Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

SUPPLEMENTARY INFORMATION

### Generalised linear model – exponent calculation

In the quasi-likelihood method (QLM), the variance function is proportional to a power (exponent) of the mean. To determine the initial value of the exponent, the sample means and variances for every combination of the categorised covariates included in the final model were calculated. A double logarithmic function was fit to the data, and the slope of the regression line was determined.[1] The initial value of the exponent was determined as 3.15, which was subsequently used as the exponent in the variance function.[1] A residual plot was generated to evaluate the model fit.[2] Because no specific trend in residuals was observed, the initial value of the exponent, 3.15, was retained. The geometric least squares (LS) mean, the geometric LS mean ratio and 95% confidence intervals for the total medical cost in the two groups were calculated.

REFERENCES

1. Blough DK, Ramsey SD. Using generalized linear models to assess medical care costs. *Health Serv Outcomes Res Methodol* 2000;1:185–202.

2. Barber J, Thompson S. Multiple regression of cost data: use of generalised linear models. *J Health Serv Res Policy* 2004;9:197–204.

1

SUPPLEMENTARY FIGURES AND TABLES

Figure S1 Mean medical cost categorised by patient characteristics
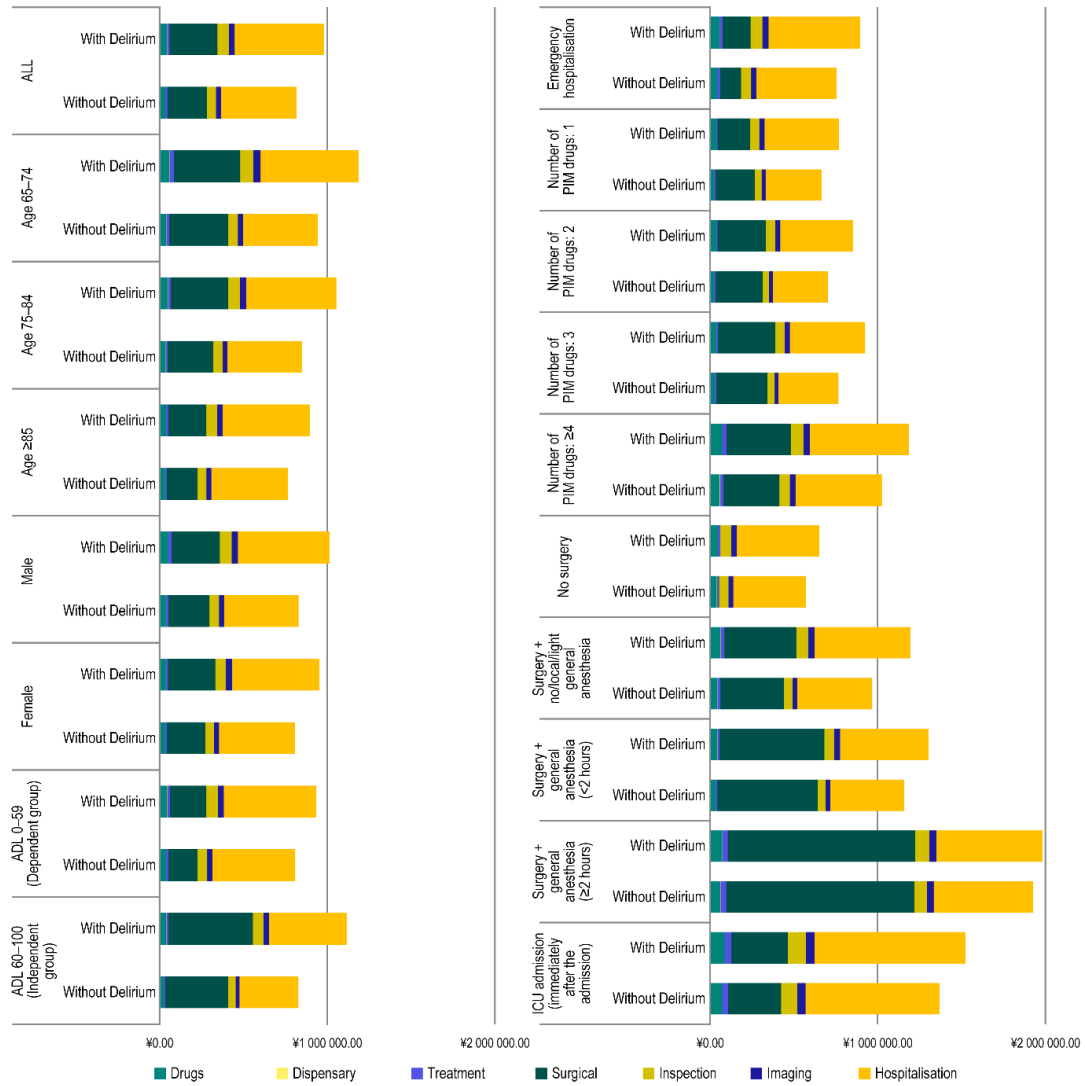
ICU, intensive care unit; PIM, potentially inappropriate medication.

