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3 **Age, multimorbidity, and dementia with health care costs in older Canadian people: a**
4 **population-based cohort study**
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35 **Running Title:** Age, morbidity and dementia
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ABSTRACT

Background: The aging of the general population is expected to lead to increases in multimorbidity and dementia. The intersection of age, dementia and multimorbidity poses potential challenges for the sustainability of health systems worldwide.

Objective: We sought to examine how age, dementia and multimorbidity jointly associate with health care costs.

Methods: We did a retrospective population-based cohort study in Alberta, Canada with 827,947 adults aged ≥ 65 years between April 2003 and March 2017. We identified comorbidities using 30 validated algorithms applied to administrative health data and assessed costs associated with hospitalization, provider billing, ambulatory care, medications, and long-term care (LTC).

Results: Dementia was associated with higher mean annual total costs and all individual mean component costs. Similarly increasing number of morbidities was associated with higher mean total costs and the component costs. Increasing age was associated with higher total costs for people with and without dementia, driven by increasing LTC costs. However, there were no consistent trends between age and non-LTC costs among people with dementia. When costs attributable to LTC were excluded, there was evidence that older age was associated with lower costs for hospitalization, medications, and ambulatory care among people with dementia.

Interpretation: Multimorbidity, older age and dementia were all associated with increased use of long-term care and thus health care costs, but some costs among people with dementia decreased at older ages. These findings illustrate the complexity of projecting the economic consequences of the aging population, which must account for the interplay between multimorbidity and dementia.

INTRODUCTION

The presence of multiple chronic conditions is termed multimorbidity¹, and is associated with worse clinical outcomes compared to good health or to the presence of a single chronic condition.²⁻⁵ Dementia is an important contributor to multimorbidity, and in fact, factors that contribute to multimorbidity (such as vascular disease) can also cause dementia. Like multimorbidity, the prevalence of dementia increases in parallel with age. Therefore, the aging of the general population is expected to lead to further increases in the burden of both multimorbidity and dementia. Since both dementia and multimorbidity are independently associated with increased health care costs and an increased likelihood of requiring long-term care (LTC),^{6,7} the intersection of age, dementia and multimorbidity poses potential challenges for the sustainability of health systems worldwide.⁸ Given the potential for overlap and statistical interactions between these various exposures, there is potential for bias if individual associations are used to examine associations with cost. Rather, an approach which simultaneously considers the joint associations between these exposures and healthcare costs is preferable.

We used a large population-based dataset of all 827,947 people aged 65 years or greater and living in a defined geographical area to characterize the frequency of dementia and 29 other common chronic conditions. We examined the joint associations between age, dementia, and burden of morbidity with total healthcare costs, comprised of costs related to hospitalization, provider billing, use of ambulatory or emergency care, medications, and long-term care (defined as care and services for those who cannot live independently or who require onsite nursing care, 24-hour supervision, or personal support).⁹ Our goal was to advance the available literature by considering joint associations rather than pairwise associations between these three key exposures and total healthcare costs.

METHODS

We reported this retrospective population-based cohort study according to the STROBE guidelines.¹⁰

The institutional review boards at the Universities of Alberta (Pro00053469) and Calgary (REB16-1575) approved this study and waived the requirement for participants to provide consent due to the large sample size. Data were de-identified.

Data sources and cohort

We used the Alberta Kidney Disease Network (AKDN) database, which incorporates data from Alberta Health (AH; the provincial health ministry) such as provider claims, hospitalizations and ambulatory care utilization; Alberta laboratory data, and Alberta Blue Cross prescription data.¹¹ All people registered with AH were included in the database; all Alberta residents are eligible for insurance coverage by AH and >99% participate in coverage. We linked postal codes for the last known residential address of each participant to Statistics Canada's Postal Code Conversion File Plus (www.statcan.ca) to obtain rural/urban status and neighbourhood (postal code) income quintiles for each relevant fiscal year. We used the database to assemble a cohort of adults aged ≥ 65 years who resided in Alberta, Canada between April 2003 and March 2017. We followed participants from April 2003, their 65th birthday, or registration with AH (whichever was later) until March 2017, death, or migration out of the province.

Comorbidities

We used a previously published list of validated algorithms for 29 chronic conditions that could be applied to claims data and had positive predictive values $\geq 70\%$ ¹²: alcohol misuse, asthma, atrial fibrillation, lymphoma, non-metastatic cancer (breast, cervical, colorectal, pulmonary, and prostate), metastatic cancer, chronic heart failure, chronic pain, chronic obstructive pulmonary disease, chronic hepatitis B, cirrhosis, severe constipation, dementia, depression, diabetes, epilepsy, hypertension,

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hypothyroidism, inflammatory bowel disease, irritable bowel syndrome, multiple sclerosis, myocardial infarction, Parkinson's disease, peptic ulcer disease, peripheral vascular disease, psoriasis, rheumatoid arthritis, schizophrenia, and stroke or transient ischemic attack. Dementia was one of the 29 conditions and was defined by the presence of 1 hospitalization or 2 physician claims within 2 years (ICD-9 290, 294.1, 331.2 or ICD-10 F00-F03, F05.1, G30, G31.1).¹³ A validated algorithm for gout¹⁴ was included in the set of comorbidities. We also considered chronic kidney disease (CKD) as a 31st condition that was defined by any of the following: mean annual estimated glomerular filtration rate (eGFR) <60 mL/min*1.73m²; a median annual presence of albuminuria (albumin:creatinine ratio ≥30 mg/g, protein:creatinine ratio ≥150 mg/g or dipstick proteinuria ≥ trace); two outpatient physician claims for dialysis; or, one hospitalization or one outpatient claim for kidney transplantation. We classified each participant with respect to the presence or absence of dementia and the 30 other chronic conditions for each fiscal year.¹⁵ If a participant developed a condition within a fiscal year or at any point previously (lookback extended as far as April 1994 where records were available), we classified him/her as having the condition. Detailed methods for classifying morbidity status and the specific algorithms used are found elsewhere.¹²

