Appendix

Assessing the Preparedness of the Health Care System Infrastructure in Six European Countries for an Alzheimer's Treatment

Jakub P. Hlávka, Soeren Mattke, Jodi L. Liu

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Appendix

This appendix provides the sources for our model parameters and supplemental results.

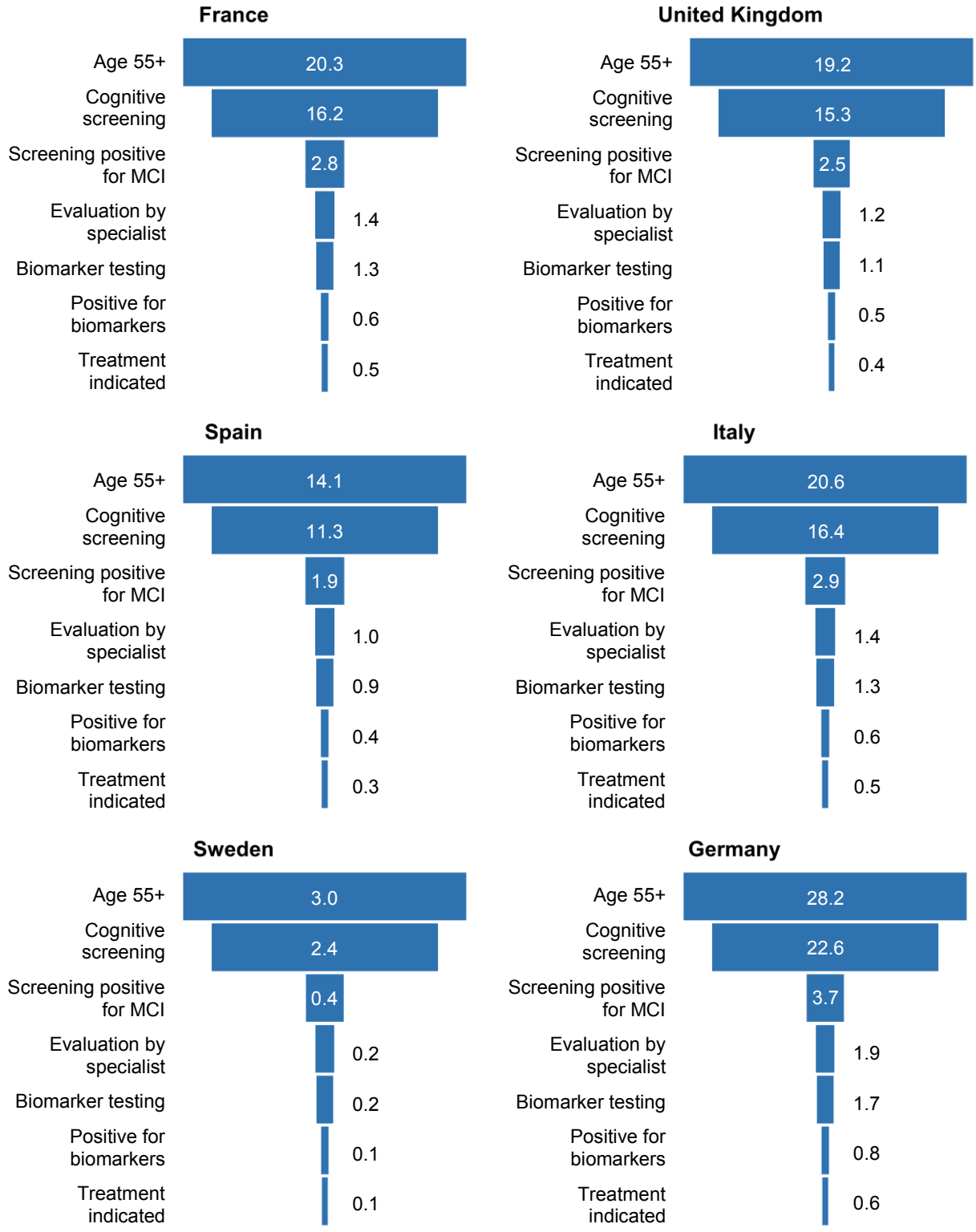
Table A.1. Model Parameters, Values, and Sources

