

# EVOLUTION DES COLONISATIONS BRONCHIQUES BACTÉRIENNES CHEZ 198 PATIENTS ADULTES APRÈS 1 AN DE TRAITEMENT PAR ETI

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# CONTEXTE

## CFF patient registry : 2021

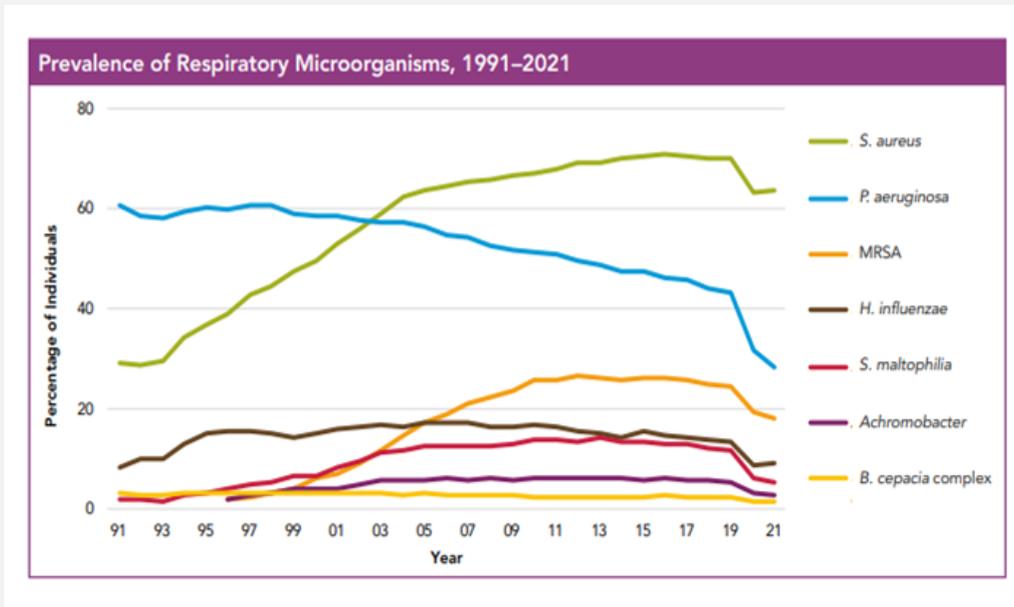


Figure 1: Prevalence of respiratory microorganisms from 1991 to 2021, CFF patient registry

## Registre Français : 2021

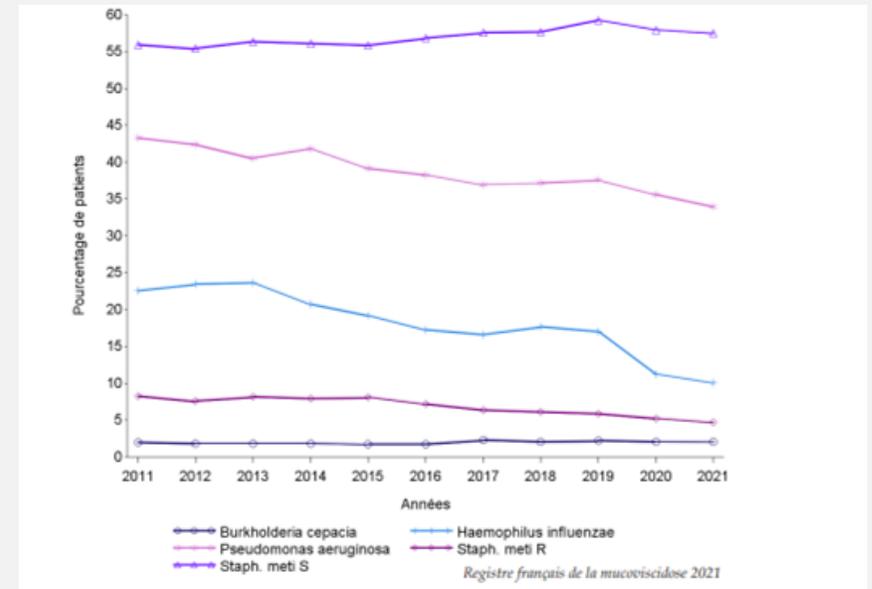


Figure 2: Prevalence of respiratory micro-organisms from 2011 to 2021, French CF patient registry

# OBJECTIFS

**=> Décrire l'impact de l'ETI sur la colonisation bronchique**

1. Le traitement par ETI modifie la prévalence des pathogènes bronchiques habituels de la mucoviscidose et la densité bactérienne bronchique globale ?
2. Comment le traitement par ETI impacte la colonisation bronchique par *Pseudomonas aeruginosa* ?
3. Est-ce qu'on identifie une corrélation entre l'amélioration clinique sous ETI et la diminution des pathogènes bronchiques (type et densité) ?

# METHODES

Etude rétrospective observationnelle

CHU de Lyon

**Critères d'inclusion** : tous les patients adultes traités par ETI (2019-2021)

**ECBC** : spontanés, à l'occasion de visites programmées de routine et/ou exacerbations, analyse microbiologique centralisée à l'institut des agents infectieux HCL

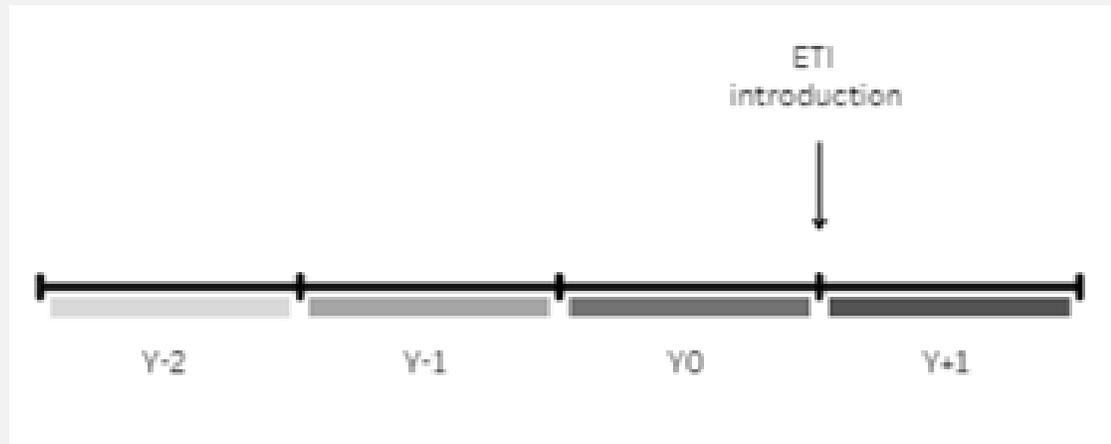


Figure 3 : schéma de l'étude

## **Définition statut de colonisation :**

- Persistant si > 50% par an
- Intermittant si < 50% par an
- "Dé"colonisé si aucun dans l'année

