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Running head: Complications of medical care in US adults

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Abstract

Background:

Total US population estimates of adverse reactions (ARs) and complications of medical care (CMs) have relied on extrapolations of state-specific estimates. Generalizability is suspect because findings are limited by geographical location or time. We describe the relationship between the annual prevalence of adverse reactions and socio-demographic characteristics in the adult US population. We used data from the National Health Interview Surveys, annual nationwide surveys of the resident, civilian, noninstitutionalized population of the United States. A total of 618,167 reports of conditions from 313,438 subjects 18 years and older from 1987 to 1994 were examined. The main outcome of interest were self-reported conditions from ARs and activity limitations that arise from such events.

Results:

In 1987, 830,386 (558 per 100,000) adults reported AR/CM. This increased by 40% to 1,174,089 (an increase in rate by 25% to 678 per 100,000) adults in 1994. One-third reported onset a year prior to the interview; two-thirds visited a doctor six months prior; half experienced limitation in major activities; a quarter reported limitation in personal care activities. In the two weeks preceding the interview, AR/CM caused an average of 1.72 days of restricted activity, 0.79 days spent in bed, and 0.58 days of work lost. Race modified the age-specific risk of AR/CM.

Conclusions:

Adverse reactions and complications of medical care impose heavier morbidity than previously considered with some indication that socio-demographic variables modify the risk for injuries.

Estimates of adverse reactions and complications of medical care in the adult US population

Background

The Harvard Medical Practice Study (HMPS) examined the epidemiology of iatrogenic injuries arising from unintended adverse reactions (ARs) and complications of medical care (CMs), termed “adverse events” [1, 2]. The study recruited a random sample of patients discharged from hospitals in New York state in 1984. Adverse events were found to occur in 3.4% of patients undergoing medical management. Of these, 14% died [1].

Apart from raising awareness of the magnitude of the problem [3-8], data from the HMPS has been used to estimate rates for the entire US general population [9]. There is concern that the scope of the HMPS might produce inappropriate population estimates, given that it was limited to a single state and collected data for a single year. For instance, a recent hospital-based study conducted in Utah and Colorado [5] reported an adverse event rate of 2.9% following hospitalization. The authors’ extrapolation of this data to the general US population produced estimates that were lower than those derived from HMPS.

We present the results of analyses of self-reported adverse events using several years of cross-sectional data from a nationwide survey of US adults. We attempted to estimate the population prevalence of adverse events and examine the relationship between the self-reported AR/CM and selected socio-demographic variables.

Materials and Methods

The US Bureau of Census, under the specifications of the National Center for Health Statistics (NCHS), conducts the National Health Interview Survey (NHIS) to obtain data on the health of the resident, civilian, noninstitutionalized population of the United States. The NHIS, one of the oldest US national health surveys, has a complex multistage probability design that uses clustering and stratification with oversampling of selected population subgroups [10, 11]. The overall response rate has consistently been about 95%.

We evaluated NHIS data from 1987 to 1994 focusing on 313,438 participants aged 18 or older. The main outcome variable of interest was the occurrence of an injury condition reported by the respondent to have been due to (1) acute or chronic conditions associated with disability days, doctor visits and/or hospitalizations in the two weeks preceding the NHIS interview; (2) chronic conditions reported to be the main or secondary cause of activity limitation; or (3) chronic conditions reported in response to a checklist of conditions for each body system.

In the NHIS, this data was collected by asking the subject to identify conditions that impacted on their health (“Is [subject] limited in any activities because of an impairment or health problem?” and “What condition caused this?”) and by reading a standard list of chronic conditions and asking the subject whether he or she had any of the listed conditions. Responses were recoded by nosologists according to classifications based on the ninth revision of the International Classification of Diseases (ICD-9) [12]. This study focuses on ICD-9 codes 996 to 999 referring to

injuries due to complications of surgical and medical care (subsequently recoded by the NHIS as an “adverse reaction or complication of medical care”).

Secondary outcomes included the onset of AR/CM; the last time a physician was visited for the condition; the level of restrictions in major, work-related, and personal care activities imposed by AR/CM; and the number of total bed-days and days lost from work in the two-week period preceding the NHIS interview. Except for the latter two outcomes, all were coded using indicator variables.

The following socio-demographic variables were considered: age (7 categories), sex, race (white, black, other), region (US Northeast, Midwest, South, West), education (7 categories), annual family income (6 categories), major activity (work, housekeeping, school, other), and health status (excellent, very good, good, fair, poor). All socio-demographic variables were coded using indicator variables.

Race was coded as White, Black, or Other following NHIS data structures. This category is obviously racially heterogeneous and contributes about 2.5% of the total survey population. Nevertheless, we recognized the paucity of extant information and chose to retain the category in all analyses.

General population estimates of AR/CM took into account the complex sampling procedure employed by the National Center for Health Statistics. All analyses used methods to account for the sampling design of the study by utilizing weights provided on the NHIS data tapes to yield population estimates.

We derived annual estimates of the prevalence AR/CM from 1987 to 1994 and according to the selected socio-demographic variables. Contingency tables were analysed using chi-square tests corrected for the complex sampling design to test for

differences between variables [13, 14]. Univariate prevalence odds ratios of AR/CM were calculated for each of the socio-demographic variables previously identified. The two-way interaction between race and age was examined by including the relevant terms into the model. Three multivariate logistic regression models were applied to adjust for potentially confounding factors. Model 1 adjusted for the year of the survey. Model 2 included survey year plus education and annual income. Model 3 adjusted for all the variables in Model 2 plus major activity and self-reported health status. Tests were considered significant at $P < 0.05$.

Results

From 1987 to 1994, the NHIS sampled a total of 313,438 subjects aged 18 years or older. These subjects provided a total of 618,167 reports of conditions of which 3,740 were AR/CM.

Annual estimates of the prevalence of the condition in the total population are shown in Figure 1. The results point to a generally increasing trend in both the number and proportion of the total population with AR/CM. In 1987, a total of 830,368 US adults (558 per 100,000) reported such a condition. This figure increased by about 40% in 1994 to 1,174,089 adults (an increase of 25% to 678 per 100,000), although in a non-monotonic manner. The average increase in rates was about 3.38% (95% confidence interval [CI]=1.85-4.93) annually over the study period.

The socio-demographic characteristics of the study population and corresponding total population estimates are presented in Table 1. Univariate analyses suggest that there were no statistically significant differences in the risk of an injury due to

AR/CM by gender ($P=0.581$). There was some evidence of an increasing trend in risk of AR/CM by age ($P<0.001$). Significant associations in risk according to regional ($P=0.041$), racial ($P<0.001$), educational ($P<0.001$), and annual income ($P=0.001$) variables were also present. A statistically significant inverse relationship was seen between health status and the risk for AR/CM ($P<0.001$).

31.6% of all subjects reporting AR/CM stated it occurred within a year of the interview (Table 2). About 75% said they had visited a doctor within the past year to discuss the condition (about 66% in the past six months). About half said they experienced some degree of limitation in the performance of their major activities and a quarter reported some limitation in performing personal care activities due to their condition.

Overall, there was an average of 1.72 days of restricted activity, 0.79 days spent in bed, and 0.58 days of work lost due to AR/CM. When limited to AR/CM occurring in the two weeks prior to the interview, the results are 3.52, 1.90, and 1.51 days, respectively.

The interaction between race and age was found to be statistically significant in the base model ($P=0.016$). In whites, Model 1 suggested a steadily increasing trend in the risk AR/CM according to age, at least until the middle of the seventh decade of life (Table 3). Full adjustment verified that subjects aged 25 and older were at a statistically significantly increased risk for AR/CM. The highest risk corresponded to an 81% increase (95% CI=38%-138%) compared to the youngest age group. In blacks, adjustment for all variables suggested a 45% greater risk for AR/CM in persons aged 25 to 35 and those 35 to 44 years compared to those aged 18 to 24. All other age groups did not show statistical significance.

Results from the base model for other races indicate a bimodal pattern with peaks at 25 to 34 years and above 65 years of age that did not change appreciably with adjustment for all other confounders. For these age groups, the risk for AR/CM was more than twice that of the youngest age group.

Risk derived after adjustment for all variables are displayed graphically in Figure 2.

Discussion

While a number of studies have quantified the occurrence of adverse events in health systems [1, 2, 8, 15, 16], none have examined the impact of these events in a population-based sample of the US population. Using eight years of cross-sectional data from an on-going, annual population-based survey of the US adult population, we have attempted to measure the burden of morbidity arising from these events and to determine the relationship between AR/CM and socio-demographic variables.

Our estimates of prevalence differ from those conducted by other studies.