Parameter	Description	France	Germany	Italy	Spain	Sweden	UK	Source
Population in 2017 (millions)								
Age 55+ without mild cognitive impairment (MCI) and Alzheimer's dementia	Population estimate of people 55 years and older, minus those with MCI and Alzheimer's dementia	17.113	23.608	17.206	11.807	2.572	16.037	Eurostat (2018), Petersen et al. (2017), Organisation for Economic Co-operation and Development (OECD) (2017a)
MCI	Estimated number of people with MCI based on a meta-analysis of MCI prevalence	2.642	3.541	2.741	1.844	0.378	2.332	Petersen et al. (2017)
Alzheimer's dementia	Estimated number of Alzheimer's dementia patients based on dementia prevalence and AD etiology estimates	0.923	1.170	0.957	0.631	0.095	0.698	OECD (2017a)
Dead	Estimated mortality among the age 55+ population	0.500	0.785	0.547	0.359	0.079	0.502	Eurostat (2018)
Annual death rates								
Age 55+ without cognitive impairment and Alzheimer's dementia	All-cause death rate among those without cognitive impairment	0.018	0.018	0.017	0.018	0.019	0.016	Eurostat (2018), Vassilaki et al. (2015), Rossetti et al. (2010), Spackman et al. (2012)
MCI	Derived from all-cause mortality of age cohort adjusted for increased mortality in MCI cohorts	0.048	0.053	0.052	0.051	0.053	0.053	Vassilaki et al. (2015)
Alzheimer's dementia	Derived from weighted average of mortality of patients in mild, moderate, and severe stages of Alzheimer's disease	0.161	0.171	0.170	0.166	0.179	0.174	Rossetti et al. (2010), Spackman et al. (2012)
Annual disease state transition probabilities								
Probability of transitioning to MCI	Interpolated from Yesavage et al. (2002) given the average age in the population ages 55+	2.5%	2.5%	2.5%	2.6%	2.5%	2.4%	Yesavage et al. (2002); Eurostat (2018)

Parameter	Description	France	Germany	Italy	Spain	Sweden	UK	Source
Probability of transitioning from MCI to Alzheimer's dementia *without* treatment	Derived from a meta-analysis			6.5%				Mitchell and Shiri-Feshki (2009)
Probability of transitioning from MCI to Alzheimer's disease *with* treatment	Calculated as a product of a transitioning from MCI to Alzheimer's disease and an assumed relative risk reduction of 50%			3.25%				—
Other epidemiological parameters								
Share of age 55+ population who receive cognitive screening each year	Assumption based on expert input from the U.S. analysis			80%				Liu et al. (2017)
Share of 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 biomarker levels	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 who test positive for biomarkers and 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 geriatric psychiatrists to diagnose Alzheimer's disease; share of psychiatrists based on expert input on the six European countries	4,327	19,699	9,501	4,424	1,799	4,848	Eurostat (2017), European Geriatric Medicine Society (2018)

Parameter	Description	France	Germany	Italy	Spain	Sweden	UK	Source
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	Base scenario: 5% Low capacity scenario: 2.5% High capacity scenario: 7.5%						Liu et al. (2017)
Positron Emission Topography (PET) scanners	Number of scanners in each country; estimated growth in PET scanners based on the growth rates from the U.S. analysis	139	125	121	76	16	72	OECD (2017a); National Cancer Research Institute (2018); Gesundheitsberichterstattung des Bundes (2018); Liu et al. (2017)
Cerebrospinal fluid (CSF) testing fraction of total biomarker testing by CSF and PET	Assumption based on expert input on the six European countries and the assumption used in the Alzheimer's Research UK analysis	90%						Alzheimer's Research UK (2018)
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 United States, and scaled to each European country based on population size and relative health care system capacity; growth rates from the U.S. analysis	See Figure A.1 for the projected infusion capacity in the United States, which was scaled to each of the six European countries based on population size and the relative health care system capacity in each country (Table A.2)						National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey 2011 and 2013 data from Centers for Disease Control and Prevention (2017); OECD (2017b); 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)

Figure A.1. Expected Patient Demand at Each Stage of the Patient Journey in 2019 (millions)



NOTES: The age 55+ population in these figures includes both cognitively normal and cognitively impaired individuals. Each subsequent patient pool is a subset of the prior patient pool.

