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Appendix 1

Description of the included cohort studies

Alameda County Study (Alameda), USA

The Alameda County Study is a prospective cohort study of a stratified random sample of Alameda County (California, USA) households with non-institutionalized residents, aged 21 and older, or aged 16-21 if married. The purpose of this survey was to explore the influence of health practices and social relationships on the physical and mental health of a typical sample of the population. The study started in 1965 with a sample of 6,928 respondents (including approximately 500 women aged 65 years and older). The 1974 questionnaire, which was used as the baseline year for the current study 6861 participants had data on BMI and a dementia follow-up, and were thus eligible to this study.

Dementia was defined using death records *ICD 9 209-294, 331.0, 331.1, 331.2, 331.8, 331.9*

Reference: Berkman L, Breslow L. Health and ways of living: the Alameda County Study. New York, 1983.

Finnish Public Sector study (FPS), Finland

The Finnish Public Sector study is a prospective cohort study comprising the entire public sector personnel of 10 towns (municipalities) and 21 hospitals in the same geographical areas. Participants, who were recruited from employers' records in 2000-2002, were individuals who had been employed in the study organisations for at least six months prior to data collection. 48 592 individuals (9 337 men and 39 255 women aged 17 to 65) responded to the questionnaire. Of these, 46,880 had data on body mass index based on self-reported weight and health and were eligible for our meta-analyses. Ethical approval was obtained from the ethics committee of the Finnish Institute of Occupational Health. Participants were linked to drug reimbursement, hospitalisation and death registers. Dementia was defined using ICD-10, codes F00, F01, F02, F03, G30 and G31 (31.0, 31.1, 31.8)

Reference: Kivimäki M, Lawlor DA, Davey Smith G, et al. Socioeconomic position, co-occurrence of behavior-related risk factors, and coronary heart disease: the Finnish Public Sector study. *Am J Public Health* 2007; **97**: 874-9.

Finnish Twin Cohort (FTC) study, Finland

The older Finnish Twin Cohort study is a longitudinal study of all Finnish same-sex twins born before 1958. At the baseline in 1975, a postal questionnaire survey consisting of questions on health and health-related behaviors was conducted. The mean age of the participants was 36.3 (range 18.3 to 95.9) years at the start of follow-up May 1, 1976. Data for self-reported height and weight were available for 12,630 men and 13,184 women resident in Finland. Responses and returning completed questionnaire were considered as consent in postal questionnaire data collection in 1975; the study was approved by the National Board of Health. The use of the cohort for register follow-up studies has been approved by the Ethical committee of the Department of Public Health, University of Helsinki. Data and permission for use of cause of death data were obtained from Statistics Finland.

Dementia death was defined according to appropriate versions of the International Classification of Diseases (ICD). In ICD8 (deaths between 1970 and 1986) the following diagnoses were counted as a dementia death: Dementia senilis et praesentis (ICD 290 category), Senilis (ICD 290,00), Morbus Alzheimer (ICD 290,01), Morbus Pick (ICD 290,11), Praesentis alia sive NUD (ICD 290,19), Senilitas, psychosi non indicata (ICD 794), Marasmus senilis (ICD 794,00), and Senilitas alia sive NUD (ICD 794,09). In ICD9 (years 1987 to 1995) the following diagnoses were categorized as a dementia death: Dementia senilis et praesentis (ICD 290 category, ICD 2900A), Morbus Alzheimer (ICD 3310A, Morbus Pick (ICD 3311A), Dementia e multis infarctibus (ICD 4378A), and Senilitas, psychosi non indicata (ICD 797). In the most recent period (years 1996 to 2011, ICD-10) the following diagnoses were considered to be a dementia death: Dementia vascularis (F01), Dementia non specificata (F03), Morbus Alzheimer (G30), and Senilitas (R54). Both underlying and contributing codes were used.

References: Kaprio J, Koskenvuo M. Genetic and environmental factors in complex diseases: the older Finnish Twin Cohort. *Twin Res* 2002; **5**: 358-65; Iso-Markku P, Waller K, Kujala UM, Kaprio J. Physical activity and dementia: long-term follow-up study of adult twins. *Ann Med*. 2015; **47** :81-7.

Gazel, France

Gazel is a prospective cohort study of 20 625 employees (15 011 men and 5 614 women) of France's national gas and electricity company, Electricité de France-Gaz de France (EDF-GDF). Since the study baseline in 1989, when the participants were aged 35–50 years, they have been posted an annual follow-up questionnaire to collect data on health, lifestyle, individual, familial, social, and occupational factors. BMI was measured from self-reported height and weight in 1997 and 11 342 had data and were eligible for our meta-analysis. The GAZEL study received approval from the national commission overseeing ethical data collection in France (Commission Nationale Informatique et Liberté). Data from Gazel, WOLF-S, WOLF-N, and HeSSup were pooled to achieve sufficient case numbers (labelled IPD-Work other).

Dementia was defined using data from annual follow-up surveys requesting reported doctor-diagnosed demensis Alzheimer.

Reference: Goldberg M, Leclerc A, Bonenfant S, Chastang JF, Schmaus A, Kaniewski N, et al. Cohort profile: the GAZEL Cohort Study. *Int J Epidemiol* 2007; **36** :32-9.

Health and Lifestyle Survey (HALS)

UK HALS is a nationwide sample survey of community dwelling adults in England, Scotland, and Wales. In 1984/1985, a total of 12,254 addresses were randomly chosen from Electoral Registers and one adult aged 18 years or over was selected from each household. A total of 9003 adults participated in the baseline examination. Ethical approval for the main HALS surveys was received from the BMA Ethical Committee before the launch of survey.

Participants were linked to mortality registers and deaths from dementia were defined using ICD 9 209-294, 331.0, 331.1, 331.2, 331.8, and 331.9.

Reference: Cox BD, Blaxter M, Buckle ALJ, et al. The Health and Lifestyle Survey: A Preliminary Report. London: Health Promotion Trust; 1987.

Health and Social Support (HeSSup), Finland

The Health and Social Support (HeSSup) study is a prospective cohort study of a stratified random sample of the Finnish population in the following four age groups: 20–24, 30–34, 40–44, and 50–54. The participants were identified from the Finnish population register and posted an invitation to participate, along with a baseline questionnaire, in 1998. A total of 16 666 had data on BMI from self-reported height and weight and were thus eligible for our meta-analyses. The Turku University Central Hospital Ethics Committee approved the study. Data from Gazel, WOLF-S, WOLF-N, and HeSSup were pooled to achieve sufficient case numbers (labelled IPD-Work other).

Participants were linked to drug reimbursement, hospitalisation and death registers.

Dementia was defined using ICD-10, codes F00, F01, F02, F03, G30 and G31 (31.0, 31.1, 31.8)

Reference: Korkeila K, Suominen S, Ahvenainen J, Ojanlatva A, Rautava P, Helenius H, et al. Non-response and related factors in a nation-wide health survey. *Eur J Epidemiol* 2001; **17**: 991-9.

