Appendix 1

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1. Goodness-of-fit of parametric survival models

Survival analysis was conducted to extrapolate the short-term clinical data observed from the HD/HP trial over time, following the methods suggested by Latimer (1). Survival models were fitted to incidence data on severe CVD events and non-CVD mortality. For each event rate, six standard parametric distributions (exponential, Weibull, Gompertz, log normal, log logistic and generalized gamma) were assessed using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and considerations of parsimony and plausibility of extrapolated data. Results are reported in Table 1.

The exponential distribution was considered to provide the most appropriate model for all parameters except the incidence rate of myocardial infarction. The incidence rate of myocardial infarction had a sharp increase in year 2 compared to year 1. As a result, all of the two parameter survival models generated implausibly high event rates when extrapolated beyond year 2. Therefore, a piecewise constant function with a boundary at 12 months was used to extrapolate the incidence rate of myocardial infarction over time. Such a model extrapolates a constant event rate over time equal to that observed in the second year.

The clinical plausibility of the extrapolated data was checked with Dr Zhenhua Yang (nephrologist consultant, Ruijin Hospital, Shanghai, China).

Table 1 Goodness-of-fit of parametric survival models [a]

Variable	AIC score	BIC score
Incidence rate of myocardial infarction		
Piecewise constant	262.97	333.58
Exponential	279.90	337.64
Weibull	258.31	321.30
Gompertz	258.65	321.65
Log normal	260.85	323.84
Log logistic	**258.30**	**321.29**
Generalized gamma	260.30	328.54
Incidence rate of stroke		
Exponential	576.57	**634.31**
Weibull	578.37	641.36
Gompertz	578.55	641.54
Log normal	574.63	637.62
Log logistic	577.97	640.96
Generalized gamma	**573.31**	641.55
Incidence rate of heart failure		
Exponential	**219.87**	**277.61**
Weibull	221.51	284.50
Gompertz	221.78	284.77
Log normal	222.92	285.91
Log logistic	221.59	284.58
Generalized gamma	223.32	291.56
Incidence rate of other severe CVD events		

Exponential	127.68	**185.42**
Weibull	129.47	192.46
Gompertz	**127.58**	190.57
Log normal	128.52	191.51
Log logistic	129.41	192.40
Generalized gamma	DNC	DNC
Mortality rate for patients with no severe CVD events		
Exponential	**552.22**	**609.96**
Weibull	553.96	616.95
Gompertz	553.98	616.97
Log normal	554.74	617.73
Log logistic	554.17	617.16
Generalized gamma	555.70	623.94

Notes:

a. For each parameter, the bolded figures highlight the best fitting distribution according to the measure of model fit.

Abbreviations:

AIC=Akaike information criterion; BIC=Bayesian information criterion.

2. Baseline demographics and clinical information of patients recruited to the HD/HP trial

Table 2. Baseline demographics and clinical information of patients recruited to the HD/HP trial

Variable	HD group (n=703)	HD+HP group (n=704)	P value
Age (years)			
Mean (interquartile range)	56.6 (49-65)	54.7 (47-63)	0.0017
Sex - N (%)			
Male	305 (43.4%)	237 (33.7%)	
Female	389 (56.6%)	467 (66.3%)	0.0002
CVD - N (%)			
Yes	100 (14.3%)	89 (12.7%)	
No	599 (86.7%)	613 (87.3%)	0.3724
Primary kidney disease diagnosis - N (%)			
Chronic glomerulonephritis	358 (50.9%)	386 (54.8%)	0.1423
Diabetic nephropathy	116 (16.5%)	102 (14.5%)	0.2970
Polycystic kidney disease	42 (6.0%)	36 (5.1%)	0.4805
Pyelonephritis	1 (0.1%)	4 (0.6%)	0.3741
Hereditary nephritis	0 (0.0%)	1 (0.1%)	1.0000
Hypertensive nephropathy	103 (14.7%)	92 (13.1%)	0.3901
Lupus nephritis	5 (0.7%)	4 (0.6%)	0.7530
Obstructive nephropathy	9 (1.3%)	11 (1.6%)	0.6547
Chronic interstitial nephritis	6 (0.9%)	9 (1.3%)	0.4378
Other	27 (3.8%)	28 (4.0%)	0.8948

Abbreviations: CVD=Cardiovascular diseases; HD=Hemodialysis; HP=Hemoperfusion.