Figure A.2. Projected Capacity for Infusions in the United States

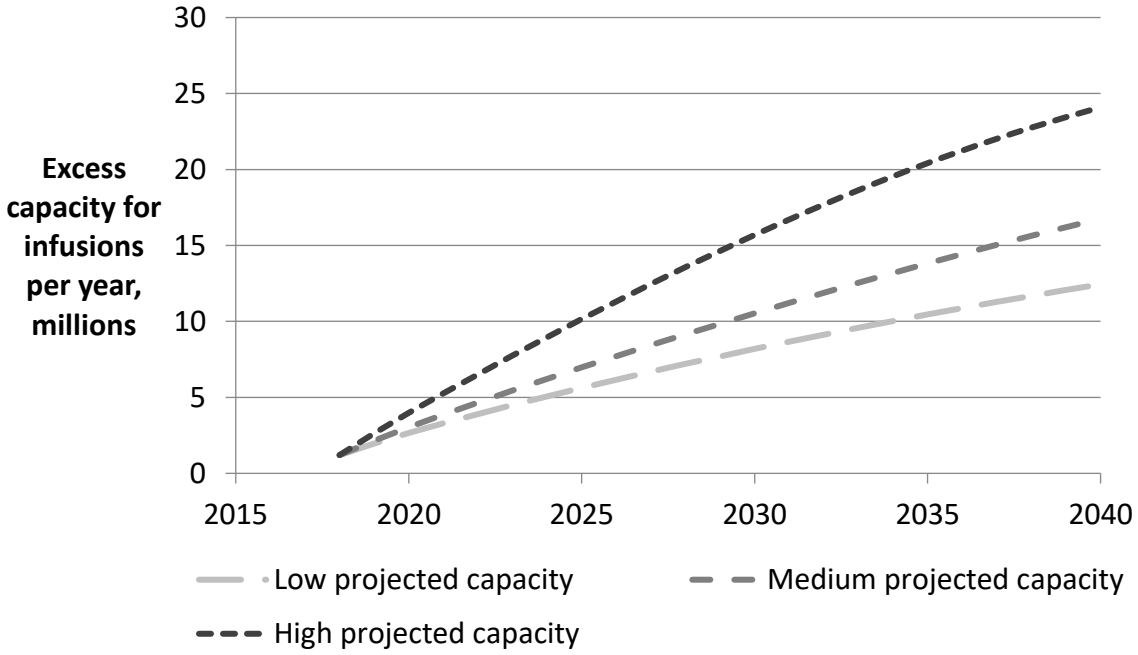


Table A.2. Health Care System Capacity Index

	Hospital Beds (%)	Active Nurses (%)	MRI Scanners (%)	PET Scanners (%)	Health Care System Capacity Index (%)
France	220	88	32	38	94
Germany	291	143	86	30	137
Italy	113	54	72	59	75
Spain	105	49	41	32	57
Sweden	90	104	N/A	31	75
UK	96	78	19	21	54

SOURCE: OECD, 2017b
NOTES: The value of each component of the index is a relative value on a per capita basis between each country and the United States. We average the four component values to calculate the health care system capacity index for each country, relative to the United States at 100 percent.