**Symptomatique ou non**

# POPULATION

## 198 patients inclus

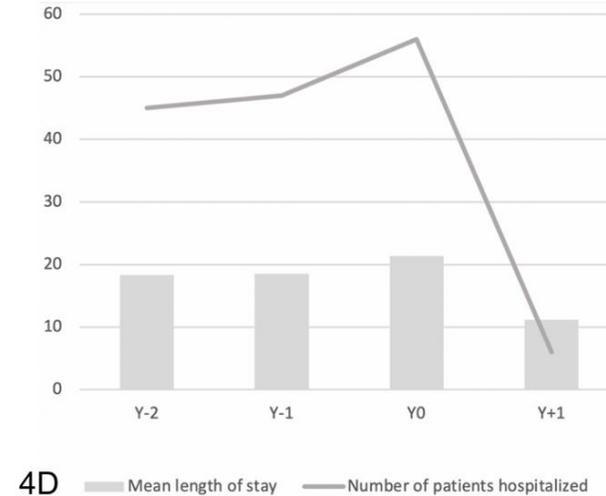
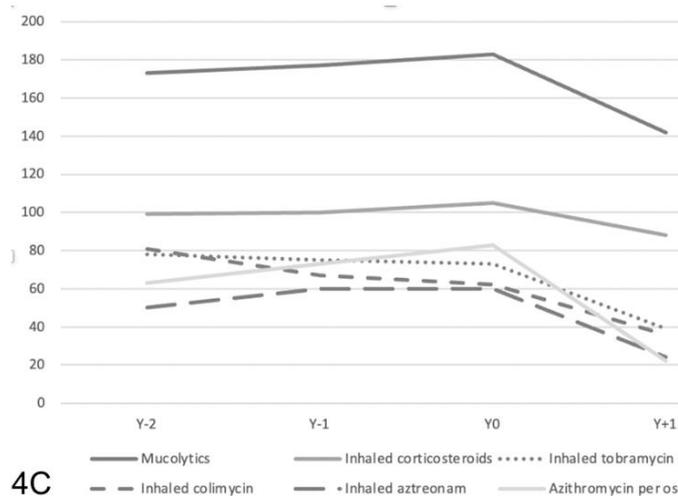
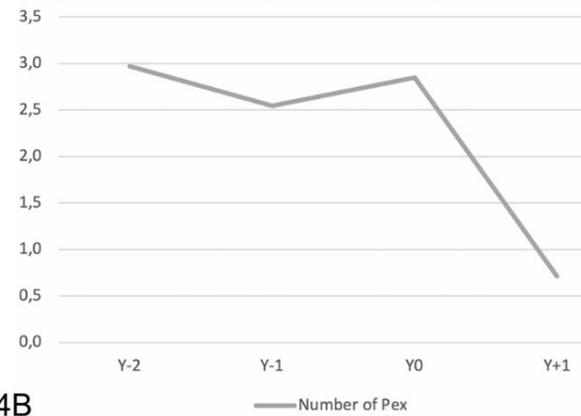
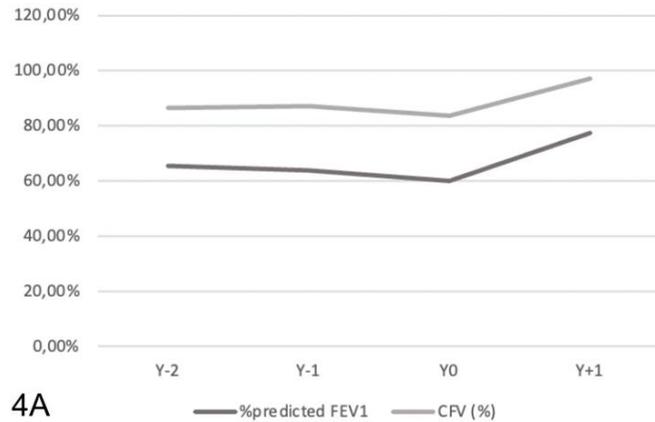
2 patients n'ont pas reçu 1 an de traitement complet

Tous les patients étaient inclus dans les analyses

	<b>At ETI initiation N =198</b>
<b>Males</b>	120 (60.6%)
Age - median (IQR)	28.8 (11.3)
BMI - median (IQR)	21.7 (3.6)
<i>Mutation</i>	
Homozygous DF508	122 (62%)
Heterozygous G542X	9 (4.5%)
Heterozygous N1303K	8 (4.4%)
<i>Modulator anteriority</i>	
Any	107 (54%)
Lumacaftor/Ivacaftor	105 (53%)
Ivacaftor/Tezacaftor	2 (0.01%)

*Table 1: Caractéristiques des patients à l'initiation de l'ETI*

# CLINICAL OUTCOMES



*Figure 4 : Evolution des paramètres cliniques*

**4A.** Evolution of lung function before and after ETI, % predicted FEV1 and CFV.

**4B.** Evolution of pulmonary exacerbations

**4C.** Evolution of treatment load, focusing on pulmonary treatments: mucolytics, inhaled corticosteroids, inhaled antibiotics, oral antibiotics

**4D.** Evolution of prevalence and length of stay of hospitalizations for respiratory reasons

# ECHANTILLONAGE DES ECBC

	Before ETI			After ETI
	2 years before N=195	1 year before N=196	Year of Introduction N=198	1 year after N=197
Number of sputum cultures – <i>mean (+/- SD)</i>	4.4 (+/- 2.0)	3.9 (+/- 1.7)	4.5 (+/- 1.8)	2.8 (+/- 1.7)

*Table 2: Nombre d'ECBC par an*

Pas d'ECBC  
pour 17  
patients non  
sécrétants

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DENSITE MICROBIENNE GLOBALE SOUS ETI ?

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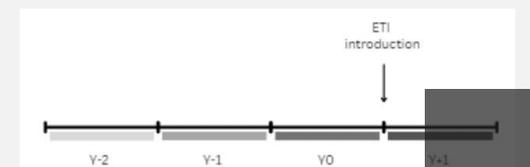
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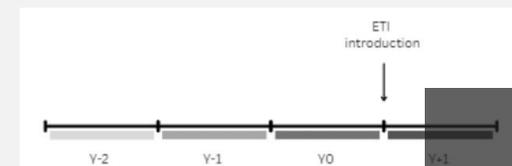
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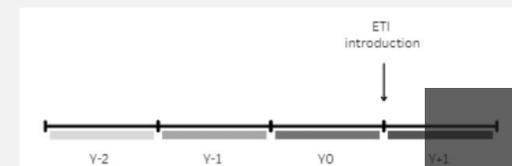
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	2 Years before N = 194 <sup>1,2</sup>	1 Year before N = 196 <sup>1,2</sup>	Year of Introduction N = 198 <sup>1,2</sup>	1 Year after N = 179 <sup>1,2</sup>	
<i>Pseudomonas aeruginosa</i>	134 (69) [62 - 75]	144 (73) [67 - 79]	142 (72) [65 - 78]	105 (59) [51 - 66]	<0.001
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<i>Stenotrophomonas maltophilia</i>	40 (21) [15 - 27]	29 (15) [10 - 21]	37 (19) [14 - 25]	13 (7.3) [4.1 - 12]	<0.001
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All Germs of interest	193 (99) [97 - 100]	194 (99) [96 - 100]	195 (98) [95 - 100]	161 (90) [84 - 94]	<0.001

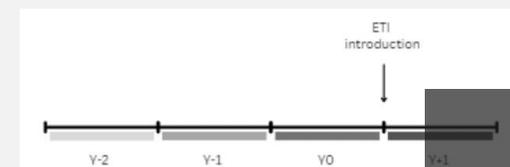
<sup>1</sup>n (prevalence in %) [CI<sup>2</sup> of prevalence according to the Wilson method]

<sup>2</sup>CI = Confidence Interval

<sup>3</sup>p-value result of mixed model before and after ETI and adjusted according to the Holm method

