



# Pathologies respiratoires en milieu agricole

## Démarche diagnostique et de prévention

**Pr Bruno DEGANO**

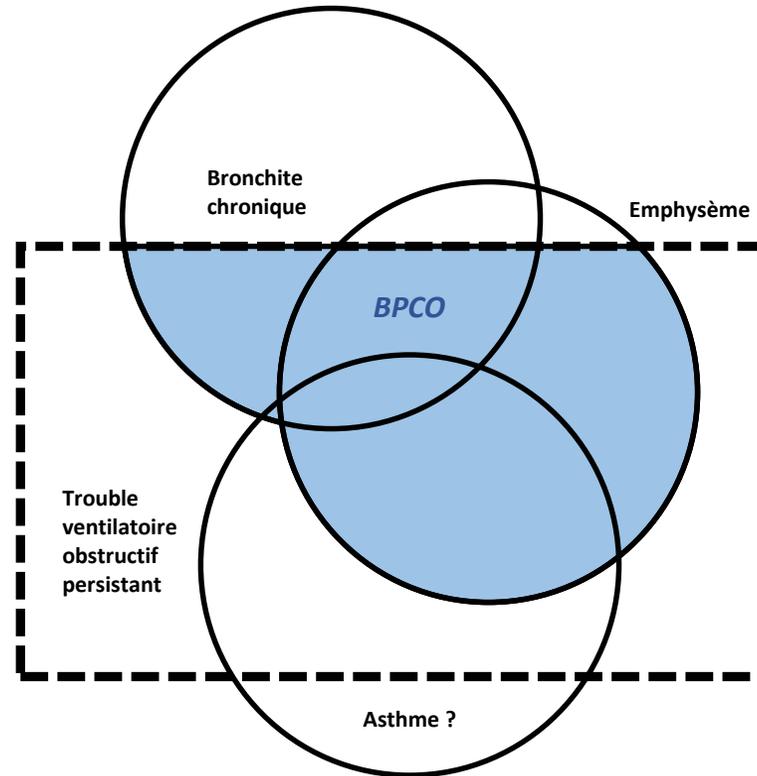
SHU Pneumologie – Physiologie

CHU Grenoble Alpes

# BPCO : définition GOLD

- Maladie caractérisée par des symptômes respiratoires chroniques et un trouble ventilatoire obstructif persistant dus à des anomalies bronchiques et/ou alvéolaire le plus souvent secondaires à une exposition significative à des gaz ou particules toxiques
- BPCO en milieu agricole
  - Secteurs concernés
    - Milieu céréalier (ouvriers des silos)
    - Élevage de porcs (et volailles ?)
    - Milieu de production laitière
    - Autres ?
  - Durée « significative » de l'exposition ?
  - Diagnostic différentiel strict
    - PHS (maladie du poumon de fermier)

# BPCO : un syndrome ?



# BPCO et asthme : les symptômes...

- Symptômes respiratoires chroniques
  - Moins de 50% des sujets symptomatiques avec exposition significative à des gaz ou particules toxiques ont un TVO persistant
  - Moins de 10% des sujets symptomatiques ont un TVO persistant en l'absence de sélection portant sur l'exposition
- Asthme vs. BPCO : une question récurrente
  - The Dutch hypothesis
    - L'asthme et la BPCO seraient des manifestations différentes d'une seule maladie, la « broncho-pneumopathie chronique non spécifique »
  - De nombreux aérocontaminants professionnels ont des propriétés allergisantes
    - Développement possible d'une atopie chez des sujets prédisposés
  - L'asthme chronique peut entraîner une obstruction bronchique non réversible
    - L'asthme chronique pourrait mener à la BPCO

