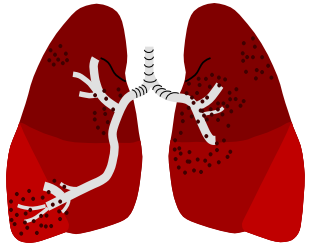
Primer Silyer Diskinezide

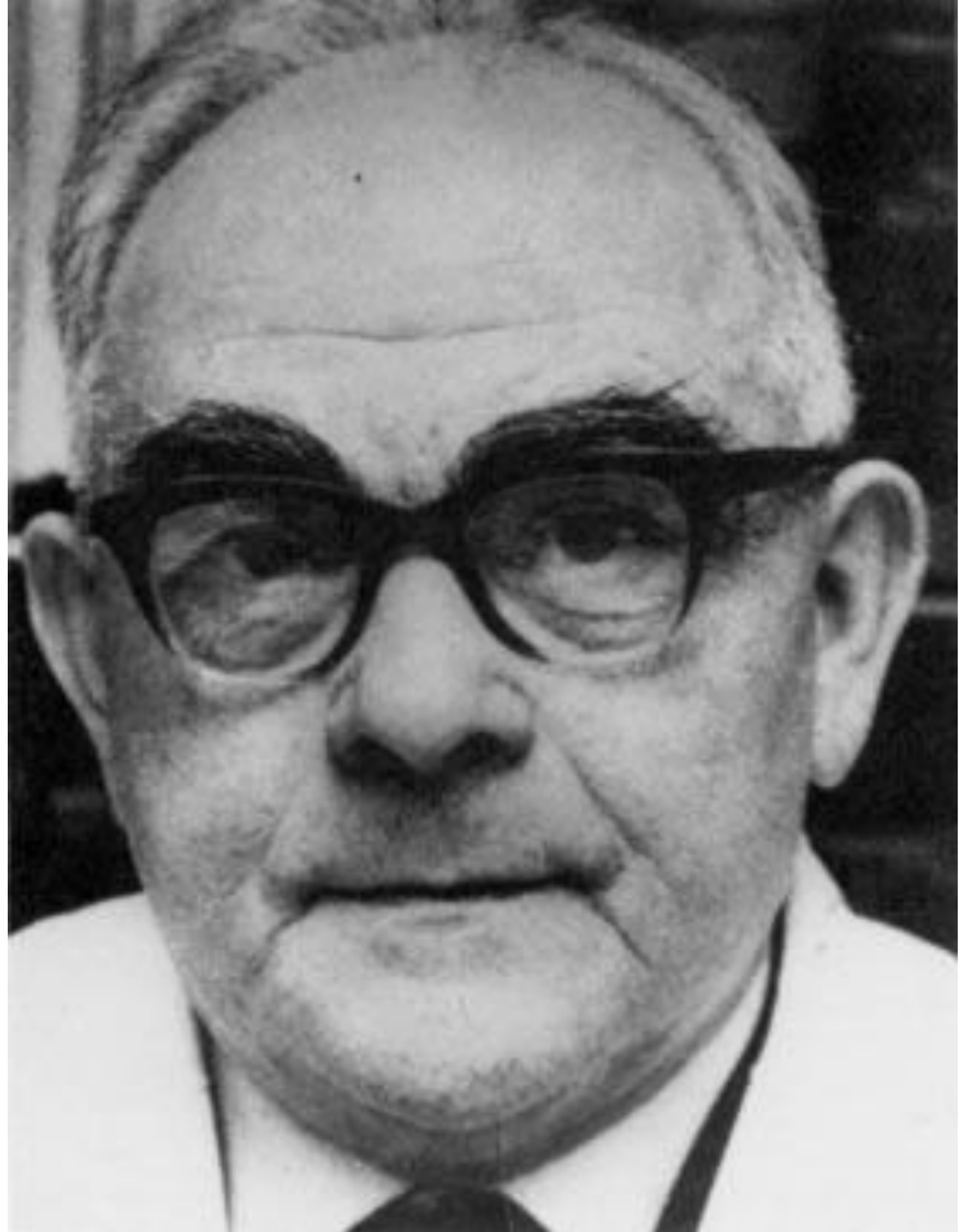
Güncel Bilgiler

Dr. Bulent KARADAG



PCD

1. Tanı
2. Klinik
2. QoL
3. Genetik
4. SFT
5. Tedavi



PCD Tanısı neden zor?

Nadir bir hastalık

Farkındalık düşük

Semptomlar nonspresifik

Kolay ve yaygın bir tanı yöntemi yok

Çoğu merkezde tanı aracı yok

Tanı yöntemleri uzmanlık istiyor ve pahalı

PCD’li hastaların en az yarısında dekstrokardi yok.

PCD Tanısı neden zor?

Tanı genellikle bronşektazi ve işitme kaybı geliştikten sonra konuluyor.

Standardize bir tanı akış şeması yok

Yeni tekniklerde standardizasyon ihtiyacı var.

Diagnostic Methods in Primary Ciliary Dyskinesia

Jane S. Lucas [1,2,*], Tamara Paff [3,4], Patricia Goggin [1,2], Eric Haarman [3]

Paediatric Respiratory Reviews 18 (2016) 8–17

Çeşitli tanısal yöntemler

Herbirinin gücü ve kısıtlılıkları var

Altın standart test YOK

İleri derecede uzmanlaşmış merkezlere ihtiyaç var.

Diagnostic Methods in Primary Ciliary Dyskinesia

Jane S. Lucas [1,2,*], Tamara Paff [3,4], Patricia Goggin [1,2], Eric Haarman [3]

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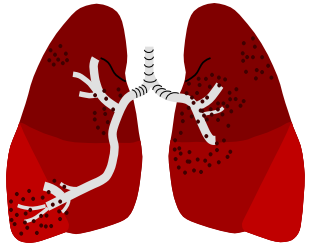
Table 2
Who to refer for diagnostic testing.

Patients with early onset of recurrent respiratory tract symptoms and any of the following: 1. Situs inversus (SI) totalis or any heterotaxic syndrome (approximately 50% have normal situs) 2. Neonatal nasal congestion and/or unexplained neonatal distress 3. Positive family history for PCD 4. Males with dysmotile sperm 5. Persistent productive cough/bronchiectasis/severe upper airway after more common causes like allergies, asthma, immune deficiencies and CF have been excluded. 6. Early onset of the combination of both severe upper and lower respiratory tract infections 7. Persistent/frequent intermittent serous otitis media (glue ear) associated with respiratory symptoms



PCD Tanısı

1.Faz-kontrast optik mikroskop için nasal fırça

2. Transmission elektron mikroskopi (TEM)

3.Nazal nitrik oksit (nNO)

4. High speed videomicroskopi (HVMA)

5. Immunofloresan mikroskopi

6. Genetik

7. Hücre kültürü

8. Izotopik mukosilyer klirens

Diagnosis of primary ciliary dyskinesia: When and how?

J.-J. Braun[a,b,*], N. Boehm[c], C. Metz-Favre[b], I. Koscinski[d], M. Teletin[d], C. Debry[a]

European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017)

Sıklık: 1/10.000-40.000

Semptom: non-spesifik

Faz kontrast mikroskopi için nazal fırçalama - Hızlı, kolay, ucuz

Yorumlamak için uzmanlaşma istiyor.

Erken tanı için standardizasyon yok.

Diagnosis of primary ciliary dyskinesia: When and how?

J.-J. Braun[a,b,*], N. Boehm[c], C. Metz-Favre[b], I. Koscinski[d], M. Teletin[d], C. Debry[a]

European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017)

Nazal silyer fırçalama:

Burun spreyi almıyor olmalı, lokal anestezi olmamalı,

sentetik bir fırça ile inferior türbinatların 2/3 ünden alınmalı

Hızlıca incelenmeli

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European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017)

Normal CBF - 9-12 Hz

Patolojik durumlar – 1-3 Hz veya hareketsiz

HSVMA ile iyi korele

Diagnosis of primary ciliary dyskinesia: When and how?

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European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017)

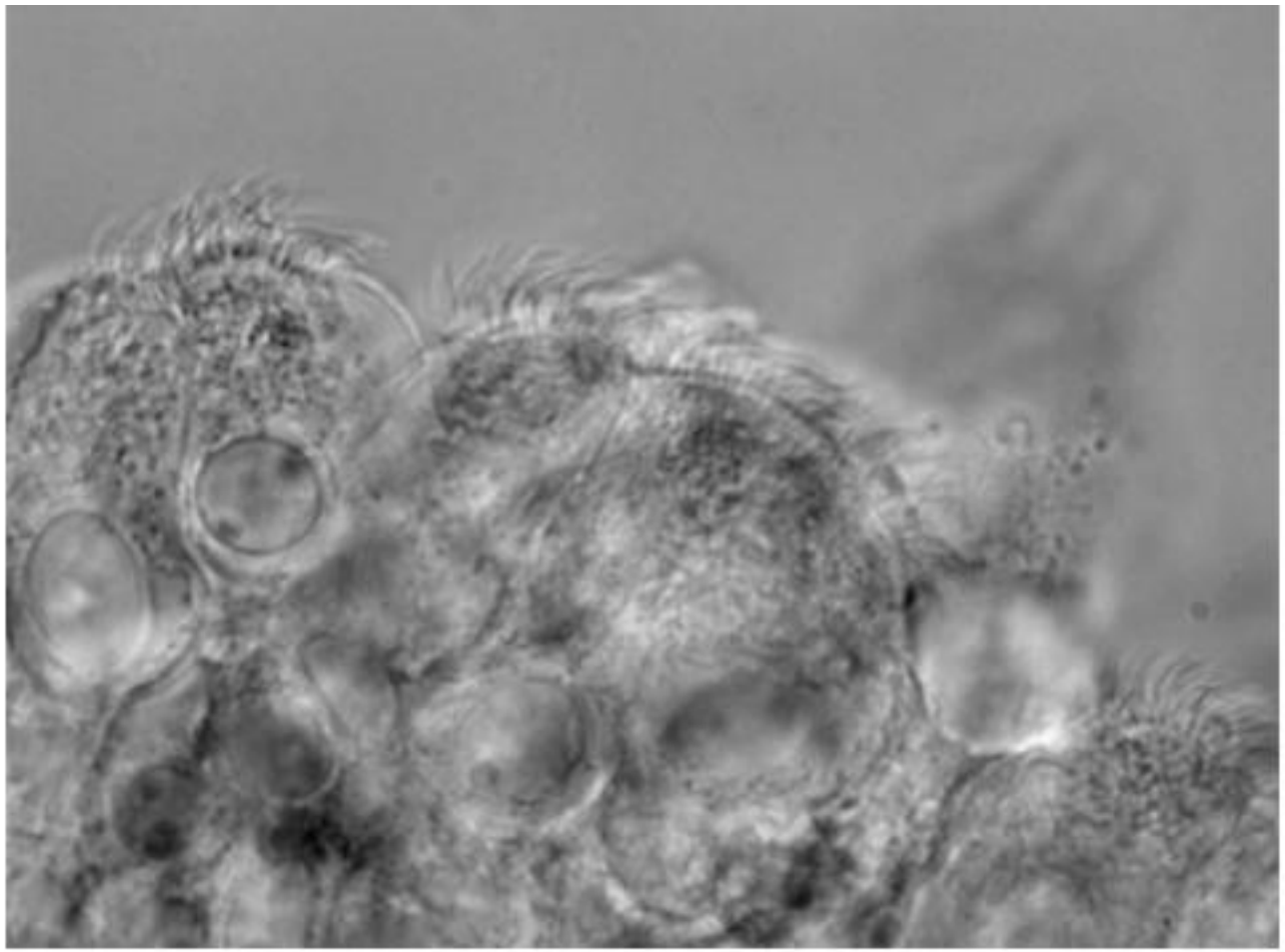
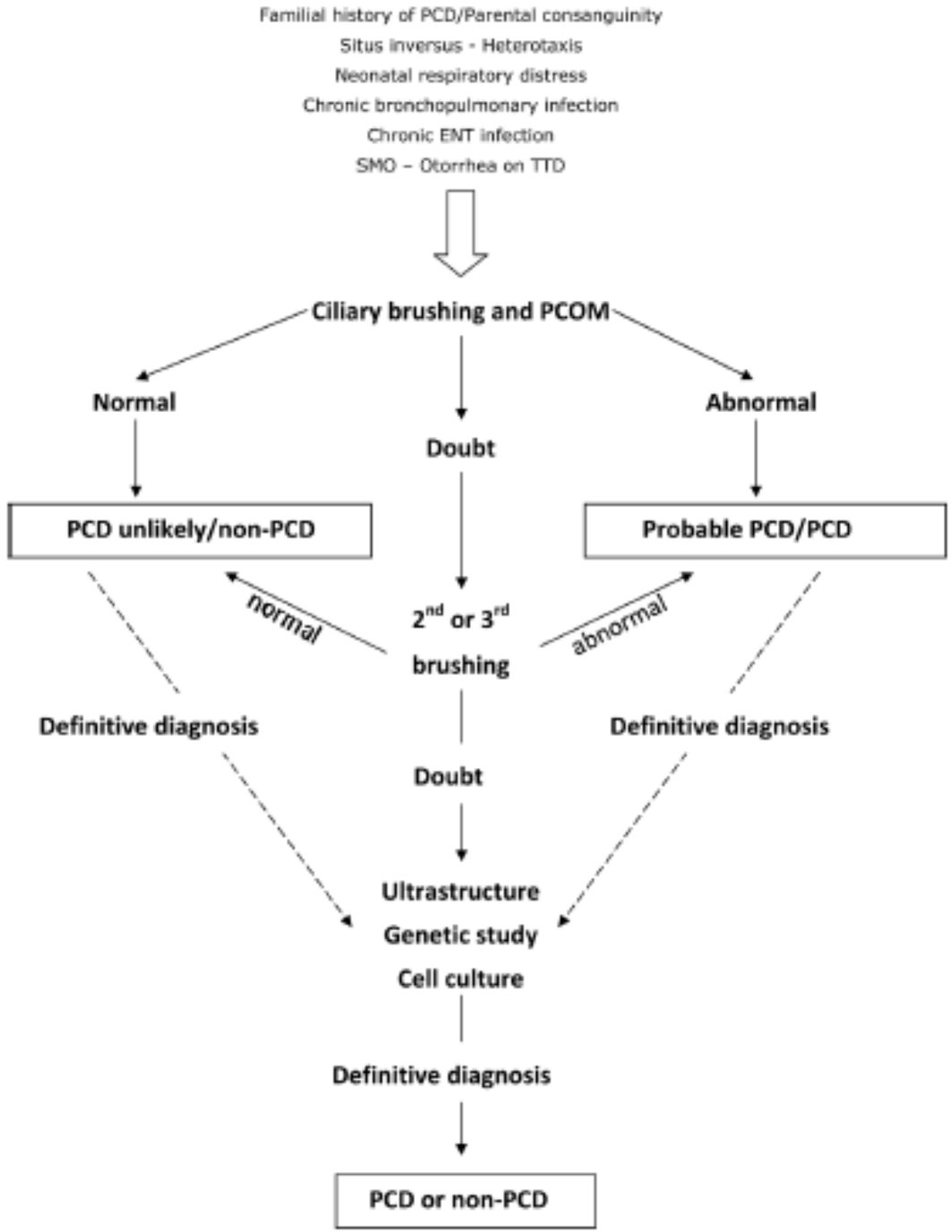
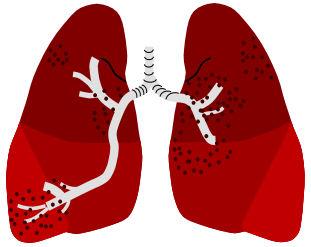


Fig. 1. Normal cilia from nasal brushing on phase-contrast optical microscopy after trypan-blue staining.