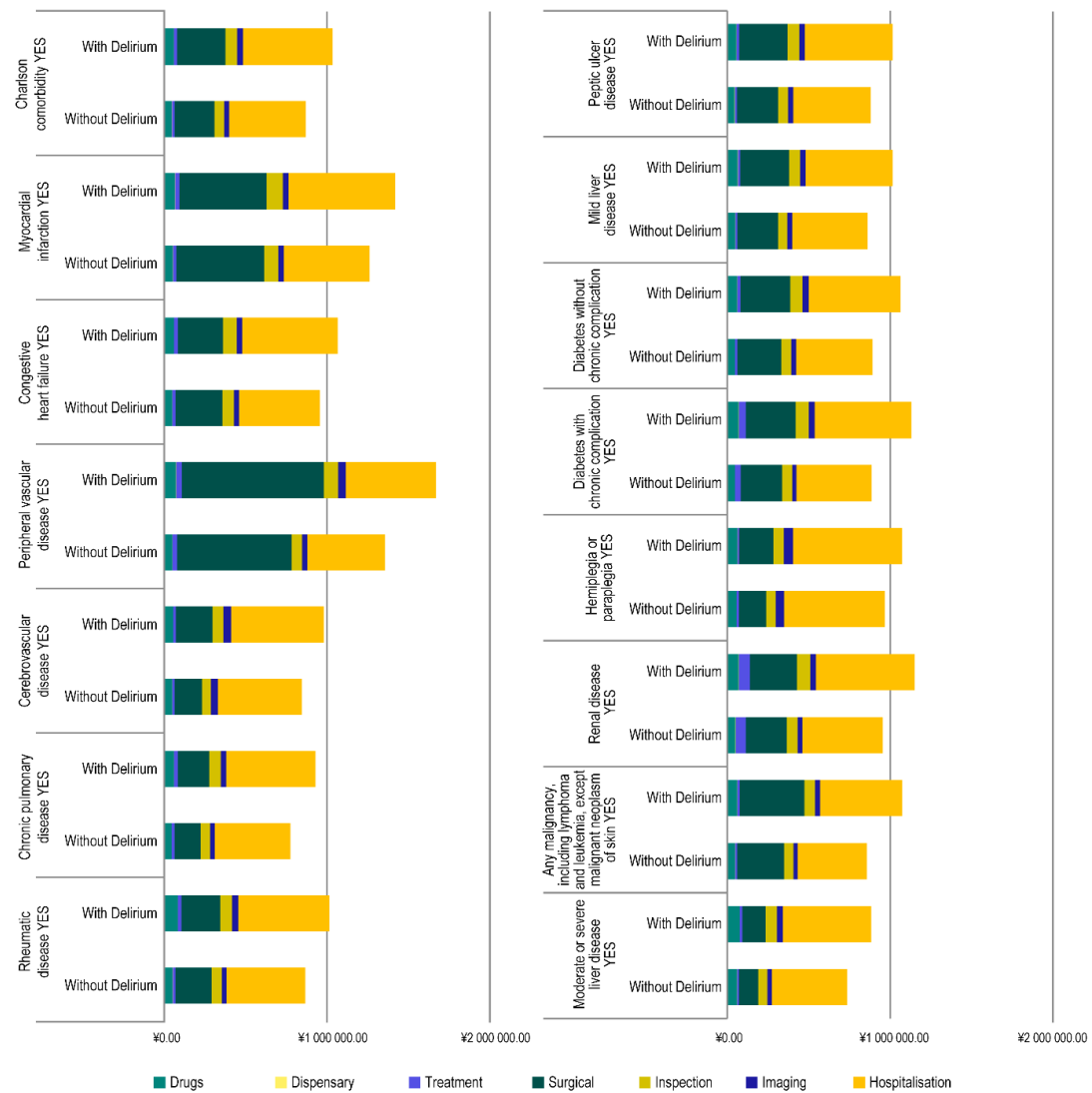**Figure S2** Medical cost categorised by comorbidities

