Appendix E1 – Health Economic Extractions –TLoC Guideline

Table 1: Model based economic evaluations

Primary details	Design	Patient characteristics	Interventions	Outcome measures	Results	Comments
Author, Year: Krahn, 1999 Country: US (government funded health care) Funding: Not stated but one author employed by IER manufacturer Type of analysis: Cost-effectiveness	Study design: Decision analytic model combing cost estimates with published data on diagnostic yield of each test Time horizon: Not stated but diagnostic pathways likely to last <2 years Discounting: None Perspective: US Societal Cost year: 1995 US$	Theoretical cohort of 100 patients undergoing cardiac investigations following a first episode of unexplained syncope 40% are assumed to have SHD	1) Holter, Echo, HUT, EER, EPS. 2) As 1) but IER after EPS 3) as 2) but Echo only if presence of SHD uncertain (50%) 4) as 2) but EPS only if SHD present 5) As 2) but echo only if presence of SHD uncertain (50%) and EPS only if SHD present	Patients diagnosed at the end of diagnostic pathway Cost (per patient) of diagnostic pathway (treatment costs not included) Incremental cost per diagnosis (reviewer calculated)	1) 84/100 2) 99/100 3) 98/100 4) 98/100 5) 98/100 1) $2398 2) $3100 3) $2601 4) $2561 5) $2287 5 dominates 1, 3, and 4. 2 vs 5 = $813,000	Results presented for incremental costs per cumulative diagnosis associated with IER do not follow from data presented. ICER for 2 vs 1 is $4680 per additional diagnosis not $1416 as presented. Univariate sensitivity shows large uncertainty in cost and diagnostic yield but does not present uncertainty in incremental cost per additional diagnosis
Author, Year: Simpson, 1999 Country: Canada (government funded health care) Funding: Not stated but one author	Study design: Decision analytic model combing cost estimates with published data on diagnostic yield of each test Time horizon: Not stated but	Theoretical cohort of 100 patients undergoing cardiac investigations following a first episode of unexplained syncope 40% are assumed to have SHD	1) Holter, Echo, HUT, EER, EPS. 2) As 1) but IER after EPS 3) as 2) but Echo only if presence of SHD uncertain (50%)	Patients diagnosed at the end of diagnostic pathway Cost (per patient) of diagnostic pathway	1) 84.8/100 2) 98.2/100 3) 98.1/100 4) 98.1/100 5) 98.1/100 6) 98.9/100 1) $391 – 810	Order of tests in strategy 6 based on ranking of cost per diagnosis. May not be clinically viable. Sensitivity analysis on cost range only

employed by IER manufacturer Type of analysis: Cost-effectiveness	diagnostic pathways likely to last <2 years Discounting: None Perspective: Canadian, third party payer Cost year: 1997 CDN$		4) as 2) but EPS only if SHD present 5) As 2) but echo only if presence of SHD uncertain (50%) and EPS only if SHD present 6) EER, HUT, Holter, EPS if SHD, IER, Echo, EPS if no SHD	(treatment costs not included) Incremental cost per diagnosis (reviewer calculated)	2) $648 – 1,327 3) $616 – 1,273 4) $891 – 1,168 5) $565 – 1,122 6) $455 – 1,032 6 dominates 2 - 5 6 vs 1 = $425 to $1566 5 dominates 2 to 4. 5 vs 1 = $1279 – 2338	
Author, Year: MSAC. 2003 Country: Australia (government funded health care) Funding: Independent adaptation of model submitted by manufacturer of IER Type of analysis: Cost-effectiveness	Study design: Decision analytic model Time horizon: 3 years Discounting: 5% Perspective: Australian health care perspective Cost year: 2003 AUS$	Theoretical cohort of patients with recurrent syncope occurring at intervals >1 week, and negative diagnosis following history and PE (BP and ECG), plus negative EER (or EER inappropriate) and no structural heart disease or low risk of sudden cardiac death	1) IER 2) Standard care (no further ECG monitoring in the majority of patients)	Diagnosis (tachy/bradycardia) Successful treatment QALY gain Incremental costs: Diagnostic testing Treatment of brady/tachycardia Treatment of injury ICERS: cost per diagnosis, cost per successful treatment cost per QALY	1) 33% 2) 0% 1) 74%, 2) 0% 1) vs 2) 0.09 QALYs Incremental costs: Diagnostic: $4,419 Treatment: $696 Injury: $970 Total: $4,145 Total incremental : $12,560 $16,973 $44,969	Univariate sensitivity analysis has range of $23,555 - $76,132 It is unclear what evidence has been used to estimate proportion of patients successfully treated and model is sensitive to this outcome Utility scores based on EQ-VAS which may not reflect preference based valuation

