Hospitalizations for acetaminophen overdose: a Canadian population-based study from 1995 to 2004

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Abstract

**Background:** Acetaminophen overdose (AO) is the most common cause of acute liver failure. We examined temporal trends and sociodemographic risk factors for AO in a large Canadian health region.

**Methods:** 1,543 patients hospitalized for AO in the Calgary Health Region (population ~1.1 million) between 1995 and 2004 were identified using administrative data.

**Results:** The age/sex-adjusted hospitalization rate decreased by 41% from 19.6 per 100,000 population in 1995 to 12.1 per 100,000 in 2004 (P < 0.0005). This decline was greater in females than males (46% vs. 29%). Whereas rates fell 46% in individuals under 50 years, a 50% increase was seen in those ≥ 50 years. Hospitalization rates for intentional overdoses fell from 16.6 per 100,000 in 1995 to 8.6 per 100,000 in 2004 (2004 vs. 1995: rate ratio [RR] 0.49; P < 0.0005). Accidental overdoses decreased between 1995 and 2002, but increased to above baseline levels by 2004 (2004 vs. 1995: RR 1.24; P < 0.0005). Risk factors for AO included female sex (RR 2.19; P < 0.0005), Aboriginal status (RR 4.04; P < 0.0005), and receipt of social assistance (RR 5.15; P < 0.0005).

**Conclusion:** Hospitalization rates for AO, particularly intentional ingestions, have fallen in our Canadian health region between 1995 and 2004. Young patients, especially females, Aboriginals, and recipients of social assistance, are at highest risk.

Background

Acetaminophen is the most commonly implicated drug in cases of acute liver failure (ALF) predominantly due to its widespread availability [1-5]. Excluding combination preparations, approximately 1.5 billion tablets are sold annually in Canada[6]. Recent data from the US ALF Study Group identified acetaminophen as the etiology in approximately 50% of cases[2,3]. Acetaminophen overdose typically has a good prognosis, even if hepatic failure has developed. Less than 5% of patients who take toxic quantities of acetaminophen (approximately 150 mg/kg body weight) develop acute liver toxicity [7], and survival without transplantation for those who develop encephalopathy (~65%) exceeds that for most other forms of ALF [2-4]. Nevertheless, nearly one-third of those developing encephalopathy will die and 8% require transplantation.
The cost of treating patients with acetaminophen overdose was estimated at over $87 million annually in the US in 1995.[8] This is likely a conservative estimate in light of current health care costs.

Due to these important public health implications, a wealth of literature has focused on the epidemiology of acetaminophen overdose[9,19]. Most reports originate in the United Kingdom (UK) where legislation in 1998 limited the size of packets of acetaminophen to 16 tablets of 500 mg[9,10]. Although results are variable, most studies suggest a benefit of this legislation. In a systematic review examining the impact of these restrictions, Morgan et al. reported a reduction in hospital admissions and liver transplants for acetaminophen overdose, but conflicting findings regarding the severity of poisonings, deaths, and over the counter sales following this legislation[11].

Recently, Prior et al. examined the epidemiology of acetaminophen overdose in Canada[6]. Between 1995 and 2002, the annual hospitalization rate for acetaminophen overdose was 27 per 100,000 population. This rate did not change significantly after the lifting of restrictions limiting sales of acetaminophen (tablets > 325 mg or quantities > 24 tablets) to pharmacies only in 1999–2000[6]. Unfortunately, this study did not describe the characteristics of patients with acetaminophen overdose, including sociodemographic factors. Studies have suggested that younger age and female gender increase the risk of acetaminophen overdose,[12,13] but Canadian data is lacking.

Therefore, we conducted a population-based study to examine risk factors for acetaminophen overdose in a large Canadian health region. We were particularly interested in the impact of Aboriginal race and low socioeconomic status on rates of acetaminophen overdose since a wealth of literature has demonstrated greater health disparities, including an increased risk of suicide, in Aboriginal[14,15] and lower income Canadians[16,17]. We also examined temporal trends in hospitalization rates for acetaminophen overdose, including both intentional and accidental ingestions. An understanding of the predisposing factors for acetaminophen overdose might permit targeting of preventive initiatives at high risk subgroups if a substantial need is uncovered by the epidemiologic analysis.

