Appendix

Assessing the Preparedness of the Canadian Health Care System Infrastructure for an Alzheimer's Treatment

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Appendix

This appendix provides an overview of the model, sources for our model parameters, and details on the capacity projections.

Model Overview

The simulation model has two parts. First, a Markov model simulates transitions between the following disease states: normal cognition (no mild cognitive impairment [MCI] and no Alzheimer's dementia) to MCI to Alzheimer's dementia. People move through the disease states based on annual transition probabilities from the literature (Table A.1).

Second, within the MCI disease state, a system dynamics model simulates three health care system capacity constraints within the diagnostic and treatment phases. The systems dynamic model uses stocks and flows to allow people to move through the phases and to delay people in phases when there is not enough capacity. For example, in the diagnosis phase, the initial constraint is the first dementia specialist visit. Based on the specialists' capacity for visits, people move to the biomarker testing step; if the number of people exceeds the specialists' capacity, then those people remain at the specialist visit step until the following year (i.e., they queue for the next year). The model uses a one-year time step for the entire diagnosis and treatment phases—i.e., if a person is delayed at any step due to inadequate capacity, they remain at that step until the following year. After exiting each capacity step, a subset of people may exit the model at each "decision point" (see the diamonds in the conceptual framework in Figure 1 in the main report) if the next step is not indicated. For example, at the first dementia specialist visit, specialists would determine whether biomarker testing is indicated for a given patient. See Table A.1 for the assumptions for the share of patients who proceed at each decision point.

Model Adjustments for the Canadian Analysis

Year of analysis: In this analysis, we consider scenarios in which an Alzheimer's disease (AD)–modifying therapy becomes available in 2021. Our prior analyses (Liu et al., 2017; Hlávka, Mattke, and Liu, 2018) of the health care system infrastructure in the United States and six European countries were published in 2017 and 2018, respectively, and analyzed scenarios in which a disease-modifying therapy becomes available in 2020. Since then, the research pipeline for AD–modifying therapies has included some terminated clinical trials and revised completion dates.

Ages included in the population studied: In this analysis, we include the population age 50 and older in Canada. In our prior analyses, the population studied was people age 55 and older. We update the population studied to age 50 and older because some of the terminated late-stage clinical trials had older eligibility criteria (e.g., age 55 and older [U.S. National Library of

Medicine, 2018a]), and several current trials have lower age eligibility criteria (e.g., ages 50 to 85 or 90 [U.S. National Library of Medicine, 2018b, 2018c]). Although the 50-to-55 age group is relatively large, the prevalence of MCI is lower compared with older age groups. Thus, the additional population extends wait lists somewhat but does not have substantial impact on the overall findings.

Age-adjusted transition and mortality rates: With the inclusion of those ages 50 to 55, we update transition and mortality rates that are age-adjusted in the model. The model does not include separate age cohorts; rather, we adjust rates to account for the average age of the entire population studied. As the included population ages over time, we revise the rates to vary over time such that, in later years, the population is older and has higher transition and mortality rates.

