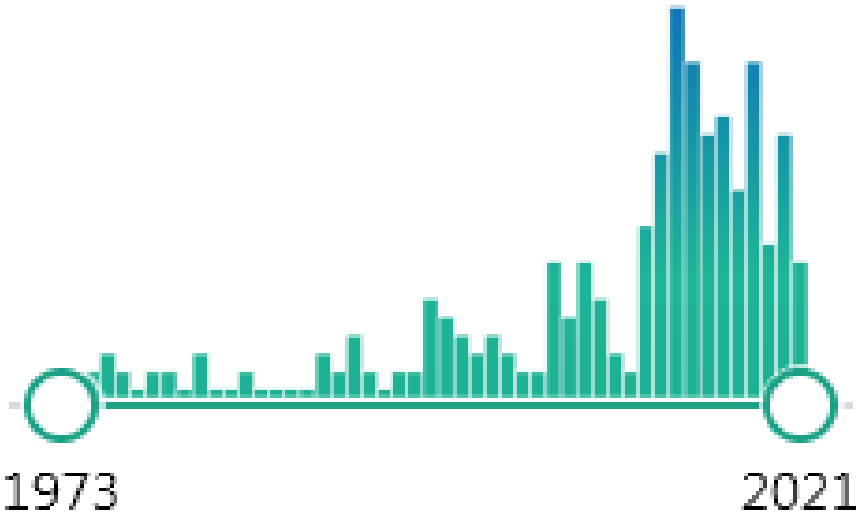
SIFC
SOCIETÀ ITALIANA
PER LO STUDIO DELLA FIBROSI CISTICA

Microbiologia delle vie aeree superiori in pazienti FC

DANIELA DOLCE
AOU Meyer, Firenze

NESSUN POTENZIALE CONFLITTO D'INTERESSI DA DICHIARARE



- ("nose" or "paranasal sinus" or "paranasal sinuses" or "sinus") AND("microbiology" or "bacteria") AND ("cystic fibrosis" or "cf")
- 189 risultati (120 negli ultimi 10 anni)
- 16 clinical trial
- 31 review

Anatomy

- cellule cilindriche ciliate
- caliciformi muco secernenti

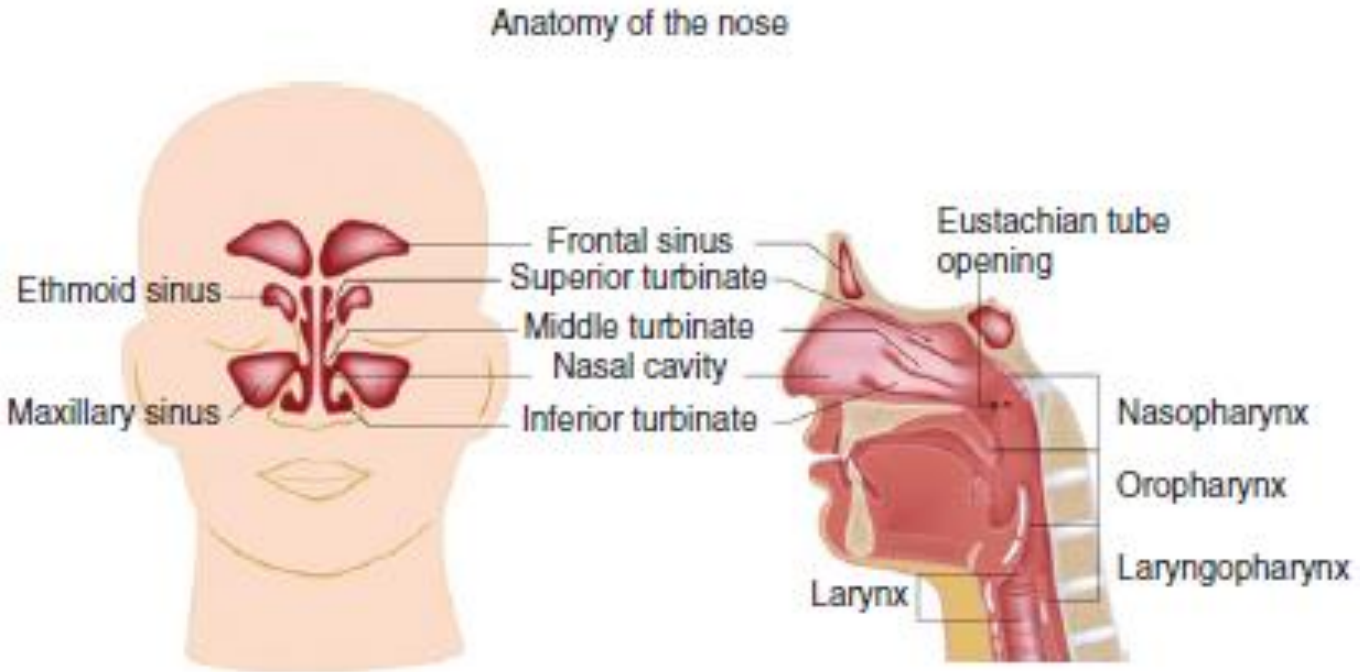
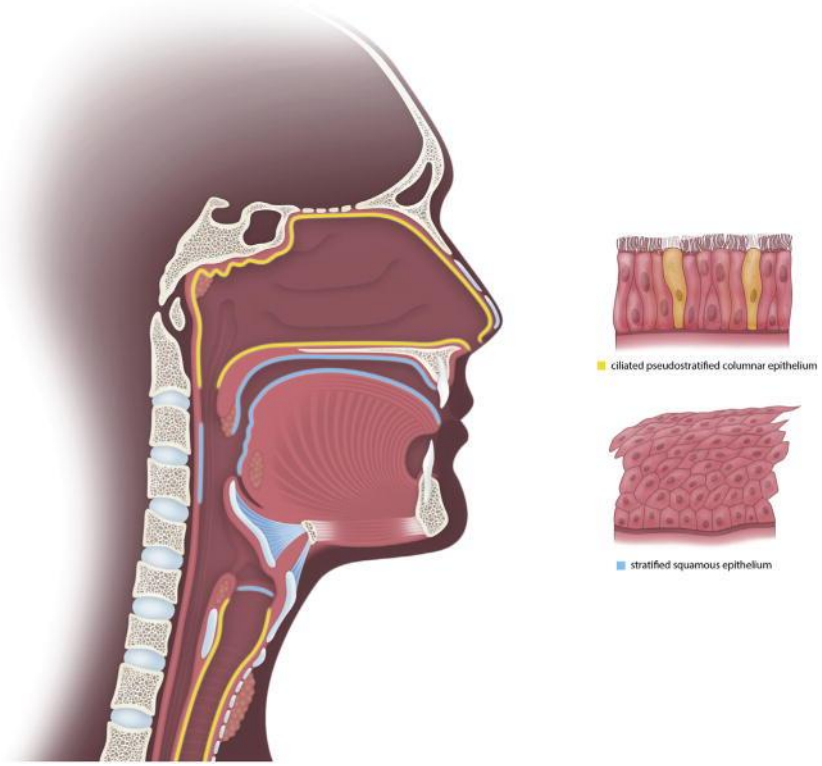


Fig. 5.1 Anatomy of nasal cavity and sinuses. (With permission from Dreamstime LLC)



A.S. Hanshew et al. / Respiratory Medicine 126 (2017) 68–74

M. P. Carroll Jr. et al. Asthma, Allergic and Immunologic Diseases During Pregnancy. 2018 Dec 30 : 61–86.

Hanshew, A. S., Jetté, M. E., Rosen, S. P., & Thibeault, S. L. (2017). Integrating the microbiota of the respiratory tract with the unified airway model. Respiratory medicine, 126, 68–74. https://doi.org/10.1016/j.rmed.2017.03.019

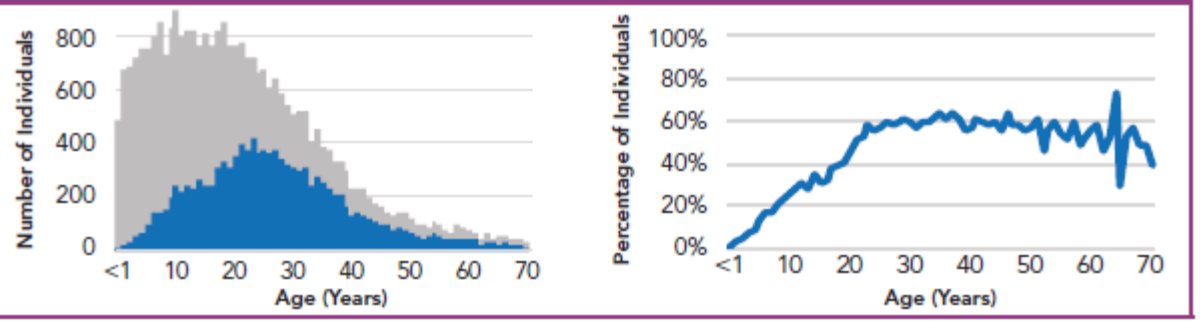
Complication of CF – 2019 US data registry

Complications of CF, 2019 *continued*

GI	Age < 18 (%)	Age ≥ 18 (%)	All (%)
Distal intestinal obstruction syndrome (DIOS)[C]	1.7	2.4	2.1
Fibrosing colonopathy/colonic stricture[C]	<0.1	<0.1	<0.1
Gastroesophageal reflux disease (GERD)	31.8	41.2	36.8
GI bleed requiring hospitalization (non-variceal)[C]	<0.1	<0.1	<0.1
History of intestinal or colon surgery	4.3	2.2	3.2
Pancreatitis[C]	0.3	1.3	0.8
Peptic ulcer disease[C]	<0.1	0.1	<0.1
Rectal prolapse[C]	0.3	0.1	0.2
Mental Health			
Anxiety disorder	5.0	23.8	15.0
Depression	3.5	28.3	16.7
Other Complications			
Cancer confirmed by histology[C]	0.0	0.4	0.2
Hearing loss	1.3	3.6	2.5
Hypertension	0.4	6.4	3.6
Kidney stones[C]	0.1	1.3	0.7
Nasal polyps requiring surgery[C]	1.3	1.2	1.3
Renal failure requiring dialysis[E]	[illegible]	0.2	[illegible]
Sinus disease	21.1	55.7	39.5

- Prevalence of sinus disease increases in adolescence and in young adults
- Remains high through the older ages

Sinus Disease



Normal Flora

Table of common microbiota found within the regions of the respiratory tract.