Methods

Study population

The study population consisted of hospitalized patients with acetaminophen overdose residing in the Calgary Health Region (CHR) between fiscal years 1995 to 2004. The CHR provides virtually all medical and surgical care to approximately 1.1 million residents of Calgary and surrounding communities in the southern part of the province of Alberta. Hospitalized acetaminophen overdose cases were identified using CHR hospital discharge abstract administrative data. This database contains 16 diagnosis and 10 procedure coding fields. Cases of acetaminophen overdose were identified via a search of the 16 diagnosis coding fields for diagnostic code 965.4 according to the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) [18] in the 1995–2001 discharge data, and T39.1 according to ICD-10 [19] in the 2002–2004 discharge data. Trained health records nosologists at each hospital code all diagnoses prior to submission of the data to Alberta Health and Wellness. Coding is based on the entire hospital record. Non-residents of the CHR were excluded. The first admission was assigned as the index admission for patients with repeated hospitalizations for acetaminophen overdose.

Definitions of variables

The identified acetaminophen overdose cases were linked with the Alberta Health Care Insurance Plan (ACHIP) Registry [20], using a unique personal health number. Since the ACHIP is a government-administered universal plan providing health care for over 99% of Albertans, this registry includes nearly all residents of Alberta[20]. Demographics and information regarding Aboriginal and socioeconomic status (SES) were extracted from this registry. Aboriginal status was ascertained using a field that identifies individuals with “Treaty status” based on treaties between their First Nations bands and the federal government, which entitle patients to comprehensive health care without insurance premiums[20,21]. As a proxy for low SES, the receipt of social assistance or an insurance premium subsidy from Alberta Health and Wellness were examined. In 2004, 2% of Albertans received social assistance and 13% received a subsidy. All individuals 65 years of age and older (herein referred to as seniors) are eligible for this subsidy regardless of income. Due to the methods of coding in the ACHIP Registry, receipt of a subsidy or social assistance could not be determined in status Aboriginals.

Comorbid depression was defined using ICD-9-CM and ICD-10 coding algorithms developed by Quan et al.[22]. Alcohol-related diagnoses were defined using a previously-validated ICD-9-CM diagnosis coding algorithm for discharge data from fiscal years 1995–2001[23,24]. We translated ICD-9-CM codes to corresponding ICD-10 codes for 2002–2004 discharge data via a search of both coding manuals. All 16 diagnosis fields were used to define these comorbidities.

The circumstance in which the overdose occurred was classified as accidental (ICD-9-CM, E850.4, E935.4; ICD-10, X40, Y45.5), intentional (ICD-9-CM, E950.0; ICD-10, X60), or other (including homicidal [ICD-9-CM,
E962; ICD-10, X85] and undetermined intent) using ‘external causes of injury’ codes (E-codes). These codes are frequently used to define injuries according to mechanism (eg. poison, firearm, motor vehicle) and intent (eg. accidental, suicide, assault)25. Any overdose involving self-inflicted poisoning by another drug, medicinal or biological substance in addition to acetaminophen (ICD-9-CM, E950.1-E952.9; ICD-10, X61-X69) was considered intentional.

Statistical methods
Descriptive statistical methods were used to describe demographic and clinical characteristics of patients with acetaminophen overdose at their first hospitalization. We also compared patients with single versus multiple hospitalizations to identify characteristics that might be particularly strong risk factors for acetaminophen overdose. Between group comparisons were made using Fisher’s exact, \( \chi^2 \), and Mann-Whitney tests, as appropriate. Hospitalization rates were calculated by considering the entire end-of-fiscal year population of the CHR (as obtained from the AHCIP Registry) as at risk. Direct age/sex-adjusted rates were calculated using the 2001 Canadian population as the standard. Temporal trends in hospitalization rates and selected risk factors (age, gender) for acetaminophen overdose were evaluated using Poisson log-linear regression26. The impact of Aboriginal status, and receipt of social assistance or an insurance premium subsidy on rates of acetaminophen overdose were determined by comparing the prevalence of these indicators among acetaminophen overdose cases versus the remainder of the population using Fisher’s exact test.