Soriano et al. *Lancet* 2009; 374: 721–732

Eisner et al. *Am J Respir Crit Care Med* 2010; 182: 693-718

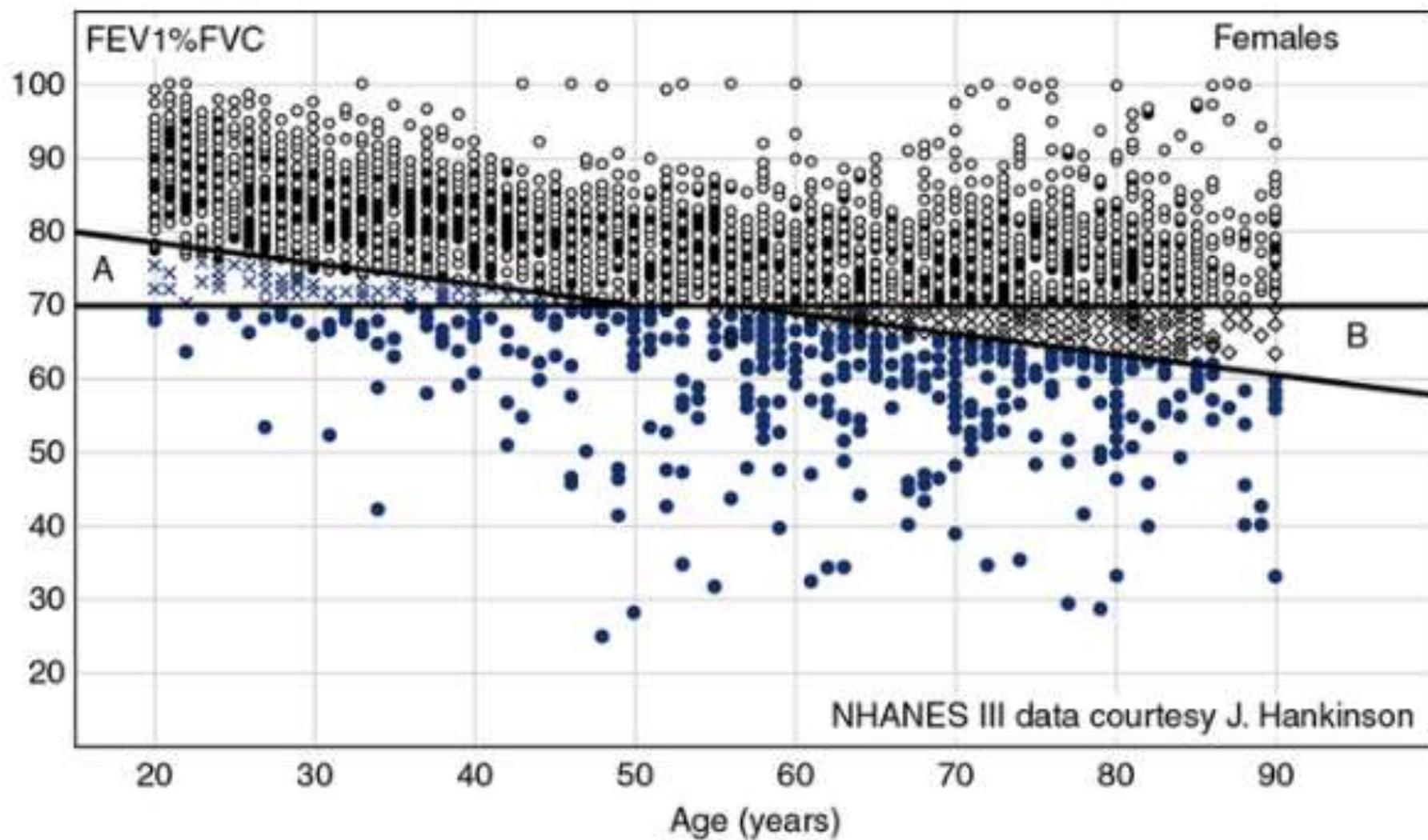
Beghe et al. *Allergy* 2010, 65:474–481

# BPCO vs. TVO persistant sans symptômes

	BPCO n = 76	TVO seul n = 51	p (BPCO vs. TVO)
Hommes, n (%)	61 (78)	44 (85)	0.364
Age, années	59 ± 9	57 ± 10	0.463
IMC, kg/m <sup>2</sup>	27.9 ± 5.5	24.7 ± 4.4	< 0.001
Fumeurs (ex ou actifs), n (%)	56 (72)	29 (56)	0.06
Tabagisme, paquets-années	21 ± 23	13 ± 17	0.034
Spirométrie post-BD			
VEMS, L	2.12 ± 0.73	2.68 ± 0.70	< 0.001
VEMS, z-score	-2.22 ± 1.09	-1.35 ± 0.82	< 0.001
VEMS < LLN, n (%)	51 (67)	19 (37)	< 0.001
CVF, L	3.65 ± 1.00	4.34 ± 0.95	< 0.001
CVF, z-score	-0.72 ± 1.26	0.12 ± 0.86	< 0.001
VEMS/CVF, %	57.7 ± 8.0	61.4 ± 5.0	0.002
VEMS/CVF, z-score	-2.62 ± 0.75	-2.26 ± 0.47	0,001

# Prévalence de la BPCO

- La prévalence de la BPCO en milieu agricole
  - Varie selon l'existence ou non d'un tabagisme
  - Dépend des critères diagnostiques
  - Varie d'une région du monde à une autre
    - DOHaD (Developmental Origin of Health and Diseases)
    - Mode d'exercice agricole
- Entre 65 et 80 % des sujets atteints de BPCO n'ont pas reçu de diagnostic
  - Perte de chances possible en l'absence de prise en charge thérapeutique
- Environ 1/3 des sujets qui ont reçu un diagnostic de BPCO n'en sont pas atteints
  - Coût et risque inhérents à des traitements inappropriés
  - Risque potentiel lié à l'absence de diagnostic approprié



# COPD, airflow limitation and chronic bronchitis in farmers: a systematic review and meta-analysis

Alicia Guillien,<sup>1</sup> Thibaud Soumagne,<sup>2</sup> Jean-Charles Dalphin,<sup>2,3</sup> Bruno Degano<sup>4,5</sup>

## Key messages

### **What is already known about this subject?**

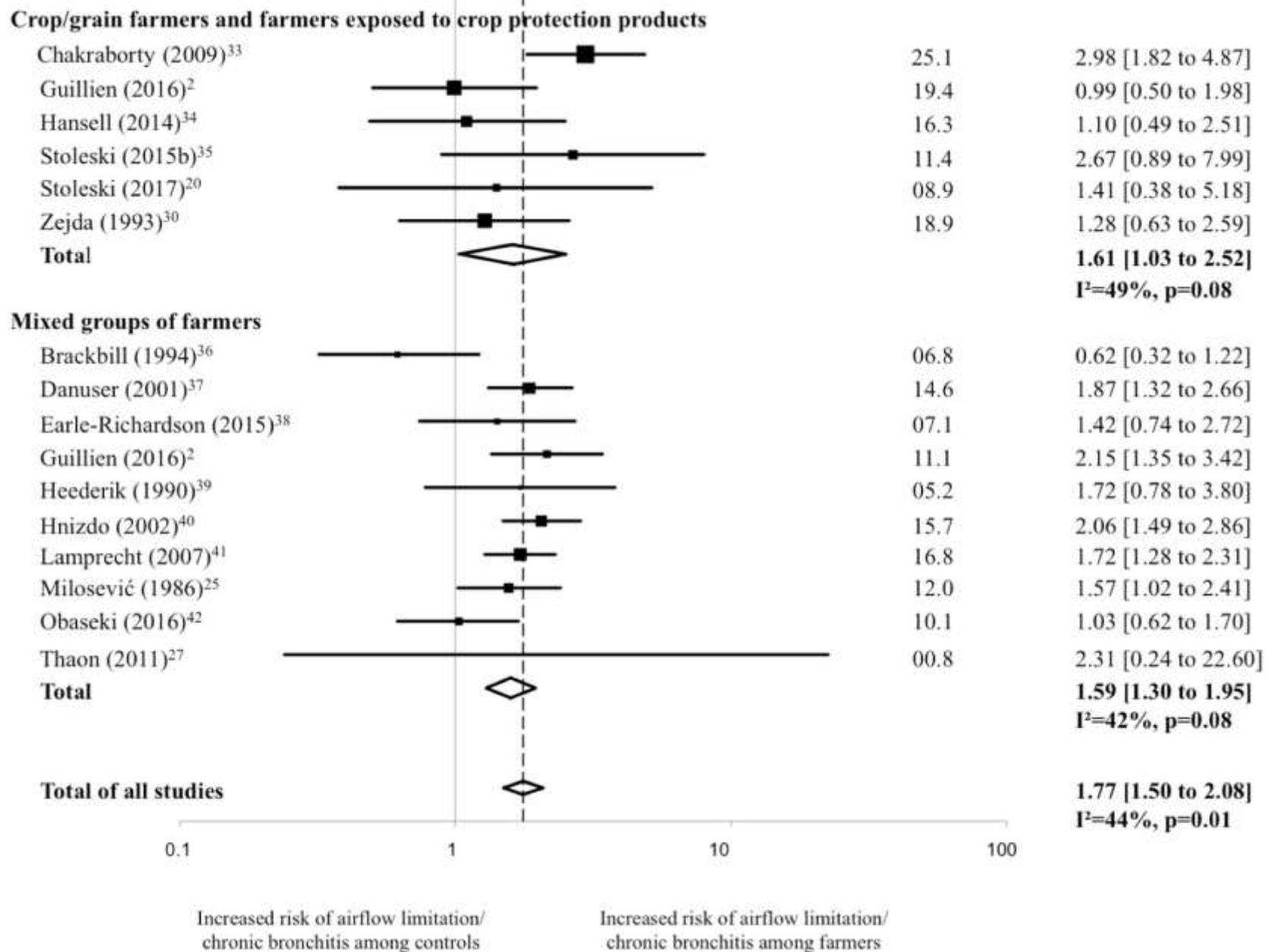
- ▶ Agriculture and farming have been associated with increased prevalence of chronic obstructive pulmonary disease (COPD).
- ▶ This association varies from one agricultural job to another, and data for some agricultural jobs are conflicting.

