

## Online Appendix - Diabetes as a Determinant of Mortality in Cystic Fibrosis

**Online Appendix Table 1 Characteristics at baseline of 4,234 individuals with CF by mortality status and hazard ratio (HR) with 95% confidence interval for each risk factor**

<i>Characteristic</i>	<i>Total (n=4,234)</i>	<i>Alive (n=3,909)</i>	<i>Died (n=325)</i>	<i>p-value*</i>	<i>HR (95%CI)<sup>†</sup></i>
Age (years), median (IQR)	16.0 (10.0 – 23.3)	15.1 (9.6 – 22.7)	21.9 (17.8 – 28.1)	<0.001	1.06 (1.05 – 1.06)
Females, No (%)	1,953 (46.1)	1,784 (45.6)	169 (52.0)	0.027	1.24 (0.99 – 1.54)
White ethnicity, No (%)	4,105 (97.0)	3,785 (96.8)	320 (98.5)	0.100	1.35 (0.56 – 3.28)
BMI, kg/m <sup>2</sup> (SD)	19.3 (3.5)	19.3 (3.5)	18.8 (2.9)	0.010	0.97 (0.94 – 1.01)
BMI z-score (SD)	-0.28 (1.20)	-0.19 (1.13)	-1.44 (1.41)	<0.001	0.52 (0.49 – 0.56)
FEV <sub>1</sub> % predicted (SD)	68.7 (28.7)	71.5 (27.5)	34.5 (19.7)	<0.001	1.07 (1.06 – 1.07)
FVC % predicted (SD)	76.1 (31.3)	78.6 (30.7)	46.5 (22.2)	<0.001	1.007 (1.006-1.007)
Diabetes, No (%)	592 (14.0)	472 (12.1)	120 (36.9)	<0.001	4.04 (3.22 – 5.06)
Pancreatic insufficiency, No (%)	3,897 (92.0)	3,583 (91.7)	314 (96.6)	0.002	1.97 (1.08 – 3.59)
CFTR functional class, No (%)					
Class I	342 (8.1)	319 (8.2)	23 (7.1)	0.115	1.00
Class II	3,439 (81.2)	3,162 (80.9)	277 (85.2)		1.19 (0.78 – 1.82)
Class III	294 (6.9)	273 (7.0)	21 (6.5)		0.90 (0.50 – 1.62)
Class IV	139 (3.3)	135 (3.5)	4 (1.2)		0.41 (0.14 – 1.19)
Class V	20 (0.5)	20 (0.5)	0 (0)		4.69e <sup>-18</sup> (0 - .)
High risk CFTR genotype, No (%)	4,075 (96.2)	3,754 (96.0)	321 (98.8)	0.013	3.18 (1.19 – 8.54)
<i>Pseudomonas aeruginosa</i> , No (%)	2,621 (61.9)	2,343 (59.9)	278 (85.5)	<0.001	3.52 (2.59 – 4.80)
<i>Burkholderia cepacia complex</i> , No (%)	213 (5.0)	153 (3.9)	60 (18.5)	<0.001	3.94 (2.97 – 5.21)
<i>Hemophilus influenzae</i> , No (%)	796 (18.8)	749 (19.2)	47 (14.5)	0.037	0.59 (0.44 – 0.81)
<i>Aspergillus fumigatus</i> , No (%)	456 (10.8)	408 (10.4)	48 (14.8)	0.015	1.61 (1.18 – 2.19)
<i>Staphylococcus aureus</i> , No (%)	1,763 (41.6)	1,636 (41.9)	127 (39.1)	0.329	0.79 (0.63 – 0.99)
MRSA, No (%)	68 (1.6)	63 (1.6)	5 (1.5)	0.920	1.11 (0.46 – 2.69)
ABPA, No (%)	262 (6.2)	228 (5.8)	34 (10.5)	0.001	1.97 (1.38 – 2.81)
Liver disease, No (%)	1,000 (23.6)	891 (22.8)	109 (33.5)	<0.001	1.79 (1.42 – 2.26)
Nutritional supplementation, No (%)	1,952 (46.1)	1,715 (43.9)	237 (72.9)	<0.001	2.96 (2.32 – 3.78)
Use of corticosteroid, No (%)	2,372 (56.0)	2,127 (54.4)	245 (75.4)	<0.001	2.56 (1.99 – 3.30)
Organ transplantation, No (%)	114 (2.7)	90 (2.3)	24 (7.4)	<0.001	4.43 (2.79 – 6.42)
CF detected by screening, No (%)	436 (10.3)	420 (10.7)	16 (4.9)	0.001	0.42 (0.22 – 0.80)

\* *p* values represent difference between individuals who died and those who were alive using t-tests or Kruskal-Wallis tests for normally or non-normally distributed continuous variables and  $\chi^2$  tests for categorical variables.

<sup>†</sup> comparisons are for each year older, for 1 unit increase in BMI or BMI z-score, for 1% increase in %predicted FEV<sub>1</sub> and FVC, high vs. low risk CFTR, CFTR class II,III,IV&V vs. class I, and Yes vs. No for other binary variables.

**Online Appendix Table 2. Population attributable fraction (PAF) of risk factors for CF mortality (n = 4,234)**

<b>Factor</b>	<b>reference</b>	<b>HR*</b>	<b>95% CI</b>		<b>prevalence<sup>†</sup></b>	<b>PAF</b>	<b>95%CI</b>	
Diabetes	no diabetes	1.62	1.27	2.06	0.37	0.14	0.08	0.19
%FEV <sub>1</sub> predicted	>= 70%	6.14	3.86	9.77	0.94	0.78	0.69	0.84
BMI z-score	> -0.23	1.92	1.43	2.58	0.81	0.39	0.24	0.50
<i>B. cepaciae</i>	No	2.50	1.88	3.32	0.18	0.11	0.09	0.13
<i>S. aureus</i>	Yes	1.34	1.06	1.68	0.39	0.10	0.02	0.16
Liver disease	No	1.27	1.00	1.62	0.34	0.07	0.00	0.13
Corticosteroid use	No	1.73	1.33	2.24	0.75	0.32	0.19	0.42
Nutritional supplementation	No	1.85	1.43	2.40	0.73	0.34	0.22	0.42
Organ Transplantation	No	2.41	1.57	3.70	0.07	0.04	0.03	0.05

\* Hazard ratio (HR) adjusted for median age, sex and all risk factors in the table

† prevalence of a risk factor in subjects who died.