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Research Report 214

Long-Term Exposure to AIR Pollution and COVID-19 Mortality and Morbidity in DENmark: Who Is Most Susceptible? (AIRCODEN)

Zorana J. Andersen et al.

Appendix A: Supplementary Tables and Figures

This Appendix was reviewed solely for spelling, grammar, and cross-references to the main text. It has not been formatted or fully edited by HEI. This document was reviewed by the HEI Review Committee.

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Appendix A. Supplementary Tables and Figures

TABLES

FIGURES

Table A1: Documentation of Danish COVID-19 data, a variable overview from June 2020 (translated from Danish from the original document 'Dokumentation af COVID-19 data' and available at *https://miba.ssi.dk/-/media/arkiv/subsites/miba-og-haiba/dokument/dokumentation-af-covid-19-data.pdf?la=da*)

Variable	Description	Definition	Source of Data
Case Definition	COVID-19 test result	1 = positive; 0 = negative; 9 = awaiting answer (first positive test will overrule earlier and later test results, both positive and negative)	EpiMiBa
Sample Date	Test date	If Case Definition = 1, the date for 1st positive test result; If Case Definition = 0, the date for 1st negative test result; If Case Definition = 9, the date of the test for results are awaited	EpiMiBa
CPR	Individual person number		EpiMiBa
COVID-19 Status	Status on whether patient is infected, recovered from infection, or dead	0 = infected; 1 = recovered from infection; 2 = dead	SampleDate (Prdate/MiBa) + LastDsc (EPiLPR/ RegionData)
COVID-19 End Date	The expected date for recovery from infection; day of death for dead patients		SampleDate (Prdate/MiBa) + LastDsc (EPiLPR/ RegionData)
COVID-19 Rule	Information for which rule for recovery from infection was used in the algorithm	Rule = 1 no admission — recovery from infection 14 days after positive test; Rule = 2 short admission — recovery from infection 14 days after positive test; Rule = 3 admission longer than 14 days, after positive test but shorter than 30 days; Rule = 4 admission longer than 30 days and recovered from infection within 30 days; Rule = 5 when a person is admitted within 14 days from the test date and is still in the intensive care unit on day 30, the date for recovery from the infection is the date for discharge from an intensive care unit	
CPR Date of Death	Date of death		
Sex	Patients gender		
Test Age	Age test date		
Region	Region residence		
KMA	Clinical microbiological department for the first test		EpiMiBa

Pregnancy	Information about patients pregnancy at the time of test date	1 = pregnant; 0 = not pregnant	DNPR/Danish Register
EpiLPRFistAdm	Information on admission with COVID-19 infection	1 = first admission date for more than 12 hours within 14 days after a positive test; 0 = no admission for more than 12 hours within 14 days after a positive test	LPR
EpiLprICU in	The date for the admission in the ICU	Based on SOR codes and procedure codes NABB, NABE, BGDA0, BGDA1, BJFD0, BGXA2, BFHC92, BFHC93, and BFH95	LPR
Travel	Patients travel history	Y = travel history outside Denmark; N = no travel history	MIS/MiBa
Country of Travel	Country of travel	Country of travel if Travel = Y	MIS/MiBa

LPR = The Danish National Hospital Register; MiBa = The Danish microbiology database.

Table A2: The association between long-term exposure to air pollution and COVID-19 related morbidity and mortality below various cut-off values

Pollutants	Cut-Off levels	Number of Participants	COVID-19 Incidence		COVID-19 Hospitalization		COVID-19 Mortality		All-Cause Mortality	
			Number of Events	HR (95% CI)	Number of Events	HR (95% CI)	Number of Events	HR (95% CI)	Number of Events	HR (95% CI)
$PM_{2.5}$	All levels	3,721,813	138,742	1.10 (1.05, 1.14)	11,270	1.09 (1.01, 1.17)	2,557	1.23 (1.04, 1.44)	62,359	1.02 (1.01, 1.03)
	< 8 μg/m^3	3,521,340	132,801	1.13 (1.09, 1.18)	10,839	1.14 (1.05, 1.23)	2,490	1.32 (1.10, 1.57)	58,905	1.02 (1.01, 1.04)
	< 7.5 μg/m^3	1,641,307	51,678	1.13 (1.07, 1.20)	4,172	1.25 (1.11, 1.40)	950	1.51 (1.09, 2.11)	27,526	1.03 (1.01, 1.05)
	< 7 μg/m^3	677,418	16,409	1.04 (0.95, 1.13)	1,263	1.19 (1.00, 1.43)	296	1.74 (1.07, 2.83)	11,640	1.04 (1.00, 1.08)
NO_2	All levels	3,721,813	138,742	1.18 (1.14, 1.23)	11,270	1.19 (1.12, 1.27)	2,557	1.18 (1.03, 1.34)	62,359	1.04 (1.01, 1.07)
	< 15 μg/m^3	3,597,855	132,137	1.26 (1.21, 1.31)	10,787	1.28 (1.19, 1.38)	2,452	1.29 (1.10, 1.51)	60,643	1.05 (1.02, 1.09)
	< 13 μg/m^3	2,961,558	96,508	1.33 (1.25, 1.41)	7,963	1.34 (1.20, 1.50)	1,760	1.39 (1.12, 1.73)	51,404	1.05 (1.01, 1.08)
	< 10 μg/m^3	1,607,400	41,419	1.10 (1.00, 1.21)	3,366	1.09 (0.89, 1.33)	740	1.05 (0.68, 1.61)	28,032	1.03 (0.97, 1.09)
	< 8 μg/m^3	432,196	9,946	0.98 (0.76, 1.25)	813	1.24 (0.68, 2.28)	186	2.37 (0.68, 8.28)	7,772	1.02 (0.90, 1.17)
BC	All levels	3,721,813	138,742	1.05 (1.01, 1.08)	11,270	1.05 (1.01, 1.08)	2,557	1.06 (1.02, 1.10)	62,359	1.01 (1.00, 1.02)
	< 0.5 μg/m^3	3,685,856	137,343	1.20 (1.16, 1.25)	11,159	1.20 (1.12, 1.29)	2,541	1.25 (1.08, 1.45)	61,834	1.02 (0.99, 1.06)
	< 0.4 μg/m^3	3,196,323	111,021	1.25 (1.18, 1.31)	9,250	1.29 (1.18, 1.42)	2,123	1.38 (1.13, 1.67)	55,368	1.05 (1.01, 1.09)
	< 0.3 μg/m^3	1,355,757	34,675	1.14 (1.02, 1.28)	2,964	1.36 (1.05, 1.77)	643	1.93 (1.00, 3.70)	24,515	1.05 (0.98, 1.12)
O_3	All levels	3,721,813	138,742	0.86 (0.84, 0.89)	11,270	0.86 (0.82, 0.91)	2,557	0.87 (0.78, 0.96)	62,359	1.00 (0.98, 1.02)
	< 60 μg/m3	3,670,474	137,676	0.86 (0.84, 0.89)	11,183	0.87 (0.82, 0.92)	2,542	0.88 (0.79, 0.99)	61,383	1.00 (0.98, 1.02)
	< 56 μg/m3	2,869,443	115,939	0.88 (0.84, 0.91)	9,236	0.88 (0.82, 0.95)	2,084	0.96 (0.81, 1.12)	46,452	1.00 (0.97, 1.04)
	< 54 μg/m3	1,701,405	80,244	0.99 (0.95, 1.05)	6,293	0.99 (0.90, 1.09)	1,415	1.10 (0.88, 1.39)	26,648	1.03 (0.98, 1.09)
	< 52 μg/m^3	398,968	19,466	1.04 (0.96, 1.12)	1,471	1.23 (0.96, 1.58)	335	2.42 (1.25, 4.68)	5,698	1.23 (1.10, 1.37)