CLINICAL SUSPICION OF PCD AFTER DIFFERENTIAL DIAGNOSIS





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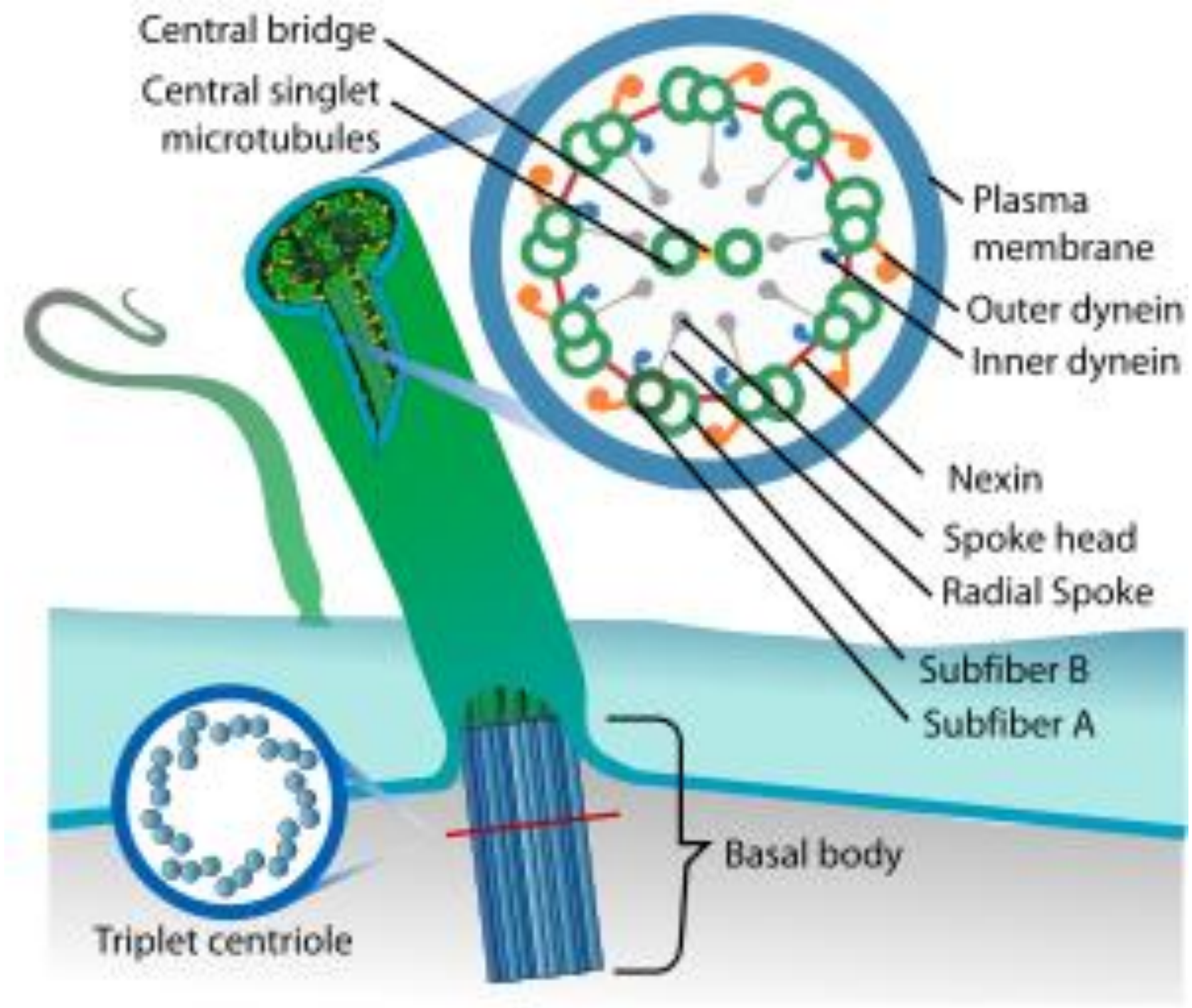

Central bridge
Central singlet microtubules
Plasma membrane
Outer dynein
Inner dynein
Nexin
Spoke head
Radial Spoke
Subfiber B
Subfiber A
Basal body
Triplet centriole

Diagnosis of primary ciliary dyskinesia: potential options for resource-limited countries

Eur Respir Rev 2017; 26: 160058

Nisreen Rumman[1,2], Claire Jackson[2,3], Samuel Collins[2,3], Patricia Goggin[3], Janice Coles[2,3] and Jane S. Lucas[2,3]

The process of preparing ciliated epithelial cells for testing by TEM is lengthy. Samples are immersed immediately after collection in 3% glutaraldehyde fixative and processed to resin blocks. Ultrathin sections are cut, placed on copper grids and stained with heavy metals to enhance contrast. Cilia are observed at high magnification (>60 000×) in transverse and longitudinal section, and the number of defects in microtubular arrangement and the dynein arms are counted. There is no global consensus to standardise the analysis of the cilia. In the UK, quantitative analysis of 100–300 cilia is usual [51, 67], while others analyse at least 30 ciliary cross-sections containing >60 high-quality cilia images [12].

Diagnosis of primary ciliary dyskinesia: potential options for resource-limited countries

Eur Respir Rev 2017; 26: 160058

Nisreen Rumman[1,2], Claire Jackson[2,3], Samuel Collins[2,3], Patricia Goggin[3], Janice Coles[2,3] and Jane S. Lucas[2,3]

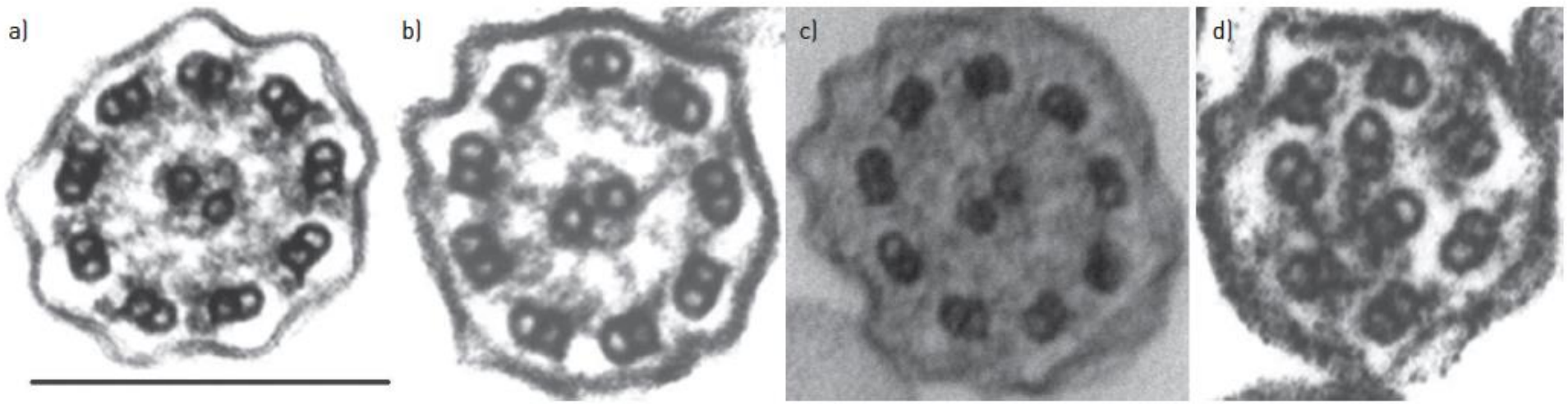
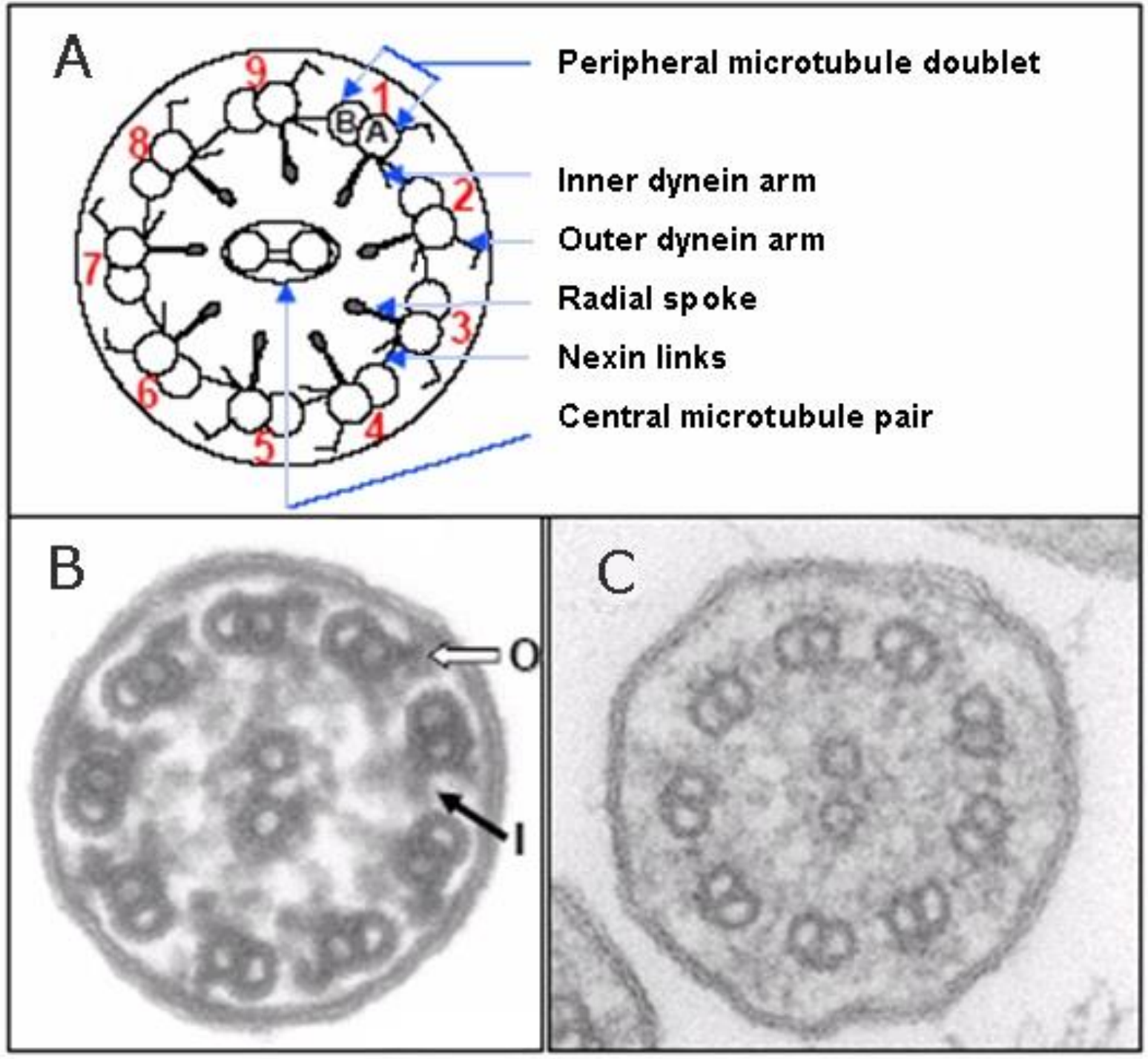
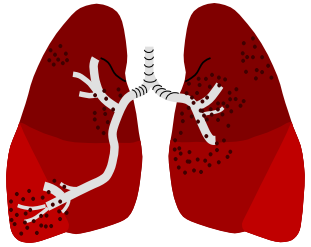


FIGURE 1 Transmission electron micrographs of human airway cilia in transverse section of a) normal subjects, and examples of hallmark defects depicting b) the absence of outer dynein arms, c) the combined absence of inner and outer dynein arms, and d) inner arm absence combined with microtubular disarrangement. Scale bar=200 nm.


A
9
1
8
2
7
3
6
4
5
B
A
Peripheral microtubule doublet
Inner dynein arm
Outer dynein arm
Radial spoke
Nexin links
Central microtubule pair
B
O
I
C



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7. Hücre kültürü

8. Izotopik mukosilyer klirens

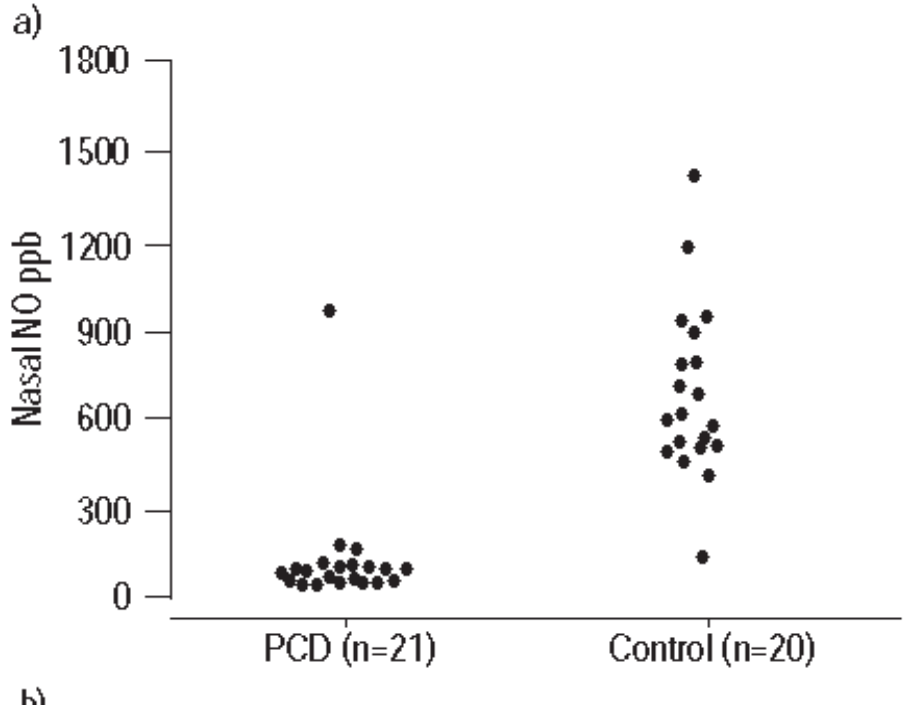
Nasal and lower airway level of nitric oxide in children with primary ciliary dyskinesia

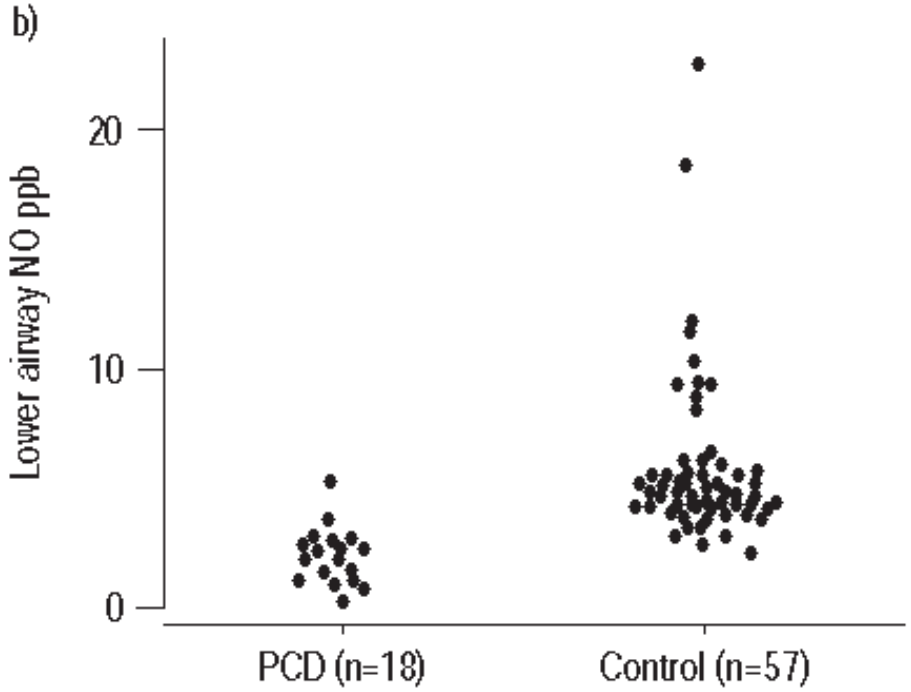
B. Karadag, A.J. James, E. Gültekin, N.M. Wilson, A. Bush

Eur Respir J 1999; 13: 1402–1405

Nazal NO – PCD'li hastalarda sağlıklı çocuklara göre belirgin düşük (n=21) (97 vs 664, $p<0.0001$).

