tries use the European Directive (ED) 2001/20/EC to govern all research (e.g. Germany regional EC), others are in an "evolving process" of coming into "adapted" compliance with the ED (e.g. France); and others have their own independent regulations that are less accessible (e.g. Saudi Arabia). Each country has varying data protection legislation. CONCLUSIONS: For some, regulatory approvals are believed to be easier to acquire from disparate regulatory bodies when no intervention is under study. However, investigators cautioned that their various regulatory authorities do not support natural history studies if they appear to be "large cheap databases" driven by outside countries. More support for such studies is likely if the natural history data serves as an untreated control arm when treatments begin to be tested.

THE IMPLICATIONS OF DIFFERING ASSUMPTIONS REGARDING THE BASIS OF PLACEBO RESPONSES ON THE ESTIMATION OF COST-EFFECTIVENESS

PMC7

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OBJECTIVES: To investigate the relationship between differing assumptions regarding the basis of placebo effects and estimates of cost-effectiveness in non-linear models. METHODS: Responses to placebos observed in randomized controlled trials have a variety of mechanisms including: a “subject-expectancy” effect specific to the experimental situation; a “subject-expectancy” effect generalisable to a clinical situation; and a “regression to the mean” effect arising from natural variation. If the placebo response in a trial with placebo and active treatment responses of $R_{PLC}$ and $R_{TX}$ arose from a trial specific “subject-expectancy”, we would expect to see no response to placebo and $R_{PLC} = R_{LCLB}$ response to treatment in a clinical situation. If the placebo response arose from generalisable “subject-expectancy” or natural variation, we would expect to see $R_{PLC}$ response to placebo and $R_{TX}$ response to treatment in a clinical situation. Estimates of cost-effectiveness from a simple model of an epilepsy treatment, where the expected costs and effects were non-linear with respect to response rate, were obtained under these differing assumptions. RESULTS: The icer assuming a trial specific “subject-expectancy” was $\leq$14,000 and assuming a general “subject-expectancy” or natural variation placebo effect was $\leq$20,000. CONCLUSIONS: For non-linear models the incremental cost-effectiveness ratios and the identification of optimum treatment choice may be sensitive to assumptions regarding the placebo response mechanism. Even where the analysis is based on the results of actively controlled trials, responses may still include an element of placebo effect and the incremental cost-effectiveness ratios may be sensitive to assumptions regarding the basis of this effect. We should also consider that the placebo effect may differ over different dimensions of response, such as initial probability and duration, and also carefully consider the appropriate estimation of the “no-treatment” comparator response rates in clinical situations where the use of placebos is not permissible.

ECONOMIC DECISION MODELLING: CALCULATION OF TOTAL NET MONETARY BENEFITS OF GUIDELINE IMPLEMENTATION INTO CLINICAL PRACTICE

PMC8

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OBJECTIVES: Despite evidence on the cost-effectiveness of clinical guidelines, patients and health care providers do not adhere to guideline recommendations. Implementation strategies aim to change guideline adherence but cost money to enact. As health care resources are limited, it becomes increasingly important to determine whether investing in guideline implementation is worthwhile. METHODS: We developed a model to calculate the total net monetary benefits of guideline implementation for an eligible patient population. By combining evidence on guidelines, current practice and implementation strategies our model allows the determination of the total potential to invest in guideline implementation and the mutual comparison of implementation strategies. We illustrated the use of our model with a hypothetical example and examined the extent to which alternative modelling assumptions influence the efficient allocation of scarce resources. RESULTS: Through illustration of the use; our model, we demonstrated the influence of the threshold value $\varepsilon$, the baseline guideline adherence and the patient population size on the total guideline implementation investment potential and the total net monetary benefits of guideline implementation. CONCLUSIONS: Using a total net monetary benefits approach, our model overcomes problems with the use of policy cost-effectiveness ratios and allows the incorporation of uncertainty surrounding evidence on guidelines, current practice and implementation strategies. Moreover, our model provides simple and useful tool to examine the value for money of guideline implementation and inform policy decisions about efficient allocation of scarce resources.

