Clinical / economic question: 2

Inpatient/Outpatient detoxification services versus no treatment

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Parrot, 2006 UK	Minor Limitations[a]	Directly applicable	Based on a single study of an outpatient detoxification service carried out at the Smithfield Centre in Manchester. Time horizon of 6 months. Not cost-effective at NICE threshold.	1316[b]	0.033	39 867	No sensitivity analysis conducted
Parrot, 2006 UK	Minor Limitations[c]	Directly applicable	Based on a single study of a partial hospitalisation programme that was performed at Plummer Court. Time horizon of 6 months. Not cost-effective at NICE threshold.	1246[d]	0.008	155 773	No sensitivity analysis conducted

[a] The effectiveness evidence came from a within-group comparison study as no external group was used. The absence of a non-treatment group/usual care group limits the validity of the study results since the changes in the outcome measures might have occurred without the intervention. In effect, the baseline values were implicitly assumed to reflect a no-intervention condition. Moreover, time-dependent confounding variables could not be controlled due to the design of the study, and this might represent a limitation of the analysis. The evidence for each programme came from a single centre, which may not be representative of other institutions. Similarly, the small number of patients and the substantial loss to follow-up further limit the robustness of the analysis.

[b] Inflated form 2003-04 UK pounds to 2009 values using Hospital and Community Health Services (HCHS) indices (Curtis, 2009)

[c] The effectiveness evidence came from a within-group comparison study as no external group was used. The absence of a non-treatment group/usual care group limits the validity of the study results since the changes in the outcome measures might have occurred without the intervention. In effect, the baseline values were implicitly assumed to reflect a no-intervention condition. Moreover, time-dependent confounding variables could not be controlled due to the design of the study, and this might represent a limitation of the analysis. The evidence for each programme came from a single centre, which may not be representative of other institutions. Similarly, the small number of patients and the substantial loss to follow-up further limit the robustness of the analysis.

[d] Inflated form 2003-04 UK pounds to 2009 values using HCHS indices (Curtis, 2009)

Inpatient versus Outpatient alcohol treatment

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Pettinati, 1999 UK	Potentially serious limitations[e]	Partially applicable[f]	Cost-effectiveness ratio was calculated by dividing treatment costs by the probability of returning to significant drinking rather than incremental costs divided by incremental effects	Unable to calculate	Unable to calculate	Unable to calculate	No Sensitivity Analysis

[e] Only costs of treatment services calculated; unclear where unit costs were obtained from; no incremental analysis of costs and outcomes
[f] US health care system; no QALYs measured – array of clinical outcomes measured

Clinical / economic question: question 3

Acamprosate versus usual care/placebo

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Annemans, 2000 Belgium	Potentially serious limitations[g]	Partially applicable[h]	Costing analysis. Treatment effect outcomes reported as well. Time Horizon: 24 months	-577[i]	7% abstinent	-82 / percentage of patients remaining abstinent	The sensitivity analysis looked at the proportion of patients followed up in an institution following detoxification (base case value: 0.541), the cost of acute hospitalisation and the effectiveness of acamprosate, expressed as the probability of relapse at 3 months (base case value: 0.586). Acamprosate was shown to be cost saving at a follow-up rate of =>24%, acamprosate was cost-saving at hospitalisation costs of =>50% of actual costs, and at relapse rates <= 59% acamprosate was cost-saving. This was the most sensitive estimate
NCCMH, 2010 UK	Minor limitations[j]	Directly applicable	Cost-utility analysis based on decision model. Time horizon 12 months	139	0.027	5,043 / QALY	Probabilistic Sensitivity Analysis (PSA): At a cost-effectiveness threshold range of £20-30,000, the probability of acamprosate being most the cost-effective treatment was 52-53%

[g] Belgian population and health care system Effectiveness estimates from several sources: Whitworth et al. 1996. NEAT study unpublished data.
[h] Conducted in Belgium –Institute of health insurance perspective; no QALYs estimated but health outcome measure may be relevant
[i] Converted from 1997 German Euros using a PPP exchange rate of 0.89(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[j] Short time horizon (12 months); Clinical efficacy data based on network meta-analysis subject to a number of assumptions