Oral cavity	Nasopharynx	Oropharynx	Larynx	Lung
Prevotella	*Corynebacterium*	*Prevotella*	*Prevotella*	*Prevotella*
Streptococcus	*Streptococcus*	*Streptococcus*	*Streptococcus*	*Streptococcus*
Veillonella	*Veillonella*	*Veillonella*	*Veillonella*	*Veillonella*
Haemophilus	*Propionibacterium*	*Haemophilus*	*Unclassified-Comamonoadaceae*	*Pseudomonas*
	Staphylococcus	*Fusobacterium*	*Cloacibacterium*	*Fusobacterium*
	Moraxella		*Helicobacter*	

A.S. Hanshew et al. / Respiratory Medicine 126 (2017) 68–74

NORMAL NASAL FLORA

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- α- and γ-streptococci
- *Propionibacterium acnes*
- Aerobic diphtheroid

NORMAL SINUS FLORA

Anaerobic bacteria:

- *Prevotella, Porphyromonas, Fusobacterium, Peptostreptococcus* spp.

Aerobic bacteria:

- *S. pyogenes, S. aureus, S. pneumoniae, H. influenzae*.

Sinus bacteriology in patients with cystic fibrosis or primary ciliary dyskinesia: A systematic review

Maria E. Møller, M.D.,[1] Mikkel C. Alanin, M.D., Ph.D.,[1] Christian Grønhøj, M.D.,[1]
Kasper Aanæs, M.D., Ph.D.,[1] Niels Høiby, M.D, D.M.Sc.,[2]
and Christian von Buchwald, M.D., D.M.Sc.[1]

- 43 studies 1718 CF patients
- Sampling methods:
  - sinus surgery with the use of endoscopy (54%)
  - lavage and/or washouts (15%)
  - swabs (30%)
  - endoscopy or other procedures (26%)
  - aspirate samples (22%),
  - biopsy specimens and/or smears
  - (11%)
  - pus and/or secretions (7%)
  - crusts (4%)
  - nose blowing 2%

- Sampling sites:
  - maxillary sinus (30%)
  - middle meatus (24%)
  - paranasal sinus unspecified (including the sinus ostia) (20%)
  - nose specified (anterior nares, posterior nares,
  - nostrils, inferior turbinate, and meatus) (20%)
  - nose unspecified (17%)
  - ethmoid sinuses (20%)
  - frontal sinuses (9%)
  - sphenoid sinuses (11%)
  - external nares (2%)

Møller et al., Am J Rhinol Allergy 31, 293-298, 2017

Sinus flora in CF - Review

Table 1 **The most common bacteria isolated from the nose and sinuses in patients with cystic fibrosis, including swab and blowing sample studies***

Bacteria	Patients, no.#	Prevalence, %
Staphylococcus aureus	513	30
Pseudomonas aeruginosa	437	25
Coagulase negative *Staphylococcus*	88	5
Haemophilus influenzae	74	4
Streptococcus pneumoniae	29	2
Corynebacteria species	21	1
Burkholderia cepacia complex	20	1
Stenotrophomonas maltophilia	19	1
Moraxella catarrhalis	16	1
Escherichia coli	15	1
Achromobacter xylosoxidans	10	1

55%

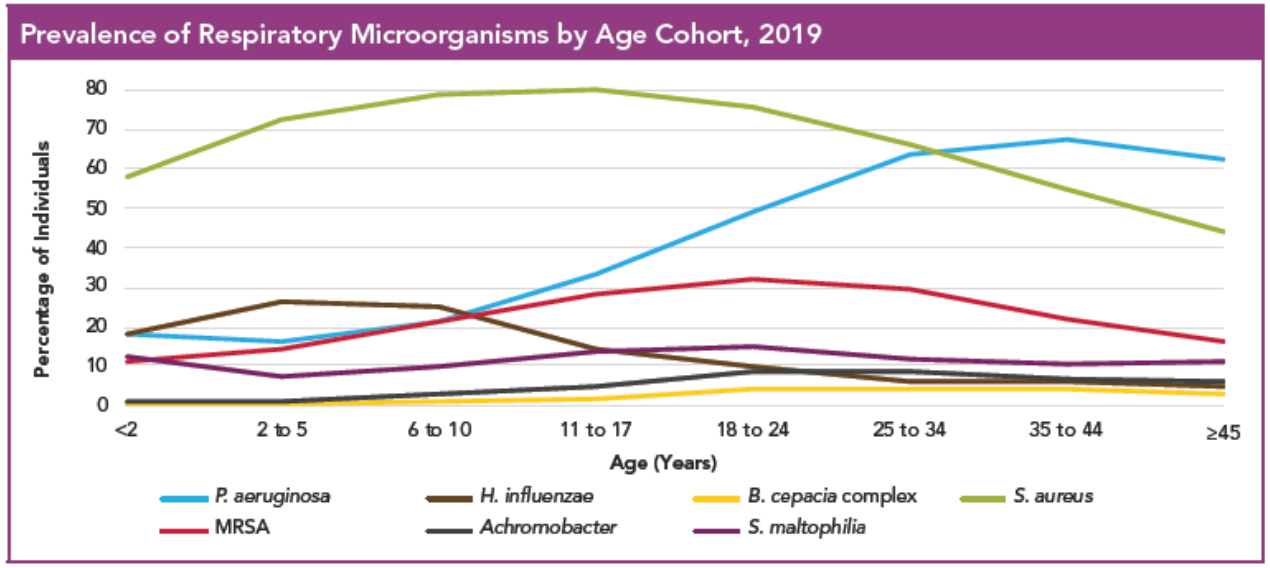
Table 4 **The most common bacteria isolated from the nose and sinuses in patients with cystic fibrosis, without swab and blowing sample studies***

Bacteria	Patients, no.#	Prevalence, %
Pseudomonas aeruginosa	383	34
Staphylococcus aureus	320	28
Haemophilus influenzae	56	5
Coagulase negative *Staphylococcus*	40	3.5
Burkholderia cepacia complex	20	2
Stenotrophomonas maltophilia	17	1.5
Streptococcus pneumoniae	17	1.5
Escherichia coli	14	1.2
Achromobacter xylosoxidans	10	1
Moraxella catarrhalis	9	1
Streptococcus viridans	8	1

62%

Møller et al., Am J Rhinol Allergy 31, 293-298, 2017

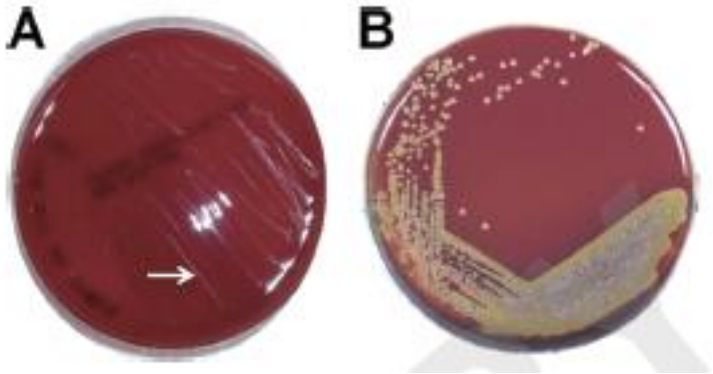
Staphylococcus aureus



- *S. aureus* and *H. influenzae* are the most common in upper airways in pediatric patients (Taylor, 1990; Robertson, 2008)
- *S. aureus* is higher in who had not received antibiotics (Goerke, 2000)
- *S. aureus* is transformed in SCV after gentamycin exposure (Gitomer, 2015)

Table I Summary of sinus culture results

Author	Patient age (years)	*P. aeruginosa* (%)	*S. aureus* (%)	*H. influenzae* (%)
Shapiro[22]	15 (mean)	38.2	–	29.4
Moss[24]	23.3 (mean)	72.9	–	–
Wise[26]	<17 yrs	22	68.2	Only recovered
	>17 yrs	75	25	in <11 years
Muhlebach[23]	9.5 (mean)	42	49	22

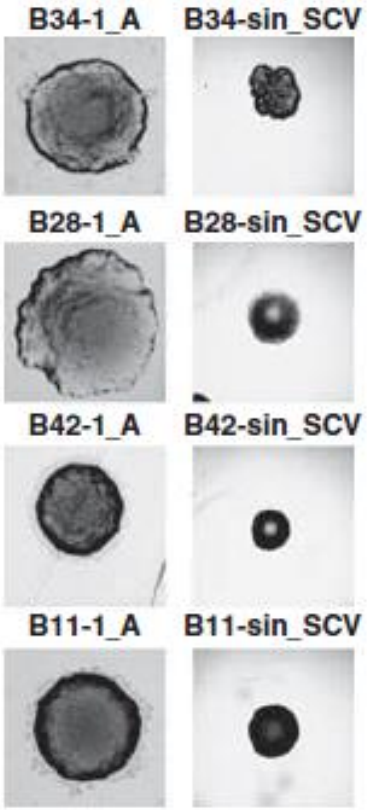


Pseudomonas aeruginosa

- *P. aeruginosa* was found more frequently increasing age (Muhlebach, 2006; Robertson , 2008)
- *P. aeruginosa* is transformed in SCV and antibiotic resistant clones (Hansen, 2012)
- Sinus represent a protected niches of adapted *P. aerugionsa* clones (Hansen, 2012; Low, 2001)

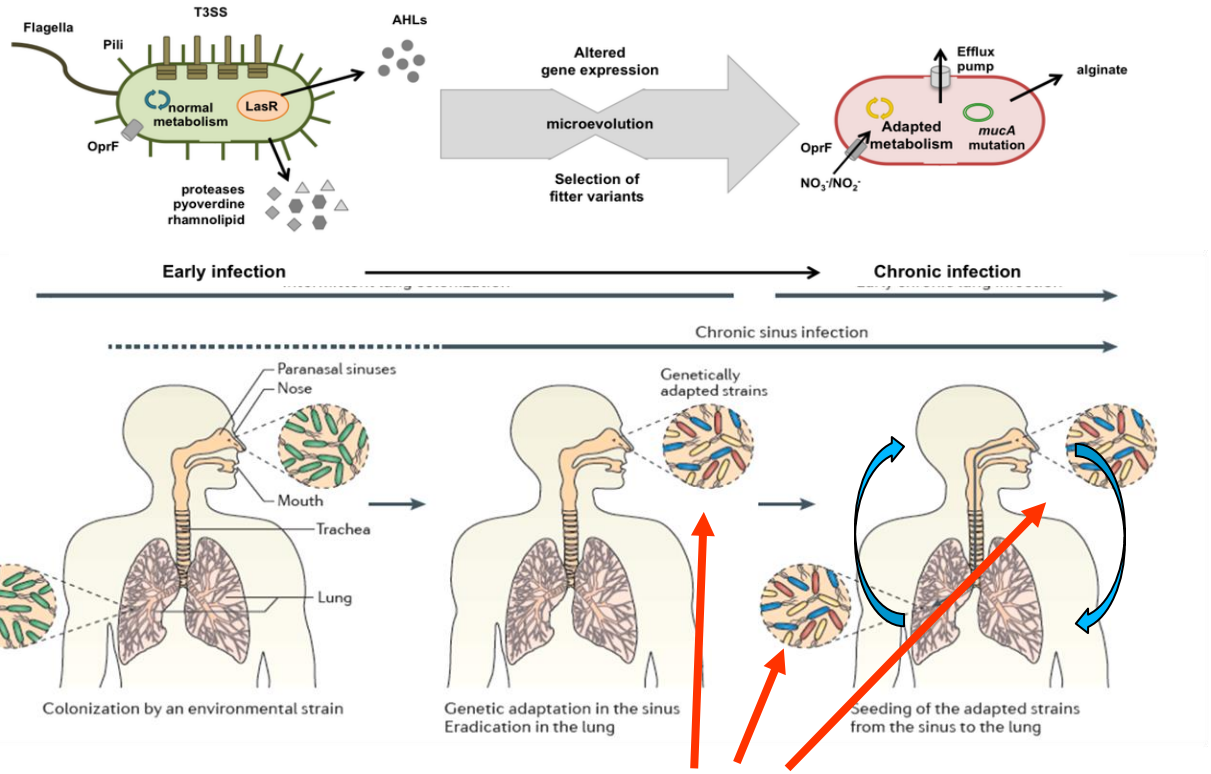
	Sinus (n = 45)[a] Freq. (%)
S. aureus	22 (49)
Age <8 years	8 (36)
Age ≥8 years	14 (61)
P. aeruginosa	19 (42)
Age <8 years	6 (27)
Age ≥8 years	13 (57)
H. influenzae	10 (22)
Age <8 years	8 (36)
Age ≥8 years	2 (9)
No pathogen[b] detected	2 (4)
Age < 8 years	2 (9)
Age ≥8 years	0 (0)