3. Unadjusted clinical outcomes of the HD/HP trial

Table 3. Unadjusted clinical outcomes of the HD/HP trial at the 96-week follow-up

Variable	HD group (n=703)	HD+HP group (n=704)	P value
Probability of developing severe CVD events – N (%)			
Myocardial infarction	17 (2.42%)	11 (1.56%)	0.2505
Heart failure	10 (1.42%)	8 (1.14%)	0.6330
Stroke	34 (4.84%)	22 (3.13%)	0.1006
Other severe CVD events	5 (0.71%)	3 (0.43%)	0.3640
Total CVD events	**66 (9.39%)**	**44 (6.25%)**	0.0283
Mortality rate			
CVD deaths – n/N (%)	51/66 (83.61%)	32/44 (72.73%)	0.5870
Non-CVD deaths – n/N (%)	33/637 (5.18%)	21/660 (3.18%)	0.0840
All-cause death – N (%)	**84 (11.95%)**	**53 (7.53%)**	0.0053

4. Regression models

This section reports the regression models used for estimating the incidence of severe CVD events (Section 4.1), the mortality for patients with no severe CVD events (Section 4.2), the KDQOL-SF score for patients with no severe CVD events (Section 4.3), and the mapped EQ-5D score for patients with no severe CVD events (Section 4.4). The covariates included in each regression model were pre-specified before the regression analyses were conducted. An exponential distribution was used for all survival models.

4.1 Regression model for incidence of severe CVD events

Table 4. Regression model for monthly incidence of myocardial infarction

Covariate	Coefficient	Standard error	z	P>z
Group[1]	-0.53484	0.407328	-1.31	0.189
No. of years since the onset of the trial[2]	-1.94025	0.540416	-3.59	0.000
Age	0.072537	0.019306	3.76	0.000
Sex[3]	1.225243	0.509862	2.4	0.016
Average number of dialysis per week	1.191887	1.475248	0.81	0.419
Hypertension[4]	-0.57787	0.39388	-1.47	0.142
Diabetes[4]	0.166059	0.634298	0.26	0.793
Diagnosis of kidney disease[4]	-0.22832	1.030462	-0.22	0.825
History of heart diseases[4]	0.078474	0.758788	0.10	0.918
Underweight[5]	0.010214	0.626514	0.02	0.987
Obese[6]	2.523985	0.67433	3.74	0.000
Constant	-16.0986	4.638898	-3.47	0.001

Notes:

1. HD+HP=1; HD=0.

2. Year1=1; Year 2 onwards=0.

3. Male=1; Female=0.

4. Yes=1; No=0.

5. (Body mass index (BMI)<18) =1; (BMI≥18) =0.

6. (BMI≥30) =1; (BMI<30) =0.

Table 5. Regression model for monthly incidence of stroke

Covariate	Coefficient	Standard error	z	P>z
Group[1]	-0.3584632	0.2770956	-1.29	0.196
No. of years since the onset of the trial[2]	0.0173334	0.0128895	1.34	0.179
Age	0.0010608	0.2790288	0	0.997
Sex[3]	0.2894877	0.8653368	0.33	0.738
Average number of dialysis per week	0.5957511	0.3314541	1.8	0.072
Hypertension[4]	0.644257	0.3778849	1.7	0.088
Diabetes[4]	-0.4310273	0.7228806	-0.6	0.551
Diagnosis of kidney disease[4]	0.8096352	0.4542963	1.78	0.075
History of heart diseases[4]	0.5769954	0.3341873	1.73	0.084
Underweight[5]	-0.2865019	1.022738	-0.28	0.779
Obese[6]	-9.999628	2.709175	-3.69	0.0000

Notes:

1. HD+HP=1; HD=0.

2. Year1=1; Year 2 onwards=0.

3. Male=1; Female=0.

4. Yes=1; No=0.

5. (Body mass index (BMI)<18) =1; (BMI≥18) =0.