Health and Retirement Study (HRS), USA

The Health and Retirement Study (HRS) is a leading source for information on the health and economic well-being of adults age 50 and older in the United States. The HRS is a longitudinal project sponsored by the National Institute on Aging and the Social Security Administration. The first cohort was interviewed in 1992. Data on height, weight plus dementia follow-up were available for 9,899 men and women.

Participants were linked to mortality registers. Deaths from dementia were defined using ICD 10 G30 (Alzheimer's disease).

References: Growing Older in America: The Health and Retirement Study. Available at <http://hrsonline.isr.umich.edu/index.php?p=dbook>. June 25, 2016.

Juster FT, Suzman R. An overview of the Health Retirement Study. *J Human Resources* 1995;30(suppl): S7–S56.

Webpage: <http://hrsonline.isr.umich.edu>

National Health and Nutrition Survey (NHANES) 1971, 1976, 1988, 1999, 2001, 2003, 2005 and 2007, USA

The National Health and Nutrition Examination Survey (NHANES) is a programme of studies designed to assess the health and nutritional status of adults in the United States. The original NHANES (original) sample included 20,729 persons 25 to 74 years of age. NHANES 1971 (original, n = 14 396), 1976 (n=9,246), 1988 (n=18,072), 1999 (n=4,900), 2001 (n=5,223), 2003 (n =5,189), 2005 (n=5,234) and 2007 (n=5,884) are independent prospective cohort studies with height and weight measurement at baseline and a follow-up for cause-specific deaths.

Available ICD codes for dementia as a cause of death varied between study baseline: For NHANES 1971, 1976 and 1988, dementia deaths were defined using ICD 9 codes: 209-294, 331.0, 331.1, 331.2, 331.8, 331.9. For NHANES 1999 to 2007, dementia deaths were defined using ICD 10 G30 (Alzheimer's disease).

References: Madans JH, Cox CS, Kleinman JC, et al. 10 years after NHANES I: mortality experience at initial follow up, 1982-84. *Public Health Rep* 1986; **101**: 474-81.

Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *JAMA* 2012; **307**: 491-7.

Webpage: <http://www.cdc.gov/nchs/nhanes/index.htm>

National Health Interview Survey (NHIS) 1986-2009, USA

The National Health Interview Survey (NHIS) is a programme of studies monitoring the health of the U. S. residents since 1957. NHIS data on a broad range of health topics are collected through personal household interviews. The U.S. Census Bureau is the data collection agent for NHIS. For self-reported weight and height at baseline with a sufficient mortality follow-up for dementia deaths, data are publicly available from surveys in 1986 (n=43,028), 1987 (n=85,100), 1988 (n=85,140), 1989 (n=81,345), 1990 (n=83,459), 1991 (n=83,102), 1992 (n=88,060), 1992 (n=75,781), 1993 (n=75,781), 1994 (n=79,291), 1995 (n=68,721), 1996 (n=42,239), 1997 (n=33,523), 1998 (n=29,768), 1999 (n=28,178), 2000 (n=29,481), 2001 (n=30,218), 2002 (n=27,736), 2003 (n= 27,153), 2004 (n=28,187), 2005 (n=28,053), 2006 (n=22,312), 2007 (n=21,552), 2008 (n=20,502), and 2009 (n=26,470). Dementia was defined using death records, ICD-9 codes 209-294, 331.0, 331.1, 331.2, 331.8, and 331.9 or ICD-10 code G30 (Alzheimer's disease).

Reference: Dawson DA. Ethnic-differences in female overweight - data from the 1985 National-Health Interview Survey. *Am J Public Health* 1988; **78**: 1326-29.

Webpage: <http://www.cdc.gov/nchs/nhis/>

WOLF (Work, Lipids, and Fibrinogen) Stockholm and WOLF Norrland studies, Sweden

The WOLF (Work, Lipids, and Fibrinogen) Stockholm study is a prospective cohort study of 5673 people aged 19-70 and with data on BMI from measured height and weight working in companies in Stockholm county. WOLF Norrland is a prospective cohort of 4708 participants with data on BMI aged 19-65 working in companies in Jämtland and Västernorrland counties. At study baseline the participants underwent a clinical examination and completed a set of health questionnaires. For WOLF Stockholm, the baseline assessment was undertaken at 20 occupational health units between November 1992 and June 1995 and for WOLF Norrland at 13 occupational health service units in 1996-98. The Regional Research Ethics Board in Stockholm, and the ethics committee at Karolinska Institutet, Stockholm, Sweden approved the study. Data from Gazel, WOLF-S, WOLF-N, and HeSSup were pooled to achieve sufficient case numbers (labelled IPD-Work other). Dementia was defined using ICD-10, codes F00, F01, F02, F03, G30 and G31 (31.0, 31.1, 31.8).

References: Peter R, Alfredsson L, Hammar N, Siegrist J, Theorell T, P. W. High effort, low reward, and cardiovascular risk factors in employed Swedish men and women: baseline results from the WOLF Study. *J Epidemiol Community Health* 1998; **52** :540-7
Alfredsson L, Hammar N, Fransson E, de Faire U, Hallqvist J, Knutsson A, et al. Job strain and major risk factors for coronary heart disease among employed males and females in a Swedish study on work, lipids and fibrinogen. *Scand J Work Environ Health* 2002; **28**: 238-48.

Whitehall II, the United Kingdom

The Whitehall II study is a prospective cohort study set up to investigate socioeconomic determinants of health. At study baseline in 1985-1988, 10 308 civil service employees (6 895 men and 3 413 women) aged 35-55 and working in 20 civil service departments in London were invited to participate in the study. Data on BMI from measured height and weight and the outcome measures from phase 3 were available for 8073 men and women who were eligible for our meta-analyses. The Whitehall II study protocol was approved by

the University College London Medical School committee on the ethics of human research. Written informed consent was obtained at each data collection wave. Comprehensive tracing of electronic health records for dementia ascertainment was undertaken using three databases: the national hospital episode statistics (HES) database, the Mental Health Services Data Set (MHSDS) and the mortality register. Record linkage until 31st of March 2015, using International Classification of Diseases Tenth Edition (ICD-10) codes F00, F01, F02, F03, F05.1, G30, G31.0, G31.1 and G31.8 identified cases of dementia. The National Health Service (NHS) in the UK (England, Scotland, Wales) provides most of the health care, including out- and in-patient care. Private medical insurance, held by around 12% of the UK population (1997 figures),²⁸ is mainly used for elective surgery rather than chronic conditions such as dementia. MHSDS is a national database which contains information for persons in contact with mental health services in hospitals, outpatient clinics, and the community. Mortality data were drawn from the British national mortality register (National Health Services Central Registry). The tracing exercise was carried out using the unique NHS identification number given to each resident in the UK.

Reference: Marmot MG, Davey Smith G, Stansfeld S, et al. Health inequalities among British civil servants: the Whitehall II study. *Lancet* 1991; **337**: 1387-93.

