Long-Term Economic and Clinical Burden of Complicated Invasive Meningococcal Disease: Evidence From a United States Managed Care Population

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BACKGROUND

- The annual incidence of invasive meningococcal disease (IMD) in the United States (US) varies from 0.5 to 1.5 cases per 100,000 population.[1]
- Individuals with IMD have a high risk of death, with a case fatality rate of approximately 10%.[2] Moreover, approximately 10% to 20% of IMD survivors experience life-long, debilitating sequelae such as hearing loss, stroke, limb amputation, brain and nervous system damage, and seizure disorders.
- Although the high prevalence of serious complications in meningococcal infections has been well documented, a paucity of data exists in regard to the additional economic burden associated with the presence of IMD-related sequelae.

OBJECTIVE

- To compare health care utilization and costs, including both the initial acute hospitalization and postdischarge follow-up care, between commercially insured patients with IMD with and without related sequelae.

METHODS

Study Design and Data Source

- Retrospective longitudinal cohort analysis of the Ingenix Impact database for the years 1997 to 2009.
- Data contain administrative insurance claims from a national sample of over 40 managed care health plans covering approximately 95 million lives.
- The age and sex distribution of the health plan enrollees is representative of national managed care enrollment.
- Individuals from all four US census regions (Northeast, Midwest, South, and West) are represented in the data, with greater representation of individuals residing in the North, North Central, and Atlantic regions.
- Data include utilization and associated cost details for medical (e.g., inpatient, emergency department [ED], outpatient, physician office, nursing home, and rehabilitation services) and pharmacy services.

Research Cohort

- Patients with an inpatient diagnosis for IMD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 036.x)[3] from January 1, 1997, through June 30, 2008, were selected. The first observed IMD inpatient diagnosis defined the study index date.
- Patients were required to have continuous health plan enrollment for at least 6 months before and 12 months after the index IMD diagnosis date.

Outcome Measures

- All-cause health care utilization and associated costs incurred during the 12-month period after the index IMD diagnosis date.
- Health care utilization documented as (1) percentage of patients with at least one claim for each category of service (i.e., inpatient, ED, physician office, pharmacy, hospital outpatient, home health/durable medical equipment (HH/DME), laboratory, and ancillary care); (2) number of unique inpatient and ED admissions; (3) total days in hospital; (4) number of physician office, outpatient, and other ancillary care visits and pharmacy claims; and (5) percentage of patients with rehospitalization during the postindex period.
- Total aggregated all-cause costs (adjusted to 2009 US$) associated with the above outlined service categories.

Primary Independent Covariate

- The primary independent (i.e., explanatory) variable that was assessed was a binary indicator for IMD-related sequelae, categorized based on the presence (complicated IMD) or absence (uncomplicated IMD) of at least one IMD-related sequelae diagnosis on or at any time during the 12-month period on or after the index IMD diagnosis date.
- IMD-related sequelae included adrenal hemorrhage, hemiparesis, cranial nerve palsy, learning disabilities, mental retardation, blindness, quadriparesis, anoxic brain damage, skin necrosis or skin grafting, ataxia, limb amputation, obstructive hydrocephalus, chronic renal failure, epilepsy, hearing loss, seizure, and stroke. The outlined conditions were selected based on a review of the literature and from clinical experience. ICD-9-CM code list is available upon request.

Statistical Analyses

- All analyses were descriptive on all variables.
- Univariate differences in health care utilization and costs between patients with complicated and uncomplicated IMD were compared using Student's t-test for continuous variables and chi-square or Fisher's exact test for categorical variables.
- Multivariable regression was conducted for outcome comparison between patients with complicated and uncomplicated IMD after adjusting for patient baseline demographics and comorbidity burden (i.e., Charlson comorbidity index [CCI] score).
  - Cox proportional hazard models for dichotomous outcomes (e.g., had an ED visit)
  - Negative binomial regression for count outcomes (e.g., number of ED visits)
  - Generalized linear model for continuous outcomes (e.g., ED-related costs)
- The covariates included in each multivariable regression model were the following: indicator for presence or absence of an IMD-related complication, age, sex, geographic region, payer type, and CCI score.
- All statistical analyses were conducted using SAS 9.1.3 (Cary, NC) statistical software.