### **What are the new findings?**

- ▶ Only a few epidemiological studies use the appropriate definition of COPD for studying the relationship between farming and COPD.
- ▶ This meta-analysis shows that cattle farming, swine farming and poultry farming are strongly associated with airflow limitation and chronic bronchitis.
- ▶ Crop/grain farmers have also a higher prevalence of airflow limitation and of chronic bronchitis compared with unexposed controls.

### **How might this impact on policy or clinical practice in the foreseeable future?**

- ▶ New epidemiological studies investigating different farming groups and using the appropriate definition of COPD are needed.





CrossMark

# Prevalence and risk factors for COPD in farmers: a cross-sectional controlled study

Alicia Guillien<sup>1</sup>, Marc Puyraveau<sup>2</sup>, Thibaud Soumagne<sup>1,3</sup>, Stéphanie Guillot<sup>4</sup>, Fabrice Rannou<sup>5</sup>, David Marquette<sup>4</sup>, Patrick Berger<sup>6</sup>, Stéphane Jouneau<sup>7</sup>, Elisabeth Monnet<sup>8</sup>, Frédéric Mauny<sup>2</sup>, Jean-Jacques Laplante<sup>9</sup>, Jean-Charles Dalphin<sup>3,10</sup> and Bruno Degano<sup>1,11</sup>

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Conflict of interest: None declared.

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TABLE 1 Population characteristics

	Controls	Farmers (all)	Farmers (by category)					
			Crop	Cattle	Swine	Poultry	≥2 types of livestock	Other farm production
<b>Subjects</b>	917	3787	411	1638	233	192	333	980
<b>Males</b>	423 [46]	2371 [63]*	272 [66]*	998 [61]*	153 [66]*	102 [53]	209 [63]*	637 [65]*
<b>Age years</b>								
40–49	307 [34]	1200 [32]	164 [40]*	450 [27]*	73 [31]	72 [38]*	98 [29]	343 [35]
50–59	288 [31]	1181 [31]	134 [33]*	501 [31]*	86 [37]	72 [38]*	102 [31]	286 [29]
≥60	322 [35]	1406 [37]	113 [27]*	687 [42]*	74 [32]	48 [24]*	133 [40]	351 [36]
<b>BMI kg·m<sup>-2</sup></b>	25.7±4.4	26.8±4.5*	26.5±4.4*	27.1±4.7*	26.1±3.8	26.0±4.2	26.4±3.7*	27.1±4.7*
<b>Smoking status</b>								
Never	540 [59]	2571 [68]*	237 [58]	1227 [75]*	169 [73]*	127 [66]	239 [72]*	572 [58]
Former	250 [27]	736 [19]*	94 [23]*	261 [16]*	49 [21]*	36 [19]	61 [18]*	235 [24]
Current	127 [14]	480 [13]*	80 [19]*	150 [9]*	15 [6]*	29 [15]	33 [10]*	173 [18]
<b>Smoking intensity</b>								
<1 pack-year	549 [60]	2599 [69]*	238 [58]	1240 [76]*	172 [74]*	128 [67]	241 [72]*	580 [59]
1–15 pack-years	189 [21]	542 [14]*	70 [17]	194 [12]*	35 [15]*	25 [13]	42 [13]*	176 [18]
>15 pack-years	179 [19]	646 [17]*	103 [25]	204 [12]*	26 [11]*	39 [20]	50 [15]*	224 [23]
Pack-years	7.14±14.4	5.70±12.6*	7.78±14.6	4.09±10.1*	3.86±9.3*	6.76±14.0	4.98±11.5*	8.11±15.4
<b>Region</b>								
Brittany	796 [87]	2925 [77]*	327 [80]*	1091 [67]*	231 [99]*	187 [97]*	320 [96]*	769 [78]*
Franche-Comté	121 [13]	862 [23]*	84 [20]*	547 [33]*	2 [1]*	5 [3]*	13 [4]*	211 [22]*
<b>mMRC dyspnoea &gt;0</b>	165 [19]	816 [22]*	92 [23]	352 [22]*	34 [15]	44 [24]	50 [16]	244 [26]*
<b>Chronic cough</b>	106 [12]	687 [19]*	77 [19]*	296 [19]*	33 [15]	31 [17]	66 [21]*	184 [19]*
<b>Chronic sputum</b>	81 [9]	538 [15]*	52 [13]*	247 [16]*	22 [10]	24 [13]	48 [15]*	145 [15]*

TABLE 2 Prevalence and odds ratios for chronic obstructive pulmonary disease (COPD) adjusted<sup>#</sup> for age, smoking status and sex, according to the definition used to identify COPD

	GOLD			LLN		
	Cases	Prevalence	Adjusted OR (95% CI)	Cases	Prevalence	Adjusted OR (95% CI)
<b>All subjects</b>	221/4704	4.70 (4.08–5.30)		131/4704	2.78 (2.31–3.26)	
<b>Controls</b>	27/917	2.94 (1.85–4.04)	1.00	14/917	1.53 (0.73–2.32)	1.00
<b>Farmers</b>	194/3787	5.12 (4.42–5.82)	<b>1.94 (1.23–3.06)</b>	117/3787	3.09 (2.54–3.64)	<b>2.28 (1.24–4.20)</b>
Crop	12/411	2.92 (1.29–4.55)	1.02 (0.48–2.20)	13/502	2.19 (0.77–3.60)	1.43 (0.56–3.66)
Cattle	79/1638	4.82 (3.79–5.86)	<b>1.84 (1.12–3.02)</b>	46/1822	2.50 (1.75–3.26)	1.86 (0.95–3.66)
Swine	13/233	5.58 (2.63–8.53)	<b>2.28 (1.06–4.87)</b>	9/266	3.86 (1.39–6.34)	<b>3.02 (1.16–7.83)</b>
Poultry	11/192	5.73 (2.44–9.02)	<b>2.60 (1.11–6.08)</b>	10/226	3.65 (0.99–6.30)	<b>3.04 (1.05–8.79)</b>
≥2 types of livestock	19/333	5.71 (3.21–8.20)	<b>2.02 (1.00–4.06)</b>	11/354	3.30 (1.38–5.22)	2.13 (0.83–5.47)
Other farm production	60/980	6.12 (4.62–7.62)	<b>2.01 (1.20–3.35)</b>	28/617	4.08 (2.84–5.32)	<b>2.47 (1.26–4.84)</b>