Costs and long-term care

The primary outcome was mean annual total health care costs; the cost components were hospitalization, provider visits (primary care or specialists), ambulatory care (including emergency department (ED) visits), medications, and long-term care. For all hospitalizations and ambulatory care classification system (ACCS) charges between fiscal years 2004 and 2017, we used the Canadian Institute for Health Information's resource intensive weights (RIW) from the administrative data and Alberta's cost of a standard hospital stay (CSHS).¹⁶ We used grouper codes for ACCS charges from fiscal years 2004 to 2010, and RIW and CSHS for the years thereafter. Costs for provider visits (inpatient and outpatient)

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3 were the actual amounts charged to Alberta Health Services or for physicians on the alternative
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5 payment program we based costs on the mean amounts charged by the other physicians. Medication
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7 costs were those listed with Alberta Blue Cross. We also measured time residing in long-term care home
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9 (e.g., nursing homes, auxiliary hospitals) and estimated costs based on the average daily cost (\$218.16
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11 CAD; from Alberta Health) of all such homes in Alberta (individual level data on the type of long-term
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13 care was not available). We classified participants as residing in long-term care if they were discharged
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15 to a long-term care home after hospitalization, or if we identified two provider claims at least 30 days
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17 apart for services provided in a long-term care home; we deemed long-term care to have begun on the
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19 earlier of the date of discharge and the date of the first claim respectively. All costs are reported in
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21 \$1000 Canadian dollar units and are inflated to 2017 costs using the consumer price index for all items
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23 in Canada. All data (demographics, morbidities and costs) were linked and organized by participant and
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Statistical analyses

We did analyses with Stata MP 15.1 (www.stata.com) and reported baseline (first fiscal year within follow-up) descriptive statistics as counts and percentages, or medians and inter-quartile ranges, as appropriate.

In order to examine the associations between dementia, increasing morbidity burden and age with cost outcomes, we used generalized linear models with a zero-inflated negative binomial distribution and a log-link. We allowed for intra-participant correlation in our standard errors – this allowed participants to contribute multiple fiscal years of cost data. We regressed outcomes on dementia, the number of other (non-dementia) morbidities (categorized as none, 1, 2, 3, 4, and 5 or more), age (categorized as 65-74, 75-84, and ≥ 85 years), their 3-way interaction and all three 2-way interactions; also sex, rural or urban

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3 residence and the lowest neighbourhood (postal code) income quintile. We allowed all covariates to
4 vary on a year-by-year basis; an offset term was used to account for partial and full years. Only
5 rural/urban residence and the lowest neighbourhood income quintile had missing values – both 7%. In
6 the models, missing values were imputed with the most frequent category (i.e., imputed as urban and
7 not the lowest neighbourhood income quintile). We also did additional analyses that further examined
8 the oldest age groups categorized as 85-89, 90-95, and ≥ 95 years. We determined independence of
9 residuals by examining plots of residuals versus fitted values. The threshold p for statistical significance
10 was set at 0.05. We reported adjusted means with 95% confidence intervals. We compared differences
11 in means between those with dementia and those without, between adjacent age categories, and
12 between adjacent morbidity categories using Chi-square tests.
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28 RESULTS

29 *Characteristics of study participants*

30 Participant flow is shown in Supplemental eFigure 1. There were 827,947 participants; median follow-up
31 was 6.5 years (range 1 day to 14.0 years; 2% of participants out-migrated before the end of follow-up).
32 Twenty-six percent of participants died during follow-up. Participants could contribute follow-up to
33 more than one age category: 661,755 participants were followed while 65-74 years of age, 354,161
34 while 75-84 years, and 158,538 while 85 years and older (Table 1). The percentage of participants with
35 dementia increased with age, from 1.4% to 21.9%. The percentage of participants who were men
36 decreased with age, from 49.8% to 37.3%. More participants living with dementia resided in a low-
37 income neighbourhood than participants without dementia in the 65-74 years group, but this difference
38 diminished with increasing age and was absent in those aged ≥ 85 years. Compared to those without
39 dementia, participants with dementia consistently had more comorbidity across all age groups.
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3 *Adjusted annual mean costs*
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5 Total adjusted annual mean costs and all individual component costs were higher if dementia was
6 present (Table 2; Figure 1). Similarly mean total costs and the component costs increased in parallel with
7 the number of morbidities, whether dementia was present or not. Mean total costs (driven by LTC costs)
8 and LTC costs increased in parallel with age, but there were no consistent trends for other component
9 costs with increasing age.
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18 Among people without dementia, mean annual costs for medications, ACCS, and claims increased from
19 65-74 years of age to 75-84 years of age and then decrease from 75-84 years of age to 85 years of age
20 (Supplemental eFigure 2). Hospitalizations and LTC costs increased in parallel with age.
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27 In participants with dementia, LTC was the largest component of costs followed by hospitalizations,
28 claims, ACCS and medications. Mean costs for LTC and mean total costs (driven by LTC costs) increased
29 with age among participants with dementia. When LTC costs were excluded, older age was associated
30 with lower costs – and there was an inverse association between hospitalization, medication, ACCS and
31 claim costs and increasing age-(Table 2; eFigure 2).
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41 In a sensitivity analysis, we further divided participants aged ≥ 85 years into the following categories: 85-
42 89 years of age, 90-94 years, and 95 years and older. There were 144,134, 69,615, and 23,736
43 participants contributing follow-up to each age group, respectively. The results were similar to that of
44 the whole study population. Dementia was associated with higher mean total costs and component
45 costs, and there was also an association between higher costs and the number of morbidities. For
46 people with and without dementia, there was an association between LTC costs (and thus total costs)
47 and increasing age. However, after LTC costs were excluded, there was evidence of decreasing costs
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3 among older participants, with those aged >95 years having the lowest non-LTC costs (Table 3;
4 Supplemental eFigure 3).
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10 Inspection of the burden of comorbidity among the oldest participants demonstrated that comorbidity
11 was surprisingly infrequent among those without dementia. For example, among participants aged >95
12 years and without dementia, 56% of the participant-years were lived with ≤ 1 comorbidity.
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18 **INTERPERTATION**