The study protocol was approved by the Conjoint Health Research Ethics Board at the University of Calgary.

Results
Study population
Between 1995 and 2004, 1,543 patients had 1,680 admissions for acetaminophen overdose. The majority (68%) was female and the median age at first hospitalization was 26 years (interquartile range [IQR], 2–85) (Table 1). Females were significantly younger than males at presentation (median age [IQR]: 24 [12–84] vs. 29 [2–76] years; \( z = -5.69; P < 0.0005 \)). Thirty-two percent (n = 486) were less than 20 years of age; only 4.5% (n = 70) were 60 years or greater. Of all patients, 7% were status Aboriginals, and 11% and 15% received social assistance or an insurance premium subsidy, respectively. Compared with patients hospitalized only once, those with multiple hospitalizations were more likely to be on social assistance (17% vs. 11%; \( z = -2.11; P = 0.04 \)) and Aboriginal (14% vs. 7%; \( z = -2.83; P = 0.005 \)) (Table 1).

Depression or at least one alcohol-related diagnosis were recorded in 55% (n = 842) and 33% (n = 515) of the patients, respectively; 17% (n = 270) had both conditions. The most common alcohol-related diagnoses were alcohol abuse (12%), alcohol dependence disorders (11%), and alcohol-related psychiatric disorders (15%). Alcohol-related diagnoses were more common in males (47% vs. 27%; \( z = -7.52; P < 0.0005 \)) and Aboriginals (65% vs. 31%; \( z = -7.29; P < 0.0005 \)), but did not differ according to receipt of social assistance or an insurance premium subsidy. Alcohol-related diagnoses, but not depression, were more common in patients with multiple versus single hospitalizations for acetaminophen overdose (Table 1).

The majority of the overdoses (85%) were intentional. Only 13% were accidental and 2% were homicidal (n = 3).

Table 1: Characteristics of patients hospitalized for acetaminophen overdose *

| Characteristic                  | All patients (n = 1,543) | Single hospitalization (n = 1,434) | Multiple hospitalizations (n = 109) | P-value ** |
|--------------------------------|--------------------------|------------------------------------|-----------------------------------|------------|
| **Demographics**               |                          |                                    |                                   |            |
| Age, years                     | 26 (2–85)                | 26 (2–85)                          | 27 (14–55)                        | 0.91       |
| Female gender                  | 68% (1,054)              | 68% (975)                          | 72% (79)                          | 0.20       |
| Aboriginal status              | 7% (109)                 | 7% (94)                            | 14% (15)                          | 0.005      |
| Social assistance              | 11% (174)                | 11% (155)                          | 17% (19)                          | 0.04       |
| Subsidy                        | 15% (226)                | 15% (215)                          | 10% (11)                          | 0.16       |
| Depression                     | 55% (842)                | 54% (774)                          | 62% (68)                          | 0.09       |
| Alcohol-related diagnosis      | 33% (515)                | 33% (467)                          | 44% (48)                          | 0.01       |
| **Circumstance of overdose**   |                          |                                    |                                   |            |
| Intentional                    | 85% (1,427)              | 85% (1,215)                        | 88% (96)                          | 0.73       |
| Accidental                     | 13% (220)                | 13% (193)                          | 11% (12)                          |            |
| Other                          | 2% (33)                  | 2% (26)                            | 1% (1)                            |            |

* Data at first hospitalization. All data are medians (interquartile range) or proportions (% [n]).
** For comparison of patients with single versus multiple hospitalizations.
\( \dagger \) Percentages calculated based on total number of overdoses (n = 1,680).
or of undetermined intent (n = 30) (Table 1). The proportion with intentional overdoses decreased with advancing age (\( \chi^2 [7 \ df] = 166.3; P = 0.0001; \) Figure 1). Only 45% (22/49) of overdoses in seniors were intentional versus 86% (1,405/1,631) in younger patients (\( z = 7.95; P < 0.0005 \)). All overdoses in patients under 10 years (n = 11) were accidental.

