Appendix files

Appendix Table 1. Probability of SVR

Parameters	Expected values (ranges)	Distribution	Reference
Genotype 1			
PR in treatment-naïve patients (48 weeks)	0.52 (0.46-0.57)	Beta ($\alpha = 69, \beta = 63.7$)	[9]
LS in treatment-naïve patients (12 weeks)	0.98 (0.91-1)	Beta ($\alpha = 36.4, \beta = 0.7$)	[11]
LS in treatment-experienced patients (12 weeks)	1 (0.83-1)	Beta ($\alpha = 37.8, \beta = 3.5$)	[11]
Genotype 2			
PR in treatment-naïve patients (24 weeks)	0.89 (0.8-0.96)	Beta ($\alpha = 52.3, \beta = 6.5$)	[9]
SR in treatment-naïve and treatment-experienced patients (12 weeks)*	1 (0.96-1)	Beta ($\alpha = 0, \beta = 0$)	[12]
Genotype 3			
PR in treatment-naïve patients (24 weeks)	0.89 (0.8-0.96)	Beta ($\alpha = 52.3, \beta = 6.5$)	[9]
SR in treatment-naïve and treatment-experienced patients (24 weeks)*	0.946 (0.892-1)	Beta ($\alpha = 63.7, \beta = 3.6$)	[12]
LSR in treatment-experienced patients (12 weeks)#	1 (0.87-1)	Beta ($\alpha = 0, \beta = 0$)	[19, 20]
LSR in treatment-experienced patients (12 weeks)#	0.82 (0.69-0.91)	Beta ($\alpha = 38.4, \beta = 8.4$)	[19, 20]
Genotype 4			
PR in treatment-naïve patients (48 weeks)	0.52 (0.46-0.57)	Beta ($\alpha = 164.8, \beta = 152.2$)	[9]
LS in treatment-naïve and treatment-experienced patients (12 weeks)*	0.97 (0.96-1)	Beta ($\alpha = 271.1, \beta = 8.4$)	[10]

* Due to the absence of data, the overall SVR data were used for treatment-naïve and treatment-experienced patients.

The efficacies of LS for genotype 2 and LSR for genotype 3 in adolescents were assumed to be similar to those in adults.

Abbreviation: PR = pegylated interferon with ribavirin, LS = ledipasvir/sofosbuvir, LSR = ledipasvir/sofosbuvir/ribavirin, SR = sofosbuvir/ribavirin, SVR = sustained virologic response.