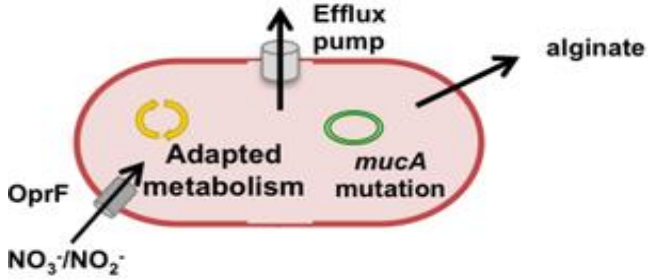
Muhlebach et al. Pediatric Pulmonology 41:445–451 (2006)



Sinuses are infection foci in CF airways
SK Hansen *et al*

Pseudomonas aeruginosa





→ **Chronic infection**

P. aeruginosa characteristics

Mucoid phenotype
Biofilm growth
Reduced virulence factors expression
Auxotrophy
Antibiotic resistance
Adapted metabolism
Increased mutation rates

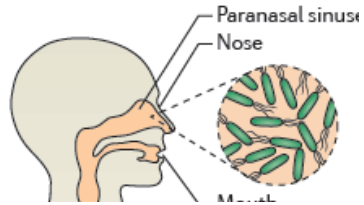
Trasformazione di un patogeno originariamente ambientale in un patogeno altamente specializzato per le vie aeree del paziente e possibile re-infezione della vie aeree inferioriFC

ISME J. **6**, 31–45 (2012).

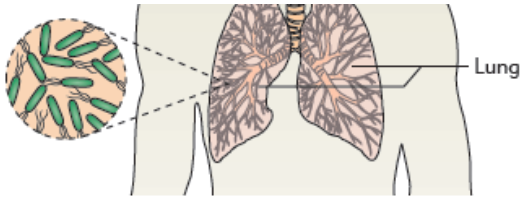
Dati preliminari sulla colonizzazione dei seni paranasali

LEEDS DEFINITION	NEVER INFECTED	PA-FREE	INTERMITTENTLY INFECTED	CHRONICALLY INFECTED	TRANSPALNTED
65 patients	**3 (4%)**	**18 (28%)**	**24 (37%)**	**9 (14%)**	**11 (17%)**
21 positive nasal lavage	**0**	**1 (5.5%)**	**4 (16.6%)**	**9 (100%)**	**7 (63.6%)**

- I ceppi di *P. aeruginosa* dalle alte e dalle basse vie respiratorie hanno lo stesso genotipo in 19 (90,5%) su 21 pazienti
- I seni paranasali possono essere un serbatoio per la re-infezione soprattutto pazienti non cronicamente infettati



90,5% stesso genotipo



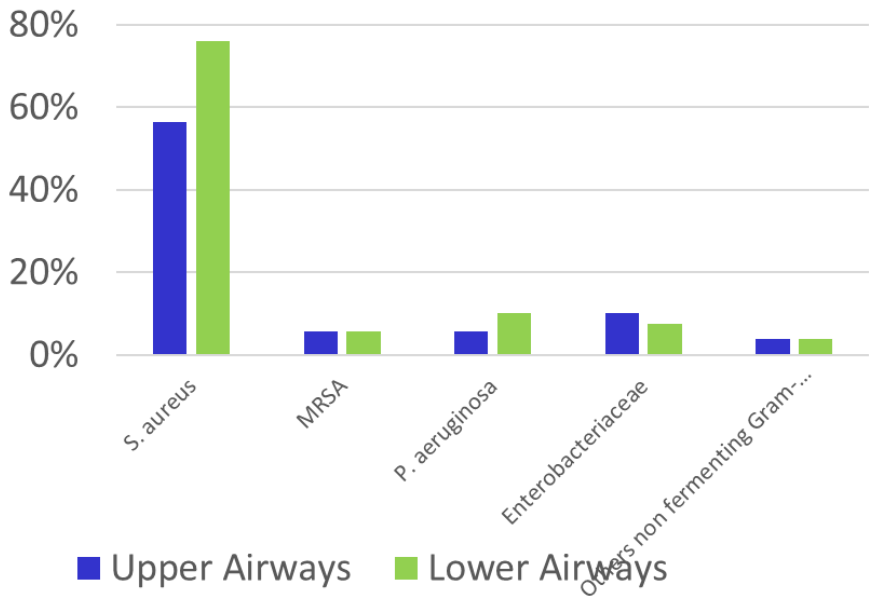
ECFC 2015

MICROBIOLOGICAL COMPARISON BETWEEN UPPER AND LOWER AIRWAYS IN PATIENTS WITH CYSTIC FIBROSIS

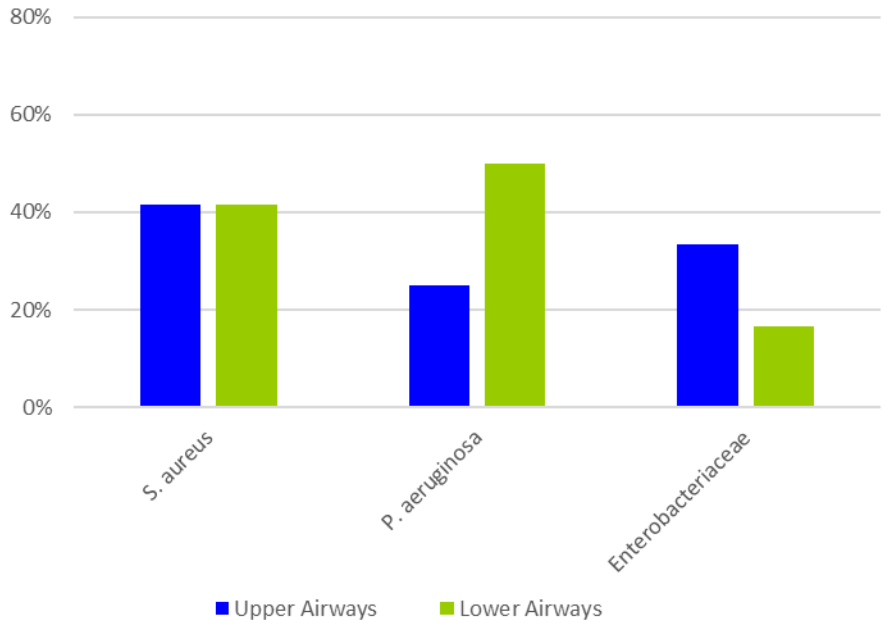
Bianchimani C[1], Campana S[1], Dolce D[1], Ravenni N[1], Francalanci M[1], Maggiore C[3], Cavicchi MC[1], Galici V[1], Neri AS[1], Terlizzi V[1], Innocenti D[1], Santini G[1], Masi E[1], Ferrari B[1], Castellani C[1], Masolini M[1], Camera E[1], Orioli T[1], Bresci S[2], Borchi B[2], Cavallo A[2], Mencarini J[2], Fevola C[1], Taccetti G[1]

Preliminary Data – Poster 13

108 patients - Not chronic



12 patients - Transplanted



Project funded by the Tuscany Region – Grant K35, K37

Microbiome

frontiers in Microbiology

ORIGINAL RESEARCH
published: 30 June 2020
doi: 10.3389/fmicb.2020.01463

The Respiratory Microbiome in Cystic Fibrosis: Compartment Patterns and Clinical Relationships in Early Stage Disease

Marian Garcia-Nuñez[1,2], Miguel Garcia-Gonzalez[3,4,5], Xavier Pomares[1,2,3], Concepción Montón[1,3], Laura Millares[1,2,6], Sara Quero[1,2,6], Elena Prina[1], Oscar Asensio[3,4], Montserrat Bosque[3,4], Silvia Capilla[7], Oscar Cuevas[4†] and Eduard Monsó[1,2,5*]*

