Anticoagulant chez le sujet âgé
Les données de la vraie vie

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Liens d’intérêt

- Novartis, Boehringer-Ingelheim, Bayer, BMS, Pfizer
- Astra-Zeneca, Servier, Vifor, Boston scientific

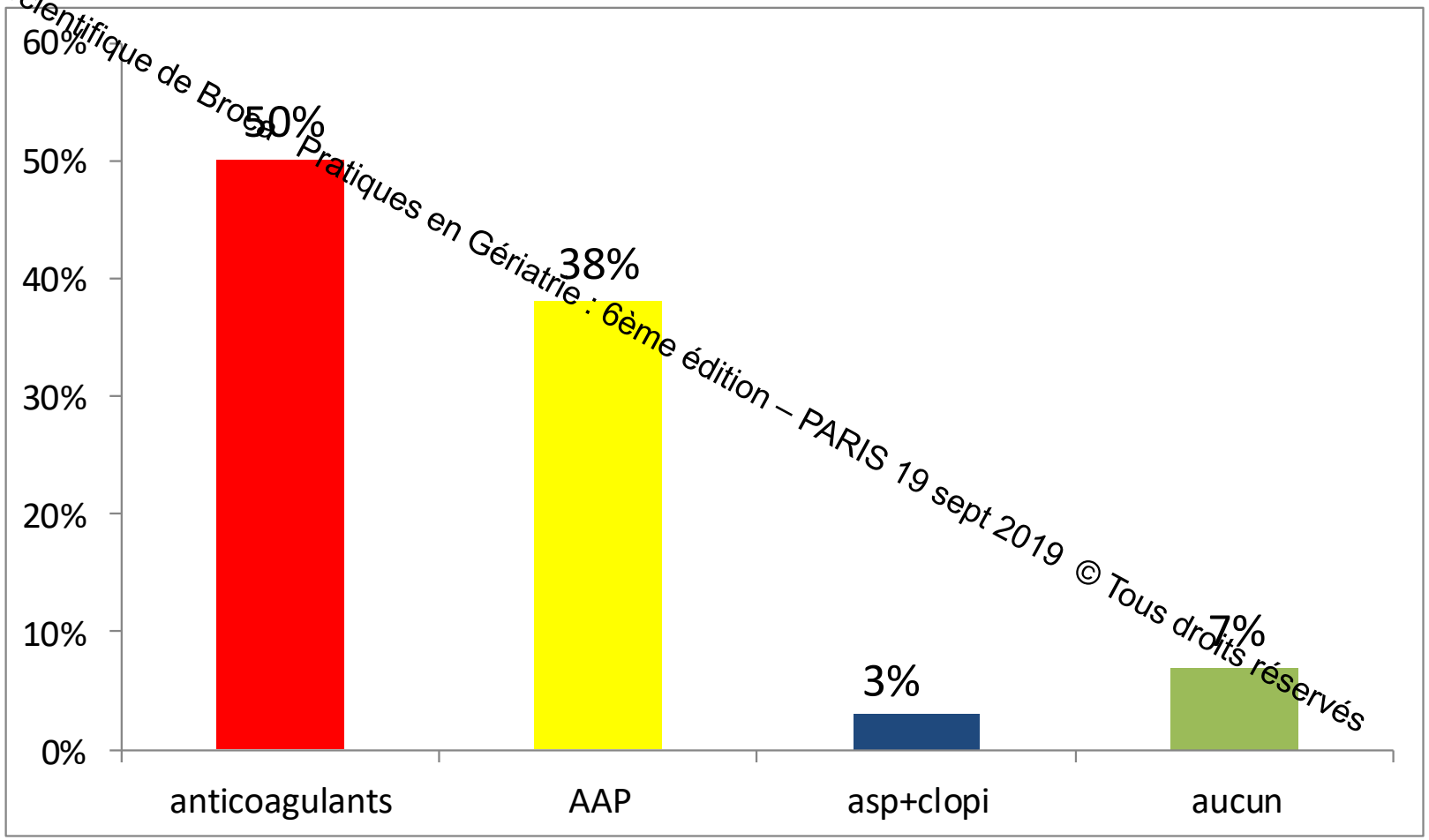
Les études de la « vraie vie »