Table S1 Definition of cognitive impairment

		Number of patients with delirium		Number of patients without delirium	
		n	%	n	%
Cognitive impairment	Yes	39 836	(100.0)	257 764	(100.0)
	Diagnosis of dementia (ICD-10)	21 341	(53.6)	112 687	(43.7)
	Prescription of anti-dementia drugs	11 963	(30.0)	66 069	(25.6)
	Low degree of independence in activities of daily living related to dementia	25 154	(63.1)	169 760	(65.9)

ICD-10, International Classification of Diseases, 10th Revision; n, number of patients.

Table S2 Identification of patients with delirium

			Number of patients with delirium		Number of patients without delirium	
Number of patients			39 836		257 764	
Patients identified by delirium identification algorithm, n (%)	Diagnosis of delirium only (ICD-10)		3685	(9.3)	0	(0.0)
	Prescription of antipsychotics only		33 611	(84.4)	0	(0.0)
	Both		2540	(6.4)	0	(0.0)
Diagnosis of delirium (ICD-10), n (%)	Yes (delirium not induced by alcohol and other psychoactive substances, F05)		6225	(15.6)	0	(0.0)
	Delirium not superimposed on dementia (F05.0)		130	(0.3)	0	(0.0)
	Delirium superimposed on dementia (F05.1)		1027	(2.6)	0	(0.0)
	Other delirium (F05.8)		8	(0.0)	0	(0.0)
	Subacute cerebral syndrome		4	(0.0)	0	(0.0)
	Acute confusional state		2	(0.0)	0	(0.0)
	Acute brain syndrome		2	(0.0)	0	(0.0)
	Delirium, unspecified (F05.9)		5100	(12.8)	0	(0.0)
	Delirium		4093	(10.3)	0	(0.0)
	Nocturnal delirium		813	(2.0)	0	(0.0)
	Senile nocturnal delirium		199	(0.5)	0	(0.0)
Prescription of antipsychotics, n (%)	Yes		36 151	(90.7)	0	(0.0)
	Haloperidol	INJ	17 188	(43.1)	0	(0.0)
		TAB	490	(1.2)	0	(0.0)
		FGR	41	(0.1)	0	(0.0)
		SOL	2	(0.0)	0	(0.0)
	Risperidone	SOL	12 081	(30.3)	0	(0.0)
		ODT	2727	(6.8)	0	(0.0)
		TAB	1762	(4.4)	0	(0.0)
		FGR	75	(0.2)	0	(0.0)
		INJ	1	(0.0)	0	(0.0)
	Quetiapine	TAB	7489	(18.8)	0	(0.0)
		FGR	278	(0.7)	0	(0.0)
		SRT	0	(0.0)	0	(0.0)
	Olanzapine	TAB	378	(0.9)	0	(0.0)
		ODT	224	(0.6)	0	(0.0)
		FGR	36	(0.1)	0	(0.0)
		INJ	1	(0.0)	0	(0.0)
	Perospirone	TAB	767	(1.9)	0	(0.0)