BC = black carbon; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 =ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively. Results are presented for interquartile range increase: 0.55 μg/m^3 for $PM_{2.5}$, 3.49 μg/m^3 for NO_2, 0.09 μg/m^3 for BC, 2.79 μg/m^3 for O_3, and 1.14 μg/m^3 for PM_{10}. Model adjusted for calendar time (time axis), sex (strata) , age at baseline (strata), and region (strata); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare. (Analysis for all-cause mortality was not stratified by regions.)

Table A3: The association between long-term exposure to air pollution and COVID-19 incidence, hospitalization, and mortality among the 3,721,813 participants of the AIRCODEN cohort: two-pollutant models

Pollutants	Single-Pollutant Model	Two-Pollutant Model (adjusted for pollutants below)				
		$PM_{2.5}$	NO_2	BC	O_3	PM_{10}
COVID-19 mortality (*N* = 2,557)						
$PM_{2.5}$	1.23 (1.04, 1.44)	/	1.16 (0.94, 1.43)	1.21 (1.00, 1.46)	1.14 (0.93, 1.39)	1.14 (0.94, 1.39)
NO_2	1.18 (1.03, 1.34)	1.09 (0.92, 1.29)	/	/	/	1.12 (0.97, 1.29)
BC	1.06 (1.02, 1.10)	1.02 (0.96, 1.07)	/	/	1.03 (0.97, 1.08)	1.03 (0.99, 1.08)
O_3	0.87 (0.78, 0.96)	0.91 (0.80, 1.04)	/	0.88 (0.79, 0.98)	/	0.89 (0.80, 1.00)
PM_{10}	1.19 (1.07, 1.33)	1.13 (0.99, 1.31)	1.15 (1.02, 1.30)	1.17 (1.05, 1.31)	1.16 (1.03, 1.30)	/
COVID-19 hospitalization (*N* = 11,270)						
$PM_{2.5}$	1.09 (1.01, 1.17)	/	0.97 (0.88, 1.06)	1.05 (0.96, 1.14)	0.94 (0.87, 1.03)	1.02 (0.94, 1.11)
NO_2	1.19 (1.12, 1.27)	1.21 (1.12, 1.30)	/	/	/	1.15 (1.08, 1.23)
BC	1.05 (1.01, 1.08)	1.04 (1.00, 1.08)	/	/	1.01 (0.97, 1.06)	1.03 (0.99, 1.07)
O_3	0.86 (0.82, 0.91)	0.84 (0.79, 0.89)	/	0.87 (0.82, 0.92)	/	0.88 (0.84, 0.93)
PM_{10}	1.14 (1.07, 1.20)	1.13 (1.06, 1.20)	1.09 (1.03, 1.16)	1.12 (1.06, 1.19)	1.10 (1.04, 1.17)	/
COVID-19 incidence (*N* = 138,742)						
$PM_{2.5}$	1.10 (1.05, 1.14)	/	0.98 (0.94, 1.03)	1.06 (1.01, 1.11)	0.96 (0.92, 1.01)	1.06 (1.01, 1.11)
NO_2	1.18 (1.14, 1.23)	1.20 (1.14, 1.25)	/	/	/	1.17 (1.12, 1.22)
BC	1.05 (1.01, 1.08)	1.03 (1.00, 1.07)	/	/	1.02 (0.99, 1.04)	1.03 (1.00, 1.07)
O_3	0.86 (0.84, 0.89)	0.85 (0.82, 0.88)	/	0.87 (0.84, 0.90)	/	0.87 (0.85, 0.90)
PM_{10}	1.09 (1.06, 1.12)	1.07 (1.03, 1.10)	1.04 (1.01, 1.07)	1.07 (1.04, 1.10)	1.05 (1.02, 1.09)	/

BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively. Results are presented for interquartile range increase: 0.55 μg/m^3 for $PM_{2.5}$, 3.49 μg/m^3 for NO_2, 0.09 μg/m^3 for BC, 2.79 μg/m^3 for O_3, and 1.14 μg/m^3 for PM_{10}. Model adjusted for calendar time (time axis), sex (strata), age at baseline (strata), and region (strata); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare. (Analysis for all-cause mortality was not stratified by regions.)