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20 In this population-based study of more than 800,000 older adults treated in a universal health system,
21 we found strong graded associations between multimorbidity, dementia and total health care costs.
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23 Older age was associated with significant increases in mean annual health care costs, driven by a strong
24 association between older age and LTC utilization. As expected, dementia was associated with high
25 health care costs that were driven by high utilization of LTC. After LTC costs were excluded, the presence
26 of dementia appeared to modify the relation between age and costs, such that older age was associated
27 with increased non-LTC costs among those without dementia, but not necessarily among those with
28 dementia. In fact, when long-term care resource use was excluded, there was evidence that older age
29 was associated with lower mean annual costs among people with dementia, including lower costs for
30 hospitalization, medications, and ambulatory care.
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46 These findings provide insight into how health care costs may change over time in parallel with the
47 anticipated aging of the general population, and therefore which interventions should be the highest
48 priority to mitigate the consequences of this demographic shift. First, to the extent that the costs
49 associated with multimorbidity and with dementia were higher among people of older age, an increased
50 prevalence of these conditions will exaggerate the economic consequences of the aging population,
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3 whereas interventions that prevent these conditions (or reduce their severity) will have the opposite
4 effect. Second, since long-term care is such an important driver of health care resource use, providing
5 additional supports to enable older people to live independently rather than entering long-term care
6 would likely yield economic benefits as well as better quality of life. This may prove more difficult for
7 adults with dementia and for those with physical comorbidities. Third, we do not have data that directly
8 explains the inverse association between costs and age among people with dementia once long-term
9 care costs were excluded. One possibility is survivorship effects, where those that survive to advanced
10 age despite dementia may have less morbidity and thus require less costly care. An alternative (not
11 mutually exclusive) is that provider attitudes or patient preferences mean that the care provided to
12 people with dementia is less aggressive than that provided to those without dementia – thus leading to
13 lower individual costs associated with hospitalization, medications, emergency care and provider claims.
14 Costs associated with acute care for older people with dementia might be reduced further if LTC homes
15 enhance their ability to provide services that are currently restricted to hospitals, which would in turn
16 require additional training and resources. The ongoing reviews of LTC that have been triggered by the
17 COVID-19 pandemic may offer an opportunity to consider these issues in detail.¹⁷

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39 Previous studies and a high-quality systematic review have demonstrated that multimorbidity (with or
40 without dementia) is correlated with higher health care costs.^{7,18-22} Prior work also demonstrates that
41 dementia is associated with increased costs, especially those due to hospitalization.^{6,23} However, most
42 such studies have not been able to assess long-term care utilization, which is an important contributor
43 to total costs in older people (representing 32% of all health care costs in our cohort). Some prior
44 studies have examined how multimorbidity associates with a broad range of health care costs, including
45 long-term care and other forms of social care.^{24,25} These studies have generally reached similar
46 conclusions to our own, but have generally not explored the intersection between dementia,
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3 multimorbidity and costs as we were able to do. We also assessed a broader range of comorbidities than
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5 most prior studies of costs and dementia (or costs and multimorbidity), many of which focus on highly
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7 prevalent conditions such as vascular disease and diabetes.²² An exception is the 2012 Symphony study
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9 from the UK, which assessed the intersection between age, dementia and a broad panel of
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11 comorbidities in a much smaller population (N with dementia = 1026).²⁶ Our findings are generally
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13 consistent with the Symphony study, which also showed that multimorbidity and dementia are more
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15 strongly correlated with cost than is age per se. Overall, the available evidence suggests that accurately
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17 projecting the economic consequences of the aging population is complicated and must account for the
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19 interplay between comorbidity and dementia as well as increasing age.
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24 Our study has important strengths, including its rigorous analytical methods, use of validated algorithms
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26 for ascertaining the presence of dementia and morbidity, and the large, geographically defined cohort
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28 on which it was based. However, our study also has limitations that should be considered. First,
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30 administrative data will underestimate the true prevalence of dementia and other morbidities
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32 compared to a gold standard such as a structured interview – and because health care utilization
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34 increases with age, our focus on older people aged ≥ 65 years should reduce the extent of such
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36 underestimation. Second, the validated algorithm that we used to classify participants with dementia
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38 has positive predictive value of 93% and sensitivity of 67%.¹³ Therefore, our findings will have
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40 misclassified some participants with respect to dementia. To the extent that such misclassification may
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42 have been random rather than systematic, this should have tended to bias our findings toward the null
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44 and thus should not have affected the observed associations between age, dementia and costs. Third,
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46 although we were able to extend further studies by including long-term care utilization, we were not
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48 able to capture costs from outside the health sector, such as those due to unpaid care (a major
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50 contributor to the societal costs of dementia²⁷), private sector care, or out-of-pocket costs for patients
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52 and families.²⁸ Fourth, the exact per-person cost of long term was not available as only average per diem
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3 cost was available; costs for patients with greater care requirements such as those with dementia are
4 likely underestimated (and overestimated for those with lower care needs). Fifth, we did not have
5 information on functional status, frailty, disabilities, or the severity of morbidities, and thus we relied on
6 the total count of morbidities, which is relatively crude. More severe morbidity for a given morbidity
7 count would be expected to increase the likelihood of LTC, which might in turn affect costs. However,
8 this misclassification of morbidity is likely to have biased toward the null and so should not have
9 affected our conclusions. Finally, we studied people from a single Canadian province and our findings
10 may not apply to other settings.
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23 To gain additional insights about how the aging population may influence health care costs, future
24 studies should combine the projected population structure in the coming decades with data examining
25 the interplay between age, multimorbidity, dementia and costs, such as the findings presented herein. A
26 more detailed examination of which conditions (or which clusters of conditions) account for most
27 multimorbidity-related costs would likely improve the precision of these future studies. Out-of-pocket
28 costs and opportunity costs (for unpaid labour) borne by caregivers and families should also be captured
29 by such studies, since they likely account for a substantial proportion of the total economic burden
30 associated with dementia. Finally, as previously noted, new methods for preventing dementia,
31 attenuating multimorbidity and promoting independent living among older adults should be extremely
32 high priority for future research.
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48 **CONCLUSION**