Webpage: <https://www.ucl.ac.uk/whitehallII>

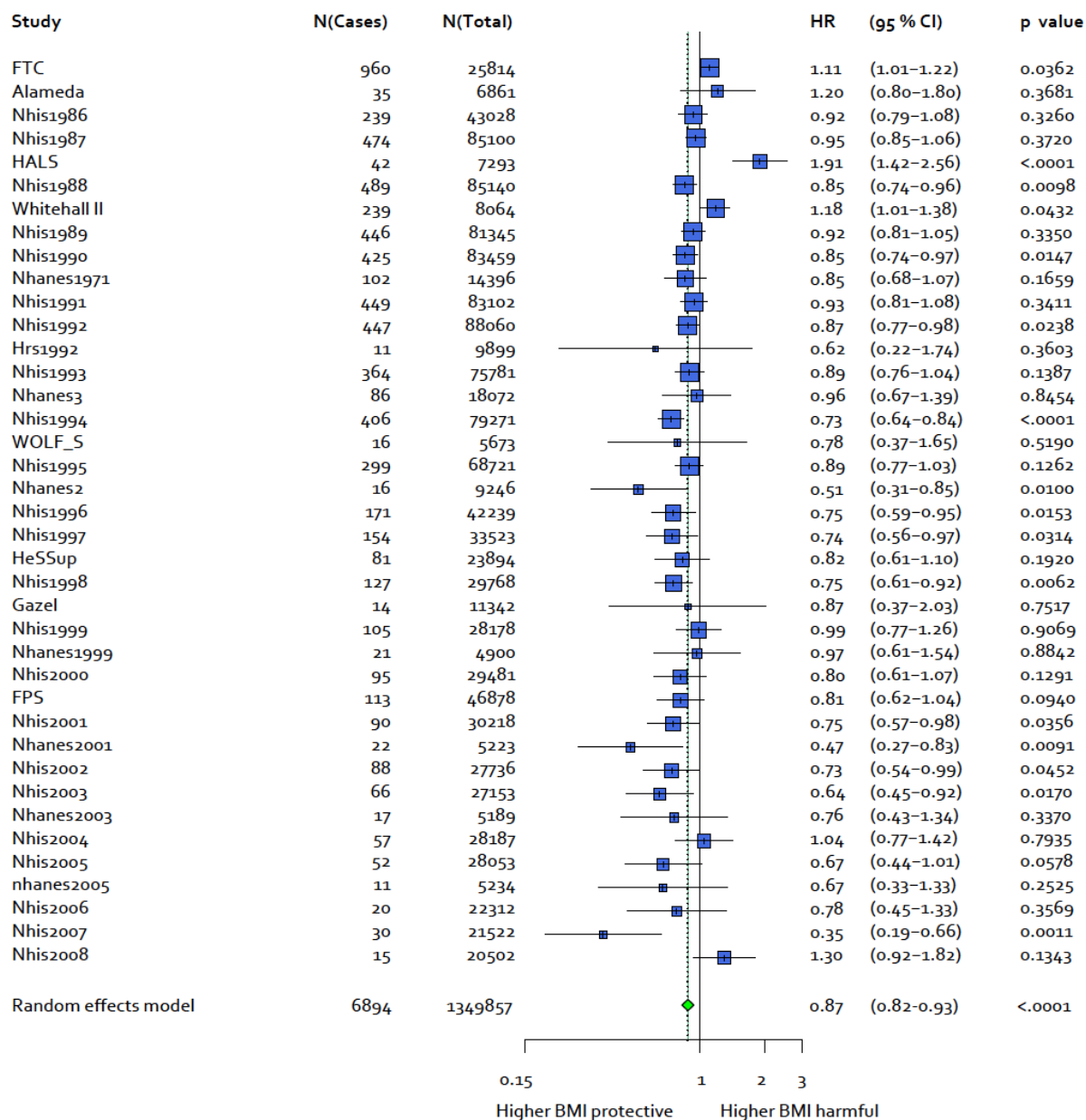
eTable 1. Characteristics of the included cohort studies

Study	Baseline	N(Total)	Mean age at BMI measurement	Proportion of women	Max follow-up, years	Person-years	N (Dementia)	Method of BMI measurement	Method of dementia ascertainment
FTC	1976	25,814	36.3	51.1	37.7	827,449	960	Measured	Deaths
Alameda	1965	6,861	43.7	54.2	35.9	193,935	35	Self-reported	Deaths
Nhis1986	1986	43,028	43.7	30.8	26.0	951,273	239	Self-reported	Deaths
Nhis1987	1987	85,100	44.0	46.3	25.0	1,822,167	474	Self-reported	Deaths
HALS	1984-1985	7,293	45.4	54.7	24.8	153,757	42	Measured	Deaths
Nhis1988	1988	85,140	44.3	46.4	24.0	1,763,067	489	Self-reported	Deaths
Whitehall II	1991 - 1993	8,064	49.6	30.8	23.9	177,486	239	Measured	Hospital & deaths
Nhis1989	1989	81,345	44.2	46.6	23.0	1,628,386	446	Self-reported	Deaths
Nhis1990	1990	83,459	44.3	46.5	22.0	1,613,081	425	Self-reported	Deaths
Nhanes1971	1971	14,396	48.9	59.7	21.4	260,397	102	Measured	Deaths
Nhis1991	1991	83,102	44.5	46.6	21.0	1,543,289	449	Self-reported	Deaths
Nhis1992	1992	88,060	44.4	46.7	21.0	1,639,100	447	Self-reported	Deaths
Hrs1992	1992	9,899	55.2	49.9	19.0	216,965	11	Self-reported	Deaths
Nhis1993	1993	75,781	44.6	46.8	19.0	1,291,418	364	Self-reported	Deaths
Nhanes3	1988-1994	18,072	46.8	53.2	18.1	238,438	86	Measured	Deaths
Nhis1994	1994	79,271	45.1	46.7	18.0	1,282,915	406	Self-reported	Deaths
WOLF_S	1992-1995	5,673	41.6	43.0	17.9	87,471	16	Measured	Hospital & deaths
Nhis1995	1995	68,721	44.6	46.8	17.0	1,063,138	299	Self-reported	Deaths
Nhanes2	1976-1980	9,246	54.3	53	16.8	122,842	16	Measured	Deaths
Nhis1996	1996	42,239	44.4	47.3	16.0	620,931	171	Self-reported	Deaths
Nhis1997	1997	33,523	46.1	56.4	15.3	465,807	154	Self-reported	Deaths
HeSSup	1998	23,894	36.7	59.0	15.0	352,597	81	Self-reported	Hospital, prescriptions, deaths
Nhis1998	1998	29,768	46.5	55.4	14.3	388,341	127	Self-reported	Deaths
Gazel	1997	11,342	50.3	27.6	14.0	154,810	14	Self-reported	Self-report, deaths
Nhis1999	1999	28,178	46.7	56.3	13.3	345,181	105	Self-reported	Deaths
Nhanes1999	1999-2000	4,900	46.3	53.1	12.8	53,590	21	Measured	Deaths
Nhis2000	2000	29,481	46.3	56	12.3	337,222	95	Self-reported	Deaths
FPS	2000	46,878	44.6	80.7	11.5	499,068	113	Self-reported	Hospital, prescriptions, deaths
Nhis2001	2001	30,218	46.3	55.6	11.3	319,395	90	Self-reported	Deaths
Nhanes2001	2001-2002	5,223	45.1	52.1	11.0	49,569	22	Measured	Deaths
Nhis2002	2002	27,736	46.7	55.4	10.3	268,815	88	Self-reported	Deaths
Nhanes2003	2003-2004	5,189	47.0	51.8	9.3	39,216	17	Measured	Deaths
Nhis2003	2003	27,153	46.7	55.7	9.3	238,863	66	Self-reported	Deaths
Nhis2004	2004	28,187	47.2	54.8	8.5	230,676	57	Self-reported	Deaths
Nhis2005	2005	28,053	47.5	55.3	7.3	195,895	52	Self-reported	Deaths
Nhanes2005	2005-2006	5,234	44.8	52	7.0	30,438	11	Measured	Deaths
Nhis2006	2006	22,312	47.0	54.8	6.3	135,425	20	Self-reported	Deaths
Nhis2007	2007	21,522	47.4	54.8	5.3	110,246	30	Self-reported	Deaths
Nhis2008	2008	20,502	47.9	55.5	4.3	85,435	15	Self-reported	Deaths
TOTAL	1965-2009	1,349,857				21,798,094	6894		