Table A4: The association between long-term exposure to air pollution and COVID-19 incidence, hospitalization, and mortality, as well as all-cause mortality among the 3,721,813 participants of the AIRCODEN cohort with additional adjustment for municipality-level monthly COVID-19 positive rates as a proxy for spatial and temporal pandemic development

Pollution	Main Model	Time-Varying Model
COVID-19 related Incidence (N = 138,742)		
$PM_{2.5}$	1.10 (1.05, 1.14)	1.09 (1.05, 1.12)
NO_2	1.18 (1.14, 1.23)	1.15 (1.11, 1.18)
BC	1.05 (1.01, 1.08)	1.04 (1.01, 1.07)
O_3	0.86 (0.84, 0.89)	0.90 (0.88, 0.92)
PM_{10}	1.09 (1.06, 1.12)	1.06 (1.03, 1.09)
COVID-19 related Hospitalization (N = 11,270)		
$PM_{2.5}$	1.09 (1.01, 1.17)	1.09 (1.02, 1.17)
NO_2	1.19 (1.12, 1.27)	1.15 (1.08, 1.22)
BC	1.05 (1.01, 1.08)	1.04 (1.01, 1.08)
O_3	0.86 (0.82, 0.91)	0.89 (0.85, 0.94)
PM_{10}	1.14 (1.07, 1.20)	1.08 (1.03, 1.14)
COVID-19 related Mortality (N = 2,557)		
$PM_{2.5}$	1.23 (1.04, 1.44)	1.22 (1.04, 1.43)
NO_2	1.18 (1.03, 1.34)	1.12 (0.98, 1.28)
BC	1.06 (1.02, 1.10)	1.05 (1.00, 1.09)
O_3	0.87 (0.78, 0.96)	0.92 (0.82, 1.02)
PM_{10}	1.19 (1.07, 1.33)	1.13 (1.01, 1.26)

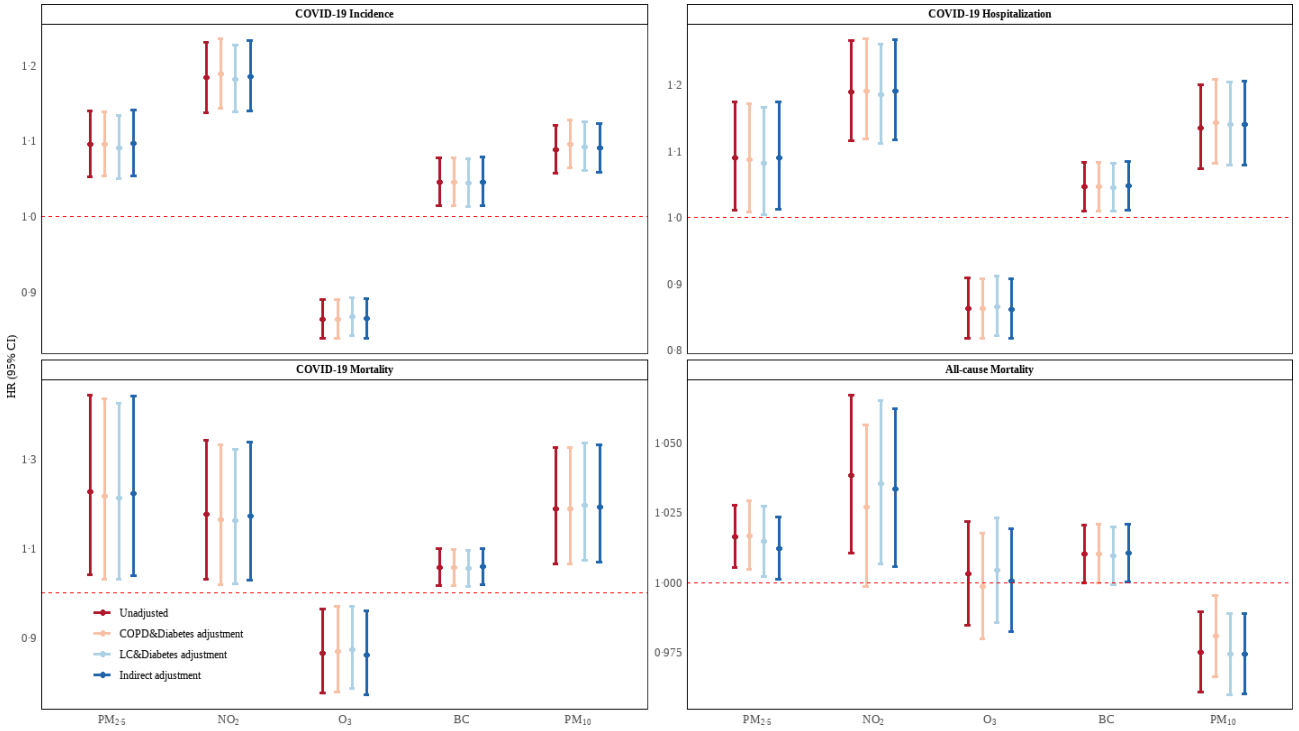
BC = black carbon; NO_2 = nitrogen dioxide; O_3 = ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively. Results are presented for interquartile range increase: 0.55 μg/m^3 for $PM_{2.5}$, 3.49 μg/m^3 for NO_2, 0.09 μg/m^3 for BC, 2.79 μg/m^3 for O_3, and 1.14 μg/m^3 for PM_{10}. Model adjusted for calendar time (time axis), sex (strata) , age at baseline (strata), and region (strata); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare. (Analysis for all-cause mortality was not stratified by regions.) *Time-varying Model further adjusted the time (monthly) and geographic (municipality-level) varying COVID-19 positive rate during the follow-up period in Denmark.