**Hospitalization rates**

Between 1995 and 2004, the age/sex-adjusted annual hospitalization rate for acetaminophen overdose was 15.5 per 100,000 population. Females were approximately twice as likely to be hospitalized. Age-adjusted rates in females and males were 21.3 and 9.7 per 100,000, respectively (rate ratio [RR]: 2.19; \( z = 472.16; P < 0.0005 \)). Hospitalization rates decreased by 41% between 1995 and 2004 (Figure 2). The adjusted hospitalization rate in 1995 was 19.6 per 100,000 versus 12.1 per 100,000 in 2004. This decline was more marked in females than males (46% vs. 29%). Hospitalization rates declined steadily for intentional overdoses from 16.6 per 100,000 in 1995 to 8.6 per 100,000 in 2004 (2004 vs. 1995: RR 0.49; \( z = -178.52; P < 0.0005 \)) (Figure 3). On the contrary, accidental overdoses decreased during the middle years of the interval and increased back above baseline levels by 2004 (2004 vs. 1995: RR 1.24; \( z = 26.49; P < 0.0005 \)) (Figure 3). Overdoses of other causes fluctuated at low levels (Figure 3).

The highest hospitalization rates were observed in the 10–19 and 20–29 year age groups (35.5 and 30.3 per 100,000 population, respectively) (Figure 4). These groups were nearly three-times as likely to have an overdose compared with patients 30 years and older (RR 2.76; \( z = 648.30; P < 0.0005 \)). Excluding patients under 10 years, hospitalization rates were significantly higher in females (Figure 4). The greatest disparity was seen in the 10–19 year age group in whom the crude hospitalization rate was 55.4 per 100,000 in females versus only 13.0 per 100,000 in males (RR 4.24; \( z = 398.04; P < 0.0005 \)).

Trends in hospitalization rates for acetaminophen overdose varied by age group (Figure 5). Between 1995 and 2004, rates declined in both males and females under 50 years (2004 vs. 1995: males, RR 0.62 [\( z = -69.71; P < 0.0005 \)]; females, RR 0.51 [\( z = -148.78; P < 0.0005 \)]; overall, RR 0.54; \( z = -164.13; P < 0.0005 \]). In patients 50 years and over, rates tended to fluctuate (Figure 5). Compared with 1995, rates in 2004 were higher in both males and females (2004 vs. 1995: males, RR 1.86 [\( z = 33.58; P < 0.0005 \)]; females, RR 1.29 [\( z = 17.43; P < 0.0005 \)]; overall, RR 1.50 [\( z = 35.60; P < 0.0005 \)].

Aboriginal status and receipt of social assistance were important risk factors for acetaminophen overdose. The RRs of Aboriginal status and social assistance were 4.04 (P.
< 0.0005) and 5.16 (<P < 0.0005), respectively. Receipt of an insurance premium subsidy was not a significant risk factor (RR 0.97; <P = 0.74).