Exhale NO- PCD'de belirgin düşük (2.17 vs 5.94 ppb, $p<0.0001$).


a)
Nasal NO ppb
1800
1500
1200
900
600
300
0
PCD (n=21)
Control (n=20)


b)
Lower airway NO ppb
20
10
0
PCD (n=18)
Control (n=57)

Nasal nitric oxide screening for primary ciliary dyskinesia: systematic review and meta-analysis

Eur Respir J 2014; 44: 1589–1599 |

Samuel A. Collins[1,2,3], Kerry Gove[1,2,3], Woolf Walker[1,2,3] and Jane S.A. Lucas[1,2,3]

TABLE 3 Summary of studies presenting sensitivity and specificity of their cut-off values for nNO for PCD *versus* healthy patients

Study	Subjects n	nNO cut-off nL·min^{-1}	Sensitivity %	Specificity %
Mateos-Corral *et al.* [26], 2011#	44	60.8	100	100
Narang *et al.* [7], 2002	157	25	75	96
		62.5	97	90
Horvath *et al.* [8], 2003	102	46.8	93	95
Corbelli *et al.* [10], 2004	34	126	94	88
Marthin and Nielsen [25], 2011	94	Breath hold 52.5	91.1	100
		Oral exhalation 72.6	94.3	100
		Tidal breathing 47.4	94.4	100
Leigh *et al.* [19], 2013	227	77	98	>99.9
Marthin and Nielsen [17], 2013	57	78.6	100	100
Harris *et al.* [32], 2014	47	38	100	95
Boon *et al.* [31], 2014	226	90	89.5	87.3

How to use nasal nitric oxide in a child with suspected primary ciliary dyskinesia

Kim Simpson,[1] Malcolm Brodlie[1,2]

Arch Dis Child Educ Pract Ed 2017;**0**:1–5. doi:10.1136/archdischild-2016-311468

Box 1 When should I investigate a child for primary ciliary dyskinesia?

- Several of the following: persistent wet cough, situs anomalies, congenital cardiac defects, persistent rhinitis, chronic middle ear disease with or without hearing loss, a term infant with neonatal upper and lower respiratory symptoms or neonatal intensive care admittance
- Patients with normal situs presenting with other features of primary ciliary dyskinesia
- Siblings of children with primary ciliary dyskinesia
- Symptoms of primary ciliary dyskinesia and predictive tool such as PICADAR score >5 (see table 1)

Adapted from Lucas *et al* (2016).[5]

How to use nasal nitric oxide in a child with suspected primary ciliary dyskinesia

Arch Dis Child Educ Pract Ed 2017;**0**:1–5. doi:10.1136/archdischild-2016-311468

Kim Simpson,[1] Malcolm Brodlie[1,2]

NO- Düz kaslarda gevşeme ve vazodilatasyon yapar.

PCD'de nNO neden düşük ?

-Metabolizmada artış

-Havayolu epitel hücrelerinde NO üretim azlığı

-Paranazal sinüslerde tıkanmaya bağlı NO düşüklüğü

-Sinüslerde üretim azlığı

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Duyarlılık ve özgüllük değişik yöntemlerde, cihazlarda ve yaşlarda farklı.

Tanısal eşik değeri? 77 nL/min okul çağı çocuklarında

How to use nasal nitric oxide in a child with suspected primary ciliary dyskinesia

Kim Simpson,[1] Malcolm Brodlie[1,2]

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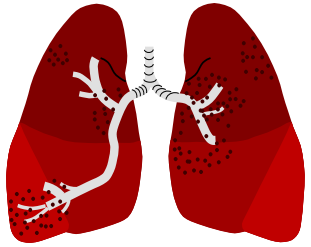
Kemiluminesan cihazlar pahalı

Taşınabilir cihazlar ucuz ve kullanışlı

Karşılaştırmalı çalışma yok

SUT'ta geri ödemede değil



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A reach-out system for video microscopy analysis of ciliary motions aiding PCD diagnosis

Israel Amirav[1,7*], Huda Mussaffi[2], Yehudah Roth[3], Miriam Schmidts[4,5], Heymut Omran[6], Claudius Werner[6]
for the Israeli PCD Consortium Investigators

BMC Research Notes (2015) 8:71

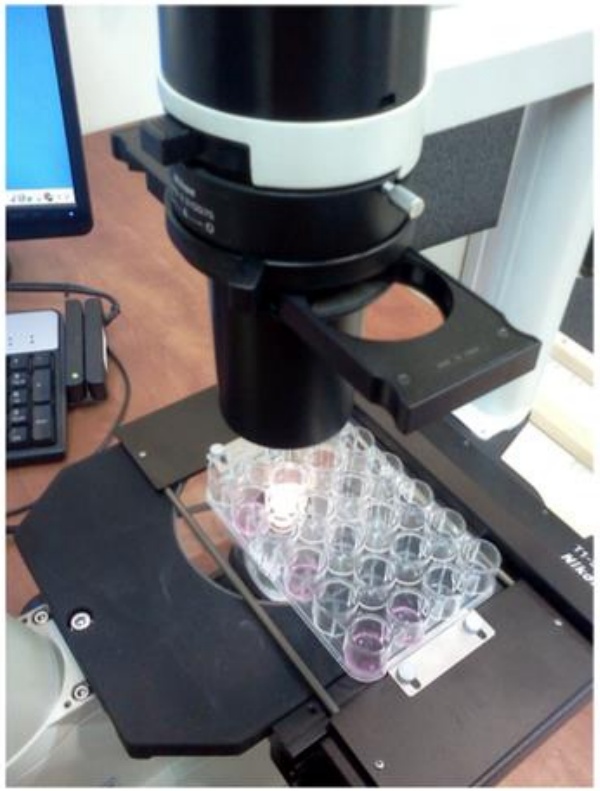
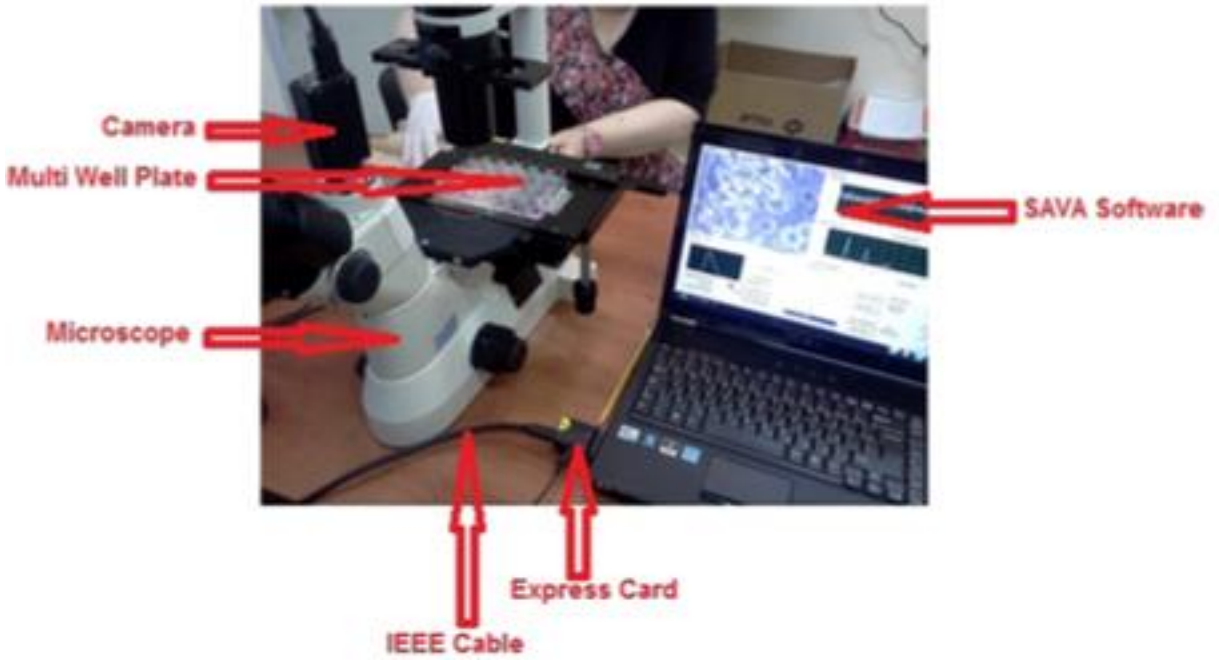


Figure 1 Use of a 24 well plate for microscopy.



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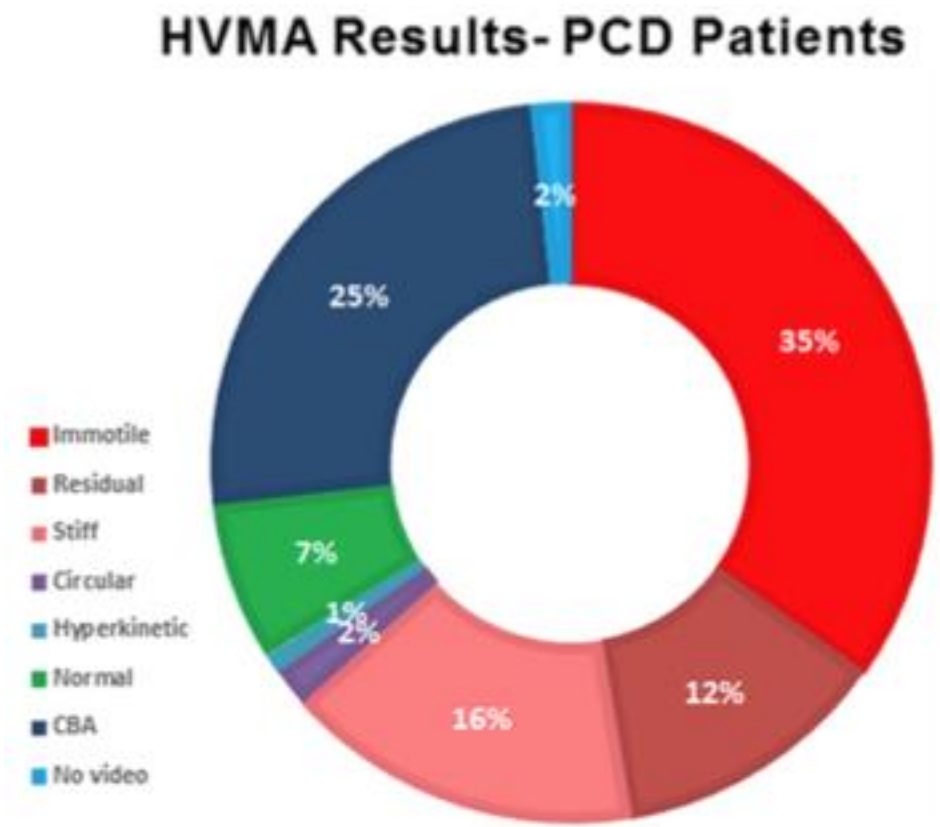
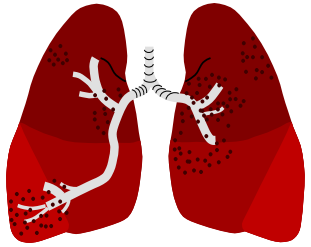


Figure 4 HVMA post-hoc results (percentage of each category) in PCD patients (n = 112).



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Ultrastructural Defect	Gene	Immunofluorescence
Outer dynein arm defect	*DNAH5* *DNAI1* *ARMC4* *CCDC114* *TXNDC3 (NME8)* *DNAI2* *DNAL1* *CCDC151*	DNAH5 Absent
Inner and outer dynein arm defect	*C21orf59* *ZYMND10* *CCDC103* *DNAFF2 (KTU)* *DNAFF1 (LRRC50)* *LRRC6* *DNAFF3 (C19orf31)* *HEATR2* *DYX1C1* *SPAG1*	DNAH5 Absent DNALI1 Absent
Central complex / transposition defect	*RSPH4A* *RSPH9* *RSPH1* *RSPH3*	RSPH9, RSPH4A,RSPH1 absent RSPH9 absent RSPH9, RSPH1 absent All present
Microtubular disorganisation with loss of inner dynein arm	*CCDC39* *CCDC40*	DNALI1 Absent GAS 8 Absent
Microtubular disorganisation with present inner dynein arms	*CCDC65* *CCDC164* *GAS8*	GAS 8 Absent
Normal ciliary ultrastructure	*HYDIN* *DNAH11* *OFD1* *RPGR*	All present
Ciliary 'aplasia'	*CCNO* *MCIDAS*	All present DNAH5& LI1Absent

Electron microscopy defect	Absent or mislocalised antibody	Number of patients with PCD tested (total n=35)
Outer dynein arm defect	DNAH5	14
Outer and inner dynein arm defect	DNAH5 DNALI1	10
Inner dynein arm and microtubular disorganisation defect	DNALI1 GAS8	7
Transposition defect / central pair absence	RSPH4A RSPH9 RSPH1	4

		Standard diagnosis	
		PCD positive	PCD negative
Immunofluorescence diagnosis	PCD positive	22	0
	PCD negative	3	252

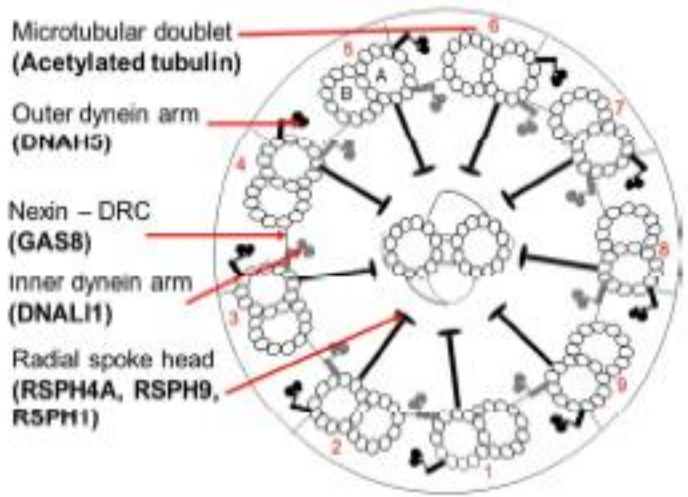


Figure 1: Diagram of the ultrastructure of a motile cilium in transverse section. Labels indicate ultrastructural features targeted by immunofluorescence with corresponding antibodies (bold text).

