

Supplementary Table 1. *CFTR* mutation allele frequency <1% stratified by ancestry, SACFR December 2018

<i>CFTR</i> mutation allele frequencies <1%	Caucasian N= 630 n	Mixed N= 174 n	Black African N=82 n	Indian N= 8 n	Total N= 894 n (%)
W1282X1 c.3846G>A / p.Trp1282Arg	4	2	0	0	6 (0.7)
1078delT c.948delT /p.Phe316LeufsX12	4	0	0	0	4 (0.4)
R1162X c.3484C>T / p.Arg1162X	0	4	0	0	4 (0.4)
621+1G>T c.489+1G>T	2	1	0	0	3 (0.3)
Leu218X	-	1	-	2	3 (0.3)
R347H c.1040G>A / p.Arg347His	3	0	0	0	3 (0.3)
S549N c.1646G>A / p.Ser549Asn	3	0	0	0	3 (0.3)
Y563N; c.1687T>A / p.Tyr563Asn	3	-	-	-	3 (0.3)
2789+5G>A c.2657+5G>A	2	0	0	0	2 (0.2)
3849+10kbC>T1 c.3717+12191C>T	0	1	0	1	2 (0.2)
c.2738A>G / p.Tyr913Cys	2	-	-	-	2 (0.2)
CFTRdele2; c.(53+1_54-1)_(164+1_165-1)del	1	0	1	0	2 (0.2)
E60X c.178G>T / p.Glu60X	2	0	0	0	2 (0.2)
p.Tyr577X	-	2	-	-	2 (0.2)
R709X; c.2125C>T/ p.Arg709X	0	0	2	0	2 (0.2)
W846X c.2537G>A / p.Trp846X	0	2	0	0	2 (0.2)
1154insTC; c.1021_1022dupTC / p.Phe342HisfsX28	1	0	0	0	1 (0.1)
1677delTA c.1545_1546delTA /p.Tyr515X	1	0	0	0	1 (0.1)
1898+1G>A c.1766+1G>A	1	0	0	0	1 (0.1)
2183AA>G c.2051_2052delAAinsG /p.Lys684SerfsX38	1	0	0	0	1 (0.1)
394delTT; c.262_263delTT / p.Leu88IlefsX22	1	0	0	0	1 (0.1)
405+1G->A; c.273+1G>A	1	-	-	-	1 (0.1)
711+1G>T c.579+1G>T	0	1	0	0	1 (0.1)
c.1520_1522delTCT/p.Phe508del	1	-	-	-	1 (0.1)
c.1680-886A>G	1	-	-	-	1 (0.1)
c.1802T>C; p.Ile601Thr	-	-	-	1	1 (0.1)
c.2788G>T	-	1	-	-	1 (0.1)
c.3454G>C p.Asp1152His	1	-	-	-	1 (0.1)
c.473G>A / p.Ser158Asn	-	1	-	-	1 (0.1)
E585X; c.1753G>T / p.Glu585X	1	-	-	-	1 (0.1)
G576A; c.1727G>C / p.Gly576Ala	1	-	-	-	1 (0.1)
Gly1173GlnfsX21	-	2	-	-	1 (0.1)
I502T; c.1505T>C / p.Ile502Thr	0	0	0	1	1 (0.1)
I507del; c.1519_1521delATC /p.Ile507del	1	0	0	0	1 (0.1)
L206W; c.617T>G / p.Leu206Trp	1	-	-	-	1 (0.1)
large deletion exon 16-20	1	-	-	-	1 (0.1)
p.Gly458Val	-	-	1	-	1 (0.1)
Q493X, p.Gln493X, c.1477C>T	1	-	-	-	1 (0.1)
R117H c.350G>A / p.Arg117His	1	0	0	0	1 (0.1)
R31L; c.92G>T / p.Arg31Leu	1	-	-	-	1 (0.1)
R352Q; c.1055G>A / p.Arg352Gln	1	-	-	-	1 (0.1)
R7758X	-	1	-	-	1 (0.1)
R792X; c.2374C>T/ p.Arg792X	-	-	1	-	1 (0.1)
S1251N c.3752G>A / p.Ser1251Asn	0	1	0	0	1 (0.1)
S1255P; c.3763T>C / p.Ser1255Pro	-	-	1	-	1 (0.1)
S466X; c.1397C>A / p.Ser466X	-	-	1	-	1 (0.1)