<sup>4</sup>Methicillin-resistant *Staphylococcus aureus*

<sup>5</sup>Methicillin-sensitive *Staphylococcus aureus*



Prevalence of documentation during the year	Before ETI			After ETI	p-value <sup>3</sup>
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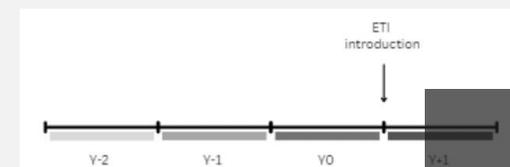
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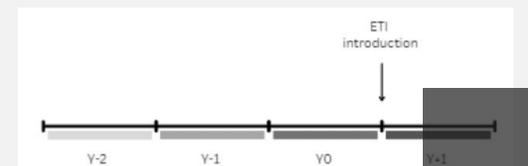
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<sup>2</sup>CI = Confidence Interval

<sup>3</sup>p-value result of mixed model before and after ETI and adjusted according to the Holm method

<sup>4</sup>Methicillin-resistant *Staphylococcus aureus*

<sup>5</sup>Methicillin-sensitive *Staphylococcus aureus*



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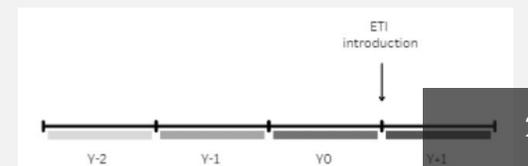
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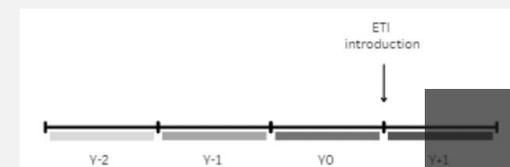
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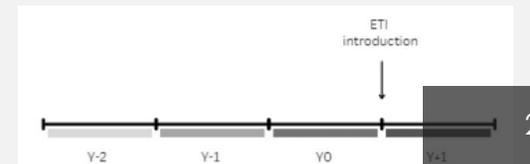
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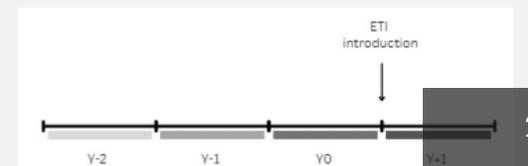
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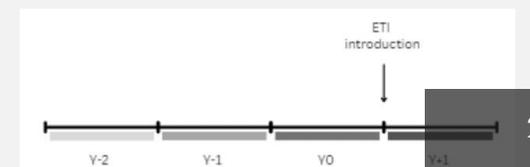
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<sup>4</sup>Methicillin-resistant *Staphylococcus aureus*

<sup>5</sup>Methicillin-sensitive *Staphylococcus aureus*

1 an après ETI : 2 *M. Avium* et 1 *M. intracellulare*  
Aucun des *M. abscessus* et *M. chimerare* de Y0 retrouvé



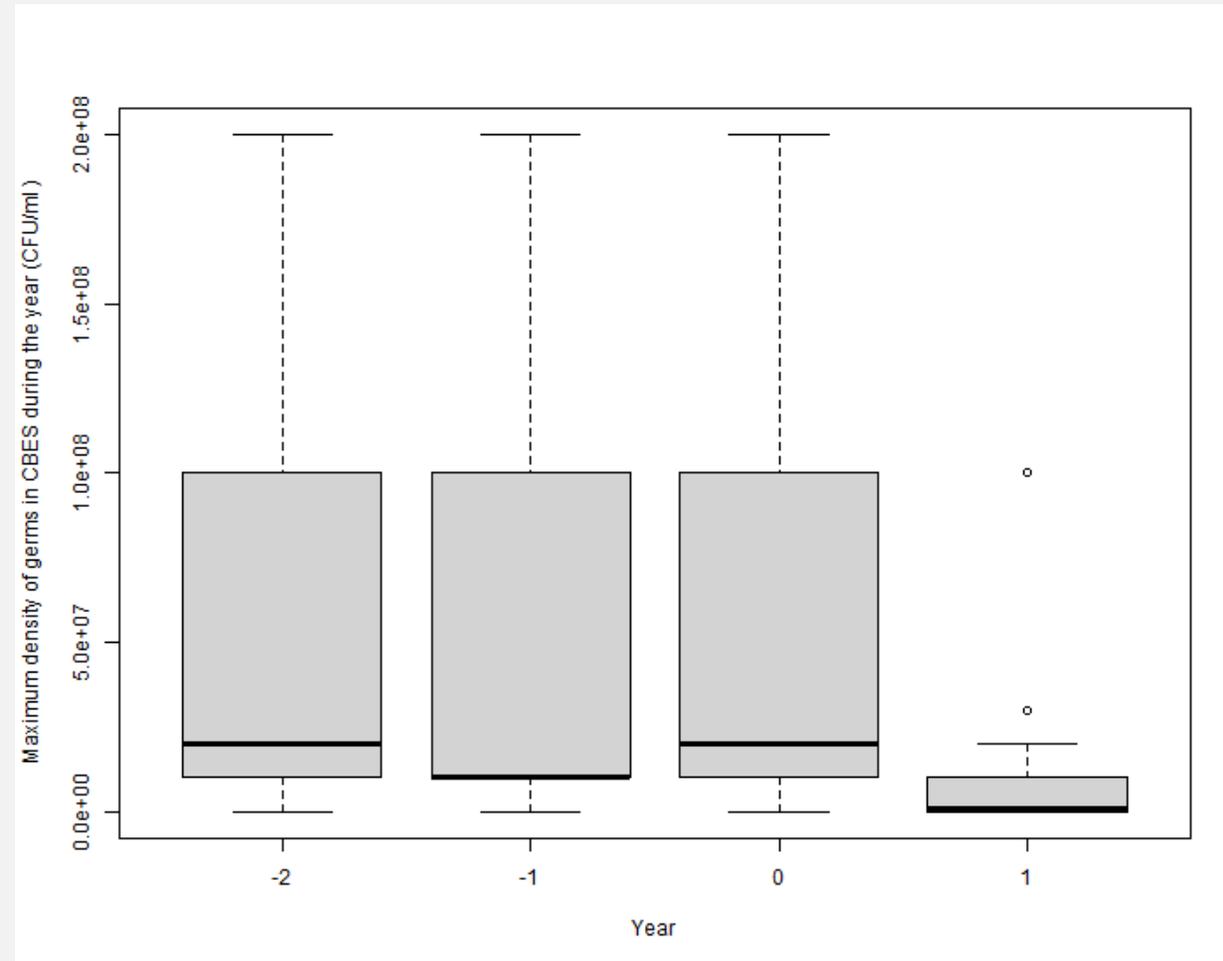


Figure 4 : Evolution de la densité globale des pathogènes dans les ECBC



## 2. *PSEUDOMONAS AERUGINOSA* ?

## Définition statut de colonisation :

- Persistant si  $> 50\%$  par an
- Intermittant si  $< 50\%$  par an
- "Dé"colonisé si aucun dans l'année
- Min 2 ECBC par an