346x559mm (72 x 72 DPI)

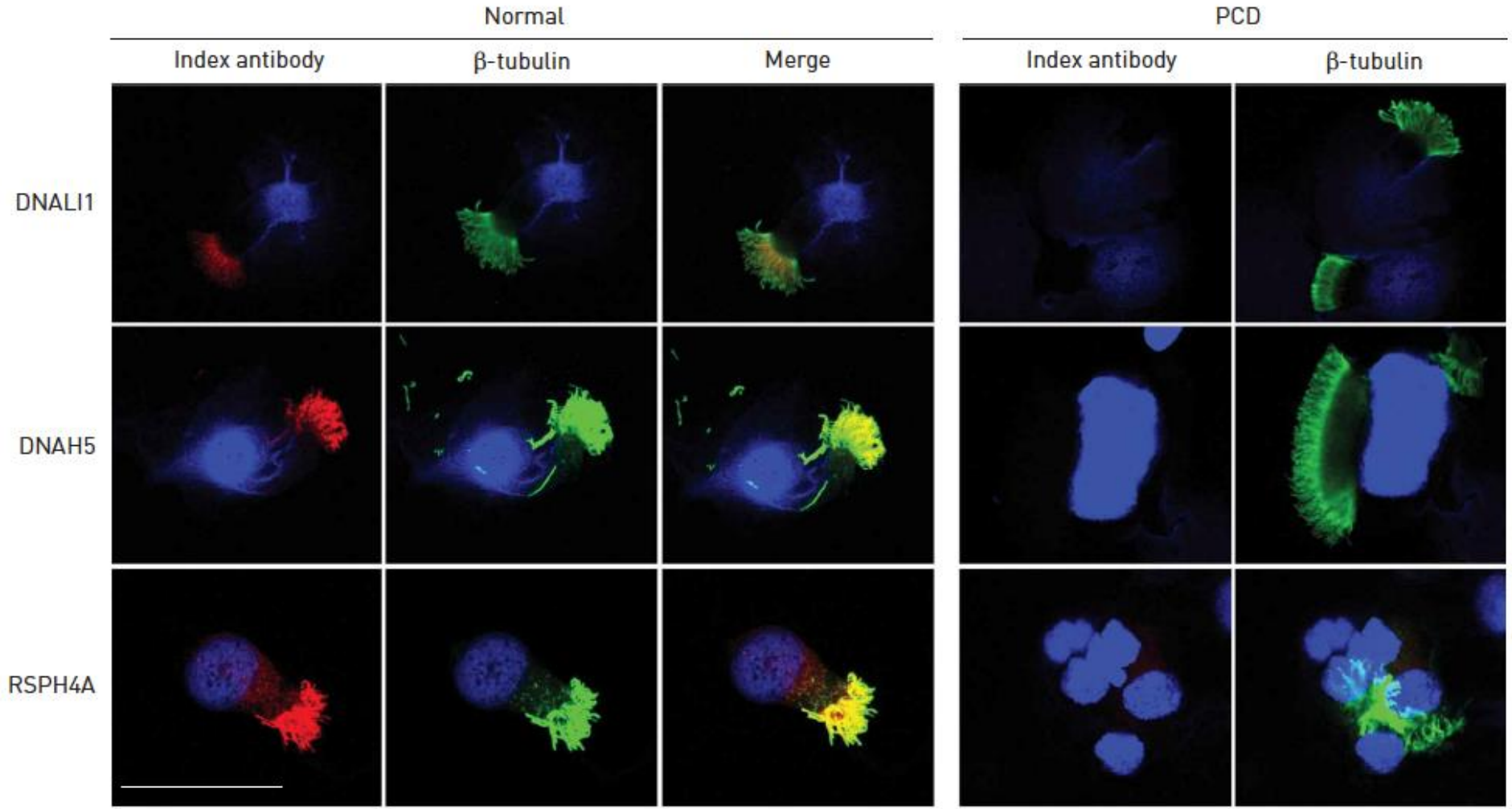
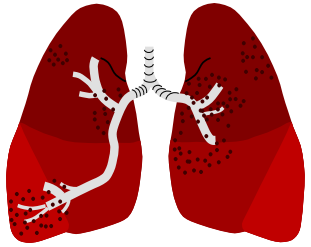


FIGURE 2 Fluorescence confocal micrograph images of human ciliated nasal epithelial cells showing presence (normal) or absence (examples were from different primary ciliary dyskinesia (PCD) patients) of ciliary proteins by labelling with antibodies against DNALI1 (inner dynein arm), DNAH5 (outer dynein arm) and RSPH4A (radial spoke head) in red. β-tubulin was used as a consistent cilium marker (green) and cell nuclei were counterstained with DAPI (blue). Scale bar=40 μm.



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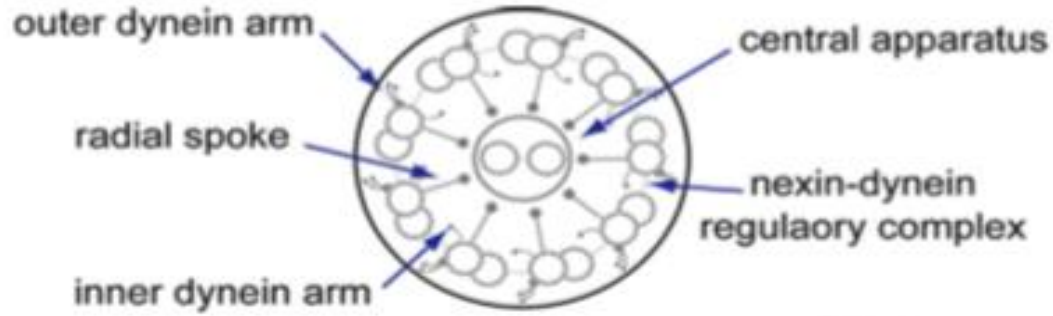
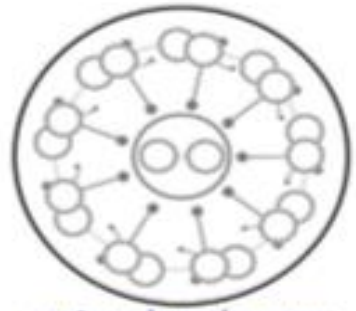
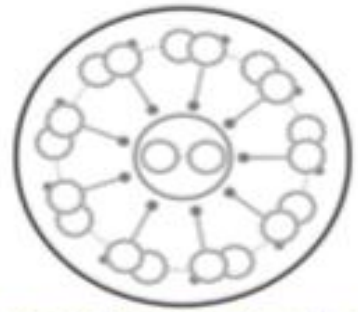
Paediatric Respiratory Reviews 18 (2016) 18–24

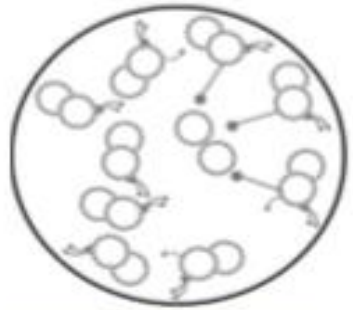




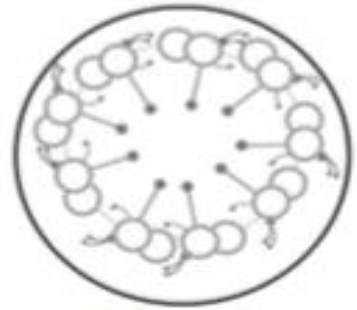
outer dynein arm
DNAH5, DNAI1, DNAI2
TXNDC3, DNAL1, ARMC4,
CCDC114, CCDC151



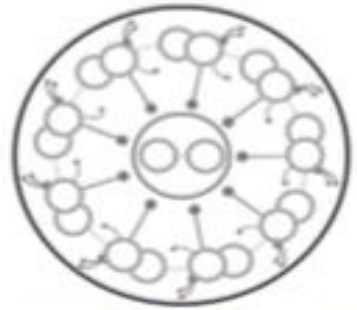
outer and inner dynein arm
LLRC6, DNAAF1, DNAAF2,
DNAAF3, CCDC103, ZMYND10,
HEATR2, DYX1C1, SPAG1, C21orf59



inner dynein arm
and axonemal
dysorganization
CCDC39, CCDC40



central apparatus
HYDIN
with disorganization
RSPH4A, RSPH9



normal ultrastructure
DNAH11, CCDC164,
CCDC65, RSPH1
with rare cilia
CCNO, MCIDAS

Ciliary beat pattern and frequency in genetic variants of primary ciliary dyskinesia

Eur Respir J 2014; 44: 1579–1588 |

Johanna Raidt[1], Julia Wallmeier[1], Rim Hjeij[1], Jörg Große Onnebrink[1], Petra Pennekamp[1], Niki T. Loges[1], Heike Olbrich[1], Karsten Häffner[2], Gerard W. Dougherty[1], Heymut Omran[1] and Claudius Werner[1]

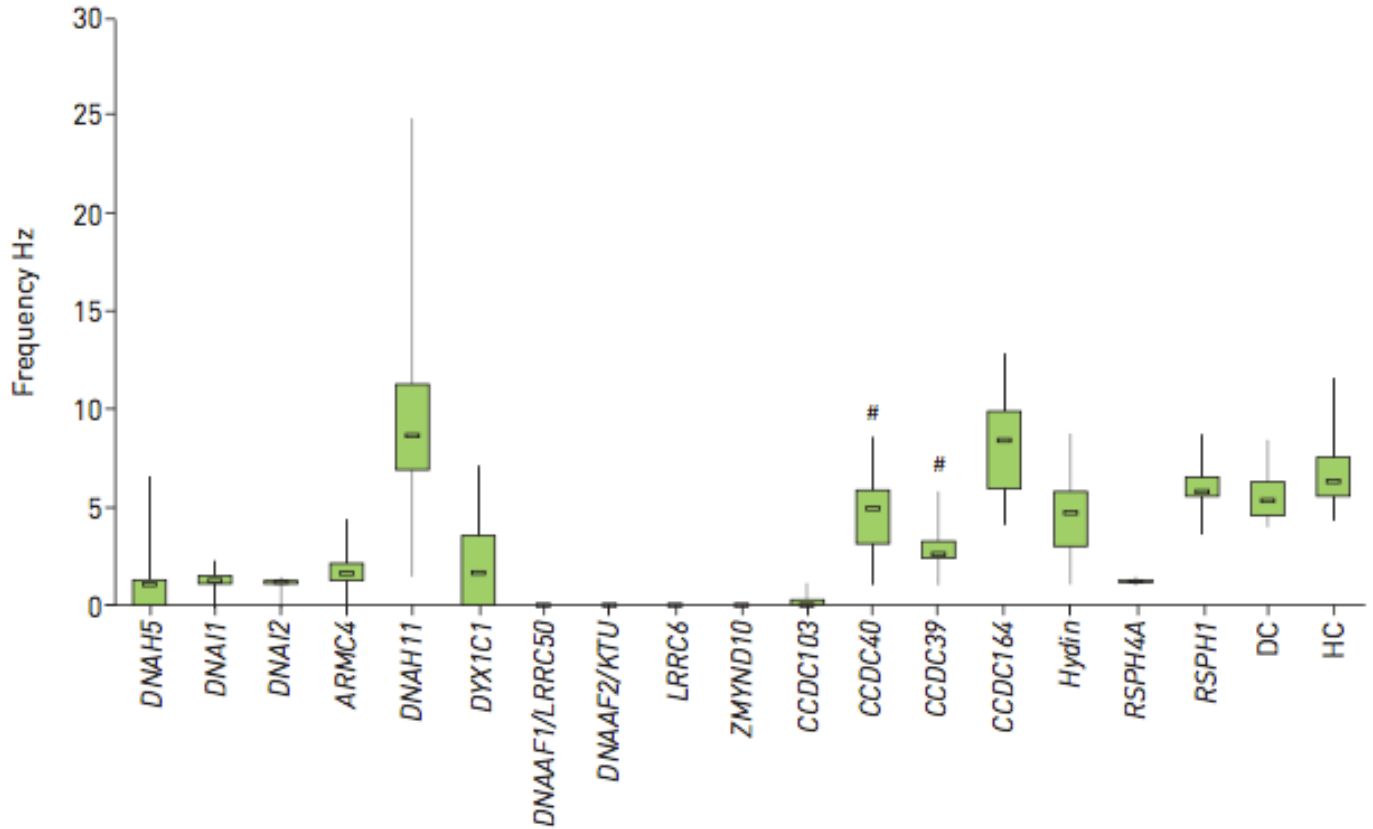


FIGURE 1 Boxplot illustrating ciliary beat frequency (CBF) measured using high-speed video-microscopy analysis in individuals with genetically confirmed primary ciliary dyskinesia sorted according to gene. The bars indicate median CBF

Genetics and biology of primary ciliary dyskinesia

Amjad Horani [1,*], Thomas W. Ferkol [1,2], Susan K. Dutcher [3,2], Steven L. Brody [4]

Paediatric Respiratory Reviews 18 (2016) 18–24

FUTURE DIRECTIONS

- Design and use of DNA microchips for the rapid diagnosis of PCD.
- Genotype-phenotype mapping to understand the heterogeneity of PCD.
- Elucidation of the mechanism of cilia assembly and function to allow for gene specific therapies.

PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia

Laura Behan[1,2,3], Borislav D. Dimitrov[4,5], Claudia E. Kuehni[6], Claire Hogg[7], Mary Carroll[1,2], Hazel J. Evans[1], Myrofora Goutaki[6], Amanda Harris[1], Samantha Packham[1], Woolf T. Walker[1,2,4] and Jane S. Lucas[1,2,4]

Eur Respir J 2016; 47: 1103–1112 |

TABLE 3 Factors for the prediction of primary ciliary dyskinesia selected by step-wise logistic regression

	Regression coefficient	Odds ratio (95% CI)	p-value	Simplified regression coefficient tool #
Situs inversus	3.54	34.48 (11.6–101.8)	<0.001	4
Gestational age (full term)	2.20	9.06 (2.9–27.4)	<0.001	2
Neonatal chest symptoms	1.91	6.79 (2.7–16.7)	<0.001	2
Neonatal unit	1.90	6.70 (2.7–16.3)	<0.001	2
Congenital cardiac defect	1.57	4.83 (1.1–22.2)	0.043	2
Rhinitis	1.22	3.40 (1.2–8.9)	0.013	1
Ear and hearing symptoms	0.95	2.59 (1.2–5.8)	0.021	1

PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia

PICADAR		
Does the patient have a daily wet cough that started in early childhood?	**Yes** – complete PICADAR **No – STOP**. PICADAR is not designed for patients without a wet cough	
1. Was the patient born pre-term or full term?	Term	2
2. Did the patient experience chest symptoms in the neonatal period (*e.g.* tachypnoea, cough, pneumonia)?	Yes	2
3. Was the patient admitted to a neonatal unit?	Yes	2
4. Does the patient have a situs abnormality (situs inversus or heterotaxy)?	Yes	4
5. Does the patient have a congenital heart defect?	Yes	2
6. Does the patient have persistent perennial rhinitis?	Yes	1
7. Does the patient experience chronic ear or hearing symptoms (*e.g.* glue ear, serous otitis media, hearing loss, ear perforation)?	Yes	1
	Total score =	

FIGURE 2 PICADAR is a predictive score with seven simple questions to predict the likelihood of having primary ciliary dyskinesia (PCD). It can be used in any patients with chronic respiratory symptoms starting in early childhood. The total score is calculated and the individual probability of having PCD diagnosis can be estimated from the probability curve shown in figure 3.

PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia

Laura Behan[1,2,3], Borislav D. Dimitrov[4,5], Claudia E. Kuehni[6], Claire Hogg[7], Mary Carroll[1,2], Hazel J. Evans[1], Myrofora Goutaki[6], Amanda Harris[1], Samantha Packham[1], Woolf T. Walker[1,2,4] and Jane S. Lucas[1,2,4]

TABLE 5 The distribution of scores (≤5, 6–9 and ≥10) in primary ciliary dyskinesia (PCD) positive and PCD-negative participants using PICADAR in the derivation group (n=288) and in the validation group (n=157) (only children <18 years included)

	Derivation group		Validation group	
	PCD-positive	PCD-negative	PCD-positive	PCD-negative
Subjects	50	238	79	78
≤5	3 (6.0)	189 (79.4)	15 (18.7)	59 (75.6)
6–9	29 (58.0)	48 (20.2)	42 (53.3)	16 (20.5)
≥10	18 (36.0)	1 (0.4)	22 (28.0)	3 (3.8)

PICADAR: a diagnostic predictive tool for primary ciliary dyskinesia

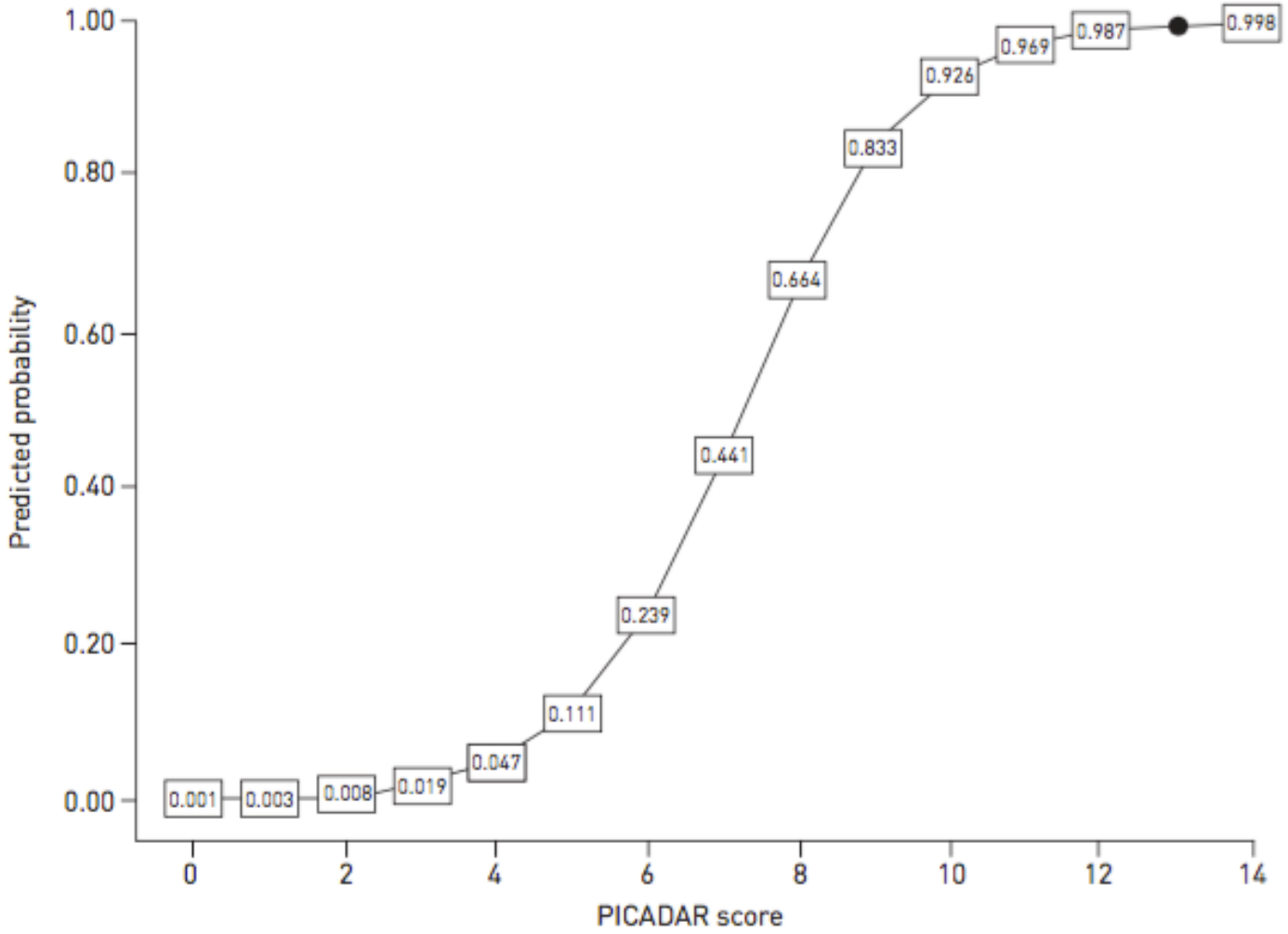
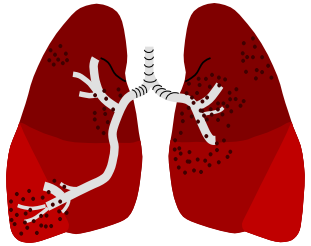


FIGURE 3 PICADAR: probability curve. Once the total PICADAR score is calculated from figure 2, the individual probability of having a primary ciliary dyskinesia diagnosis is estimated from the probability curve.



PCD

1. Tanı
2. Klinik
2. QoL
3. Genetik
4. SFT
5. Tedavi

Clinical Features of Childhood Primary Ciliary Dyskinesia by Genotype and Ultrastructural Phenotype

Stephanie D. Davis[1]*, Thomas W. Ferkol[2], Margaret Rosenfeld[3], Hye-Seung Lee[4], Sharon D. Dell[5], Scott D. Sagel[6], Carlos Milla[7], Maimoona A. Zariwala[8], Jessica E. Pittman[2]*, Adam J. Shapiro[9]*, Johnny L. Carson[10,11], Jeffrey P. Krischer[4], Milan J. Hazucha[11,12], Matthew L. Cooper[13], Michael R. Knowles[12], and Margaret W. Leigh[10]

Am J Respir Crit Care Med Vol 191, Iss 3, pp 316–324, Feb 1, 2015

Table 3. Markers of Disease Severity by PCD Group

	All (*n* = 118)	ODA Only (*n* = 54)	ODA+IDA (*n* = 18)	IDA/CA/MTD (*n* = 40)	CA or IDA Alone (*n* = 6)	*P* Value*
Height, percentile†	42 (19 to 70) n = 106	42 (20 to 83) n = 51	63 (15 to 77) n = 16	36 (13 to 60) n = 34	44 (24 to 62) n = 5	0.036
Weight, percentile	52 (17 to 80) n = 118	67 (30 to 91) n = 54	76 (34 to 82) n = 18	39 (13 to 52) n = 40	62 (47 to 81) n = 6	<0.0001
BMI, percentile†	63 (32 to 82) n = 106	68 (32 to 92) n = 51	74 (41 to 82) n = 16	46 (26 to 65) n = 34	80 (71 to 84) n = 5	0.003
FEV_1, % pred	89 (67 to 99) n = 86	93 (78 to 101) n = 46	91 (74 to 99) n = 12	72 (58 to 88) n = 24	86 (77 to 93) n = 4	0.003
$FEF_{25–75}$, % pred	68 (48 to 80) n = 86	73 (57 to 80) n = 46	78 (59 to 94) n = 12	49 (32 to 64) n = 24	75 (53 to 88) n = 4	0.002
Infant $FEV_{0.5}$, *z* score	0.22 (0.12 to 0.31) n = 13	1.00 (0.57 to 1.43) n = 2	0.20 (0.02 to 0.31) n = 3	0.14 (0.01 to 0.22) n = 7	0.38 n = 1	0.144
Infant $FEF_{25–75}$, *z* score	−0.91 (−1.02 to −0.81) n = 13	0.77 (0.57 to 0.97) n = 2	−0.84 (−0.91 to −0.82) n = 3	−1.02 (−1.25 to −0.91) n = 7	−0.05 n = 1	0.023
Chest CT						
Number of lobes with bronchiectasis	3 (1 to 5) n = 118	3 (1 to 4) n = 54	3 (0 to 5) n = 18	3.5 (1 to 5) n = 40	4.5 (3 to 6) n = 6	0.243
Number of lobes with alveolar consolidation	2 (1 to 3) n = 118	1.5 (1 to 3) n = 54	2 (1 to 3) n = 18	3 (2 to 4) n = 40	2 (1 to 2) n = 6	0.001

Definition of abbreviations: BMI = body mass index; CA = central apparatus; CT = computed tomography; $FEF_{25–75}$ = forced expiratory flow, midexpiratory phase; IDA = inner dynein arm; MTD = microtubular disorganization; ODA = outer dynein arm; PCD = primary ciliary dyskinesia.

Median (first quartile to third quartile).

**P* values for the comparison between the group of IDA/CA/MTD defect and the combined groups of ODA defect only and ODA+IDA defect.

†Subjects <2 years not included.

Growth and nutritional status, and their association with lung function: a study from the international Primary Ciliary Dyskinesia Cohort

Eur Respir J 2017; 50: 1701659

Myrofora Goutaki[1,2], Florian S. Halbeisen[1], Ben D. Spycher[1], Elisabeth Maurer[1], Fabiën Belle[1], Israel Amirav[3,4] on behalf of the PCD Israeli Consortium, Laura Behan[5,6], Mieke Boon[7], Siobhan Carr[8], Carmen Casaulta[2] on behalf of the Swiss PCD Group, Annick Clement[9] on behalf of the French Reference Centre for Rare Lung Diseases, Suzanne Crowley[10], Sharon Dell[11], Thomas Ferkol[12], Eric G. Haarman[13], Bulent Karadag[14], Michael Knowles[15], Cordula Koerner-Rettberg[16], Margaret W. Leigh[17], Michael R. Loebinger[18], Henryk Mazurek[19], Lucy Morgan[20], Kim G. Nielsen[21], Maria Phillipsen[21], Scott D. Sagel[22], Francesca Santamaria[23], Nicolaus Schwerk[24], Panayiotis Yiallouros[25], Jane S. Lucas[5] and Claudia E. Kuehni[1]

TABLE 2 Height and body mass index (BMI) of primary ciliary dyskinesia (PCD) patients of the iPCD Cohort compared to national and World Health Organization (WHO) references (constant only models)

Characteristic	Population	Reference	Subjects	z-score	p-value
Height	Overall study	National#	1601	−0.27 (−0.33 to −0.21)	<0.001
	Overall study	WHO	1609	−0.12 (−0.17 to −0.06)	<0.001
	Paediatric (<20 years)	National#	1226	−0.26 (−0.33 to −0.20)	<0.001
	Adult (⩾20 years)	National#	439	−0.31 (−0.42 to −0.20)	<0.001
	Definite PCD¶	National#	1054	−0.26 (−0.33 to −0.19)	<0.001
	Overall study+	National#	1601	−0.30 (−0.36 to −0.24)	<0.001
BMI	Overall study	National#	1549	0.06 (0.002 to 0.13)	0.043
	Overall study	WHO	1539	0.21 (0.14 to 0.27)	<0.001
	Paediatric (<20 years)	National#	1184	0.02 (−0.05 to 0.09)	0.582
	Definite PCD¶	National#	1019	0.05 (−0.02 to 0.13)	0.172
	Overall study+	National#	1549	0.03 (−0.04 to 0.09)	0.424

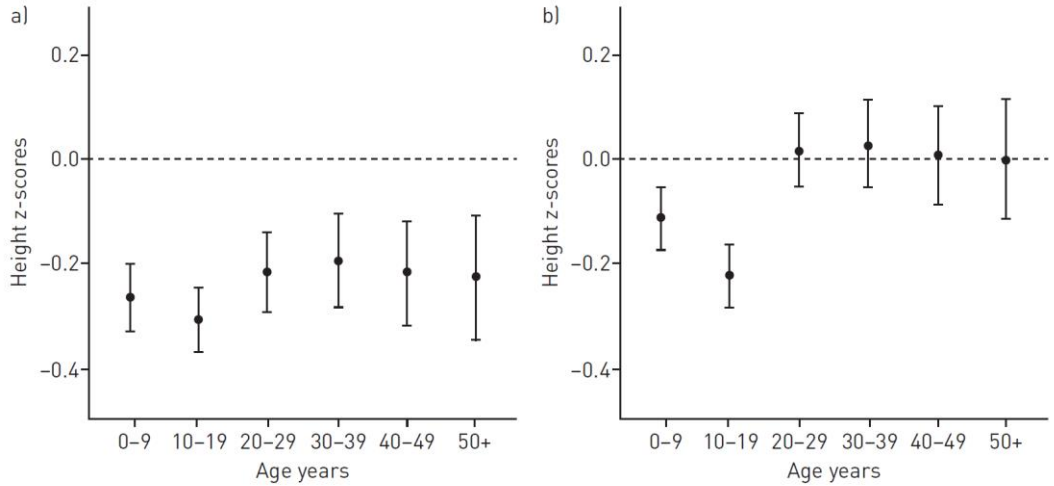
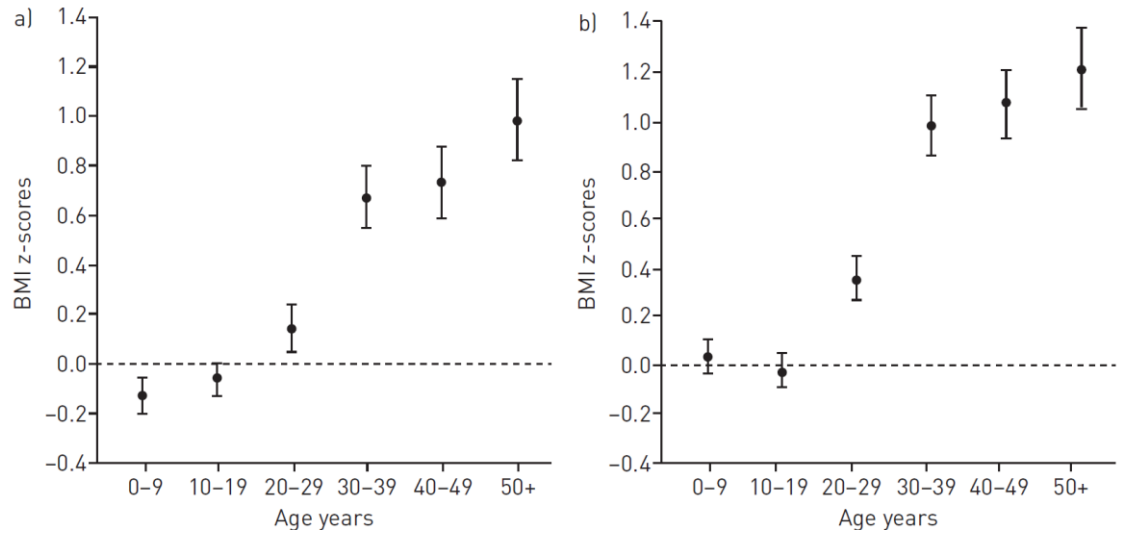
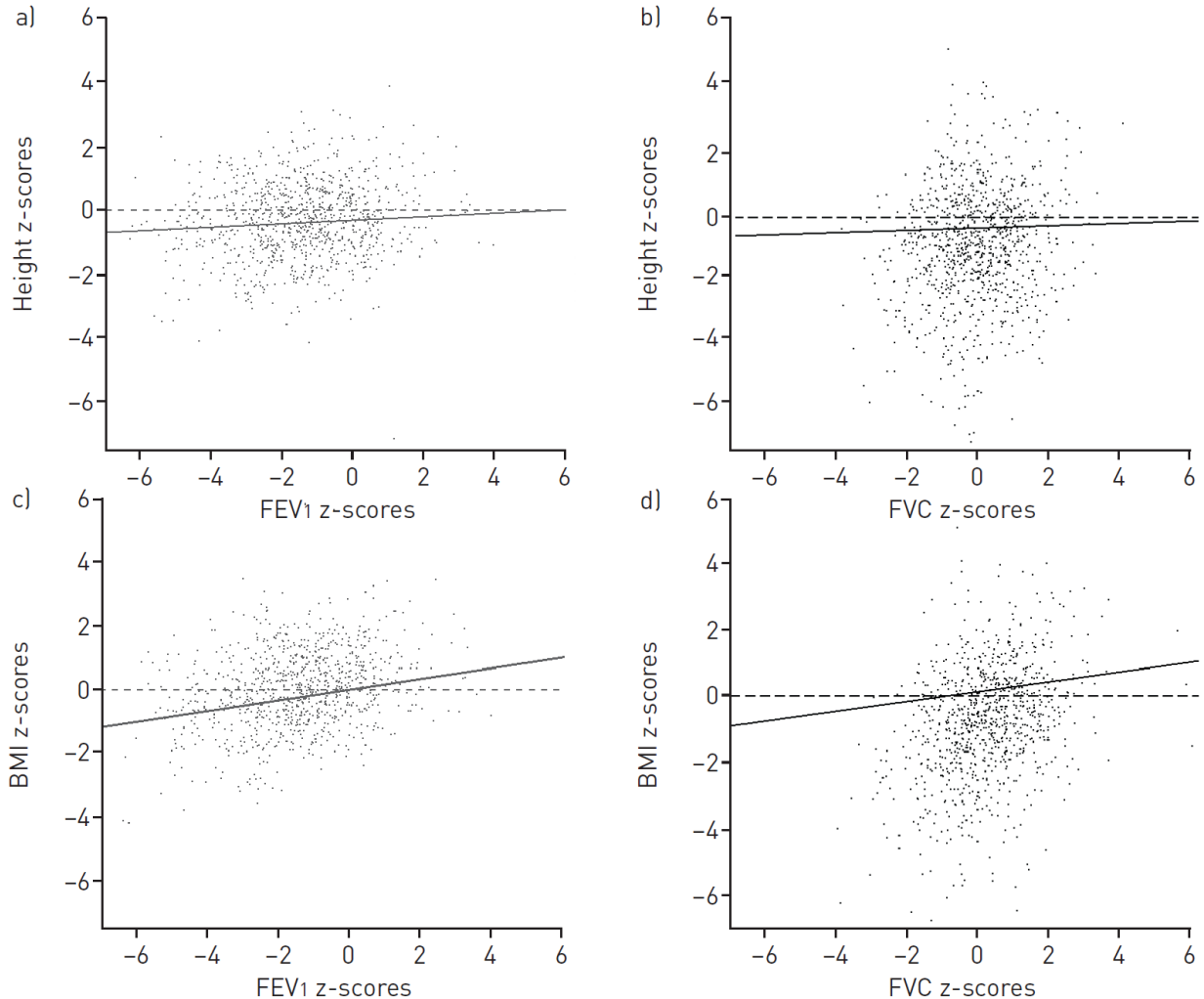


