

# Health Economics Extraction for Question

## Which interventions are effective in increasing adherence to prescribed medication?

<b>No</b>	1518	<b>Cost effectiveness of an adherence-improving programme in hypertensive patients</b>
<b>Author:</b>	Brunenberg-Danielle EM;Wetzels-Gwenn EC;Nelemans PJ;Dirksen CD;Severens JL;Stc 2007 Henri EH;Schouten-Jan SG;Prins MH;de-Leeuw PW;Joore MA;	
<b>Relevance</b>		
<b>Intervention:</b>	Medication events monitoring system (MEMS) plus adherence training	
<b>Comparison:</b>	usual care alone	
<b>Population:</b>	164 hypertensive patients in the MEMS arm and 89 in usual care group with systolic BP >160mm Hg and/or diastolic >95mm Hg despite use of antihypertensive drug eligible. Adherence was defined as intake minimum 85% of days as prescribed.	
<b>Perspective:</b>	health care and societal	
<b>Study type:</b>	CUA	
<b>Methods:</b>	RCT	
<b>Health valuations:</b>	TTO	
<b>Cost components</b>	Healthcare utilization (intervention, drug, consultation etc) and patient borne medical costs (Health care perspective) as non-medical costs (societal perspective).	
<b>Currency:</b>	EURO	
<b>Cost year:</b>	2002	
<b>Time horizon:</b>	5 months	

**Discount rate:** not applicable

**Results-cost** MEMS cost EUR26 per patient, but led to a saving of drug costs of EUR40. Reduction in drug costs is mainly due to percentage of patients with drug additions or dose escalations in the MEMS arm. The mean total health care costs amounted to EUR827 in the experimental group and 927 in the usual care arm. This is a non significant negative diff of EUR100 (95%CI -415 to 189).

**Results-effectiveness** At 5 months, 53.7% of MEMS patients had NBP compared to 50.6% in usual care (diff +3.1% 95CI -9.7 to 15.8). An incremental 0.003 QALYs were generated (95CI -0.005 to 0.01) in the experimental arm.

**Results-ICER:** From the healthcare perspective, electronic monitoring led to a cost saving of EUR100 and an additional 3.1% patients achieved NBP than in the usual care arm and was therefore dominating. From a societal perspective, and when using as outcome measure, the incremental costs for the 5month programme of EUR47 resulted in an ICER of EUR15 667 QALY gained.

**Result-Uncertainty:** Univariate SA revealed considerable uncertainty. From a healthcare perspective, the probability that MEMS is cost effective is estimated to be at maximum 77%. This dropped to 69% in sensitivity analysis. The effect sizes were small and not statistically significant, and results varied depending on what perspective and outcome measure was chosen. From both perspectives, the CEA bootstrap replicates on the CE plane covered the origin. The CEAC from the societal perspective suggests the very high uncertainty by ranging from 45% to 51% in the base case analysis, which did not improve in sensitivity analysis.

**Source Funding:** Public

**Comments:** The probability that this AEI in hypertensive patients is cost effective is at best moderate as there is considerable uncertainty around the ICER. However, if in the UK the costs for electronic monitoring do not exceed those of a potential drug cost saving, even a moderate increase in adherence would be cost effective. It appears uncertain as to whether certain conclusions can be drawn from this analysis.

**No** 1514 **Cost effectiveness of long-acting risperidone injection versus alternative antipsychotic agents in with schizophrenia in the USA**

**Author:** Edwards NC;Locklear JC;Rupnow MF;Diamond RJ; 2005

**Relevance**

<b>Intervention:</b>	Long acting risperidone
<b>Comparison:</b>	Oral atypical antipsychotic agents (oral risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole) and depot haloperidol injections
<b>Population:</b>	Patients with schizophrenia in community dwelling who have previously suffered relapse requiring hospitalisation.
<b>Perspective:</b>	NHS (health care)
<b>Study type:</b>	CEA
<b>Methods:</b>	DECISION ANALYSIS
<b>Health valuations:</b>	NOT APPLICABLE
<b>Cost components</b>	Health care resource utilization estimates from literature and expert opinion. Pricing with published unit costs to derive direct and indirect medical costs.
<b>Currency:</b>	US\$
<b>Cost year:</b>	2003
<b>Time horizon:</b>	One year
<b>Discount rate:</b>	Not applicable
<b>Results-cost</b>	Using long acting risperidone rather than an oral atypical antipsychotic agent is predicted to result in US\$161 of health savings per patient per year compared with oral risperidone and higher costs savings when compared with other agents seems largely attributable to a reduction in relapse rates on the basis that compliance was imputed in the model as tripled with long acting risperidone.
<b>Results-effectiveness</b>	The model predicts that patients receiving long acting risperidone will have the best clinical outcomes in terms of the frequency and duration of relapses over the one year duration. For example, on long acting risperidone 26% of patients experience relapse requiring hospitalisation and 24% relapse not requiring hospitalisation. On haloperidol nearly two patients are predicted to have relapses requiring hospitalisation and over 60% not requiring hospitalisation.
<b>Results-ICER:</b>	This analysis predicts dominance of long acting risperidone over the comparators, with providing a health outcome improvement in terms of days of relapse averted whilst costing less over the time horizon of one year.
<b>Result-Uncertainty:</b>	Univariate sensitivity analysis was reported to have been robust. However, at the upper bound of the 95%CI for relapse requiring hospitalisation there was an incremental cost for long acting risperidone with an ICER of US\$821 per days of relapse averted.