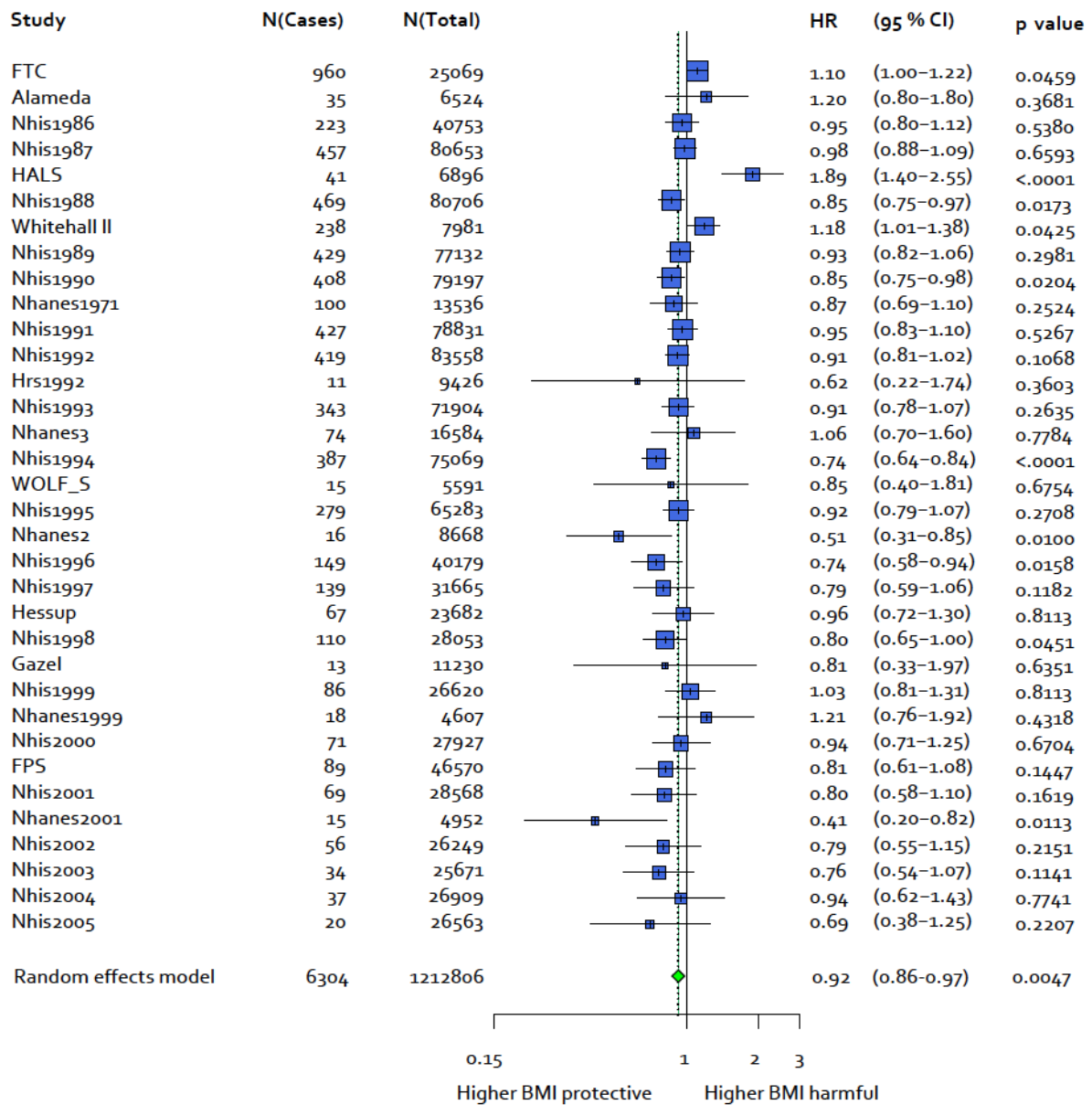
Appendix 2

Forest plots for meta-analysis of dementia risk per 5-unit increment in BMI after incremental exclusions to the follow-up

