intervals HPV-based screening was more effective than cytology alone, with a rela-
tive reduction in cervical cancer incidence of 49%-90% and mortality of 33%-80% with
cytology alone (depending on screening intervals). In HPV- compared to cytology
screening the incremental gain in effectiveness was higher with extended screening
intervals and the increase in harms lower. Based on the BII, 12 of 17 screening strate-
gies were evaluated pharmaco-economics, conducted in Germany. Biennial HPV-screening was similarly effective as annual cytology and
reduced unnecessary treatment. Moving from biennial HPV- with cytologic triage
to annual HPV-screening alone results in an incremental harm-benefit ratio of 15.52.
unnecessary treatments per additional prevented cervical cancer case (depending
on screening adherence rate). CONCLUSIONS: The benefit-harm frontier is a useful tool
to demonstrate the trade-off between expected gains and risks of different screening
strategies. Based on the BII, HPV-based cervical screening is more effective
than cytology alone, but has a higher risk of overtreatment when used in annual
screening. In the German health care context, depending on screening adherence
rates of 70%-80% or 90%-95% or 95%-99% or 100%
and quality of life (QoL) by HTA bodies, IQWiG and G-BA, were compared to those
Institute for Quality and Efficiency in Health Care (IQWiG) assessments, and G-BA
Joint Committee (G-BA) website was used to obtain manufacturers’ value dossiers,
the specified level of reduction to define a relevant response varied;
among trials reporting PANS total, five different levels of reduction were defined (≥20%, ≥25%, ≥30%, ≥40%, ≥50%). Common outcomes were also measured differ-
ently in terms of improvement from baseline and proportion achieving response/
remission, with little consensus on clinical meaningfulness. CONCLUSIONS: The
RCTs included in this review reported a broad range of outcomes, making com-
parison of different therapies a complex task. The disparity in outcomes between
chronic obstructive pulmonary disease (COPD) in terms of trough forced expiratory
volume in 1 second (FEV1) at 12 weeks.

OBJECTIVES: To identify and assess the clinical outcomes assessments and endpoint strategies
that can establish treatment benefits. We describe a systematic literature review
of endpoints and outcomes used in schizophrenia trials to determine treatment
METHODS: The therapies selected in the search strategy included pharma-
co- and non-pharmacological therapeutic, interventions and music therapy. These were chosen to reflect the range of interventions in current
use, and to allow comparison between outcomes reported for different therapies.
The interventions were designed to include all outcomes for each therapy area, and
were evaluated in 2012
and to non-pharmacological outcomes scales highlights the chal-
lenge of selecting endpoints that can establish treatment benefits.

PM6M MULTI-DIMENSIONAL CAPTURE OF PATIENT-RELEVANT ENDPOINTS
IN REGULATORY TRIALS AND HEALTH TECHNOLOGY ASSESSMENTS
IN ONCOLOGY TWO YEARS AFTER INTRODUCTION OF THE GERMAN AMNOG
HEALTH CARE REFORM

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OBJECTIVES: With the introduction of AMNOG in January 2011, an early benefit
assessment (EBA) was required for new medicines in Germany. EBA is based on the
additional therapeutic benefit of a drug on patient-relevant endpoints (PREs).
We compared the acceptance of PREs for oncology in regulatory trials, and in EBA
conducted by German health technology assessment (HTA) bodies. METHODS: EBA
on oncology drugs and the respective regulatory trials were reviewed. The Federal
Joint Committee (G-BA) was used to obtain manufacturers’ value dossiers, Institute
for Quality and Efficiency in Health Care (IQWiG) assessments, and G-BA
resolutions. Acceptance of endpoints in the dimensions of mortality, morbidity and
quality of life (QoL) by HTA bodies, IQWiG and G-BA, were compared to those
accepted for regulatory trials. Data on endpoints used in regulatory trials were
obtained from the manufacturers’ value dossiers. RESULTS: Overall survival (OS) and
measures of disease morbidity, such as progression-free survival (PFS), were
prerequisite in stated in the regulatory trials. OS was accepted by IQWiG and G-BA as
a mortality endpoint for evaluating additional benefit. Widely accepted morbidity
endpoints such as PFS were not deemed patient-relevant by IQWiG and G-BA.
In general, questionnaires and psychological regulatory trials were seen.
the accept-
ance of mortality and QoL endpoints typically evaluated in oncology. Considerable
variation was observed in the acceptance of PREs in morbidity. Evaluating addi-
tional benefit only based on mortality and QoL endpoints underestimate the poten-
tial value of new drugs. Multiple endpoints, which capture all three dimensions,
ought to be evaluated in regulatory trials and accepted by IQWiG and G-BA to confirm
patient-relevant additional benefit.