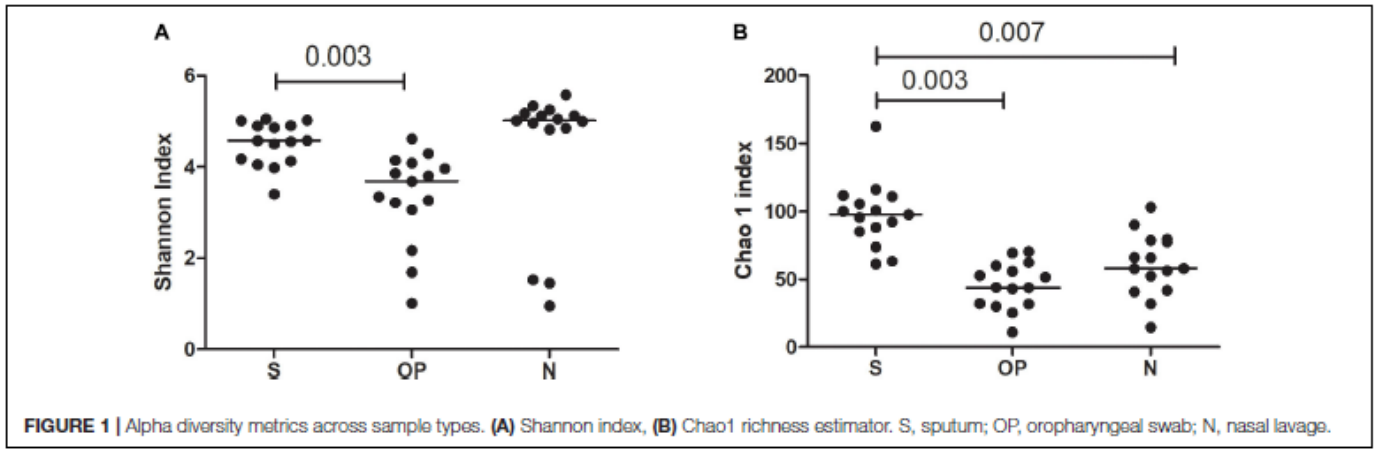
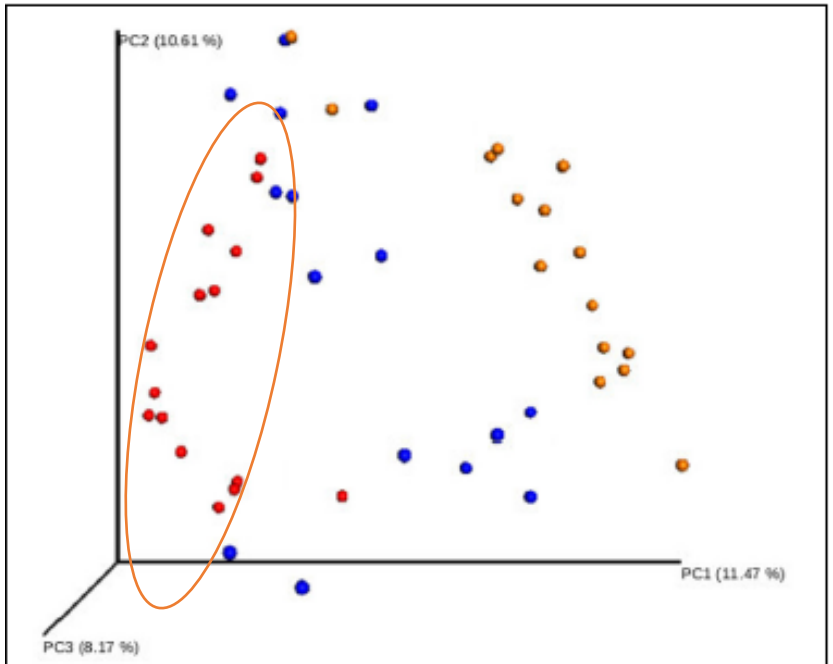


FIGURE 1 | Alpha diversity metrics across sample types. **(A)** Shannon index, **(B)** Chao1 richness estimator. S, sputum; OP, oropharyngeal swab; N, nasal lavage.

TABLE 1 | Patient characteristics at baseline.

N	**17**
Age (years), median (IQR)	13 (11–20)

Microbioma bronchiale mostra una maggiore diversità rispetto alla flora microbica nell'orofaringe e nel principalmente a causa di una sovrarappresentazione di batteri anaerobi nelle secrezioni bronchiali.



Principal Coordinates Analysis

FIGURE 2 | Beta-diversity analysis of the bacterial communities of different respiratory compartments. Principal coordinate analysis (PCoA) of sputum (yellow), oropharyngeal swab (blue), and nasal lavage samples (red). Adonis test of Bray Curtis dissimilarity matrix, $p = 0.001$.

Garcia-Nuñez M, Garcia-Gonzalez M, Pomares X et al / Frontiers in Microbiology, 2020, Vol. 11, 1463

Microbiome

PLOS ONE

RESEARCH ARTICLE

Comparison of Microbiomes from Different Niches of Upper and Lower Airways in Children and Adolescents with Cystic Fibrosis

Sébastien Boutin[1,4], Simon Y. Graeber[2,3,4], Michael Weitnauer[1], Jessica Panitz[1,4], Mirjam Stahl[2,3,4], Diana Clausznitzer[5], Lars Kaderali[5], Gisli Einarsson[6], Michael M. Tunney[6,7], J. Stuart Elborn[6,8], Marcus A. Mall[2,3,4☯], Alexander H. Dalpke[1,4☯*]

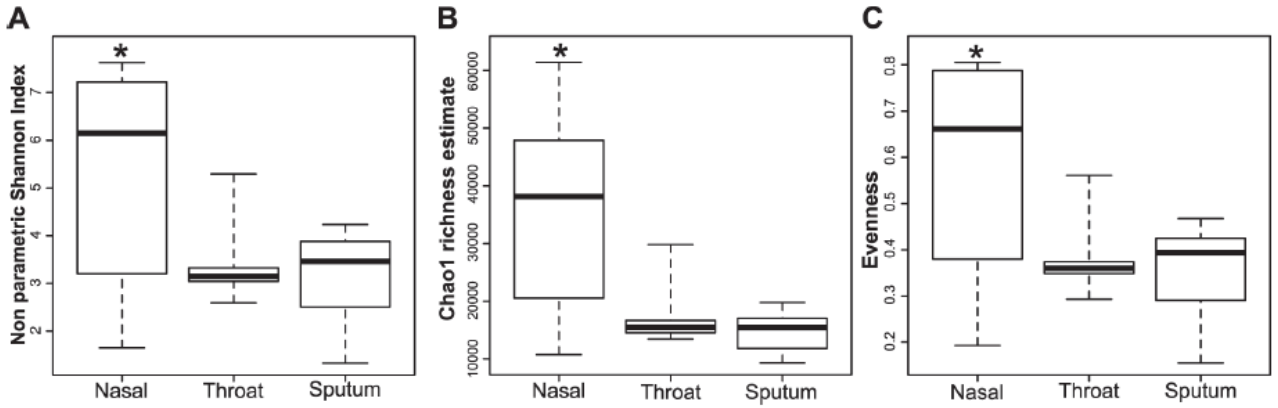


Fig 3. Alpha-diversity of the upper and lower airways microbiomes from clinically stable children with CF. Alpha-diversity was calculated with the non parametric Shannon index (A), richness was estimated with the Chao1 estimate (B) and evenness was calculated based on the Shannon index (C). Alpha-diversity variation among nose, throat and sputum microbiome was analyzed with a linear mixed model with random effects for CF patients and paired comparisons were done with a Tukey post-hoc test for pairwise comparison.

Table 1. Patients' characteristics.

	mean ± SD (range) or n (%)
Number of patients	20
Age, years	16.1 ± 3.8 (7.0–22.0)

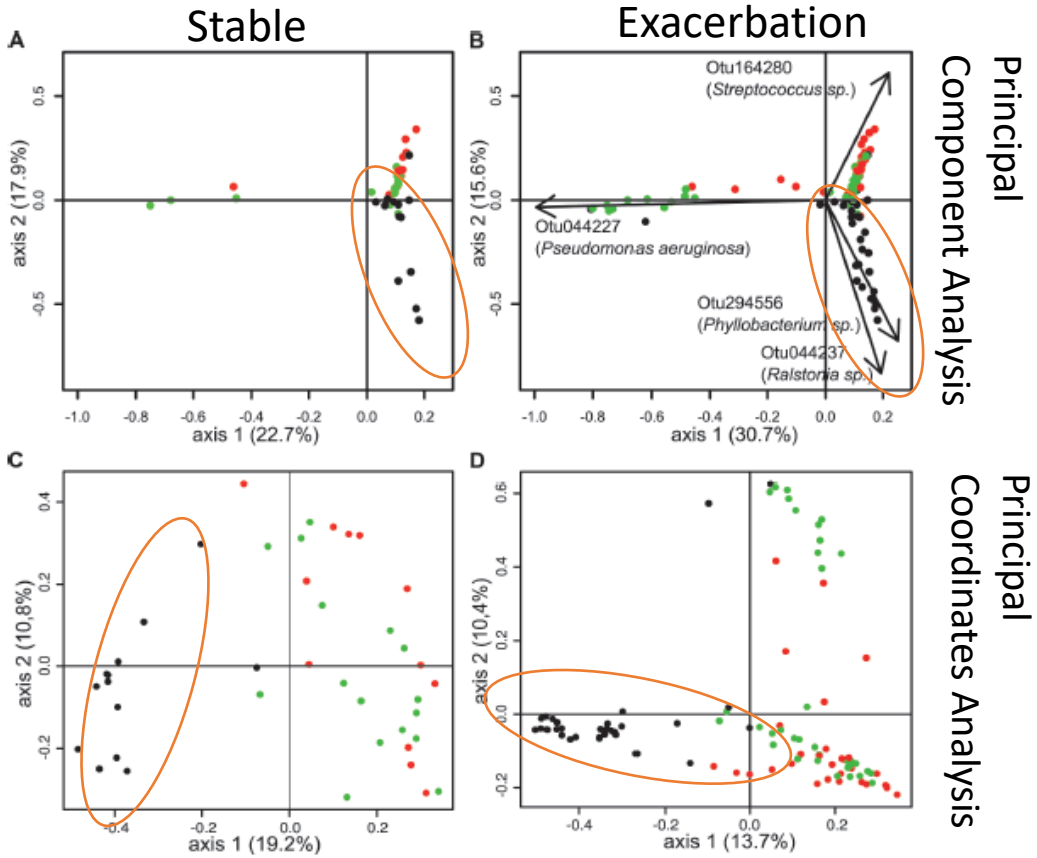
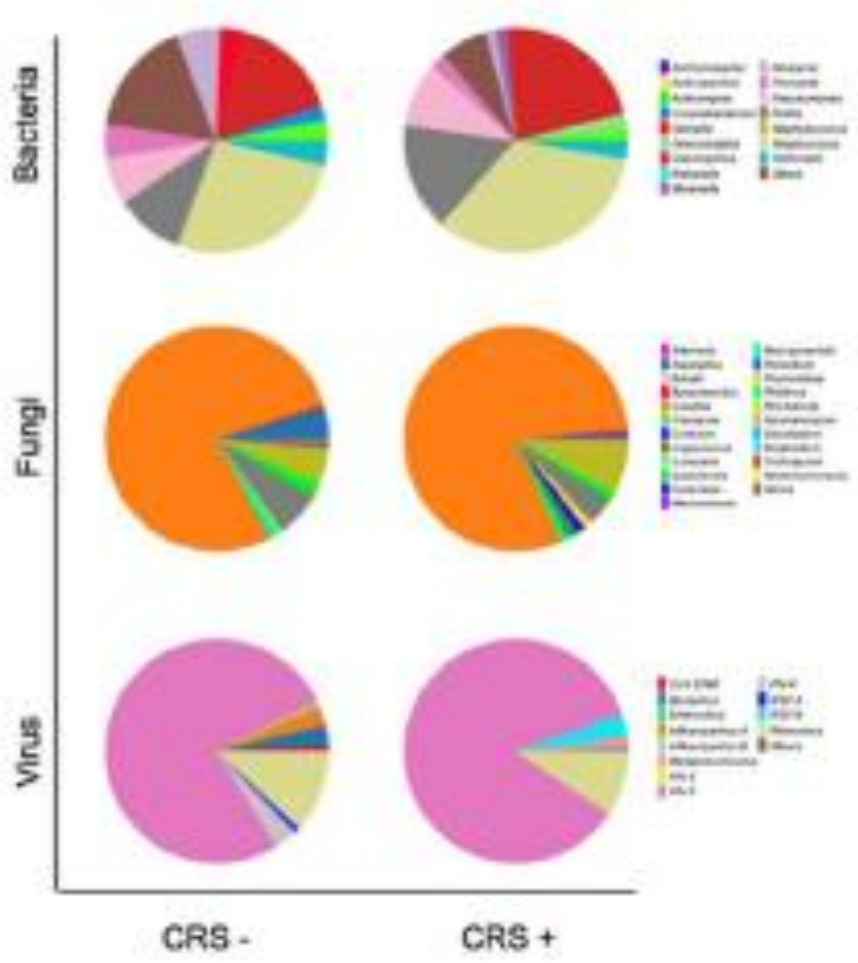