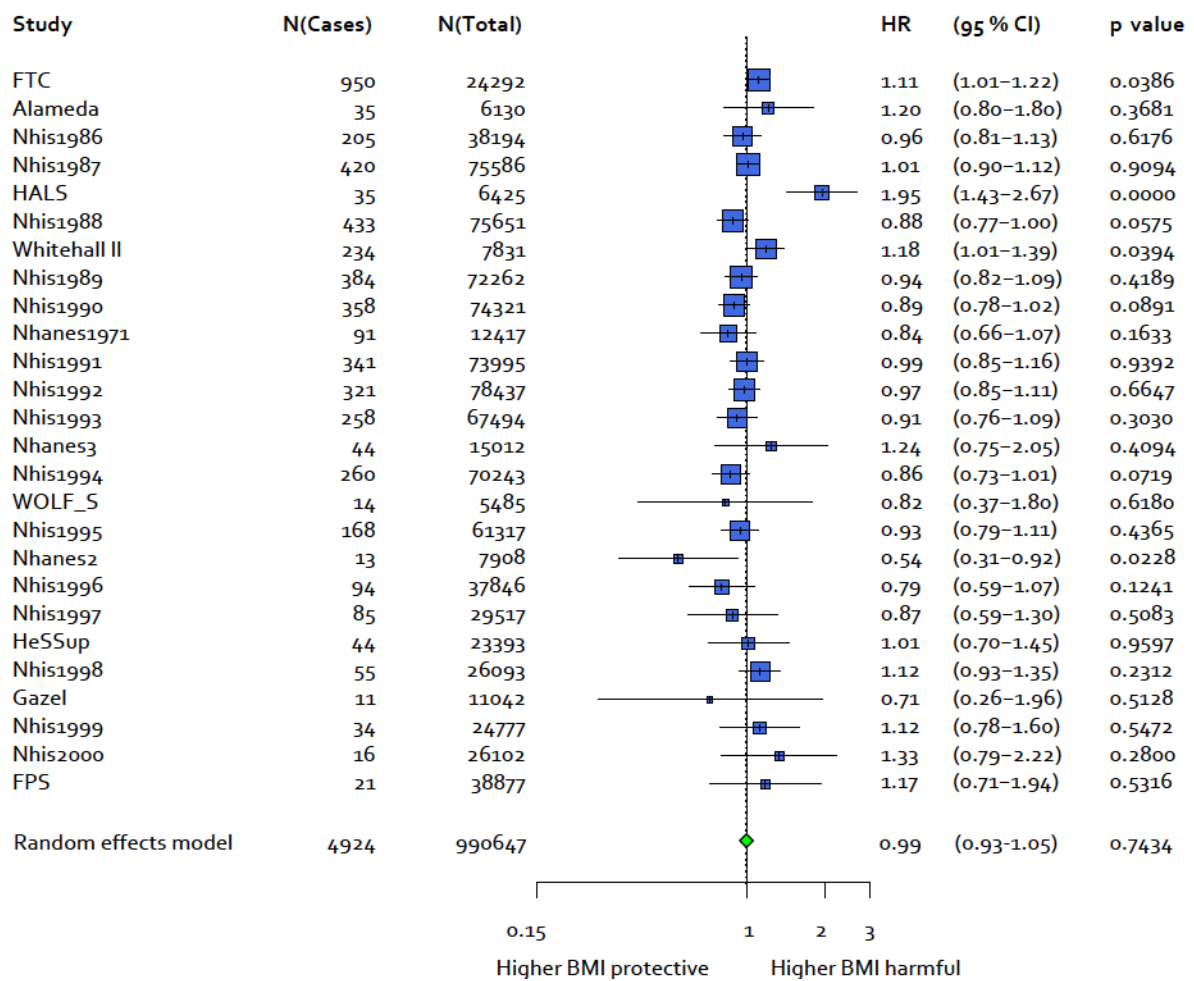
eFigure 1. Age-, sex-, and ethnicity-adjusted hazard ratio for dementia per 5-unit increment in BMI after no exclusions to the follow-up



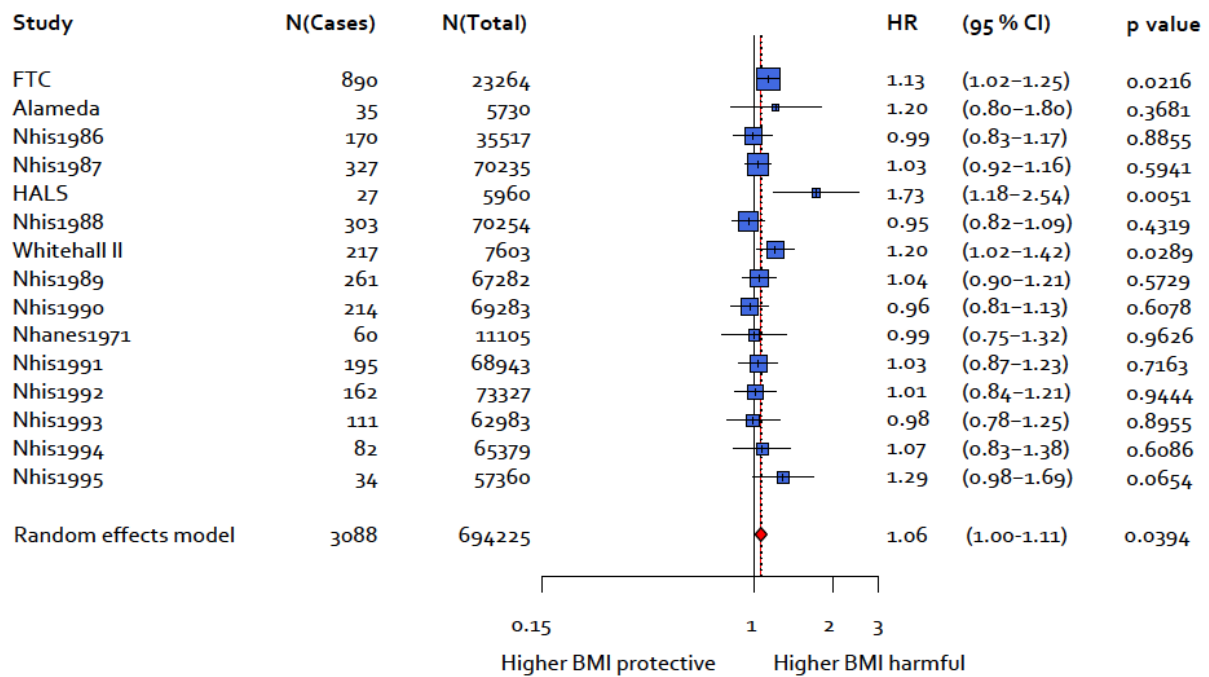
eFigure 2. Age-, sex-, and ethnicity-adjusted hazard ratio for dementia per 5-unit increment in BMI after excluding the first 5 years of the follow-up



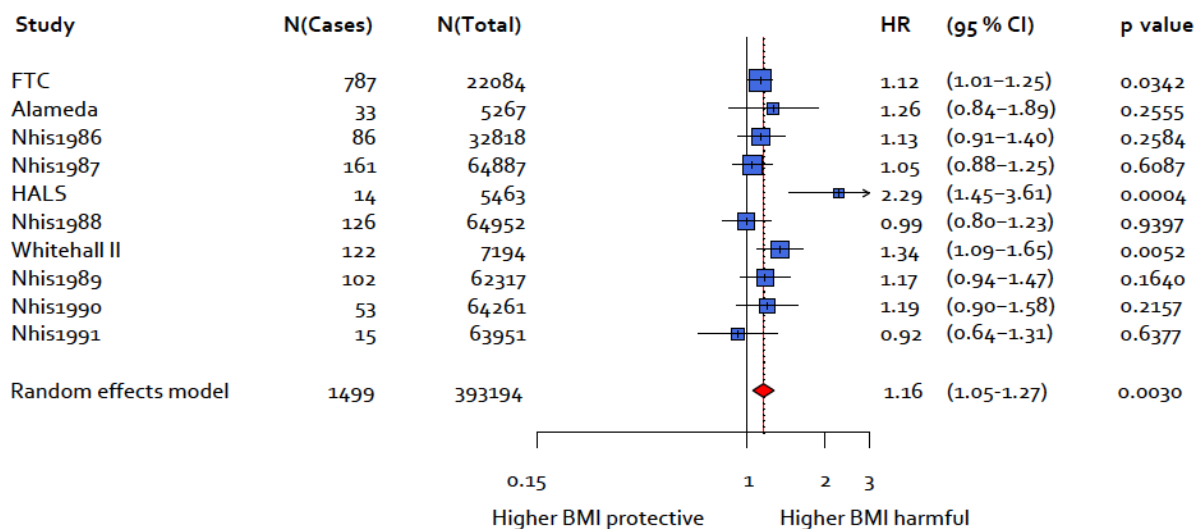
eFigure 3. Age-, sex-, and ethnicity-adjusted hazard ratio for dementia per 5-unit increment in BMI after excluding the first 10 years of the follow-up



eFigure 4. Age-, sex-, and ethnicity-adjusted hazard ratio for dementia per 5-unit increment in BMI after excluding the first 15 years of the follow-up