S945L; c.2834C>T / p.Ser945Leu	-	-	1	-	1 (0.1)
Ser158IlefsX2	-	1	-	-	1 (0.1)
Ser877PhefsX29	-	1	-	-	1 (0.1)
V456A; c.1367T>C / p.Val456Ala	1	-	-	-	1 (0.1)
W679; c.2037G>A / p.Trp679X	1	-	-	-	1 (0.1)
Total	46 (7.3)	22 (12.6)	8 (9.8)	5 (62.5)	81 (9.1)

Supplementary Table 3: Univariable model results - factors for severe lung disease in children  $\geq 6$  years and adults in the SA CF registry, 2018

Factor	Level	n	Odds Ratio (95% CI)	Unadjusted p-value	Adjusted p-value
Sex	Male (Ref: Female)	292	1.33 (0.82,2.18)	0.249	1
Current age (units: 10-years)	Present (Ref: No)	292	1.99 (1.55,2.54)	<0.001	<0.001
Age diagnosis (units: 10-years)	Present (Ref: No)	285	1.26 (0.90,1.76)	0.18	1
p.Phe508del	Homozygous (Ref: Neither)	292	0.77 (0.37,1.57)	0.069	1
	Heterozygous (Ref: Neither)	292	1.45 (0.70,3.01)		
3120+1G>A; c.2988+1G>A homozygous/heterozygous	Present (Ref: No)	292	0.88 (0.40,1.92)	0.737	1
Caucasian	Present (Ref: other ancestry)	292	1.50 (0.83,2.72)	0.171	1
Pancreatic insufficient	Present (Ref: No)	290	1.54 (0.69,3.41)	0.279	1
Neonatal bowel obstruction	Present (Ref: No)	275	0.58 (0.28,1.19)	0.126	1
Household cigarette smoke	Present (Ref: No)	292	0.62 (0.30,1.28)	0.181	1
Informal housing with no water or electricity	Present (Ref: No)	292	2.05 (0.13,33.17)	0.616	1
Receiving social welfare grant	Present (Ref: No)	292	1.38 (0.72,2.65)	0.331	1
Private health insurance	Present (Ref: No)	292	0.83 (0.51,1.37)	0.467	1
Ever had <i>P.aeruginosa</i>	Present (Ref: No)	279	4.36 (1.65,11.49)	0.001	0.013
Time since first <i>P.aeruginosa</i> isolate (per 10-year interval) <sup>†</sup>	Present (Ref: No)	133	2.12 (1.38,3.25)	<0.001	0.007
Chronic <i>P.aeruginosa</i>	Present (Ref: No)	201	3.81 (2.08,6.95)	<0.001	<0.001
Chronic MSSA	Present (Ref: No)	200	0.57 (0.30,1.10)	0.089	1
Ever had MRSA	Present (Ref: No)	261	2.46 (0.98,6.18)	0.055	1
Chronic MRSA	Present (Ref: No)	198	8.88 (1.89,41.73)	0.001	0.024
Chronic <i>B. cepacia</i>	Present (Ref: No)	198	1.62 (0.50,5.22)	0.421	1
Chronic <i>aspergillus spp</i>	Present (Ref: No)	201	0.79 (0.34,1.88)	0.597	1
Another fungus/mould	Present (Ref: No)	292	2.19 (1.22,3.93)	0.009	0.187
Ever had <i>Achromobacter</i>	Present (Ref: No)	263	1.66 (0.54,5.11)	0.378	1
Ever had <i>Stenotrophomonas</i>	Present (Ref: No)	262	0.52 (0.16,1.61)	0.232	1
CF-related diabetes	Present (Ref: No)	286	3.79 (2.10,6.84)	<0.001	<0.001
ABPA	Present (Ref: No)	261	0.29 (0.06,1.30)	0.064	1
CF-liver disease	Yes, without cirrhosis (Ref: No)	282	1.02 (0.53,1.94)	0.073	1
	Yes, with cirrhosis (Ref: No)	282	2.87 (1.15,7.14)		
WAZ < -1.0 at diagnosis	Present (Ref: $\geq -1$ )	179	1.42 (0.66,3.08)	0.362	1
Undernutrition <sup>#</sup>	Present (Ref: No)	292	3.17 (1.80,5.61)	<0.001	0.002

Legend Supplementary Table 3:

† Included as an interaction term, to apply only to those who have had ever had *P.aeruginosa*

‡ Undernutrition includes: WHZ < -1.0, < 2 years age; BMIz < -1.0, 2-17 years; or BMI < 18.5 kg/m<sup>2</sup>, ≥ 18 years

Severe lung disease: FEV<sub>1z</sub> < -3 in children ≥ 6 years

Chronic *H.Influenzae*, any non-tuberculosis mycobacteria isolated, any mycobacterium tuberculosis and pneumothorax showed extreme OR estimates and extremely wide CIs, arising from very small samples and were excluded from univariable analysis.