Table A5: Risk ratio (RR) and hazard ratio (HR) in estimating the association between long-term exposure to air pollution and COVID-19 incidence, hospitalization, and mortality among the 3,721,813 participants of the AIRCODEN cohort with Poisson and Cox Regression models, respectively

	Poisson Regression RR (95% CI)	Cox Regression HR (95% CI)
COVID-19 Incidence* (*N* = 138,742)		
$PM_{2.5}$	1.09 (1.08, 1.11)	1.10 (1.05-1.14)
NO_2	1.18 (1.16, 1.19)	1.18 (1.14-1.23)
BC	1.05 (1.04, 1.05)	1.05 (1.01-1.08)
O_3	0.87 (0.86, 0.88)	0.86 (0.84-0.89)
PM_{10}	1.08 (1.07, 1.10)	1.09 (1.06-1.12)
COVID-19 Hospitalization* (*N* = 11,270)		
$PM_{2.5}$	1.09 (1.04, 1.14)	1.09 (1.01-1.17)
NO_2	1.19 (1.14, 1.24)	1.19 (1.12-1.27)
BC	1.05 (1.03, 1.06)	1.05 (1.01-1.08)
O_3	0.86 (0.83, 0.89)	0.86 (0.82-0.91)
PM_{10}	1.13 (1.09, 1.18)	1.14 (1.07-1.20)
COVID-19 Mortality (*N* = 2,557)		
$PM_{2.5}$	1.22 (1.10, 1.36)	1.23 (1.04-1.44)
NO_2	1.17 (1.07, 1.29)	1.18 (1.03-1.34)
BC	1.06 (1.02, 1.10)	1.06 (1.02-1.10)
O_3	0.87 (0.80, 0.93)	0.87 (0.78-0.96)
PM_{10}	1.19 (1.09, 1.29)	1.19 (1.07-1.33)

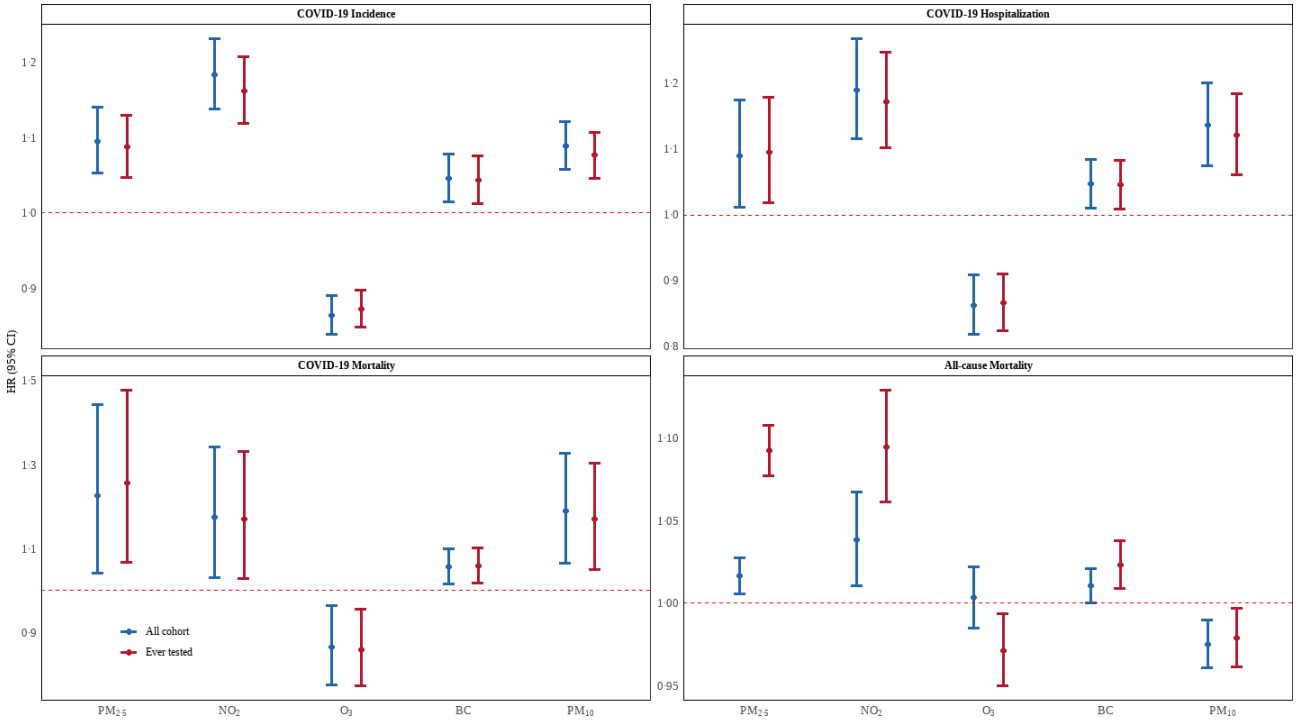
BC = black carbon; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 = ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively; RR = risk ratio. Results are presented for interquartile range increase: 0.55 $\mu g/m^3$ for $PM_{2.5}$, 3.49 $\mu g/m^3$ for NO_2, 0.09 $\mu g/m^3$ for BC, 2.79 $\mu g/m^3$ for O_3, and 1.14 $\mu g/m^3$ for PM_{10}. Model adjusted for sex (strata), age at baseline (strata), region (strata), civil status, household size, individual wealth, family income, education, occupational status, parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the difference of those variables between parish and municipality, and municipality-level access to healthcare. Besides, COX regression considers calendar time as time scale and robust estimate by parish, which are not considered in Poisson regression model.