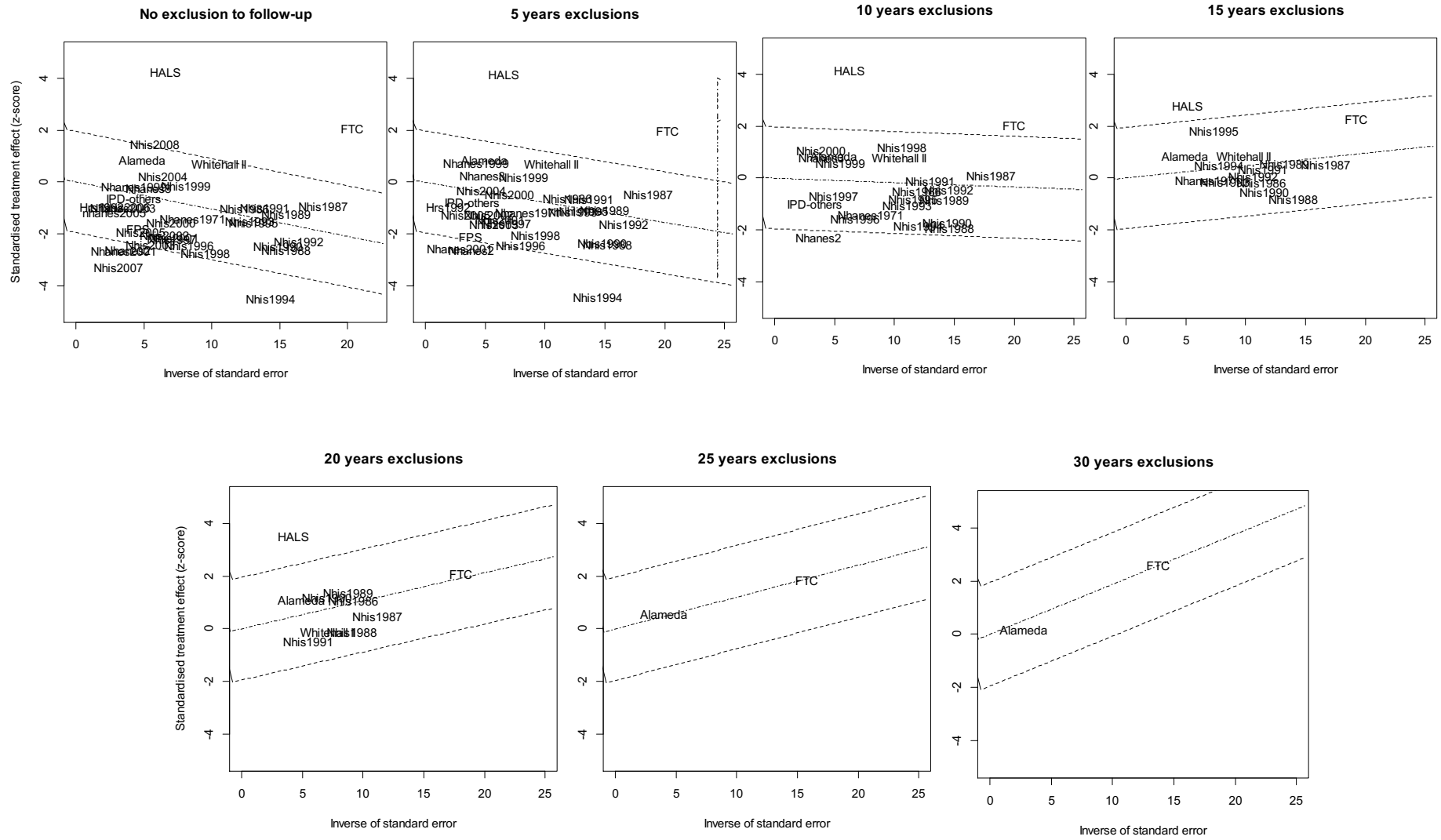
eFigure 5. Age-, sex-, and ethnicity-adjusted hazard ratio for dementia per 5-unit increment in BMI after excluding the first 20 years of the follow-up



Appendix 3

Galbraith plots for the association between BMI and dementia after gradual exclusions to follow-up

eFigure 6. Galbraith plots for the association between BMI and dementia after gradual exclusions to follow-up