Palmer, 2000 Germany	Potentially serious Limitations[k]	Partially applicable[l]	A Markov model was used in addition to a set of sub-models simulating the progression of important complications of was constructed in parallel to allow for the patients to develop more than one complication concurrently. Time Horizon: Lifetime (5% discount rate)	-1672[m]	0.52 LYG	-3 216 / Life Year Gained	The sensitivity analyses suggested that, on the life expectancy side, the probabilities of hepatic disease, suicide and relapse rate had the greatest impact on the study results. On the cost side, the probability of relapse in the first year, suicide at age 45, various liver complications, alcohol psychosis, and the costs of treatment of chronic pancreatitis and alcohol dependence, had the greatest impact on the study results.
Rychlik, 2003 Germany	Potentially serious limitations[n]	Partially applicable[o]	Cost-effective analysis. Average cost ratios reported as costs per abstinent rate	-342[p]	Additional 12% of cohort abstinent over 12 mo	-2 853 / % of cohort abstinent over 12 mo	No sensitivity analysis
Schadlich 1998 Germany	Potentially serious limitations[q]	Partially applicable[r]	Cost-effective analysis. Average cost ratios reported. Time Horizon: 48 weeks treatment and 48 weeks of follow up	-59 9421[s]	226 additional patients who were abstinent	-2 652/ [t]additional abstinent patient	-414 to -9002/ additional abstinent patient (Lower and upper cost boundary) Acamprosate was found to be cost saving in 78% of the scenarios tested. The parameter with the greatest impact on results was the rate of abstinence under acamprosate therapy.
Slattery, 2003 Scotland	Minor Limitations [u]	Partially applicable[v]	Effectiveness data based on SIGN meta-analysis and combined with Scottish NHS cost data. 12 months of drug treatment	-10 3713[w]	84 additional patients abstinent	-1 237 / additional abstinent patient	4643 - -3477/ additional abstinent patient: range in one way sensitivity analysis

[k] Data used to estimate costs and effects are not reported or described adequately. This may potentially bias results. Funded by industry
[l] Conducted in Germany –health insurance perspective; no QALYs estimated but health outcome measure may be relevant
[m] Converted from 1996 German DM using a PPP exchange rate of 0.99(www.oecd.org/std/ppp) then inflated by using HCHS indices (Curtis, 2009)
[n] German population and health care system Results not subject to sensitivity analysis, effectiveness data based on naturalistic study, funded by industry
[o] Conducted in Germany –health insurance perspective; cost year not clear, no QALYs estimated but health outcome measure may be relevant
[p] Converted from 1998 German euro using a PPP exchange rate of 0.88(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[q] Some uncertainty over the applicability of German trial data (PRAMA study) to the UK. Maybe differences in population as well as healthcare resource use and unit costs in Germany. Efficacy data derived selectively from PRAMA study; funded by industry
[r] Conducted in Germany –German health care system perspective; no QALYs estimated but health outcome measure may be relevant
[s] Converted from 1995 German DM using a PPP exchange rate of 1.00(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[t] Negative ICER indicates that Intervention is dominant i.e. cheaper and more effective
[u] Some limitations in reporting e.g. sources of effectiveness data not explicitly stated. However, costings based on Scottish NHS perspective. Measure of benefit does not follow NICE reference case, however the health outcome may be relevant
[v] Some uncertainty over the applicability of trial data to UK because of differences in populations and severity. However, resources use, costs and perspectives are Scottish-UK specific. However the discount rate does not follow the NICE reference case.
[w] 2002 Scottish pounds inflated using HCHS indices (Curtis, 2009)

Naltrexone versus placebo/usual care

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Mortimer, 2005 Australia	Potentially serious Limitations[x]	Partially applicable[y]	Uses Markov modelling. Only study to use QALYs as measure of benefit. Time horizon: Life time	404[z]	0.0528	7647/ QALY	2196 - ∞ £/ QALY range in one way sensitivity analysis
NCCMH, 2010 UK	Minor limitations[aa]	Directly applicable	Cost-utility analysis based on decision model. Time horizon 12 months	133	0.024	5,395 / QALY	Probabilistic Sensitivity Analysis (PSA): At a cost-effectiveness threshold range of £20-30,000, the probability of naltrexone being most the cost-effective treatment was 44-45%