A REVIEW OF FACTORS AFFECTING THERAPEUTIC COMPLIANCE

PMC9

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OBJECTIVE: To explore the definition of therapeutic compliance and evaluate the most common factors causing therapeutic non-compliance. METHODS: A qualitative review was undertaken by a literature search of the Medline database from 1970 to 2005. The following key words were used: treatment refusal, patient compliance, patient dropouts, factors, predictors and determinants. RESULTS: A total of 7372 articles were retrieved by the literature review process. From the literature review, the most commonly accepted definition of therapeutic compliance is patient’s behaviors (in terms of taking medication, following diets, or executing life style changes) coincide with health care providers’ recommendation for health and medical advice. The preliminary evaluation revealed a number of factors that contributed to therapeutic noncompliance. These factors include: Patient-centered factors: demographic factors (age, gender, ethnicity, education background, marriage status), patients’ beliefs, motivation and attitude about The rapy, patient-prescriber relationship, health literacy, patients’ education, physical difficulties, smoking and alcohol intake, poor quality of life, forgetfulness, a history of noncompliance. Therapy-related factors: treatment complexity, duration of the treatment period, medication side effects, degree of behavioral change required. Social and economic factors: cost, income, social support, health care system factors, and characteristics of the disease. Broadly speaking, factors related to poor therapeutic compliance can be categorized to intentional factors and non-intentional factors. They are complicated and not fully predictive. CONCLUSION: From the review, it would appear that there are numerous studies on the issue of therapeutic noncompliance, the definition of therapeutic compliance is adequately addressed and generally accepted by the clinical communities. Regarding reasons for therapeutic non-compliance, there are many factors being reported and studied over the years, but the evidence is sometimes con-
tradictory and variable except a few important issues. From the perspective of clinical health care delivery, therapeutic noncompliance remains a major problem in enhancing health care outcomes.

**Abstracts**

**PMCI0**

**ESTIMATING UTILITY VALUES FOR HEALTH STATUS USING THE SPANISH VERSION OF THE SF-36, IS IT WORTHY TO CALCULATE WEIGHT VALUES FOR UTILITY MEASURES?**

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**OBJECTIVES:** A new utility index derived of the SF-36, the SF-6D, was recently developed and has an increasing research in different groups of patients and has also been compared with other utility measures, as it is the EQ-5D. The purpose of present work was to evaluate the differences between the weighted and not weighted version of two utility measures: the Spanish SF-6D and EQ-5D.

**METHODS:** A total of 1843 complete measures of the SF-36 and the EQ-5D (5 items and visual analogic scale-VAS) from 1283 patients who received a solid organ transplant (kidney, liver, heart or lung) were used. Data were collected at different moments during the first year after the surgery in the context of the Spanish Research Network on Transplantation. SF-6D values were calculated using the model proposed by its creator (weighted version) and without tariff values, as has been proposed by some authors (not weighted). EQ-5D values were calculated using Spanish VAS tariff (VAS-t), the time-trade off tariff (TTO-t) and also without tariff values (not weighted). Spearman correlation coefficients were calculated between SF-6D (weighted and not weighted) and EQ-5D values (VAS-t, TTO-t and not weighted). RESULTS: Mean value of weighted SF-6D was 0.67 (0.15) and not weighted, 0.72 (0.15). Mean values of EQ-5D VAS-t was 0.69 (0.24), of TTO-t, 0.70 (0.32) and of not weighted EQ-5D, 0.63 (0.33). SF-6D values had moderate correlation with EQ-5D VAS-t (r = 0.734) and EQ-5D TTO-t (r = 0.731) (both p < 0.001). Using the SF-6D index without tariff values, it had a high correlation with the weighted version of SF-6D (r = 0.969, p < 0.001), and moderate with the EQ-5D VAS-t (r = 0.754), EQ-5D TTO-t (r = 0.750) and no weighted EQ-5D (r = 0.784) (p < 0.001). CONCLUSIONS: The efforts made to get the preferences values and calculate the weights in utility indexes do not seem to add enough information to make them worthy.