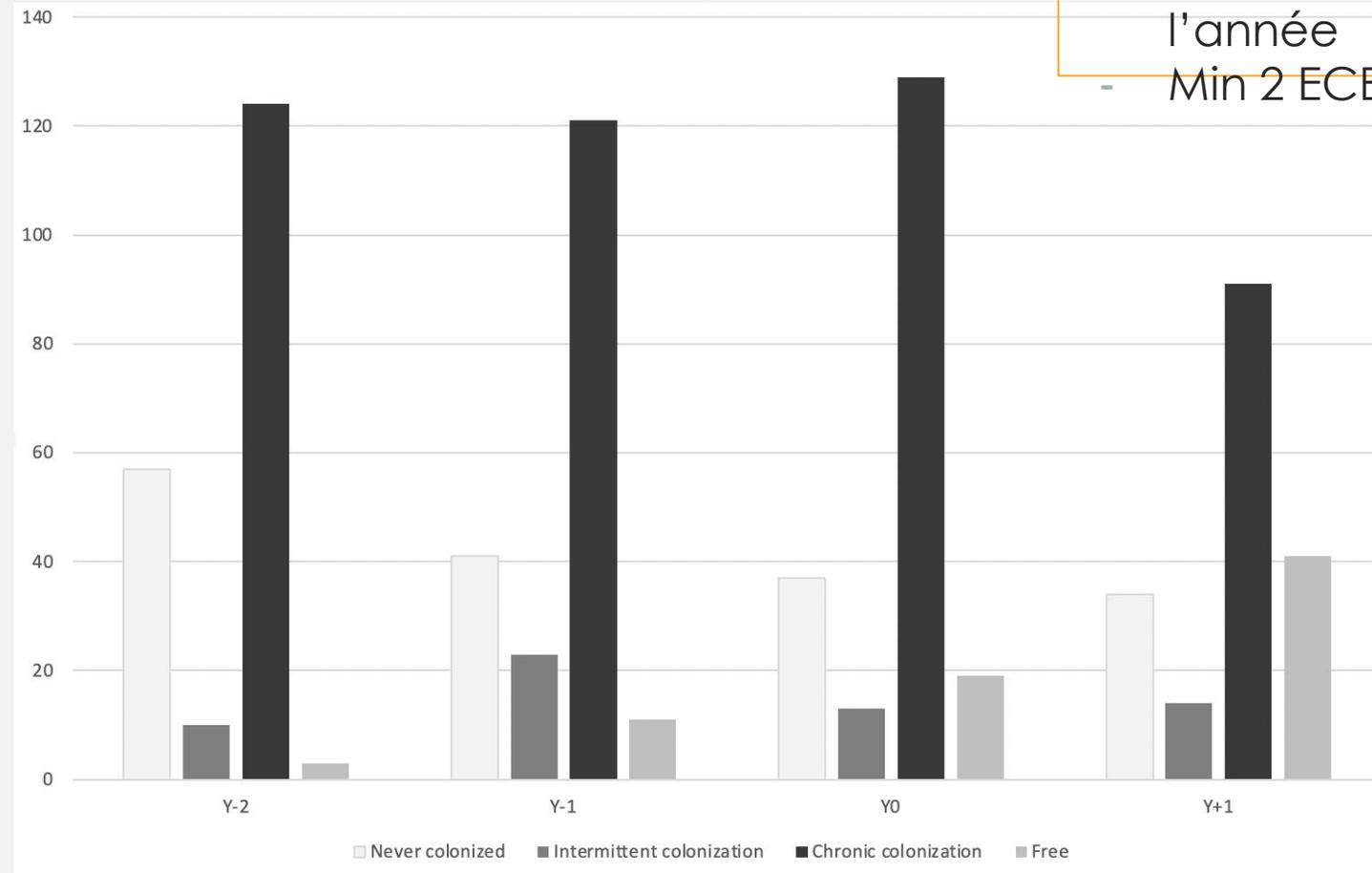


Figure 5 : Evolution du statut de la colonisation à *Pseudomonas*