FGR, fine granule; ICD-10, International Classification of Diseases, 10th Revision; INJ, injectable; N, number of patients; ODT, oral disintegrating tablet; SOL, solution; SRT, sustained release tablet; TAB, tablet.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Table S3 Clinical practice

		Number of patients with delirium		Number of patients without delirium	
Number of patients		39 836		257 764	
Prescription of PIM, n (%)	Yes	18 370	(46.1)	108 326	(42.0)
	PIM class				
	Benzodiazepines	7666	(19.2)	45 166	(17.5)
	Opioids	5183	(13.0)	26 293	(10.2)
	Corticosteroids	3933	(9.9)	28 048	(10.9)
	H2-receptor antagonists	3925	(9.9)	24 036	(9.3)
	Non-benzodiazepines	2606	(6.5)	12 624	(4.9)
	H1-receptor antagonists	2488	(6.2)	11 214	(4.4)
	Antidepressants	72	(0.2)	578	(0.2)
	Anticholinergic drugs	62	(0.2)	459	(0.2)
Duration of hospitalisation (days)	Mean (SD)	15.9 (11.6)		14.2 (13.4)	
	Median	14.0		12.0	
	[Q1, Q3]	[9.0, 20.0]		[7.0, 18.0]	
	[Min, Max]	[3, 495]		[3, 1357]	
	≤ 1 week	6429	(16.1)	69 819	(27.1)
	1 week < - ≤ 2 weeks	14 771	(37.1)	88 409	(34.3)
	2 weeks < - ≤ 3 weeks	10 600	(26.6)	55 885	(21.7)
	3 weeks < - ≤ 4 weeks	4860	(12.2)	26 227	(10.2)
	4 weeks < - ≤ 12 weeks	3049	(7.7)	16 523	(6.4)
	>12 weeks	127	(0.3)	901	(0.3)
Use of ICU	Yes	5942	(14.9)	20 975	(8.1)
Duration of ICU stay (days)	Mean (SD)	3.2 (2.9)		2.9 (2.9)	
	Median	2.0		2.0	
	[Q1, Q3]	[1.0, 4.0]		[1.0, 4.0]	
	1 day	2038	(5.1)	8692	(3.4)
	2 days	1232	(3.1)	4204	(1.6)
	3 days	829	(2.1)	2773	(1.1)
	4 days	535	(1.3)	1649	(0.6)
	5 days	389	(1.0)	1042	(0.4)
	6 days	277	(0.7)	691	(0.3)
	≥7 days	642	(1.6)	1,924	(0.8)

ICU, intensive care unit; n, number of patients; PIM, potentially inappropriate medication.

