Appendices

Contents

Appendix 1

Table A1
Volume and Issue numbers for Health Technology Assessment monographs included in analysis of projects including trials with economic evaluations. Underlined issue numbers indicate those that contained at least on comparison that had "doubly null" results. (For example 8.46 in Volume 8 had a "doubly null" result.)

Year	Volume	Issue																
2004	8	8	16	17	26	29	46	48	50									
2005	9	1	4	5	16	18	31	32	33	34	37	39	40	41				
2006	10	2	13	17	19	21	22	29	37	40								
2007	11	10	16	24	25	31	35	38	40									
2008	12	4	13	14														
2009	13	9	13	15	21	22	28	30	33	37	39	47	51	53	54	55	56	
2010	14	1	6	13	14	15	20	22	23	26	35	41						
2011	15	3	8	12	13	21	23	24	32									
2012	16	8	9	10	18	26	47	48	49									
2013	17	2	7	18	21	25	26	39	45	46	47	57						
2014	18	6	13	19	20	22	26	29	30	31	36	44	48	54	57	66	67	71
2015	19	12	13	17	19	23	24	25	27	38	40	54	59	61	63	64	66	70
		cont.	71	72	73	76	79	80	84	88	97	101	102					
2016	20	11	14	15	18	20	21	28	29	41	45	52	53	56	59	60	63	64
		cont.	68	71	73	75	80	84	88	89	93	95						
2017	21	1	3	4	8	10	11	12	13	16	17	20	24	28	32	34	37	46
		cont.	49	50	53	57	60	62	65	67	70							

Appendix 2
Overall conclusions: extracts from abstracts along with probability that the intervention was cost effective

Appendix 2 Table A1 provides excerpts on the overall conclusions drawn in the abstracts of HTA published randomised trials with "doubly null" results, in which economics favours the intervention. The projects are divided into three groups, those with overall conclusions in favour of the intervention, the control and those which favoured neither, that is those which were uncertain

10 projects with "doubly null" results drew concluded in favour of the intervention. These were 21.24, 20.93, 20.53, 19.88, 18.57, 18.36, 18.19 (3 comparisons), 14.15 (2 comparisons) and 9.41 (2 comparisons). These contained 14 comparisons. (First section Table A2.)

The 7 projects that included a conclusion in favour on the control were 20.95, 20.60, 20.52, 20.41, 17.25, 17.07, 9.34. These contained 7 comparisons. (Second section, Table A".)

The 7 projects that concluded in favour of uncertainty were 21.12 (2 comparisons), 19.80, 19.38, 16.47,13.33, 10.22, 9.16 (2 comparisons) . These contained 9 comparisons. (Third section, Table A2.)

The average probability of being cost effective at a willingness to pay of £20k per QALY is also shown for those comparisons for which this was available. For those overall comparisons in favour of an intervention the average probability of being cost effective was put at 82%. For those with conclusions favouring the control arm, the average was 79%. And for with mixed or uncertain conclusions the mean probability was 68%. The presence of other factors which might have influenced the overall conclusion is also noted where relevant.

Appendix 2

Table A1

HTA RCTs with "doubly null" results, in which economics favours the intervention, divided between those whose overall conclusions favour the intervention, control or were uncertain