Figure A1: The association between long-term exposure to air pollution and COVID-19 incidence, hospitalization, and mortality, as well as all-cause mortality among the 3,721,813 participants of the AIRCODEN cohort with additional adjustment for missing information on individual lifestyle.*



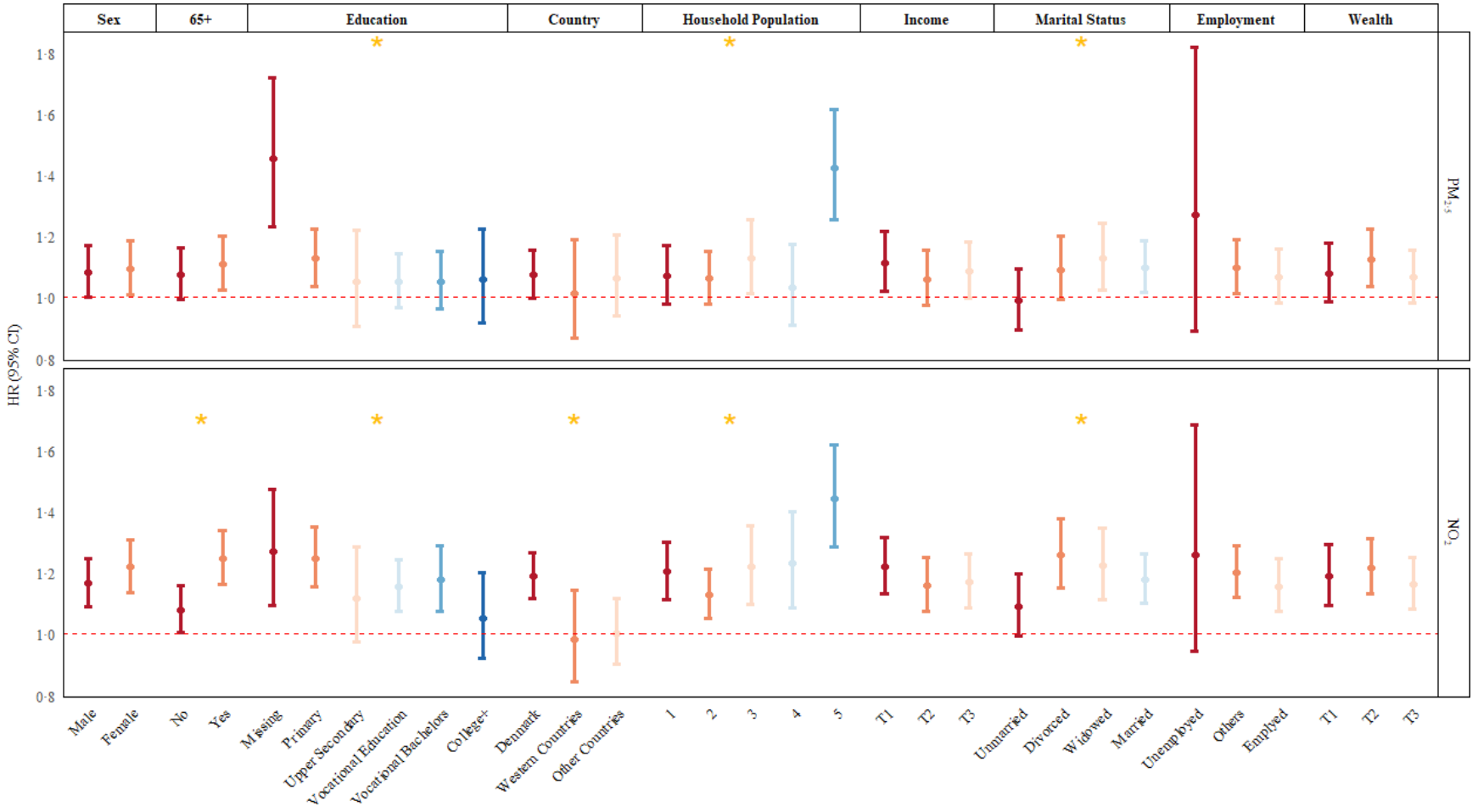
BC = black carbon; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 =ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively. Results are presented for interquartile range increase: 0.55 μg/m^3 for $PM_{2.5}$, 3.49 μg/m^3 for NO_2, 0.09 μg/m^3 for BC, 2.79 μg/m^3 for O_3, and 1.14 μg/m^3 for PM_{10}. Model adjusted for calendar time (time axis), sex (strata), age at baseline (strata), and region (strata); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare. (Analysis for all-cause mortality was not stratified by regions.) *COPD (smoking indicator), lung cancer (smoking indicator), and diabetes (BMI indicator) prevalence rates at parish-level. Indirect adjustment refers to Shin et al. methods for indirect adjustment for missing data on individual-levels of smoking and physical activity.

Figure A2: The association between long-term exposure to air pollution and COVID-19 incidence, hospitalization, and mortality, as well as all-cause mortality among the subset of 2,902,932 participants of the AIRCODEN cohort who were tested for COVID-19 (excluding 818,881 (22%) participants who were never tested for COVID-19 in the study period from March 1, 2020 until April 26, 2021).