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50 In conclusion, multimorbidity or dementia were associated with higher mean annual health care costs.
51 As expected, older age was associated with increased use of long-term care and thus health care costs
52 among those with and without dementia, and dementia was associated with substantially increased
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3 utilization of long-term care. However, whereas older age was associated with higher costs of
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5 hospitalization, medications, acute care and provider claims among those without dementia, the
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7 converse was true among those with dementia, for whom there was an inverse association between
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9 older age and total costs once costs attributable to long-term care were excluded. These findings
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11 suggest that projecting the economic consequences of the aging population is complicated and must
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13 account for the interplay between comorbidity and dementia as well as increasing age.
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Confidential

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3 **Competing Interests:** None reported.
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5 **Author Contributions:** MT and SK conceived the study. MT, NW and SK designed the study and drafted
6 the manuscript. NW performed the statistical analyses. All authors have made substantial contributions
7 to the development of the manuscript, all have been involved in revising it for important intellectual
8 content and all approved the final version. MT had full access to all the data in the study and takes
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11

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21 **Data Sharing Statement:** We are not able to make our dataset available to other researchers due to our
22 contractual arrangements with the provincial health ministry (Alberta Health), who is the data
23 custodian. Researchers may make requests to obtain a similar dataset at
24 <https://sporresources.researchalberta.ca>.
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27 **Disclaimer:** This study is based in part by data provided by Alberta Health and Alberta Health Services.
28 The interpretation and conclusions contained herein are those of the researchers and do not represent
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31

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33 and Sophanny Tiv, BSc, University of Alberta provided technical support.
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Table 1. Demographic and clinical characteristics at first year within each age group

Characteristic	Age 65-74y		Age 75-84y		Age 85y+	
	Dementia	No dementia	Dementia	No dementia	Dementia	No dementia
N	9,135	652,620	23,747	330,414	34,752	123,786
Women	50.0	50.2	56.7	54.3	66.7	61.5
Men	50.0	49.8	43.3	45.7	33.3	38.5
Rural	11.6	13.1	10.9	12.6	10.3	11.0
Lowest SES neighbourhood quintile	25.8	18.3	23.5	20.0	22.7	22.8
Non-dementia morbidities						
None	4.7	24.0	3.7	12.8	2.4	11.2
One	10.0	25.0	8.8	17.6	6.7	10.9
Two	13.4	20.5	13.1	20.2	11.8	16.1
Three	15.5	14.0	15.5	18.0	15.8	17.8
Four or more	56.3	16.5	59.0	31.4	63.3	44.0
Alcohol misuse	19.5	2.4	10.0	2.0	4.2	1.2
Asthma	6.5	2.7	5.6	3.5	5.0	4.0
Atrial fibrillation	12.1	4.5	19.9	11.0	26.8	18.5
Cancer, lymphoma	1.2	0.6	1.1	0.8	1.0	0.9
Cancer, metastatic	3.2	1.5	3.5	2.3	3.0	2.6
Cancer, non-metastatic	5.6	4.5	7.4	7.1	7.2	7.1
Chronic heart failure	20.1	4.9	27.0	11.7	35.2	22.3
Chronic kidney disease	39.2	21.8	50.7	40.0	66.3	56.9
Chronic pain	18.5	14.7	17.1	16.8	15.0	16.0
Chronic pulmonary disease	34.3	14.2	34.8	21.3	34.4	25.1
Chronic viral hepatitis B	0.2	0.1	0.0	0.1	0.0	0.0
Cirrhosis	1.7	0.3	0.7	0.2	0.2	0.1
Constipation, severe	5.1	0.8	5.6	1.7	6.7	3.1
Depression	33.6	7.0	27.1	6.5	21.2	6.4
Diabetes	32.0	17.8	30.4	21.6	25.5	19.9
Epilepsy	11.8	1.3	5.9	1.3	3.7	1.2
Gout	10.6	8.6	12.5	11.5	13.7	13.0
Hypertension	64.8	50.6	73.5	67.7	79.0	74.2
Hypothyroidism	17.9	11.3	20.8	15.5	24.8	19.2
Inflammatory bowel disease	1.5	1.0	1.4	1.0	1.0	0.8
Irritable bowel syndrome	4.1	2.0	3.6	2.1	3.1	2.0
Multiple sclerosis	4.1	0.7	1.4	0.4	0.7	0.3
Myocardial infarction	5.6	3.3	7.1	5.1	7.9	6.5
Parkinson's disease	10.4	0.7	11.4	1.7	9.3	2.4
Peptic ulcer disease	1.3	0.2	1.1	0.4	0.9	0.4
Peripheral vascular disease	5.4	1.5	5.8	3.0	5.5	3.9
Psoriasis	1.7	0.8	1.3	0.9	1.0	0.8
Rheumatoid arthritis	5.4	2.7	5.6	4.2	6.3	5.0
Schizophrenia	15.6	0.8	7.0	0.5	3.5	0.3
Stroke or TIA	31.1	7.1	35.0	13.7	38.2	21.1