Appendix Table 2. Transition probabilities and other clinical inputs

Parameters	Expected values (ranges)	Distribution	Reference
F0 → F1 (Age <20 years)	0.107 (0.059-0.196)	Beta (α = 8.4, β = 69.9)	[23]
F1 → F2 (Age <20 years)	0.106 (0.094-0.12)	Beta (α = 228.3, β = 1925.8)	[23]
F2 → F3 (Age <20 years)	0.16 (0.125-0.205)	Beta (α = 51.6, β = 271.1)	[23]
F3 → F4 (Age <20 years)	0.087 (0.047-0.16)	Beta (α = 8.3, β = 87.3)	[23]
F0 → F1 (Age 20-29 years)	0.073 (0.064-0.084)	Beta (α = 189.8, β = 2409.9)	[23]
F1 → F2 (Age 20-29 years)	0.134 (0.103-0.175)	Beta (α = 46.1, β = 297.9)	[23]
F2 → F3 (Age 20-29 years)	0.14 (0.093-0.212)	Beta (α = 18.3, β = 112.4)	[23]
F3 → F4 (Age 20-29 years)	0.102 (0.092-0.113)	Beta (α = 325.5, β = 2866.1)	[23]
F0 → F1 (Age ≥30 years)	0.187 (0.156-0.225)	Beta (α = 91.8, β = 398.9)	[23]
F1 → F2 (Age ≥30 years)	0.109 (0.063-0.186)	Beta (α = 10.8, β = 87.9)	[23]
F2 → F3 (Age ≥30 years)	0.105 (0.092-0.12)	Beta (α = 193.4, β = 1648.5)	[23]
F3 → F4 (Age ≥30 years)	0.158 (0.133-0.187)	Beta (α = 110.8, β = 590.3)	[23]
F3 → DC	0.012 (0.01-0.014)	Beta (α = 136.6, β = 11249.9)	[26]
F4 → DC	0.039 (0.03-0.048)	Beta (α = 69.3, β = 1708.2)	[26]
SVR F3 → DC	0.001 (0.001-0.002)	Beta (α = 10, β = 18.5)	[26]
SVR F4 → DC	0.003 (0.002-0.005)	Beta (α = 13.5, β = 99.2)	[26]
F3 → HCC	0.007 (0-0.027)	Beta (α = 6.5, β = 4.7)	[26]
F4 → HCC	0.019 (0.017-0.055)	Beta (α = 11.7, β = 37)	[26]
Proportion of SVR F1 → SVR F0 regression post-SVR	0.35 (0.17-0.52)	Beta (α = 8.3, β = 9.7)	[26]
Proportion of SVR F2 → SVR F0 regression post-SVR	0.12 (0.06-0.18)	Beta (α = 14, β = 141.4)	[26]
Proportion of SVR F2 → SVR F1 regression post-SVR	0.58 (0.29-0.87)	Beta (α = 13.2, β = 81.2)	[26]
Proportion of SVR F3 → SVR F1 regression post-SVR	0.24 (0.12-0.36)	Beta (α = 12, β = 42.5)	[26]
Proportion of SVR F3 → SVR F2 regression post-SVR	0.46 (0.23-0.69)	Beta (α = 16.2, β = 15764.2)	[26]
Proportion of SVR F4 → SVR F1 regression post-SVR	0.09 (0.05-0.14)	Beta (α = 19, β = 5668)	[26]
Proportion of SVR F4 → SVR F2 regression post-SVR	0.14 (0.07-0.21)	Beta (α = 1.1, β = 154.1)	[26]
Proportion of SVR F4 → SVR F3 regression post-SVR	0.22 (0.11-0.33)	Beta (α = 3.8, β = 194.6)	[26]
SVR F3 → HCC	0.005 (0.001-0.007)	Beta (α = 9.6, β = 2009.6)	[26]
SVR F4 → HCC	0.012 (0.006-0.019)	Beta (α = 13.9, β = 1103.9)	[26]
Spontaneous resolution (Age 12-17 years)	0.0198 (0.005-0.039)	Beta (α = 1.8, β = 89.7)	[2-4]
Spontaneous resolution (Age ≥18 years)	0.002 (0-0.005)	Beta (α = 2.5, β = 1224.4)	[26]
DC → HCC in the United States	0.014 (0.011-0.017)	Beta (α = 82.5, β = 5809.7)	[26]
DC → LT in the United States	0.017 (0.0169-0.045)	Beta (α = 5.5, β = 319.7)	[26]
DC → Death in the United States	0.129 (0.103-0.155)	Beta (α = 83.7, β = 564.8)	[26]

HCC → LT in the United States	0.017 (0.0169-0.045)	Beta (α = 5.5, β = 319.7)	[26]
HCC → Death in the United States	0.427 (0.342-0.512)	Beta (α = 55, β = 74)	[26]
LT → Death in the United States in 1st year	0.107 (0.09-0.13)	Beta (α = 98.2, β = 819.5)	[26]
LT → Death in the United States in subsequent year	0.0485 (0.0385-0.0585)	Beta (α = 86, β = 1686.8)	[26]
DC → HCC in China	0.037 (0.01-0.083)	Beta (α = 19901.8, β = 522873.6)	[25]
DC → LT in China	0.0003 (0.0002-0.0011)	Beta (α = 0, β = 0.1)	[25]
DC → Death in China	0.052 (0.032-0.084)	Beta (α = 9.2, β = 167.3)	[25]
HCC → LT in China	0.0005 (0-0.0024)	Beta (α = 4.1, β = 8788.8)	[25]
HCC → Death in China	0.368 (0.36-0.375)	Beta (α = 220386, β = 378838)	[25]
LT → Death in China in 1st year	0.0003 (0.0002-0.0011)	Beta (α = 0, β = 0.1)	[25]
LT → Death in China in subsequent year	0.0005 (0-0.0024)	Beta (α = 0, β = 0.1)	[25]
RR of CHC progression post SVR	0.086 (0.065-0.108)	Normal (Mean = 0.086, sd = 0.022)	[26]
HR of fibrosis progression between Eastern and Western	1.28 (1.02-1.61)	Normal (Mean = 1.28, sd = 0.151)	[24]

Abbreviation: F0–F4 = METAVIR liver fibrosis scores, CC = compensated cirrhosis, DC = decompensated cirrhosis, HCC = hepatocellular carcinoma, LT = liver transplant, SVR = sustained virologic response, RR= risk ratio, HR= hazard ratio.