6. (BMI≥30) =1; (BMI<30) =0.

Table 6. Regression model for monthly incidence of heart attack

Covariate	Coefficient	Standard error	z	P>z
Group[1]	0.0005574	0.4835321	0	0.999
No. of years since the onset of the trial[2]	0.0686182	0.0267898	2.56	0.010
Age	-0.4428715	0.499203	-0.89	0.375
Sex[3]	1.638272	2.022195	0.81	0.418
Average number of dialysis per week	0.1948334	0.5903978	0.33	0.741
Hypertension[4]	1.111731	0.5672732	1.96	0.050
Diabetes[4]	1.597166	0.6566357	2.43	0.015
Diagnosis of kidney disease[4]	1.313364	0.6131606	2.14	0.032
History of heart diseases[4]	-0.0861219	0.7704673	-0.11	0.911
Underweight[5]	0.5972018	1.078201	0.55	0.580
Obese[6]	-18.17078	6.378463	-2.85	0.004

Notes:

1. HD+HP=1; HD=0.

2. Year1=1; Year 2 onwards=0.

3. Male=1; Female=0.

4. Yes=1; No=0.

5. (Body mass index (BMI)<18) =1; (BMI≥18) =0.

6. (BMI≥30) =1; (BMI<30) =0.

Table 7. Regression model for monthly incidence of other severe CVD events

Covariate[1]	Coefficient	Standard error	z	P>z
Group[2]	-0.35877	0.739737	-0.48	0.628
Age	0.052434	0.036182	1.45	0.147
Sex[3]	-0.44923	0.712596	-0.63	0.528
Constant	-12.2877	2.302815	-5.34	0.000

Notes:

1. The number of patients experiencing other severe CVD events was very small (8/1407). Therefore, only three covariates (group, age and sex) were included in the regression model.

2. HD+HP=1; HD=0.

3. Male=1; Female=0.

4.2 Regression model for mortality for patients with no severe CVD events

Table 8. Regression model for monthly mortality rate for patients with no severe CVD events

Covariate	Coefficient	Standard error	z	P>z
Group[1]	-0.36962	0.28498	-1.3	0.195
No. of years since the onset of the trial[2]	0.035515	0.013563	2.62	0.009
Age	-0.11881	0.280279	-0.42	0.672
Sex[3]	0.264635	0.893858	0.3	0.767
Average number of dialysis per week	0.003739	0.300756	0.01	0.990
Hypertension[4]	1.324063	0.331048	4	0.000
Diabetes[4]	-0.99723	1.012102	-0.99	0.324
Diagnosis of kidney disease[4]	-0.64234	0.736302	-0.87	0.383
History of heart diseases[4]	0.270976	0.375332	0.72	0.47
Underweight[5]	0.458956	0.741048	0.62	0.536
Obese[6]	-10.5094	2.801466	-3.75	0.000

Notes:

1. HD+HP=1; HD=0.

2. Year1=1; Year 2 onwards=0.

3. Male=1; Female=0.

4. Yes=1; No=0.

5. (Body mass index (BMI)<18) =1; (BMI≥18) =0.

6. (BMI≥30) =1; (BMI<30) =0.

4.3 Regression model for KDQOL-SF score of patients with no severe CVD events

Table 9. Regression model for KDQOL-SF score of patients with no severe CVD events - PCS12

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	3.049751	1.292583	2.36	0.019
Baseline utility	0.756099	0.031747	23.82	0.000

	Coefficient	Standard error	t	P>|t|
Age	-0.06028	0.058466	-1.03	0.303
Sex[2]	-0.81017	1.340497	-0.60	0.546
Constant	14.7578	4.011779	3.68	0.000

Abbreviations:

PCS12= Physical Component Summary of the 12-Item Short Form Health Survey (SF-12).