Volume	Technology comparison	Disease	Conclusion as in the Abstract, divided between those pro intervention, uncertain/mixed and those pro control	Probability cost effective at £20k/QALY	Comment
1.			**PRO INTERVENTION**		
21.24	Podiatry versus usual care plus falls prevention leaflet	Elderly, falls	"The intervention was safe and potentially effective. Although the primary outcome measure did not reach significance, a lower fall rate was observed in the intervention group. The reduction in the proportion of older adults who experienced a fall was of borderline statistical significance. The economic evaluation suggests that the intervention could be cost-effective."	65%	Borderline significance may have affected conclusion..
20.93	GP letter in addition to and versus usual care	Asthma exacerbations, school children	"The intervention did not reduce unscheduled care in September, although it succeeded in increasing the proportion of children collecting prescriptions in August as well as having scheduled contacts in the same month. These unscheduled contacts in September could be a result of the intervention, as GPs may have wanted to see patients before issuing a prescription. The economic analysis estimated a high probability that the intervention was cost-saving, for baseline-adjusted costs, across both base-case and sensitivity analyses. There was no increase in QALY."	93% (cost saving)	Probability refers to cost saving only. Concluding chapter more strongly pro intervention.
20.53	Zoledoninc acid (ZA) versus placebo	Prostate cancer	The additional costs and small positive QALY changes in favour of ZA resulted in ICERs of £42,047 (Zometa) and £8005 for the generic alternative; thus, generic ZA represents a cost-effective option."	64%	Probability of cost effectiveness refers to the generic version.
19.88	Levonorgestrel-releasing intrauterine system (LNG-IUS) versus usual treatment	Menhorragia	"The LNG-IUS, compared with usual medical therapies, resulted in greater improvement over 2 years in women's assessments of the effect of HMB on their daily routine, including work, social and family life, and psychological and physical well-being. At 5 years, the differences were no longer significant. A similar low proportion of women required surgical intervention in both groups. The LNG-IUS is cost-effective in both the short and medium term, using the method generally recommended by the National Institute for Health and Care Excellence."	>90%	Primary outcome was statistically significant in short but not in longer term.
18.57	Two Layer (2LB) hosiery versus 4 layer dressings	Venous ulcers	"Trial data … found no evidence of a difference in venous ulcer healing between 2LB and the 4LB. 2LB may reduce ulcer recurrence rates compared with the 4LB and be a cost-effective treatment. When all available high-compression treatments were considered, the 2LB had the highest probability of being clinically effective and cost-effective. However, the underpinning evidence was sparse and more research is needed."	>95%	Time to recurrence, a secondary outcome, was statistically significant in favour of the intervention
18.36	Polymerase chain reaction (PCR) v conventional viral culture	Influenza diagnosis	"The total costs and QALYs of each diagnostic strategy were similar, although, incrementally, PCR was the most cost-effective strategy. The analysis does not support routine use of POCTs for either influenza or pneumococcal antigen for adults presenting with acute cardiopulmonary conditions, but suggests that conventional viral culture for clinical diagnosis should be replaced by PCR."	78%	Two diagnostic tests compared with each other and conventional led to a conclusion in favour of PCR.
18.19	i) Resurfacing versus not. ii) Metal versus poly backed tibia.	Hip Replacement (3 comparisons)	"The results provide evidence to support the routine resurfacing of the patella and the use of metal-backed tibial components even in the elderly. Further follow-up is required to assess the stability of these findings over time and to inform the decision between mobile and fixed bearings."	96% 91% 86%	3 comparisons in factorial trial, two of which favoured an intervention

	iii) Mobile versus fixed bearings.				
14.15	i) Out patient versus inpatient, ii) Specialiast versus generalist treatment	Anorexia nervosa	However, this study provides little support for lengthy inpatient psychiatric treatment on clinical or health economic grounds. These findings are broadly consistent with existing guidelines on the treatment of anorexia nervosa, which suggest that outpatient treatments should be offered to the majority, with inpatient treatment offered in rare cases, though our findings lend little support to a stepped-care approach in which inpatient care is offered to outpatient non-responders. Outpatient care, supported by brief (medical) inpatient management for correction of acute complications may be a preferable approach. The health economic analysis and user views both support NICE guidelines, which suggest that anorexia nervosa should be managed in specialist services that have experience and expertise in its management	QALY not included QALY not included n.a.	
9.41	i) arthroplasty versus THR, ii) fixation versus THR)	Displaced intracapsular hip fractures in previously fit, mobile patients aged 60 years or over	In fit, older patients the results of the study show a clear advantage for arthroplasty over fixation; arthroplasty was more clinically effective and probably less costly over a 2-year period post surgery. The results suggest that total hip replacement has long-term advantages over bipolar hemiarthroplasty, but these findings are less definite. This study provided support for the use of total hip replacement to treat displaced intracapsular hip fractures in fit, older patients.	Cost/QALY not reported Cost/QALY not resported	Reporting requirements were not as stringent as later when this project reported
8.46	Supplementing home exercise with class	Osteoarthritis of the knees	The supplementation of a home-based exercise programme with a class-based exercise programme led to superior improvement in the supplemented group. These differential improvements were still evident at review 12 months after treatment had ceased. The additional cost of the supplemented group was offset by reductions in resource use elsewhere in the system. Compliance with the home exercise programme did not differ between the groups. Based on this evidence, the supplementation of a home-based exercise programme with an 8-week class-based exercise programme can be confidently expected to produce small improvements in locomotor function and clinically important reductions in pain.	70%	Reporting requirements were not as stringent as later when this project reported
2.			**PRO CONTROL**		
20.95	Mesh versus standard repair	Vaginal wall prolapse.	"In women who were having primary repairs, there was evidence of no benefit from the use of mesh inlay or biological graft compared with standard repair in terms of efficacy, Quality of Life or adverse effects (other than mesh complications) in the short term."	83%	2 comparisons, only one (mesh) included
20.60	Restrictive versus liberal thresholds for blood transfusion	post cardiac surgery	"A restrictive transfusion threshold is not superior to a liberal threshold after cardiac surgery. This finding supports restrictive transfusion due to reduced consumption and costs of red blood cells. However, secondary findings create uncertainty about recommending restrictive transfusion and prompt a new hypothesis that liberal transfusion may be superior after cardiac surgery."	65%	Uncertainty of cost effectiveness emphasised.
20.52	Psychoeducation (PEPS) versus usual treatment	Personality disorder	"We found no evidence to support the use of PEPS therapy alongside standard care for improving social functioning of adults with personality disorder living in the community."	64%	Relatively low probability of being cost effective
20.41	Progesterone versus placebo	Miscarriage	"There is no evidence that first-trimester progesterone therapy improves outcomes in women with a history of unexplained recurrent miscarriage."	71%	Cost effecivness based on longer term modelling.