**PMCI1**

**EFFECTIVE USE OF ELECTRONIC DATA CAPTURE (EDC) TO IMPROVE THE QUALITY AND EFFICIENCY OF THE ANALYSIS OF PATIENT REPORTED OUTCOMES**

Ooms KL

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**OBJECTIVES:** It is well recognised that electronic data capture (EDC) is revolutionising the data collection and management of clinical trials data especially for pre-registration Phase I to III studies. We will discuss the benefits of the use of EDC for patient reported outcomes especially within the context of large observational studies.

**METHODS:** Using EDC, patient reported outcome data are collected directly by the patient onto the data capture device; this can be either a tablet pc at the study site or using a PDA for diary data. Whilst the patient is entering data, the device will prompt them if they do not fill in the questionnaire correctly or do not complete particular questions.

**RESULTS:** Even this simple interaction with the patient of ensuring the answer provided is the most appropriate one improves the quality of the patient reported outcome data. For example, the query rate for these data is usually reduced from 6 to 10 fold compared with paper CRF collection and of course for patient reported data these queries usually cannot be updated so that these data remain inconsistent and of poorer quality. Other benefits include the on-line reporting of data which is especially beneficial for observational studies of moderate to long duration. Often several statistical reports are made from these data for example by conducting interims for baseline data, 3-month, 6-month, and 1-year data, etc. These reports were often produced several months after the last data were collected due to the delay between data processing of paper CRF data and the processes involve with statistical reporting. **CONCLUSIONS:** Now it is possible to provide near real-time access to reports via EDC working with a suite of pre-validated statistical programs. These can be produced on an on-going basis, for example we can update our reports daily.

**PMCI2**

**REVIEW ON THE IMPACT OF DOSE FREQUENCY ON COMPLIANCE AND HEALTH OUTCOMES**

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**OBJECTIVE:** Conduct a systematic review of the literature on delayed-action dose preparation compared to regular dose preparation, and to examine the impact of a change in dose frequency on compliance and health outcomes (e.g., health-related quality of life, patient satisfaction, treatment costs), as well as efficacy and tolerability profile.

**METHODS:** The medical literature databases MEDLINE and Cochrane Library were reviewed from 1966 through 2006 for published, peer-reviewed articles. Search terms were combinations of “delayed-action preparations”, “dose frequency”, “dose administration schedule”, “dosing” and “efficacy”, “safety”, “clinical effectiveness”, “preferences”, “adherence”, “compliance”, “persistence”, “health-related quality of life”, “patient satisfaction”, “resource use”, and “costs”. References from identified articles were not used to expand the search. Two reviewers independently reviewed titles, abstracts, and finally full-text articles. A total of 57 peer-review articles were selected for the full-text review, including 14 literature/systematic reviews and 2 meta-analysis articles.

**RESULTS:** All of the clinical studies, except 2, support better or comparable efficacy when using a simple dose (e.g., weekly dose vs. multiple doses per week or once-daily versus twice-daily or three-times-daily) to treat clinical symptoms in the following disease areas: cardiovascular disorders, diabetes, neurological/psychological disorders, rheumatoid/muscle disorders, nephrology/urology disorders. Along with literature/systematic reviews and meta-analysis articles, these studies have supported the general advantages of reducing dosing frequency on improved compliance (16 studies), improved quality of life or patient satisfaction (8 studies), greater control over side effects (3 studies), and improved economic outcomes using extended-release formulation (2 studies).

**CONCLUSION:** In general, reducing dose frequency by using a delayed-action dose may offer benefits for patients in terms of improving medication compliance, effectiveness and adverse effect profiles, while possibly reducing health care costs. However, physicians and patients need to bear in mind that the wide variety of delivery systems are available to find the most appropriate one for a particular patient.