Model Parameters and Capacity Projections

Table A.1. Model Parameters, Values, and Sources

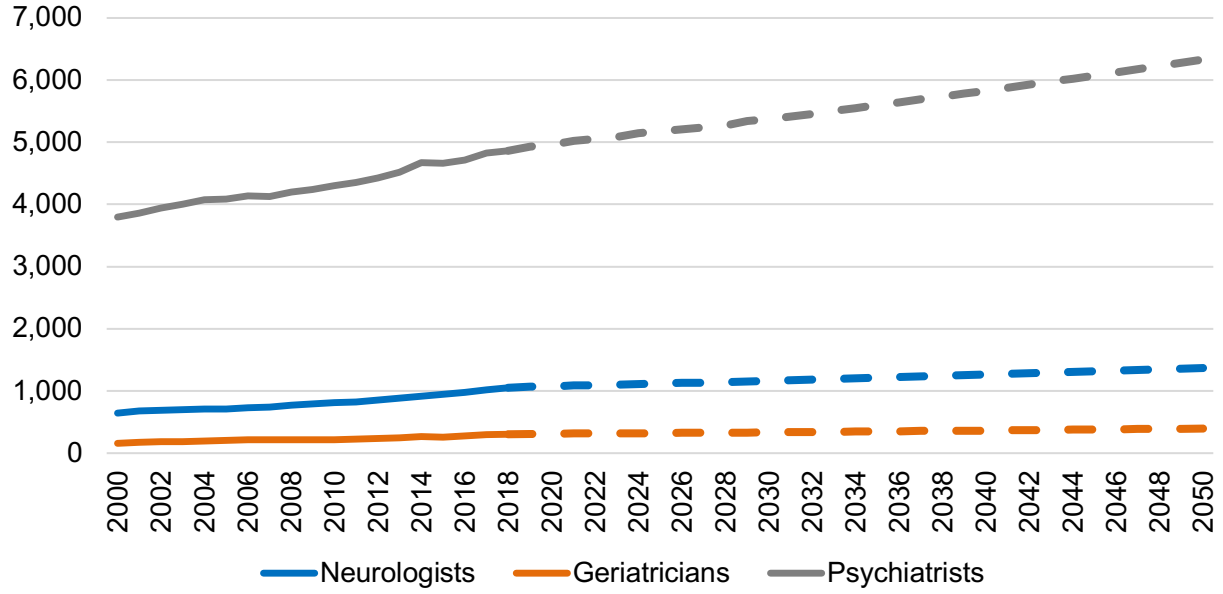
Parameter	Description	Value	Source
Population in 2017 (millions)			
Age 50+ without MCI and Alzheimer's dementia	Population estimate of people 50 years and older, minus those with MCI and Alzheimer's dementia	11.707	Statistics Canada (2018), Petersen et al. (2018), Alzheimer Society Population Health Expert Panel (2016)
MCI	Estimated number of people with MCI based on a meta-analysis of MCI prevalence	1.331	Petersen et al. (2018)
Alzheimer's dementia	Estimated number of Alzheimer's dementia patients based on dementia prevalence and AD etiology estimates	0.376	Alzheimer Society Population Health Expert Panel (2016)
Dead	Estimated mortality among the age 50+ population	0.250	Statistics Canada (2018)
Annual mortality rates			
Age 50+ without cognitive impairment and Alzheimer's dementia	Derived from all-cause mortality rate among those without cognitive impairment, adjusted to the average age each year from 2017 to 2050	1.4–2.6%	Statistics Canada (2018), Vassilaki et al. (2015), Rossetti et al. (2010), Spackman et al. (2012)
MCI	Derived from all-cause mortality rate, adjusted to the average age each year from 2017 to 2050, and adjusted for increased mortality in MCI cohorts	4.9–6.7%	Statistics Canada (2018), Vassilaki et al. (2015)
Alzheimer's dementia	Derived from weighted average of mortality rate for patients in mild, moderate, and severe stages of AD, adjusted to the average age each year from 2017 to 2050	15.0–15.2%	Statistics Canada (2018), Rossetti et al. (2010), Spackman et al. (2012)
Annual disease state transition probabilities			
Probability of transitioning to MCI	Interpolated from Yesavage et al. (2002) based on the average age each year from 2017 to 2050	1.5–2.3%	Yesavage et al. (2002), Statistics Canada (2018)

Parameter	Description	Value	Source
Probability of transitioning from MCI due to AD to Alzheimer's dementia *without* treatment	Derived from a meta-analysis	6.5%	Mitchell and Shiri-Feshki (2009)
Probability of transitioning from MCI due to AD to Alzheimer's dementia *with* treatment	Calculated as a product of a transitioning from MCI due to AD to Alzheimer's dementia and an assumed relative risk reduction of 50%	3.25%	—
Patient uptake and epidemiological parameters			
Share of the population who receive cognitive screening each year	Assumption based on expert input from the U.S. analysis	80%	Liu et al. (2017)
Share of the MCI population who receive further evaluation by a dementia specialist each year	Assumption based on expert input from the U.S. analysis	50%	Liu et al. (2017)
Share of MCI patients eligible for biomarker test	Assumption based on expert input from the U.S. analysis	90%	Liu et al. (2017)
Share of MCI patients who have clinically relevant amyloid burden	Average of two estimates by Ong et al. (2015) and Doraiswamy et al. (2014)	45%	Ong et al. (2015), Doraiswamy et al. (2014)
Share of MCI patients with amyloid who have no contradictions for treatment	Assumption based on expert input from the U.S. analysis	80%	Liu et al. (2017)
Capacity parameters			
Dementia specialists	Estimated total number of neurologists, geriatricians, and psychiatrists able to diagnose MCI due to AD; 10% of all psychiatrists based on expert input from Canadian subject-matter experts	1,772 in 2018 See Figure A.1 for the projected number of specialists	Canadian Medical Association (2018); 2018–2030 Fraser Institute projections from Globerman, Barua, and Hasan (2018)
Average visits by a dementia specialist per year	Estimated annual number of ambulatory visits by a full-time clinical neurologist	2,860	Dall et al. (2013)
Dementia specialists fraction of excess capacity	Assumption based on expert input from the U.S. analysis	5%	Liu et al. (2017)
PET scanners	Number of scanners; estimated growth in PET scanners based on projecting historical trends forward	51 in 2017 See Figure A.2 for the projected number of PET scanners	OECD (2018a)

