Appendix 1 (as supplied by the authors): Detailed methods

This retrospective population-based cohort study is reported according to the STROBE guidelines.[1] The institutional review boards at the Universities of Alberta and Calgary approved this study.

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 physician claims, hospitalizations and ambulatory care utilization; the Northern and Southern Alberta Renal Programs (NARP and SARP); and the clinical laboratories in Alberta. This database has been widely used[2–4] because of its population-based coverage of a geographically defined area, including demographic characteristics, health services utilization, and clinical outcomes. Additional information on the database is available elsewhere, including the validation of selected data elements.[5] 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. The database was used to assemble a cohort of adults aged ≥ 65 years who resided in Alberta, Canada between May 2002 and March 2013. We followed participants from May 2002, their 65th birthday, or registration with AH (whichever was later) until March 2013, death, or migration out of the province.

Comorbidities

Informed by a systematic review of multimorbidity measures,[6] the Quality and Outcomes Framework of the UK General Practice contract, and health service planning by NHS Scotland, Barnett et al identified a set of 40 morbidities and used them to generate a comprehensive assessment of multimorbidity in the UK. We aimed to use the same set of morbidities in our work, but the Barnett study used administrative codes from NHS Scotland, which are not

available in Canada. From this set, we found and published validated algorithms for 29 chronic conditions that could be applied to Canadian claims data and had positive predictive values ≥ 70%:[7] 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, 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).[8] We also considered chronic kidney disease (CKD) as a 30th condition that was defined by mean annual estimated glomerular filtration rate (eGFR) < 60 mL/min*1.73m^2 or a median annual presence of albuminuria (albumin:creatinine ratio ≥ 30 mg/g, protein:creatinine ratio ≥ 150 mg/g or dipstick proteinuria ≥ trace). Each participant was classified with respect to the presence or absence of dementia and 29 other chronic conditions for each fiscal year.[9] 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), they were classified as having the condition. Detailed methods for classifying morbidity status and the specific algorithms used are found elsewhere.[7]

Clinical outcomes

The primary outcome was time to all-cause death. Key secondary outcomes included the rate of physician visits (primary care or specialists), the rate of emergency department (ED) visits, and the rate of hospitalizations. We also evaluated loss of capacity for independent living, which was

defined by first discharge to a public or private long-term care facility (e.g., nursing homes, auxiliary hospitals) following any hospital admission.

Statistical analyses

We did analyses with Stata MP 13·1 (www.stata.com) and reported baseline (first year within follow-up) descriptive statistics as counts and percentages, or medians and inter-quartile ranges, as appropriate. Spine plots (multi-variable stacked bar graphs) were used to depict mortality, discharge to long-term care, and burden of dementia by age and number of morbidities. Secular trend of prevalent dementia was assessed using an autoregressive model of order 1. Analyses were aimed at the interactions between the specific exposures of dementia, number of non-dementia morbidities, and age.

In order to examine the associations between dementia, increasing morbidity burden and age with the clinical outcomes, we used a number of models: Cox regression for mortality and long-term care placements; and generalized linear regression using the Poisson distribution with a log-link for the rates of physician claims, ED visits, and hospitalizations (all separately) and a random intercept term for participant. To meet Poisson modelling assumptions, we analyzed the doubling of events (claims, ED visits, and hospitalizations) rather than absolute increments of 1 event. Outcomes were regressed 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 3 2-way interactions; also sex, Aboriginal status (registered First Nations or recognized Inuit), social assistance, and rural or urban residence. All covariates were allowed to vary on a year-by-year basis. We also did additional analyses that further examined the oldest age groups categorized as 85–89, 90–95, and ≥ 95 years.

Appendix to: Tonelli M, Wiebe N, Straus S, et al. Multimorbidity, dementia and health care in older people: a population-based cohort study. *CMAJ Open* 2017. doi: 10.9778/cmajo.20170052.

The requirement for 3-way interaction terms was confirmed by plotting the natural logarithm of the outcome ratio against age category for each number of morbidity groups (a separate connected line for each group) for both the dementia group and the group without dementia and checking for non-additive lines. We determined that the proportional hazard assumption was satisfied by examining plots of the log-negative-log of within-group survivorship probabilities versus log-time. For Poisson modelling, we verified that the variances approximately equaled the means. The threshold *p* for statistical significance was set at 0·05.

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This study is based in part by data provided by Alberta Health and Alberta Health Services. The interpretation and conclusions are those of the researchers and do not represent the views of the Government of Alberta. The funders had no role in the design or analysis of this study, nor the drafting or approval of this manuscript. Neither the Government of Alberta nor Alberta Health express any opinion in relation to this study. The corresponding author has access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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