Figure A.3. Projected Number of Patients Waiting for Diagnosis, Testing, and Treatment (millions)

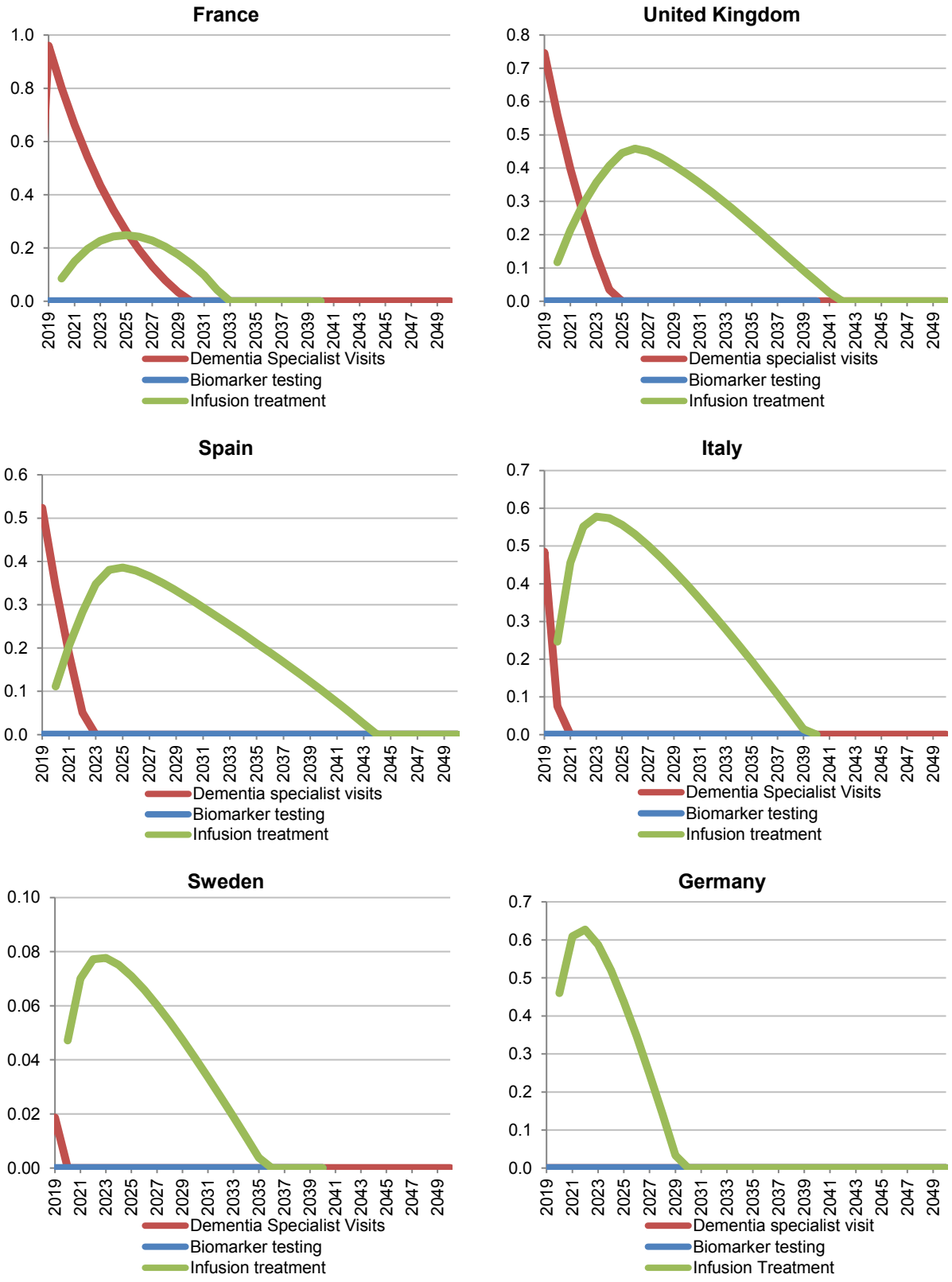
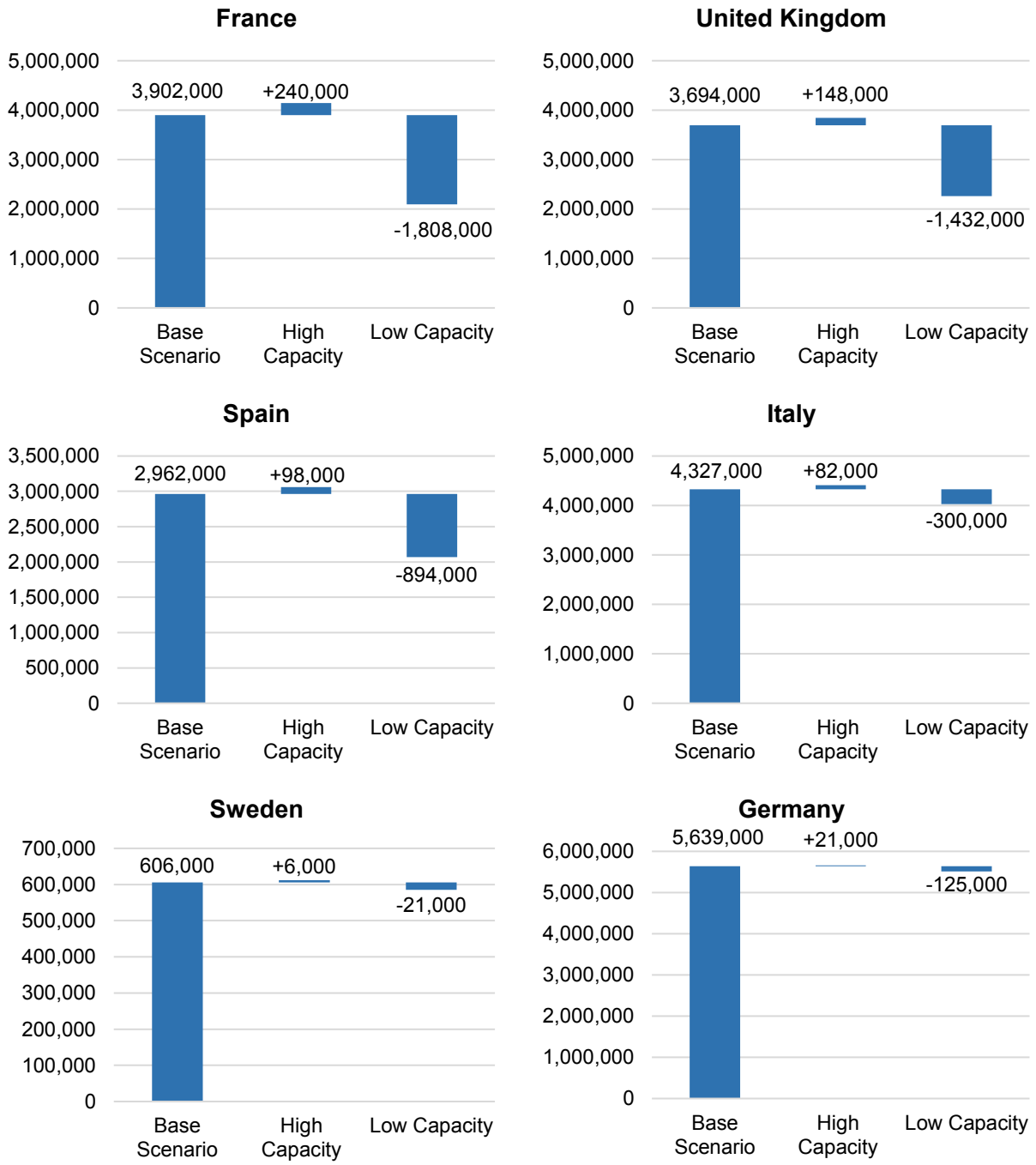
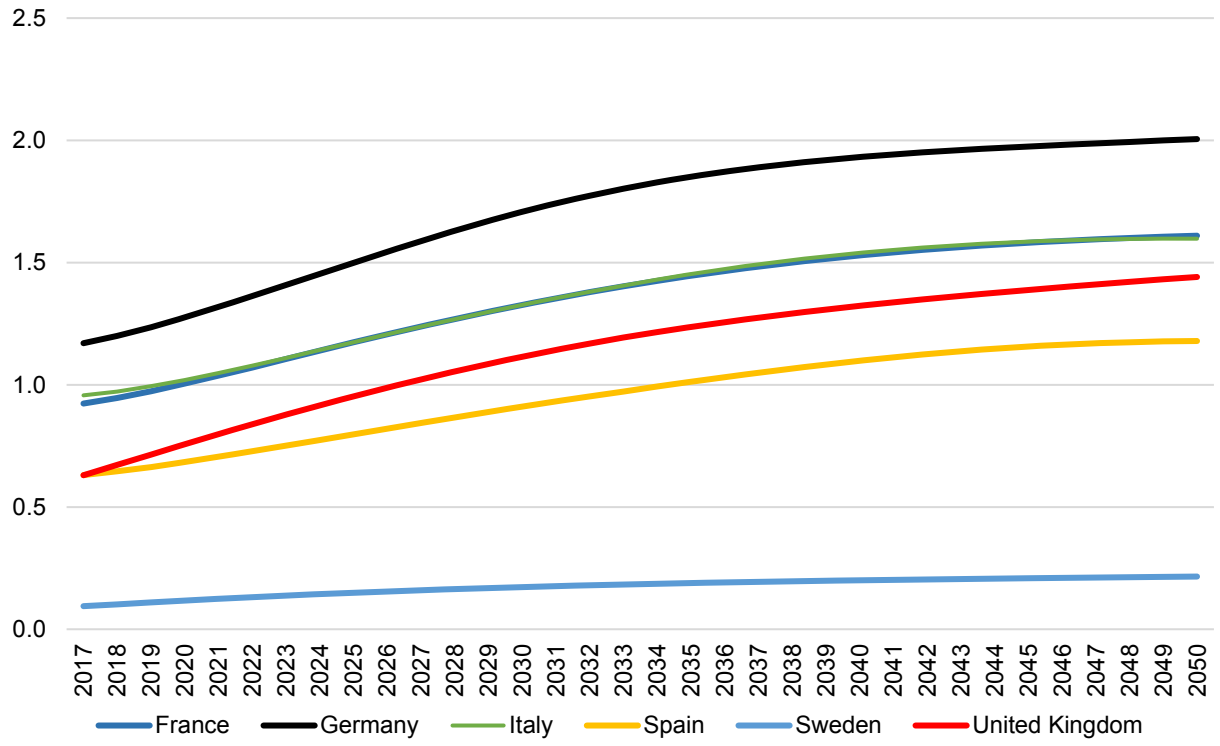