17.25	Brief intervention ("stepped care)" versus minimal brief consultation	Hazardous drinking	"Stepped care does not confer an advantage over minimal intervention in terms of reduction in alcohol consumption at 12 months post intervention when compared with a 5-minute brief (minimal) intervention."	94%	Primary outcome pro control, QALY pro intervention.
17.07	Mertazipine versus placebo	Depression in Alzheimer's Disease (AD)	" This is a trial with negative findings but important clinical implications. The data suggest that the antidepressants tested, given with normal care, are not clinically effective (compared with placebo) for clinically significant depression in AD. This implies a need to change current practice of antidepressants being the first-line treatment of depression in AD".	89%	Concerned with inappropriate use of anti depressants
9.34	Aggressive versus usual symptomatic therapy	Rheumatoid arthritis	"This trial showed no benefit of aggressive treatment in patients with stable established rheumatoid arthritis."	90%	Patients more able to control medication use with symptomatic treatment
3.			**MIXED/UNCERTAIN OVERALL CONCLUSIONS**		
21.12	i) Cognitive Behaviour Therapy (CBT) versus Brief Intervention, ii) Short Term Psychoanalytic Psychotherapy (STPP) versus Brief Intervention	Childhood depression	"The three psychological treatments differed markedly in theoretical and clinical approach and are associated with a similar degree of clinical improvement, cost-effectiveness and subsequent maintenance of lowered depressive symptoms. Both STPP and BPI offer an additional patient treatment choice, alongside CBT, for depressed adolescents attending specialist Child and Adolescent Mental Health Services."	CBT v Brief >50% STPP v Brief STPP v CBT >50%	
19.80	Arthroscopic versus open surgery	Rotator cuff tear	"In patients aged > 50 years with a degenerative rotator cuff tear there is no difference in clinical effectiveness or cost-effectiveness between open repair and arthroscopic repair at 2 years for the primary outcome (OSS) and all other prespecified secondary outcomes."	54%	Non-inferiority conclusions drawn from superiority trial.
19.38	Supplementing Childrens Cognitive Behaviour Therapy (CCBT) with Mother Child Interaction therapy (MCI)	Childhood anxiety disorder	There was no evidence of a benefit to child outcome of supplementing CCBT with either intervention focusing on maternal anxiety disorder or maternal cognitions and behaviours. However, supplementing CCBT with treatment that targeted maternal cognitions and behaviours represented a cost-effective use of resources, although the high percentage of missing data on some economic variables is a shortcoming	75%	MCI was seen as cost effective, MCBT was not.
16.47	Nitrofurazone-impregnated impregnated catheter versus standard	Urinary tract infection	"The trial estimate of clinical effectiveness for nitrofurazone-impregnated catheters was less than the pre-specified minimum absolute risk difference that we considered important (−3.3%), and the surrounding CI included zero, indicating that any reduction in catheter-associated UTI was uncertain. Economic analysis, although associated with uncertainty, suggested that nitrofurazone-impregnated catheters may be cost-effective for the NHS."	80%	Cost effectiveness was based on modelling due to poor trial data.
13.33	Continuous positive airway pressure (CPAP) versus usual care	pulmonary oedema	"Non-invasive ventilatory support delivered by ….CPAP … safely provides earlier improvement and resolution of breathlessness, respiratory distress and metabolic abnormality. However, this does not translate into improved short- or longer-term survival."	71%	Primary outcome was 7 day mortality. Cost effectiveness based on long term modelling.
10.22	Pressure mattress versus underlay	Pressure sores	"There is no difference between alternating pressure mattress replacements and overlays in terms of the proportion of patients developing new pressure ulcers; however, alternating pressure mattress replacements are more likely to be cost-saving."	64% (dominance)	Difference in cost was due to duration not incidence of pressure sores.

9.16	i) SSRI versus Tricylic (TCA), ii) Lofepramine versus TCA	Depression	"When comparing the different treatment options, no significant differences were found in outcomes or costs within the sample, but when outcomes and costs were analysed together, the resulting cost-effectiveness acceptability curves suggested that SSRIs were likely to be the most cost-effective option, although the probability of this did not rise above 0.6."	SSRI v TCA 60% SSRI v Lofepramine Lofepramine v TCA	Overall conclusion that drugs compared are equally effective and cost effective

Notes

1. The heading Volume in the first column refers to the HTA Monograph series. Each volume can be accessed free at https://www.journalslibrary.nihr.ac.uk/hta/#/
2. Technology comparison refers to the intervention technology and its control. Which is usually a placebo or usual care, but sometimes another intervention which may constitute usual care.
3. The extracts in the column headed conclusions are all quotations from the abstracts of the relevant reports in the HTA monograph series
4. The figures in the column headed Probability cost effective at £20k/QALY are from the chapters on cost effectiveness in the relevant reports in the HTA monograph series.