Table S4 Univariate and multivariable analyses for total medical cost

Categories	n‡	Univariate analysis			Multivariable analysis		
		Geometric LS Mean§ [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value	Geometric LS Mean§ [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value
Delirium							
Without	257 764	816 137.39 [813 142.03, 819 143.79]	Ref		745 294.95 [743 312.18, 747 283.02]	Ref	
With	39 836	979 907.90 [969 783.64, 990 137.85]	1.20 [1.19, 1.21]	p<0.001	815 721.23 [810 206.11, 821 273.88]	1.09 [1.09, 1.10]	p<0.001
Age (years)							
65–74	32 220	970 981.96 [960 264.35, 981 819.19]	Ref		791 810.64 [785 966.32, 797 698.42]	Ref	
75–84	111 176	875 684.51 [870 766.49, 880 630.30]	0.90 [0.89, 0.91]	p<0.001	759 844.50 [756 869.58, 762 831.11]	0.96 [0.95, 0.97]	p<0.001
≥85	154 204	783 162.50 [779 657.12, 786 683.63]	0.81 [0.80, 0.82]	p<0.001	742 836.46 [740 330.23, 745 351.18]	0.94 [0.93, 0.95]	p<0.001
Sex							
Male	121 417	856 423.75 [851 758.80, 861 114.26]	Ref		760 340.59 [757 466.10, 763 225.98]	Ref	
Female	176 183	825 403.68 [821 747.47, 829 076.15]	0.96 [0.96, 0.97]	p<0.001	750 235.54 [747 864.66, 752 613.94]	0.99 [0.98, 0.99]	p<0.001
ADL score (points)							
0–59	206 443	827 168.97 [823 776.86, 830 575.05]	Ref		782 325.73 [779 918.81, 784 740.08]	Ref	
60–100	87 360	858 426.56 [852 905.30, 863 983.56]	1.04 [1.03, 1.05]	p<0.001	692 121.10 [688 983.95, 695 272.52]	0.88 [0.88, 0.89]	p<0.001
Comorbidities†							
Myocardial infarction							
Yes	8464	1 283 247.71 [1 250 209.84, 1 317 158.63]	Ref		858 222.93 [844 622.77, 872 042.08]	Ref	

7

Categories	n[‡]	Univariate analysis			Multivariable analysis		
		Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value	Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value
No	289 136	825 030.17 [822 176.08, 827 894.16]	0.64 [0.63, 0.66]	p<0.001	751 501.99 [749 592.23, 753 416.62]	0.88 [0.86, 0.89]	p<0.001
Congestive heart failure							
Yes	51 355	971 424.84 [962 803.22, 980 123.68]	Ref		880 345.55 [875 051.97, 885 671.14]	Ref	
No	246 245	810 245.79 [807 278.03, 813 224.46]	0.83 [0.83, 0.84]	p<0.001	730 461.61 [728 508.10, 732 420.35]	0.83 [0.82, 0.84]	p<0.001
Peripheral vascular disease							
Yes	8850	1 411 778.68 [1 374 850.80, 1 449 698.41]	Ref		974 908.71 [959 465.71, 990 600.27]	Ref	
No	288 750	820 506.76 [817 721.02, 823 302.00]	0.58 [0.57, 0.60]	p<0.001	748 457.71 [746 561.13, 750 359.11]	0.77 [0.76, 0.78]	p<0.001
Cerebrovascular disease							
Yes	62 901	859 792.08 [853 239.47, 866 395.01]	Ref		832 895.13 [828 462.74, 837 351.23]	Ref	
No	234 699	832 234.89 [829 005.98, 835 476.38]	0.97 [0.96, 0.98]	p<0.001	734 578.88 [732 566.05, 736 597.24]	0.88 [0.88, 0.89]	p<0.001
Chronic pulmonary disease							
Yes	17 563	797 779.79 [786 809.06, 808 903.50]	Ref		781 634.02 [774 427.35, 788 907.75]	Ref	
No	280 037	840 585.61 [837 587.48, 843 594.47]	1.05 [1.04, 1.07]	p<0.001	752 656.84 [750 723.74, 754 594.92]	0.96 [0.95, 0.97]	p<0.001
Rheumatic disease							
Yes	4017	885 481.30 [858 673.54, 913 125.99]	Ref		787 870.87 [772 432.04, 803 618.27]	Ref	
No	293 583	837 410.51 [834 498.94, 840 332.25]	0.95 [0.92, 0.98]	p<0.001	753 889.45 [751 985.70, 755 798.02]	0.96 [0.94, 0.98]	p<0.001
Peptic ulcer disease							