# Aucune nouvelle colonisation sous ETI

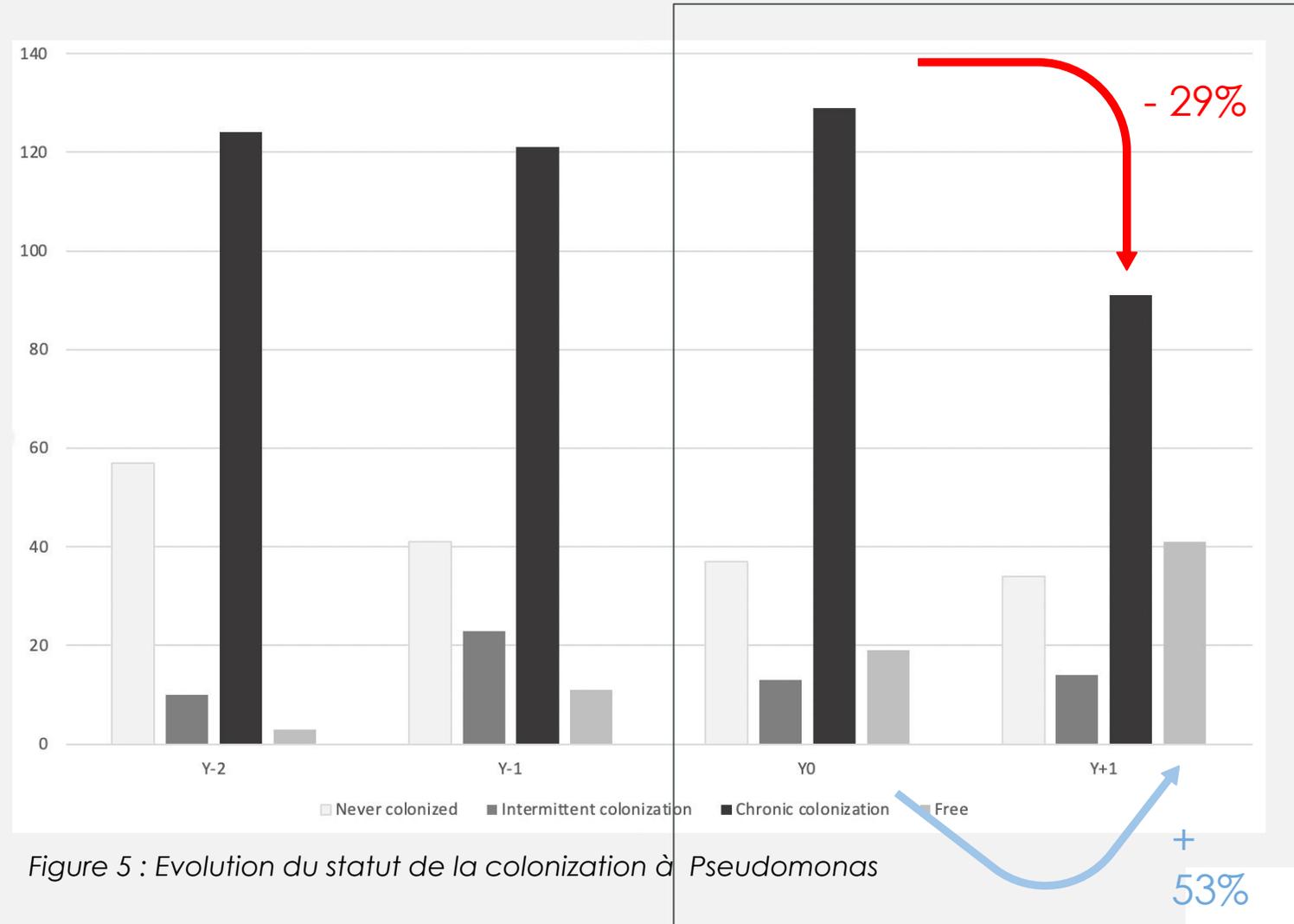
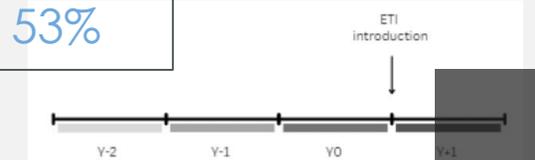