N count, SES socioeconomic status, TIA transient ischemic attack

Percentages are reported. Many participants will have data within multiple age groups

Morbidities	Participant-years ¹	Hospital costs Mean (95%CI)	Medication costs Mean (95%CI)	ACCS costs Mean (95%CI)	Claim costs Mean (95%CI)	LTC costs Mean (95%CI)	Total costs Mean (95%CI)

ACCS Ambulatory Care Classification System, CAD Canadian dollars, CI confidence interval, LTC long-term care

Costs are adjusted for sex, and rural/urban. These models include 3-way and 2-way interactions terms for dementia, age, and number of morbidity.

The Table shows the mean costs (i.e., long-term care, hospitalizations, provider claims, ACCS, medications, and total costs) that is associated with dementia. All costs are reported in \$1000 Canadian dollar units and are inflated to 2017 costs using the consumer price index for all items in Canada.

¹Participant-years correspond to number of full or partial fiscal-years for each participant

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Morbidities	Participant-years ¹	Hospital costs Mean (95%CI)	Medication costs Mean (95%CI)	ACCS costs Mean (95%CI)	Claim costs Mean (95%CI)	LTC costs Mean (95%CI)	Total costs Mean (95%CI)

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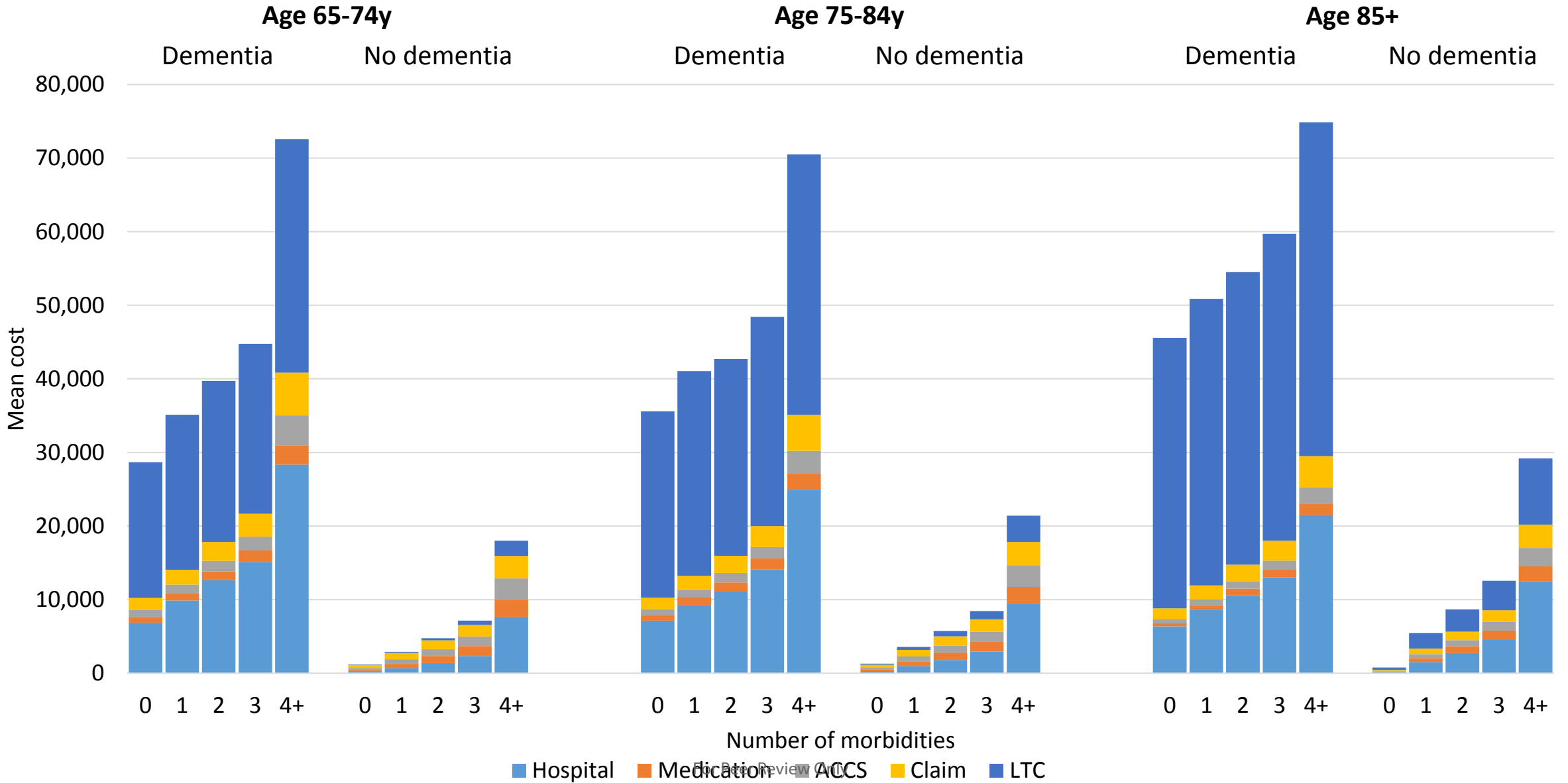
Figure 1. Adjusted annual mean costs (in CAD) for dementia by age and number of morbidities in participants ≥65 years