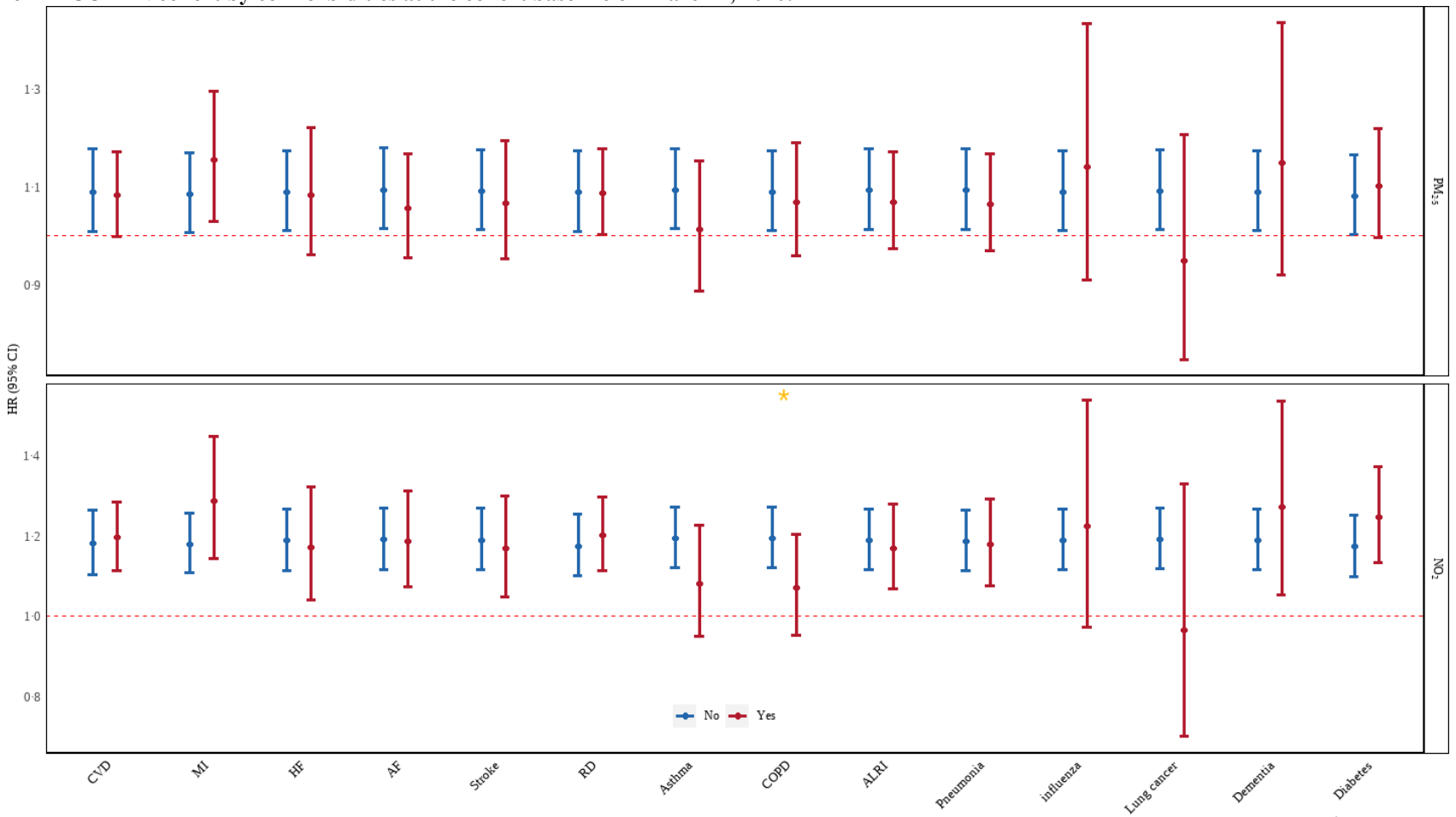
BC = black carbon; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; O_3 =ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 μm, respectively. Results are presented for interquartile range increase: 0.55 μg/m^3 for $PM_{2.5}$, 3.49 μg/m^3 for NO_2, 0.09 μg/m^3 for BC, 2.79 μg/m^3 for O_3, and 1.14 μg/m^3 for PM_{10}. Model adjusted for calendar time (time axis), sex (strata), age at baseline (strata), and region (strata); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare. (Analysis for all-cause mortality was not stratified by regions.)

Figure A3: Effect modification* of the association between long-term exposure to air pollution and COVID-19 hospitalization among the 3,721,810 participants of the AIRCODEN cohort by sex, age, and individual-level SES characteristic at the cohort baseline on March 1, 2020.



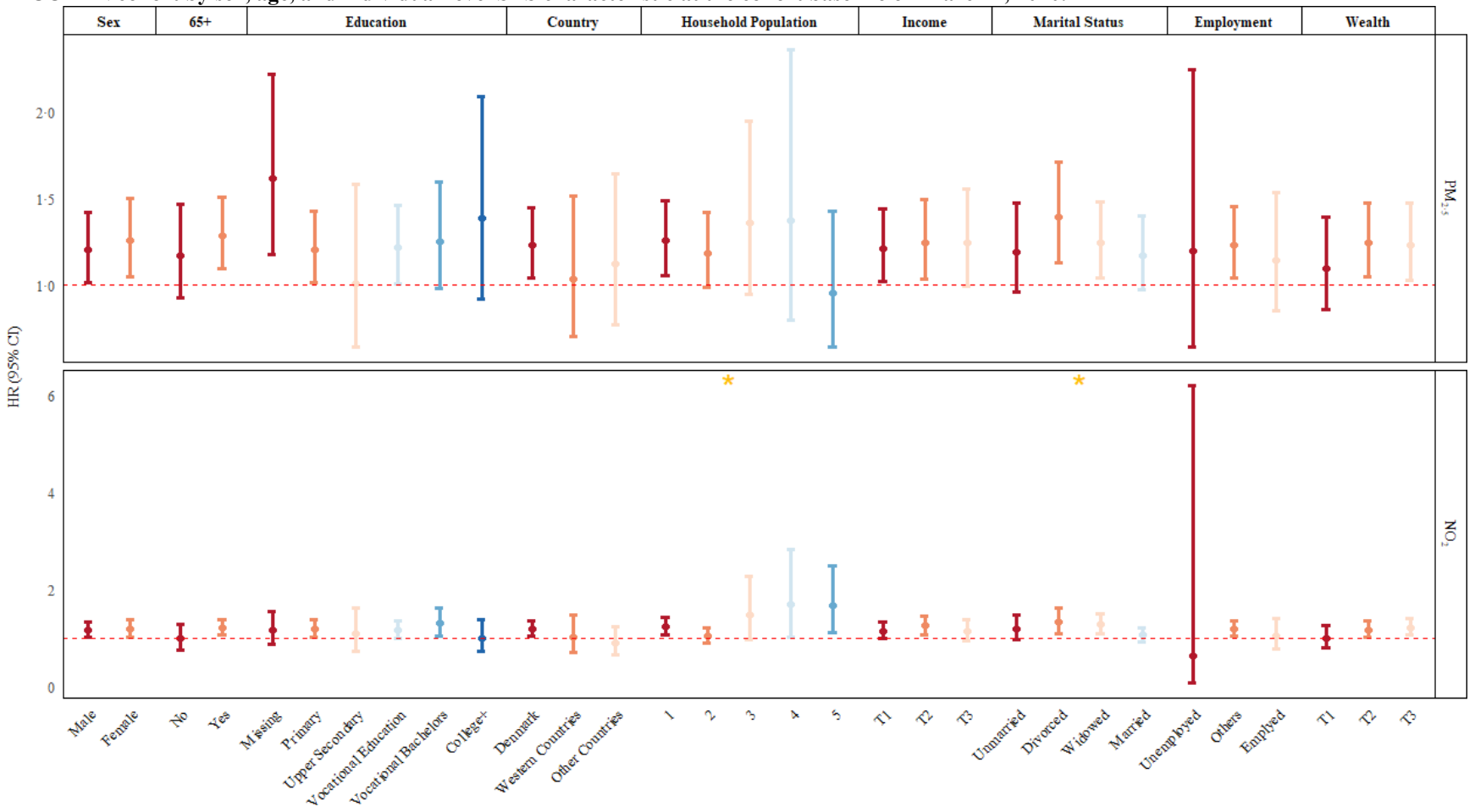
CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter with diameter ≤ 2.5 µm. Results are presented for interquartile range increase: 0.55 µg/m^3 for $PM_{2.5}$ and 3.49 µg/m^3 for NO_2. *Wald test was used to calculate the global *P*-value, and results with *P*-value <0.05 are highlighted with a star.