- Patients **« Real world »**
  - conditions réelles de prescription
  - sans les critères de sélection d'un essai randomisé
  - Sujets > 80 ans
  - avec comorbidités gériatriques (démences, dénutrition, chutes ….)
- **Larges** effectifs
- Données rétrospectives des bases médico-économiques (Assurance maladie, PMSI)

  => biais : pas de randomisation, qualité des données, pas de biologie …

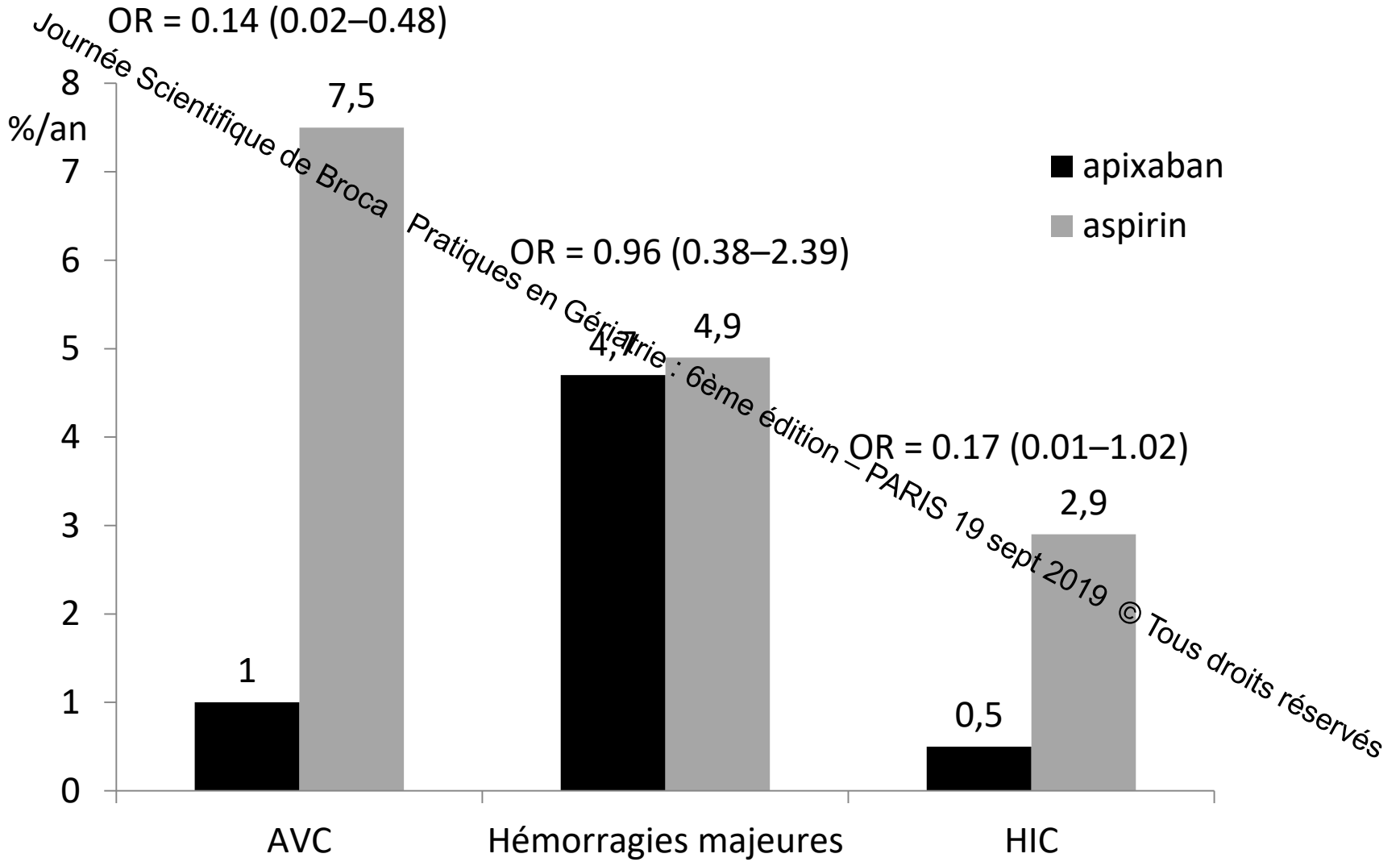
- **Les études « vraie vie » permettent de donner des signaux et de confirmer des résultats sur des populations spécifiques (par ex sujets > 80 ans)**
- **Mais elles ne remplacent pas l'essai randomisé = référence**