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

Table 10. Regression model for KDQOL-SF score of patients with no severe CVD events - MCS12

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	3.481582	1.432423	2.43	0.015
Baseline utility	0.714466	0.033517	21.32	0.000
Age	-0.1009	0.06426	-1.57	0.117
Sex[2]	-1.40904	1.476961	-0.95	0.341
Constant	21.73768	4.508863	4.82	0.000

Abbreviations:

MCS12= Mental Component Summary of SF-12.

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

Table 11. Regression model for KDQOL-SF score of patients with no severe CVD events - Symptoms/problems

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	0.578551	0.847137	0.68	0.495
Baseline utility	0.756752	0.028867	26.21	0.000
Age	-0.03463	0.038051	-0.91	0.363
Sex[2]	-0.11173	0.877332	-0.13	0.899
Constant	20.39339	3.206442	6.36	0.000

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

Table 12. Regression model for KDQOL-SF score of patients with no severe CVD events - Effects of kidney disease

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	1.522936	1.155942	1.32	0.188
Baseline utility	0.776116	0.026516	29.27	0.000
Age	-0.08395	0.051837	-1.62	0.106
Sex[2]	-0.97463	1.195145	-0.82	0.415
Constant	14.94506	3.380844	4.42	0.000

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

Table 13. Regression model for KDQOL-SF score of patients with no severe CVD events - Burden of kidney disease

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	0.9748625	1.46505	0.67	0.506
Baseline utility	0.8161408	0.029527	27.64	0.000
Age	-0.0956213	0.0658886	-1.45	0.147
Sex[2]	-0.3993965	1.51078	-0.26	0.792
Constant	11.73611	4.143638	2.83	0.005

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

4.4 Regression model for EQ-5D score of patients with no severe CVD events

Table 14. Regression model for calculation of EQ-5D score of patients with no severe CVD events

Covariate	Coefficient	Standard error	t	P>|t|
Group[1]	0.0036747	0.0014126	2.60	0.010
Baseline utility	0.7864141	0.0292573	26.88	0.000
Age	-0.0001212	0.0000643	-1.88	0.060
Sex[2]	-0.000863	0.0014734	-0.59	0.558
Constant	0.1980354	0.0273775	7.23	0.000

Notes:

1. HD+HP=1; HD=0.

2. Male=1; Female=0.

5. KDQoL-SF score and EQ-5D score

Table 15. KDQoL-SF score and EQ-5D score at baseline and the 96-week follow-up

	Baseline		96-week follow-up	
	HD group	HD+HP group	HD group	HD+HP group
KDQoL-SF				
PCS12	55.90	55.61	53.00	55.79
MCS12	67.07	64.11	63.00	64.54
Symptoms/problems	78.44	78.45	77.35	78.74
Effects of kidney disease	50.74	54.84	48.89	54.38
Burden of kidney disease	41.04	40.50	40.00	39.21
Mapped EQ-5D score				
EQ-5D score	0.89	0.87	0.89	0.92

Abbreviations:

PCS12= Physical Component Summary of the 12-Item Short Form Health Survey (SF-12)

MCS12= Mental Component Summary of SF-12.

6. Results of one-way sensitivity analysis

39 parameters were tested using one-way sensitivity analysis. The results (Table 16) show that the base case conclusion (HD+HP being the most cost-effective intervention) is robust to all scenarios tested except the following:

- HR of non-CVD mortality increased to 0.83 (base case value: 0.69)
- frequency of HP increased to 0.63 per week (base case value: 0.50 per week)
- cost of HP increased to 1,446 RMB (base case value: 1,149 RMB)
- discount rate for costs reduced to 3.00% (base case value: 5.00%)
- discount rate for QALYs increased to 6.78% (base case value: 5%)
- cost of HD per session increased to 566 RMB (base case value: 400 RMB)
- monthly incidence rate of heart failure in the HD group increased to 0.85% (base case value: 0.04%)

