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# Achalasia: incidence, prevalence and survival. A population-based study

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**Abstract**

***Background*** *Studies of achalasia epidemiology are important as they often yield new insights into disease etiology. In this study, our objective was to carry out the first North American population-based study of achalasia epidemiology using a governmental administrative database.* ***Methods*** *All residents in the province of Alberta, Canada receive universal healthcare coverage as a benefit. The provincial health ministry, Alberta Health and Wellness, maintains a central stakeholder database of patient demographic information and physician billing claims. We defined an achalasia case as a billing claim submitted for the years 1996–2007 with an ICD-9-CM code of 530.0 or 530 and a Canadian Classification of Procedure treatment code of 54.92A (endoscopic balloon dilation) or 54.6 (esophagomyotomy). A preliminary validation study of the case definition demonstrated a sensitivity of 85% and specificity of 99% for known cases and controls.* ***Key Results*** *A total of 463 achalasia cases were identified from 1995 to 2008 (59.6% males). Mean age at diagnosis was 53.1 years. In 2007, the achalasia incidence was 1.63/100 000 (95% CI 1.20, 2.06) and the prevalence was 10.82/100 000 (95% CI 9.70, 11.93). We observed a steady increase in the overall prevalence rate from 2.51/100 000 in 1996 to 10.82/100 000 in 2007. Survival of achalasia cases was significantly less than age–sex matched population controls (P < 0.0001).* ***Conclusions & Inferences*** *Using a population-based approach, the incidence and prevalence of treated achalasia is 1.63/100 000 and 10.82/100 000, respectively. The disease appears to have a stable incidence but a rising prevalence. Survival of achalasia cases is significantly less than age-matched healthy controls.*

***Keywords*** *achalasia, epidemiology.*

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## INTRODUCTION

### 1. What is current knowledge?

- Achalasia is the best-characterized and most treatable gastrointestinal motility disease and serves as a prototype for disorders of the enteric nervous system.
- Previous studies of achalasia epidemiology have been limited to small manual reviews of hospital discharge data.

### 2. What is new here?

- In the first North American population-based study, the incidence and prevalence of treated achalasia is 1.63/100 000 and 10.82/100 000, respectively.
- The disease appears to have a stable incidence but a rising prevalence.
- Survival of achalasia cases is significantly less than age-matched healthy controls.

Achalasia is a disorder of esophageal motor function resulting in dysphagia, chest pain, and malnutrition. While rare, achalasia is the best-characterized and most treatable gastrointestinal motility disease and

serves as a prototype for disorders of the enteric nervous system. The characteristic disturbance of esophageal motility is known to be a consequence of selective loss of inhibitory neurons in the esophageal myenteric plexus.[1] The cause of this neuronal loss is unknown but possible initiating mechanisms range from viral infection and immune-mediated destruction to an unknown combination of genetic and environmental factors.[2–5]

Inquiry into the epidemiology of achalasia is important as it can yield important clues to illusive, inciting causes and provide information about secular trends in disease prevalence for a given population. Previous studies of achalasia epidemiology have been limited to estimates of disease incidence using retrospective manual reviews of hospital discharge data.[6–8] Observations of disease prevalence are more difficult as this requires a population-based approach and in the case of achalasia have been restricted to small studies in Iceland and Singapore.[9,10] To date, there have been no population-based studies of achalasia epidemiology or disease survival in North America. Our purpose was to carry out an investigation of achalasia incidence, prevalence, and survival in a well-defined North American population.

## METHODS

### Objective

In this study, our objective was to estimate the incidence, prevalence, and survival of achalasia cases in the entire Alberta population for the years 1996–2007 using a system of governmental administrative health databases. The University of Alberta ethics review board approved the study protocol.