Underuse of Oral Anticoagulation for Individuals with Atrial Fibrillation in a Nursing Home Setting in France: Comparisons of Resident Characteristics and Physician Attitude



J Am Geriatr Soc. 2015 Jan;63(1):71-6

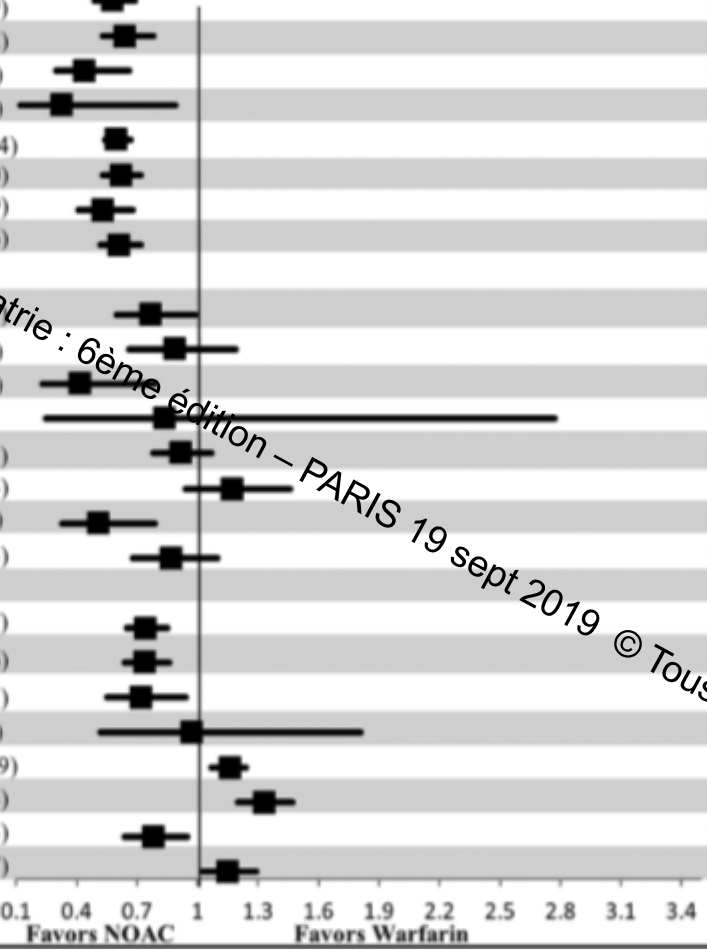
AVERROES : AOD vs aspirin
Aged ≥85 Years



Age and ageing 2016, 45:77-83

Comparisons between Oral Anticoagulants among Older Nonvalvular Atrial Fibrillation Patients