Data are presented as n/N or % (95% CI), unless otherwise stated. Data presented in bold are statistically significant. GOLD: Global Initiative for Chronic Obstructive Lung Disease; LLN: lower limit of normal. <sup>#</sup>: odds ratio for COPD adjusted for age (as a continuous variable), smoking status (1–15 pack-years, >15 pack-years or <1 pack-year (as reference)) and sex (female as reference).

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TABLE 4 Adjusted odds ratios<sup>#</sup> for chronic obstructive pulmonary disease (COPD) according to region and definition used to identify COPD

	GOLD				LLN			
	Brittany		Franche-Comté		Brittany		Franche-Comté	
	Cases	OR	Cases	OR	Cases	OR	Cases	OR
<b>Controls</b>	24/796	1.00	3/121	0.62 (0.17–2.25)	13/796	1.00	1/121	0.40 (0.05–3.26)
<b>Farmers (all)</b>	129/2925	1.00	65/862	<b>1.55 (1.11–2.16)</b>	81/2925	1.00	36/862	1.41 (0.92–2.15)
Cattle	34/1091	1.00	45/547	<b>2.46 (1.49–4.06)</b>	18/1091	1.00	23/547	<b>2.54 (1.29–5.01)</b>
Crop	8/327	1.00	4/84	1.22 (0.28–5.25)	7/327	1.00	2/84	0.67 (0.11–4.20)
Other farm production	44/769	1.00	16/211	1.34 (0.71–2.52)	29/769	1.00	11/211	1.45 (0.68–3.05)

Data are presented as n/N or OR (95% CI). Data presented in bold are statistically significant. GOLD: Global Initiative for Chronic Obstructive Lung Disease; LLN: lower limit of normal. <sup>#</sup>: odds ratio for COPD adjusted for age (as a continuous variable), smoking status (1–15 pack-years, >15 pack-years or <1 pack-year [as reference]) and sex (female as reference).

# Screening, détection ou diagnostic ?

- Symptômes
- VEMS/VEM6
- Combinaison d'un questionnaire et du VEMS/VEM6
- VEMS/CVF
- VEMS/CVF avec test de bronchodilatation
- Spirométrie complète

American Journal of  
Preventive Medicine

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RESEARCH ARTICLE

Case-Finding for Persistent Airway Obstruction in  
Farmers: A Questionnaire With Optimal Diagnosis Criteria



Alicia Guillien, MS,<sup>1</sup> Thibaud E. Soumagne, MD,<sup>2</sup> Marc Puyraveau, PhD,<sup>3</sup> Patrick Berger, MD, PhD,<sup>4</sup>  
Stéphanie L. Guillot, MD,<sup>5</sup> Fabrice Rannou, MD,<sup>6</sup> Stéphane Jouneau, MD, PhD,<sup>7</sup> Frédéric J. Mauny, MD, PhD,<sup>3</sup>  
Jean-Jacques Laplante, MD,<sup>8</sup> Jean-Charles Dalphin, MD,<sup>2,9</sup> Bruno Degano, MD, PhD<sup>1,10</sup>

**Table 1.** Prediction of the probability of persistent airway obstruction in the development population

Parameter	OR (95% CI)	$\beta$
History of respiratory disease		
No	1	0
Yes	5.02 (3.03, 8.32)	1.613
BMI		
$\geq 25$	1	0
<25	2.32 (1.43, 3.75)	0.840
Dyspnea		
mMRC=0	1	
mMRC>0	2.49 (1.52, 4.09)	0.913
Sex		
Female	1	0
Male	2.24 (1.27, 3.95)	0.808
Smoking status		
Never smokers	1	0
Former smokers	1.61 (0.82, 3.18)	0.479
Current smokers	9.32 (5.23, 16.62)	2.232
Age, years		
40-54	1	0
55-64	1.27 (0.70, 2.31)	0.242
65-75	2.65 (1.44, 4.88)	0.976
Occupation at risk		
No	1	0
Yes	2.47 (1.44, 4.23)	0.902
Constant	-	-7.033