Table 1: Trial based economic evaluations

Primary details	Design	Patient	Interventions	Outcome measures	Results	Comments

		characteristics				
Author, Year: Rockx, 2005 Country: Canada (government funded health care) Funding: No conflict identified Type of analysis: Cost-effectiveness	Study design: RCT with optional cross-over Discounting: None Perspective: Third-party payer Cost year: 2003 CND$ converted to 2005 $US	Patients (N=100) referred for ambulatory monitoring (mostly from primary care) with symptoms of syncope and/or presyncope. This is described by the authors as "community acquired syncope" to reflect the fact that it is unlikely to include high risk patients who would be admitted and investigated promptly.	1a) 1 mth of external event recorder 1b) as for 1a) but with cross over to 48 hour Holter if failed activation or no recurrence during 1mth 2a) 48 hour Holter monitoring 2b) As for 2a) with cross over to 1 mth external event recorder if no symptom recurrence during 48hr	Symptom rhythm correlation defined as arrhythmia recorded during symptoms (arrhythmia diagnosis) or normal sinus rhythm recorded during symptoms (arrhythmia excluded). Cost per patient (treatment costs not included) Incremental cost per additional diagnosis	1a) 31/49 1b) 31/49 2a) 12/51 2b) 25/51 1a) $533.56 1b) $551 2a) $175.18 2b) $481 1a) vs 2a) $902 per additional diagnosis 1b) vs 2b) $500 per additional diagnosis	Only 22% of those offered cross-over following EER and 74% of those offered cross-over following Holter monitoring took up the option of further monitoring. This may reflect the prevalence of previous negative Holter monitoring in this cohort. Hoch 2006 reports CEAC with mean ICER of $1,096 with a 97% likelihood of being under $2000
Author, Year: Krahn, 2003 Country: Canada (government funded health care) Funding: Devices provided by manufacturer Type of analysis: Cost-effectiveness	Study design: RCT with optional cross-over Discounting: None Perspective: Societal (direct medical costs only) Cost year: 2002 CND$	Patients (N=60) with recurrent unexplained syncope (or first episode with injury) referred for cardiovascular investigation. Assessment: Postural BP, 24hour ECG and echo prior to enrolment. Excluded if LV ejection fraction <35%, unlikely to survive 1 year or presentation typical of neurally mediated at baseline	1a) 1 year IER monitoring 1b) As for 1a) with cross over to comparator (without EER) if undiagnosed 2a) Conventional testing consisting of EER (2-4 weeks), HUT and EPS 2b) As for 2a) with cross over to IER if undiagnosed	Diagnosis: defined as symptom / rhythm correlation for IER and standard criteria for other tests. Recurrence free during follow-up after diagnosis Cost per patient (treatment costs not included) Incremental cost per additional diagnosis	1a) 14/30 1b) 15/30 2a) 6/30 2b) 14/30 1a) $2,731 1b) $2,937 2a) $1,683 2b) $3,683 1a) vs 2a) $3,930 per additional diagnosis 1b) dominates 2b)	Only 31% offered cross over after IER and 88% offered cross over after conventional testing took up further monitoring.

Author, Year: Farwell 2004 (Farwell 2006 reports final results) Country: UK NHS Funding: IER manufacturer Type of analysis: RCT reporting costs	Study design: RCT Perspective: NHS local estimates Cost year: 2000-2001 Mean follow-up 276 days (+-134), minimum of 6 mths Discounting: none	Patients presenting acutely with recurrent syncope (>2 in past 12 mths) and no diagnosis following history, PE, ECG, FBC, urea and electrolytes, plasma glucose, Holter monitoring (if cardiac cause suspected)., CSM and HUT. Patients with SHD and patients requiring cardiac pacing following CSM and HUT were excluded.	1) IER with automatic and patient activation (n=103 with 2 lost to follow-up) 2) Conventional testing (n=98 with 1 lost to follow-up)	Time to ECG diagnosis Time to first recurrence Time to second recurrence Time to ECG guided therapy QoL (SF-12 and VAS) Mean difference in costs (2 minus 1): Investigation Hospitalisation Total (excl IER cost and treatment of diagnosed cause)	HR: 8.98 (3.17 – 25.19, p<0.0001) HR: 1.12 (0.71-1.78, p=0.62) HR 0.88 (0.43 -1.80, p=0.44) HR: 7.9 (2.8 – 22.3, p<0.0001) No sig difference at 0, 3, 6 or 12 mths £61.4 (£35.2-92.9) £747 (£72.8-2730) £809 (£123-2770) IER device £1350	Cost of treating diagnosed cause and costs associated with IER monitoring not estimated. Resource use not reported separately from costs
Author, Year: Farwell 2006 (Farwell 2004 reports intermediate results) Country: UK NHS Funding: IER manufacturer Type of analysis: RCT reporting costs	Study design: RCT Perspective: NHS local estimates Cost year: 2000-2002 Median follow-up 17mths (IQ 9-23 mths) Discounting: none	Patients presenting acutely with recurrent syncope (>2 in past 12 mths) and no diagnosis following history, PE, ECG, FBC, urea and electrolytes, plasma glucose, Holter monitoring (if cardiac cause suspected)., CSM and HUT. Patients with SHD and patients requiring cardiac pacing following CSM and HUT were excluded.	1) IER with automatic and patient activation (n=103 with 2 lost to follow-up) 2) Conventional testing (n=98 with 1 lost to follow-up)	Time to ECG diagnosis Time to first recurrence Time to second recurrence Time to ECG guided therapy QoL (SF-12 and VAS) Mean difference in costs (2 minus 1): Investigation cost Total cost (excl IER cost and treatment of diagnosed cause)	HR: 6.53 (3.73 – 11.4, p<0.0001) HR: 1.03 (0.67-1.58, p=0.9) p=0.04 (longer for IER) HR: 6.53 (3.73 – 11.4, p<0.0001) No change in SF-12 Significant increases in VAS, p=0.03 £70.1 (£40.3-99.3) No sig difference, p=0.28	Cost of treating diagnosed cause and costs associated with IER monitoring not estimated. Resource use not reported separately from costs