	NOAC	Warfarin	Hazard Ratio (95% CI)	P-value
	No. of events (incidence per 100 person-years)			
Apixaban vs. Warfarin				
Stroke/SE	197 (1.80)	382 (2.89)	0.58 (0.49 – 0.69)	<0.001
Ischemic	161 (1.47)	280 (2.12)	0.64 (0.53 – 0.78)	<0.001
Hemorrhagic	32 (0.29)	86 (0.65)	0.44 (0.30 – 0.66)	<0.001
SE	5 (0.05)	17 (0.13)	0.33 (0.12 – 0.89)	0.029
Major Bleeding	540 (4.96)	1,024 (7.84)	0.60 (0.54 – 0.67)	<0.001
GI Bleeding	274 (2.50)	502 (3.80)	0.62 (0.53 – 0.72)	<0.001
ICH	82 (0.75)	185 (1.39)	0.53 (0.41 – 0.68)	<0.001
Other Bleeding	218 (1.99)	404 (3.06)	0.61 (0.52 – 0.72)	<0.001
Dabigatran vs. Warfarin				
Stroke/SE	103 (2.18)	137 (2.89)	0.77 (0.60 – 0.99)	0.045
Ischemic	84 (1.78)	97 (2.01)	0.89 (0.66 – 1.19)	0.421
Hemorrhagic	14 (0.29)	34 (0.70)	0.42 (0.23 – 0.79)	0.007
SE	5 (0.11)	6 (0.12)	0.84 (0.25 – 2.77)	0.769
Major Bleeding	295 (6.30)	329 (6.91)	0.92 (0.78 – 1.07)	0.281
GI Bleeding	172 (3.66)	151 (3.14)	1.17 (0.94 – 1.46)	0.160
ICH	31 (0.65)	62 (1.28)	0.51 (0.33 – 0.79)	0.003
Other Bleeding	119 (2.52)	141 (2.93)	0.87 (0.68 – 1.10)	0.244
Rivaroxaban vs. Warfarin				
Stroke/SE	396 (2.20)	541 (2.97)	0.74 (0.65 – 0.85)	<0.001
Ischemic	288 (1.60)	394 (2.16)	0.74 (0.64 – 0.86)	<0.001
Hemorrhagic	92 (0.51)	130 (0.71)	0.72 (0.55 – 0.94)	0.016
SE	19 (0.11)	20 (0.11)	0.97 (0.52 – 1.81)	0.918
Major Bleeding	1,512 (8.50)	1,331 (7.39)	1.16 (1.07 – 1.26)	<0.001
GI Bleeding	857 (4.78)	659 (3.63)	1.33 (1.20 – 1.47)	<0.001
ICH	173 (0.96)	225 (1.23)	0.78 (0.64 – 0.95)	0.015
Other Bleeding	612 (3.40)	540 (2.97)	1.15 (1.03 – 1.29)	0.017