Table 16. One-way sensitivity analysis results

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
Base case analysis results						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the monthly incidence rate of myocardial infarction in the HD group (year 1) to 0.00% (base case value:0.02%)						
HD	¥515,342	5.40	–	–	–	2
HD+HP	¥748,900	6.74	¥233,558	1.34	173,888	1
Set the monthly incidence rate of myocardial infarction in the HD group (year 1) to 0.06% (base case value:0.02%)						
HD	¥512,589	5.37	–	–	–	2
HD+HP	¥746,462	6.72	233,873	1.35	173,121	1
Set the monthly incidence rate of myocardial infarction in the HD group (year 2 onwards) to 0.00% (base case value:0.13%)						
HD	¥544,519	5.72	–	–	–	2
HD+HP	¥783,045	7.06	¥238,526	1.34	178,328	1
Set the monthly incidence rate of myocardial infarction in the HD group (year 2 onwards) to 0.39% (base case value:0.13%)						
HD	¥473,984	4.93	–	–	–	2
HD+HP	¥698,934	6.27	¥224,951	1.34	168,351	1
Set the monthly incidence rate of heart failure in the HD group to 0.00% (base case value:0.04%)						
HD	¥523,128	5.49	–	–	–	2
HD+HP	¥765,017	6.90	¥241,889	1.41	171,684	1
Set the monthly incidence rate of heart failure in the HD group to 0.93% (base case value:0.04%)						
HD	¥378,497	3.82	–	–	–	1
HD+HP	¥509,842	4.43	¥131,345	0.61	214,938	2
Set the monthly incidence rate of stroke in the HD group to 0.00% (base case value:0.21%)						
HD	¥555,011	5.85	–	–	–	2

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD+HP	¥801,115	7.25	¥246,104	1.40	175,985	1
Set the monthly incidence rate of stroke in the HD group to 0.63% (base case value:0.21%)						
HD	¥456,521	4.73	–	–	–	2
HD+HP	¥670,136	5.97	¥213,615	1.25	171,128	1
Set the monthly incidence rate of other severe CVD events in the HD group to 0.00% (base case value:0.03%)						
HD	¥518,419	5.43	–	–	–	2
HD+HP	¥753,330	6.78	¥234,911	1.35	173,846	1
Set the monthly incidence rate of other severe CVD events in the HD group to 2.53% (base case value:0.03%)						
HD	¥371,320	3.77	–	–	–	2
HD+HP	¥547,914	4.80	¥176,595	1.03	171,463	1
Set the HR of myocardial infarction (HD+HP vs. HD, year 1) to 0.264 (base case value: 0.583)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,534	6.74	¥234,112	1.35	173,422	1
Set the HR of myocardial infarction (HD+HP vs. HD, year 1) to 1.000 [a] (base case value: 0.583)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥747,512	6.73	¥233,089	1.34	173,901	1
Set the HR of myocardial infarction (HD+HP vs. HD, year 2 onwards) to 0.264 (base case value: 0.586)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥766,784	6.91	¥252,362	1.52	165,839	1
Set the HR of myocardial infarction (HD+HP vs. HD, year 2 onwards) to 1.000 [a] (base case value: 0.586)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥725,746	6.52	¥211,324	1.14	186,106	1
Set the HR of heart failure (HD+HP vs. HD) to 0.388 (base case value: 1.001)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥758,342	6.83	¥243,920	1.44	168,838	1
Set the HR of heart failure (HD+HP vs. HD) to 1.001 (base case value: 1.001)						
HD	¥514,422	5.39	–	–	–	2

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD+HP	¥748,096	6.73	¥233,673	1.35	173,626	1
Set the HR of stroke (HD+HP vs. HD) to 0.406 (base case value: 0.699)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥768,954	6.94	¥254,532	1.55	164,322	1
Set the HR of stroke (HD+HP vs. HD) to 1.000 [a] (base case value: 0.699)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥728,544	6.54	¥214,122	1.16	185,319	1
Set the HR of other severe CVD events (HD+HP vs. HD) to 0.164 (base case value: 0.699)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥752,131	6.77	¥237,709	1.38	171,662	1
Set the HR of other severe CVD events (HD+HP vs. HD) to 1.000 [a] (base case value: 0.699)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥745,846	6.71	¥231,424	1.32	174,771	1
Set the mortality for patients with no severe CVD events in the HD group to 0.10% (base case value: 0.19%)						
HD	¥664,351	6.91	–	–	–	1
HD+HP	¥948,093	8.49	283,742	1.58	179,878	2
Set the mortality for patients with no severe CVD events in the HD group to 0.97% (base case value: 0.19%)						
HD	¥232,105	2.49	–	–	–	2
HD+HP	¥333,008	3.06	¥100,903	0.57	177,641	1
Set the HR of mortality for patients with no severe CVD events (HD+HP vs. HD) to 0.395 (base case value: 0.691)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥931,248	8.34	¥416,826	2.95	141,180	1
Set the HR of mortality for patients with no severe CVD events (HD+HP vs. HD) to 1.000 [a] (base case value: 0.691)						
HD	¥514,422	5.39	–	–	–	1
HD+HP	¥631,233	5.70	¥116,811	0.31	370,887	2
Set mortality rate for patients with myocardial infarction (acute phase) to 60% (base case value: 85.71%)						