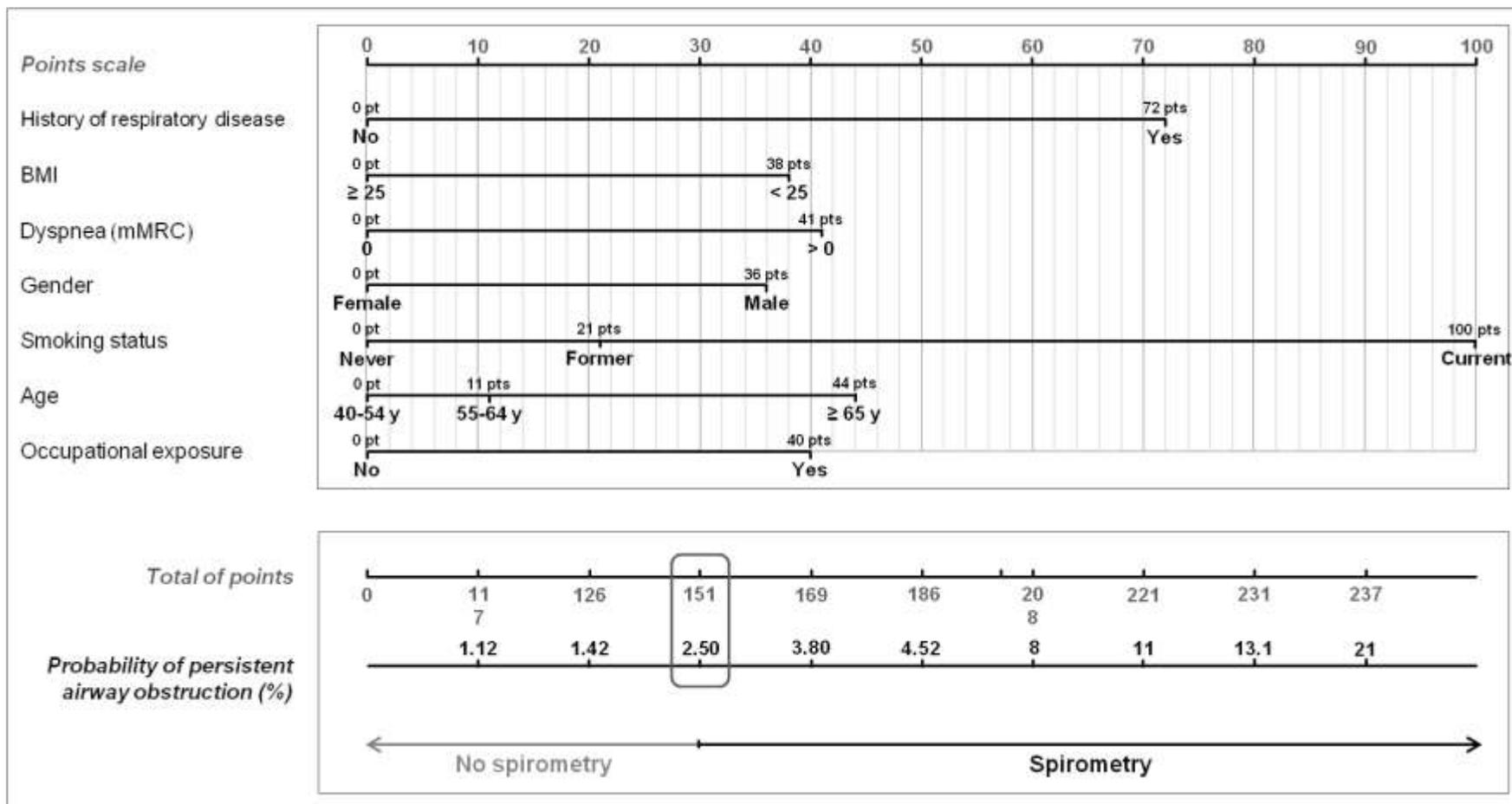
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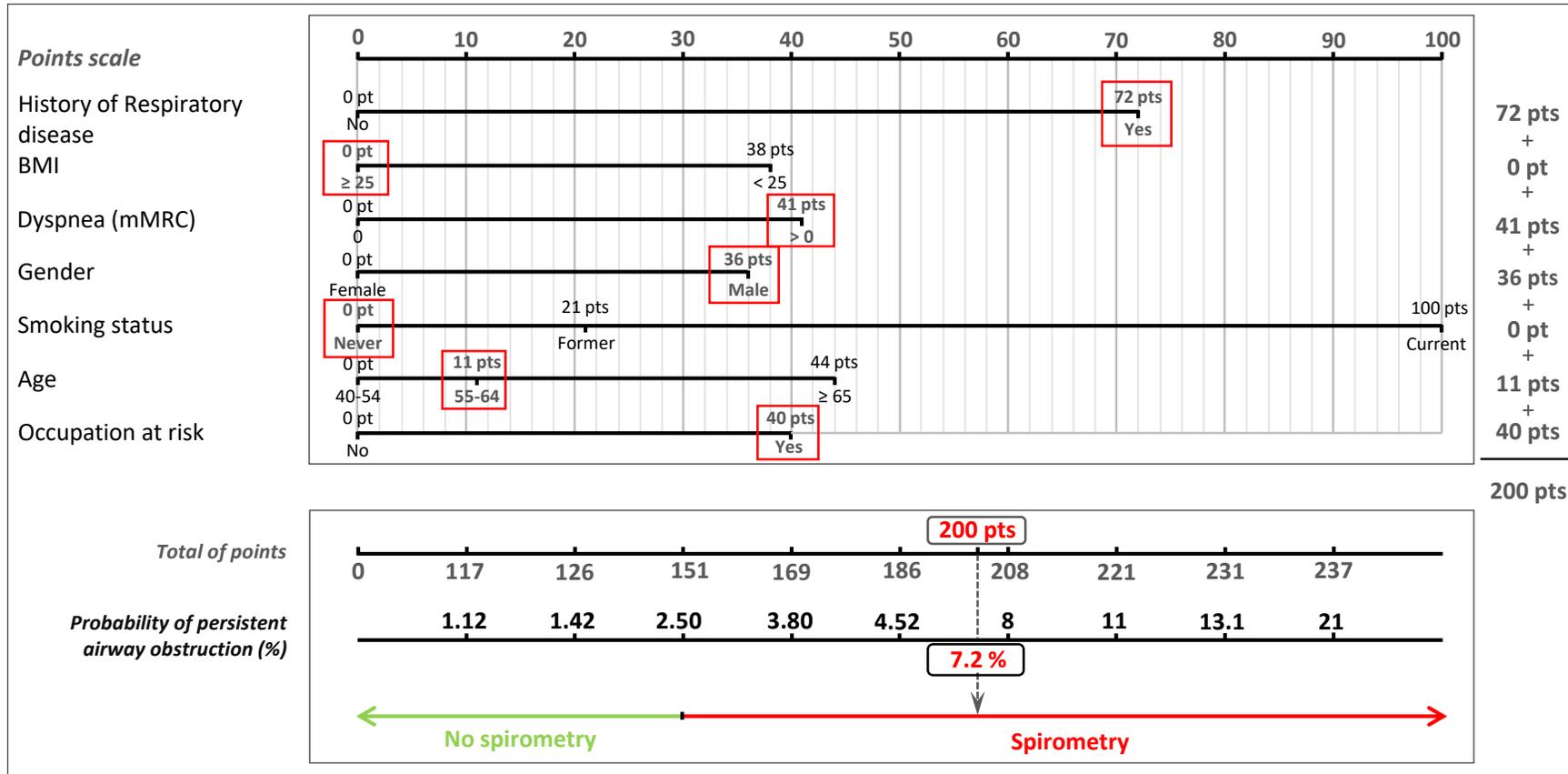
Odds (PAO=1) =  $-7.033 + 1.613 \times (\text{atcd maladie respi} = \text{oui}) + 0.84 \times (\text{IMC} < 25) + 0.808 \times (\text{sexe} = \text{Homme}) + 0.479 \times (\text{Ex fumeur} = \text{oui}) + 2.232 \times (\text{Fumeur actif} = \text{oui}) + 0.242 \times (\text{Age} = 55-64 \text{ ans}) + 0.976 \times (\text{Age} = 65-75 \text{ ans}) + 0.902 \times (\text{expo prof} = \text{oui})$

$\text{Proba}(\text{PAO}=1) = \text{odds}(\text{PAO}=1) / [1 + \text{odds}(\text{PAO}=1)]$