Discussion
In this population-based study, we examined trends in hospitalization rates for acetaminophen overdose in a large Canadian health region. Between 1995 and 2004, the adjusted annual hospitalization rate for acetaminophen overdose was 15.5 per 100,000 population. This rate is approximately one-fifth of that reported in the UK despite legislation limiting sales of acetaminophen in that country[12,27,28]. Although the explanations for this discrepancy are beyond the scope of this study, differences in acetaminophen availability seem unlikely considering the relatively liberal sale of acetaminophen in Canada. Moreover, suicide rates are similar in the UK and Canada[29,30]. Presumably, this discrepancy reflects different methods of suicide in the two countries (eg. more frequent use of firearms, hanging, and suffocation in Canada versus poisoning in the UK)[29,30]. We also report a 41% decline in the annual rate of hospitalization between 1995 and 2004. This decline was more pronounced in females, younger patients (under 50 years), and for intentional overdoses. Our study is at odds with a recent Canadian epidemiologic investigation of acetaminophen overdose[6]. In this analysis of Canada-wide hospital discharge data, Prior et al. reported only a slight decrease (~10%) in hospitalization rates for acetaminophen overdose between 1995 and 2001 (vs. 30% in our study). The purpose of this study was to examine the impact of the lifting of place-of-sale restrictions in 1999 on rates of acetaminophen overdose. Provincial data for Alberta was aggregated with that of other provinces (Nova Scotia and Prince Edward Island) that did not have restrictions prior to this time point. Therefore, data specific to our health region or Alberta cannot be extracted from this report. Of pertinence is that overdose rates in our health region appear to differ from other regions, even within Alberta. For example, Colman et al. reported much lower rates of emergency department visits for self-inflicted injuries in Calgary compared with Edmonton (the other major city in the province) during the same time period[31]. This finding likely reflects differences in the underlying populations. Since low SES appears to be associated with acetaminophen overdose (see below), the relative prosperity of the CHR due to its high concentration of petroleum companies may account for the lower rates that we observed. The majority of the data from other countries supports our observation. Although US data is limited, Nourjah et al. reported a 10% decline in acetaminophen-related ‘poison control calls’ to centers involved in the Toxic Exposure Surveillance System between 1997 and 2001[13]. Similarly, Turvill et al. reported declines of 21% and 64% in all acetaminophen overdoses and severe overdoses, respectively, presenting to the Royal Free Hospital in London between 1995 and 2002[28]. In Scotland, Bateman et al. reported an increase in hospitalizations from 1990 to 1997 followed by an approximate 20% decrease between 1997 and 1999 (2000–2004 data was not reported)[12]. Hughes et al. also reported a fall in hospital admissions for acetaminophen overdose in Birmingham between 1995 and 1999[32]. These reductions have been attributed to legislation limiting the sale of acetaminophen in the UK. The fall in hospitalization rates in our region is somewhat surprising since efforts to reduce acetaminophen overdose, including package size restrictions, have not been undertaken. Colman et al. actually reported an increase in visits to emergency departments in Alberta for self-inflicted injuries during this time period (but trends in acetaminophen overdose were not reported)[31]. In addition, Canadian suicide rates have remained stable during

Figure 4
Crude hospitalization rates for acetaminophen overdose by age and sex (1995–2004).

Figure 5
Trends in crude hospitalization rates for acetaminophen overdose by age group (< vs. ≥ 50 years) and sex (1995–2004).
the past two decades[29]. Presumably this conflicting data relates to shifting trends in methods of suicide[29]. Huc-
croft et al. observed a decline in self-poisoning deaths in Canadian females, but an increase in suicides due to hang-
ing, strangulation and suffocation in males[33]. An alter-
native explanation is that thresholds for hospitalizing patients with acetaminophen overdose have become more stringent. Increasing demand for hospital beds and greater experience managing these patients are possible explanations. Because our data does not represent all inci-
dent cases, we cannot confirm these speculations.

Hospitalization rates for accidental acetaminophen over-
dose appeared to rise during the latter years of our study follow-
ing an initial decline between 1995 and 2002. Such 'therapeutic misadventures' [34,35] occurred in 13% of our study population. This finding is in keeping with data from the US ALF Study Group reporting that a striking 50% of ALF cases due to acetaminophen were accident-
al[2]. Based on this data, it has been estimated that approximately 500 ALF cases and 150 deaths attributable to unintentional overdoses occur annually in the US[36]. Since accidental ingestions have been linked with a greater risk of hepatotoxicity, [3,37-39] our observation of a recent increase is of public health importance. Currently over 100 products containing sometimes large amounts of acetaminophen are available over-the-counter, and many patients (and physicians) are unaware of their acetaminophen content[36]. The observed increase in hospitalization rate coincides with the availability of extended release acetaminophen preparations in Canada (since 1999); misinformation about the proper dosing of these formulations may have played a role. Our data emphasizes the necessity of educational initiatives regarding the safe use of acetaminophen and clear labeling of medications with their acetaminophen content so that this trend does not continue.