FIGURE 1 Height in primary ciliary dyskinesia (PCD) patients by age group compared to national references (a) and World Health Organization (WHO) references (b). Height is presented as mean z-score (95% CI) after adjusting for sex, country and level of diagnostic certainty.




a)
b)
c)
d)
Height z-scores
BMI z-scores
FEV1 z-scores
FVC z-scores
6
4
2
0
−2
−4
−6

Sleep Disordered Breathing in Patients With Primary Ciliary Dyskinesia

Sedat Oktem, MD,[1]* Bulent Karadag, MD,[2] Ela Erdem, MD,[2] Yasemin Gokdemir, MD,[2] Fazilet Karakoc, MD,[2] Elif Dagli, MD,[2] and Refika Ersu, MD[2]

Pediatric Pulmonology 48:897–903 (2013)

TABLE 1—Demographic, Pulmonary Function, Sleep Questionnaire, and PSQI Data for Primary Ciliary Dyskinesia Patients and Control Subjects

	PCD (n = 29)	Control (n = 29)	*P*
Age (years)	10 ± 5.9	10 ± 5.6	NS
Male/female	15/14	14/15	NS
Weight *Z*-score	−0.87 ± −0.90	0.10 ± 1.35	0.002
Height *Z*-score	−1.35 ± 0.87	0.10 ± 1.26	<0.001
FVC (% predicted normal)	74	99	<0.001
FEV_1 (% predicted normal)	74	103	<0.001
FEV_1/FVC (% predicted normal)	101 ± 12	107 ± 7	NS
Habitual snoring (%)	65.5	6.9	<0.001
Witnessed sleep apnea (%)	27.6	0	0.002
Excessive daytime sleepiness (%)	20.7	3.4	0.04
Difficulty breathing during sleep (%)	27.6	3.4	0.011
Increased parental anxiety about child's sleep (%)	48.3	3.4	<0.001
Restless sleep/irritability (%)	27.6	0	0.002
Profuse sweating (%)	24.1	3.4	0.02
Blue color during sleep (%)	3.4	0	NS
Parental shaking for apnea (%)	13.8	0	0.03
PSQI	3.9 ± 2.1	2.3 ± 1.1	NS
Poor sleepers	11	1	0.002
Good sleepers	18	28	

NS, non significant, FVC, forced vital capacity, FEV_1, forced expiratory volume in one second, PSQI, Pittsburgh Sleep Quality Index.

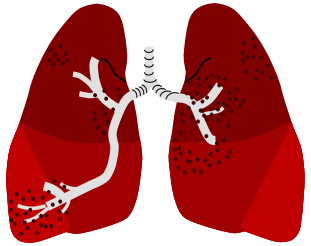
Sleep Disordered Breathing in Patients With Primary Ciliary Dyskinesia

Sedat Oktem, MD,[1]* Bulent Karadag, MD,[2] Ela Erdem, MD,[2] Yasemin Gokdemir, MD,[2] Fazilet Karakoc, MD,[2] Elif Dagli, MD,[2] and Refika Ersu, MD[2]

Pediatric Pulmonology 48:897–903 (2013)

TABLE 3—Sleep Characteristics of the PCD Patients

	Mean ± standard deviation
Total sleep time (min)	382 ± 76
Sleep efficiency (%)	86.1 ± 6.9
Arousal index (n/hr)	13.3 ± 2.8
Stage 1 (%TST)	6 ± 3
Stage 2 (%TST)	46 ± 8
Slow wave sleep (%TST)	28 ± 8
Rapid eye movement sleep (%TST)	20 ± 6
Mean saturation (%)	95 ± 2
Mean lowest saturation	92 ± 5
Obstructive apnea (n/hr)	6.8 ± 8.8
Mixed apnea (n/hr)	1 ± 1.9
Hypopnea (n/hr)	2.7 ± 2.8
Apnea–hypopnea index (n/hr)	1.6 ± 2



PCD

1. Tanı
2. Klinik
3. QoL
4. Genetik
5. SFT
6. Tedavi

A quality-of-life measure for adults with primary ciliary dyskinesia: QOL–PCD

Jane S. Lucas[1,2,3,7], Laura Behan[1,2,3,4,7], Audrey Dunn Galvin[4], Adrianne Alpern[5], Anjana M. Morris[5], Mary P. Carroll[1,2,3], Michael R. Knowles[6], Margaret W. Leigh[6] and Alexandra L. Quittner[5]

Eur Respir J 2015; 46: 375–383 |

TABLE 2 Participant quotes by topic

Topic	Quote	Country of interviewee/sex/age band in years
Impact of respiratory symptoms	"I had to tell the group not to worry because I start huffing and spluttering as I'm walking."	UK/female/36–50
	"When I listen to myself breathe, I always wheeze."	USA/female/18–35
Impact of sinus symptoms	"I'm always blowing my nose, doesn't matter what weather it is."	UK/female/36–50
	"I always have to blow my nose before I eat if I wanna taste anything."	USA/female/36–50
Impact of ear symptoms/ hearing loss	"You have to ask people to repeat themselves so many times, they're just, like, 'oh don't worry about it'."	UK/male/18–35
	"I can't go white water rafting because I have tubes in my ears and my ears can't get wet."	USA/female/18–35

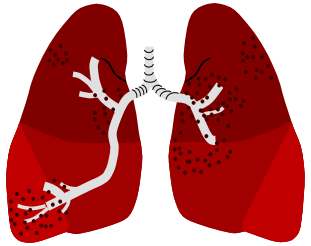
Quality of Life Questionnaire for Turkish Patients with Primary Ciliary Dyskinesia

Nagehan Emiralioğlu[1], Bülent Karadağ[2], H. Uğur Özçelik[1]

Turk Thorac J 2017; 18: 19-22

Table 1. The sub-groups of the quality of life scale in different age groups

Measurement	Children in the age group of 6-12 years	Adolescents in the age group of 13-18 years	Parents of children in the age group of 6-12 years	Adults in the age group of 18 years and above
Evaluation of physical functions	X	X	X	X
Evaluation of emotions	X	X	X	X
Evaluation of treatment	X	X	X	X
Evaluation of ears and hearing	X	X	X	X
Evaluation of respiratory symptoms	X	X	X	X
Evaluation of sinus symptoms	X	X	X	X
Evaluation of social functions	X	X		X
Evaluation of social role		X		X
Evaluation of vitality		X	X	X
Evaluation of health perception			X	X
Evaluation of school functions			X	
Evaluation of				



PCD

1. Tanı
2. Klinik
3. QoL
4. SFT
5. Tedavi

Primary Ciliary Dyskinesia

Diagnostic and Phenotypic Features

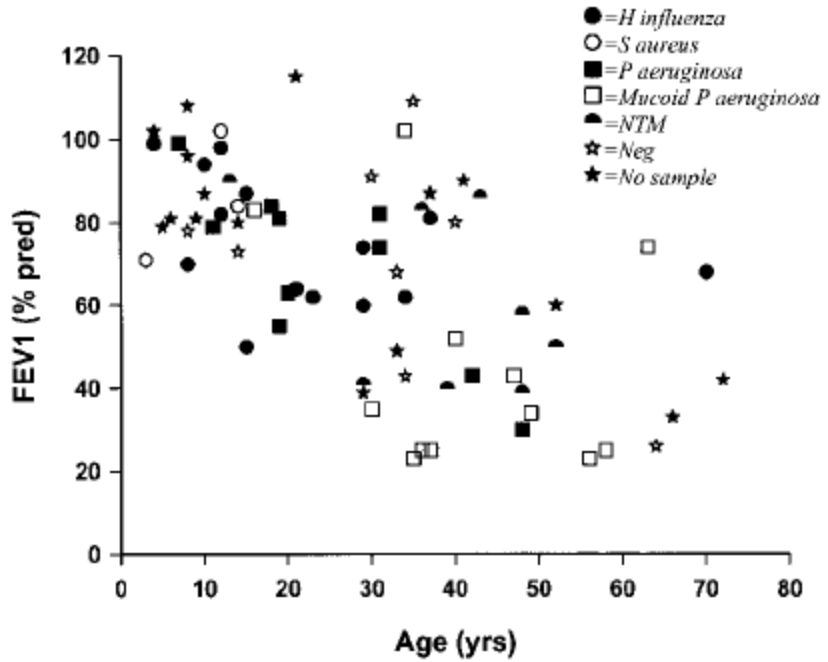
Peadar G. Noone, Margaret W. Leigh, Aruna Sannuti, Susan L. Minnix, Johnny L. Carson, Milan Hazucha, Maimoona A. Zariwala, and Michael R. Knowles

Am J Respir Crit Care Med Vol 169. pp 459–467, 2004

TABLE 1. "CLASSIC" PRIMARY CILIARY DYSKINESIA

	Cough n (%)	Bronchiectasis* n (%)	Sinusitis† n (%)	Otitis Media n (%)	NRS n (%)	Situs Inversus n (%)	FEV_1 (% predicted)	Nasal NO (nl/min)
Adults (≥ 18 yr; n = 47 [31 females]; median age, 36 yr; range, 19–73 yr)	47 (100%)	46 (98)	22 (47)	43 (92)	30 (65)	22 (46)	60 ± 4	23 ± 4
Pediatric subjects (< 18 yr; n = 31 [11 females]; median age, 8 yr; range, 1–17 yr)	31 (100%)	19 (61)	20 (65)	31 (100)	27 (87)	21 (68)	85 ± 3	16 ± 4

Yıllık düşüş
FEV1 : 0.8%



Lung Function in Patients with Primary Ciliary Dyskinesia

A Cross-Sectional and 3-Decade Longitudinal Study

June K. Marthin[1], Nadia Petersen[1], Lene T. Skovgaard[2], and Kim G. Nielsen[1]

Am J Respir Crit Care Med Vol 181. pp 1262–1268, 2010

1/3 okul öncesi çocuk FEV1 <80%

1/3 çocukta >10% FEV1'de düşüş 30 yıl içinde

Erken tanı önlemiyor

Ventilation inhomogeneity in children with primary ciliary dyskinesia

Kent Green,[1] Frederik F Buchvald,[1] June Kehlet Marthin,[1] Birgitte Hanel,[1]
Per M Gustafsson,[2] Kim Gjerum Nielsen[1]

Thorax 2012;**67**:49–53.

Multipl breath inert gas washout (MBW) test- Lung clearance index (LCI) değişiklikleri daha iyi gösterir.

LCI:

PCD %85 anormal

Normal FEV1 %81 anormal

LCI, diğer SFT parametreleri ile daha iyi korele.

Lung function in patients with primary ciliary dyskinesia: an iPCD Cohort study

Eur Respir J 2018; 52: 1801040 |

Florian S. Halbeisen[1], Myrofora Goutaki[1,2], Ben D. Spycher[1,2], Israel Amirav[3,4,5], Laura Behan[6,7], Mieke Boon[8], Claire Hogg[9], Carmen Casaulta[2,10], Suzanne Crowley[11], Eric G. Haarman[12], Bulent Karadag[13], Cordula Koerner-Rettberg[14], Michael R. Loebinger[15], Henryk Mazurek[16], Lucy Morgan[17], Kim G. Nielsen[18], Heymut Omran[19], Francesca Santamaria[20], Nicolaus Schwerk[21], Guillaume Thouvenin[22,23,24], Panayiotis Yiallouros[25], Jane S. Lucas[6], Philipp Latzin[2] and Claudia E. Kuehni[1,2]

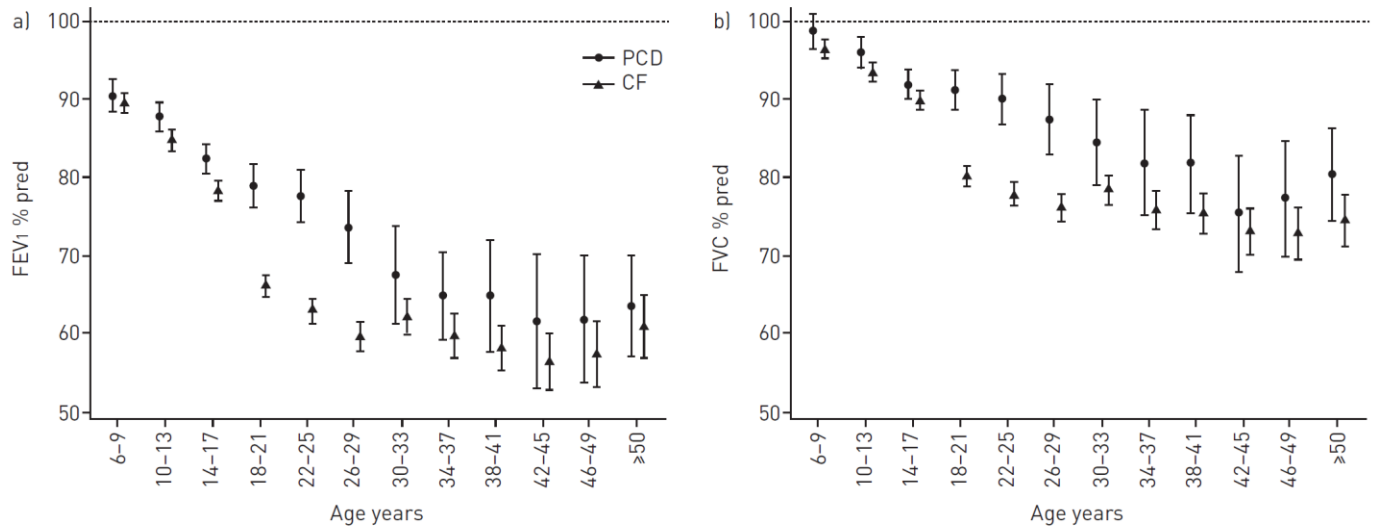
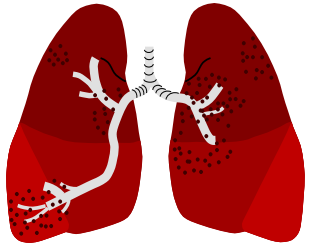


FIGURE 4 Association of a) forced expiratory volume in 1 s (FEV_1) and b) forced vital capacity (FVC) of primary ciliary dyskinesia (PCD) patients with cystic fibrosis (CF) patients. FEV_1 and FVC are presented as mean % predicted (95% CI), without adjusting for other factors. The dashed line shows the mean of the normal population.



PCD

1. Tanı
2. Klinik
3. QoL
4. SFT
5. Tedavi

Kanıta dayalı tedavi

?