PM65 THRESHOLD SELECTION IN BIOMARKERS USING COX REGRESSION.
AN APPLICATION TO NON-SMALL-CELL LUNG CANCER

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OBJECTIVES: To select thresholds for predictive biomarkers using Cox regres-
sion. METHODS: We used data from a Cuban trial designed to assess the efficacy
of immunotherapy against the epithelial growth factor (EGF) to test our approach.
The trial included 122 patients diagnosed with non-small-cell lung cancer (NSCLC) who had basal EGF concentration available. The EGF concentration was analysed as a predictor of immunotherapy success over the range of all possible values of the biomarker. RESULTS: (a) We selected a threshold. The ratio of the C-index adjusted to assess survival. We then identified the \( w_{th} \) with significant treatment
to find (a) the lowest biomarker threshold where the effect of treatment was
shown, (b) also to find (b) the biomarker thresholds where the effect of treatment was
highest difference between treatments. RESULTS: For NSCLC we observed that EGF
concentration thresholds range from 870 pg/ml to 2000 pg/ml were significant. At the lowest
threshold (870 pg/ml) the immunotherapy group showed a 6-month difference for the
analyzed. Both based on clinical and non-pharmacological aspects at the three most significant differences between treatments (EGF - 1750 pg/ml) the immunotherapy group
pre-
ented a 10-month difference for the median survival (p = 0.004).
CONCLUSIONS: The evaluation of p-values of the effect of treatment for each \( w_{th} \) allows the selection of the thresholds where the treatment result is significant. Whereas the
PRM7 SYSTEMATIC LITERATURE REVIEW AND VALIDATION OF THE EXPANDED DISABILITY STATUS SCALE (EDSS) AND THE MULTIPLE SCLEROSIS FUNCTIONAL COMPOSITE (MSFC) IN PATIENTS WITH MULTIPLE SCLEROSIS

Objective: To conduct a systematic literature search in relevant databases (MEDLINE, PubMed, ISI Web of Science, EMBASE, PsycINFO & PsycNDEX, CINAHL) yielding 3,860 results. The identification of relevant full-text publications was conducted using abstract and key words, and manual search was performed. A total of 1,554 articles were included in the full-text review. The full-text review included both instruments. The EDSS has some documented weaknesses in reliability and sensitivity to change. For the MSFC, the main limitations are the learning effects and the 2-scores method used to calculate the total score. However, the methodological criterion of validity applies sufficiently for both instruments. For use in clinical trials, it is important to consider that the EDSS has been used in a secondary outcome measure in recent studies (50 EDSS, 9 MSFC).

Conclusion: Recognizing their strengths and weaknesses, both EDSS and MSFC are suitable to be used as measures of clinical improvement and to monitor disease progression. Almost all publications identify the EDSS as the most widely used tool to measure disease outcomes in clinical trials. Despite some limitations, both instruments are able to generate “hard endpoints”. In the case of MSFC, different models are suggested as surrogates parameters. A great advantage of the EDSS is the international acceptance (e.g. by EMA) as a primary endpoint in clinical trials and its broad use in trials, enabling cross-study comparisons.

PRM9 IMPACT OF MEDICATION ADHERENCE ON HEALTH CARE COST IN COPD

Objective: To evaluate the impact of medication adherence on health care utilization and costs of the patients with COPD in Hungary. The authors conducted a retrospective observation of the patients continuously enrolled in medical and prescription benefit plans from July 2007 to June 2012. The study is based on patient attendance data of Hungarian National Health Insurance Fund -NHIFA. The accessible resource uniquely contains the detailed provision data (medicine, out- and inpatient services) about the whole 10 millions Hungarian populations. No precise job description was provided, however, and the Danish counties request evidence for the effect of case management (CM). The aim of this study was to (1) determine medication adherence, (2) estimate events and resource usage, and (3) determine adherence and all-cause related medical costs, drug costs, and hospitalization risk were measured. These measures were modeled at varying levels of medication adherence using regression analysis. The study included 150 COPD patients are randomized into two groups after referral to pulmonary rehabilitation. The study is expected to provide further insight to the future organization of CM, and if being cost-effective, the intervention could be applied to comparable health care settings.

PRM10 USING SATURN PLOTS TO DESCRIBE CO-MORBIDITY PATTERNS WITHIN COHORTS

Objective: It is a common practice in outcomes research studies to examine several co-medications over two or more cohorts to develop some intuition about the benefit of one medication against another and to provide additional evidence for the clinical relevance of this medication. The authors used a novel graphical procedure (a Saturn plot) allows an investigator to examine co-morbidity patterns readily when the number of binary co-medications is 10 without having to recode or rescale large tables of indicator variables coded over several binary co-medications based on co-medications. CONCLUSIONS: A newly developed graphical data analysis called a Saturn plot allows investigators to indentify the relative frequency of various subgroups (as defined by their co-morbidity pattern) within a cohort without the need to study large sets of tables.