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD	¥520,625	5.44	–	–		2
HD+HP	¥755,272	6.79	¥234,647	1.35	174,253	1
Set mortality rate for patients with myocardial infarction (acute phase) to 100% *(base case value: 85.71%)*						
HD	¥510,977	5.36	–	–	–	2
HD+HP	¥744,094	6.70	¥233,118	1.35	173,284	1
Set mortality rate for patients with heart failure (acute phase) to 65% *(base case value: 82.14%)*						
HD	¥516,283	5.40	–	–	–	2
HD+HP	¥751,524	6.76	¥235,241	1.36	173,553	1
Set mortality rate for patients with heart failure (acute phase) to 100% *(base case value: 82.14%)*						
HD	¥512,484	5.37	–	–	–	2
HD+HP	¥744,506	6.71	¥232,022	1.34	173,712	1
Set mortality rate for patients with stroke (acute phase) to 25% *(base case value: 50.00%)*						
HD	¥527,648	5.51	–	–	–	2
HD+HP	¥765,558	6.87	¥237,910	1.36	174,508	1
Set mortality rate for patients with stroke (acute phase) to 70% *(base case value: 50.00%)*						
HD	¥503,842	5.29	–	–	–	2
HD+HP	¥734,109	6.62	¥230,267	1.33	172,912	1
Set mortality rate for patients with other severe CVD events (acute phase) to 10% *(base case value: 37.50%)*						
HD	¥516,383	5.41	–	–	–	2
HD+HP	¥750,679	6.75	¥234,296	1.35	173,753	1
Set mortality rate for patients with other severe CVD events (acute phase) to 50% *(base case value: 37.50%)*						
HD	¥513,531	5.38	–	–	–	2
HD+HP	¥746,908	6.72	¥233,377	1.34	173,574	1
Set the cost of HD per session to 165 RMB *(base case value: 400 RMB)*						
HD	¥381,120	5.39	–	–	–	2
HD+HP	¥540,162	6.73	¥159,043	1.35	118,181	1
Set the cost of HD per session to 635 RMB *(base case value: 400 RMB)*						

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD	¥647,725	5.39	–	–	–	1
HD+HP	¥956,011	6.73	¥308,286	1.35	229,080	2
Set the cost of HP per session to 473 RMB (base case value: 1,149 RMB)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥628,464	6.73	¥114,041	1.35	84,741	1
Set the cost of HP per session to 1,825 RMB (base case value: 1,149 RMB)						
HD	¥514,422	5.39	–	–	–	1
HD+HP	¥867,709	6.73	¥353,287	1.35	262,519	2
Set the weekly frequency of using HP to 0.25 in the HD+HP group (base case value: 0.5)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥646,425	6.73	¥132,002	1.35	98,088	1
Set the weekly frequency of using HP to 1 in the HD+HP group (base case value: 0.5)						
HD	¥514,422	5.39	–	–	–	1
HD+HP	¥951,410	6.73	¥436,987	1.35	324,715	2
Set the cost of per follow-up to 113 RMB (base case value: 214 RMB)						
HD	¥507,261	5.39	–	–	–	2
HD+HP	¥739,150	6.73	¥231,889	1.35	172,312	1
Set the cost of per follow-up to 412 RMB (base case value: 214 RMB)						
HD	¥528,462	5.39	–	–	–	2
HD+HP	¥765,605	6.73	¥237,144	1.35	176,216	1
Set the cost of treating acute myocardial infarction per episode to 7,454 RMB (base case value: 38,788 RMB)						
HD	¥512,639	5.39	–	–	–	2
HD+HP	¥746,735	6.73	¥234,096	1.35	173,951	1
Set the cost of treating acute myocardial infarction per episode to 66,022 RMB (base case value: 38,788 RMB)						
HD	¥515,973	5.39	–	–	–	2
HD+HP	¥749,262	6.73	¥233,289	1.35	173,352	1
Set the cost of treating acute heart failure per episode to 21,977 RMB (base case value: 33,796 RMB)						