Figure A.4. Projected Cumulative Number of New Alzheimer's Dementia Cases Averted Between 2020 and 2050 Under Low and High Capacity Assumptions, by Country



NOTES: This figure demonstrates the sensitivity of our projections to the capacity assumptions. The base scenario reflects medium capacity assumptions; the high- and low-capacity scenarios represent high and low parameter values of our specialist, biomarker testing, and infusion capacity. The displayed values for the high- and low-capacity scenarios are relative to the cumulative number of Alzheimer's dementia cases averted in the base scenario. For specialists, our alternative assumptions range from 2.5 percent (low) to 7.5 percent (high), relative to the base case 5 percent excess capacity among specialists. For PET scanners, we assume an annual increase of 1 percent (low), 3 percent (base), and 5 percent (high) in 2019, which decay gradually to 0.1 percent (low), 0.4 percent (base), and 0.7 percent (high) in 2050; note that PET scans are not a binding constraint. Our infusion capacity assumption ranges from 8 percent (low) to 15 percent (high), relative to the base case of 10 percent excess capacity among specialists in 2019, which decay to 1.1 percent (low), 1.3 percent (base), and 0.4 percent (high) in 2050.

Figure A.5. Projected Burden of Alzheimer's Dementia with No Treatment (millions)



NOTES: This figure shows the projected number of Alzheimer's dementia cases in the six European countries without a disease-modifying therapy in our model. These projections are consistent with projections by Alzheimer's Disease International, which estimates more than a doubling of the prevalence of dementia in high-income countries between 2015 and 2050 (Prince et al., 2015), and with other sources also reporting approximately a doubling of projected Alzheimer's disease and related dementia cases by 2050 in France (Mura, Dartigues, and Berr, 2010), Germany ("Germany Sees Increase of Dementia Cases," 2013), Italy ("Dementia Sufferers in Italy to Nearly Double by 2050—Experts," 2016), Spain (Soto-Gordoba et al., 2015), Sweden ("Sweden 'Lacks National Dementia Plan,'" 2015), and the United Kingdom (Mashta, 2007). Approximately 60 to 80 percent of dementia cases are due to Alzheimer's disease (OECD, 2017a).