Extrapolations to the US general population of data from HMPS [1, 2] conducted in New York State in 1984 have indicated that over a million hospitalized patients suffered an injury due to medical treatment [9, 16]. Using similar methodology, a more recent study made similar extrapolations from data collected in Utah and Colorado, arriving at a total population figure slightly less than one million [5]. Even when limited to adults, our results point to population numbers averaging about 1 million over the seven-year period, with a suggestion of a generally increasing trend to values above this level. The inclusion of individuals less than 18 years of age increases the prevalence by about 25% to 33% (data not shown).

Our findings are strengthened by the use of data from subjects randomly selected from the total US population over eight years. Previous research has used hospital-based data to reach conclusions about the experience of the total population. The external validity of such inferences are conditioned on the representativeness of the study population on which the results are based. Hospitals often lack clear indications of the catchment populations to which such generalizations are to be made. This progressive hierarchical leap is hard to justify, especially if primary data from the total population of interest is publicly available, as is the NHIS. Furthermore, our data suggest that a statistically significant relationship exists between such injuries and certain US geographical regions, implying that estimates derived from localities may not correctly reflect the total population's experience.

The NHIS lacks both the ability to externally validate the veracity of self-reported claims of AR/CM and the specificity of classification offered by hospital-based studies. For instance, one cannot measure the extent to which subjects reported conditions that were due to some disease process instead of a particular complication of medical care. In some cases, ARs are an unavoidable outcome of therapy. In spite of this, our data captures a feature of inquiry that is missed by hospital-based studies: population estimates include injuries that arise from community-based sources. Thus, two different aspects of the same question are addressed.

A recent Australian study attempted to measure such incidents arising from the general practice setting. Of about 1,500 reports of adverse events received, 44% were due to premature or inappropriate use and 26% reported problems occurring during therapeutic use. About 15% of adverse events were due to the use of contraindicated medication and 11 percent were due to unintended medications or use that was not

medically indicated at the time [17]. It has been estimated that such incidents give rise to comparable costs to the health system as that due to all other forms of injury combined (including suicide, falls, homicide, etc.) [18].

In this study, injuries arising from adverse reactions were self-reported. Plausible situations arise that might account for differential reporting. These might take the form of differences in awareness that injuries may be related to certain adverse reactions, or local or nationwide publicity related to high-profile cases of adverse reactions being applied to personal situations. We do not have enough data to speculate as to how, or to what extent, these differences might have affected the results. However, biases arising from misclassification in this setting will tend to attenuate any relationships found, since there is no *a priori* evidence that one categorization was more likely than another. We propose four situations in which misclassification might be plausible.

Firstly, reporting behaviour, as with medication compliance or dietary recall, is a complex activity affected by numerous external factors [19, 20]. Secondly, subjects may attribute outcomes of the disease to outcomes of therapy, or vice-versa. Thirdly, the litigious character of participants in the US health system (in both providers and consumers of medical care) has been widely recognized [21, 22]. Lastly, increased media publicity about the impact of adverse events is known to make evaluation of symptoms difficult [23].

When modelling the risk for injuries due to adverse reactions, we found significant interaction between age and race. The effect of age had been previously examined in the HMPS [2]. In that study, subjects above 64 years of age were more than twice as likely to have an adverse event compared to those under 45 years. We hypothesized

that some degree of residual confounding was present when broad age ranges were used. Our unadjusted results mirror those of the HMPS findings. However, after adjustment for multiple variables, differences emerged. To our knowledge, this is the first indication of the presence of such an interaction. We explored the possibility that these results were due to some bias in the design of the study. The NHIS is known for the consistency of its data checks and response rates for the analysis period were consistently above 90%. Selection bias is unlikely in this setting.

We recognize the limitation of the racial classifications used by the NHIS, especially in the category labelled “Others”. However, the lack of available information for persons that could potentially be included in this category prompted us to keep the three-category coding. The results are admittedly unstable, given that analyses were based on much smaller sample sizes. Future research could examine this issue more finely.

If present, non-differential misclassification will generally tend to attenuate predicted differences between groups. For instance, this attenuation might have been the cause of the non-significant results seen in the older age groups. However, if present, the results for the younger age groups are expected to be underestimates of the true value.

Prevalence data was used to estimate risk. The prevalence odds ratio is an unbiased estimate of the incidence odds ratio if the exposure is unrelated to prognosis (ie., duration of illness is the same for exposed and unexposed groups). Since self-reported, cross-sectional data were used, we have no direct information on the longitudinal features of the condition. However, data from previous studies indicate that up to 10% of events lead to death [5], a figure not likely to impact heavily on these results.

Conclusions

These data suggest that self-reported injuries due to adverse reactions impose heavier morbidity than previously considered with some indication that socio-demographic variables modify the risk for injuries. Further studies are required to better understand these relationships.

Abbreviations

AR, adverse reaction; CI, confidence interval; CM, complication of medical care;
HMPS, Harvard Medical Practice Study; ICD-9, Ninth Revision of the International
Classification of Diseases; NCHS, National Center for Health Statistics; NHIS,
National Health Interview Survey; OR, odds ratio;

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Figures

Figure 1. Proportion and number of subjects with self-reported adverse reactions or complications of medical care by year, National Health Interview Surveys, 1987 to 1994.

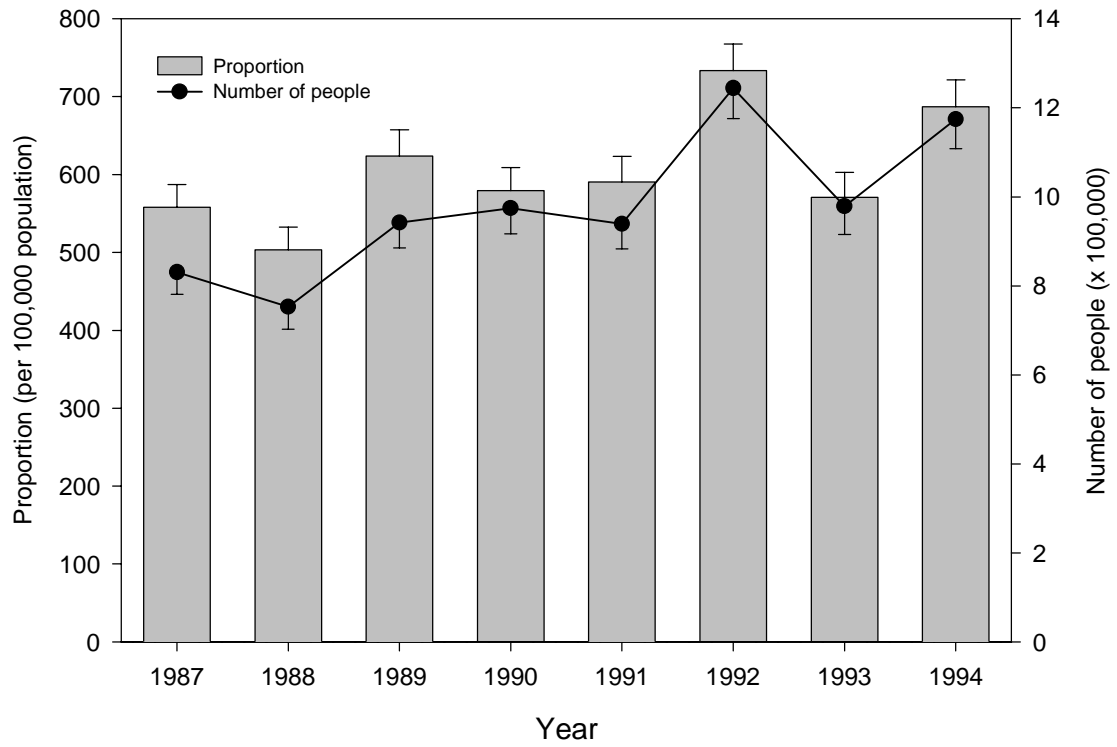
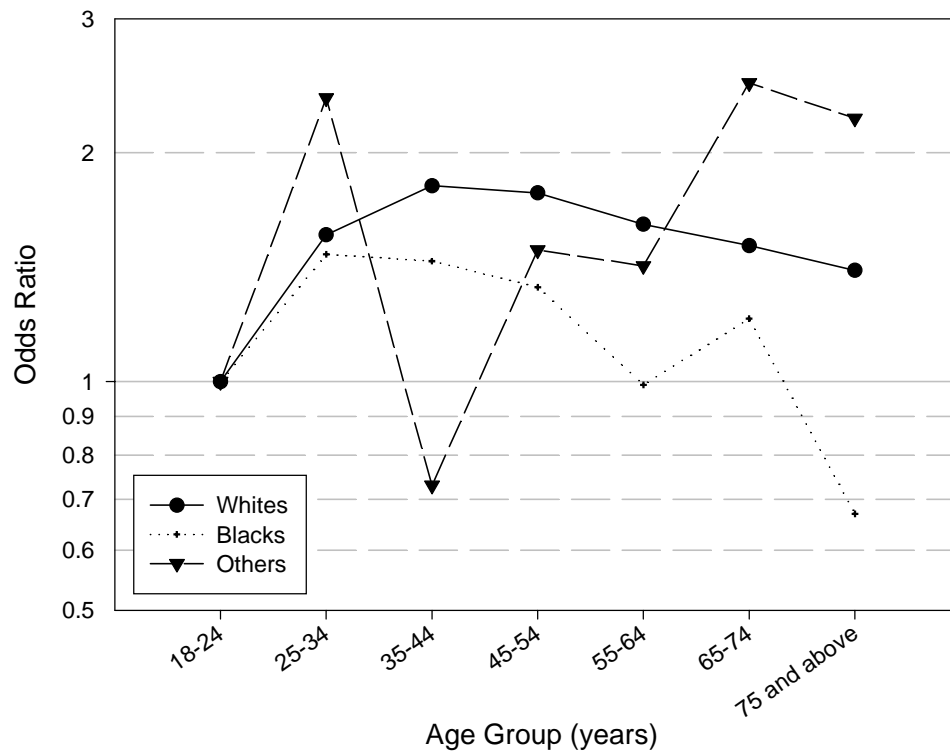