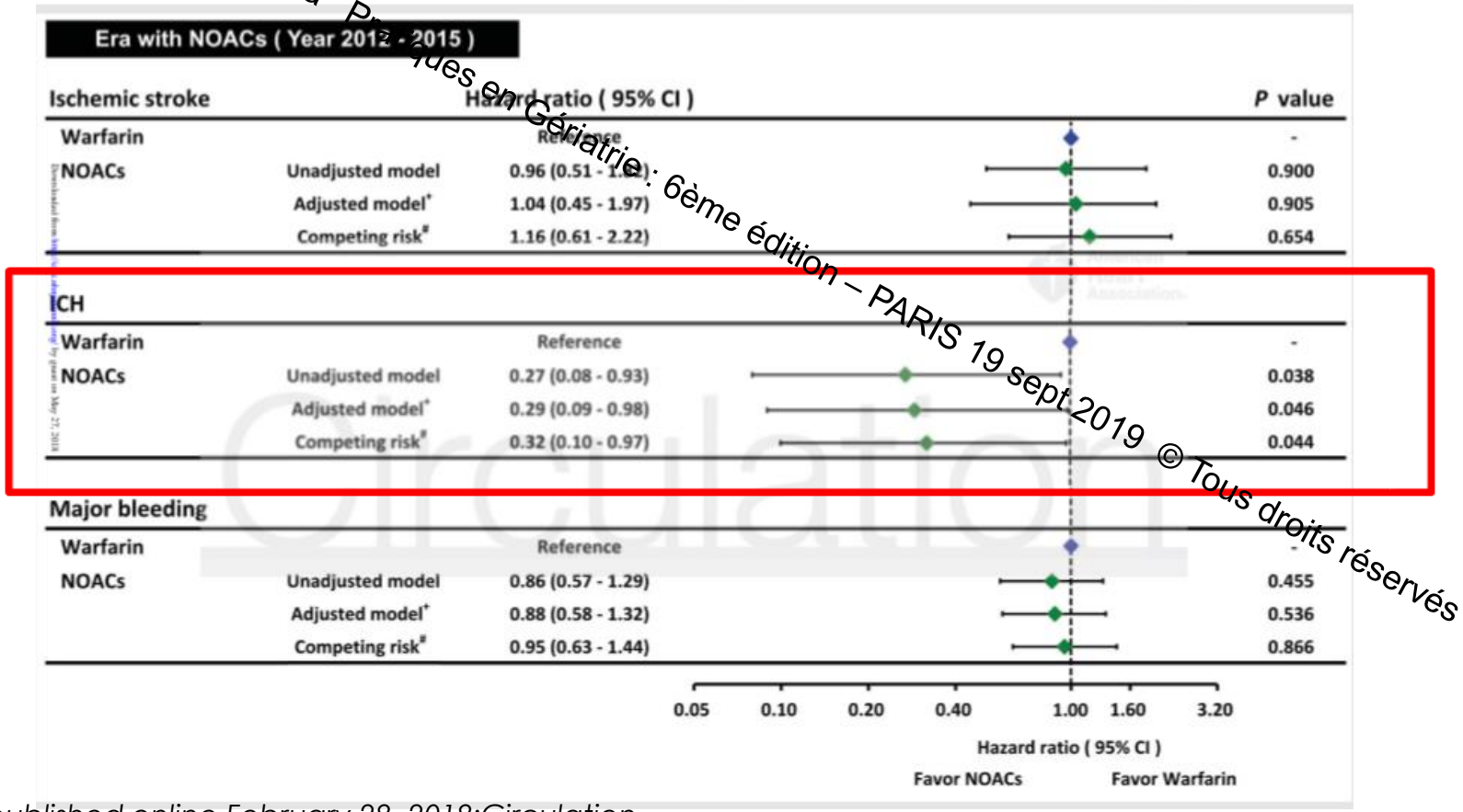
J Am Geriatr Soc 67:1662–1671, 2019.

Oral Anticoagulation in Very Elderly Patients with Atrial Fibrillation - A Nationwide Cohort Study

Circulation

"National Health Insurance Research Database" in Taiwan.

AF patients (n=15,756) **aged ≥90** years from year 1996 to 2011.



published online February 28, 2018;Circulation.

NAXOS

Apixaban in patients with atrial fibrillation in French Real Life Study

Comparative safety and effectiveness of apixaban versus VKAs and other DOACs in patients with nonvalvular atrial fibrillation: the NAXOS study

*Eric Van Ganse[1,2], Nicolas Danchin[3], Isabelle Mahé[4,5,6], Olivier Hanon[6,7], Flore Jacoud[1], Maëva Nolin[1], Faustine Dalon[1], Cinira Lefevre[8], François-Emery Cotte[8], Sabrina Gollety[8], Bruno Falissard[9], Manon Belhassen[1], **Ph. Gabriel Steg**[10,11,12]*

PMSI – SNIIRAM, Janvier 2014 – decembre 2016,

initiation de traitement, FA, **n= 411 077**

VKA, apixaban, rivaroxaban, Dabigatran

NAXOS

Apixaban in patients with atrial fibrillation in Real Life French Study

Study design

- NAXOS is a historical cohort study generated from the French National Health System (NHS) claims data. **(bases de données du SNIIRAM et du PMSI)**
- All patients aged ≥18 years with NVAF and newly initiating an OAC* between January 2014 and December 2016 were identified in the NHS and allocated to four different treatment cohorts, according to the OAC started (VKA, Apixaban, Dabigatran or Rivaroxaban).
- The study was approved by the French Institute for Health Data (INDS) on Sept 8, 2015), conducted using anonymised data, approved by the National Informatics and Liberty Committee (CNIL) on 17 March 2016.
- NAXOS is registered at ClinicalTrials.gov (NCT02640222).