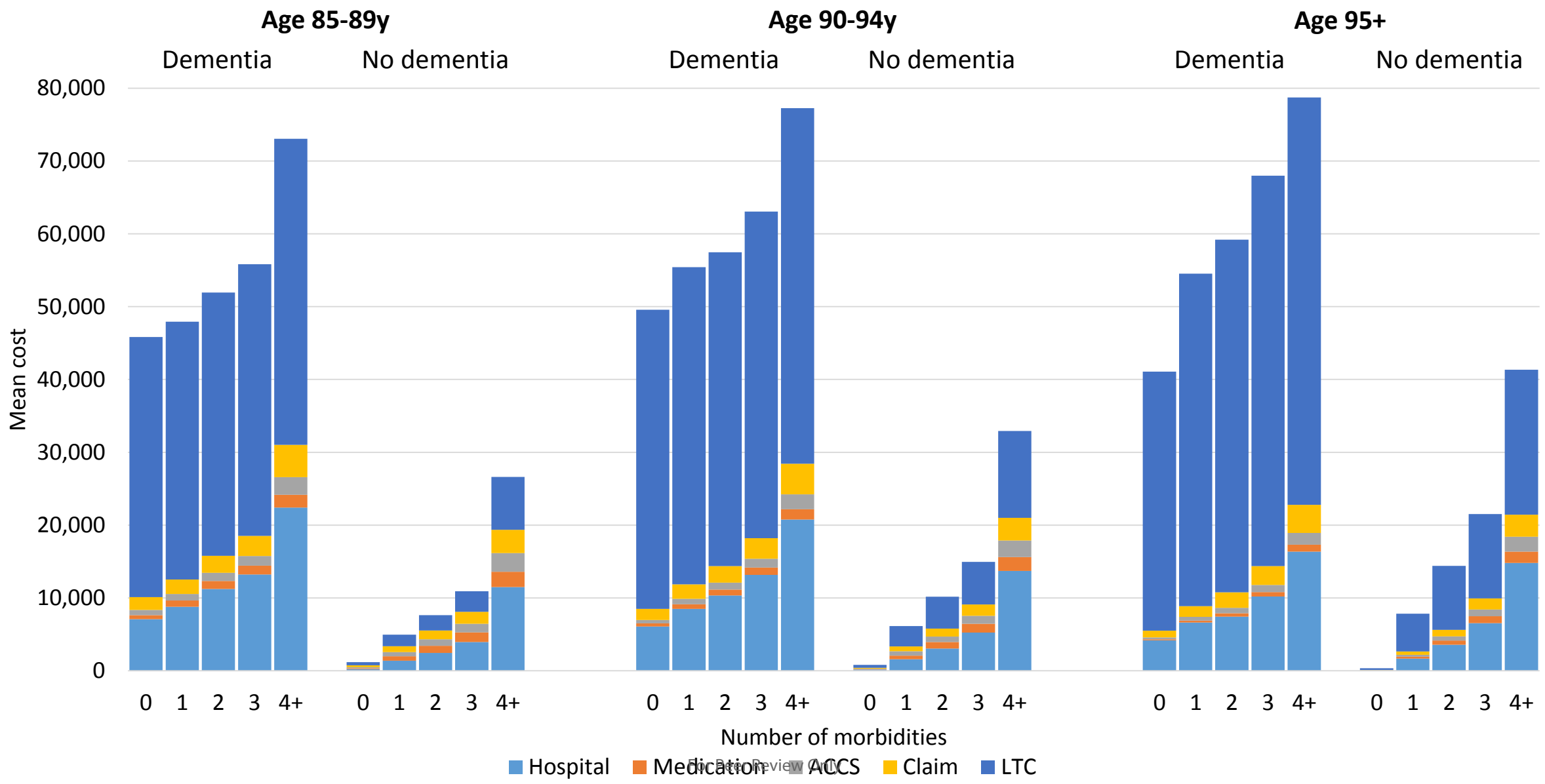
ACCS Ambulatory Care Classification System, CAD Canadian dollars, LTC long-term care

Figure 2. Adjusted annual mean costs (in CAD) for dementia by age and number of morbidities in participants ≥85 years

ACCS Ambulatory Care Classification System, CAD Canadian dollars, LTC long-term care