8

		Univariate analysis			Multivariable analysis		
Categories		**Geometric LS Mean[§]**	**Geometric LS Mean Ratio**		**Geometric LS Mean[§]**	**Geometric LS Mean Ratio**	
	n[‡]	**[95% CI]**	**[95% CI]**	**P-value**	**[95% CI]**	**[95% CI]**	**P-value**
Yes	15 858	898 974.79	Ref		769 874.99	Ref	
		[885 049.60, 913 119.07]			[762 026.48, 777 804.34]		
No	281 742	834 630.71	0.93	p<0.001	753 478.83	0.98	p<0.001
		[831 673.42, 837 598.52]	[0.91, 0.94]		[751 542.42, 755 420.23]	[0.97, 0.99]	
Mild liver disease							
Yes	9482	883 934.28	Ref		787 281.56	Ref	
		[866 433.60, 901 788.44]			[776 793.81, 797 910.91]		
No	288 118	836 549.62	0.95	p<0.001	753 275.38	0.96	p<0.001
		[833 614.25, 839 495.33]	[0.93, 0.97]		[751 357.62, 755 198.05]	[0.94, 0.97]	
Diabetes without chronic complication							
Yes	40 046	914 169.39	Ref		794 680.73	Ref	
		[905 205.75, 923 221.79]			[789 536.56, 799 858.41]		
No	257 554	826 225.36	0.90	p<0.001	748 257.02	0.94	p<0.001
		[823 201.28, 829 260.54]	[0.89, 0.91]		[746 268.72, 750 250.62]	[0.94, 0.95]	
Diabetes with chronic complication							
Yes	8959	915 347.36	Ref		783 602.75	Ref	
		[896 366.30, 934 730.35]			[773 012.63, 794 337.96]		
No	288 641	835 660.47	0.91	p<0.001	753 449.92	0.96	p<0.001
		[832 737.34, 838 593.86]	[0.89, 0.93]		[751 534.01, 755 370.71]	[0.95, 0.97]	
Hemiplegia or paraplegia							
Yes	3955	976 219.29	Ref		873 678.85	Ref	
		[944 738.52, 1 008 749.07]			[854 561.54, 893 223.84]		
No	293 645	836 198.54	0.86	p<0.001	752 855.32	0.86	p<0.001
		[833 292.41, 839 114.80]	[0.83, 0.89]		[750 954.84, 754 760.61]	[0.84, 0.88]	
Renal disease							
Yes	18 117	981 851.58	Ref		829 892.85	Ref	
		[967 029.48, 996 900.86]			[821 699.57, 838 167.82]		

9

Categories	n[‡]	Univariate analysis			Multivariable analysis		
		Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value	Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value
No	279 483	828 738.49 [825 830.94, 831 656.27]	0.84 [0.83, 0.86]	p<0.001	749 684.48 [747 756.51, 751 617.42]	0.90 [0.89, 0.91]	p<0.001
Any malignancy, including lymphoma and leukaemia, except malignant neoplasm of skin							
Yes	34 770	894 940.92 [885 556.43, 904 424.87]	Ref		756 333.75 [750 844.57, 761 863.06]	Ref	
No	262 830	830 534.45 [827 488.96, 833 591.14]	0.93 [0.92, 0.94]	p<0.001	754 076.15 [752 060.81, 756 096.88]	1.00 [0.99, 1.00]	0.450
Moderate or severe liver disease							
Yes	1293	759 638.71 [722 861.93, 798 286.57]	Ref		763 512.80 [737 776.84, 790 146.51]	Ref	
No	296 307	838 401.58 [835 498.51, 841 314.73]	1.10 [1.05, 1.16]	p<0.001	754 300.54 [752 402.34, 756 203.54]	0.99 [0.95, 1.02]	0.488
Metastatic solid tumour							
Yes	5601	844 997.61 [823 846.20, 866 692.06]	Ref		799 764.56 [786 066.03, 813 701.82]	Ref	
No	291 999	837 926.28 [835 003.64, 840 859.16]	0.99 [0.97, 1.02]	0.520	753 493.48 [751 586.47, 755 405.34]	0.94 [0.93, 0.96]	p<0.001
Emergency hospitalisation							
Yes	220 990	774 165.90 [771 234.05, 777 108.89]	Ref		801 606.91 [798 857.56, 804 365.73]	Ref	
No	56 736	972 011.84 [963 755.28, 980 339.13]	1.26 [1.24, 1.27]	p<0.001	607 271.67 [602 729.33, 611 848.24]	0.76 [0.75, 0.76]	p<0.001
Number of PIM drugs							
0	170 904	799 179.22 [795 776.56, 802 596.43]	Ref		773 552.61 [771 014.71, 776 098.86]	Ref	
1	23 553	675 395.61 [668 382.66, 682 482.15]	0.85 [0.84, 0.85]	p<0.001	632 724.36 [627 952.83, 637 532.13]	0.82 [0.81, 0.82]	p<0.001