References

Alzheimer's Research UK, *Thinking Differently: Preparing Today to Implement Future Dementia Treatments*, Cambridge, UK, March 2018. As of May 25, 2018: https://www.alzheimersresearchuk.org/wp-content/uploads/2018/04/thinking_differently_report-180328-single.pdf

Aneshensel, C. S., L. I. Pearlin, L. Levy-Storms, and R. H. Schuler, "The Transition from Home to Nursing Home Mortality Among People with Dementia," *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, Vol. 55, No. 3, 2000, pp. S152–S162.

Dall, T. M., M. V. Storm, R. Chakrabarti, O. Drogan, C. M. Keran, P. D. Donofrio, and T. R. Vidic, "Supply and Demand Analysis of the Current and Future U.S. Neurology Workforce," *Neurology*, Vol. 81, No. 5, 2013, pp. 470–478.

"Dementia Sufferers in Italy to Nearly Double by 2050—Experts," Agenzia Nazionale Stampa Associata, 2016. As of July 1, 2018: http://www.ansa.it/english/news/2016/01/19/dementia-sufferers-in-italy-to-nearly-double-by-2050-experts_0b792431-0c26-4dbe-aa32-836e7b566ccc.html

Doraiswamy, P. M., R. A. Sperling, K. Johnson, E. M. Reiman, T. Z. Wong, M. N. Sabbagh, C. H. Sadowsky, A. S. Fleisher, A. Carpenter, A. D. Joshi, M. Lu, M. Grundman, M. A. Mintun, D. M. Skovronsky, M. J. Pontecorvo, and the AV45-A11 Study Group, "Florbetapir F 18 Amyloid PET and 36-Month Cognitive Decline: A Prospective Multicenter Study," *Molecular Psychiatry*, Vol. 19, No. 9, 2014, pp. 1044–1051.

European Geriatric Medicine Society, "National Societies," webpage, Genoa, Italy, 2018. As of May 25, 2018: http://www.eugms.org/our-members/national-societies.html

Eurostat, "Physicians by Medical Speciality," database, 2017. As of May 25, 2018: http://appsso.eurostat.ec.europa.eu/nui/show.do?query=BOOKMARK_DS-052274_QID_7C5B3907_UID_-3F171EB0&layout=TIME,C,X,0;MED_SPEC,L,X,1;GEO,L,Y,0;UNIT,L,Z,0;INDICATORS,C,Z,1;&zSelection=DS-052274INDICATORS,OBS_FLAG;DS-052274UNIT,NR;&rankName1=UNIT_1_2_-1_2&rankName2=INDICATORS_1_2_-1_2&rankName3=TIME_1_0_0_0&rankName4=MED-SPEC_1_2_1_0&rankName5=GEO_1_2_0_1&sortC=ASC_-1_FIRST&rStp=&cStp=&rDCh=&cDCh=&rDM=true&cDM=true&footnes=false&empty=false&wai=false&time_mode=NONE&time_most_recent=false&lang=EN&cfo=%23%23%23%2C%23%23%23.%23%23%23

Eurostat, "Your Key to European Statistics," homepage, 2018. As of May 25, 2018: http://ec.europa.eu/eurostat/data/database

"Germany Sees Increase of Dementia Cases," *Deutsche Welle*, 2013. As of July 1, 2018: https://www.dw.com/en/germany-sees-increase-of-dementia-cases/a-16722825

Gesundheitsberichterstattung des Bundes, "Medizinisch-Technische Großgeräte," database, 2018. As of May 25, 2018: http://www.gbe-bund.de/gbe10/I?I=160:28777873D

Liu, J. L., J. P. Hlavka, R. Hillestad, and S. Mattke, *Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment*, Santa Monica, Calif.: RAND Corporation, RR-2272-BIOG, 2017. As of August 21, 2018: https://www.rand.org/pubs/research_reports/RR2272.html

Mashta, O., "Number of People in UK with Dementia Will More Than Double by 2050," *British Medical Journal*, Vol. 334, No. 7591, 2007, p. 447.