[x] Some uncertainty over applicability of the study to the UK due to potential differences in populations. Effectiveness data sourced from Streeton and Whelon, 2001 meta-analysis. Perspective of the department of Health and Ageing adopted. 5% discount rate used which is not in keeping with NICE reference case. Sources of certain data e.g. Unit costs not explicit.
[y] This is the only study that reports QALYs. However, the source and methods of determining the utility data was not adequately described.
[z] Converted from 2003 AUD using a PPP exchange rate of 1.35(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[aa] Short time horizon (12 months); Clinical efficacy data based on network meta-analysis subject to a number of assumptions

Slattery, 2003 Scotland	Minor Limitations [bb]	Partially applicable[cc]	Effectiveness data based on SIGN meta-analysis and combined with Scottish NHS cost data. 6 months of treatment	125 536[dd]	55	2 289/ additional abstinent patient	29 476 - -2945/ additional abstinent patient: range in one way sensitivity analysis

[bb] Some limitations in reporting e.g. sources of effectiveness data not explicitly stated. However, costings based on Scottish NHS perspective. Measure of benefit does not follow NICE reference case, however the health outcome may be relevant

[cc] Some uncertainty over the applicability of trial data to UK because of differences in populations and severity. However, resources use, costs and perspectives are Scottish-UK specific. However the discount rate does not follow the NICE reference case.

[dd] 2002 Scottish pounds inflated using HCHS indices (Curtis, 2009)

Disulfiram or Combinations of Drugs versus placebo/usual care

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Slattery, 2003 Scotland	Minor Limitations[ee]	Partially applicable[ff]	Effectiveness data based on RCTs of unsupervised disulfiram therapy. Costs of supervision however included. 6 months of treatment	230 496[gg]	38	6 103/ additional abstinent patient	40 716/ additional abstinent patient - Std care dominates :range in one way sensitivity analysis
Zarkin 2008 USA	Potentially serious limitations[hh]	Partially applicable	Based on COMBINE study set in 11 US study centres. 9 combinations of drugs and psychological interventions compared. Results were sensitive to the price of drugs. Time horizon: 16 weeks	226[ii]	0.5 % days abstinent (PDA)	452/ PDA[jj]	Under the high pharmaceutical price scenario, naltrexone was approximately 3 times more expensive than the baseline case; acamprosate was approximately 15% more expensive. The results of the 2-way sensitivity analysis were the same as the 1-way analysis when pharmaceutical prices are varied.

[ee] Some limitations in reporting e.g. sources of effectiveness data not explicitly stated. Furthermore, effectiveness data based on unsupervised disulfiram studies; however, costings include supervision costs. Costings, are however, based on Scottish NHS perspective. Measure of benefit does not follow NICE reference case, however the health outcome may be relevant

[ff] Some uncertainty over the applicability of trial data to UK because of differences in populations and severity. However, resources use, costs and perspectives are Scottish-UK specific. However the discount rate does not follow the NICE reference case.

[gg] 2002 prices inflated using HCHS indices (Curtis, 2009)

[hh] Some uncertainty over the applicability of US trial data to the UK. Differences in health care systems may result in differences in population (insured only) as well as healthcare resource use and unit costs.

[ii] Converted from 2007 US $ using a PPP exchange rate of 0.65(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)

[jj] This is the ICER for the most cost effective intervention i.e. Medical management, acamprosate and naltrexone

Acamprosate versus Naltrexone

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
NCCMH, 2010 UK	Minor limitations[kk]	Directly applicable	Cost-utility analysis based on decision model. Time horizon 12 months	5	0.003	1,899 / QALY	Probabilistic Sensitivity Analysis (PSA): At a cost-effectiveness threshold range of £20-30,000, the probability of acamprosate being most the cost-effective treatment was 52-53%

[kk] Short time horizon (12 months); Clinical efficacy data based on network meta-analysis subject to a number of assumptions (see Guideline chapter 7)