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD	¥514,206	5.39	–	–		2
HD+HP	¥747,816	6.73	¥233,610	1.35	173,590	1
Set the cost of treating acute heart failure per episode to 46,256 RMB (base case value: 33,796 RMB)						
HD	¥514,650	5.39	–	–	–	2
HD+HP	¥748,372	6.73	¥233,722	1.35	173,673	1
Set the cost of treating acute stroke per episode to 5,570 RMB (base case value: 9,958 RMB)						
HD	¥513,902	5.39	–	–	–	2
HD+HP	¥747,631	6.73	¥233,730	1.35	173,679	1
Set the cost of treating acute stroke per episode to 17,933 RMB (base case value: 9,958 RMB)						
HD	¥515,369	5.39	–	–	–	2
HD+HP	¥748,914	6.73	¥233,545	1.35	173,542	1
Set the cost of treating other severe CVD events per episode to 4,537 RMB (base case value: 6,482 RMB)						
HD	¥514,390	5.39	–	–	–	2
HD+HP	¥748,058	6.73	¥233,668	1.35	173,633	1
Set the cost of treating other severe CVD events per episode to 8,427 RMB (base case value: 6,482 RMB)						
HD	¥514,455	5.39	–	–	–	2
HD+HP	¥748,115	6.73	¥233,660	1.35	173,627	1
Set the monthly cost of treating post-acute myocardial infarction to 104 RMB (base case value: 322 RMB)						
HD	¥514,328	5.39	–	–	–	2
HD+HP	¥747,991	6.73	¥233,663	1.35	173,629	1
Set the monthly cost of treating post-acute myocardial infarction to 541 RMB (base case value: 322 RMB)						
HD	¥514,517	5.39	–	–	–	2
HD+HP	¥748,183	6.73	¥233,666	1.35	173,632	1
Set the monthly cost of treating post-acute heart failure to 1,150 RMB (base case value: 1,451 RMB)						
HD	¥514,357	5.39	–	–	–	2
HD+HP	¥747,980	6.73	¥233,623	1.35	173,600	1
Set the monthly cost of treating post-acute heart failure to 1,752 RMB (base case value: 1,451 RMB						

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD	¥514,487	5.39	–	–		2
HD+HP	¥748,193	6.73	¥233,706	1.35	173,661	1
Set the monthly cost of treating post-acute stroke to 128 RMB (base case value: 304 RMB)						
HD	¥513,817	5.39	–	–	–	2
HD+HP	¥747,393	6.73	¥233,577	1.35	173,565	1
Set the monthly cost of treating post-acute stroke to 613 RMB (base case value: 304 RMB)						
HD	¥515,486	5.39	–	–	–	2
HD+HP	¥749,303	6.73	¥233,817	1.35	173,744	1
Set the monthly cost of treating post-acute other severe CVD events to 71 RMB (base case value: 222 RMB)						
HD	¥514,334	5.39	–	–	–	2
HD+HP	¥747,985	6.73	¥233,651	1.35	173,621	1
Set the monthly cost of treating post-acute other severe CVD events to 372 RMB (base case value: 222 RMB)						
HD	¥514,511	5.39	–	–	–	2
HD+HP	¥748,187	6.73	¥233,677	1.35	173,640	1
Set the utility of patients with no severe CVD events in the HD group to 0.853 (base case value: 0.907)						
HD	¥514,422	5.07	–	–	–	2
HD+HP	¥748,086	6.33	¥233,664	1.27	184,447	1
Set the utility of patients with no severe CVD events in the HD group to 0.960 (base case value: 0.907)						
HD	¥514,422	5.71	–	–	–	2
HD+HP	¥748,086	7.13	¥233,664	1.42	164,024	1
Set the incremental impact of HP on utility of patients with no severe CVD events to 0.001 (base case value: 0.004)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.71	¥233,664	1.33	176,224	1
Set the incremental impact of HP on utility of patients with no severe CVD events to 0.006 (base case value: 0.004)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.75	¥233,664	1.36	171,437	1
Set the disutility of myocardial infarction (acute phase) to 0.139 (base case value: 0.147)						