Figure A4: Effect modification* of the association between long-term exposure to air pollution and COVID-19 hospitalization among the 3,721,810 participants of the AIRCODEN cohort by co-morbidities at the cohort baseline on March 1, 2020.



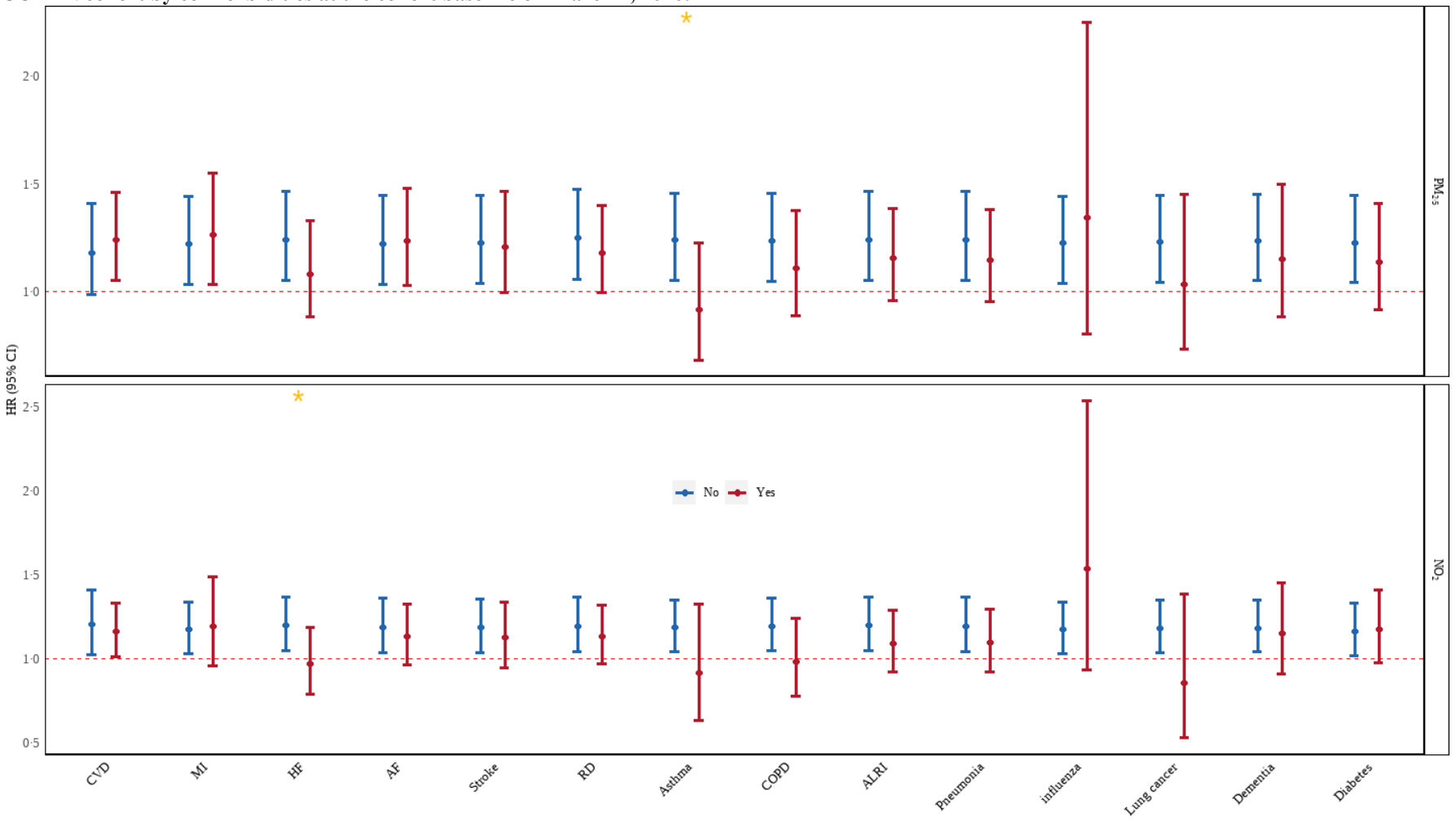
CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter with diameter ≤ 2.5 µm. Results are presented for interquartile range increase: 0.55 µg/m^3 for $PM_{2.5}$ and 3.49 µg/m^3 for NO_2. *Wald test was used to calculate the global *P*-value, and results with *P*-value <0.05 are highlighted with a star.

Figure A5: Effect modification* of the association between long-term exposure to air pollution and COVID-19 mortality among the 3,721,810 participants of the AIRCODEN cohort by sex, age, and individual-level SES characteristic at the cohort baseline on March 1, 2020.