10

Categories	n[‡]	Univariate analysis			Multivariable analysis		
		Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value	Geometric LS Mean[§] [95% CI]	Geometric LS Mean Ratio [95% CI]	P-value
2	22 405	717 867.17 [709 955.60, 725 866.90]	0.90 [0.89, 0.91]	p<0.001	609 627.10 [604 829.38, 614 462.89]	0.79 [0.78, 0.79]	p<0.001
3	15 929	786 527.42 [775 709.98, 797 495.71]	0.98 [0.97, 1.00]	0.031	651 387.10 [645 148.52, 657 686.00]	0.84 [0.83, 0.85]	p<0.001
≥4	64 809	1 053 920.10 [1 045 398.80, 1 062 510.86]	1.32 [1.31, 1.33]	p<0.001	839 977.97 [835 377.19, 844 604.09]	1.09 [1.08, 1.09]	p<0.001
ICU admission (Immediately after the admission)							
Yes	21 843	1 400 460.24 [1 377 051.74, 1 424 266.67]	Ref		1 200 167.33 [1 186 502.18, 1 213 989.87]	Ref	
No	275 757	793 510.74 [790 796.18, 796 234.61]	0.57 [0.56, 0.58]	p<0.001	727 493.58 [725 647.54, 729 344.32]	0.61 [0.60, 0.61]	p<0.001
Type of surgery							
No surgery	163 428	582 783.35 [581 113.35, 584 458.15]	Ref		521 053.69 [519 281.97, 522 831.45]	Ref	
Surgery + no/local/light general anaesthesia	88 164	992 997.25 [987 747.24, 998 275.17]	1.70 [1.69, 1.71]	p<0.001	1 010 902.09 [1 005 260.17, 1 016 575.68]	1.94 [1.93, 1.95]	p<0.001
Surgery + general anaesthesia (<2 hours)	29 725	1 178 860.92 [1 167 047.13, 1 190 794.29]	2.02 [2.00, 2.04]	p<0.001	1 349 139.14 [1 335 579.50, 1 362 836.45]	2.59 [2.56, 2.62]	p<0.001
Surgery + general anaesthesia (≥2 hours)	16 283	1 939 178.48 [1 904 403.92, 1 974 588.02]	3.33 [3.27, 3.39]	p<0.001	2 179 481.16 [2 141 798.56, 2 217 826.74]	4.18 [4.11, 4.26]	p<0.001

ADL, activities of daily living; ICU, intensive care unit; JPY, Japanese Yen; LS, least squares; n, number of patients; PIM, potentially inappropriate medication; Ref, reference category.

[†] *15 comorbidities excluding dementia and AIDS/HIV from the 17 Charlson comorbidities were examined.*

[‡] *Patients with missing data for the corresponding variable are not included. The multiple imputation method was applied only in the multivariable analysis.*

[§] *Unit: JPY.*

11