Mura, T., J. F. Dartigues, and C. Berr, "How Many Dementia Cases in France and Europe? Alternative Projections and Scenarios 2010–2050," *European Journal of Neurology*, Vol. 17, No. 2, 2010, pp. 252–259.

National Cancer Research Institute PET Core Lab, "PET Facilities," webpage, 2018. As of May 25, 2018: http://www.ncri-pet.org.uk/pet_facilities.php

OECD—*See* Organisation for Economic Co-operation and Development.

Ong, K. T., V. L. Villemagne, A. Bahar-Fuchs, F. Lamb, N. Langdon, A. M. Catafau, A. W. Stephens, J. Seibyl, L. M. Dinkelborg, C. B. Reininger, B. Putz, B. Rohde, C. L. Masters, and C. C. Rowe, "A Beta Imaging with 18F-Florbetaben in Prodromal Alzheimer's Disease: A Prospective Outcome Study," *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 86, No. 4, 2015. pp. 431–436.

Organisation for Economic Co-operation and Development, *Health at a Glance 2017: OECD Indicators*, 2017a. As of August 9, 2018: http://www.oecd.org/health/health-systems/health-at-a-glance-19991312.htm

Organisation for Economic Co-operation and Development, "Health Care Resources," database, 2017b. As of May 25, 2018: http://stats.oecd.org/Index.aspx?DataSetCode=HEALTH_REAC

Petersen, R., O. Lopez, M. J. Armstrong, T. S. D. Getchius, M. Ganguli, D. Gloss, G. S. Gronseth, D. Marson, T. Pringsheim, G. S. Day, M. Sager, J. Stevens, and A. Rae-Grant, "Practice Guideline Update Summary: Mild Cognitive Impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology," *Neurology*, Vol. 90, No 3, 2018, pp. 126–135.

Prince, M., A. Wirno, M. Guerchet, G. Ali, Y. Wu, and M. Prina, *World Alzheimer Report 2015: The Global Impact of Dementia, An Analysis of Prevalence, Incidence, Cost and Trends*, London: Alzheimer's Disease International, 2015. As of May 25, 2018: https://www.alz.co.uk/research/WorldAlzheimerReport2015.pdf

Soto-Gordoa, M., A. Arrospide, F. Moreno-Izco, P. Martínez-Lage, I. Castilla, and J. Mar, *The Long-Term Impact (2010 to 2050) of Obesity and Hypertension Prevalence on Alzheimer's Disease–Related Dementia*, presented at IV Taller EvaluAES, Asociatión Economía de la Salud, Barcelona, April 17, 2015. As of July 1, 2018: http://www.aes.es/evaluaes/presentaciones_taller_iv/

Spackman, D. E., S. Kadiyala, J. Neumann, P. L. Veenstra, and D. S. Sullivan, "Measuring Alzheimer Disease Progression with Transition Probabilities: Estimates from NACC-UDS," *Current Alzheimer Research*, Vol. 9 No. 9, 2012, pp. 1050–1058.

"Sweden 'Lacks National Dementia Plan,'" Sveriges Radio, 2016. As of July 1, 2018: https://sverigesradio.se/sida/artikel.aspx?programid=2054&artikel=6486987

Vassilaki, M., R. H. Cha, Y. E. Geda, M. M. Mielke, D. S. Knopman, R. C. Petersen, and R. O. Roberts, "Mortality in Mild Cognitive Impairment Varies by Subtype, Sex, and Lifestyle Factors: The Mayo Clinic Study of Aging," *Journal of Alzheimer's Disease*, Vol. 45, No. 4, 2015, pp. 1237–1245.