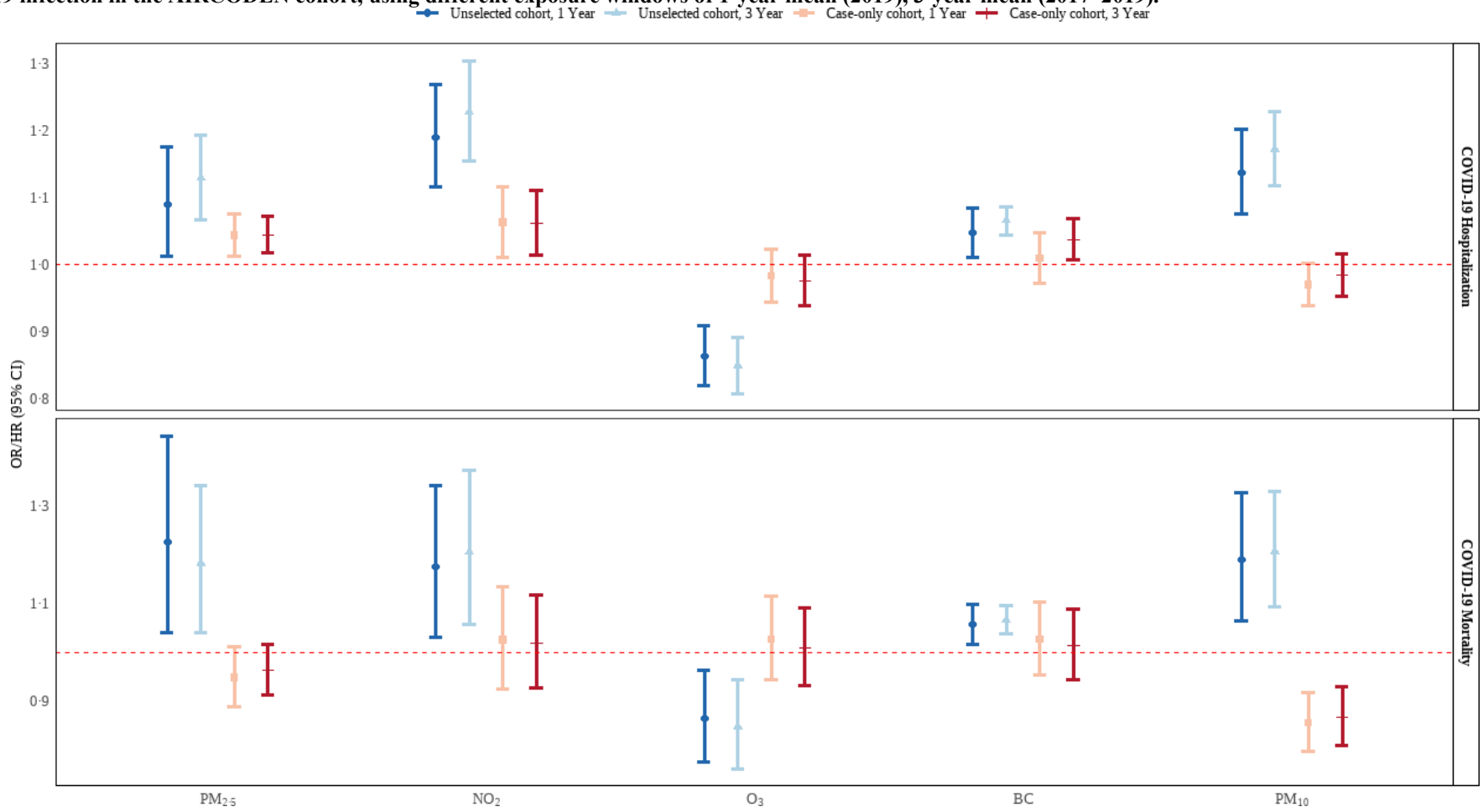
CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter with diameter ≤ 2.5 µm. Results are presented for interquartile range increase: 0.55 µg/m^3 for $PM_{2.5}$ and 3.49 µg/m^3 for NO_2. *Wald test was used to calculate the global *P*-value, and results with *P*-value <0.05 are highlighted with a star.

Figure A6: Effect modification* of the association between long-term exposure to air pollution and COVID-19 mortality among the 3,721,810 participants of the AIRCODEN cohort by co-morbidities at the cohort baseline on March 1, 2020.



CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter with diameter ≤ 2.5 µm. Results are presented for interquartile range increase: 0.55 µg/m^3 for $PM_{2.5}$ and 3.49 µg/m^3 for NO_2. *Wald test was used to calculate the global *P*-value, and results with *P*-value <0.05 are highlighted with a star.

Figure A7: The association between long-term exposure to air pollution and COVID-19 hospitalization, and mortality among the 138,742 participants with COVID-19 infection in the AIRCODEN cohort, using different exposure windows of 1-year mean (2019), 3-year mean (2017–2019).



BC = black carbon; CI = confidence interval; HR = hazard ratio; NO_2 = nitrogen dioxide; OR = odds ratio; O_3 =ozone; PM_{10} and $PM_{2.5}$ = particulate matter with diameter ≤ 10 and 2.5 µm, respectively. Results are presented for interquartile range increase: 0.55 µg/m^3 for $PM_{2.5}$, 3.49 µg/m^3 for NO_2, 0.09 µg/m^3 for BC, 2.79 µg/m^3 for O_3, and 1.14 µg/m^3 for PM_{10}. Model adjusted for calendar time, sex, age at baseline, and region (for unselected cohort); individual covariates (civil status, household size, individual wealth, family income, education, and occupational status); and area-level covariates (parish-level population density, mean income, median wealth, unemployment rate, primary or low education rate, the differences of socioeconomic variables between parish and municipality, and municipality-level access to healthcare.

Figure A8: COVID-19 Vaccination rollout in Denmark from 1st December 2020 until 25th January 2022 (Source: https://ourworldindata.org/covid-vaccinations?country=DNK).