Appendix Table 3. Costs data

Parameters	United States[26, 28]		China[25]	
	Expected values (ranges)	Distribution	Expected values (ranges)	Distribution
Pegylated interferon alfa-2a per week	1044 (1016-1084)	Gamma (65229, 0.016)	153 (140-177)	Gamma (α = 2469, λ = 0.062)
Pegylated interferon alfa-2b per week	898 (873-939)	Gamma (47243, 0.019)	305 (290-351)	Gamma (α = 5978, λ = 0.051)
LS per 12 week	96418 (48,209-96,418) #	Fixed	10708 (5354-10708) #	Fixed
Sofosbuvir per 12 and 24 weeks	85709 (42,854-85,709) #	Fixed	9074 (4537-9074) *#	Fixed
Ribavirin per 12 weeks	8.02 (5.28-10.48)	Gamma (49, 0.165)	0.353 (0.212-0.564)	Gamma (α = 1, λ = 0.255)
Annually managing F0-F2 disease	831 (416-3326)	Gamma (931, 0.893)	917 (620-1214)	Gamma (α = 5558, λ = 0.165)
Annually managing F3 disease	2207 (1103-8828)	Gamma (2471, 0.893)	917 (620-1214)	Gamma (α = 5558, λ = 0.165)
Annually managing F4 disease	2643 (1321-10,571)	Gamma (2960, 0.893)	2610 (925-4295)	Gamma (α = 7933, λ = 0.329)
Annually managing DC disease	31301 (29,377-33,227)	Gamma (1009715, 0.031)	5813 (3532-8094)	Gamma (α = 29065, λ = 0.2)
Annually managing HCC disease	49,928 (44,809-55,041)	Gamma (960163, 0.052)	12270 (8824-15717)	Gamma (α = 85804, λ = 0.143)
Annually managing LT in 1st year	198,212 (182,784-213,635)	Gamma (4955305, 0.04)	53231 (38462-76923)	Gamma (α = 289298, λ = 0.184)
Annually managing LT in subsequent year	43,169 (35,274-51,064)	Gamma (464185, 0.093)	8462 (7692-9457)	Gamma (α = 159652, λ = 0.053)
Relative costs in post SVR F3-F4	0.709 (0.592-0.855)	Normal (Mean = 0.709, sd = 0.01)	0.709 (0.592-0.855)	Normal (Mean = 0.709, sd = 0.01)

#The range was assumed for one-way sensitivity analysis.

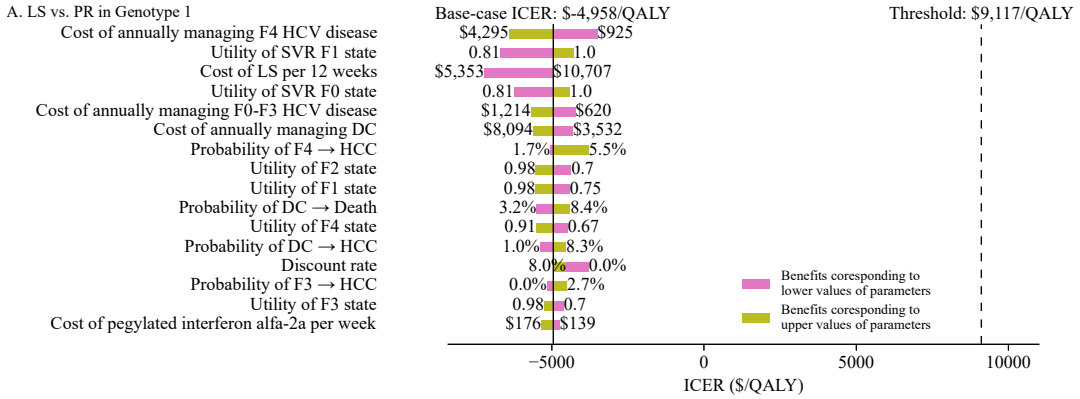
*Sofosbuvir would be donated by the producer after the first 12-week treatment.