Management of primary ciliary dyskinesia in European children: recommendations and clinical practice

Marie-Pierre F. Strippoli, Thomas Frischer, Angelo Barbato, Deborah Snijders, Elisabeth Maurer, Jane S.A. Lucas, Ernst Eber, Bulent Karadag, Petr Pohunek, Zorica Zivkovic, Amparo Escribano, Chris O'Callaghan, Andrew Bush and Claudia E. Kuehni, for the ERS Task Force on primary ciliary dyskinesia in children

ERS Task Force

26 ülke, 194 merkez

Merkez başına düşen hasta : 4 (2-9)

Çok değişken tedaviler

Eur Respir J 2012; 39: 1482–1491

Management of primary ciliary dyskinesia in European children: recommendations and clinical practice

Marie-Pierre F. Strippoli, Thomas Frischer, Angelo Barbato, Deborah Snijders, Elisabeth Maurer, Jane S.A. Lucas, Ernst Eber, Bulent Karadag, Petr Pohunek, Zorica Zivkovic, Amparo Escribano, Chris O'Callaghan, Andrew Bush and Claudia E. Kuehni, for the ERS Task Force on primary ciliary dyskinesia in children

Tedavi

1. FT ve egzersiz ile havayolu temizliği (79%, sadece 28% formal program),
2. Sık AB tedavisi (89%)
3. Profilaktik oral AB ve uzun dönem nebulize anti-Pseudomonas AB

Eur Respir J 2012; 39: 1482–1491

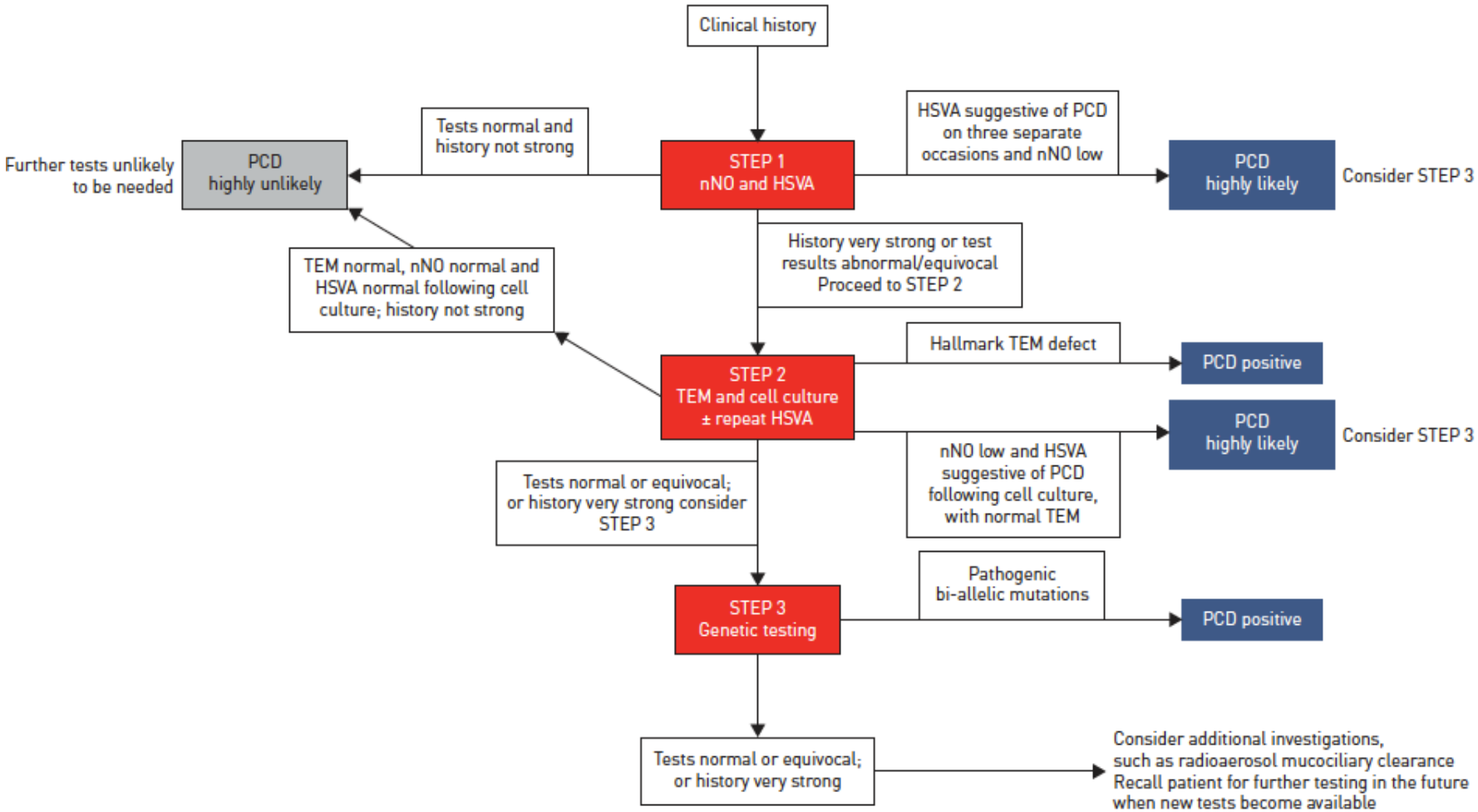
Management of primary ciliary dyskinesia in European children: recommendations and clinical practice

Marie-Pierre F. Strippoli, Thomas Frischer, Angelo Barbato, Deborah Snijders, Elisabeth Maurer, Jane S.A. Lucas, Ernst Eber, Bulent Karadag, Petr Pohunek, Zorica Zivkovic, Amparo Escribano, Chris O'Callaghan, Andrew Bush and Claudia E. Kuehni, for the ERS Task Force on primary ciliary dyskinesia in children

Tedavi

4. Inhale bronkodilatör (20%)
   Inhale steroid (11%)
5. Dnase (50% bazen/rutin)
   Hipertonik salin

Eur Respir J 2012; 39: 1482–1491


Clinical history
STEP 1
nNO and HSVA
Tests normal and history not strong
Further tests unlikely to be needed
PCD highly unlikely
HSVA suggestive of PCD on three separate occasions and nNO low
PCD highly likely
Consider STEP 3
History very strong or test results abnormal/equivocal Proceed to STEP 2
TEM normal, nNO normal and HSVA normal following cell culture; history not strong
STEP 2
TEM and cell culture ± repeat HSVA
Hallmark TEM defect
PCD positive
PCD highly likely
Consider STEP 3
nNO low and HSVA suggestive of PCD following cell culture, with normal TEM
Tests normal or equivocal; or history very strong consider STEP 3
STEP 3
Genetic testing
Pathogenic bi-allelic mutations
PCD positive
Tests normal or equivocal; or history very strong
Consider additional investigations, such as radioaerosol mucociliary clearance
Recall patient for further testing in the future when new tests become available

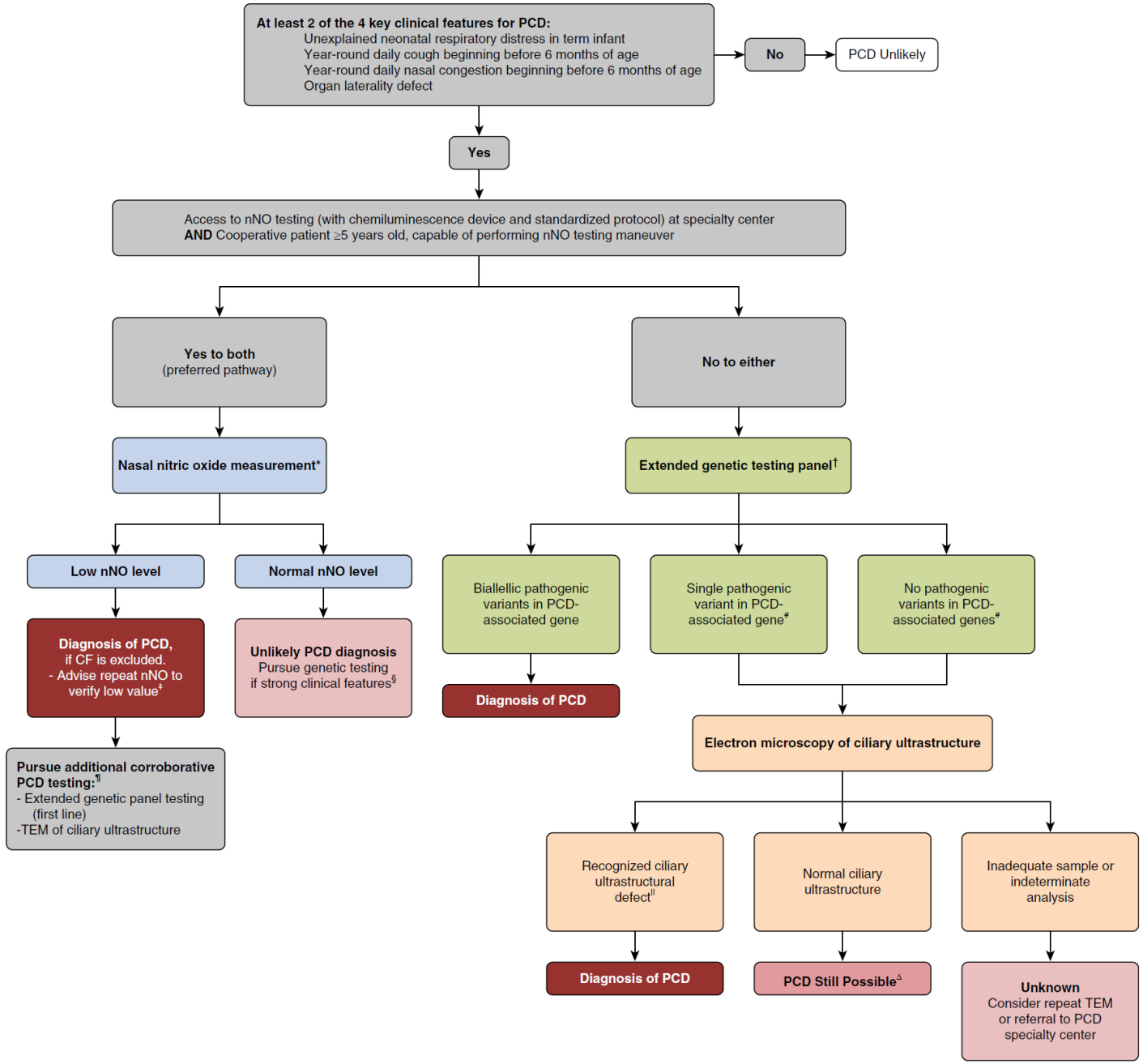
AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Primary Ciliary Dyskinesia

An Official American Thoracic Society Clinical Practice Guideline

Adam J. Shapiro, Stephanie D. Davis, Deepika Polineni, Michele Manion, Margaret Rosenfeld, Sharon D. Dell, Mark A. Chilvers, Thomas W. Ferkol, Maimoona A. Zariwala, Scott D. Sagel, Maureen Josephson, Lucy Morgan, Ozge Yilmaz, Kenneth N. Olivier, Carlos Milla, Jessica E. Pittman, M. Leigh Anne Daniels, Marcus Herbert Jones, Ibrahim A. Janahi, Stephanie M. Ware, Sam J. Daniel, Matthew L. Cooper, Lawrence M. Nogee, Billy Anton, Tori Eastvold, Lynn Ehrne, Elena Guadagno, Michael R. Knowles, Margaret W. Leigh, and Valery Lavergne; on behalf of the American Thoracic Society Assembly on Pediatrics

This official clinical practice guideline of the American Thoracic Society was approved May 2018


At least 2 of the 4 key clinical features for PCD:
Unexplained neonatal respiratory distress in term infant
Year-round daily cough beginning before 6 months of age
Year-round daily nasal congestion beginning before 6 months of age
Organ laterality defect
No
PCD Unlikely
Yes
Access to nNO testing (with chemiluminescence device and standardized protocol) at specialty center
AND Cooperative patient ≥5 years old, capable of performing nNO testing maneuver
Yes to both
(preferred pathway)
No to either
Nasal nitric oxide measurement*
Extended genetic testing panel†
Low nNO level
Normal nNO level
Biallellic pathogenic variants in PCD-associated gene
Single pathogenic variant in PCD-associated gene#
No pathogenic variants in PCD-associated genes#
Diagnosis of PCD,
if CF is excluded.
- Advise repeat nNO to verify low value‡
Unlikely PCD diagnosis
Pursue genetic testing
if strong clinical features§
Diagnosis of PCD
Electron microscopy of ciliary ultrastructure
Pursue additional corroborative PCD testing:¶
- Extended genetic panel testing (first line)
-TEM of ciliary ultrastructure
Recognized ciliary ultrastructural defect||
Normal ciliary ultrastructure
Inadequate sample or indeterminate analysis
Diagnosis of PCD
PCD Still Possible△
Unknown
Consider repeat TEM or referral to PCD specialty center

Mukus temizleme teknikleri

- Kanıt yok
- Öksürük ve balgam çıkarma teşvik edilmeli
- Egzersiz
- DNase?
- Hipertonik salin?
- Mannitol ?
- SABA normal silyalarda in vitro ortamda CBF'i arttırabiliyor.

Comparison of Conventional Pulmonary Rehabilitation and High-Frequency Chest Wall Oscillation In Primary Ciliary Dyskinesia

Yasemin Gokdemir, MD,[1]* Evrim Karadag-Saygi, MD,[2] Ela Erdem, MD,[1] Ozun Bayindir, MD,[2] Refika Ersu, MD,[1] Bulent Karadag, MD,[1] Nimet Sekban, Physiotherapist,[2] Gulseren Akyuz, MD,[2] and Fazilet Karakoc, MD[1]

Pediatr Pulmonol.

24 hasta

7-18 yaş

SFT değerleri iki yöntemle arttı

HFCWO hastalar tarafından daha çok tercih edildi

Düşük uyum gösteren hastalarda seçenek?

Comparison of Conventional Pulmonary Rehabilitation and High-Frequency Chest Wall Oscillation In Primary Ciliary Dyskinesia

Yasemin Gokdemir, MD,[1]* Evrim Karadag-Saygi, MD,[2] Ela Erdem, MD,[1] Ozun Bayindir, MD,[2] Refika Ersu, MD,[1] Bulent Karadag, MD,[1] Nimet Sekban, Physiotherapist,[2] Gulseren Akyuz, MD,[2] and Fazilet Karakoc, MD[1]

Pediatr Pulmonol.