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Occupation at risk		
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Yes	2.47 (1.44, 4.23)	0.902
Constant	-	-7.033



**Exemple** : Homme de 60 ans, producteur laitier, non-fumeur, IMC à 27.5 kg/m<sup>2</sup>, avec un antécédent de maladie respiratoire, dyspnéique



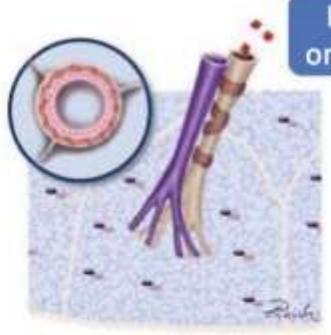
**Probabilité = 7.2%**

**Décision** : Réaliser une spirométrie

# Pneumopathie d'hypersensibilité (PHS)

<b>Classification</b>	<b>Evolution clinique</b>	<b>TDM</b>
<b>Forme <u>aiguë</u></b> qq semaines/mois ( $< 6$ mois)	Réversible Complètement résolutive Symptômes en lien avec l'exposition	<b>Verre dépoli prédominant aux lobes supérieurs et moyen</b> <b>Mosaïque</b> <b>Nodules centro-lobulaire</b> <b>Trappage</b>
<b>Forme <u>chronique</u></b> plusieurs mois ( $> 6$ mois)	En partie réversible Risque de progression	<b>Fibrose prédominant aux lobes supérieurs et moyen,</b> péribronchovasculaire Épargnant relativement les bases

Inhaled small organic particles



a) Bronchiolocentric inflammation

The diagram shows a bronchiole with a thickened wall and an inset showing a magnified view of the wall. The CT scan shows centrilobular ground-glass nodules.

Centrilobular ground-glass nodules

b) Narrowing of small airways

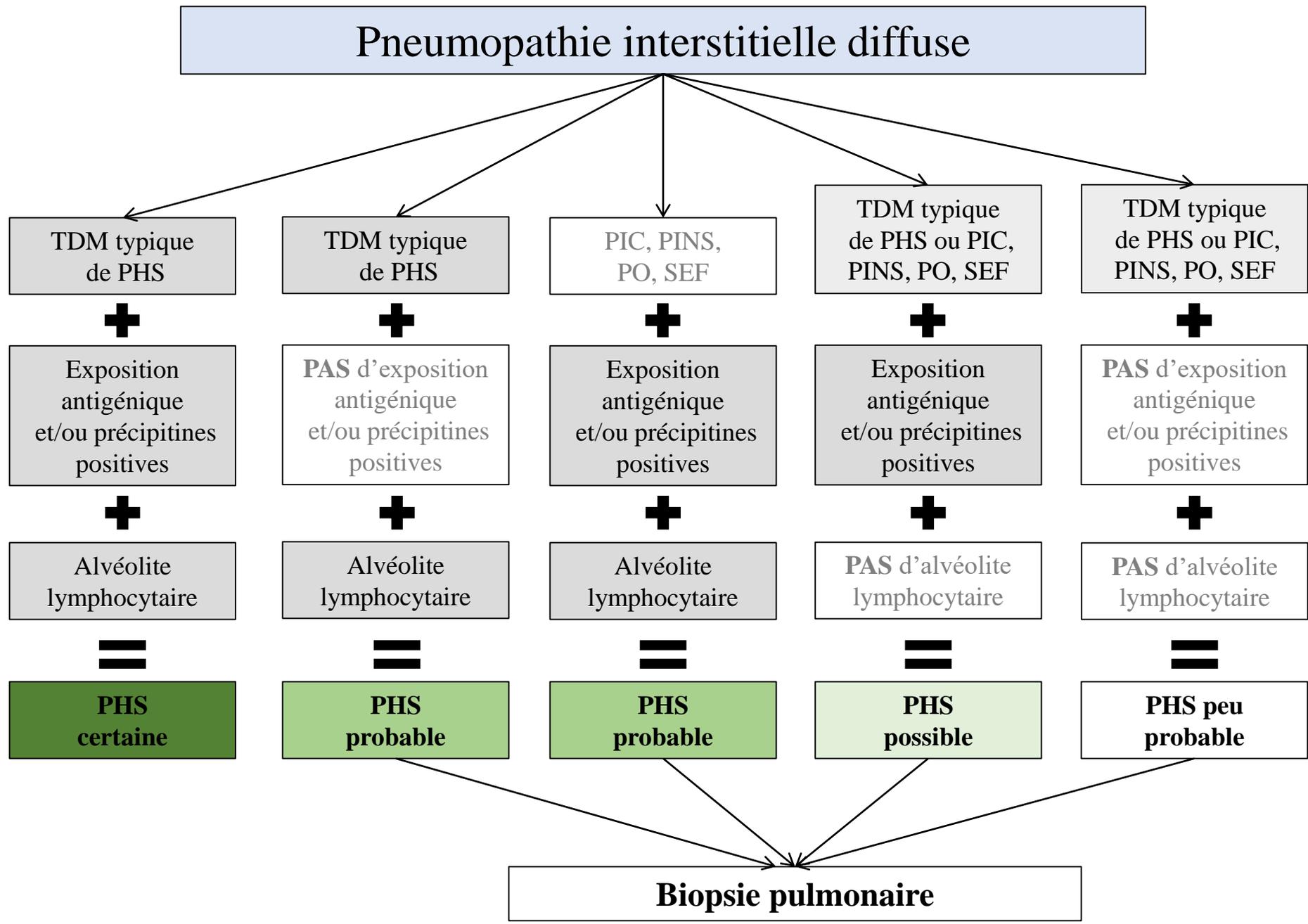
The diagram shows a bronchiole with a thickened wall and an inset showing a magnified view of the wall. The CT scan shows air-trapping, indicated by asterisks (\*).