### Setting

Alberta is a Canadian province of approximately 3.4 million people and provides a publicly funded, universally available healthcare system. All residents of the province receive universal healthcare coverage as a benefit and all residents of the province must register with the Alberta Health Care Insurance Plan. All physicians submit billing claims to a single payer (Alberta Health and Wellness). Each claim requires up to three ICD-9-CM (International Classification of Diseases, 9th Revision, Clinical Modification) diagnostic codes as well as a procedure code (Canadian Classification of Procedures – CPP). For our study, we were able to utilize the fact that there are two unique CCP billing codes for the treatment of achalasia: 54.92A for endoscopic achalasia balloon dilatation, and 54.6 for surgical esophagomyotomy.

### Databases

Two administrative Alberta health ministry databases were used: the Central Stakeholder Registry (CSR) and the Alberta Health Physicians Fee-for-Service database (AHPFS).

1. Central Stakeholder Registry: The CSR essentially includes all residents of Alberta, as registration is mandatory. Each resident is provided with a Personal Health Number (PHN), a unique lifetime identifier that must be presented at the time of service. Contained within this registry is demographic information including: name, date of birth, sex, and address. The CSR also tracks all births, deaths, and migrations.
2. Alberta Health Physicians Fee for Service: The Alberta government maintains an electronic fee-for-service data system for the purpose of administering payment to physicians and other healthcare professionals who provide services covered under the provincial health insurance plan. Virtually, all Alberta physicians bill the provincial government on a fee-for-service basis. To support the payment of a claim, physicians must supply the PHN, up to three diagnostic codes (4-digit ICD-9-CM), a procedure code (CCP), and service location. In addition, the specialty of the billing physician (e.g., gastroenterologist, thoracic surgeon) is also tracked with each claim. For achalasia, two unique CCP billing codes exist: 54.92A for endoscopic achalasia balloon dilatation and 54.6 for surgical esophagomyotomy (Heller myotomy).

### Development of the case definition

In order to develop a robust achalasia case definition, we utilized local hospital separations data to retrieve a cohort of patients with a previous diagnosis of achalasia who had been treated with either endoscopic balloon dilatation or surgical esophagomotomy ($n$ = 163) (Table 1). As controls, we identified a cohort of patients who had been treated with endoscopic esophageal dilatation for disorders unrelated to achalasia (e.g., benign esophageal stricture) or with surgical Nissen fundoplication for gastro-esophageal reflux disease (GERD, $n$ = 6256). See Appendix 1 for a complete description of the methodology. Using the PHN of individuals from these two cohorts, billing claims data from the AHPFS database were retrieved. An initial review of the data revealed that up to 50% of

**Table 1** Validation of achalasia case definition according to physician billing codes

| Parameter | Achalasia cases with this coding (%) | Endoscopy/surgical control cases with this coding (%) |
|---|---|---|
| 530 or 530.0 | 159/163 (97.5) | 3112/6256 (49.7) |
| 530/530.0 + Specialist* | 154/163 (94.5) | 1882/6256 (30.1) |
| 530/530.0 + Specialist + CCP treatment codes† | 140/163 (85.9) | 32/6256 (0.01) |

*Gastroenterologist, general surgeon, internal medicine, thoracic surgery, pediatrics.
†54.92A (endoscopic achalasia balloon dilatation) and 54.6 (surgical esophagomyotomy – Heller myotomy).

cases had been miscoded with the ICD-9 CM code 530 (general esophageal disorders) rather than 530.0 (achalasia). In an iterative fashion, the various combinations of ICD-9 code, physician specialist and CCP were probed for their ability to separate cases from controls (see Table 2). Using all three parameters together resulted in a search strategy that yielded a sensitivity of 85% for achalasia cases and a specificity of 99% for control cases. Restriction of those cases with relevant diagnostic testing (esophageal manometry, barium esophogram, or gastroscopy) did not improve the diagnostic accuracy of the case definition (data not shown). Thus, we defined an achalasia case as a billing claim submitted with an ICD-9-CM code of 530.0 or 530 and a CCP treatment code of 54.92A or 54.6 (endoscopic balloon dilatation or surgical esophagomyotomy). We also restricted cases to those claims made by appropriate specialists; gastroenterologist, pediatrician, or surgeon (thoracic and general).