Clinical / economic question: question 4

Any psychological intervention versus standard care							
Study & country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)**	**Incremental effect (QALYs)**	**ICER (£/QALY)**	**Uncertainty**
Slattery, 2002 Scotland -UK	Minor Limitations [ll]	Partially applicable [mm]	Effectiveness data based on SIGN meta-analysis and combined with Scottish NHS cost data. Intervention- Coping/Social Skills training.	-412 287[nn]	122 additional patients abstinent	-3379 Dominate	Coping/Social Skills Training Dominates Standard care to ICER of 82 654/ additional abstinent patient: range in one way sensitivity analysis
Slattery, 2002 Scotland -UK	Minor Limitations	Partially applicable	Intervention: BSCT	-121 052	86	-1408 Dominate	BSCT Dominates Standard care to ICER of 219 706/ additional abstinent patient: range in one way sensitivity analysis
Slattery, 2002 Scotland –UK	Minor Limitations	Partially applicable	Intervention: MET	-228 290	99	-2306 Dominate	MET Dominates Standard care to ICER of 103 767/ additional abstinent patient: range in one way sensitivity analysis
Slattery, 2002 Scotland -UK	Minor Limitations	Partially applicable	Intervention: Marital/Family Therapy	-276 548	105	-2634 Dominate	Marital/Family Therapy Dominates Standard care to ICER of 24 943/ additional abstinent patient: range in one way sensitivity analysis

[ll] Some limitations in reporting e.g. sources of effectiveness data not explicitly stated. However, costings based on Scottish NHS perspective. Measure of benefit does not follow NICE reference case, however the health outcome may be relevant

[mm] Some uncertainty over the applicability of trial data to UK because of differences in populations and severity. However, resources use, costs and perspectives are Scottish-UK specific. However the discount rate does not follow the NICE reference case.

[nn] 2002 prices inflated using HCHS indices (Curtis, 2009)

Any psychological intervention versus Any other psychological intervention							
Study & country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)**	**Incremental effect (QALYs)**	**ICER (£/QALY)**	**Uncertainty**
Mortimer, 2005 Australia	Potentially serious Limitations [oo]	Partially applicable[pp]	Uses QALYs as measure of benefit. Interventions: MOCE vs. BSCT. The use of different effectiveness outcomes results in different results- CEA and CUA conducted with Markov model	147[qq]	0.116	1265 or BSCT dominates MOCE	353/QALY to BSCT dominates MOCE: range in sensitivity analysis
Mortimer, 2005 Australia	Potentially serious Limitations[rr]	Partially applicable[ss]	Interventions: MET vs. No further counselling (NFC) after initial assessment and feedback/education	229[tt]	0.116	1984 or MET dominates NFC	400/QALY to NFC dominates MET: range in sensitivity analysis
Mortimer, 2005 Australia	Potentially serious Limitations [uu]	Partially applicable[vv]	Interventions: Non-directive reflective listening (NDRL) vs. No further counselling after initial assessment and feedback/education	-	-	NFC dominates	590/QALY to NFC dominates NDRL: range in sensitivity analysis

[oo] Some uncertainty over applicability of the economic study to the UK due to potential differences in health care settings. Effectiveness data sourced from Heather et al.2000 RCT based in England. Perspective of the department of Health and Ageing adopted. 5% discount rate used which is not in keeping with NICE reference case. Sources of certain data e.g. Unit costs not explicit.
[pp] This study reports QALYs. However, the source and methods of determining the utility data was not adequately described- the estimate of QALYs gained from the modelled cost-utility analysis was derived from a number of data sources with varying levels of error and uncertainty.
[qq] Converted from 2003 AUD using a PPP exchange rate of 1.35(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[rr] Some uncertainty over applicability of the study to the UK due to potential differences in populations. Effectiveness data sourced from RCT set in New Zealand by Selman et al. 2001. Perspective of the department of Health and Ageing adopted. 5% discount rate used which is not in keeping with NICE reference case. Sources of certain data e.g. Unit costs not explicit.
[ss] This study reports QALYs. However, the source and methods of determining the utility data was not adequately described.
[tt] Converted from 2003 AUD using a PPP exchange rate of 1.35(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009)
[uu] Some uncertainty over applicability of the study to the UK due to potential differences in populations. Effectiveness data sourced from RCT set in New Zealand by Selman et al. 2001. Perspective of the department of Health and Ageing adopted. 5% discount rate used which is not in keeping with NICE reference case. Sources of certain data e.g. Unit costs not explicit.