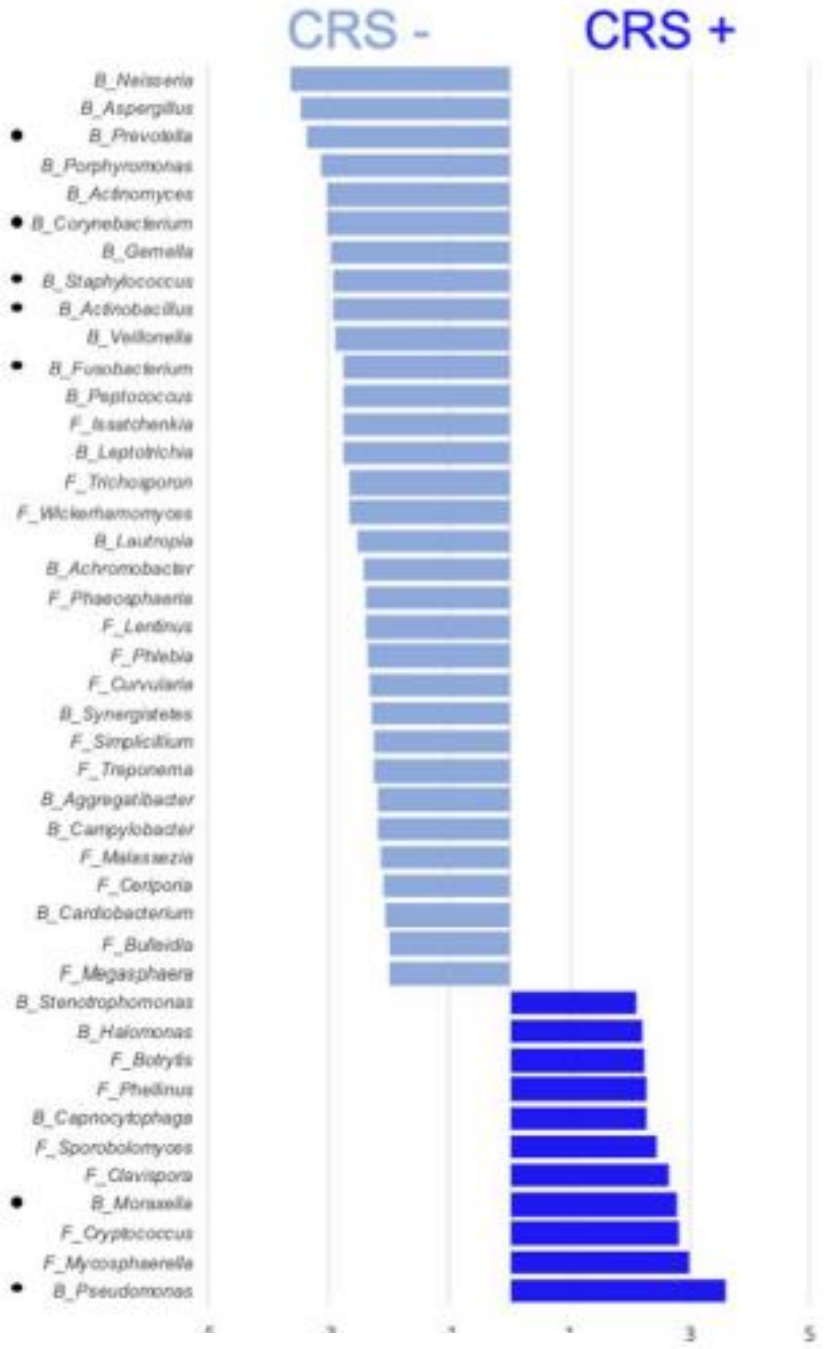
Fig 5. Spatial analysis of the airways microbiome. Nasal swabs are represented by black dots, throat swabs by red dots, sputum samples by green dots. (A) Principal Component Analysis of samples obtained from clinically stable children with CF. In panel (B) samples from patients during exacerbation were added. Pearson correlations were performed to highlight which OTUs were responsible for the divergence among the samples. Correlation was considered significant when the coefficient of correlation was higher than 0.6 and p-value < 0.01. (C) Principal Coordinates Analysis was performed on samples obtained from clinically stable CF patients or (D) on all available samples from CF patients irrespective of the clinical status.

Our first important result is that the microbiome compo
in the nose differed considerably
from corresponding throat and sputum samples

Boutin S, Graeber SY, Weitnauer M, et al. / PLoS ONE 2015 10(1)

Microbiome - Chotirmall





Mac Aogáin et al, Nature Medicine | VOL 688 27 | April 2021 | 688–699

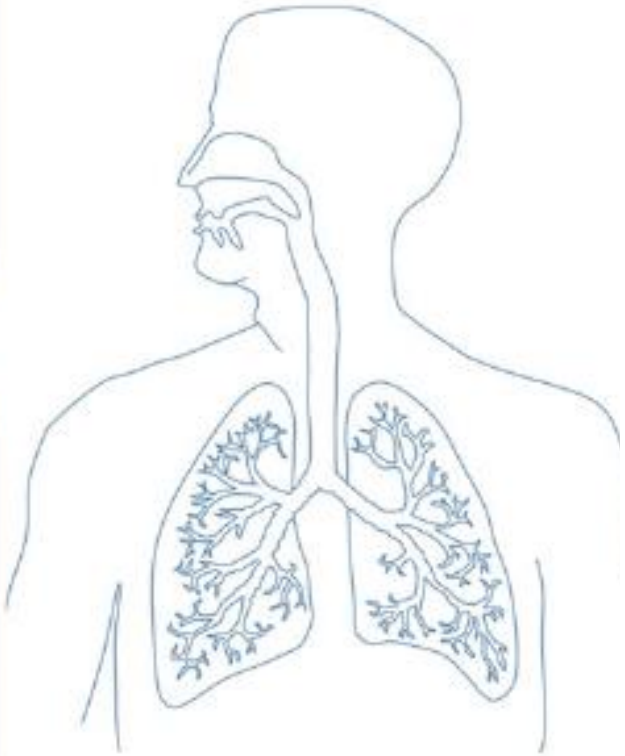
Virus

Upper airways :

Rhinovirus 2-4,6,8,9,11-19
Influenza viruses 2,3,6,7,9,11-16,18
Respiratory syncytial virus 2,3,6,7,9,11-16,18
Parainfluenza viruses 2,4,11-14,16,18,19,22
Adenovirus 8,11,14,15,18,20
Coronavirus 4-8, 18-20
Enterovirus 6,8,18,20
Polyomavirus 25
Metapneumovirus 2,6,9,11,12,15,16,18,20
Bocavirus 18
Cocksackie/Echovirus 14

Lower airways :

Rhinovirus 1,3,5,8-11,14-16,23,24
Influenza viruses 1,5,9,11,15,16,22-24
Respiratory syncytial virus 1,4,5,11,16,15,22-24
Adenovirus 8,11,14
Coronavirus 1,4,5,8,16
Parainfluenza viruses 1,4,11,14,16,22
Enterovirus 8
Polyomavirus 25
Metapneumovirus 9,11,15
Bocavirus 1
Cocksackie/Echovirus 14



CRITICAL REVIEWS IN MICROBIOLOGY, 2017
http://dx.doi.org/10.1080/1040841X.2017.1297763

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

Check for updates

Viruses in cystic fibrosis patients' airways

Lisa Billard[a], Rozenn Le Berre[a,b], Léa Pilorgé[a,c], Christopher Payan[a,c], Geneviève Héry-Arnaud[a,c] and Sophie Vallet[a,c]

[a]EA 3882-Laboratoire Universitaire de Biodiversité et Ecologie Microbienne (LUBEM), Groupe de Bactériologie-Virologie, Faculté de Médecine et des Sciences de la Santé, Université Bretagne Loire, Brest Cedex, France; [b]Département de Médecine Interne et Pneumologie, Centre Hospitalier Régional et Universitaire de Brest, Hôpital de la Cavale Blanche, Brest cedex, France; [c]Département de Bacteriologie-Virologie, Hygiène et Parasitologie-Mycologie, Pôle de Biologie-Pathologie, Centre Hospitalier Régional et Universitaire de Brest, Hôpital de la Cavale Blanche, Brest cedex, France

Rhinovirus

- Prevalence is the same in upper respiratory tract samples as in sputum
- RV viral load is also important: the higher the load in CF nasopharyngeal samples, the higher the viremia, and the more severe the clinical impact, especially in the lower respiratory tract

Influenza virus

- IV prevalence reaches 13.8% in CF adults' sputum
- It is significantly associated with exacerbation, during which it seems to infect mainly the upper respiratory tract

Respiratory syncytial virus

- RSV is associated with impaired pulmonary function, increased morbidity
- RSV infection has been linked to earlier *P. aeruginosa* colonization in infants with CF

Virus

Journal of Cystic Fibrosis 20 (2021) 432–435

Contents lists available at ScienceDirect

Journal of Cystic Fibrosis

journal homepage: www.elsevier.com/locate/jcf

Sputum versus nasopharyngeal samples for the molecular diagnosis of respiratory viral infection in cystic fibrosis: A pilot study ☆

Emilie Cardot-Martin[b], Hélène Le Guillou-Guillemette[c], Rozenn Le Berre[a,d], Sophie Ramel[e], Jean Le Bihan[e], Dominique Grenet[f], Eric Farfour[b], Françoise Troussier[g], Thierry Urban[h], Lisa Billard[a], Léa Pilorgé[i], Adissa Minoui-Tran[i], Christopher Payan[a,i], Marie-Reine Munck[j], Geneviève Héry-Arnaud[a,k], Sophie Vallet[a,i,*]

Table 1
Viral screening spectra in the three participant centres.