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,631	1
Set the disutility of myocardial infarction (acute phase) to 0.155 (base case value: 0.147)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the disutility of heart failure (acute phase) to 0.111 (base case value: 0.117)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the disutility of heart failure (acute phase) to 0.123 (base case value: 0.117)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the disutility of stroke (acute phase) to 0.214 (base case value: 0.226)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173632	1
Set the disutility of stroke (acute phase) to 0.238 (base case value: 0.226)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,629	1
Set the disutility of other CVD events (acute phase) to 0.055 (base case value: 0.058)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the disutility of other CVD events (acute phase) to 0.061 (base case value: 0.058)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1
Set the disutility of myocardial infarction (post-acute phase) to 0.037 (base case value: 0.039)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,630	1

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
Set the disutility of myocardial infarction (post-acute phase) to 0.041 (base case value: 0.039)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,631	1
Set the disutility of heart failure (post-acute phase) to 0.037 (base case value: 0.039)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,627	1
Set the disutility of heart failure (post-acute phase) to 0.041 (base case value: 0.039)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,633	1
Set the disutility of stroke (post-acute phase) to 0.065 (base case value: 0.069)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,609	1
Set the disutility of stroke (post-acute phase) to 0.073 (base case value: 0.069)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,652	1
Set the disutility of other CVD events (post-acute phase) to 0.039 (base case value: 0.041)						
HD	¥514,422	5.39	–	–	–	2
HD+HP	¥748,086	6.73	¥233,664	1.35	173,629	1
Set the disutility of other CVD events (post-acute phase) to 0.043 (base case value: 0.041)						
HD	514,422	5.39	–	–	–	2
HD+HP	748,086	6.73	233,664	1.35	173,632	1
Set the discount rate for cost outcomes to 0% (base case value: 5%)						
HD	683,813	5.39	–	–	–	1
HD+HP	1,100,793	6.73	416,980	1.35	309,848	2
Set the discount rate for cost outcomes to 8% (base case value: 5%)						
HD	449,003	5.39	–	–	–	2
HD+HP	629,550	6.73	180,547	1.35	134,160	1

Intervention	Cost (RMB)	QALY	Incremental cost (RMB)	Incremental QALY	ICER	Ranking of NMB (WTP=RMB 212,676 per QALY)
Set the discount rate for QALYs to 0% (base case value: 5%)						
HD	514,422	7.15	–	–	–	2
HD+HP	748,086	9.89	233,664	2.74	85,347	1
Set the discount rate for QALYs to 8% (base case value: 5%)						
HD	514,422	4.70	–	–	–	1
HD+HP	748,086	5.67	233,664	0.97	242,052	2

Abbreviations:

HR: hazard ratio; ICER: incremental cost-effectiveness ratio; NMB: net monetary benefit; QALY: quality-adjusted life of years; RR: relative risk. SA: sensitivity analysis.

Notes:

a. It was assumed that use of HP will not have any harmful impact on patients' clinical outcomes, including the incidence of severe CVD event rate and mortality for patients with no severe CVD

events. Therefore, the maximum value for the HR of HP was set as zero.

References

1. Latimer NR. Survival analysis for economic evaluations alongside clinical trials--extrapolation with patient-level data: inconsistencies, limitations, and a practical guide. Med Decis Making 2013;33:743-54.