TABLE 3—PFTs of Patients' Before and After Treatment With CPR and HFCWO

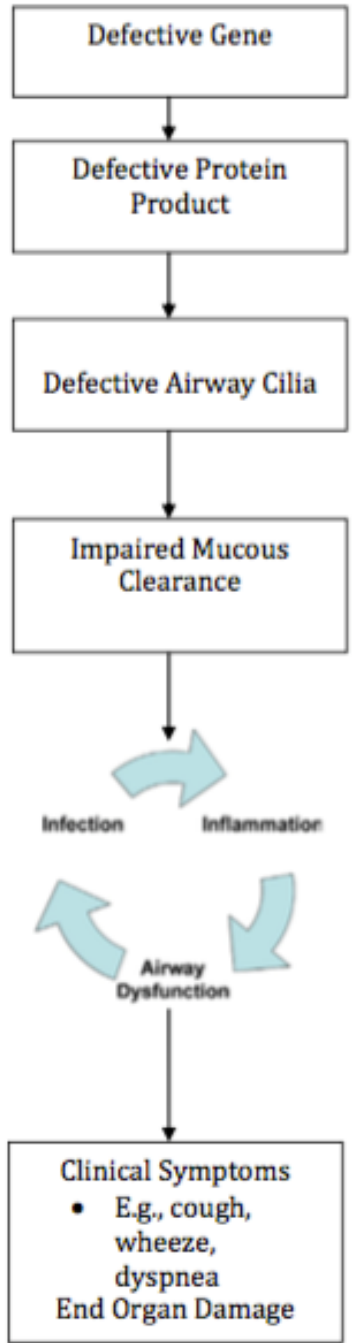
PFT	Before CPR, mean ± SD (% predicted)	After CPR, mean ± SD (% predicted)	*P*	Before HFCWO, mean ± SD (% predicted)	After HFCWO, mean ± SD (% predicted)	*P*
FVC	77.0 ± 14.1	81.8 ± 13.0	0.002	75.1 ± 15.3	80.3 ± 13.9	0.002
FEV_1	72.9 ± 14.2	78.7 ± 13.5	0.001	71.4 ± 16.1	77.4 ± 14.6	0.001
PEF	73.8 ± 14.5	82.5 ± 14.5	0.001	70.9 ± 18.0	78.3 ± 17.7	0.002
FEF_{25-75}	68.6 ± 27.6	74.9 ± 29.3	0.007	70.5 ± 23.4	76.4 ± 25.6	0.006

TABLE 4—Comparison of CPR With HFCWO

	CPR	HFCWO	*P*
△FVC (% change)	7.5	9.0	0.53
△FEV_1 % change)	8.8	9.7	0.80
△PEF (% change)	12.9	12.8	0.98
△FEF_{25-75} (% change)	9.8	9.7	0.81
SpO_2	95.8	96.7	0.89
Comfort (mean)	3.6	4.3	0.04
Effectiveness (mean)	4.5	4.0	0.09

PCD Lung Disease Pathophysiology

Existing Therapeutics



- Hypertonic Saline
- Mannitol
- Dornase Alpha
- Chest Physiotherapy

- Oral or IV Antibiotics
- Inhaled Antibiotics
- Macrolides
- Inhaled corticosteroids
- Systemic corticosteroids

Treatment recommendations in Primary Ciliary Dyskinesia

Deepika Polineni [1], Stephanie D. Davis [2], Sharon D. Dell [3,*]

Paediatric Respiratory Reviews 18 (2016) 39–45

FUTURE DIRECTIONS FOR RESEARCH

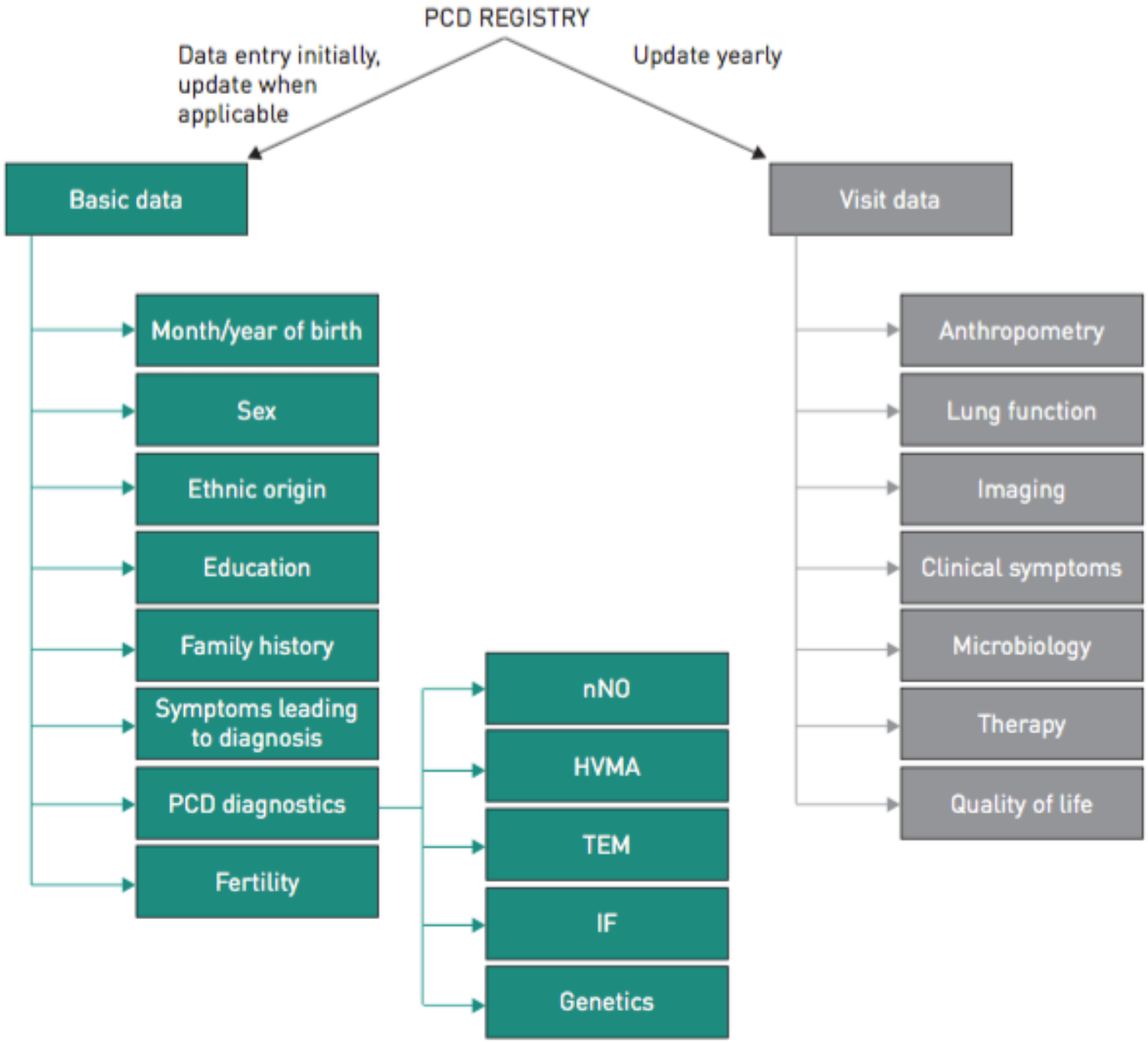
- Prospective randomized clinical trials of interventions used in patients with PCD
- Correlations of genotype and phenotype in PCD cohorts
- Genotype-based precision based medicine trials
- Determining the underlying mechanisms of disease progression

An international registry for primary ciliary dyskinesia

Claudius Werner[1], Martin Lablans[2], Maximilian Ataian[2], Johanna Raidt[1], Julia Wallmeier[1], Jörg Große-Onnebrink[1], Claudia E. Kuehni[3], Eric G. Haarman[4], Margaret W. Leigh[5], Alexandra L. Quittner[6], Jane S. Lucas[7], Claire Hogg[8], Michal Witt[9], Kostas N. Priftis[10], Panayiotis Yiallouros[11], Kim G. Nielsen[12], Francesca Santamaria[13], Frank Ückert[2] and Heymut Omran[1]

Eur Respir J 2016; 47: 849–859 |

www.pcdregistry.eu


PCD REGISTRY
Data entry initially, update when applicable
Update yearly
Basic data
Visit data
Month/year of birth
Sex
Ethnic origin
Education
Family history
Symptoms leading to diagnosis
PCD diagnostics
Fertility
nNO
HVMA
TEM
IF
Genetics
Anthropometry
Lung function
Imaging
Clinical symptoms
Microbiology
Therapy
Quality of life

The international primary ciliary dyskinesia cohort (iPCD Cohort): methods and first results

Myrofora Goutaki[1,2], Elisabeth Maurer[1], Florian S. Halbeisen[1], Israel Amirav[3], Angelo Barbato[4] on behalf of the PCD Italian Consortium, Laura Behan[5], Mieke Boon[6], Carmen Casaulta[2] on behalf of the Swiss PCD Group, Annick Clement[7] on behalf of the French Reference Centre for Rare Lung Diseases, Suzanne Crowley[8], Eric Haarman[9], Claire Hogg[10], Bulent Karadag[11], Cordula Koerner-Rettberg[12], Margaret W. Leigh[13] on behalf of the Genetic Disorders of Mucociliary Clearance Consortium, Michael R. Loebinger[14], Henryk Mazurek[15], Lucy Morgan[16], Kim G. Nielsen[17], Heymut Omran[18], Nicolaus Schwerk[19], Sergio Scigliano[20], Claudius Werner[18], Panayiotis Yiallouros[21], Zorica Zivkovic[22,23], Jane S. Lucas[5] and Claudia E. Kuehni[1]

Eur Respir J 2017; 49: 1601181

3013 hasta, 18 ülke
542 hasta uzun dönem izlem

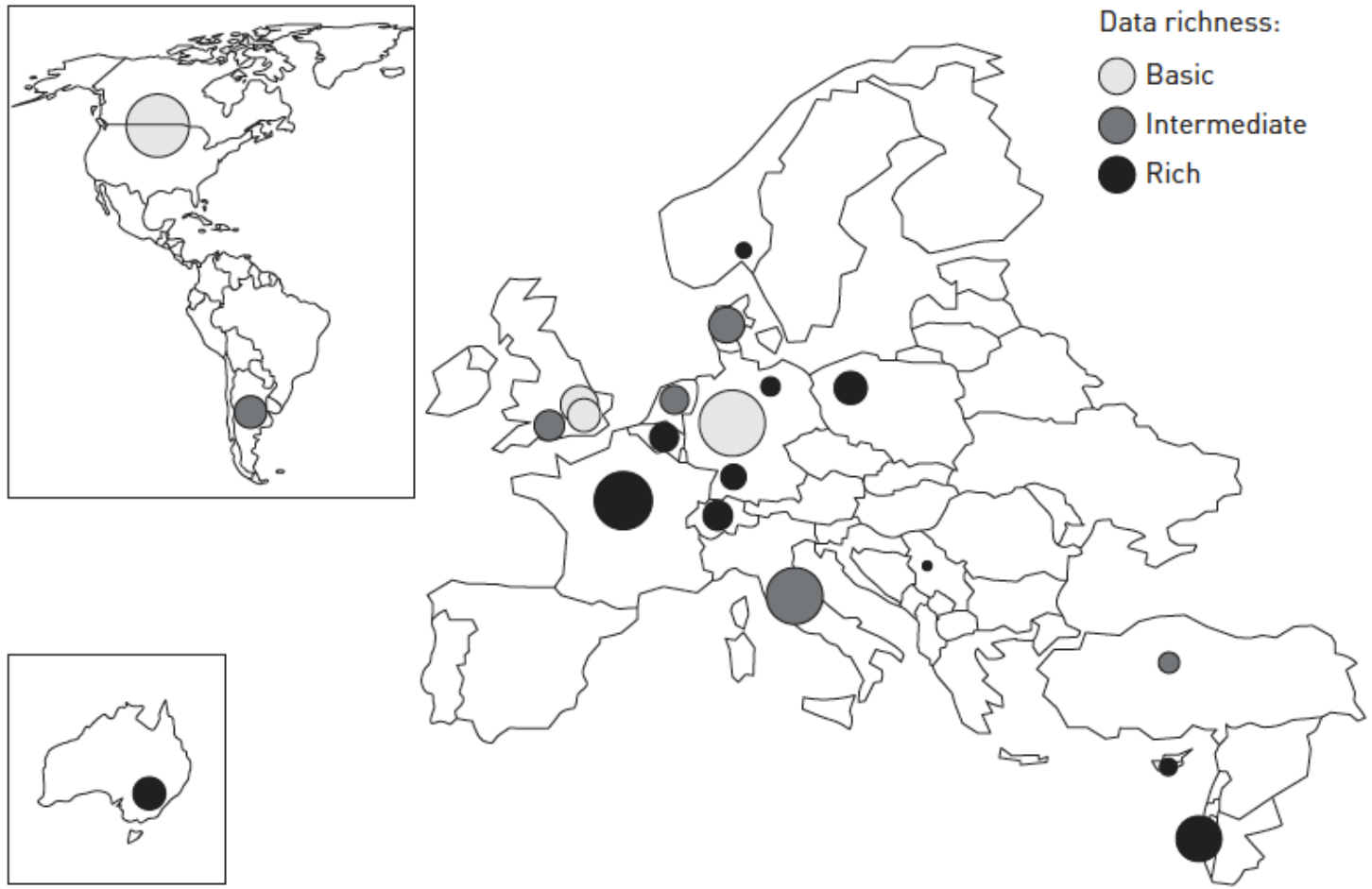


FIGURE 1 Countries contributing data to the international primary ciliary dyskinesia cohort (iPCD Cohort). The circle size reflects the size of the dataset and the shades of grey reflect the data richness (semiquantitative measure based on the number of delivered variables).

TABLE 2 Characteristics of the international primary ciliary dyskinesia cohort (iPCD Cohort)

Country	Principal investigator	Patients n	Age range years[#]	Males %	Type of data delivered	Data richness[¶]
Argentina	S. Scigliano	101	6–57	42	Cross-sectional	Intermediate
Australia	L. Morgan	109	0–76	60	Longitudinal	High
Belgium	M. Boon	82	0–69	45	Cross-sectional	High
Cyprus	P. Yiallouros	31	0–66	48	Longitudinal	High
Denmark	K.G. Nielsen	120	0–70	48	Longitudinal	Intermediate
France	A. Clement	337	0–69	52	Longitudinal	High
Germany (Bochum)	C. Koerner-Rettberg	64	0–27	40	Cross-sectional	High
Germany (Muenster)	H. Omran	436	3–75	52	Cross-sectional	Basic
Germany (Hannover)	N. Schwerk	37	0–39	68	Longitudinal	High
Israel	I. Amirav	210	0–60	56	Cross-sectional	High
Italy	Italian PCD group	331	0–73	50	Cross-sectional	Intermediate
The Netherlands	E. Haarman	82	3–69	50	Longitudinal	Intermediate
Norway	S. Crowley	23	0–18	65	Longitudinal	High
Poland	H. Mazurek	105	1–22	56	Cross-sectional	High
Serbia	Z. Zivkovic	10	6–19	45	Longitudinal	High
Switzerland	Swiss PCD group	108	3–70	51	Longitudinal	High
Turkey	B. Karadag	37	3–21	43	Cross-sectional	Intermediate
UK (Paediatric Pulmonology Dept, Brompton)	C. Hogg	116	1–18	47	Cross-sectional	Basic
UK (Adult Pulmonology Dept, Brompton)	M. Loebinger	152	20–76	38	Cross-sectional	Basic
UK (Southampton)	J. Lucas	104	0–68	49	Longitudinal	Intermediate
USA/Canada	Genetic Diseases of Mucociliary Clearance Consortium	418	0–77	44	Cross-sectional	Basic
iPCD Cohort		3013	0–77	50		

TABLE 3 Available data from different modules of the standardised dataset of 3013 primary ciliary dyskinesia (PCD) patients in the international PCD cohort (iPCD Cohort) (April 2016)

Type of data	Patients
General information	3013 (100)
Diagnostics	3013 (100)
nNO	1021 (33)
TEM	1913 (62)
VM	1088 (35)
Genetics	276 (9)
Baseline characteristics[#]	2286 (74)
Growth	1609 (53)
Lung function	1042 (34)
Clinical manifestations	1352 (44)
Therapy	843 (27)
Microbiology	732 (24)
Imaging	526 (17)
Neonatal period	1179 (38)

Data are presented as n (%). nNO: nasal nitric oxide; TEM: transmission electron microscopy; VM: light or high-frequency video microscopy. [#]: mainly data on situs anomalies and congenital heart disease.

Cerrahi

Sadece özel durumlarda, seçilmiş hastalarda!

- Segmentektomi
- Lobektomi
- AC nakli – ne zaman?

  Bilateral hastalık, ağır fonksiyonal etkilenme, oksijen bağımlılığı, tedaviye yanıtsızlık

Gelecek ?

- PCD merkezleri (en az 10-15 hasta)
- Kanıta dayalı tedavi yaklaşımları
- Değişik mutasyonların klinik fenotiplere etkisi?
- İnfeksiyon/inflamasyonun akut alevlenme ve hastalığın kötüleşmesine etkisi

Gelecek ?

- PCD-spesifik HRQL ölçümleri
- Hasta bildirimine dayalı sonuçlar (HRQL)
- AC hastalığının erken belirteçleri (LCI, inflamatuar biyobelirteçler)
- PCD Kayıt Sisteminin kurulması

Overview: PCD Clinical Centers - Why Now?

'Mission Possible!':

NOW is the time for PCD Clinical Centers