Air-trapping

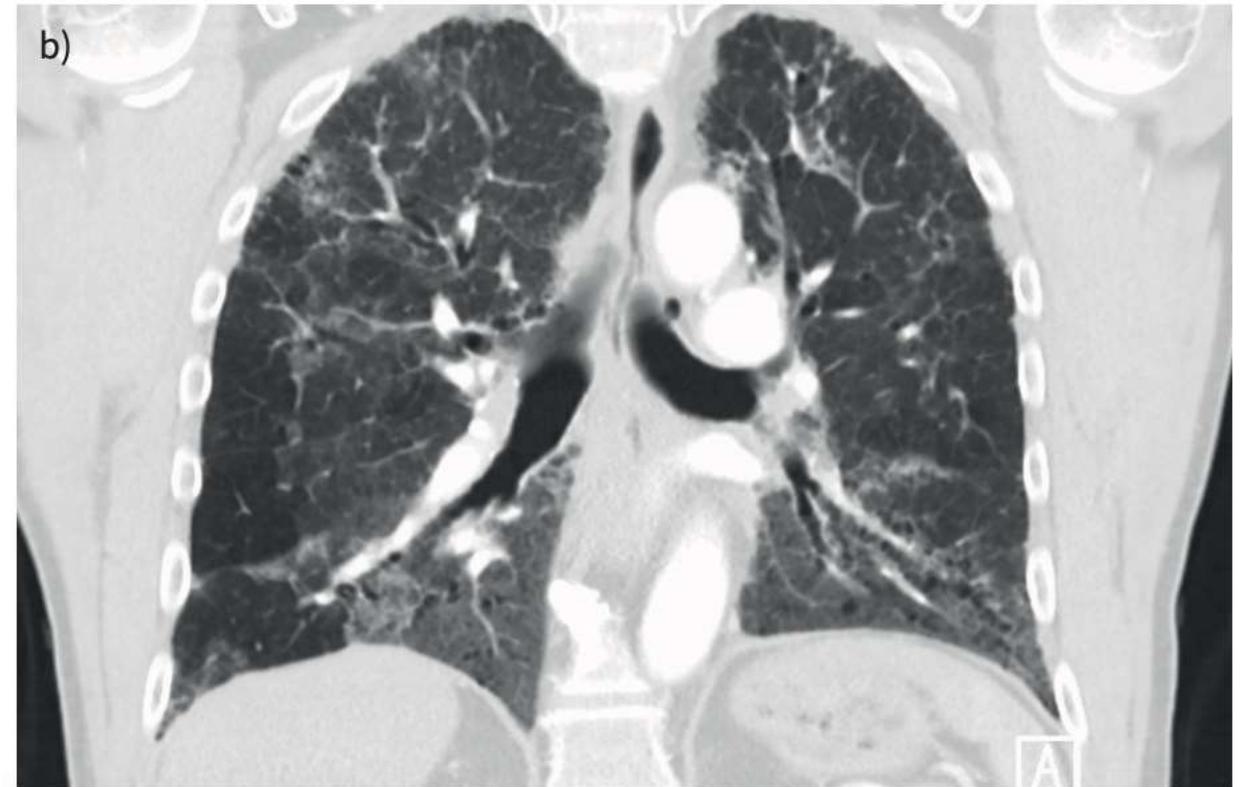
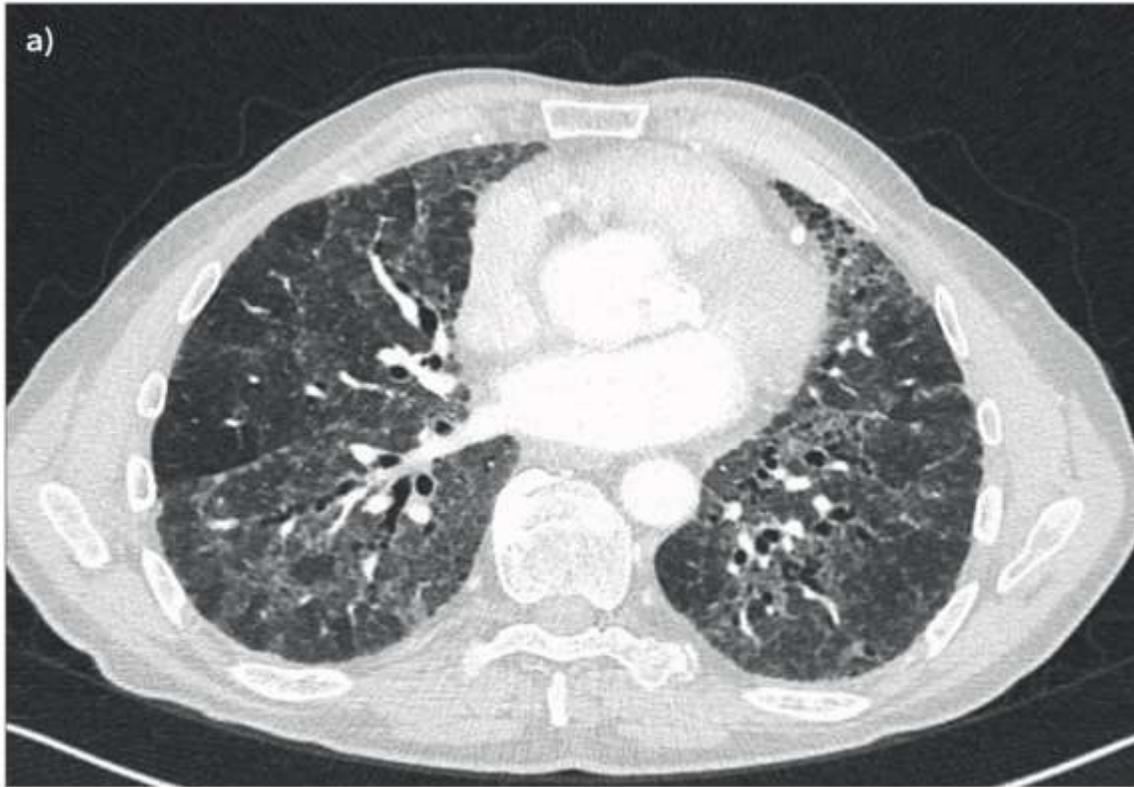
c) Interstitial inflammation

The diagram shows a bronchiole with a thickened wall and an inset showing a magnified view of the wall. The CT scan shows ground glass.