Centre	Multiplex Technique	Viral screening	patients	Age range (years)
A	*Multi Well System MWS R-GENE® bioMerieux* *	*ADV, EV, RV, IVA, IVB, PIV 1-4, RSV A and B, HCoV 229E, NL63 and OC43, and HKU1, HMPV, HBoV*	*5*	*6-43 3 childs 2 adults*
B	*RespiFinder® SMART 22 Fast v2.0, PathoFinder***	*ADV, EV/RV, IVA, IVA(H1N1) vpdm09, IVB, PIV1-4, RSV A and B, HCoV 229E, OC43, NL63 and HKU1, HMPV, HBoV*	*13*	*2-29 2 childs 11 adults*
C	*Anyplex II RV16® Seegene****	*ADV, EV, RV, IVA,IVB, PIV1-4, RSV A and B, HCoV229E, OC43, NL63, HMPV, HBoV*	*12*	*12 adults*

83% concordance

n=30	Sputum	NP
	Concordances (n=25)	
n=4	*Influenza virus B*	*Influenza virus B*
n=2	*Influenza virus A*	*Influenza virus A*
n=1	*Influenza virus A + respiratory syncytial virus*	*Influenza virus A + respiratory syncytial virus*
n=1	*Rhinovirus*	*Rhinovirus*
n=3	*Rhinovirus/Enterovirus*	*Rhinovirus/Enterovirus*
n=2	*Human coronavirus OC43*	*Human coronavirus OC43*
n=12	no virus detected	no virus detected

17% disconcordance

	Discordances (n=5)	
n=1	*Adenovirus*	*no virus detected*
n=1	*Human Bocavirus*	*no virus detected*
n=1	*Influenza virus B + rhinovirus*	*Influenza virus B*
n=1	no virus detected	*Influenza virus B*
n=1	no virus detected	*Rhinovirus/Enterovirus*

E. Cardot-Martin, H.L. Guillou-Guillemette and R.L. Berre et al. / Journal of Cystic Fibrosis 20 (2021) 432–435

Lung Transplant

Case Studies

Sinonasal persistence of *Pseudomonas aeruginosa* after lung transplantation

J.G. Mainz [a,*], J. Hentschel [a], C. Schien [a], N. Cramer [b], W. Pfister [c], J.F. Beck [a], B. Tümmler [b]

- Persistence of identical *P. aeruginosa* genotype after LTX (Mainz, 2012)

Original Article

P. aeruginosa in the paranasal sinuses and transplanted lungs have similar adaptive mutations as isolates from chronically infected CF lungs☆

Oana Ciofu [a,*], Helle Krogh Johansen [b], Kasper Aanaes [c], Tina Wassermann [a], Morten Alhede [a,b], Christian von Buchwald [c], Niels Høiby [a,b]

- Same genotype and phenotype from sinuses after LTX (Ciofu, 2013)

Correlation between sinus and lung cultures in lung transplant patients with cystic fibrosis

Kevin J. Choi, MD, MS[1], Tracy Z. Cheng, AB[1], Adam L. Honeybrook, MBBS[1], Alice L. Gray, MD[2], Laurie D. Snyder, MD, MHS[2,3], Scott M. Palmer, MD, MHS[2,3], Ralph Abi Hachem, MD, MS[1] and David W. Jang, MD[1]

SINUS CULTURES

	Pretransplant (n = 34)	Posttransplant (n = 64)
Pseudomonas	21 (62%)	51 (80%)
MRSA	10 (29%)	22 (34%)
Burkholderia	3 (9%)	5 (8%)
Achromobacter	1 (3%)	5 (8%)
Stenotrophomonas	1 (3%)	3 (5)
Other[a]	14 (41%)	33 (52%)
Fungus	4 (12%)	9 (14%)
Mycobacteria	0 (0%)	2 (1%)
No bacteria	2 (6%)	1 (2%)

(Choi, 2017)

Post transplant sinus surgery in lung transplant

Eur Arch Otorhinolaryngol (2013) 270:135–139
DOI 10.1007/s00405-012-2002-y

RHINOLOGY

Posttransplant sinus surgery in lung transplant recipients with cystic fibrosis: a single institutional experience

Domenic Vital · Markus Hofer · Annette Boehler · David Holzmann

- 94 CF patients for lung transplantation (LTx).
- After LTx, patients are treated with at least two antibiotics active against *P. aeruginosa* for a minimal duration of 2 weeks.
- 82 (87%) sinus surgery is performed after clinical recovery from lung transplantation.

Table 2 Sinus microbiology before (preSS) and after (postSS) sinus surgery

	PreSS	PostSS	Eradication rate (%)
S. aureus	6 (8 %)	4 (5 %)	33
P. aeruginosa	61 (79 %)	40 (52 %)	35
A. xyloxidans	4 (5 %)	0	100
S. maltophilia	3 (4 %)	0	100
B. cepacia complex	2 (3 %)	1 (1 %)	50

Vital et al, Eur Arch Otorhinolaryngol (2013) 270:135–139

A protocol involving surgery and daily irrigations decreased the rate of lower airway infection in lung transplant patients with CF.

Holzmann D, Speich R, Kaufmann T, et al. Effects of sinus surgery in patients with cystic fibrosis after lung transplantation: a 10-year experience. *Transplantation.* 2004;77:134–136.

Post transplant sinus surgery in lung transplant

Respiration

Clinical Investigations

Respiration 2013;86:25–31
DOI: 10.1159/000339627

Received: December 19, 2011
Accepted after revision: May 21, 2012
Published online: August 22, 2012

Impact of Sinus Surgery on Pseudomonal Airway Colonization, Bronchiolitis Obliterans Syndrome and Survival in Cystic Fibrosis Lung Transplant Recipients

Domenic Vital[a] Markus Hofer[b] Christian Benden[b] David Holzmann[a]
Annette Boehler[b]

- 94 CF patients were transplante
- 82 (87%) underwent sinus surgery after transplantation
- 66 (65%) patients with pre-transplant PA had persistent PA after transplantation.
- Upper and lower PA is related.
- Patients without PA after transplantation had a significantly better survival rate, and BOS was less frequent with a later onset.

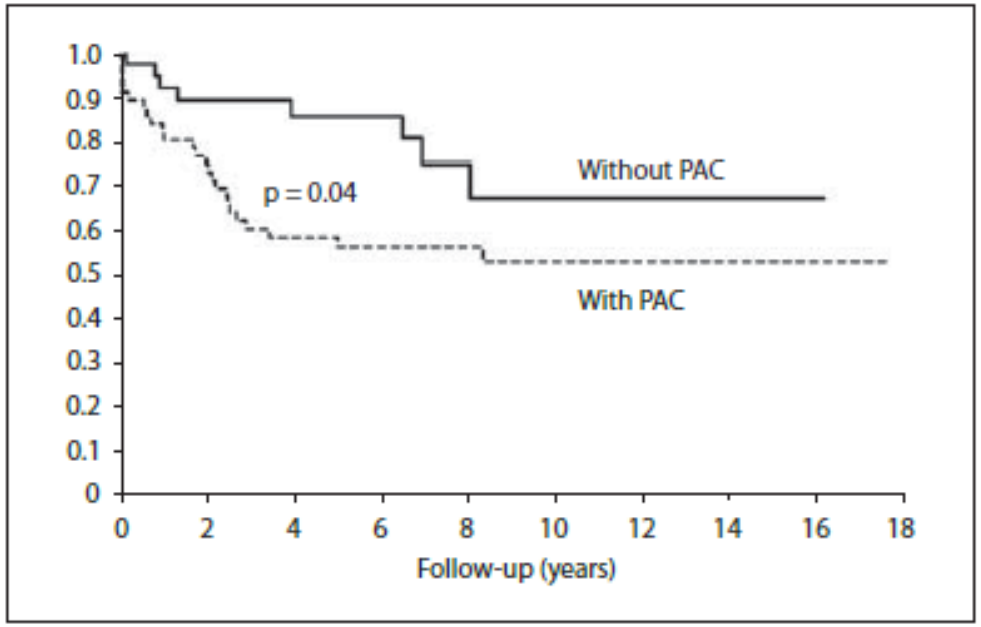


Fig. 1. Survival in patients without PA and BCC 1 year after LTx (without PAC) compared to infected patients with PA or BCC (with PAC). The log rank test was used.

- Sinus surgery and daily nasal douching reduced PA in LTx recipients. Absence of post-transplant PA had a positive impact on post-transplant survival and the development of BOS

Vital *et al,* Respiration 2013;86:25–31

CFTR modulators and sinusitis

International Forum of Allergy & Rhinology / Volume 9, Issue 3 / p. 292-297

ORIGINAL ARTICLE

Ivacaftor improves rhinologic, psychologic, and sleep-related quality of life in G551D cystic fibrosis patients

Justin McCormick MD, Do-Yeon Cho MD, Brooks Lampkin BS, Joshua Richman MD, PhD, Heather Hathorne PhD, Steven M. Rowe MD, MSPH, Bradford A. Woodworth MD

The first study noted improved patient-reported outcomes using the validated 20-item Sino-Nasal Outcome Test (SNOT-20) questionnaire, with significant improvement with respect to rhinological symptoms (e.g., rhinorrhea, postnasal drip, and thick nasal discharge) and psychological symptoms (e.g., fatigue, reduced concentration, and sadness

Clinical Otolaryngology / Volume 40, Issue 1 / p. 16-21

Original Article

Ivacaftor improves appearance of sinus disease on computerised tomography in cystic fibrosis patients with G551D mutation

S.I. Sheikh, F.R. Long, K.S. McCoy, T. Johnson, N.A. Ryan-Wenger, D. Hayes Jr,

A smaller prospective observational study assessed the appearance of sinus disease on computed tomography before and after IVA initiation. Improvement was noted in all but one patient, whereas 4/12 patients moved from a “severe” to a “mild” category

Several case reports have noted more dramatic improvements, including complete reversal of chronic rhinosinusitis and a complete resolution of symptoms.

Chang EH, Tang XX, Shah VS, Launspach JL, Ernst SE, Hilkin B, *et al*. Medical reversal of chronic sinusitis in a cystic fibrosis patient with ivacaftor. *Int Forum Allergy Rhinol* 2015;5:178–181.
Vreede CL, Berkhout MC, Sprij AJ, Fokkens WJ, Heijerman HGM. Ivacaftor and sinonasal pathology in a cystic fibrosis patient with genotype deltaF508/S1215N. *J Cyst Fibros* 2015;14:412–413.
Hayes D Jr, McCoy KS, Sheikh SI. Improvement of sinus disease in cystic fibrosis with ivacaftor therapy. *Am J Respir Crit Care Med* 2014;190:468.