Figure 2. Multivariably adjusted race- and age-specific odds ratios for adverse reactions or complications of medical care in US adults, National Health Interview Surveys, 1987-1994.



Tables

Table 1. Descriptive characteristics of the study population according to selected socio-demographic variables, National Health Interview Surveys, 1987-1994.

Characteristic	Number (%*) of subjects	Number (%*) reporting adverse reaction or complication of medical care	Estimated size of total population reporting adverse reaction or complication of medical care	Estimated percentage of total population reporting adverse reaction or complication of medical care (95% confidence interval)†	Univariate prevalence odds ratio (95% confidence interval)‡
Sex					
Male	133,533 (42.61)	1,467 (39.22)	3,148,699	0.59 (0.55-0.62)	1.00
Female	179,885 (57.39)	2,273 (60.78)	4,686,767	0.62 (0.59-0.65)	0.98 (0.91-1.05)
Age, y					
18-24	26,484 (8.45)	137 (3.66)	318,035	0.36 (0.30-0.42)	1.00
25-34	54,177 (17.28)	437 (11.68)	964,060	0.52 (0.46-0.57)	1.48 (0.21-1.80)
35-44	58,533 (18.67)	593 (15.86)	1,234,644	0.59 (0.54-0.64)	1.68 (1.37-2.05)
45-54	47,343 (15.10)	582 (15.56)	1,202,700	0.64 (0.58-0.70)	1.77 (1.45-2.16)
55-64	46,321 (14.78)	675 (18.05)	1,402,819	0.67 (0.61-0.73)	1.77 (1.46-2.14)
65-74	46,266 (14.76)	774 (20.70)	1,577,256	0.70 (0.65-0.76)	1.80 (1.48-2.18)
75 and older	34,314 (10.95)	542 (14.49)	1,135,952	0.63 (0.56-0.69)	1.58 (1.30-1.93)
Race					
White	264,759 (84.47)	3,248 (86.84)	6,964,509	0.62 (0.59-0.65)	1.00
Black	40,936 (13.06)	416 (11.12)	681,855	0.49 (0.44-0.55)	0.78 (0.70-0.88)
Other	7,743 (2.47)	76 (2.03)	189,102	0.60 (0.46-0.75)	0.98 (0.77-1.26)
Region					
Northeast	60,690 (19.36)	640 (17.11)	1,301,268	0.54 (0.49-0.60)	1.00
Midwest	79,717 (25.43)	1,020 (27.27)	2,063,524	0.65 (0.59-0.70)	1.20 (1.06-1.37)
South	107,068 (34.16)	1,325 (35.43)	2,844,560	0.62 (0.57-0.66)	1.14 (1.01-1.29)
West	65,963 (21.04)	755 (20.19)	1,626,114	0.60 (0.55-0.65)	1.16 (1.02-1.31)
Education					
None	2,338 (0.75)	17 (0.46)	36,156	0.34 (0.17-0.50)	1.00
Elementary	38,727 (12.48)	627 (16.86)	1,253,608	0.65 (0.59-0.71)	1.99 (1.20-3.31)
Some high school	42,311 (13.63)	626 (16.83)	1,270,559	0.69 (0.63-0.75)	2.19 (1.31-3.65)
High school graduate	113,582 (36.60)	1,304 (35.06)	2,753,220	0.61 (0.57-0.65)	1.95 (1.17-3.24)
Some college	59,247 (19.09)	643 (17.29)	1,380,437	0.59 (0.54-0.64)	1.90 (1.14-3.17)
College graduate	30,244 (9.75)	286 (7.69)	631,982	0.56 (0.49-0.63)	1.74 (1.04-2.92)
Post-graduate	23,901 (7.70)	216 (5.81)	464,106	0.50 (0.44-0.57)	1.56 (0.93-2.63)
Annual family income, × \$1,000					
less than 5	14,133 (5.39)	209 (6.53)	399,542	0.59 (0.50-0.68)	1.00
5-14	58,044 (22.12)	910 (28.42)	1,840,201	0.65 (0.60-0.70)	1.10 (0.92-1.31)
15-24	54,733 (20.86)	760 (23.74)	1,593,795	0.70 (0.64-0.75)	1.19 (1.01-1.40)
25-34	42,195 (16.08)	450 (14.05)	976,522	0.60 (0.54-0.65)	1.02 (0.85-1.22)
35-44	30,964 (11.80)	310 (9.68)	676,843	0.59 (0.52-0.66)	1.00 (0.83-1.22)
45 and over	62,295 (23.74)	563 (17.58)	1,225,607	0.54 (0.49-0.59)	0.91 (0.76-1.09)
Major activity					
Work	160,556 (51.22)	1,320 (35.29)	2,817,570	0.50 (0.47-0.54)	1.00
Housekeeping	72,629 (23.17)	1,094 (29.25)	2,213,449	0.67 (0.63-0.71)	1.25 (1.14-1.36)
School	12,911 (4.12)	94 (2.51)	219,536	0.48 (0.37-0.59)	0.95 (0.75-1.21)
Other	67,342 (21.48)	1,232 (32.94)	2,584,911	0.73 (0.68-0.78)	1.40 (1.28-1.53)
Health status					
Excellent	63,171 (20.23)	397 (10.65)	864,061	0.45 (0.40-0.50)	1.00
Very good	79,749 (25.54)	581 (15.59)	1,216,534	0.45 (0.41-0.49)	0.98 (0.86-1.13)
Good	92,786 (29.71)	1,067 (28.64)	2,201,757	0.60 (0.56-0.64)	1.33 (1.17-1.50)
Fair	51,499 (16.49)	938 (25.17)	1,949,144	0.72 (0.66-0.78)	1.57 (1.37-1.80)
Poor	25,092 (8.03)	743 (19.94)	1,571,466	0.87 (0.80-0.94)	1.89 (1.64-2.17)

- * Figures are percentages of the total characteristic.
- † Figures take into consideration sampling weights due to complex sampling methodology.

Table 2. Characteristics of adverse reactions or complications of medical care in US adults, National Health Interview Surveys, 1987-1994.

Characteristic	Estimate	Estimated size of total population	Estimate for those with onset within the last two weeks
Onset of injury, % (SE)			
Within last 2 weeks	8.36 (0.48)	655,431	
2 weeks to less than 3 months	8.77 (0.48)	687,454	
3 months to less than 1 year	14.50 (0.72)	1,136,380	
1 year to less than 5 years	27.09 (0.78)	2,122,473	
5 years or more	41.27 (0.88)	3,233,728	
Last seen doctor for injury, % (SE)			
Within last 2 weeks	33.23 (0.83)	2,603,844	
2 weeks to less than 6 months	33.07 (0.76)	2,591,469	
6 months to less than 1 year	9.24 (0.52)	724,278	
1 to less than 2 years	6.34 (0.41)	496,974	
2 to less than 5 years	6.06 (0.43)	474,608	
5 years or more	6.46 (0.45)	506,082	
Doctor seen but not known when	1.15 (0.18)	89,916	
Not known whether doctor seen	0.48 (0.12)	38,015	
No doctor seen for condition	3.96 (0.34)	310,280	
Activity limitation due to injury, % (SE)			
Inability to perform major activity	27.58 (0.86)	2,161,159	
Limited in kind or amount of major activity	22.68 (0.76)	1,776,688	
Limited in other activities	16.68 (0.68)	1,307,326	
Not limited	33.06 (0.90)	2,590,293	
Assistance with personal care, % (SE)			
Inability to perform personal care needs	7.57 (0.67)	313,375	
Limited in performing other routine needs	17.93 (1.14)	742,373	
Not limited	74.50 (1.22)	3,084,719	
Number of days of restricted activity within the last two weeks, mean (SE)	1.72 (0.08)		3.52 (0.23)
Number of bed-days within the last two weeks, mean (SE)	0.79 (0.06)		1.90 (0.21)
Number of days of work lost within the last two weeks, mean (SE)	0.58 (0.06)		1.51 (0.20)

Table 3. Odds ratios for adverse reactions or complications of medical care with control for socio-demographic variables, by race and age, in US adults.