hospitalisation averted compared to oral risperidone. The model seems also sensitive to the cost of hospitalisation at frequency rates of relapse.

**Source Funding:** Private

**Comments:** Compliance was assumed to be improved by long acting formula. It was estimated that a 20% point difference in cost would predict a 3.1 point improvement in the PANSS (Positive and Negative Syndrome Scale for Schizophrenia). Such improvement in turn stabilised patients so that a further 6.1 point in PANSS was achieved by further improved medication taking behaviour, and aversion of relapse.

The analysis seems of interest, but there are issues with its robustness. Values used in the SA seem relatively conservative. The short time horizon could be an issue and has not been thoroughly discussed. Quantifying treatment effect and quality of life losses in one measurement such as the QALY could considerably help interpret the findings from the analysis.

**No** 1513 **Clinical and economic outcomes of nonadherence to highly active antiretroviral therapy in patients with human immunodeficiency virus**

**Author:** Munakata J;Benner JS;Becker S;Dezii CM;Hazard EH;Tierce JC;Munakata J;Benner JS;Becker S;Dezii CM;Hazard EH;Tierce JC; 2006

**Relevance**

**Intervention:** HAART, ideal adherence (based on RCT data)

**Comparison:** HAART, typical adherence (based on observational data)

**Population:** HIV positive, mean age 33 (20-60) with assumed proportion of drugs consumed of 0.98 (0.95-1.0) if adherent and 0.55 (0.3-0.88) if nonadherent. Proportion of patients adherent in the typical comparator arm 0.52 (0.3-0.88).

**Perspective:** SOCIETAL

**Study type:** CUA

**Methods:** DECISION ANALYSIS

**Health valuations:** n/a

**Cost components** Drug costs, annual costs per HIV and AIDS event, AIDS related end of life event, costs of treatment failure.

**Currency:** US\$

**Cost year:** 2002

**Time horizon:** Lifetime horizon

**Discount rate:** 3% for costs and outcomes, varied between 0 to 5%.

**Results-cost** Lifetime discounted costs in the typical and ideal scenarios were \$308 000 and \$341 000, respectively. This gives an incremental cost of \$33 000.

**Results-effectiveness** People in the ideal scenario generated 10.2 QALYs per patient compared to 9.0 QALYs per patient in the typical scenario. This gives an incremental effect of 1.2 QALYs.

**Results-ICER:** The iCER resulted in \$29 400 per QALY. This means that there is scope for an AEI. The authors calculated a wTP value for an intervention to increase adherence. They conclude that \$1 600 could be spent per patient to increase adherence to ideal levels, giving 15-33% reductions in treatment failure.

**Result-Uncertainty:** Univariate sensitivity analysis for all parameters, as well as multivariate SA for selected values. The analysis was deemed robust in SA.

**Source Funding:** Private

**Comments:** In severe diseases where adherence and related comorbidities are a big issue, adherence improving interventions are more effective. Given that there are interventions that are effective in increasing adherence, this analysis found that \$1 600 per patient could be spent.

**No** 1512 **The economic implications of non-adherence after renal transplantation**

**Author:** Cleemput I;Kesteloot K;Vanrenterghem Y;De GS; 2004

**Relevance**

<b>Intervention:</b>	Renal transplantation
<b>Comparison:</b>	Haemodialysis
<b>Population:</b>	126 Patients with chronic renal failure, aged > 18 and varying adherence levels. Of these, 23 received renal transplanta electronic event monitoring (EEM), 5 were defined nonadherent with medication which account for 21%.
<b>Perspective:</b>	SOCIETAL
<b>Study type:</b>	CUA
<b>Methods:</b>	DECISION ANALYSIS on the basis of a prospective study
<b>Health valuations:</b>	EQ-5D based TTO
<b>Cost components</b>	Direct costs of treatment and hospitalisation, costs of follow up, indirect costs and patient travel expenses. Productivi were considered but not included as only few patients were working.
<b>Currency:</b>	EURO
<b>Cost year:</b>	2000
<b>Time horizon:</b>	1 year follow up
<b>Discount rate:</b>	3% for costs and outcomes. Tested in SA.
<b>Results-cost</b>	Lifetime costs after transplantation in the adherent patient group are higher than lifetime costs in the non adherent gr mainly because adherent patients live longer after transplantation.
<b>Results-effectiveness</b>	Compared with dialysis, renal transplantation offers better outcome in both adherent and nonadherent patients.
<b>Results-ICER:</b>	Transplant dominated haemodialysis on all adherence levels and was therefore found to be more cost effective. When adherence is assumed, transplant generates a cost saving relative of dialysis and 5.19 additional QALYs. In a heterc group of adherent and nonadherent patients, the saving was greater but fewer QALYs were generated (5.06). This w due to a reduced life expectancy. Among transplant patients, adherence with immunosuppressants after transplantat associated with a QALY gain, albeit at a higher cost which was mainly due to a longer overall life span. Mean costs   QALY in adherent patients relative to nonadherent patients after transplantation was EUR 35 021 (95%CI 26 959 - 4 This leaves scope for an adherence enhancing intervention, assuming a willingness to pay of £20 000 per QALY or of 2004.