Parameter	Description	Value	Source
CSF testing fraction of total biomarker testing by CSF and PET	Assumption based on input from Canadian subject-matter experts	Base case scenario: 20% Alternative scenarios 1 and 2: 50%	–
Current PET scanners' fraction of excess capacity	Assumption based on expert input from the U.S. analysis	50%	Liu et al. (2017)
New PET scanners' fraction of excess capacity	Assumption based on expert input from the U.S. analysis	80%	Liu et al. (2017)
Infusions	Estimated based on the historical number of infusions of therapeutic or prophylactic substances, excluding chemotherapy and biologic response modifiers, in the U.S., and scaled to Canada based on population size and relative health care system capacity; growth rates from the U.S. analysis	See Figure A.3 for the projected infusion capacity in Canada, which is based on U.S. data scaled to the Canadian population and relative health care system capacity (Table A.2)	NAMCS and NHAMCS 2011 and 2013 data from Centers for Disease Control and Prevention (2017), OECD (2018b), Liu et al. (2017)
Current infusion centers' fraction of excess capacity	Assumption based on expert input from the U.S. analysis	10%	Liu et al. (2017)
New infusion centers' fraction of excess capacity	Assumption based on expert input from the U.S. analysis	80%	Liu et al. (2017)

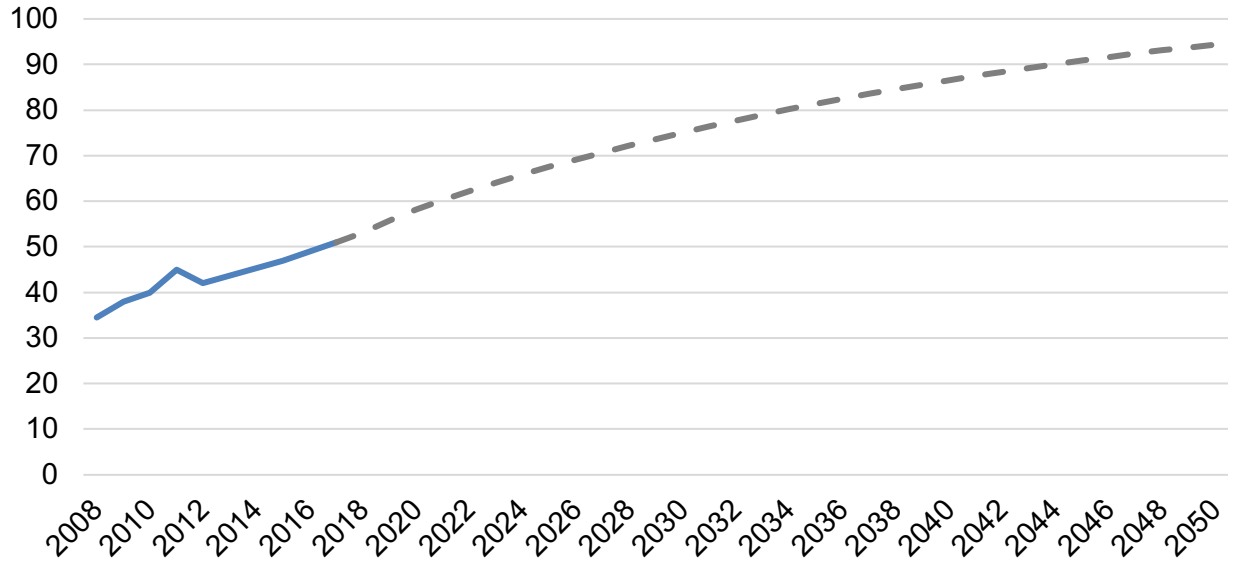
NOTE: CSF = cerebrospinal fluid, NAMCS = National Ambulatory Medical Care Survey; NHAMCS = National Hospital Ambulatory Medical Care Survey; OECD = Organisation for Economic Co-operation and Development; PET = positron emission tomography.