A major strength of our data is the examination of popu-
lation-based, sociodemographic risk factors for acetami-
nophen overdose. As reported in other studies, females, especially those in their teenage years and twenties, are at greatest risk[6,12,28,32,40-44]. Hospitalization rates are four to five-fold higher among individuals who require social assistance and status Aboriginals. High rates of sui-
cidal behaviour have been reported in the Aboriginal communities of Canada and other countries,[45,46], emphasizing the necessity of suicide prevention strategies in this population. Presumably sociodemographic factors contribute to this risk, but this could not be examined spe-
cifically due to coding methods among Aboriginals in our databases. The high rate of alcohol-related diagnoses in our study cohort (33%), particularly among status Aborig-
inals (64%), likely contributed to the risk of acetami-
nophen overdose in these subgroups[47].

Another strength of our study is the use of population-
Based studies have originated in referral centres, including liver transplant units, and are prone to selection bias[2-5,38]. For example, from the US ALF Study Group suggests that the proportion of ALF cases due to acetaminophen overdose is on the rise[2]. However, since denominator data is not available in this type of study due to the recruit-
ment methods, population-based studies such as our own are necessary to truly appreciate trends in rates of acetami-
nophen overdose. Moreover, part of the explanation for the apparently increasing rates in this study (versus the decrease that we observed) is that the proportion of ALF cases due to viral hepatitis has fallen presumably as a result of widespread vaccination. This shift in etiologies has likely led to an overemphasis of the importance of acetaminophen overdose in current data.

Our study has several limitations. First, the validity of cod-
ing suicidal intent in patients with acetaminophen over-
dose has not been validated. However, studies of other conditions have suggested that E-codes provide a reliable indication of suicidal intent[48,49]. For example, LeMier et al. reported 95% agreement between E-codes obtained from administrative data and medical record review for defining suicidal intent in a variety of injuries including poisonings, falls, and firearm incidents. For poisonings specifically, agreement was 87%[48]. In another study of adult subscribers to a health maintenance organization in California, medical record reviews confirmed that 86% of hospitalizations assigned "intentional" E-codes were suicide attempts[49]. An additional limitation of our study is the reliance on discharge data to identify only hospital-
ized cases, which clearly underestimates the true inci-
dence of acetaminophen overdose. Patients who didn't seek medical attention or weren't hospitalized would not have been captured by our search strategy. However, we have identified the most clinically relevant cases at the highest risk of adverse outcomes and consumption of health care resources.

**Conclusion**
Rates of acetaminophen overdose, particularly intentional ingestions, have fallen in our Canadian health region between 1995 and 2004. Young patients, especially females, Aboriginals, and recipients of social assistance, are at highest risk.

**Abbreviations**
AHCIP, Alberta Health Care Insurance Plan; ALF, acute liver failure; CHR, Calgary Health Region; RR, rate ratio; SES, socioeconomic status
Competing interests
The author(s) declare that they have no competing interests.

Authors’ contributions
Dr. Myers conceived the study idea, performed all statistical analyses, and drafted the manuscript. B. Li and A. Fong performed data extraction and revised the manuscript critically for important intellectual content. Drs. A. Shaheen and H. Quan assisted with statistical analysis and revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript. Dr. Myers is the guarantor of the study.