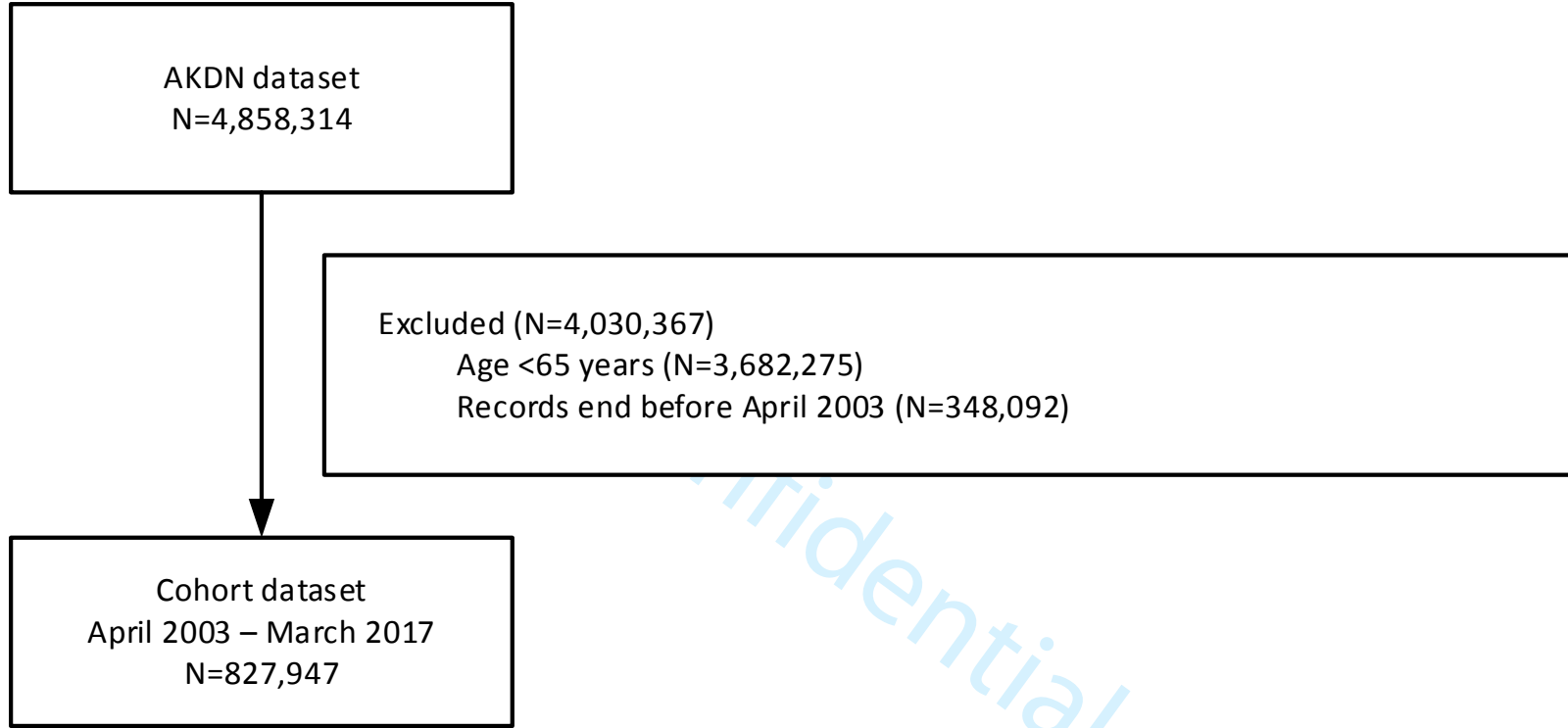
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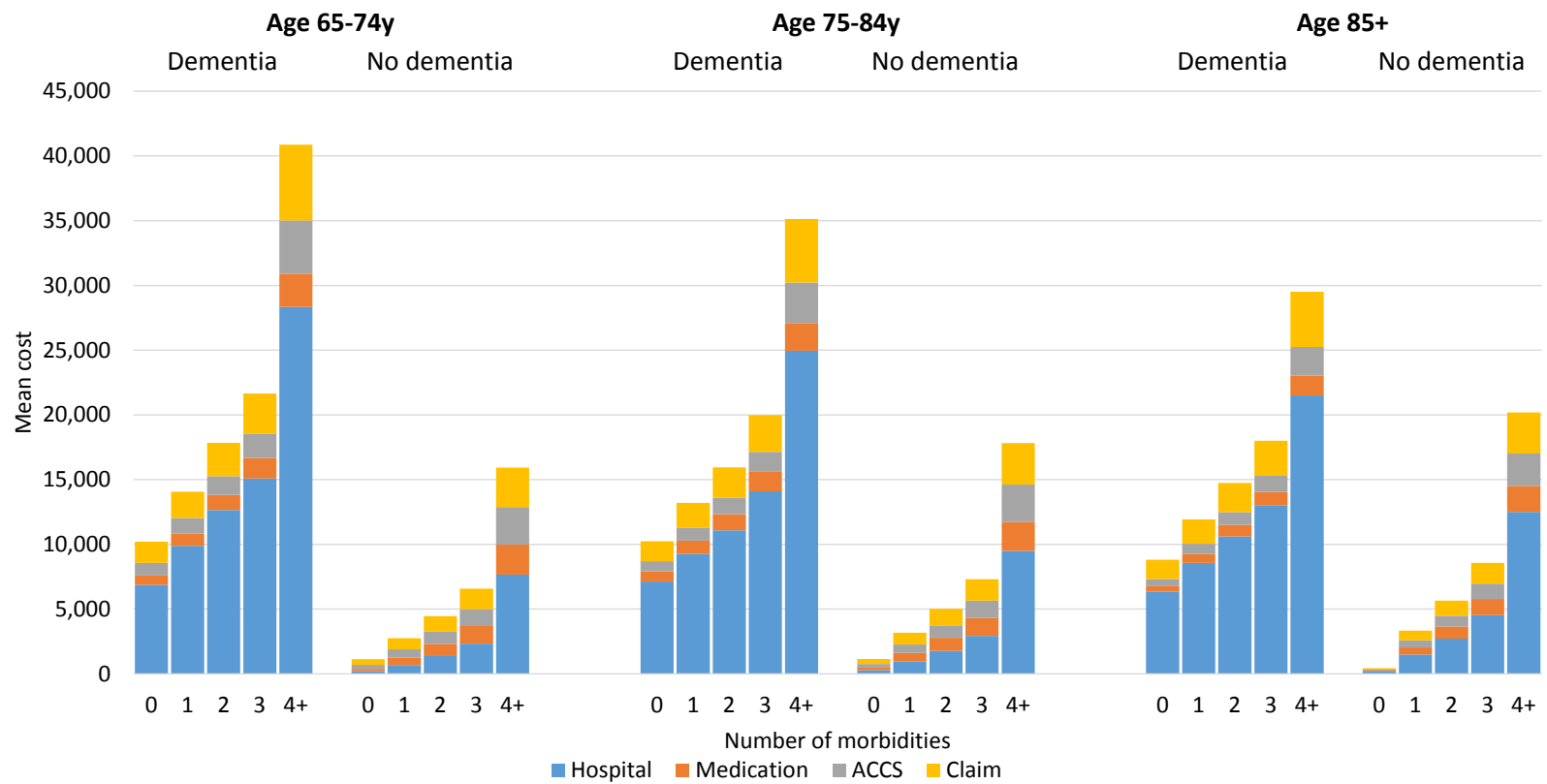
eFigure 1. Participant flow diagram