Age, y	White, odds ratio (95% confidence interval)		
	Model 1*	Model 2†	Model 3‡
18-24	1.00	1.00	1.00
25-34	1.48 (1.18-1.86)	1.53 (1.19-1.96)	1.56 (1.19-2.05)
35-44	1.75 (1.39-2.19)	1.88 (1.47-2.41)	1.81 (1.38-2.38)
45-54	1.83 (1.47-2.28)	1.97 (1.54-2.51)	1.77 (1.34-2.32)
55-64	1.89 (1.51-2.35)	1.93 (1.52-2.45)	1.61 (1.22-2.12)
65-74	1.85 (1.50-2.28)	1.85 (1.46-2.33)	1.51 (1.14-2.00)
75 and older	1.67 (1.34-2.08)	1.71 (1.34-2.18)	1.40 (1.06-1.86)
	Blacks, odds ratio (95% CI)		
18-24	1.00	1.00	1.00
25-34	1.40 (1.00-1.96)	1.50 (1.04-2.17)	1.47 (1.01-2.15)
35-44	1.60 (1.20-2.14)	1.61 (1.18-2.20)	1.44 (1.02-2.02)
45-54	1.47 (1.07-2.04)	1.60 (1.12-2.28)	1.33 (0.90-1.97)
55-64	1.22 (0.87-1.70)	1.23 (0.85-1.77)	0.99 (0.67-1.47)
65-74	1.45 (1.05-1.99)	1.48 (1.03-2.13)	1.21 (0.82-1.78)
75 and older	0.81 (0.52-1.26)	0.82 (0.49-1.36)	0.67 (0.40-1.12)
	Others, odds ratio (95% CI)		
18-24	1.00	1.00	1.00
25-34	2.26 (1.28-4.01)	2.44 (1.31-4.56)	2.36 (1.26-4.41)
35-44	0.66 (0.28-1.52)	0.80 (0.34-1.86)	0.73 (0.31-1.72)
45-54	1.72 (0.93-3.19)	1.73 (0.86-3.49)	1.49 (0.74-3.02)
55-64	1.51 (0.78-2.90)	1.72 (0.88-3.36)	1.42 (0.72-2.79)
65-74	2.58 (1.48-4.52)	3.04 (1.69-5.45)	2.47 (1.37-4.47)
75 and older	2.12 (0.92-4.87)	2.88 (1.20-6.92)	2.22 (0.93-5.33)

* Adjustment for survey year

† Model 1 plus adjustment for education and annual income

‡ Model 2 plus adjustment for major activity and health status

13 March 2001
Reviewers' reports

Estimates of adverse reactions and complications of medical care in the adult US population

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Jeremy N Anderson

Report from Peter Chyka

The objective of this manuscript is to estimate the population prevalence of adverse events based on self-reported complications reported in a national health survey during 1987 to 1994. The approach has merit as a means to characterize the problem of medical complications from a vantage point not previously reported. There are several major issues that require greater clarification in order to appropriately appreciate the findings.

1. Recall of events by patients. The authors should more fully address the apparent shortcoming of patient recall – one-third reported onset one year prior to the survey interview.

2. Causality: This issue is also related to patient recall. It is difficult enough to assess causality soon after an event in hospitalized patients by health care professionals. It would be surprising that patients would be better trained to determine causality unless their physician attributed the complication to a medical/surgical event. The following papers address the issues of patient perceptions and reporting practices regarding adverse drug events and medicine use.

Ottervanger JP, Valkenburg HA, Grobbee DE, et al. Differences in perceived and presented adverse drug reactions in general practice. *J Clin Epidem* 1998; 51: 795-799.

Bedell SE, Jabbour S, Goldberg R, et al. Discrepancies in the use of medications. *Arch Intern Med* 2000; 160: 2129-2134.

Barnes J, Mills SY, Abbot NC, et al. Different standards for reporting ADRs to herbal remedies and conventional OTC medicines; face-to-face interviews with 515 users of herbal remedies. *J Clin Pharmacol* 1998; 45: 496-500.

The estimates and odds ratios really represent self-reported, self-perceived complications that may over or under estimate the population prevalence. Instead of a problem with the denominator, there may be serious flaws in the numerator. At the conclusion of the study, we still don't know the true, verified prevalence of the problem. These issues should be expanded in the discussion and are major limitations of the study.

3. ICD-9 codes: The authors have chosen a series of ICD-9 codes that are primarily, but not exclusively, complications from surgical procedures or use of blood products or vaccines. This range of codes does not include adverse drug reactions. Accordingly, the authors should consider several approaches.

A) Provide some rationale for excluding adverse drug reactions. Most other studies include adverse drug reactions and the casual reader would assume that adverse drug reactions are included.

B) Create a table that lists the ICD-9 codes studied and provide the seven-year aggregate frequency distribution for each code represented. C) Limit the conclusion and findings to "complications" as opposed to "complications and adverse events" unless adverse drug reactions are included.

4. A minor point to consider: The authors should consider the points raised in the paper below that highlights the difference in definitions between the Harvard Medical Practice Study and the Utah-Colorado study. This may suggest a reason, in part, for the differing rates that were reported in these two papers as stated in the introduction.

McDonald CJ, Weiner M, Hui SL. Deaths due to medical errors are exaggerated in Institute of Medicine Report. JAMA 2000; 284: 93-97.

Level of interest

A paper whose findings are important to those with closely related research interests

Advice on publication

Unable to decide on acceptance or rejection until I see revised version

Quality of written English

Acceptable, readable and clearly written

Competing interests

Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this paper? If so, please specify.

No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper? If so, please specify.

No

Do you have any other financial competing interests? If so, please specify.

No

Are there any non-financial competing interests you would like to declare in relation to this paper? If so, please specify.

No

Open peer review

Do you consent to making your signed report accessible on the website should the paper be published?

Yes

Report from Tim Lesar

This is an interesting report which adds to the presently limited epidemiologic information related to adverse outcomes of medical care. The report utilizes a data source (NHIS from 87 TO 94) not previously evaluated for estimating population estimates AR and association with geographic and socio-demographic characteristics. The results further support previously available data suggesting a considerable and increasing incidence of AR of medical care in the US.

I have only a few comments regarding this manuscript.

1. The conclusions of the paper are clearly supported by the data.
2. The methods are well described and appropriate and is adequate for comparison with other similar work or replication of the work.
3. Work adheres to all standards for data reporting by clearly defining data source, analyses of such data. Relevant results are appropriately provided in adequate detail. Results are well displayed in tables and figures. Statistical analyses appropriately defined. Study limitations identified and discussed.
4. Conclusions well organized and appropriate.
5. All sections of the paper are well written.

Minor Comments / questions to consider:

1. NHIS data from 1987-1994. More current data (ie after 1995-97) would be of considerable interest given recent major changes in US health care. Are the authors planning on extending there data to include these years?
2. Any public policy implications from the results.
3. Does the data allow any estimate of national economic impact of AR to be determined?
4. Are changes in NHIS needed to better capture information related to AR? What might those changes entail?
5. Are the regional differences noted due to differences in healthcare spending / availability of services or other measurable factors?

Level of interest

A paper whose findings are important to those with closely related research interests

Advice on publication

Accept without revision

Quality of written English

Acceptable

Competing interests

Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this paper? If so, please specify.

No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper? If so, please specify.

No

Do you have any other financial competing interests? If so, please specify.

No

Are there any non-financial competing interests you would like to declare in relation to this paper? If so, please specify.

No

Open peer review

Do you consent to making your signed report accessible on the website should the paper be published?