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References
1. Hawton K, Ware C, Mistry H, Hewitt J, Kingsbury S, Roberts D, Weitzel H: Why patients choose paracetamol for self poisoning and their knowledge of its dangers. BMJ 1995, 310(6973):164.
2. Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, Hynan LS, Reisch JS, Schiodt FV, Ostapowicz G, Shakkil AO, Lee WM: Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. Hepatology 2005, 42(6):1364-1372.
3. Lee WM: Acetaminophen and the U.S. Acute Liver Failure Study Group: lowering the risks of hepatic failure. Hepatology 2004, 40(6):6-9.
4. Ostapowicz G, Fontana RJ, Schiodt FV, Larson A, Davern TJ, Han SH, McCashland TM, Shakkil AO, Hay JE, Hynan L, Crippin JS, Biehl AT, Samuel G, Reisch J, Lee WM: Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. Ann Intern Med 2002, 137(12):947-954.
5. Schiodt FV, Atillasoy E, Shakkil AO, Schiff ER, Caldwell C, Kowdley KV, Stribbling R, Crippin JS, Flamm S, Somborg KA, Rosen H, McCashland TM, Hay JE, Lee WM: Etiology and outcome for 295 patients with acute liver failure in the United States. Liver Transpl Surg 1999, 5(1):29-34.
6. Prior MJ, Cooper K, Cummins P, Bowden D: Acetaminophen availability increases in Canada with no increase in the incidence of reports of inpatient hospitalizations with acetaminophen overdose and acute liver toxicity. Am J Ther 2004, 11(6):443-452.
7. Rumack BH: Acetaminophen hepatotoxicity: the first 35 years. J Toxicol Clin Toxicol 2002, 40(1):3-20.
8. Bond GB, Novak JE: The human and economic cost of paracetamol (acetaminophen) overdose. Pharmacoeconomics 1995, 8(3):177-181.
9. Medicines Control Agency, Department of Health. Analgesics medicines available without prescription: proposed changes to product information and sale or supply of paracetamol (MLX231). London: Department of Health, 1996 November 22.
10. Committee of Safety of Medicines MCA. Paracetamol and Aspirin. Current Problems in Pharmacovigilance 1997;23:9.
11. Morgan O, Majed A: Restricting paracetamol in the United Kingdom to reduce poisoning: a systematic review. J Public Health (Oxf) 2005, 27(1):12-18.
12. Bateman DN, Bain M, Gorman D, Murphy D: Changes in paracetamol, antidepressants and opiod poisoning in Scotland during the 1990s. QJM 2003, 96(2):125-132.
13. Nourjah P, Ahmad SR, Karwowski C, Willy M: Estimates of acetaminophen (paracetamol)-associated overdoses in the United States. Pharmacoepidemiol Drug Saf 2005.
14. MacMillan HL, MacMillan AB, Ollford DR, Dingle JL: Aboriginal health. Can J Nurs 1996, 155(11):1569-1578.
15. Allard YE, Wilkins R, Berthelot JM: Premature mortality in health regions with high aboriginal populations. Health Rep 2004, 15(1):51-60.
16. Lemstra M, Neudorf C, Opondo J: Health disparity by neighbourhood income. Can J Public Health 2006, 97(4):435-439.
17. Shah CP, Kahan M, Krauser J: The health of children of low-income families. Can J 1987, 137(6):485-490.
18. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). Los Angeles, Practice Management Information Corporation; 2001.
19. International Statistical Classifications of Diseases and Related Health Problems, 10th Revision (ICD-10). Volume 3. 2003, World Health Organization: 2005.
20. Data Disclosure Handbook. Alberta Health and Wellness: 2003:1-15.
21. Status: Most often asked questions. 2004 [http://www.ainc-isc.gc.ca/pr/pub/ywtk/index_e.html]. Indian and Northern Affairs Canada
22. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luchi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005, 43(11):130-139.
23. Sarnz R, Ghali WA, Moskowitz MA: The impact of alcohol-related diagnoses on pneumoconiosis outcomes. Arch Intern Med 1997, 157(13):1446-1452.
24. Adams WL, Yuan Z, Barborkis JJ, Rimm AA: Alcohol-related hospitalizations of elderly people. Prevalence and geographic variation in the United States. JAMA 1993, 270(10):1222-1225.
25. Sniezek JE, Finklea JF, Graiter PL: Injury coding and hospital discharge data. JAMA 1989, 262(16):2270-2272.
26. Cameron AC, Trivedi PK: Regression Analysis of Count Data. Edited by: Cameron AC, Trivedi PK. New York, NY, Cambridge University Press; 1998:1-404.
27. Wilkinson S, Taylor G, Templeton L, Misstral W, Salter E, Bennett P: Admissions to hospital for deliberate self-harm in England 1995-2000: an analysis of hospital episode statistics. J Public Health Med 2002, 24(3):179-183.
28. Turvill JL, Burroughs AK, Moore KP: Change in occurrence of paracetamol overdose in UK after introduction of blister packs. Lancet 2000, 355(9220):2048-2049.
29. Langlois S, Morrison P: Suicide deaths and suicide attempts. Health Rep 2002, 13(2):9-22.
30. Trends in suicide in England and Wales, 1982-1996 1998 [http://www.statistics.gov.uk/articles/population_trends/suicide_l992pdf.pdf]. UK Office for National Statistics
31. Colman I, Yanmakkoulias N, Schopflocher D, Svenson LW, Rosychuk RJ, Rowe BH: Population-based study of medically treated self-inflicted injuries. Can J Emerg Med 2004, 6(5):313-320.
32. Hughes B, Durran A, Langford NJ, Nutimer D: Paracetamol poisoning--impact of pack size restrictions. J Clin Pharm Ther 2003, 28(4):307-310.
33. Huchcroft SA, Tanney BL: Sex-specific trends in suicide method, Canada, 1971-1985. Can J Public Health 1989, 80(2):120-123.
34. Seef L, Cucherini BA, Zimmerman HJ, Adler E, Benjamin SB: Acetaminophen hepatotoxicity in alcoholics. A therapeutic misadventure. Ann Intern Med 1986, 104(3):399-404.
35. Rumack BH: Acetaminophen misconceptions. Hepatology 2004, 40(1):10-15.
36. Fontana R, Adams PC: “Unintentional” acetaminophen overdose on the rise: Who is responsible? Can J Gastroenterol 2006, 20(5):319-324.
37. Gyamli GN, Parikh CR: Acetaminophen toxicity: suicidal vs. accidental. Crit Care 2002, 6(2):155-159.
38. Schiodt FV, Rochling FA, Casey DL, Lee WM: Acetaminophen toxicity in an urban county hospital. N Engl J Med 1997, 337(16):1112-1117.
39. Whitecomb DC, Block GD: Association of acetaminophen hepatotoxicity with fasting and ethanol use. JAMA 1994, 272(23):1845-1850.
40. Gunnell D, Hawton K, Murray V, Garnier R, Bismuth C, Fagg J, Simkin S: Use of paracetamol for suicide and non-fatal poisoning in...
41. Hawton K, Treasure J, Deeks J, Appleby L, Gunnell D, Bennewith O, Cooper J. Effects of legislation restricting pack sizes of paracetamol and salicylate on self poisoning in the United Kingdom: before and after study. *BMJ* 2001, 322(7296):1203-1207.