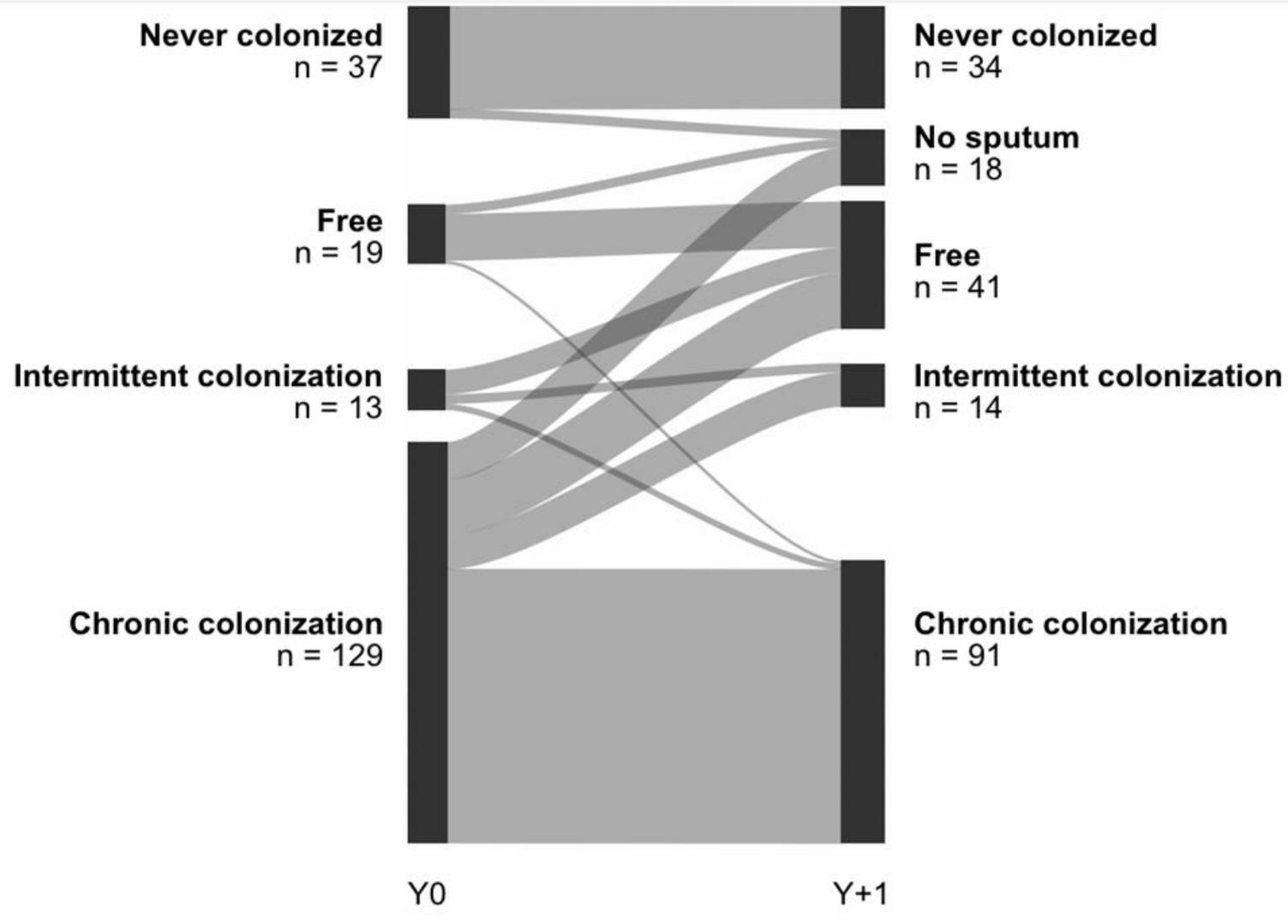
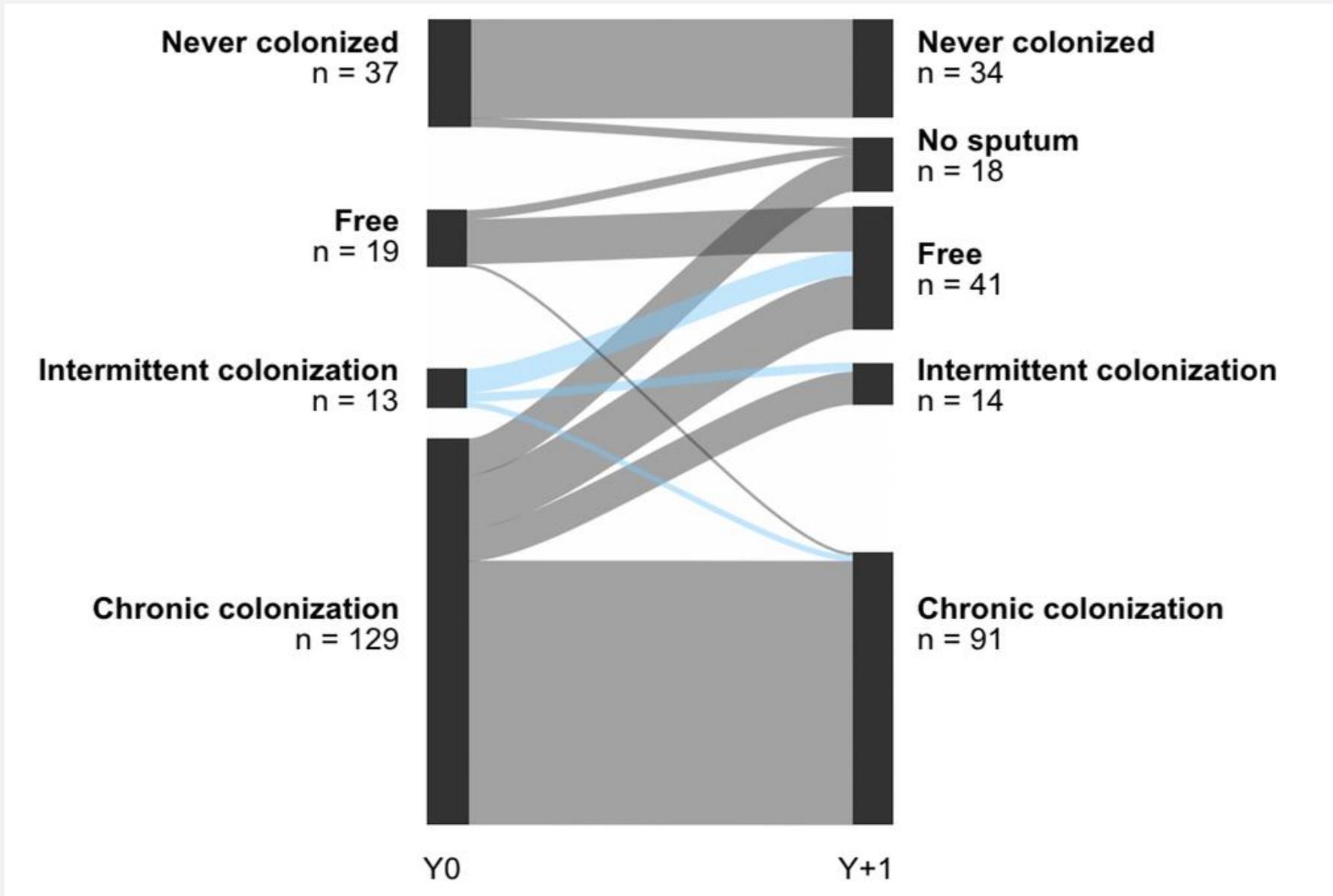
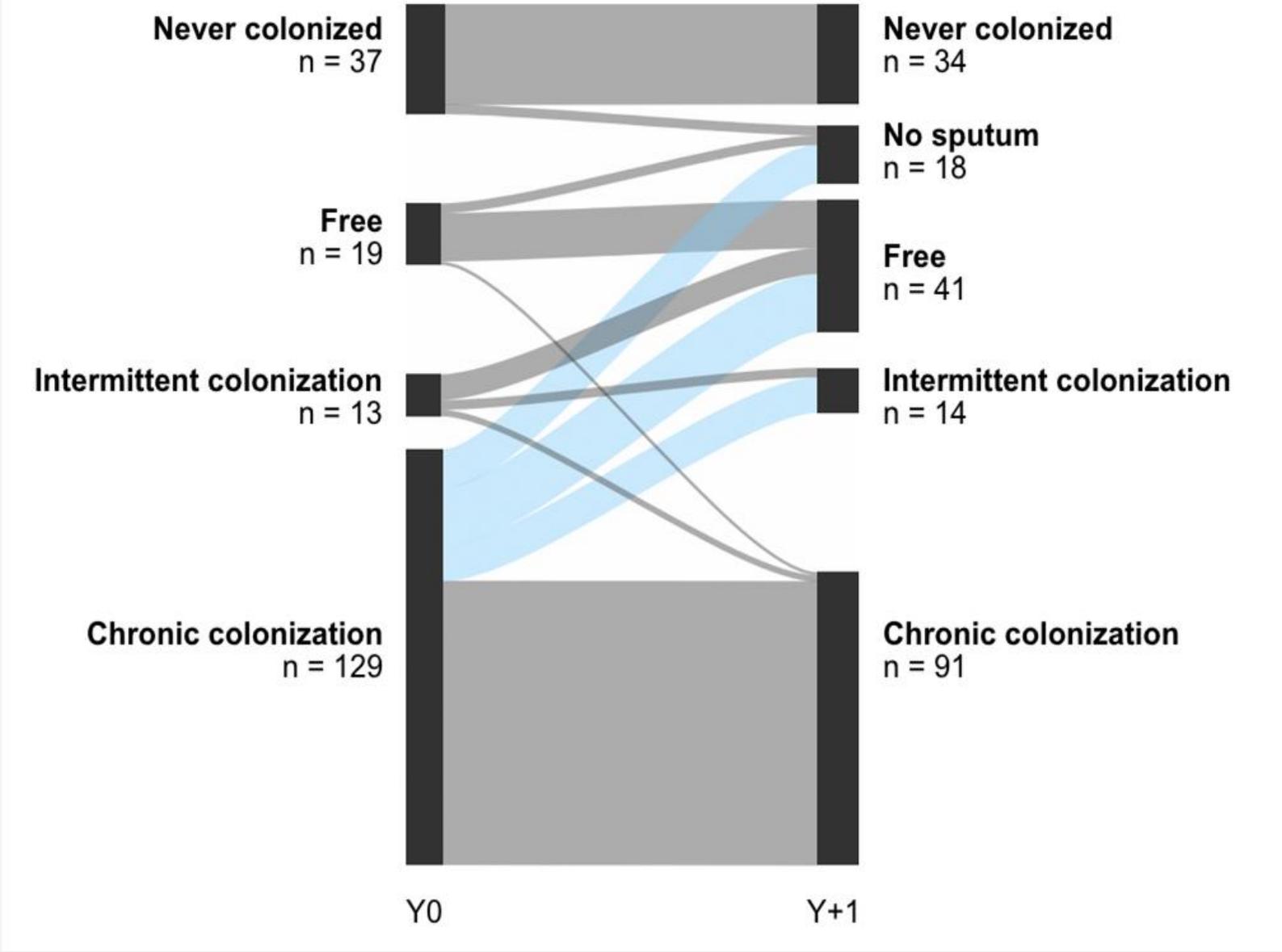