Ground glass

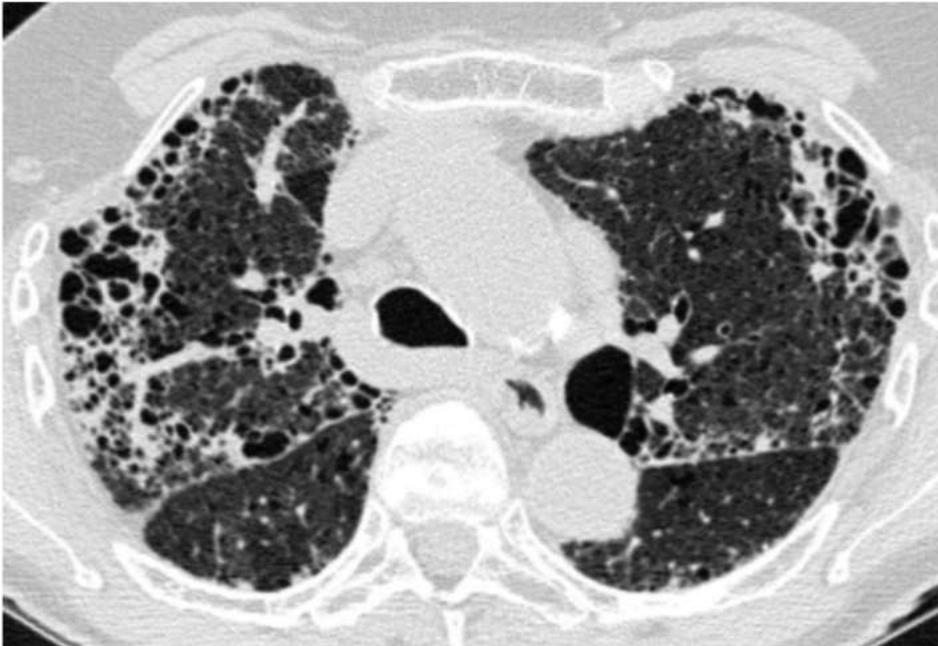


# Formes chroniques (fibreuses) de PHS



# Formes chroniques fibreuses de PHS vs. FPI

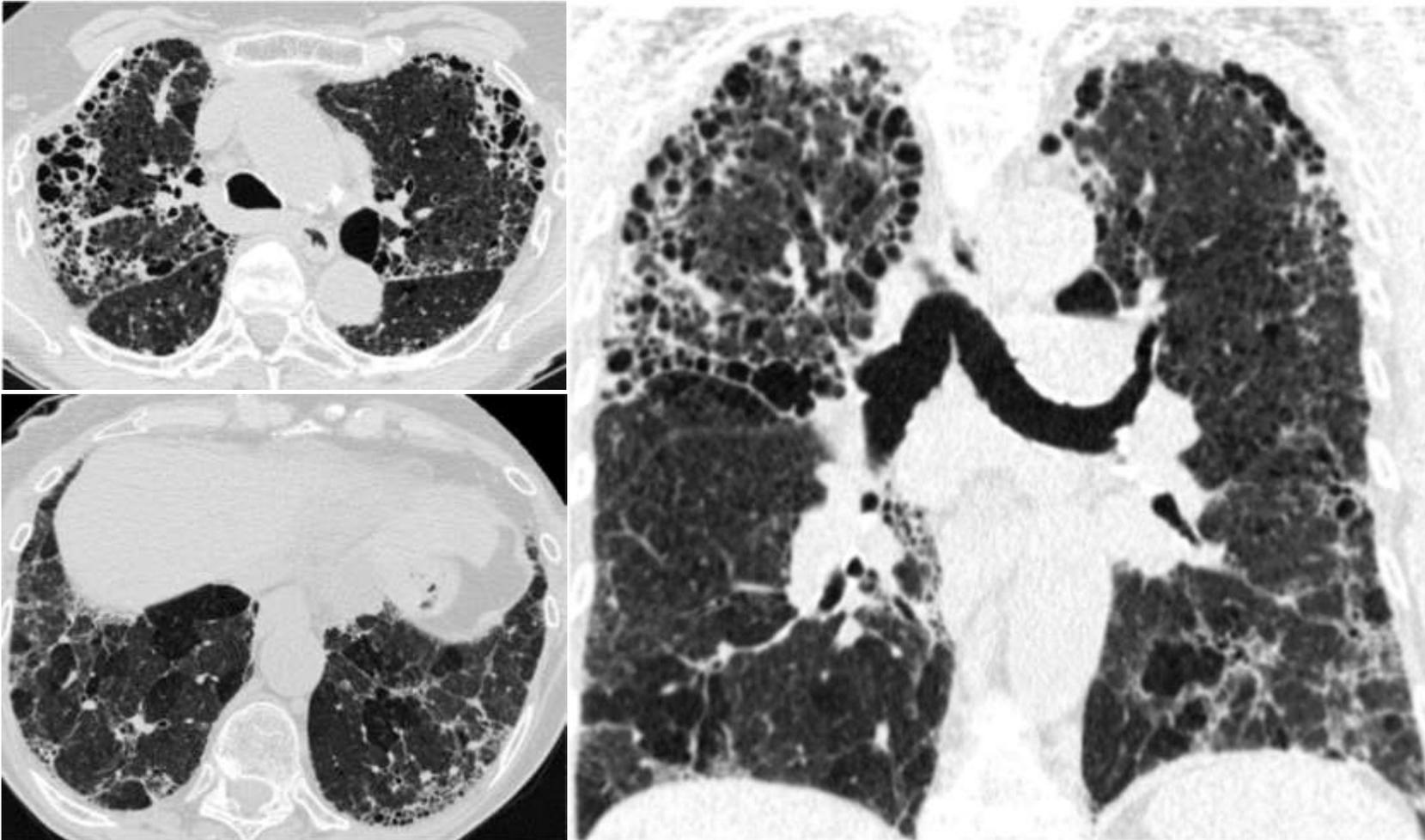
**PHS**



**FPI**



# Formes chroniques fibreuses de PHS vs. FPI



- **trappage**
- **verre dépoli centrolobulaires**
- **absence de prédominance basale**

**TABLE 1** Factors associated with mortality in patients with HP

<b>Intrinsic factors</b>	Older age
	Male sex
	Genetic predisposition
<b>Exposures</b>	Unidentifiable inciting antigen
	Duration of exposure to inciting antigen
	History of smoking
<b>Physiology</b>	Low FVC
	Low $D_{LCO}$
	Decline in FVC
<b>Radiology</b>	Lower BAL lymphocytosis
	Presence of fibrosis on HRCT
	Extent of fibrosis on HRCT
<b>Histology</b>	UIP pattern on HRCT
	UIP pattern
	Fibrotic NSIP pattern

BAL: bronchoalveolar lavage;  $D_{LCO}$ : diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; HRCT: high-resolution computed tomography; NSIP: non-specific interstitial pneumonia; UIP: usual interstitial pneumonia.

# En guise de conclusion

- Il faut s'acharner à expliquer un symptôme (dyspnée, toux, expectoration, fièvre récurrente,...)
  - Un mauvais diagnostic est associé à une « perte de chance »
- La BPCO et la PHS sont spécifiquement associées à la profession d'agriculteur
  - Mais l'asthme est une maladie fréquente, et la BPCO des agriculteurs a des caractéristiques proches de celles de l'asthme
- La spirométrie est indispensable pour identifier la BPCO, mais est moins utile pour l'asthme et rarement pertinente pour la PHS
  - Interrogatoire
  - Imagerie
  - Avis spécialisé