RESULTS

Background Characteristics (Table 1)

- 343 patients with IMD who met all study inclusion criteria were identified.
- Mean (standard deviation [SD]) age of patients with complicated IMD (41.4 [24.6]) was significantly higher than the mean age of patients with uncomplicated IMD (30.4 [20.6]; $P < 0.001$).

**Table 1. Patient Baseline Characteristics**

Characteristic	Overall IMD		Complicated IMDª		Uncomplicated IMD		P Value
	n	%	n	%	n	%	
All patients	343	100.00	117	100.00	226	100.00	
Mean age (SD)	34.2 (22.6)		41.4 (24.6)		30.4 (20.6)		< 0.001
Age group, years							
0-4	21	6.1	6	5.1	15	6.6	
5-10	27	7.9	8	6.8	19	8.4	0.148
11-18	54	15.7	12	10.3	42	18.6	
≥ 19	241	70.3	91	77.8	150	66.4	
Sex							
Male	190	55.4	64	54.7	126	55.8	0.853
Female	153	44.6	53	45.3	100	44.3	
Geographic region							
Northeast	135	39.4	45	38.5	90	39.8	
Midwest	44	12.8	18	15.4	26	11.5	
South	82	23.9	27	23.1	55	24.3	0.893
West	32	9.3	10	8.6	22	9.7	
National/other	50	14.6	17	14.5	33	14.6	
Payer type							
Medicare	9	2.6	6	5.1	3	1.3	
Medicaid	3	0.9	2	1.7	1	0.4	0.039
Commercial	331	96.5	109	93.2	222	98.2	
Insurance type							
HMO	93	27.1	36	30.8	57	25.2	
PPO	122	35.6	36	30.8	86	38.1	0.464
POS	101	29.5	34	29.1	67	29.7	
Other	27	7.9	11	9.4	16	7.1	

HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization.
ªComplicated IMD is defined as the presence of any sequelae of interest.

Prevalence of IMD-Related Sequelae (Figure 1)

- 117 of the selected IMD patients had evidence of one or more IMD-related sequelae.
- Stroke (n = 49, 14.3%), seizures (n = 40, 11.7%), hearing loss (n = 36, 10.5%), and epilepsy (n = 24, 7%) were the most commonly observed IMD-related sequelae.
- Prevalence of other sequelae ranged from 0.0% to 4.4%.

Figure 1. Percentage of Patients With IMD-Related Sequelae During the 12-Month Follow-Up Period
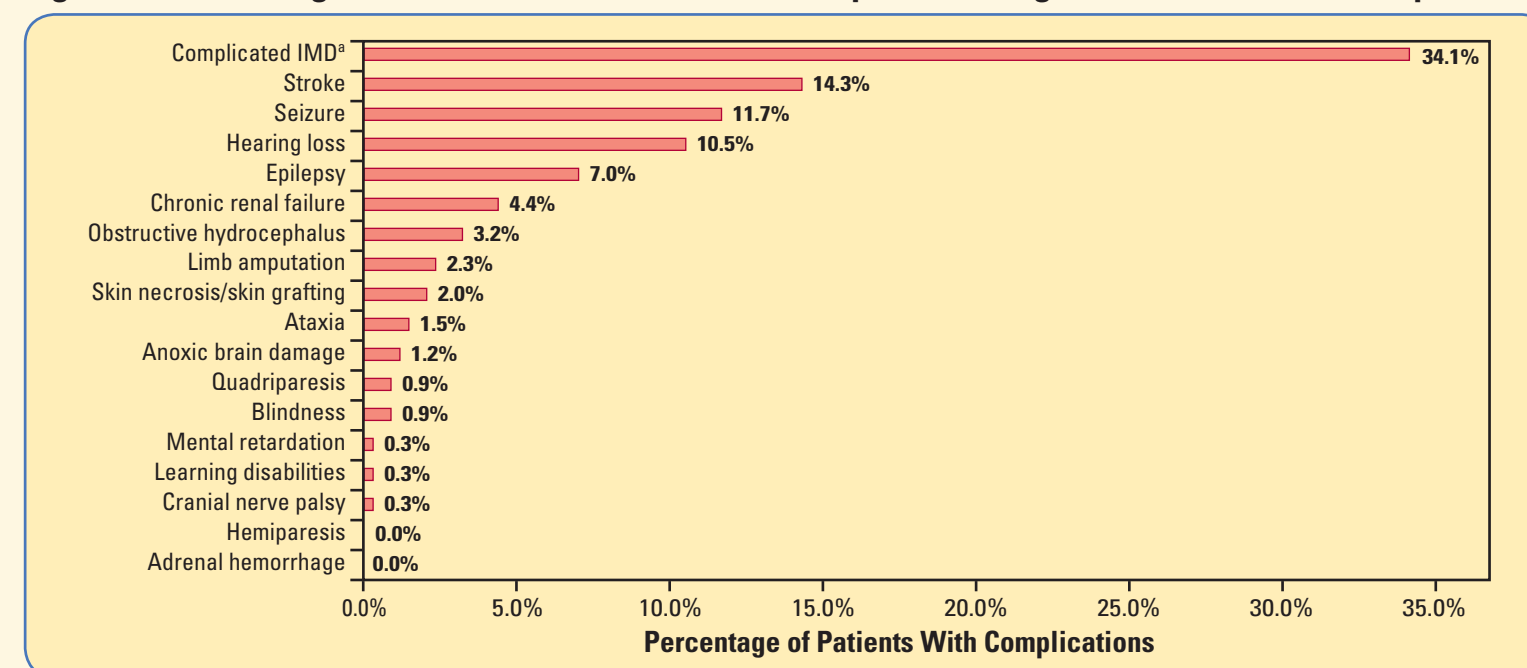
ªPatients with diagnosis for one or more of the listed IMD-related sequelae during the 12-month follow-up period.