Yes

20 March 2001
Revised version submitted

Estimates of complications of medical care in the adult US population

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Estimates of complications of medical care in the adult US population

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Abstract

Background:

Total US population estimates of complications of medical care (CMs) have relied on extrapolations of state-specific estimates. Generalizability is suspect because findings are limited by geographical location or time. We describe the relationship between the annual prevalence of adverse reactions and socio-demographic characteristics in the adult US population. We used data from the National Health Interview Surveys, annual nationwide surveys of the resident, civilian, noninstitutionalized population of the United States. A total of 618,167 reports of conditions from 313,438 subjects 18 years and older from 1987 to 1994 were examined. The main outcome of interest were self-reported conditions from CMs and activity limitations that arise from such events.

Results:

In 1987, 830,386 (558 per 100,000) adults reported CM. This increased by 40% to 1,174,089 (an increase in rate by 25% to 678 per 100,000) adults in 1994. One-third reported onset a year prior to the interview; two-thirds visited a doctor six months prior; half experienced limitation in major activities; a quarter reported limitation in personal care activities. In the two weeks preceding the interview, CM caused an average of 1.72 days of restricted activity, 0.79 days spent in bed, and 0.58 days of work lost. Race modified the age-specific risk of CM.

Conclusions:

Complications of medical care impose heavier morbidity than previously considered with some indication that socio-demographic variables modify the risk for injuries.

Estimates of complications of medical care in the adult US population

Background

The Harvard Medical Practice Study (HMPS) examined the epidemiology of iatrogenic injuries arising from unintended adverse reactions (ARs) and complications of medical care (CMs), termed “adverse events” [1, 2]. The study recruited a random sample of patients discharged from hospitals in New York state in 1984. Adverse events were found to occur in 3.4% of patients undergoing medical management. Of these, 14% died [1].

Apart from raising awareness of the magnitude of the problem [3-8], data from the HMPS has been used to estimate rates for the entire US general population [9]. There is concern that the scope of the HMPS might produce inappropriate population estimates, given that it was limited to a single state and collected data for a single year. For instance, a recent hospital-based study conducted in Utah and Colorado [5] reported an adverse event rate of 2.9% following hospitalization. The authors’ extrapolation of this data to the general US population produced estimates that were lower than those derived from HMPS.

We present the results of analyses of self-reported complications of medical care using several years of cross-sectional data from a nationwide survey of US adults. We attempted to estimate the population prevalence of adverse events and examine the relationship between the self-reported CM and selected socio-demographic variables.

Materials and Methods

The US Bureau of Census, under the specifications of the National Center for Health Statistics (NCHS), conducts the National Health Interview Survey (NHIS) to obtain data on the health of the resident, civilian, noninstitutionalized population of the United States. The NHIS, one of the oldest US national health surveys, has a complex multistage probability design that uses clustering and stratification with oversampling of selected population subgroups [10, 11]. The overall response rate has consistently been about 95%.

We evaluated NHIS data from 1987 to 1994 focusing on 313,438 participants aged 18 or older. The main outcome variable of interest was the occurrence of a injury condition reported by the respondent to have been due to (1) acute or chronic conditions associated with disability days, doctor visits and/or hospitalizations in the two weeks preceding the NHIS interview; (2) chronic conditions reported to be the main or secondary cause of activity limitation; or (3) chronic conditions reported in response to a checklist of conditions for each body system.

In the NHIS, this data was collected by asking the subject to identify conditions that impacted on their health (“Is [subject] limited in any activities because of an impairment or health problem?” and “What condition caused this?”) and by reading a standard list of chronic conditions and asking the subject whether he or she had any of the listed conditions. Responses were recoded by nosologists according to classifications based on the ninth revision of the International Classification of Diseases (ICD-9) [12]. This study focuses on ICD-9 codes 996 to 999 referring to injuries due to complications of surgical and medical care (subsequently recoded by the NHIS as an “adverse reaction or complication of medical care”).

Secondary outcomes included the onset of CM; the last time a physician was visited for the condition; the level of restrictions in major, work-related, and personal care activities imposed by CM; and the number of total bed-days and days lost from work in the two-week period preceding the NHIS interview. Except for the latter two outcomes, all were coded using indicator variables.

The following socio-demographic variables were considered: age (7 categories), sex, race (white, black, other), region (US Northeast, Midwest, South, West), education (7 categories), annual family income (6 categories), major activity (work, housekeeping, school, other), and health status (excellent, very good, good, fair, poor). All socio-demographic variables were coded using indicator variables.

Race was coded as White, Black, or Other following NHIS data structures. This category is obviously racially heterogeneous and contributes about 2.5% of the total survey population. Nevertheless, we recognized the paucity of extant information and chose to retain the category in all analyses.

General population estimates of CM took into account the complex sampling procedure employed by the National Center for Health Statistics. All analyses used methods to account for the sampling design of the study by utilizing weights provided on the NHIS data tapes to yield population estimates.

We derived annual estimates of the prevalence CM from 1987 to 1994 and according to the selected socio-demographic variables. Contingency tables were analysed using chi-square tests corrected for the complex sampling design to test for differences between variables [13, 14]. Univariate prevalence odds ratios of CM were calculated for each of the socio-demographic variables previously identified. The two-way interaction between race and age was examined by including the relevant terms into

the model. Three multivariate logistic regression models were applied to adjust for potentially confounding factors. Model 1 adjusted for the year of the survey. Model 2 included survey year plus education and annual income. Model 3 adjusted for all the variables in Model 2 plus major activity and self-reported health status. Tests were considered significant at $P < 0.05$.

Results

From 1987 to 1994, the NHIS sampled a total of 313,438 subjects aged 18 years or older. These subjects provided a total of 618,167 reports of conditions of which 3,740 were CM.

Annual estimates of the prevalence of the condition in the total population are shown in Figure 1. The results point to a generally increasing trend in both the number and proportion of the total population with CM. In 1987, a total of 830,368 US adults (558 per 100,000) reported such a condition. This figure increased by about 40% in 1994 to 1,174,089 adults (an increase of 25% to 678 per 100,000), although in a non-monotonic manner. The average increase in rates was about 3.38% (95% confidence interval [CI]=1.85-4.93) annually over the study period.

The socio-demographic characteristics of the study population and corresponding total population estimates are presented in Table 1. Univariate analyses suggest that there were no statistically significant differences in the risk of an injury due to CM by gender ($P=0.581$). There was some evidence of an increasing trend in risk of CM by age ($P < 0.001$). Significant associations in risk according to regional ($P=0.041$), racial ($P < 0.001$), educational ($P < 0.001$), and annual income ($P=0.001$) variables were also

present. A statistically significant inverse relationship was seen between health status and the risk for CM ($P<0.001$).

31.6% of all subjects reporting CM stated it occurred within a year of the interview (Table 2). About 75% said they had visited a doctor within the past year to discuss the condition (about 66% in the past six months). About half said they experienced some degree of limitation in the performance of their major activities and a quarter reported some limitation in performing personal care activities due to their condition.

Overall, there was an average of 1.72 days of restricted activity, 0.79 days spent in bed, and 0.58 days of work lost due to CM. When limited to CM occurring in the two weeks prior to the interview, the results are 3.52, 1.90, and 1.51 days, respectively.

The interaction between race and age was found to be statistically significant in the base model ($P=0.016$). In whites, Model 1 suggested a steadily increasing trend in the risk CM according to age, at least until the middle of the seventh decade of life (Table 3). Full adjustment verified that subjects aged 25 and older were at a statistically significantly increased risk for CM. The highest risk corresponded to an 81% increase (95% CI=38%-138%) compared to the youngest age group. In blacks, adjustment for all variables suggested a 45% greater risk for CM in persons aged 25 to 35 and those 35 to 44 years compared to those aged 18 to 24. All other age groups did not show statistical significance.

Results from the base model for other races indicate a bimodal pattern with peaks at 25 to 34 years and above 65 years of age that did not change appreciably with adjustment for all other confounders. For these age groups, the risk for CM was more than twice that of the youngest age group.

Risk derived after adjustment for all variables are displayed graphically in Figure 2.

Discussion

While a number of studies have quantified the occurrence of adverse events in health systems [1, 2, 8, 15, 16], none have examined the impact of these events in a population-based sample of the US population. Using eight years of cross-sectional data from an on-going, annual population-based survey of the US adult population, we have attempted to measure the burden of morbidity arising from these events and to determine the relationship between CM and socio-demographic variables.

Our estimates of prevalence differ from those conducted by other studies.

Extrapolations to the US general population of data from HMPS [1, 2] conducted in New York State in 1984 have indicated that over a million hospitalized patients suffered an injury due to medical treatment [9, 16]. Using similar methodology, a more recent study made similar extrapolations from data collected in Utah and Colorado, arriving at a total population figure slightly less than one million [5]. Even when limited to adults, our results point to population numbers averaging about 1 million over the seven-year period, with a suggestion of a generally increasing trend to values above this level. The inclusion of individuals less than 18 years of age increases the prevalence by about 25% to 33% (data not shown).