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Apixaban in patients with atrial fibrillation in Real Life French Study

Statistical analysis

- Risks were compared using **propensity scores (PS)-adjusted models** –either Cox or Fine and Gray- based on known confounding factors (sociodemographics, specialty of the prescriber who initiated OAC treatment, comorbidities, drugs dispensed within 3 months of index date).

- **Sensitivity analyses** used adjustment for
  - confounding factors,
  - PS matching
  - High-Dimensional Propensity Score (HDPS) matching.

- **Subgroup analyses** performed to compare patients treated with the standard dose of apixaban and of the other OACs using PS-adjusted models.

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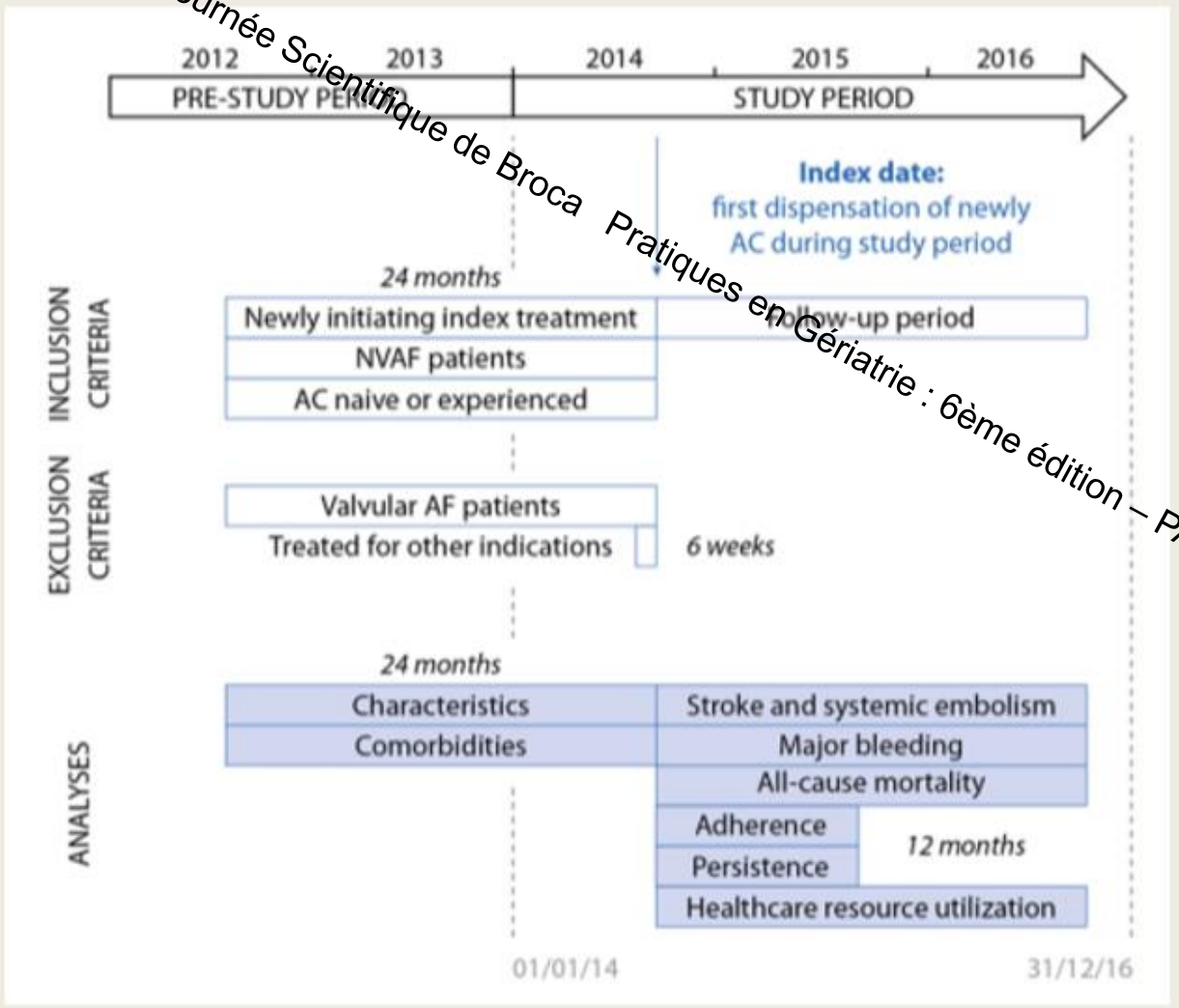
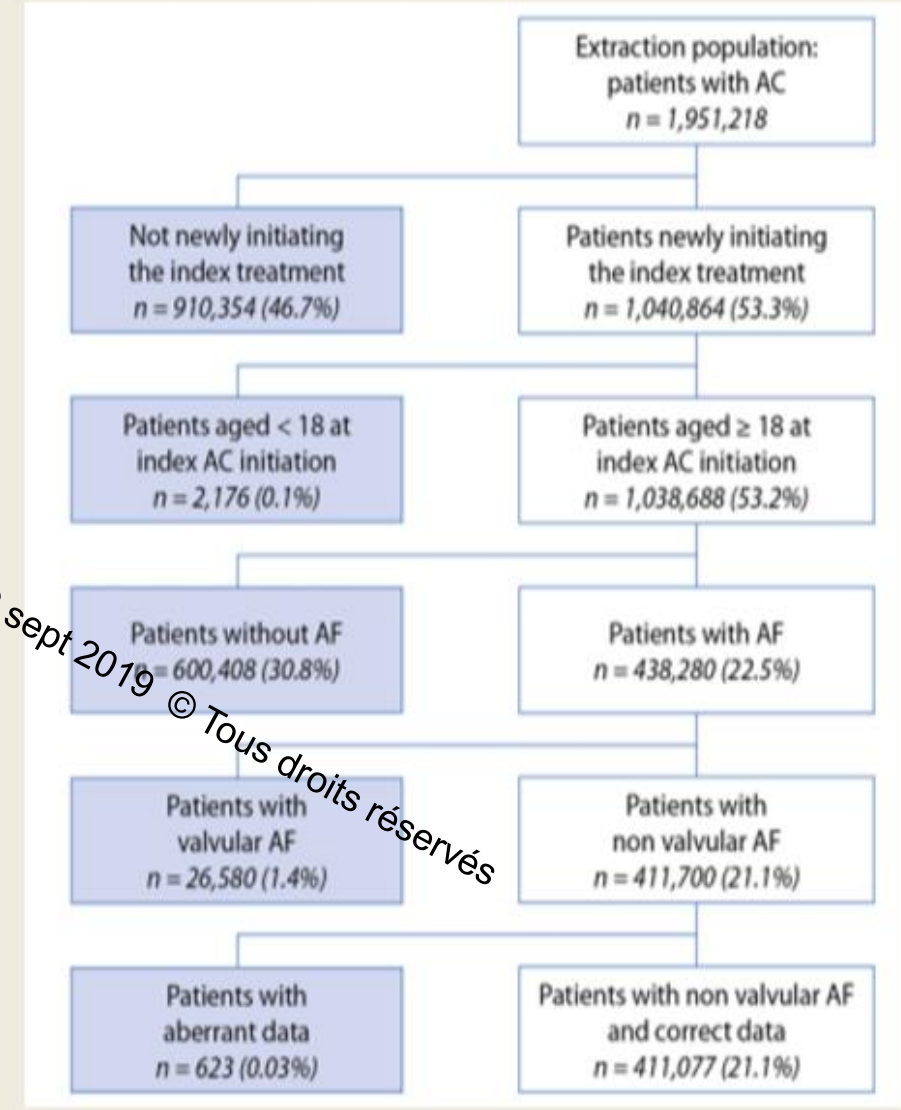
Apixaban in patients with atrial fibrillation in Real Life French Study

Patient flow





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Apixaban in patients with atrial fibrillation in Real Life French Study