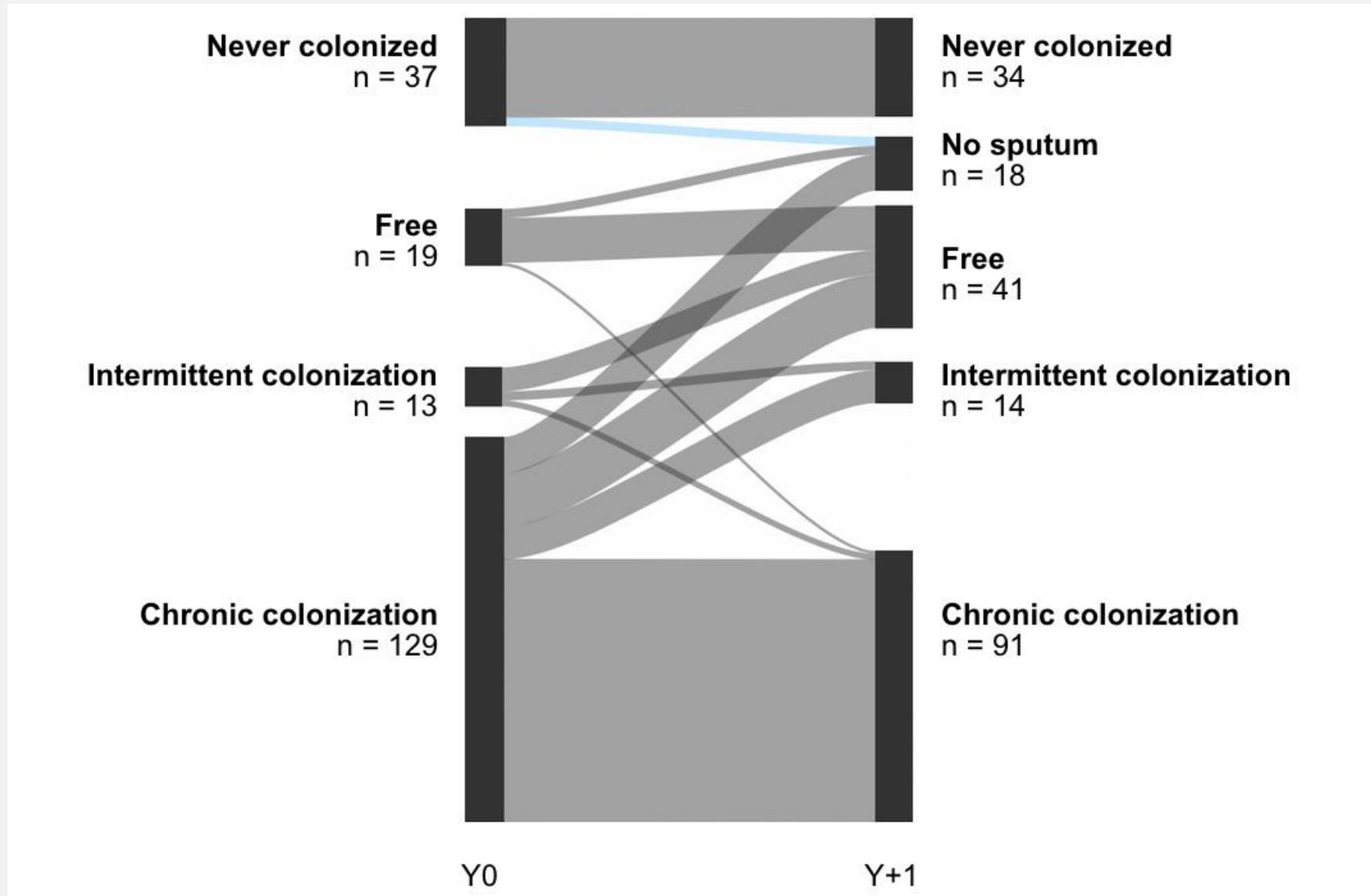
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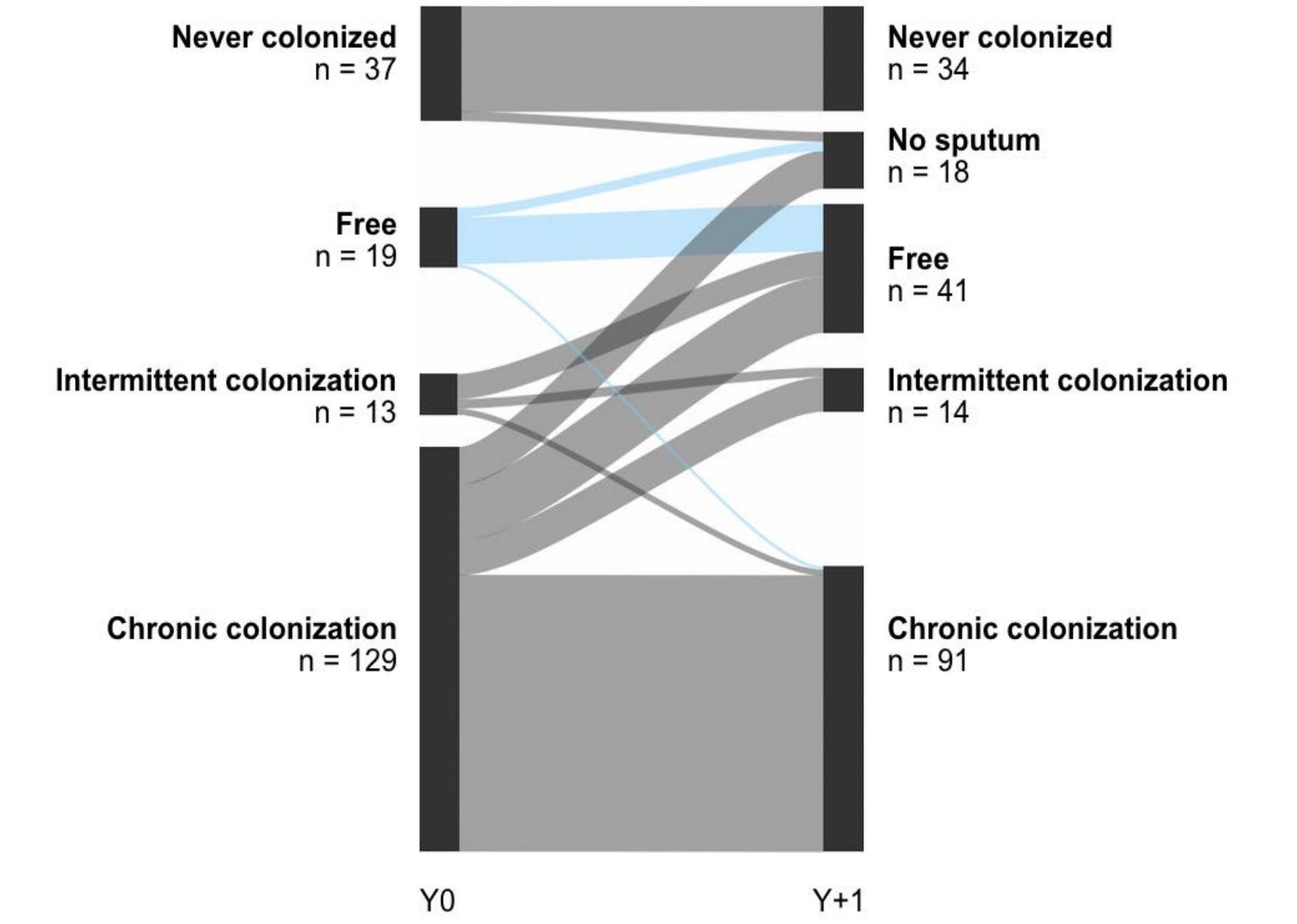