Our findings are strengthened by the use of data from subjects randomly selected from the total US population over eight years. Previous research has used hospital-based data to reach conclusions about the experience of the total population. The external validity of such inferences are conditioned on the representativeness of the

study population on which the results are based. Hospitals often lack clear indications of the catchment populations to which such generalizations are to be made. This progressive hierarchical leap is hard to justify, especially if primary data from the total population of interest is publicly available, as is the NHIS. Furthermore, our data suggest that a statistically significant relationship exists between such injuries and certain US geographical regions, implying that estimates derived from localities may not correctly reflect the total population's experience.

The NHIS lacks both the ability to externally validate the veracity of self-reported claims of CM and the specificity of classification offered by hospital-based studies. For instance, one cannot measure the extent to which subjects reported conditions that were due to some disease process instead of a particular complication of medical care. In some cases, ARs are an unavoidable outcome of therapy. In spite of this, our data captures a feature of inquiry that is missed by hospital-based studies: population estimates include injuries that arise from community-based sources. Thus, two different aspects of the same question are addressed.

A recent Australian study attempted to measure such incidents arising from the general practice setting. Of about 1,500 reports of adverse events received, 44% were due to premature or inappropriate use and 26% reported problems occurring during therapeutic use. About 15% of adverse events were due to the use of contraindicated medication and 11 percent were due to unintended medications or use that was not medically indicated at the time [17]. It has been estimated that such incidents give rise to comparable costs to the health system as that due to all other forms of injury combined (including suicide, falls, homicide, etc.) [18].

In this study, injuries arising from adverse reactions were self-reported. This dependence on the subject's self-reported recall of events is problematic only if differential recall is related to the outcome of interest. However, due to a lack of validation from external sources (i.e., medical records, case notes, etc.), we are unable to exclude the possibility that point estimates within populations or specific subgroups are misrepresented, especially since some subjects were asked to recall events that took place up to one year from the interview.

Plausible situations arise that might account for differential reporting or misclassification. These might take the form of differences in awareness that injuries may be related to certain adverse reactions, or local or nationwide publicity related to high-profile cases of adverse reactions being applied to personal situations. We do not have enough data to speculate as to how, or to what extent, these differences might have affected the results. However, biases arising from misclassification in this setting will tend to attenuate any relationships found, since there is no *a priori* evidence that one categorization was more likely than another. We propose four situations in which misclassification might be plausible.

Firstly, reporting behaviour, as with medication compliance or dietary recall, is a complex activity affected by numerous external factors [19, 20]. Secondly, subjects may attribute outcomes of the disease to outcomes of therapy, or vice-versa. Thirdly, the litigious character of participants in the US health system (in both providers and consumers of medical care) has been widely recognized [21, 22]. Lastly, increased media publicity about the impact of adverse events is known to make evaluation of symptoms difficult [23].

Prevalence data was used to estimate risk, but its interpretation is relevant only insofar as it is related to the associations with relevant covariates or groups of covariates suggested by the statistical models. Any suggestion that these results imply causality is an inappropriate appreciation of the complexity of the subject matter and the inadequacy of the primary design of the NHIS. For instance, the prevalence odds ratio is an unbiased estimate of the incidence odds ratio only if the exposure is unrelated to prognosis (ie., duration of illness is the same for exposed and unexposed groups). Since self-reported, cross-sectional data were used, we have no direct information about the longitudinal features of the condition. Hence, even the most fundamental criterion in arguing for the presence of causation – temporality - is unfulfilled.

When modelling the risk for injuries due to adverse reactions, we found significant interaction between age and race. The effect of age had been previously examined in the HMPS [2]. In that study, subjects above 64 years of age were more than twice as likely to have an adverse event compared to those under 45 years. We hypothesized that some degree of residual confounding was present when broad age ranges were used. Our unadjusted results mirror those of the HMPS findings. However, after adjustment for multiple variables, differences emerged. To our knowledge, this is the first indication of the presence of such an interaction. We explored the possibility that these results were due to some bias in the design of the study. The NHIS is known for the consistency of its data checks and response rates for the analysis period were consistently above 90%. Selection bias is unlikely in this setting.

We recognize the limitation of the racial classifications used by the NHIS, especially in the category labelled “Others”. However, the lack of available information for persons that could potentially be included in this category prompted us to keep the

three-category coding. The results are admittedly unstable, given that analyses were based on much smaller sample sizes. Future research could examine this issue more finely.

If present, non-differential misclassification will generally tend to attenuate predicted differences between groups. For instance, this attenuation might have been the cause of the non-significant results seen in the older age groups. However, if present, the results for the younger age groups are expected to be underestimates of the true value.

The potential immediate and long-term research and policy implications of these findings are many and have been discussed previously in other fora. This study lends support for the development of common definitions and systems for the routine collection and analysis of data from adverse events and complications of medical care. These information systems should not only have the capacity to exploit the inherently hierarchical nature of specific health service boundaries (ie., hospitals within counties within states within regions), but also provide a means of promoting a systematic method to the strengthening of approaches to quality of care within the larger health care community.

Conclusions

These data suggest that self-reported injuries due to adverse reactions impose heavier morbidity than previously considered with some indication that socio-demographic variables modify the risk for injuries. Further studies are required to better understand these relationships.

Abbreviations

CI, confidence interval; CM, complication of medical care; HMPS, Harvard Medical Practice Study; ICD-9, Ninth Revision of the International Classification of Diseases; NCHS, National Center for Health Statistics; NHIS, National Health Interview Survey; OR, odds ratio;

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Figures

Figure 1. Proportion and number of subjects with self-reported complications of medical care by year, National Health Interview Surveys, 1987 to 1994.

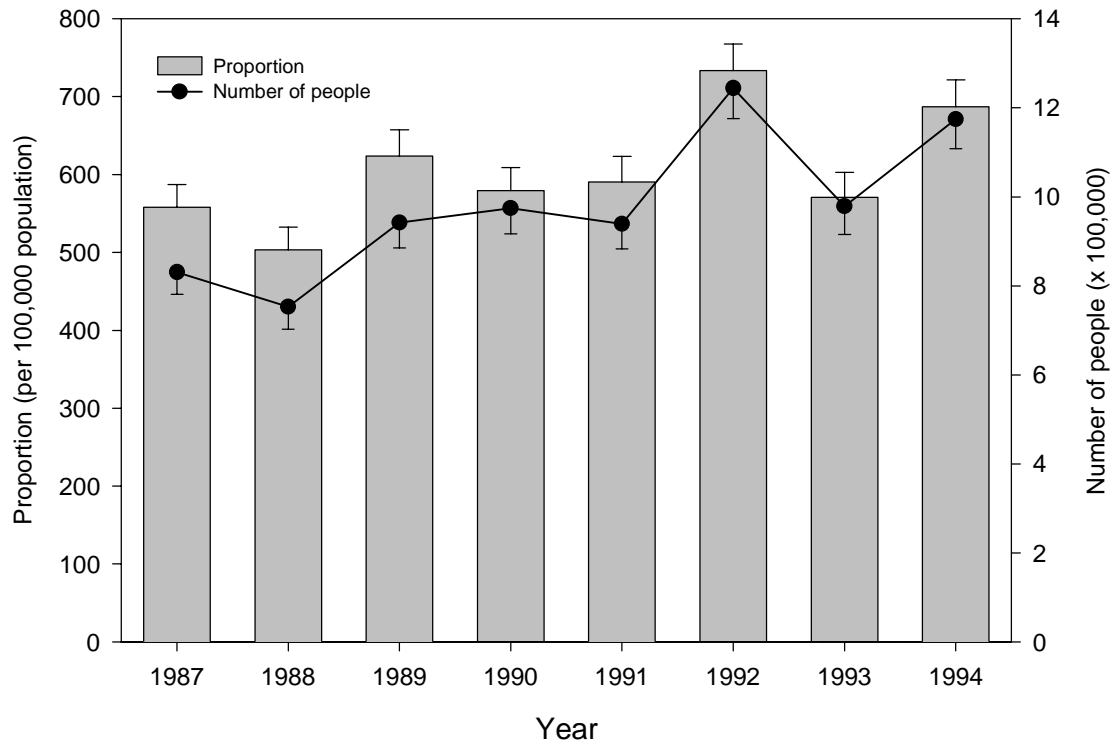
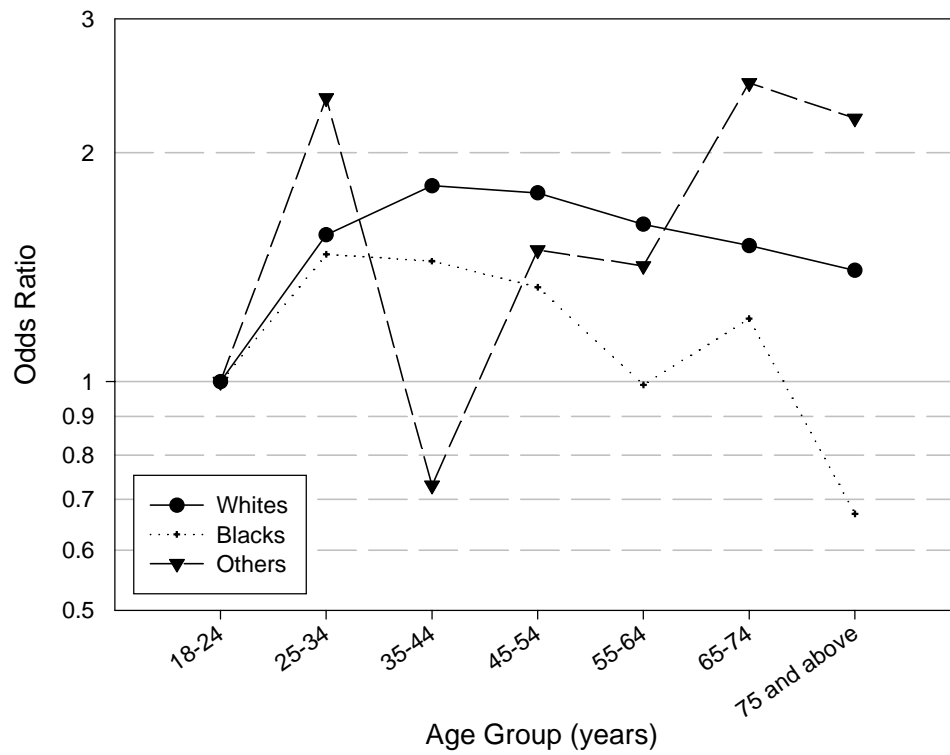