## Case definitions

- Achalasia case: a billing claim, made by an appropriate specialist in the AHPFS database, with an ICD-9-CM code of 530.0 or 530 and a CCP treatment code of 54.92A (endoscopic balloon dilatation) or 54.6 (surgical esophagomyotomy).
- Incident achalasia case: a billing claim for a diagnosis of achalasia from 1996 onwards and had not been previously diagnosed as achalasia in the prior 2 years
- Prevalent achalasia case: claims made during the study period (1996–2007) for patients who had neither moved out of the province nor died.

Rates were standardized, using the direct method, to the 1991 Canadian census population. The rate denominator was the total number of registered citizens in the CSR database at the beginning of the corresponding year. The time period studied was 1996 to the end of 2007.

**Table 2** Age standardized rates of achalasia in Alberta for 2007

| | Males (95% CI) | Females (95% CI) | Total (95% CI) |
|---|---|---|---|
| Incidence | 1.85 (1.18, 2.52) | 1.43 (0.87, 1.99) | 1.63 (1.20, 2.06) |
| Prevalence | 13.43 (11.63, 15.23) | 8.34 (6.99, 9.69) | 10.82 (9.70, 11.93) |

## Survival curve analysis

Kaplan–Meier survival curves were constructed from three groups: achalasia cases, endoscopy/surgical controls, and age–sex matched population controls using all-cause mortality rates. The endoscopy/surgical controls were those patients retrieved according to the methodology in Appendix 1. In order to create a cohort of age–sex matched population controls, three individuals were randomly selected from the general population, age and sex matched for each achalasia case. The date of diagnosis for the index achalasia case was used as time zero for the matched population controls. The date of death or migration out of the province was identified from the CSR database. Data were censored for cases still alive at the end of the observation period. Significant differences in survival functions between groups were probed using the Bonferroni test of multiple comparisons.

# RESULTS

Using the case definition search strategy, a total of 463 achalasia cases were identified in the Alberta population from 1996 to 2007 (59.6% males). The mean age at diagnosis was 53.1 (range, 5–97) years. There was no significant difference in the age of diagnosis between males and females. In 2007 (the last full year studied), the population achalasia incidence was 1.63/100 000 (95% CI 1.20, 2.06) and the prevalence was 10.82/100 000 (95% CI 9.70, 11.93) (see Table 2). During the observation period, the incidence rate remained constant. However, we observed a steady increase in the overall prevalence rate from 2.51/100 000 in 1996 to 10.82/100 000 in 2007. While this increase was seen in both sexes, the trend was significantly more pronounced in males (see Fig. 1). Survival curves analysis demonstrated that the achalasia and endoscopy/surgical control groups had a significantly reduced survival function compared with age–sex matched population controls ($P < 0.0001$; Fig. 2). Achalasia patients also had a significantly better survival function than endoscopy/surgical controls ($P < 0.0001$).