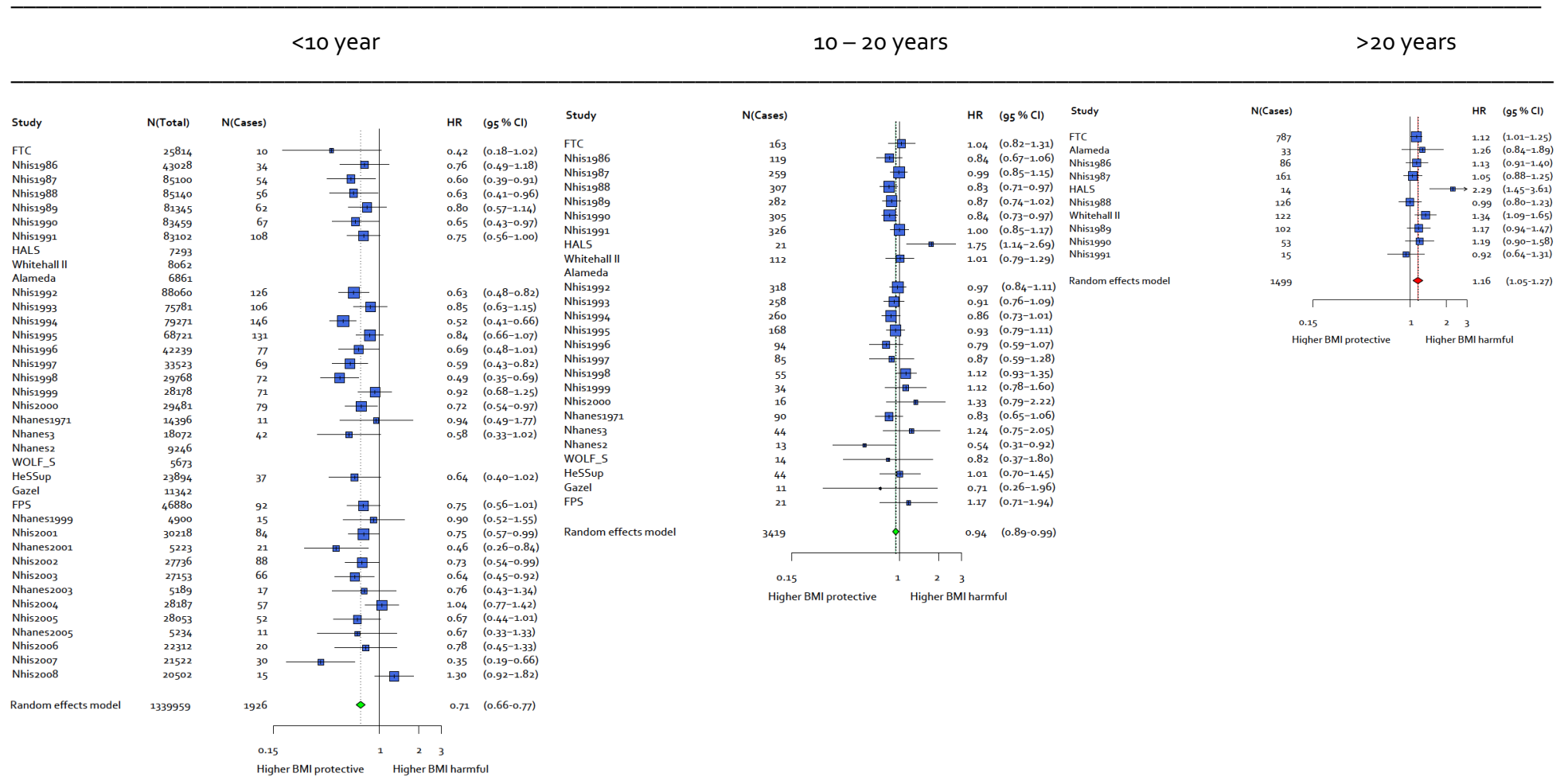


Appendix 4

Forest plots for meta-analyses of dementia risk per 5-unit increment in BMI stratified by the duration of follow-up

eFigure 7. Age-, sex- and ethnicity-adjusted hazard ratios for dementia risk per 5-unit increment in BMI stratified by the duration of follow-up