Figure 2. Multivariably adjusted race- and age-specific odds ratios for complications of medical care in US adults, National Health Interview Surveys, 1987-1994.



Tables

Table 1. Descriptive characteristics of the study population according to selected socio-demographic variables, National Health Interview Surveys, 1987-1994.

Characteristic	Number (%*) of subjects	Number (%*) reporting complication of medical care	Estimated size of total population reporting complication of medical care	Estimated percentage of total population reporting complication of medical care (95% confidence interval)†	Univariate prevalence odds ratio (95% confidence interval)†
Sex					
Male	133,533 (42.61)	1,467 (39.22)	3,148,699	0.59 (0.55-0.62)	1.00
Female	179,885 (57.39)	2,273 (60.78)	4,686,767	0.62 (0.59-0.65)	0.98 (0.91-1.05)
Age, y					
18-24	26,484 (8.45)	137 (3.66)	318,035	0.36 (0.30-0.42)	1.00
25-34	54,177 (17.28)	437 (11.68)	964,060	0.52 (0.46-0.57)	1.48 (0.21-1.80)
35-44	58,533 (18.67)	593 (15.86)	1,234,644	0.59 (0.54-0.64)	1.68 (1.37-2.05)
45-54	47,343 (15.10)	582 (15.56)	1,202,700	0.64 (0.58-0.70)	1.77 (1.45-2.16)
55-64	46,321 (14.78)	675 (18.05)	1,402,819	0.67 (0.61-0.73)	1.77 (1.46-2.14)
65-74	46,266 (14.76)	774 (20.70)	1,577,256	0.70 (0.65-0.76)	1.80 (1.48-2.18)
75 and older	34,314 (10.95)	542 (14.49)	1,135,952	0.63 (0.56-0.69)	1.58 (1.30-1.93)
Race					
White	264,759 (84.47)	3,248 (86.84)	6,964,509	0.62 (0.59-0.65)	1.00
Black	40,936 (13.06)	416 (11.12)	681,855	0.49 (0.44-0.55)	0.78 (0.70-0.88)
Other	7,743 (2.47)	76 (2.03)	189,102	0.60 (0.46-0.75)	0.98 (0.77-1.26)
Region					
Northeast	60,690 (19.36)	640 (17.11)	1,301,268	0.54 (0.49-0.60)	1.00
Midwest	79,717 (25.43)	1,020 (27.27)	2,063,524	0.65 (0.59-0.70)	1.20 (1.06-1.37)
South	107,068 (34.16)	1,325 (35.43)	2,844,560	0.62 (0.57-0.66)	1.14 (1.01-1.29)
West	65,963 (21.04)	755 (20.19)	1,626,114	0.60 (0.55-0.65)	1.16 (1.02-1.31)
Education					
None	2,338 (0.75)	17 (0.46)	36,156	0.34 (0.17-0.50)	1.00
Elementary	38,727 (12.48)	627 (16.86)	1,253,608	0.65 (0.59-0.71)	1.99 (1.20-3.31)
Some high school	42,311 (13.63)	626 (16.83)	1,270,559	0.69 (0.63-0.75)	2.19 (1.31-3.65)
High school graduate	113,582 (36.60)	1,304 (35.06)	2,753,220	0.61 (0.57-0.65)	1.95 (1.17-3.24)
Some college	59,247 (19.09)	643 (17.29)	1,380,437	0.59 (0.54-0.64)	1.90 (1.14-3.17)
College graduate	30,244 (9.75)	286 (7.69)	631,982	0.56 (0.49-0.63)	1.74 (1.04-2.92)
Post-graduate	23,901 (7.70)	216 (5.81)	464,106	0.50 (0.44-0.57)	1.56 (0.93-2.63)
Annual family income, × \$1,000					
less than 5	14,133 (5.39)	209 (6.53)	399,542	0.59 (0.50-0.68)	1.00
5-14	58,044 (22.12)	910 (28.42)	1,840,201	0.65 (0.60-0.70)	1.10 (0.92-1.31)
15-24	54,733 (20.86)	760 (23.74)	1,593,795	0.70 (0.64-0.75)	1.19 (1.01-1.40)
25-34	42,195 (16.08)	450 (14.05)	976,522	0.60 (0.54-0.65)	1.02 (0.85-1.22)
35-44	30,964 (11.80)	310 (9.68)	676,843	0.59 (0.52-0.66)	1.00 (0.83-1.22)
45 and over	62,295 (23.74)	563 (17.58)	1,225,607	0.54 (0.49-0.59)	0.91 (0.76-1.09)
Major activity					
Work	160,556 (51.22)	1,320 (35.29)	2,817,570	0.50 (0.47-0.54)	1.00
Housekeeping	72,629 (23.17)	1,094 (29.25)	2,213,449	0.67 (0.63-0.71)	1.25 (1.14-1.36)
School	12,911 (4.12)	94 (2.51)	219,536	0.48 (0.37-0.59)	0.95 (0.75-1.21)
Other	67,342 (21.48)	1,232 (32.94)	2,584,911	0.73 (0.68-0.78)	1.40 (1.28-1.53)
Health status					
Excellent	63,171 (20.23)	397 (10.65)	864,061	0.45 (0.40-0.50)	1.00
Very good	79,749 (25.54)	581 (15.59)	1,216,534	0.45 (0.41-0.49)	0.98 (0.86-1.13)
Good	92,786 (29.71)	1,067 (28.64)	2,201,757	0.60 (0.56-0.64)	1.33 (1.17-1.50)
Fair	51,499 (16.49)	938 (25.17)	1,949,144	0.72 (0.66-0.78)	1.57 (1.37-1.80)
Poor	25,092 (8.03)	743 (19.94)	1,571,466	0.87 (0.80-0.94)	1.89 (1.64-2.17)

* Figures are percentages of the total characteristic.

† Figures take into consideration sampling weights due to complex sampling methodology.

Table 2. Characteristics of complications of medical care in US adults, National Health Interview Surveys, 1987-1994.