Unadjusted Mean Health Care Utilization and Costs (Table 2)

- Compared with patients with uncomplicated IMD, patients with complicated IMD had a significantly higher mean number of inpatient admissions office visits, hospital outpatient visits, HH/DME visits, laboratory services, pharmacy claims, and ancillary encounters during the 12-month follow-up period.
- Unadjusted mean (SD) total health care costs for the overall study cohort were $55,001.96 ($108,858.35), with significantly higher mean total health care costs observed among patients with complicated IMD compared with patients with uncomplicated IMD.
- For both groups, inpatient costs accounted for over 75% of the total health care costs during the 12-month follow-up period.

Table 2. Unadjusted Mean Health Care Utilization and Costs During 12-Month Period After First IMD Diagnosis

| Health Care Service	Overall IMD		Complicated IMDª		Uncomplicated IMD		P Value
	n	%	n	%	n	%	
Inpatient services							
Had ≥ 1 hospital admission	343	100.00	117	100.00	226	100.00	—
Mean (SD) number of unique admissions	1.5 (1.3)		2.0 (2.0)		1.2 (0.6)		< 0.001
Mean (SD) total days in hospital	14.0 (27.6)		25.6 (42.3)		8.1 (11.3)		< 0.001
Mean (SD) total inpatient costs ($)	41,552.30 (96,517.64)		74,879.35 (155,443.34)		24,298.91 (28,741.16)		< 0.001
Had ≥ 1 rehospitalization	81	23.6	53	45.3	28	12.4	< 0.001
Mean (SD) number of unique rehospitalizations	0.5 (1.3)		1.0 (2.0)		0.2 (0.6)		< 0.001
ED visits							
Had ≥ 1 ED visit	253	73.8	93	79.5	160	70.8	0.083
Mean (SD) number of ED visits	1.3 (2.0)		1.6 (1.4)		1.2 (2.2)		0.074
Mean (SD) total ED costs ($)	879.16 (1,253.75)		1,227.60 (1,622.00)		698.77 (968.02)		0.002
Office visits							
Had ≥ 1 office visit	329	95.9	115	98.3	214	94.7	0.11
Mean (SD) number of office visits	11.7 (12.0)		15.1 (12.6)		9.9 (11.3)		< 0.001
Mean (SD) total office visit costs ($)	2,301.34 (4,738.07)		2,776.74 (3,137.70)		2,055.23 (5,372.97)		0.118
Pharmacy claims							
Had ≥ 1 prescription	212	61.8	75	64.1	137	60.6	0.529
Mean (SD) number of prescriptions obtained	10.9 (21.0)		18.6 (30.2)		6.9 (12.3)		< 0.001
Mean (SD) total pharmacy costs ($)	1,049.01 (2,458.18)		1,771.44 (3,173.83)		675.01 (1,892.02)		< 0.001
Hospital outpatient visits							
Had ≥ 1 hospital outpatient visit	286	83.4	113	96.58	173	76.6	< 0.001
Mean (SD) number of hospital outpatient visits	6.4 (11.9)		12.7 (17.9)		3.1 (4.5)		< 0.001
Mean (SD) total hospital outpatient costs ($)	5,624.06 (19,371.85)		13,224.15 (31,660.58)		1,689.50 (2,834.36)		< 0.001
HH/DME services							
Had ≥ 1 HH/DME service	161	46.9	64	54.7	97	42.9	0.038
Mean (SD) number of HH/DME services	4.6 (12.9)		9.1 (20.2)		2.3 (5.2)		< 0.001
Mean (SD) total HH/DME costs ($)	1,740.86 (4,937.84)		3,285.54 (7,809.36)		941.18 (1,932.92)		0.002