**Result-Uncertainty:** First and second order MonteCarlo simulations and non parametric bootstrapping revealed that the model results are robust against changes in values. The 95% confidence interval did not exceed the upper bound of the WTP threshold that were not based on published evidence (discount factors, QALY loss) were specifically subjected to sensitivity analysis but not found to have a decision rule changing impact. Recent papers on rates of graft loss may indicate that the ICER between adherent and nonadherent patients is lower as adherent patients may benefit more from better prognosis.

**Source Funding:** Public

**Comments:** This study illustrates the effect nonadherence can have on the findings of an economic evaluation. Assuming full or perfect adherence, which seems common in RCTs, has the tendency to overestimate cost effectiveness by producing more favorable results in a scenario like this study.

This study could not measure long term comorbidities of nonadherence. Had their costs in terms of treatment and QALYs been factored in, this would have resulted in a higher potential WTP for an AEI.

## Does change in dosing regime affect adherence?

**No** 1517 **Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants**

**Author:** Bosmans JE;Brook OH;Van-Hout HJ;De-Bruijne MC;Nieuwenhuysen H;Bouter LM;Stalm 2007  
WB;Van-Tulder MW;

### Relevance

**Intervention:** Pharmacist led education and coaching intervention (3 personal contacts, 1 take home video) plus standard care

**Comparison:** Usual care including standard oral and written information

**Population:** Adults in urban and rural areas with 'new episode (not used antidepressant in previous six month period)' prescription of tricyclic antidepressant from GP for depressive complaints.

**Perspective:** SOCIETAL

<b>Study type:</b>	CEA
<b>Methods:</b>	RCT
<b>Health valuations:</b>	NOT APPLICABLE
<b>Cost components</b>	Direct medical (not hospitalisation!), treatment and intervention costs as well as productivity losses due to work absence
<b>Currency:</b>	EURO
<b>Cost year:</b>	2002
<b>Time horizon:</b>	Six months
<b>Discount rate:</b>	Not applicable
<b>Results-cost</b>	In both groups, the main contributor to costs were productivity costs. Mean total costs were EUR3275 in the intervention group and EUR2961 in the control group. This resulted in an insignificant cost difference between intervention and control groups of EUR315 (95% CI -1922, 2416).
<b>Results-effectiveness</b>	Adherence was measured using an electronic pill container (eDEM) and was primary outcome, with the Hopkins depression 13 item subscale (SCL) used as secondary outcome for depressive symptoms. Mean adherence did not differ significantly between the intervention group (88%) and the control group (86%) at six months (mean difference 2.1%, 95% CI -5.6 to 5.4). In respect to SCL subscale, there was no statistically significant difference between the groups either despite a slight improvement in the pharmacist intervention group (-0.15, 95% CI -0.54, 0.23).
<b>Results-ICER:</b>	The ICER for coaching and education by pharmacists compared with usual care was EUR149 per 1% improvement in adherence and EUR2550 per point improvement in the SCL depression mean item score.
<b>Result-Uncertainty:</b>	Uncertainty was considerable, reflected by insignificance of mean differences. Pairs of costs and effects were distributed in all four quadrants of the cost effectiveness plane. The CEAC for adherence was extremely uncertain, guiding decision makers to have little belief that coaching and education by pharmacists is cost effective as a means of increasing adherence to antidepressants compared with usual care. Changes in Sensitivity analysis (per protocol analysis, univariate parameter changes) had little impact on results.
<b>Source Funding:</b>	Public



**Comments:**

Patients with higher levels of education had higher completion rates of follow up assessments, which in turn had a significant association with compliance levels. Further limitations include the use of the eDEM, which is described as the gold standard for adherence measurement, however, its use itself could have increased adherence. Withdrawal rates were found to be relatively high which the authors attempted to account for by additional analysis. Also there may be an issue with effectiveness; however, the authors state that more data from participants was unlikely to make the intervention appear favourable.