AKDN Alberta Kidney Disease Network

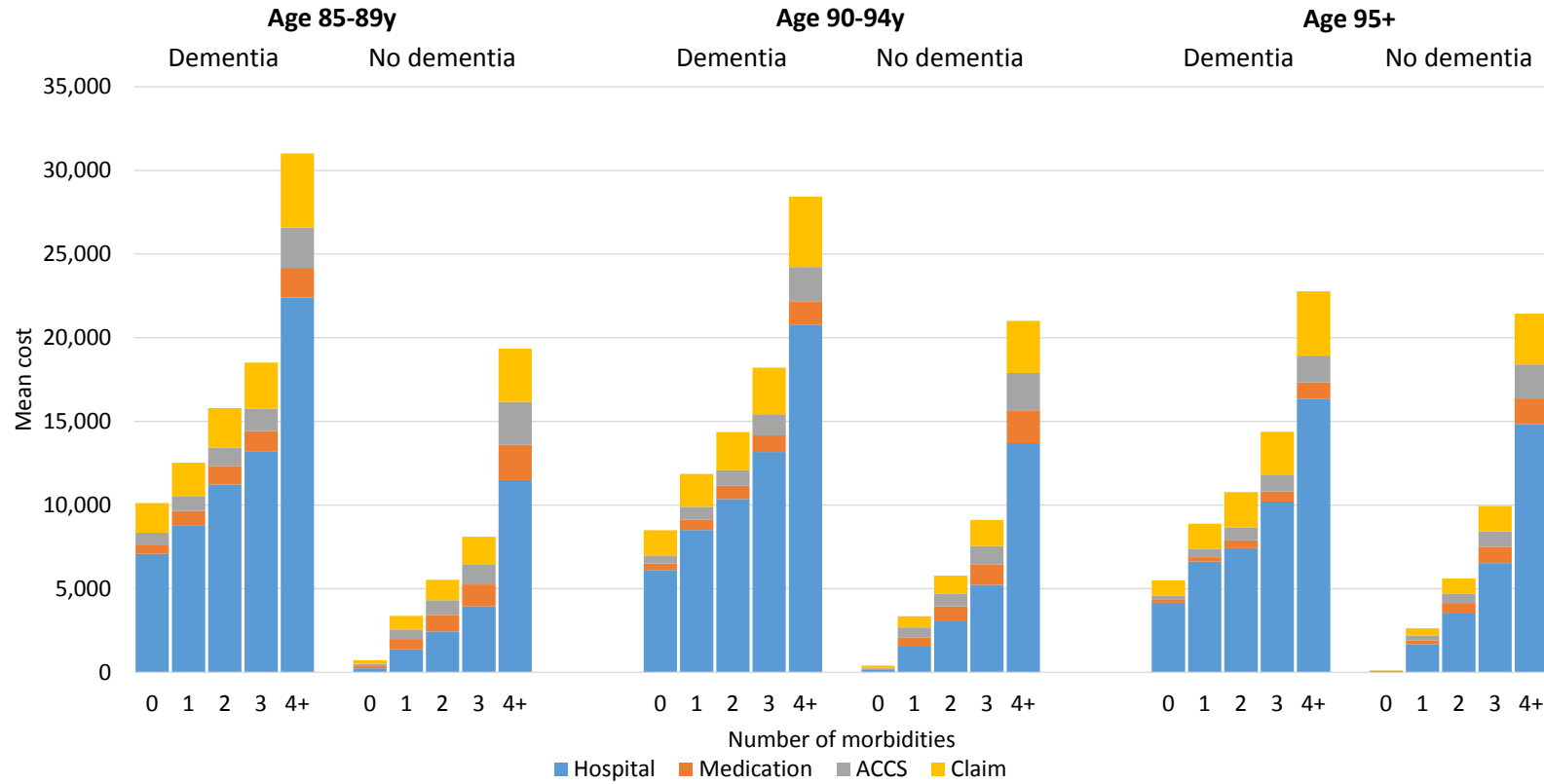
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eFigure 2. Adjusted annual mean costs (in CAD) for dementia by age and number of morbidities in participants ≥65 years, excluding costs of long-term care



ACCS Ambulatory Care Classification System, CAD Canadian dollars, LTC long-term care

eFigure 3. Adjusted annual mean costs (in CAD) for dementia by age and number of morbidities in participants ≥85 years, excluding costs of long-term care



ACCs Ambulatory Care Classification System, CAD Canadian dollars, LTC long-term care