Conclusion: what we know

Bacteria Upper airways	• ***S. aureus, P. aeruginosa,*** coagulase negative staphylococci, and *H. influenzae* dominated in the upper airways of patients with CF.
Age of colonization	• ***S. aureus*** and *H. influenzae* most common in **pediatric patients.** • ***P. aeruginosa*** more frequently in **adult patients**.
Bacteria evolution	• *S. aureus* and *P. aeruginosa*: **SCV** and **antibiotic resistant clones.**
Lung transplant	Persistence of identical *P. aeruginosa* and other bacteria genotype after LTX Sinus surgery and daily nasal douching reduced bacteria in LTX patients

Conclusion: what we still need to know

Standard of care	• The sinus microbiological analysis isn't in the standard of care
Microbiological analysis	• Very difficult site to study • Very heterogeneous methods and a better standardization of procedures and outcomes is needed
Microbiome	• The **microbiome composition** in the **nose differed** considerably from corresponding throat and sputum samples
CFTR modulator	No data about CFTR modulators and sinus bacteriology
Viruses	Few data about viruses in the upper airways

Thanks for your attention

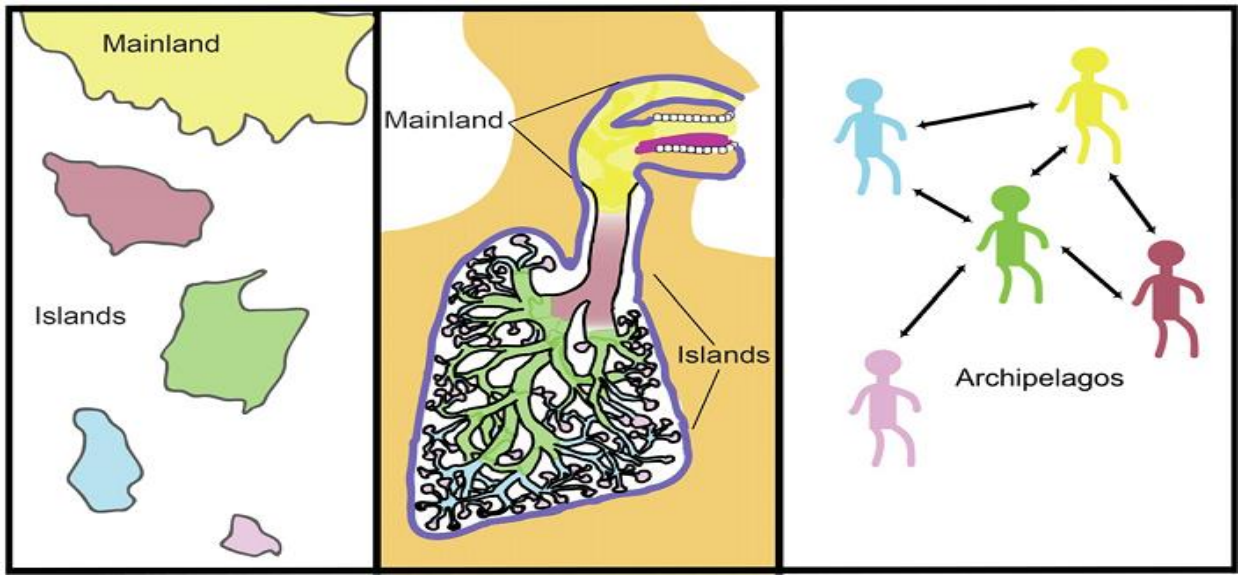
Centro Regionale Toscano per la Ricerca sulla Fibrosi Cistica
AOU Meyer - Firenze

The Upper Respiratory Tract as a Microbial Source for Pulmonary Infections in Cystic Fibrosis

Parallels from Island Biogeography

Katrine L. Whiteson[1], Barbara Bailey[2], Megan Bergkessel[3], Douglas Conrad[4], Laurence Delhaes[5], Ben Felts[6], J. Kirk Harris[7], Ryan Hunter[8], Yan Wei Lim[1], Heather Maughan[9], Robert Quinn[1], Peter Salamon[6], James Sullivan[10], Brandie D. Wagner[11], and Paul B. Rainey[12,13]

Am J Respir Crit Care Med Vol 189, Iss 11, pp 1309–1315, Jun 1, 2014



The respiratory tract measures approximately 50–75 m_2 and is an open door to our environment.

Human airway microbial colonization is likely to display a similar dependence on the distance from the mainland (largely the oral cavity, shown in yellow, which is the richest and most diverse source of microbes with proximity to the lung).

Concordance between upper and lower airway microbiota in infants with cystic fibrosis

Sabine M.P.J. Prevaes[1], Wouter A.A. de Steenhuijsen Piters[1,4], Karin M. de Winter-de Groot[1,4], Hettie M. Janssens[2], Gerdien A. Tramper-Stranders[1], Mei Ling J.N. Chu[1], Harm A. Tiddens[2], Mireille van Westreenen[3], Cornelis K. van der Ent[1], Elisabeth A.M. Sanders[1] and Debby Bogaert[1]

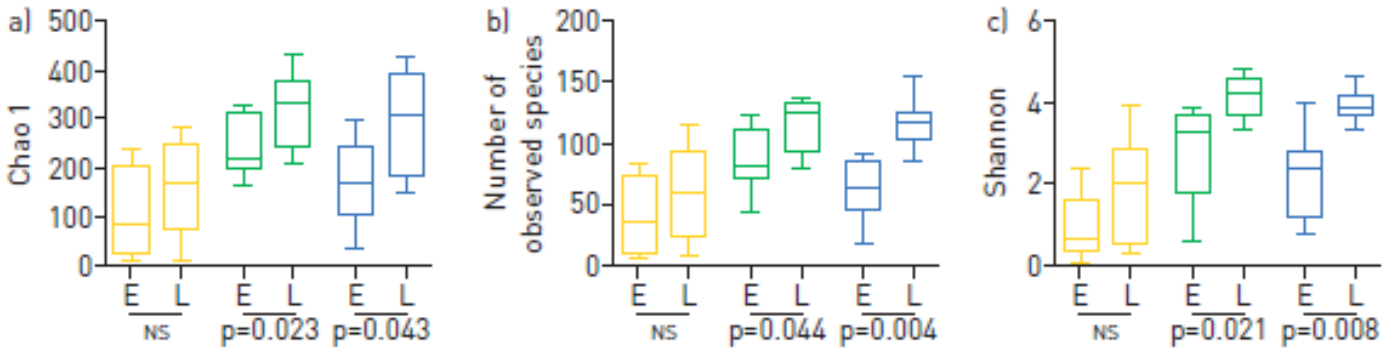


FIGURE 1 Boxplot of α-diversity analyses for nasopharyngeal (NP, yellow), oropharyngeal (OP, green) and bronchoalveolar lavage (BAL, blue) samples over time. a) Chao 1 diversity index, b) number of observed species, c) Shannon diversity index. Eight infants with cystic fibrosis were sampled twice, i.e. when 3–8 months of age (E) and when ⩾9 months (L). Statistical significance in relative abundance between early and later obtained samples was assessed by paired t-tests (p values depicted) and between the niches by repeated ANOVA with Bonferroni post hoc tests (data in main text). NS: not significant.

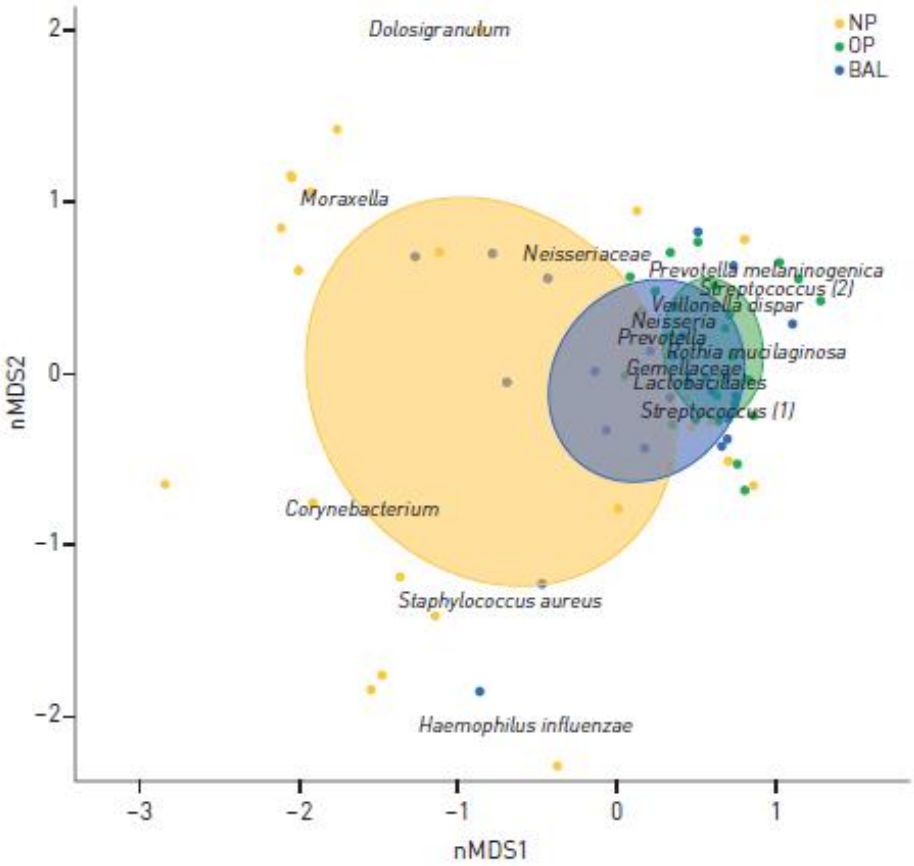


FIGURE 2 Two-dimensional non-metric multidimensional scaling (nMDS) plot of the microbial Community composition in the nasopharyngeal (NP), oropharyngeal (OP) and bronchoalveolar lavage (BAL) samples.

