

## **ONLINE ONLY MATERIAL**

### **SUPPLEMENTAL METHODS**

#### **Subjects**

Undiagnosed patients (>5 years old) with suspected CF included those with: (1) idiopathic chronic sino-pulmonary disease (RESP), (2) idiopathic recurrent acute/chronic pancreatitis (PANC), or (3) male infertility from obstructive azoospermia (AZOOSP). Idiopathic chronic sino-pulmonary disease was defined as recurrent or chronic sinusitis (including sinusoidal pain, nasal discharge, post-nasal drip), nasal polyps, recurrent or chronic bronchitis, recurrent pneumonia and/or bronchiectasis for at least 6 months. All RESP subjects had  $\geq 3$  of these symptoms. If not done prior to referral, RESP subjects were tested for immunodeficiency, alpha-1-antitrypsin deficiency, allergic bronchopulmonary aspergillosis, non-tuberculous mycobacteria, and primary ciliary dyskinesia. Patients were also screened for conditions associated with bronchiectasis (e.g. rheumatoid arthritis and other inflammatory diseases). Patients diagnosed with any of these disorders were excluded from the study. A diagnosis of idiopathic recurrent acute pancreatitis was accepted following at least 2 episodes of abdominal pain associated with: (1) raised serum amylase and/or lipase (>2 times the upper limit of the reference range), and/or (2) imaging evidence of acute pancreatitis. Patients with chronic pancreatitis had chronic pain in association with pancreatic calcifications and/or characteristic ductal changes. Obstructive azoospermia (congenital unilateral or bilateral absence of vas deferens) was confirmed by physical examination, transrectal ultrasound and evidence of azoospermia on two occasions.

## **SUPPLEMENTAL RESULTS**

### **Subject characteristics**

The ethnic origin of the 202 subjects with single-organ manifestations of CF are as follows:

- 86.5% (n=174) European Caucasian
- 4.5% (n=9) Asian and Far East Asian
- 4% (n=8) Indian subcontinent
- 2% (n=4) Middle Eastern non-Jewish
- 1.5% (n=3) Middle Eastern Jewish
- 1% (n=2) Latin American
- 0.5% (n=1) Native Indian

## **SUPPLEMENTAL TABLE**

A comparison of concordance analysis between sweat test and NPD using different borderline sweat chloride cut-offs. According to the Kappa statistic there was no difference in the levels of agreement, when the 40 mmol/L cut-off was compared with 30 mmol/L. In comparison with the 40 mmol/L cut-off, observed agreement was reduced (i.e. more disagreement with the 30 mmol/L cut-off). When borderline results were excluded, the levels of agreement remained unchanged for all subgroups. Observed agreement increased marginally in PANC and RESP but remained unchanged with RESP.

**Sweat chloride cut-off of 40 mmol/L used**

Group	All Subjects			Subjects with borderline sweat test and/or NPD results excluded		
	N	Observed agreement	Kappa (95%CI)	N	Observed agreement	Kappa (95%CI)
<b>RESP</b>	68	0.65	0.48 (0.29 to 0.66)	49	0.86	0.67 (0.46 to 0.89)
<b>PANC</b>	42	0.55	0.05 (-0.15 to 0.26)	33	0.67	0.06 (-0.18 to 0.30)
<b>AZOOSP</b>	92	0.44	0.23 (0.07 to 0.38)	46	0.72	0.40 (0.13 to 0.67)

**Sweat chloride cut-off of 30 mmol/L used**

Group	All Subjects			Subjects with borderline sweat test and/or NPD results excluded		
	N	Observed agreement	Kappa (95%CI)	N	Observed agreement	Kappa (95%CI)
<b>RESP</b>	68	0.63	0.48 (0.30 to 0.66)	44	0.86	0.70 (0.48 to 0.92)
<b>PANC</b>	42	0.40	0.03 (-0.21 to 0.17)	23	0.70	0.10 (0 to 0.45)
<b>AZOOSP</b>	92	0.35	0.26 (0.11 to 0.40)	37	0.78	0.55 (0.28 to 0.82)