ABPA: allergic bronchopulmonary aspergillosis

MSSA: methicillin sensitive *S. aureus*

MRSA: methicillin resistant *S. aureus*

Supplementary Table 4: Univariable model results – factors for undernutrition in children and adults in the SA CF registry, 2018

Factor	Level	n	Odds Ratio (95% CI)	Unadjusted p-value	Adjusted p-value
Sex	Male (Ref: Female)	398	0.97 (0.61,1.55)	0.9	1
p.Phe508del	Homozygous (Ref: Neither)	398	0.50 (0.27,0.92)	0.043	0.941
	Heterozygous (Ref: Neither)	398	0.85 (0.46,1.58)		
3120+1G>A; c.2988+1G>A homozygous/heterozygous	Present (Ref: No)	398	2.55 (1.42,4.58)	0.002	0.057
Ever had <i>P.aeruginosa</i>	Present (Ref: No)	385	1.24 (0.67,2.27)	0.486	1
Caucasian	Present (Ref: other ancestry)	398	0.35 (0.22,0.57)	<0.001	0.001
Pancreatic insufficient	Present (Ref: No)	396	1.28 (0.57,2.88)	0.54	1
Neonatal bowel obstruction	Present (Ref: No)	380	0.83 (0.43,1.62)	0.586	1
Household cigarette smoke	Present (Ref: No)	398	0.95 (0.49,1.84)	0.869	1
Informal housing with no water or electricity	Present (Ref: No)	398	1.36 (0.26,7.12)	0.724	1
Receiving social welfare grant	Present (Ref: No)	398	2.99 (1.70,5.25)	<0.001	0.005
Private health insurance	Present (Ref: No)	398	0.46 (0.28,0.73)	0.001	0.027
Chronic <i>P.aeruginosa</i>	Present (Ref: No)	256	1.76 (1.00,3.12)	0.05	1
Chronic MSSA	Present (Ref: No)	255	1.17 (0.64,2.17)	0.61	1
Ever had MRSA	Present (Ref: No)	351	1.86 (0.80,4.35)	0.165	1
Chronic MRSA	Present (Ref: No)	255	2.31 (0.77,6.94)	0.145	1
Chronic <i>B. cepacia</i>	Present (Ref: No)	254	1.80 (0.57,5.72)	0.328	1
Chronic <i>aspergillus spp</i>	Present (Ref: No)	258	1.49 (0.64,3.50)	0.368	1
Another fungus/mould	Present (Ref: No)	398	0.91 (0.50,1.65)	0.749	1
Ever had <i>Achromobacter</i>	Present (Ref: No)	353	0.91 (0.25,3.35)	0.89	1
Ever had <i>Stenotrophomonas</i>	Present (Ref: No)	353	0.83 (0.27,2.56)	0.743	1
CF-related diabetes	Present (Ref: No)	391	0.98 (0.51,1.87)	0.948	1
ABPA	Present (Ref: No)	361	1.53 (0.52,4.54)	0.455	1
WAZ < -1.0 at diagnosis	Present (Ref: ≥ -1))	270	2.18 (1.07,4.44)	0.024	0.558
CF-liver disease	Yes, without cirrhosis (Ref: No)	386	0.99 (0.52,1.88)	0.504	1
	Yes, with cirrhosis (Ref: No)	386	0.50 (0.14,1.75)		
Current age (units: 10-years)	Present (Ref: No)	398	0.82 (0.66,1.01)	0.062	1
Age diagnosis (units: 10-years)	Present (Ref: No)	391	1.12 (0.80,1.59)	0.519	1
Time since first <i>P.aeruginosa</i> isolate (per 10-year interval)†	Present (Ref: No)	188	0.83 (0.56,1.23)	0.348	1

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