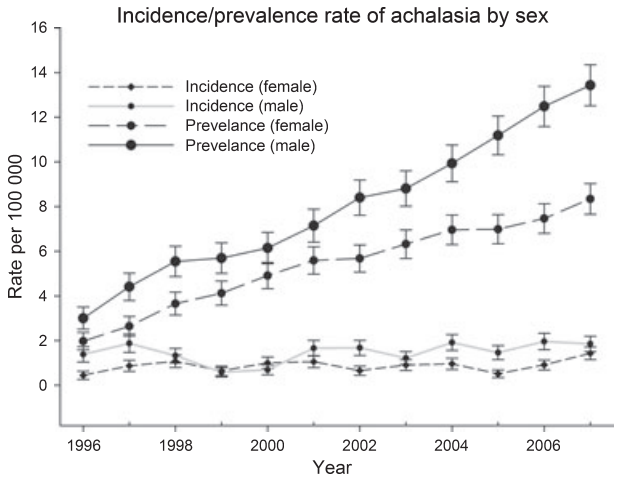


**Figure 1** Age standardized rates for achalasia incidence and prevalence (Alberta 1996–2007).

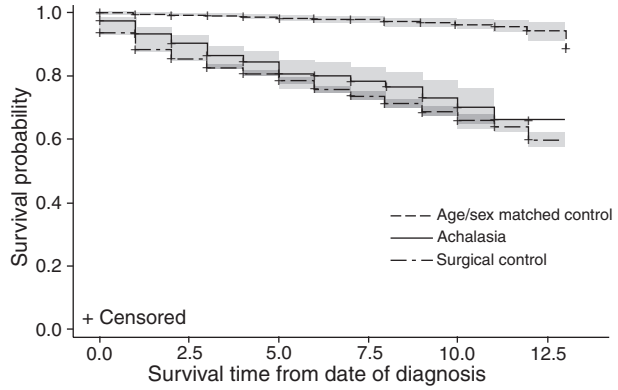


**Figure 2** Survival of achalasia cases and controls from date of diagnosis.

## DISCUSSION

In the first North American population-based study, we report secular trends in the epidemiology of achalasia over the past 12 years. We observed a stable incidence rate in the Alberta population for achalasia of 1.63/100 000. This rate is higher than previous smaller studies in countries such as Singapore (0.3/100 000), Iceland (0.55/100 000), the United Kingdom (0.8/100 000), and New Zealand (0.95/100 000).[9–12] The lower rate in older observations may reflect the fact that some of these studies relied on case finding from hospital discharge data only. In our preliminary validation analysis, 67% of cases were treated by outpatient procedures only, implying that the true rate in older studies is probably higher. Our observations also confirm prior inquiries that achalasia can occur at any age from childhood to old age, but the peak incidence is in middle age with both sexes equally affected. These data together would suggest that if the etiologic factor is infectious or environmental, it is present only at low levels in the environment and widely distributed across disparate geographical areas. Likewise, if genetic susceptibility factors (such as class II HLA genes) exist, the accumulating data would indicate that they distributed uniformly among differing racial groups.[10,13–15]

While the incidence of achalasia in our study remained relatively stable during the observation period, the prevalence rate increased fourfold from 1996 to 2007. A similar observation was made in a study of achalasia epidemiology in Iceland with the authors suggesting a low disease-specific mortality rate as an explanation.[9] However, a recent observational study found that while death primarily as a consequence of achalasia does occur (e.g., aspiration pneumonia, malignancy, and malnutrition), the majority of deaths in achalasia are due to unrelated causes.[16] In our analysis of all-cause mortality, we observed that patients with achalasia had a significantly reduced survival compared with age-matched controls but a better survival than endoscopic or surgical controls. The control group consisted mainly of patients undergoing either endoscopic dilatation or surgical fundoplication for GERD. This group would be expected to have a reduced survival because of the development of Barrett's esophagus and lifestyle factors such as obesity, which predispose to cardiovascular disease.[17] For our analysis, we did not have access to the cause of death and accordingly the proportion of cases that succumbed to the consequences of achalasia or its treatment is unknown. Thus, the explanation for the observed rising prevalence is unclear, but cannot be attributed solely to low disease-specific mortality. Paradoxically, the rising prevalence rate was most apparent in males, where males in Alberta tend to have a slightly lower survival rate than females. One explanation is that achalasia is primarily a disorder of middle age and as the common diseases of this age group (such as hypertension and diabetes) receive earlier diagnosis and medical care, a survival advantage is conferred along with any rare diseases that are also present in that age group.[18] Disease prevalence is a function of illness duration; slowly progressive processes such as achalasia can exhibit a rising prevalence rate provided that mortality is lower than the incidence rate.