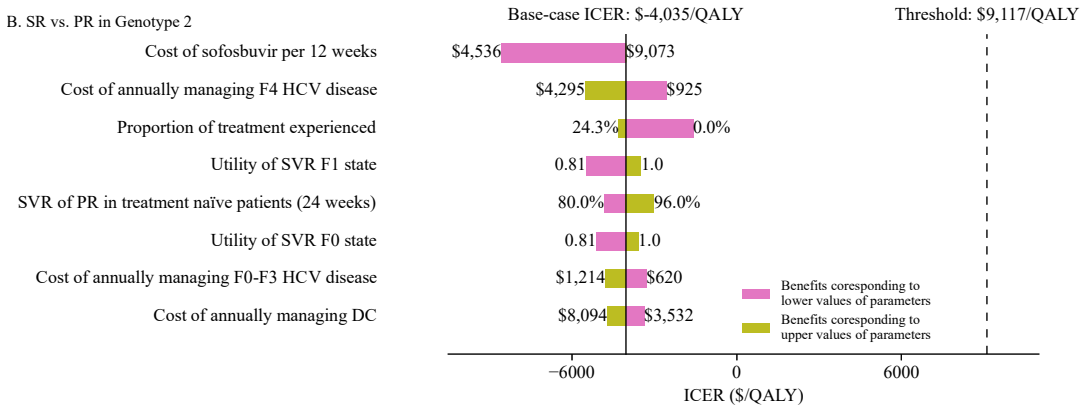
Abbreviation: F0–F4 = METAVIR liver fibrosis scores, CC = compensated cirrhosis, DC = decompensated cirrhosis, HCC = hepatocellular carcinoma, LT = liver transplant, LS = ledipasvir/sofosbuvir.