UKATT, 2005 UK	Minor Limitations	Directly applicable	MET vs. Social Behaviour Network Therapy. Inflated ICER above NICE threshold.	279[ww]	0.0113	24 652	The cost-effectiveness acceptability curves for MET relative to social behaviour and network therapy demonstrated that the two therapies were equally cost-effective. If decision-makers are willing to pay nothing for an extra QALY gained then social therapy would be preferable to motivational therapy in 747 of the 1,000 samples (i.e. 514 samples where the health gains from motivational therapy have no value and 233 samples where social therapy dominates). If a cost of 100,000 per QALY is considered acceptable, then motivational therapy is preferable to social network therapy in 662 of the 1,000 samples. In the case where an additional QALY is valued at 30,000, motivational therapy has a 57.6% probability of being more cost-effective than social behaviour and network therapy.

[vv] This study reports QALYs. However, the source and methods of determining the utility data was not adequately described.
[ww] 2000/1 UK pounds inflated using HCHS indices (Curtis, 2009)

Clinical / economic question: 5

CBT versus CBT + Naltrexone							
Study & country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)**	**Incremental effect (QALYs)**	**ICER (£/QALY)**	**Uncertainty**
Walters, 2009 UK	Potentially serious limitations[xx]	Partially applicable[yy]		Unable to calculate	Unable to calculate	Unable to calculate	No Sensitivity analysis conducted. Highly uncertain results as when compared to other studies the results varied.

[xx] Not a full economic evaluation
[yy] Health care setting limits its transferability as well as the costs used. The outcome measures also do not prove helpful from the NHS perspective

CBT versus MET versus Twelve-step facilitation (TSF)

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[zz]	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Holder, 2000 US	Potentially serious limitations[aaa]	Partially applicable[bbb]	Authors calculated average monthly costs for three interventions – incremental costs here based on total average costs over 3 year study period CBT versus MET	503	NA	NA	No sensitivity analysis
Holder, 2000 US	Potentially serious limitations	Partially applicable	CBT versus TSF	-1960	NA	NA	No sensitivity analysis
Holder, 2000 US	Potentially serious limitations	Partially applicable	MET vs TSF	-2463	NA	NA	No sensitivity analysis

[zz] Converted from 1984 US $ using a PPP exchange rate of 0.52(www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009) from 1987/88 (baseline index)
[aaa] Little detail given on resource use and cost data; no incremental analysis presented
[bbb] US health care system; cost analysis only – no synthesis with health outcomes

Brief Relationship Therapy (BRT) vs. Standard behavioural couples therapy (S-BCT) vs. Individual-based treatment (IBT) vs. Psychoeducational attention control treatment (PACT)							
Study & country	**Limitations**	**Applicability**	**Other comments**	**Incremental cost (£)[ccc]**	**Incremental effect (QALYs)**	**ICER (£/QALY)**	**Uncertainty**
Fals-Stewart, 2005 US	Potentially serious limitations[ddd]	Partially applicable[eee]	Authors calculated mean change in PDHD over 12 months divided by mean cost of treatment delivery (in $100 units) – higher ratios indicate greater cost-effectiveness BRT vs. S-BCT	-295	NA	NA	No sensitivity analysis
Fals-Stewart, 2005 US	Potentially serious limitations	Partially applicable	BRT vs. IBT	42	NA	NA	No sensitivity analysis
Fals-Stewart, 2005 US	Potentially serious limitations	Partially applicable	BRT vs. PACT	9	NA	NA	No sensitivity analysis

[ccc] Converted from 2005 US $ using a PPP exchange rate of 0.64 (www.oecd.org/std/ppp) then inflated using HCHS indices (Curtis, 2009) from 2004/05
[ddd] No incremental analysis of costs and outcomes presented; 12 month time horizon
[eee] US health care system; health outcomes not expressed as QALYs; societal cost perspective

Clinical / economic question: 6

Stepped care versus minimal intervention

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Drummond et al. 2009, UK	Minor Limitations [fff]	Directly applicable[ggg]		Unable to calculate[hhh]	Unable to calculate	Unable to calculate	98% probability of stepped care intervention being cost-effective at UK £20-30,000 threshold- based on 1000 bootstrap samples

[fff] Short time horizon; no formal synthesis of incremental costs and effectiveness
[ggg] Societal perspective including criminal justice costs;
[hhh] Not possible to calculate ICER with data available. Authors did not report total costs over 6-month period