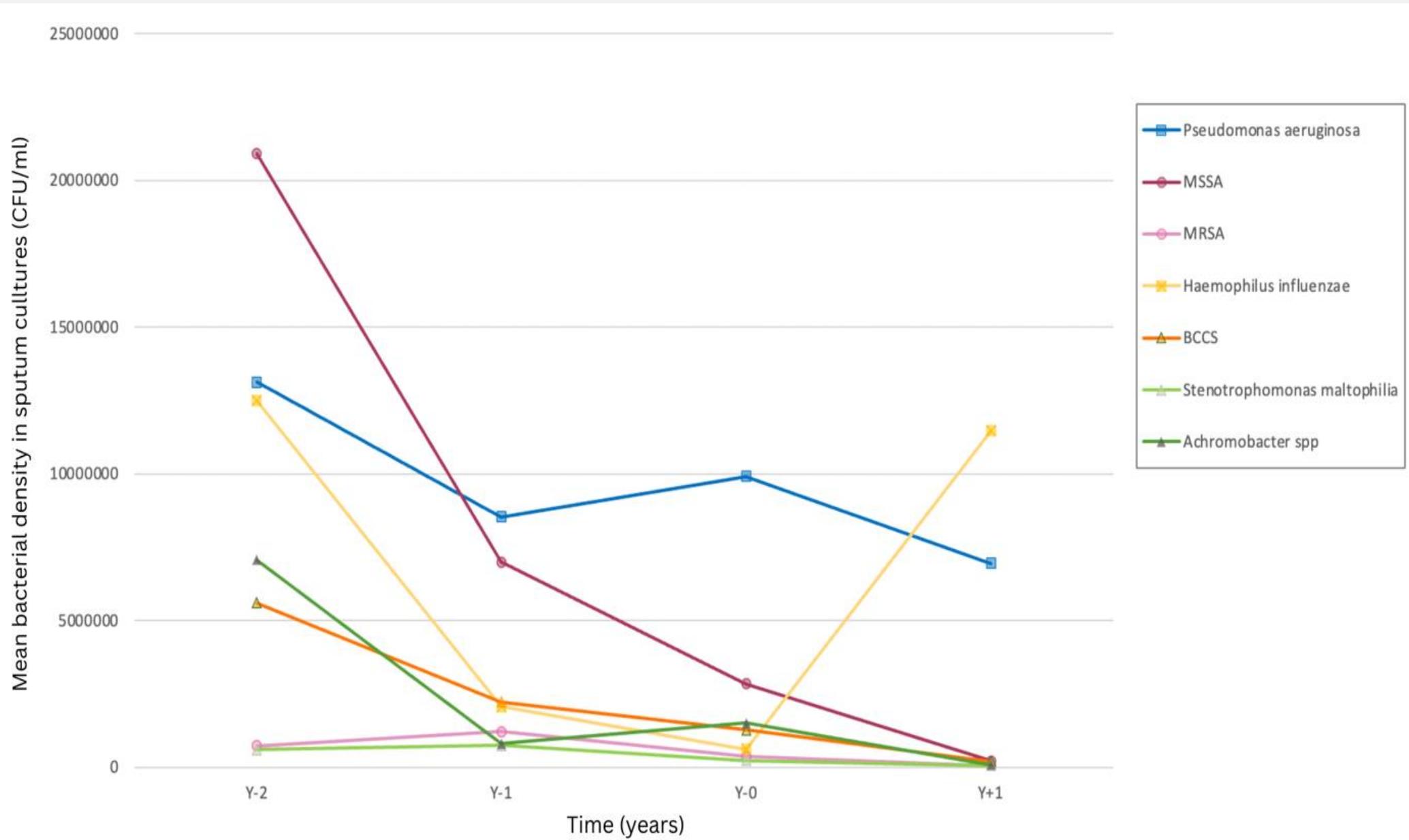


### 3. CORRELATION ENTRE AMELIORATION CLINIQUE ET DIMINUTION COLONISATION BRONCHIQUE ?

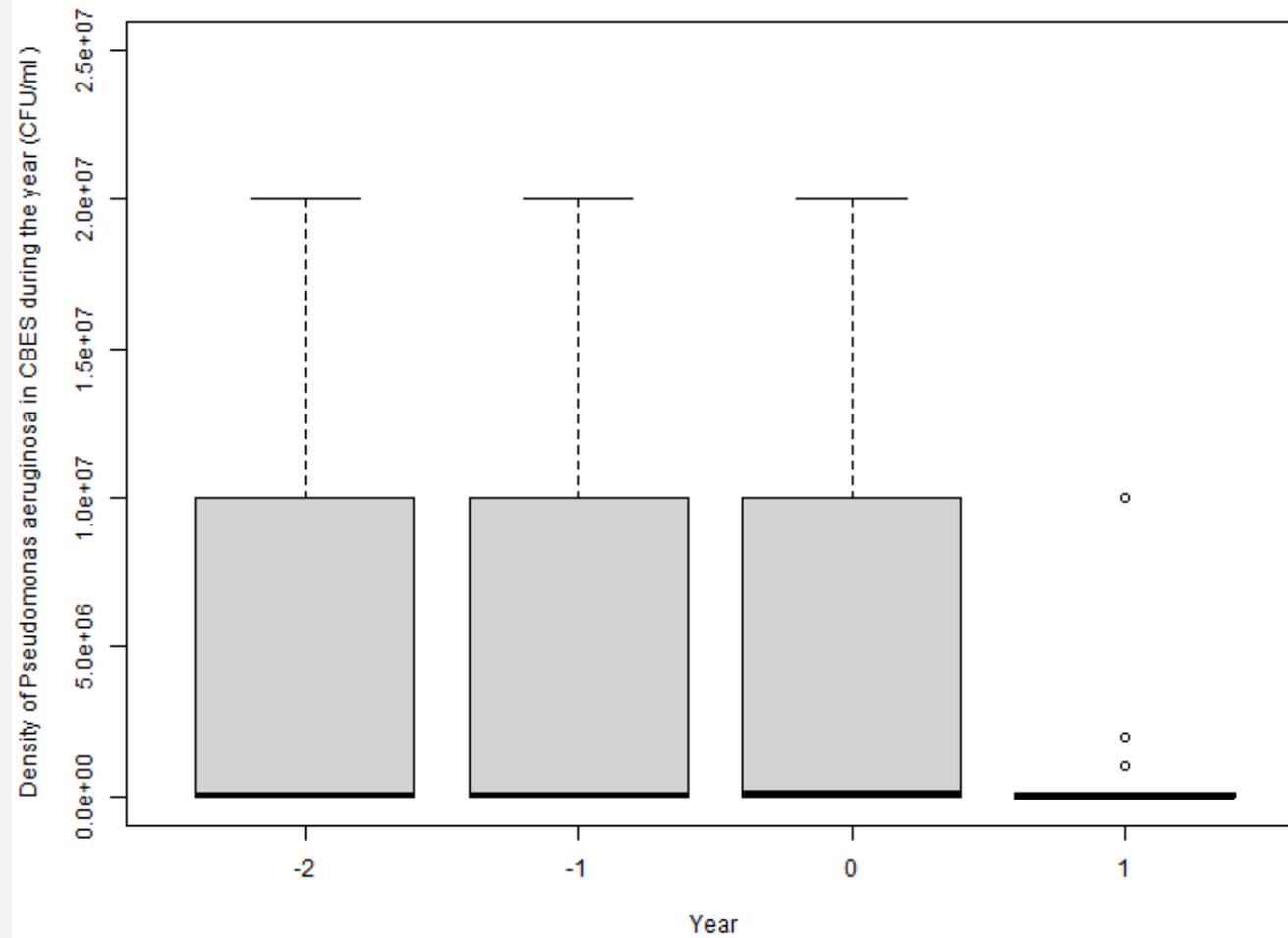
	Y-2 N = 194	Y-1 N = 196	Y0 N = 198	Y+1 N = 179	p-value <sup>1</sup>
<b>Prevalence of colonisation with at least one bacteria of interest - % (n)</b>					
<b>Age range (years)</b>					
18-23	98 (49)	96 (48)	96 (50)	81 (39)	<i>p=0.03</i>
23-28	100 (46)	100 (46)	100 (46)	87 (34)	
28-34	100 (51)	100 (51)	100 (51)	100 (44)	
34-60	100 (45)	100 (47)	98 (46)	91 (42)	
<b>ppFEV1 at Y0 (%)</b>					
<30%	100 (11)	100 (12)	100 (12)	100 (12)	<i>p=0.06</i>
30-50%	100 (63)	100 (63)	98 (62)	97 (57)	
50-70%	100 (53)	100 (53)	98 (54)	84 (41)	
≥ 70%	98 (62)	97 (62)	98 (63)	86 (48)	
<b>Change in ppFEV1 with ETI (%)</b>					
0-15%	100 (63)	100 (64)	98 (65)	88 (51)	<i>p=0.88</i>
15-20%	100 (65)	98 (65)	98 (65)	92 (56)	
20-35%	98 (65)	98 (65)	98 (65)	92 (54)	

# CONCLUSION

- Diminution de la densité bactérienne globale et de la prévalence de la plupart des pathogènes CF (PA, SM, MRSA, MSSA, Achromobacter, NTM)
- Diminution de la colonisation chronique à *Pseudomonas aeruginosa*
- Pas de corrélation entre la clairance bactérienne et la fonction respiratoire
  
- Mécanismes ?
- Stratégie surveillance ECBC : qualité et quantité ECBC ? Nouvelles techniques ?
- Traitements respiratoires associés ?
- Utilisation des antibiotiques ?



Mean density of CF pathogens in sputum cultures (CFU/ml) at a one-year interval from ETI introduction



Evolution of the density of *Pseudomonas aeruginosa* in sputum cultures at one-year interval from ETI introduction