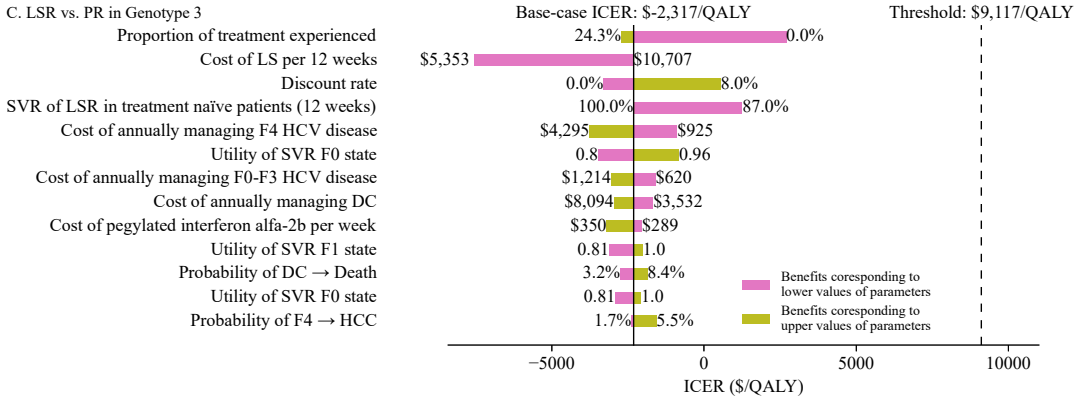
Appendix Table 4. Health preferences

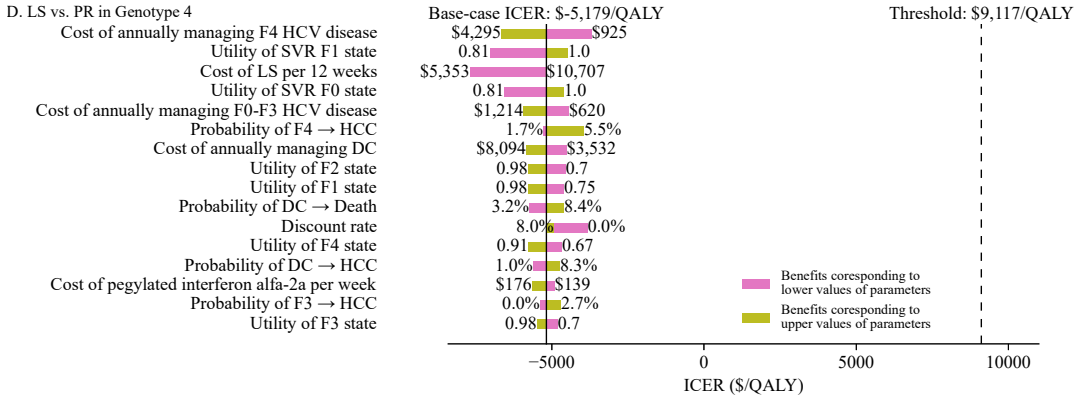
Parameters	Expected values (ranges)	Distribution	Reference
Utility scores			
F0-F1	0.878 (0.751-0.985)	Beta (α = 26.5, β = 3.7)	26, 30-32
SVR F0 - SVR F1	0.928 (0.806-1)	Beta (α = 11.9, β = 0.9)	26, 30-32
F2-F3	0.863 (0.701-0.985)	Beta (α = 19.5, β = 3.1)	26, 30-32
SVR F2	0.911 (0.791-1)	Beta (α = 30.1, β = 2.9)	26, 30-32
SVR F3	0.893 (0.766-1)	Beta (α = 30, β = 3.6)	26, 30-32
F4	0.792 (0.67-0.907)	Beta (α = 35.5, β = 9.3)	26, 30-32
SVR F4	0.85 (0.722-0.955)	Beta (α = 44.1, β = 7.8)	26, 30-32
DC	0.713 (0.517-0.837)	Beta (α = 40.8, β = 16.4)	26, 30-32
HCC	0.685 (0.532-0.821)	Beta (α = 22.2, β = 10.2)	26, 30-32
LT in 1st year	0.663 (0.563-0.8)	Beta (α = 42.1, β = 21.4)	26, 30-32
LT in subsequent year	0.773 (0.636-0.85)	Beta (α = 25, β = 7.4)	26, 30-32
Disutility scores			
Interferon-based therapy	0.1 (0.04-0.16)	Beta (α = 9.6, β = 86.4)	26, 30-32
Oral regimens therapy	0.05 (0-0.1)	Beta (α = 3.6, β = 69.3)	26, 30-32

Abbreviation: F0–F4 = METAVIR liver fibrosis scores, CC = compensated cirrhosis, DC = decompensated cirrhosis, HCC = hepatocellular carcinoma, SVR = sustained virologic response, LT = liver transplant.









Appendix Figure 1: Tornado diagrams showed the effects of the lower and upper values of each parameter on the ICER of the novel regimens versus the PR strategy in four genotypes in the Chinese context.

Abbreviation: QALY = quality-adjusted life year, ICER = incremental cost-effectiveness ratio, PR = pegylated interferon α with ribavirin, LS = ledipasvir/sofosbuvir, LSR = ledipasvir/sofosbuvir/ribavirin, SR = sofosbuvir/ribavirin.

CHEERS Checklist

Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section	Item No	Recommendation	Reported on page No/line No
Title and Abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title page/1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract page/1-19
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Text page 1/1-30
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Text page 2/28-30; Text page 3/1-3
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Text page 2/6-8
Study perspective	6	Describe the perspective of the study and relate	Text page

		this to the costs being evaluated.	4/12-13
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Text page 2/8-11
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Text page 2/6
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Text page 2/20
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Text page 2/19-20
Measurement of effectiveness	11a	*Single study-based estimates*: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	NA
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Text page 3/6-18
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Text page 4/28-30
Estimating resources and costs	13a	*Single study-based economic evaluation*: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
	13b	*Model-based economic evaluation*: Describe approaches and data sources used to estimate resource use associated with model health states.	Text page 4/17-25

		Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Text page 4/12-16
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Text page 1/12-18
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Text page 3/17-24; Text page 4/1-22
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Text page 5/1-9
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Appendix Table 1-4
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Table 1

Characterizing uncertainty	20a	*Single study-based economic evaluation*: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	**NA**
	20b	*Model-based economic evaluation*: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Text page 5/21-30
Characterizing heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	NA
Discussion			
Study findings, limitations, generalizability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Text page 7/3-30
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Title page
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Text page 7/16

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT
statement checklist

The ISPOR CHEERS Task Force Report provides examples and further discussion of the 24-item

CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices
webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.