Characteristic	Estimate	Estimated size of total population	Estimate for those with onset within the last two weeks
Onset of injury, % (SE)			
Within last 2 weeks	8.36 (0.48)	655,431	
2 weeks to less than 3 months	8.77 (0.48)	687,454	
3 months to less than 1 year	14.50 (0.72)	1,136,380	
1 year to less than 5 years	27.09 (0.78)	2,122,473	
5 years or more	41.27 (0.88)	3,233,728	
Last seen doctor for injury, % (SE)			
Within last 2 weeks	33.23 (0.83)	2,603,844	
2 weeks to less than 6 months	33.07 (0.76)	2,591,469	
6 months to less than 1 year	9.24 (0.52)	724,278	
1 to less than 2 years	6.34 (0.41)	496,974	
2 to less than 5 years	6.06 (0.43)	474,608	
5 years or more	6.46 (0.45)	506,082	
Doctor seen but not known when	1.15 (0.18)	89,916	
Not known whether doctor seen	0.48 (0.12)	38,015	
No doctor seen for condition	3.96 (0.34)	310,280	
Activity limitation due to injury, % (SE)			
Inability to perform major activity	27.58 (0.86)	2,161,159	
Limited in kind or amount of major activity	22.68 (0.76)	1,776,688	
Limited in other activities	16.68 (0.68)	1,307,326	
Not limited	33.06 (0.90)	2,590,293	
Assistance with personal care, % (SE)			
Inability to perform personal care needs	7.57 (0.67)	313,375	
Limited in performing other routine needs	17.93 (1.14)	742,373	
Not limited	74.50 (1.22)	3,084,719	
Number of days of restricted activity within the last two weeks, mean (SE)	1.72 (0.08)		3.52 (0.23)
Number of bed-days within the last two weeks, mean (SE)	0.79 (0.06)		1.90 (0.21)
Number of days of work lost within the last two weeks, mean (SE)	0.58 (0.06)		1.51 (0.20)

Table 3. Odds ratios for complications of medical care with control for socio-demographic variables, by race and age, in US adults.

Age, y	White, odds ratio (95% confidence interval)		
	Model 1*	Model 2†	Model 3‡
18-24	1.00	1.00	1.00
25-34	1.48 (1.18-1.86)	1.53 (1.19-1.96)	1.56 (1.19-2.05)
35-44	1.75 (1.39-2.19)	1.88 (1.47-2.41)	1.81 (1.38-2.38)
45-54	1.83 (1.47-2.28)	1.97 (1.54-2.51)	1.77 (1.34-2.32)
55-64	1.89 (1.51-2.35)	1.93 (1.52-2.45)	1.61 (1.22-2.12)
65-74	1.85 (1.50-2.28)	1.85 (1.46-2.33)	1.51 (1.14-2.00)
75 and older	1.67 (1.34-2.08)	1.71 (1.34-2.18)	1.40 (1.06-1.86)
	Blacks, odds ratio (95% CI)		
18-24	1.00	1.00	1.00
25-34	1.40 (1.00-1.96)	1.50 (1.04-2.17)	1.47 (1.01-2.15)
35-44	1.60 (1.20-2.14)	1.61 (1.18-2.20)	1.44 (1.02-2.02)
45-54	1.47 (1.07-2.04)	1.60 (1.12-2.28)	1.33 (0.90-1.97)
55-64	1.22 (0.87-1.70)	1.23 (0.85-1.77)	0.99 (0.67-1.47)
65-74	1.45 (1.05-1.99)	1.48 (1.03-2.13)	1.21 (0.82-1.78)
75 and older	0.81 (0.52-1.26)	0.82 (0.49-1.36)	0.67 (0.40-1.12)
	Others, odds ratio (95% CI)		
18-24	1.00	1.00	1.00
25-34	2.26 (1.28-4.01)	2.44 (1.31-4.56)	2.36 (1.26-4.41)
35-44	0.66 (0.28-1.52)	0.80 (0.34-1.86)	0.73 (0.31-1.72)
45-54	1.72 (0.93-3.19)	1.73 (0.86-3.49)	1.49 (0.74-3.02)
55-64	1.51 (0.78-2.90)	1.72 (0.88-3.36)	1.42 (0.72-2.79)
65-74	2.58 (1.48-4.52)	3.04 (1.69-5.45)	2.47 (1.37-4.47)
75 and older	2.12 (0.92-4.87)	2.88 (1.20-6.92)	2.22 (0.93-5.33)

* Adjustment for survey year

† Model 1 plus adjustment for education and annual income

‡ Model 2 plus adjustment for major activity and health status

22 March 2001

Second round of reviewers' reports

Estimates of complications of medical care in the adult US population

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Jeremy N Anderson

Report from Peter Chyka

Re: Villanueva and Anderson,
'Estimates of complications of medical care in the adult US population'

Reviewer's Comments: Peter A. Chyka

March 21, 2001

The authors have addressed many of the issues raised in the previous review in a swift and acceptable manner. In reviewing the revision, there are several additional or remaining issues that could benefit with further clarification. My comments are shown in brackets [] and in blue.

1. P2 Results: In 1987, 830,386 (558 per 100,000) adults reported CM. [To this sentence I would suggest adding something as follows so that the numbers make sense to the reader based on the actual number of 313,438 subjects in the survey. "...based on an extrapolation to the US population."]
2. [A minor point: Why abbreviate CM since space is not a limitation of this medium? It would be more readable without CM abbreviated.]
3. P5 We attempted to estimate the population prevalence of adverse events and examine the relationship between the self-reported CM and selected socio-demographic variables. [Since adverse events are not really included in the dataset, I would suggest limiting it here, as the authors have elsewhere to "medical complication."]
4. P6 This study focuses on ICD-9 codes 996 to 999 referring to injuries due to complications of surgical and medical care (subsequently recoded by the NHIS as an "adverse reaction or complication of medical care"). [To make the reader aware that adverse drug reactions are not included, the authors may want to consider adding a sentence such as. "This range of ICD-9 codes excludes adverse drug reactions (ICD-9 995 and E930 to E949)."]
5. P8 [Could the authors describe what computerized statistical program they used for multivariate regression and other statistical tests? Either reference it or include as a parenthetical entry.]
6. P9 In 1987, a total of 830,368 US adults (558 per 100,000) reported such a condition. This figure increased by about 40% in 1994 to 1,174,089 adults (an increase of 25% to 678 per 100,000), although in a non-monotonic manner. [To these sentences I would suggest adding something as follows so that the numbers make sense to the reader based on the actual number of 313,438 subjects in the survey. "...based on an extrapolation to the US population."]
7. P12 . The inclusion of individuals less than 18 years of age increases the prevalence by about 25% to 33% (data not shown). [Since this not the focus of the study, this observation is irrelevant and should be deleted.]

8. P13 In some cases, ARs are an unavoidable outcome of therapy. [Adverse reactions are not fully described in this dataset and it would be more appropriate to refer to the events as medical complications as the authors have done elsewhere.]
9. P14 In this study, injuries arising from adverse reactions were self-reported. [Adverse reactions are not fully described in this dataset and it would be more appropriate to refer to the events as medical complications as the authors have done elsewhere.]
10. P16 When modeling the risk for injuries due to adverse reactions, we found significant interaction between age and race. [Adverse reactions are not fully described in this dataset and it would be more appropriate to refer to the events as medical complications as the authors have done elsewhere.]
11. P17 The potential immediate and long-term research and policy implications of these findings are many and have been discussed previously in other fora. [For completeness, could the authors cite one or two of the other fora?]
12. P20 [While I was flattered to be listed in the acknowledgement, it is really unnecessary. My comments are simply those of a peer-reviewer.]
13. P25 Figure 1. Proportion and number of subjects with self-reported complications of medical care by year, National Health Interview Surveys, 1987 to 1994. [To this sentence I would suggest adding something as "...based on an extrapolation to the US population."]
14. P28 [Why was SE and not SD used to report variability around the mean?]
15. Add Table. [I still think that a table of the ICD-9 conditions and the aggregate counts by condition would be valuable to the reader to understand the items included in the dataset. Since this journal format is not limited by size, this seems to be a perfect medium to provide such a list.]

These are the codes as I understand them.

996.0 Mechanical complications of cardiac device, implant and graft
996.1 Mechanical complications of other vascular device, implant and graft
etc.
996.8 Complications of transplanted organ
996.9 Complications of reattached extremity or body part
997.0 Central nervous systems complications during or resulting from a procedure
997.1 Cardiac complications during or resulting from a procedure
997.2 Peripheral vascular complications during or resulting from a procedure
etc.
998.0 Postoperative shock during or resulting from a procedure
998.1 Hemorrhage or hematoma complicating a procedure
998.2 Accidental laceration or puncture during a procedure

etc.

999.0 Generalized vaccinia

999.1 Air embolism following infusion, perfusion or transfusion

999.2 Other vascular complications following infusion, perfusion or transfusion

999.3 Other infections following infusion, injection, perfusion or transfusion

999.4 Anaphylactic shock due to serum

999.5 Other serum reaction

999.6 ABO incompatibility reaction

999.7 Rh incompatibility

999.8 Other transfusion reaction

999.9 Other and unspecified complications of medical care, not elsewhere classified.