Figure A.1. Projected Number of Specialists in Canada



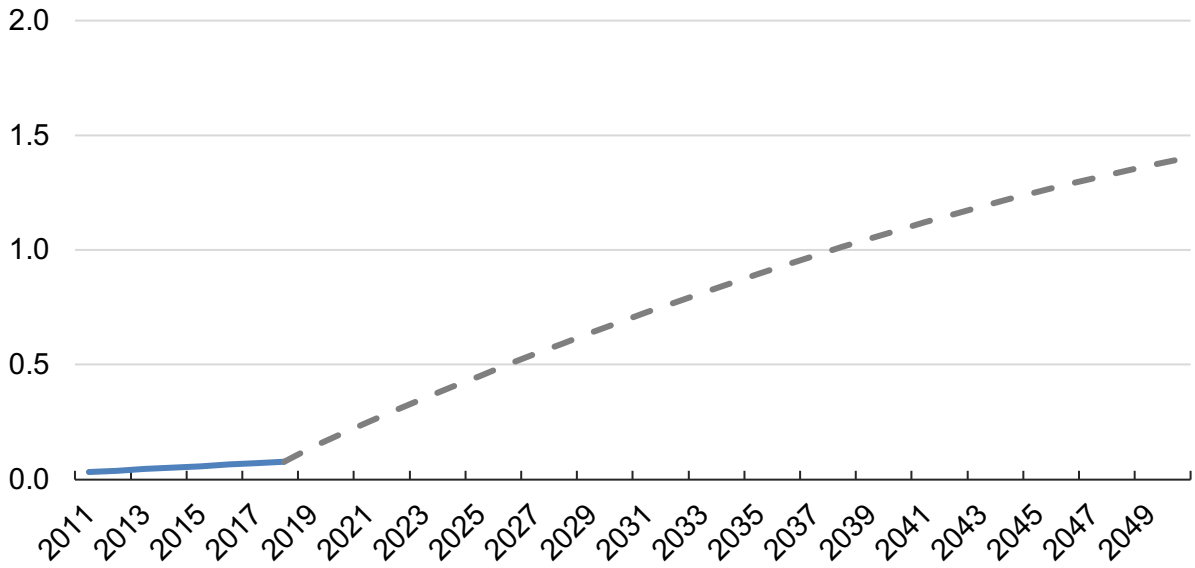
NOTES: The solid lines reflect historical data from the Canadian Medical Association (2018). The dotted lines reflect projections based on the Fraser Institute forecast for specialist growth between 2018 and 2030 (Globerman, Barua, and Hasan, 2018) and our projection that carries forward the Fraser's 2030 growth rate of 0.83 percent as the annual growth rate between 2030 and 2050. Based on expert input, we assume 10 percent of psychiatrists are able to evaluate and diagnose Alzheimer's pathology in patients with MCI.

Figure A.2. Projected Number of PET Scanners in Canada



NOTES: The blue line reflects historical data on the number of PET scanners in Canada (OECD, 2018a) for years 2008–2017. The dotted line is our projection assuming the historical trend continues with a 5-percent annual growth rate initially, decreasing to a 0.7-percent growth rate in 2050.

Figure A.3. Projected Excess Capacity for Infusions in Canada (millions)



NOTES: The blue line reflects historical data on the number of infusions in Canada based on our health care system capacity index relative to the number of infusions administered in the United States and our assumption of 10-percent excess capacity for additional infusions. The dotted line is our projection assuming the historical trend continues with a 10-percent annual growth rate initially, decreasing to a 1.3-percent growth rate in 2050, and that new infusion services could dedicate 80 percent of their capacity to an AD-modifying therapy.

Table A.2. Relative Capacity of the Canadian Health Care System Derived from Four Indicators

	Hospital Beds	Active Nurses	MRI Scanners	PET Scanners	Health Care System Capacity Index
Canada	93%	27%	26%	85%	58%

NOTES: Each component of the index is a relative value on a per capita basis between Canada and the United States based on OECD data (OECD, 2018b). We average the four component values to calculate the health care system capacity index for Canada, relative to the United States at 100 percent.

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