ORIGINAL ARTICLE
CYSTIC FIBROSIS

Longitudinal monitoring of sinonasal and oral bacterial reservoirs to prevent chronic lung infection in people with cystic fibrosis

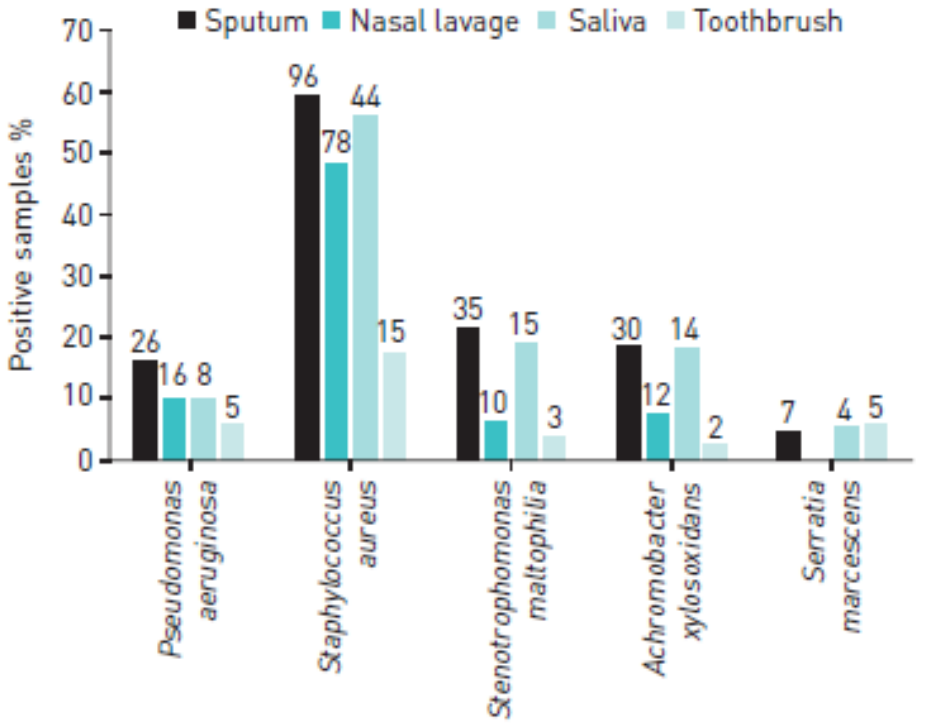
Rebeca Passarelli Mantovani[1,3], Angela Sandri[1,3], Marzia Boaretti[1], Gloria Burlacchini[1], Veronica Li Vigni[1], Mattia Scarazzai[1], Paola Melotti[2], Caterina Signoretto[1,4] and Maria M. Lleo[1,4]

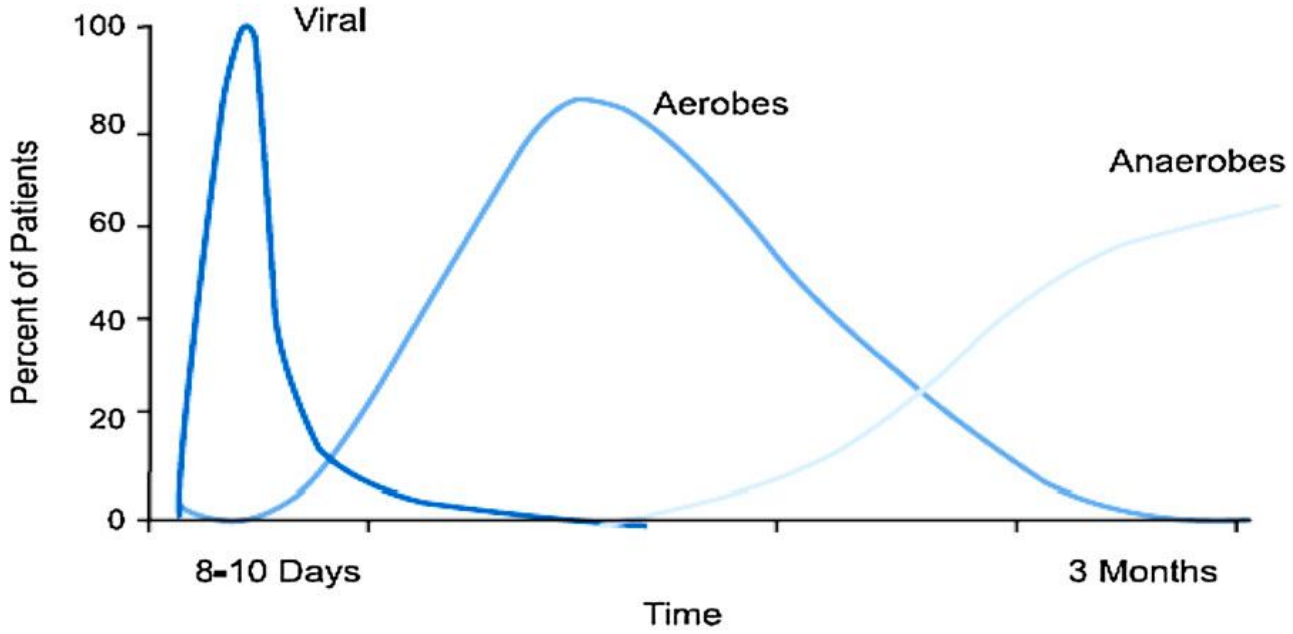
TABLE 1 Characteristics of study patients, including classification based on the status of *Pseudomonas aeruginosa* lung colonisation at the beginning of the study

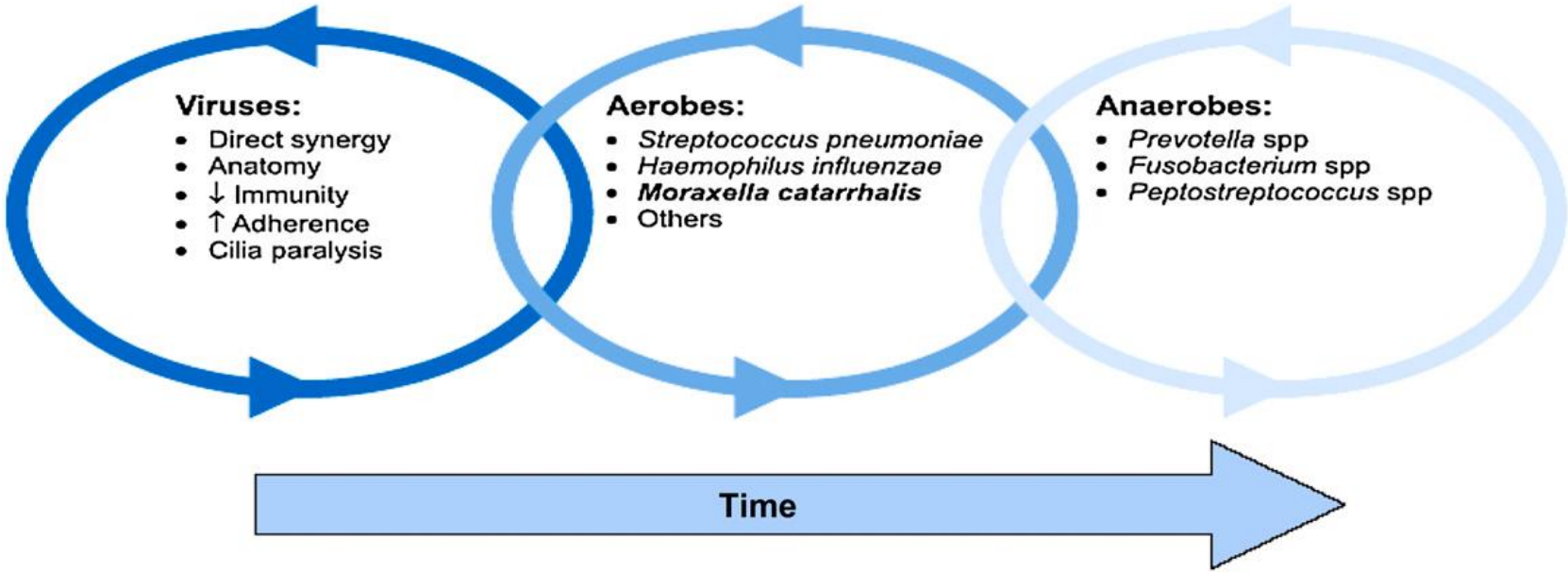
	Study patients			
Group	**AC**	**AN**	**PN**	**PO**
Number of patients	9	15	25	10
Age years	21 (18–24)	22.5 (18–27)	12.5 (7–<18)	12.5 (7–<18)
Male	3 (33.3%)	10 (66.7%)	9 (36%)	4 (40%)
Female	6 (66.7%)	5 (33.3%)	16 (64%)	6 (60%)

Data are presented as number of patients per group mean age and gender numbers (%). AC: adults with chronic *P. aeruginosa* infection; AN: adults free from *P. aeruginosa*; PN: paediatrics free from *P. aeruginosa*; PO: paediatrics with occasional *P. aeruginosa* infection.

50 patients - Not chronic



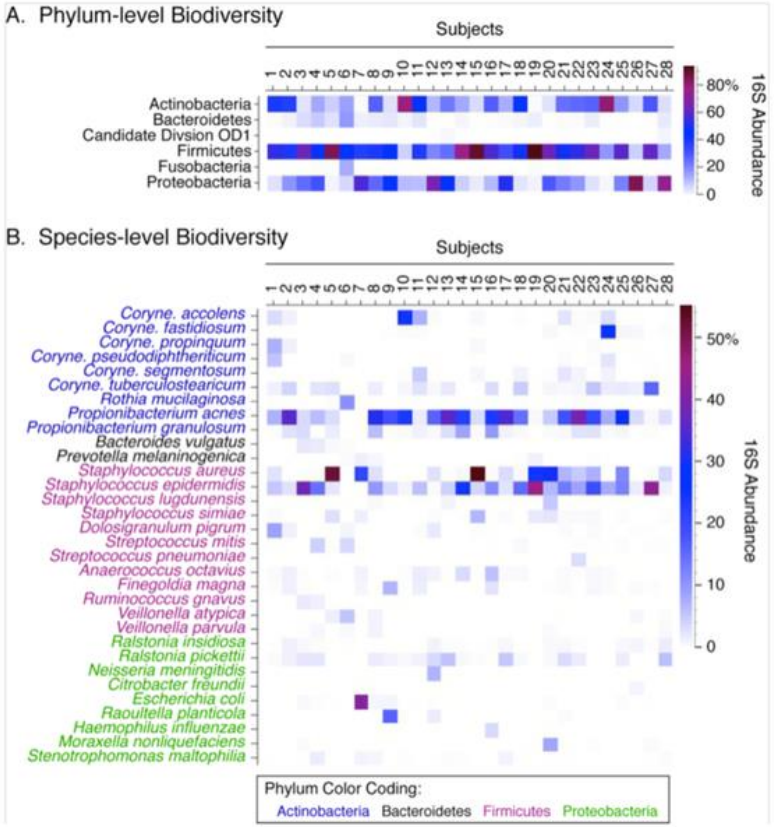




Brooks, Proc Am Thorac Soc Vol 8. pp 90–100, 2011

The Microbiome of the Middle Meatus in Healthy Adults

Figure 1. Phylum- and species-level diversity.



Ramakrishnan VR, Feazel LM, Gitomer SA, Ir D, Robertson CE, et al. (2013) The Microbiome of the Middle Meatus in Healthy Adults. PLOS ONE 8(12): e85507. https://doi.org/10.1371/journal.pone.0085507
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0085507