42. Sheen CL, Dillon JF, Bateman DN, Simpson KJ, MacDonald TM. Paracetamol pack size restriction: the impact on paracetamol poisoning and the over-the-counter supply of paracetamol, aspirin and ibuprofen. *Pharmacoepidemiol Drug Saf* 2002, 11(4):329-331.

43. Sheen CL, Dillon JF, Bateman DN, Simpson KJ, MacDonald TM. Paracetamol-related deaths in Scotland, 1994-2000. *Br J Clin Pharmacol* 2002, 54(4):430-432.

44. Thomas MR, Jowett NJ. Severity of overdose after restriction of paracetamol availability. Restriction has not reduced admissions with self poisoning. *BMJ* 2001, 322(7285):554.

45. Malchy B, Enns MW, Young TK, Cox BJ. Suicide among Manitoba's aboriginal people, 1988 to 1994. *CMAJ* 1997, 156(8):1133-1138.

46. Clayer JR, Czechowicz AS. Suicide by aboriginal people in South Australia: comparison with suicide deaths in the total urban and rural populations. *Med J Aust* 1991, 154(10):683-685.

47. Wilcox HC, Connor KR, Caine ED. Association of alcohol and drug use disorders and completed suicide: an empirical review of cohort studies. *Drug Alcohol Depend* 2004, 76(Suppl):S11-9.

48. LeMier M, Cummings P, West TA. Accuracy of external cause of injury codes reported in Washington State hospital discharge records. *Inj Prev* 2001, 7(4):334-338.

49. Iribarren C, Sidney S, Jacobs DR Jr., Weisner C. Hospitalization for suicide attempt and completed suicide: epidemiological features in a managed care population. *Soc Psychiatry Psychiatr Epidemiol* 2000, 35(7):288-296.

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