Population-based studies of rare disease epidemiology are subject to potential biases which arise as a result of differential access to care related to factors such as age, social economic status, ethnicity, and

employment status. As the entire Alberta population receives universal healthcare coverage as a benefit, bias as a result of skewed healthcare access in this study should be minimal. Our study utilized the fact that in Alberta, there are two unique billing codes for endoscopic and surgical treatment of achalasia. It should be noted that our case definition would not have included those cases of achalasia that were managed conservatively due to severe co-morbidity, received botulinum toxin injection as therapy or underwent total surgical esophagectomy. However, as botulinum toxin injection therapy for achalasia provides only transient relief of dysphagia symptoms, it would be reasonable to assume that patients treated in this way would eventually require more definitive endoscopy or surgical treatment over time.[19,20] As well, total esophagectomy is rarely the initial treatment for achalasia and thus most patient would first have a trial of more conventional balloon dilatation or esophagomyotomy.[21] This analysis is unable to capture the proportion of achalasia patients that were managed conservatively, but in the experience of the authors this subset would be likely <10% of cases.

A potential problem with the use of administrative databases is the accuracy of the information entered.[22] Alberta Health and Wellness databases have been previously validated for accuracy of coding and have been extensively used to study disease epidemiology and outcomes.[23–26] In our validation analysis, we found a sensitivity of 85% and a specificity of 99% for our case definition. This level of diagnostic accuracy is similar to that of other commonly used validated search algorithms for diseases such as diabetes.[27] By choosing to base our achalasia case definition on a search algorithm with an estimated sensitivity of 85%, we recognize that we have likely underestimated the true number of cases. However, as we applied the same case definition across time during the study, we think it is unlikely to introduce substantial bias.

In conclusion, in the first North American population-based study of achalasia epidemiology, we found a stable rate of achalasia incidence with a rising prevalence in the face of a reduced disease survival. The factors contributing to these findings will require further study.

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## AUTHOR CONTRIBUTIONS

Daniel Sadowski was responsible for conception of the study and study design as well as writing of the manuscript. Fred Ackah and Lawrence Svenson were responsible for data acquisition and data analysis. Bei Jiang carried out the statistical analysis and survival curve analysis.

## CONFLICT OF INTEREST

All authors have no conflict of interest to declare.

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## APPENDIX 1

In order to validate the case definition, a cohort of known achalasia cases along with appropriate controls was required. Hospital separations data from the Edmonton, Alberta region were used. This region has a catchment area of approximately 1.2 million people and is served by four hospitals.

Cases were retrieved according to the following parameters:

### Achalasia cases

- For cases January 1, 1995 – April 1, 2002: ICD-9 code of 427 (esophagomyotomy) or 42.92 (dilatation of esophagus) and ICD-9 code 530.0 (achalasia).
- For cases April 2, 2002 – December 31, 2007: CCI code 1NA72 (release esophagus) or 1.NA.50 (dilatation of esophagus with sub-codes BA-BD or BA-BL) and ICD-10 diagnostic code K22.0 (achalasia of cardia).
- Using this search strategy, a total of 163 cases were retrieved The hospital record for each case was reviewed manually to confirm the achalasia diagnosis.

### Control cases (Nissen fundoplication or endoscopic dilatation of benign esophageal stricture)

- For cases from January 1, 1995 – April 1, 2002 ICD-9 code 4466 (other procedures for creation of esophago-gastro sphincter competence) or 42.92 (endscopic dilatation of esophagus).
- For cases April 2, 2002 – December 31, 2007: CCI code: 1NA.80 – Surgical Repair Esophagus/Nissen fundoplication) or CCI code 1.NA.50 dilatation of esophagus: subcodes BA-BJ (flexible dilator), BA-BP (rigid dilatation of esophagus), BA-NR (stent placement in esophagus).
- Using this search strategy, a total of 6256 control cases were retrieved.