Liaison Unit (PASLU) in October 2009 and the publication of the Pharmaceutical Price Regulation Scheme (PPRS) are two such developments, both of which are steps to address a system where medicine progression is a common used strategy to address ethical issues associated with the use of placebo controls, but could lead to statistical challenges for the analysis of key end points such as overall survival. While an advan- tage from the perspective of the treated patient enrolled in the trial, cross-over leads to loss of information and dilution of the comparative clinical efficacy and cost- effectiveness results. OBJECTIVES: The purpose of the study is to compare alternative methods for analyzing overall survival data in the presence of cross-over, thus illuminat- ing differences between methods, and providing guidance on choice of methodology. METHODS: Two promising methods for dealing with cross-over are inverse probabil- ity of censoring weighting and the rank-preserving structural failure time model. The methods are compared with naive censoring of data at cross-over and intention-to-treat analysis ignoring cross-over using two recent examples of trials in oncology: the receptor tyrosine kinase inhibitor sunitinib in renal cell carcinoma (RCC) and in gastrointestinal stromal tumor (GIST). RESULTS: The analyses showed that for a trial with a low proportion of cross-over from placebo to active treatment (RCC), the choice of statistical method did not affect the results to a great extent; the range of relative mortality risk for active treatment versus control was narrow. With a high proportion of cross-over (GIST), the range of relative mortality risks was broader. CONCLUSIONS: Naïve censoring at cross-over can lead to bias and should be avoided. If cross-over occurs frequently, the inverse probability of censoring weighting method or the rank-preserving structural failure time model are recommended depend- ing on the characteristics of cross-over in the trial, trial size, and available data.

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MULTIPLE COHORT MODELING OF LONG-TERM INTERVENTIONS: QUESTIONING TIME HORIZONS AND AGGREGATION ACROSS COHORTS

BACKGROUND: Models are widely used in the cost-effectiveness analysis of health-care interventions. Most models only simulate one patient cohort, but some use multiple cohorts. Advocates of multicotocoh model contend it better represents actual health-care implementation, especially where interventions are applied over specific age ranges, as in cancer screening. When such an intervention is introduced, cohorts already older than the starting age only receive a partial intervention, possibly
resulting in cost-effectiveness different to that of younger cohorts that receive the complete intervention: multi-cohort models can include both these “complete” and “partial” cohorts. Some multi-cohort models described as population models impose finite time horizons at which the intervention is assumed to cease, although health effects are typically assessed until death. ANALYSIS: If cost-effectiveness differs between partial and complete cohorts, then the overall cost-effectiveness estimate from a multi-cohort model will depend on the relative numbers of partial and complete cohorts. The total number of complete cohorts depends on how long the intervention is used, which is uncertain. Therefore, the overall estimate may depend, in part, on the number of future cohorts assumed. The appropriateness of time horizons depends on whether a cross-sectional or a longitudinal cohort approach is used. Assuming an intervention ceases at a time horizon is unrepresentative of actual implementation and many errors in economic models are frequent, many errors often go unnoticed and have significant impact upon a model’s results. This analysis has highlighted the relative importance of each type of error and has provided suggestions as to how these might be avoided.

CONCLUSIONS: Discrepancies in diagnosis, treatment, or prognosis may emerge among physicians. A known decision-making bias is the tendency to shift personal opinion either toward or away from a previous opinion. We sought to evaluate such biases in the context of second-opinion medical consultations. METHODS: We distributed a survey questionnaire to a nationwide sample of orthopedic surgeons and neurologists. The questionnaires presented eight scenarios, each with conventional treatment options with no clear-cut preference. In four scenarios, the physicians were told that a previous opinion had already been given by another physician, or that a second opinion will be given, and the other four scenarios were used as controls. The physicians’ responses were coded according to the level of intervention (conservative to multi-cohort). RESULTS: 172 orthopedic surgeons and 160 neurologists filled out the questionnaires, which represent about 50% of these specialties in Israel. In the orthopedic group, when a first opinion had already been given, there was a shift toward a more interventionist treatment (P = 0.05). This was especially prominent when the first opinion was known to be the opinion of another physician. When the patient intended to seek a second opinion, there was a shift toward a more conservative treatment. No such effect was found among neurologists. CONCLUSIONS: Physicians’ judgements may be affected by another physician’s opinion (compared to their choices without a first opinion). This bias mainly tends toward a more interventionist treatment. Due to the immense impact of any decision on patient health and resource use, further research should address such biases and develop tools to address them.