Laboratory services							
Had ≥ 1 laboratory service	203	59.2	81	69.2	122	54	0.006
Mean (SD) number of laboratory services	2.3 (4.1)		3.8 (5.7)		1.5 (2.6)		< 0.001
Mean (SD) total laboratory service costs ($)	361.49 (1,114.87)		563.56 (1,479.28)		256.88 (853.73)		0.04
Ancillary care							
Had ≥ 1 other ancillary care service	189	55.1	87	74.4	102	45.1	< 0.001
Mean (SD) number of ancillary care services	2.0 (5.1)		3.5 (6.6)		1.2 (3.9)		< 0.001
Mean (SD) total ancillary care costs ($)	1,493.74 (3,451.85)		2,014.19 (3,763.53)		1,224.31 (3,254.99)		0.055
Total health care utilization							
Had ≥ 1 medical encounter	343	100	117	100	226	100	—
Mean (SD) number of encounters	40.20 (44.22)		66.3 (60.1)		27.3 (25.0)		< 0.001
Mean (SD) total costs ($)	55,001.96 (108,858.35)		99,742.57 (172,815.09)		31,839.78 (32,176.91)		< 0.001

Risk-Adjusted Mean Health Care Utilization and Annual Costs (Table 3, Figure 2)

- During the 12-month follow-up period, patients with complicated IMD had a 54% higher rate of hospitalizations compared with patients with uncomplicated IMD (Table 3).
- Compared with patients with uncomplicated IMD, utilization rates were significantly higher among patients with complicated IMD for other service categories, including physician office visits, outpatient office visits, HH/DME visits, laboratory encounters, ancillary encounters, and pharmacy visits (Table 3).
- The risk of rehospitalization after discharge from the index IMD admission was higher among patients with complicated IMD (hazard ratio = 1.69; 95% confidence interval [CI]: 1.04-2.74) than in patients with uncomplicated IMD (tabular data available upon request).
- Significant differences in risk-adjusted predicted mean health care costs were observed among patients with both complicated and uncomplicated IMD across all service categories except for ancillary care, with the largest between-group difference in follow-up costs being for inpatient services ($71,646 vs. $24,838; $P < 0.001$) (Figure 2).
- Compared with patients with uncomplicated IMD, the total mean predicted health care costs were significantly high for patients with complicated IMD ($96,826 vs. $32,414; $P < 0.001$) (Figure 2).

Table 3. Risk of Event Estimated Using Negative Binomial Regressions: Complicated Versus Uncomplicated IMD

Event	Incident Rate Ratio	95% CI		P Value
		Lower Limit	Upper Limit	
Hospitalization	1.54	1.28	1.86	< 0.001
ED visit	1.27	1.00	1.62	0.054
Office visit	1.27	1.03	1.56	0.024
Outpatient visit	3.06	2.36	3.99	< 0.001
HH/DME visit	2.50	1.55	4.03	< 0.001
Laboratory encounter	1.87	1.33	2.65	< 0.001
Other ancillary encounter	2.15	1.50	3.08	< 0.001
Pharmacy visit	1.56	1.02	2.39	0.041