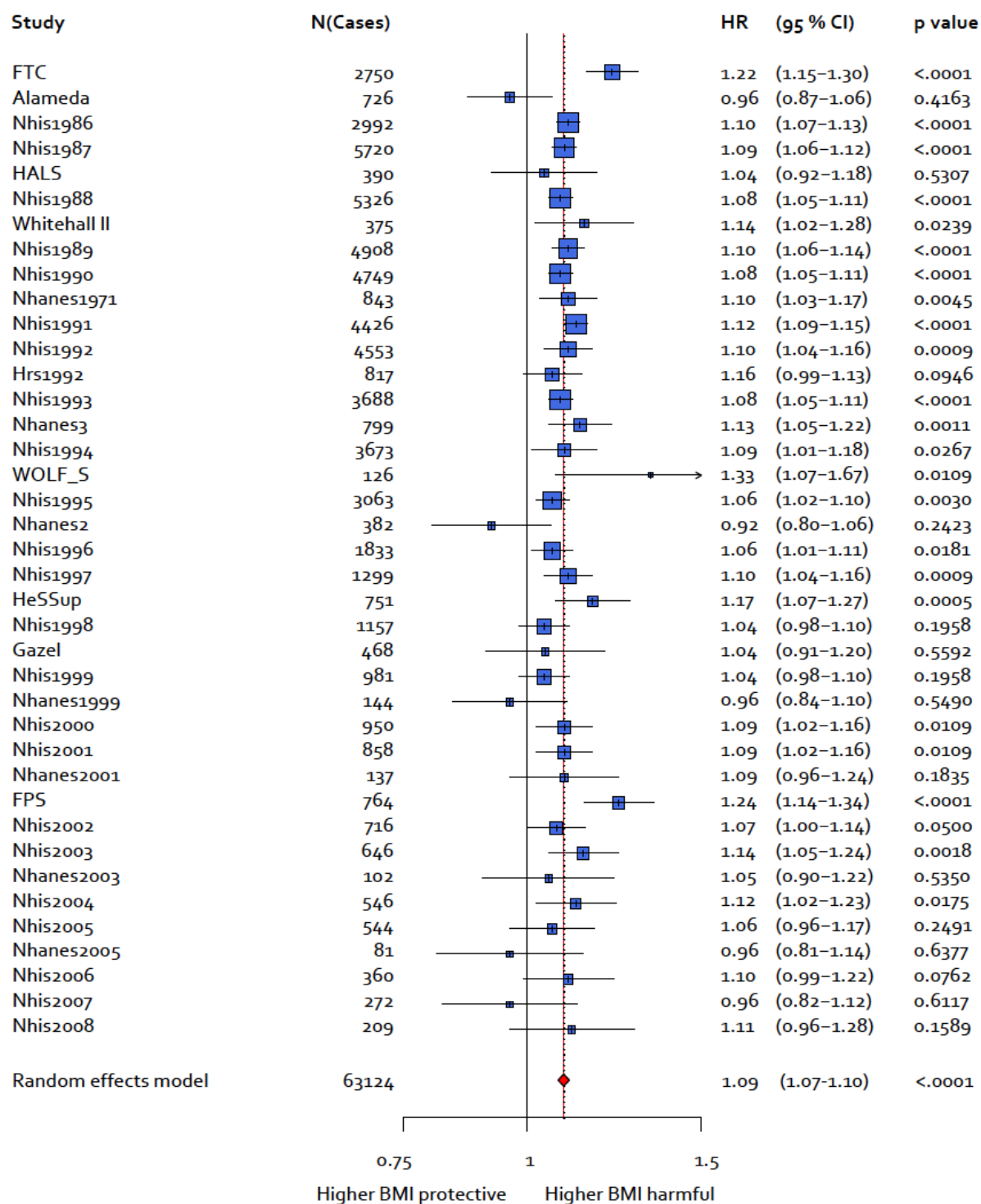
Follow-up period



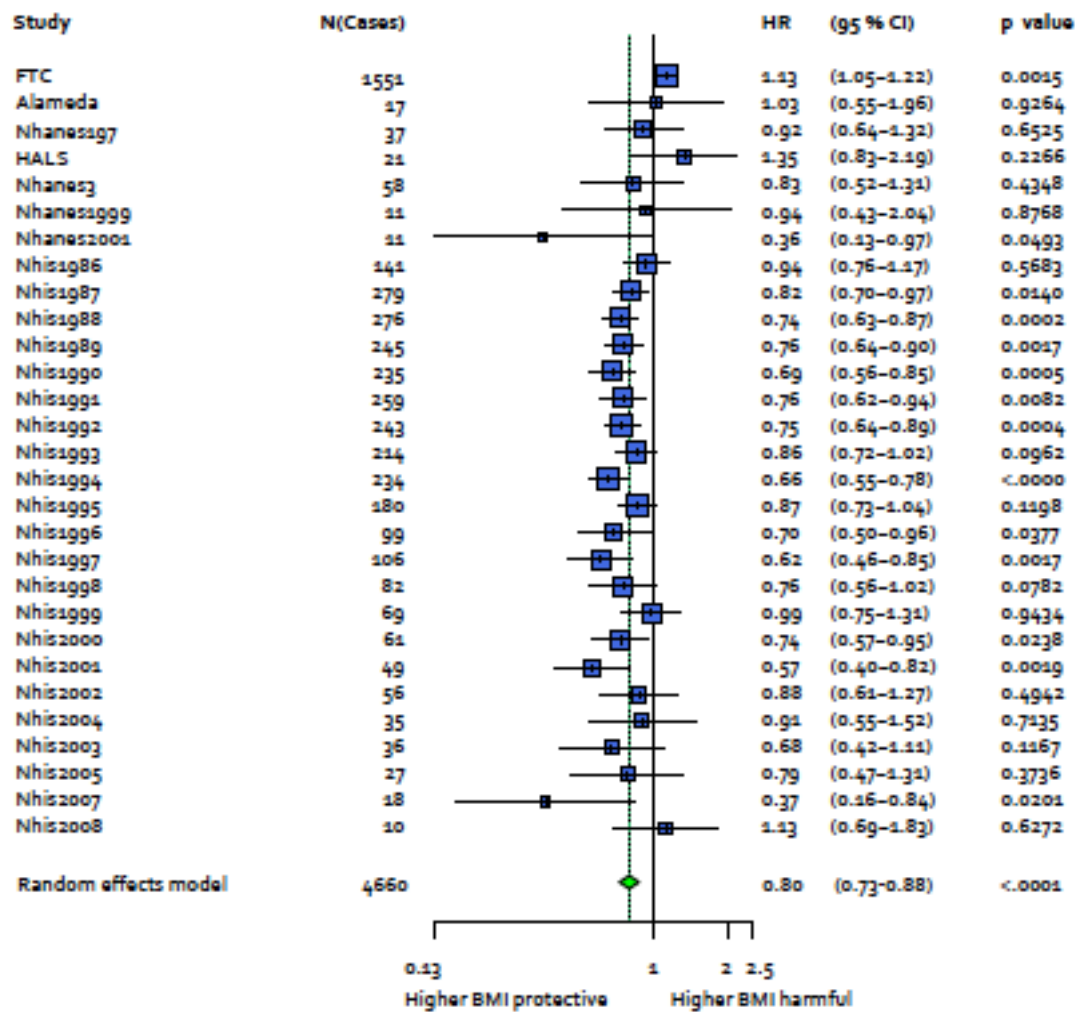
Appendix 5

Forest plots for meta-analyses of mortality risk before age 65 and after age 85 per 5-unit increment in BMI

eFigure 8. Age-, sex- and ethnicity-adjusted hazard ratio for the association between BMI (per 5-unit increment) and mortality before age 65



eFigure 9. Age-, sex- and ethnicity-adjusted hazard ratio for the association between BMI (per 5-unit increment) and mortality after age 85



Appendix 6

Study-specific estimates for the association between BMI and dementia after excluding dementia cases ascertained from death registries.

eTable 2. Study-specific estimates for the association of BMI per 5-unit increase with dementia after excluding dementia cases ascertained from death registries in analyses with serial exclusions to the follow-up

Study	N (cases)	N (total)	Hazard ratio (95% CI)	P-value
No exclusions				
Whitehall II	224	8064	1.15 (0.98 – 1.36)	0.0907
WOLF S	10	5673	0.55 (0.20 – 1.51)	0.2457
HeSSup	79	23,894	0.83 (0.62 – 1.11)	0.2110
GAZEL	12	11,342	1.00 (0.41 – 2.43)	0.9997
FPS	112	46,878	0.81 (0.63 – 1.05)	0.1108
Total	437	95,851	0.92 (0.74 – 1.15)	0.475
$I^2=51.7\%$, $P=0.0816$				
5 years excluded				
Whitehall II	223	7981	1.15 (0.98 – 1.36)	0.0894
WOLF S	9	5591	0.62 (0.22 – 1.75)	0.3664
HeSSup	67	23,682	0.96 (0.72 – 1.30)	0.8113
GAZEL	12	11,230	1.00 (0.41 – 2.43)	0.9997
FPS	88	46,570	0.82 (0.62 – 1.09)	0.1714
Total	399	95,054	0.99 (0.84 – 1.18)	0.947
$I^2=25.8\%$, $P=0.2493$				
10 years excluded				
Whitehall II	220	7831	1.15 (0.98 – 1.36)	0.0929
WOLF S	8	5485	0.55 (0.18 – 1.69)	0.2983
HeSSup	44	23,393	1.01 (0.70 – 1.45)	0.9597
GAZEL	10	11,042	0.93 (0.34 – 2.55)	0.8863
FPS	21	38,898	1.17 (0.71 – 1.94)	0.5316
Total	303	86,649	1.11 (0.97 – 1.28)	0.139
$I^2=0.0\%$, $P=0.7110$				
15 year excluded				
Whitehall II	205	7603	1.17 (0.98 – 1.39)	0.0776
WOLF S	3	4286	1.12 (0.22 – 5.59)	0.8917
Total	208	11,889	1.17 (0.98 – 1.39)	0.077
$I^2=0.0\%$, $P=0.9581$				
20 years excluded				
Whitehall II	118	7194	1.33 (1.08 – 1.65)	0.0081

eTable 3. Study-specific estimates for the association of BMI per 5-unit increase with dementia after excluding dementia cases ascertained from death registries in analyses stratified by follow-up period

Study and follow-up	N (cases)	N (total)	Hazard ratio (95% CI)	P-value
<10 years				
Whitehall II	4	8064	1.14 (0.31 – 4.21)	0.8465
WOLF S	2	5673	0.55 (0.05 – 5.83)	0.6199
HeSSup	35	23,894	0.61 (0.37 – 1.00)	0.0497
GAZEL	2	11,342	1.30 (0.22 – 7.64)	0.7695
FPS	91	46,878	0.73 (0.55 – 0.98)	0.0384
Total	134	95,851	0.72 (0.56 – 0.92)	0.008
I ² = 0.0%, P=0.8429				
10 – 20 years				
Whitehall II	102	7831	0.95 (0.73 – 1.24)	0.6996
WOLF S	8	5485	0.55 (0.18 – 1.69)	0.2983
HeSSup	44	23,393	1.01 (0.70 – 1.45)	0.9597
GAZEL	10	11,042	0.93 (0.34 – 2.55)	0.8863
FPS	21	38,898	1.17 (0.71 – 1.94)	0.5316
Total	185	86,649	0.98 (0.81 – 1.19)	0.828
I ² =0.0%, P=0.8092				
>20 years				
Whitehall II	118	7194	1.33 (1.08 – 1.65)	0.0081