Figure 2. Risk-Adjusted Mean Predicted Health Care Costsª
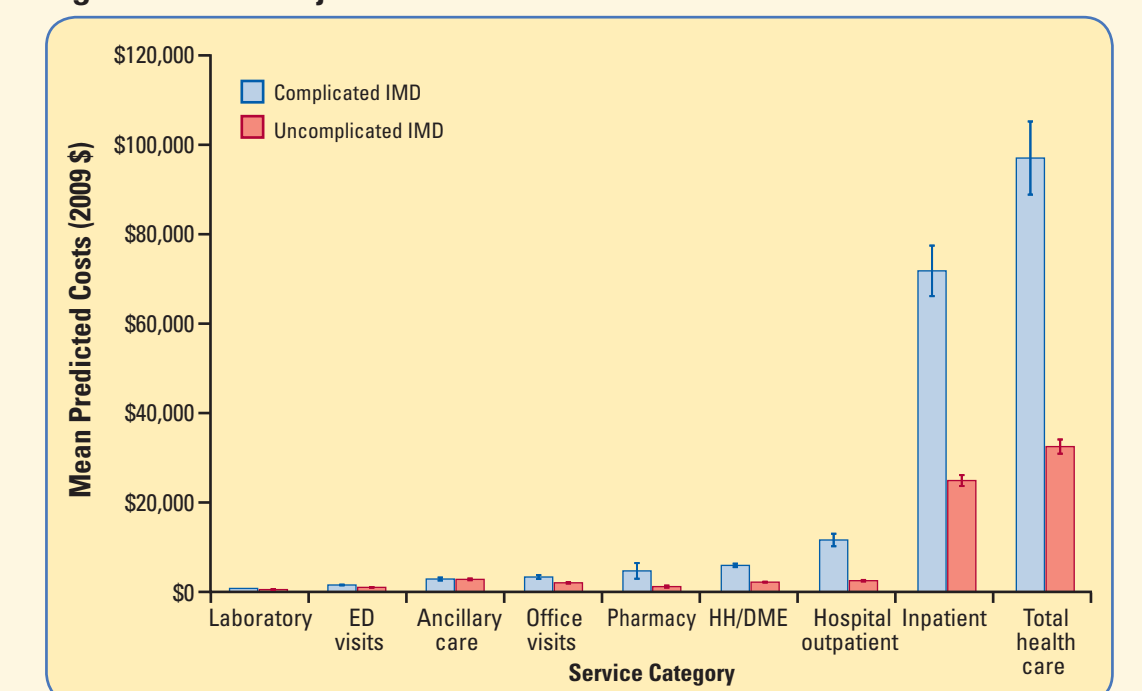
ªError bars represent 95% CIs for the mean predicted cost estimates.

LIMITATIONS

- Patient selection was based on diagnosis codes that, if recorded inaccurately, may have caused some misidentification of IMD.
- Study was limited to individuals enrolled in commercial managed care health plans and as a result may not be generalizable to persons in noncommercial health plans (e.g., Medicaid, Medicare, Veterans Affairs) or to the US population as a whole.
- Analyses were limited to direct treatment costs. Additional research on the indirect costs (e.g., loss of wages for employed patients with IMD; rehabilitative care provided by parents, guardians, and other caregivers) is warranted.

DISCUSSION AND CONCLUSIONS

- Approximately one-third of the selected IMD patients had evidence for one or more IMD-related sequelae during the follow-up period.
- As observed among prior studies,[4] seizures and hearing loss were commonly observed IMD-related sequelae. However, stroke was the most commonly observed IMD-related sequelae in our study, which is a finding that has not been documented previously. Future studies evaluating the prevalence of stroke among patients with IMD, particularly in larger populations, may help corroborate this finding.
- In general, IMD (both complicated and uncomplicated) is costly to payers, with an estimated average annual direct per-person cost of approximately $55,000. The presence of complications more than triples the total direct annual per-person cost from approximately $32,000 among patients with uncomplicated IMD to approximately $99,000 among patients with complicated IMD.
- Our study findings should serve as a useful resource for policy makers and researchers in designing and conducting cost-effectiveness analyses of meningococcal vaccination programs.

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DISCLOSURE

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