Demographic and clinical characteristics

		VKA N=112,628	Apixaban N=87,565	Dabigatran N=21,245	Rivaroxaban N=100,063
Age at index date, years	Mean (SD)	78.5 (11.1)	74.7 (11.5)	72.7 (11.8)	72.0 (12.0)
>80 years	%	54.5	38.5	32.1	29.6
Sex	% Male	48.8	51.2	54.1	55.1
Time between NVAF diagnosis and index date	Months; Mean (SD)	89.4 (189.1)	69.7 (183.5)	73.9 (190.7)	71.7 (187.8)
Past hospital stays*	% of patients	85.4	73.7	69.7	69.0
	Mean number of hospital stays (SD)	2.7 (2.4)	2.1 (1.9)	2.1 (1.6)	2.1 (1.8)
Cumulative duration of past hospital stays	Mean (SD)	22.4 (22.8)	12.5 (14.9)	11.[illegible] (14.9)	11.8 (14.9)

P values <0.0001 for all 2 x 2 comparisons

Note that VKA used are 70% fluindione, 3% acenocoumarol, 27% warfarin

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Apixaban in patients with atrial fibrillation in Real Life French Study

Sociodemographic and clinical characteristics of OAC-naive patients

	VKAs N=112,428	Apixaban N=87,565	Dabigatran N=21,245	Rivaroxaban N=100,063	P value Apixaban vs VKA	P value Apix. vs Riva.	P value Apix. vs Dabi.
More frequent LTD status (%)							
Severe heart failure, arrhythmias, valvular cardiomyopathy, congenital heart disease	28.6	24.7	24.5	23.1	<0.0001	<0.0001	0.6305
Diabetes (type 1 or 2)	19.9	15.6	14.4	14.2	<0.0001	<0.0001	<0.0001
Cancer	15.7	13.4	12.5	12.7	<0.0001	<0.0001	0.0002
Coronary heart disease	16.3	11.9	9.2	10.1	<0.0001	<0.0001	<0.0001

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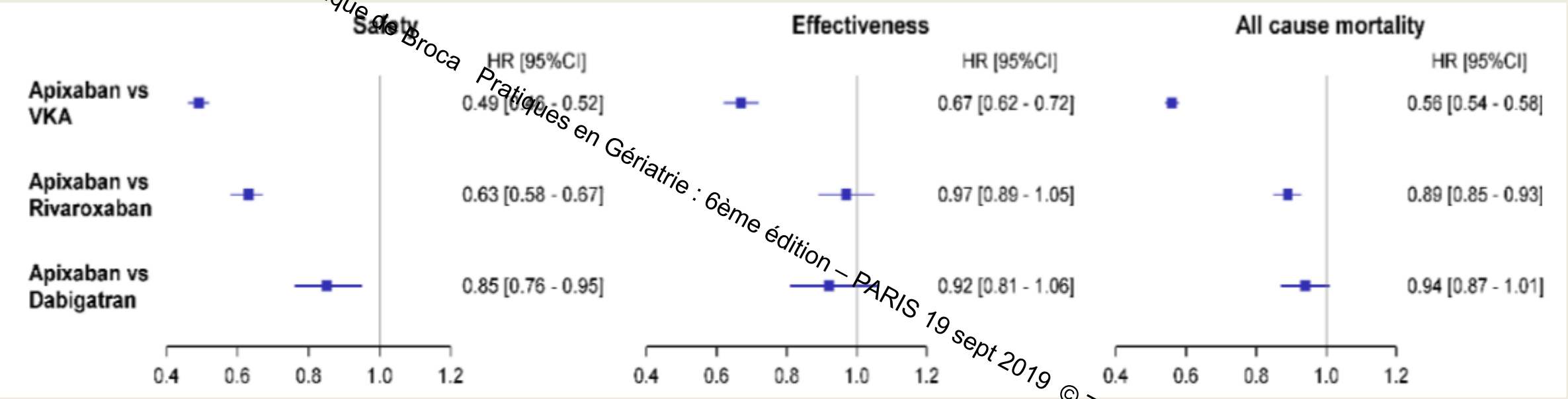
Apixaban in patients with atrial fibrillation in Real Life French Study

Comparative safety and effectiveness (propensity score adjusted comparison)



major bleeding events leading to hospitalisation

Stroke and systemic thromboembolism

NAXOS

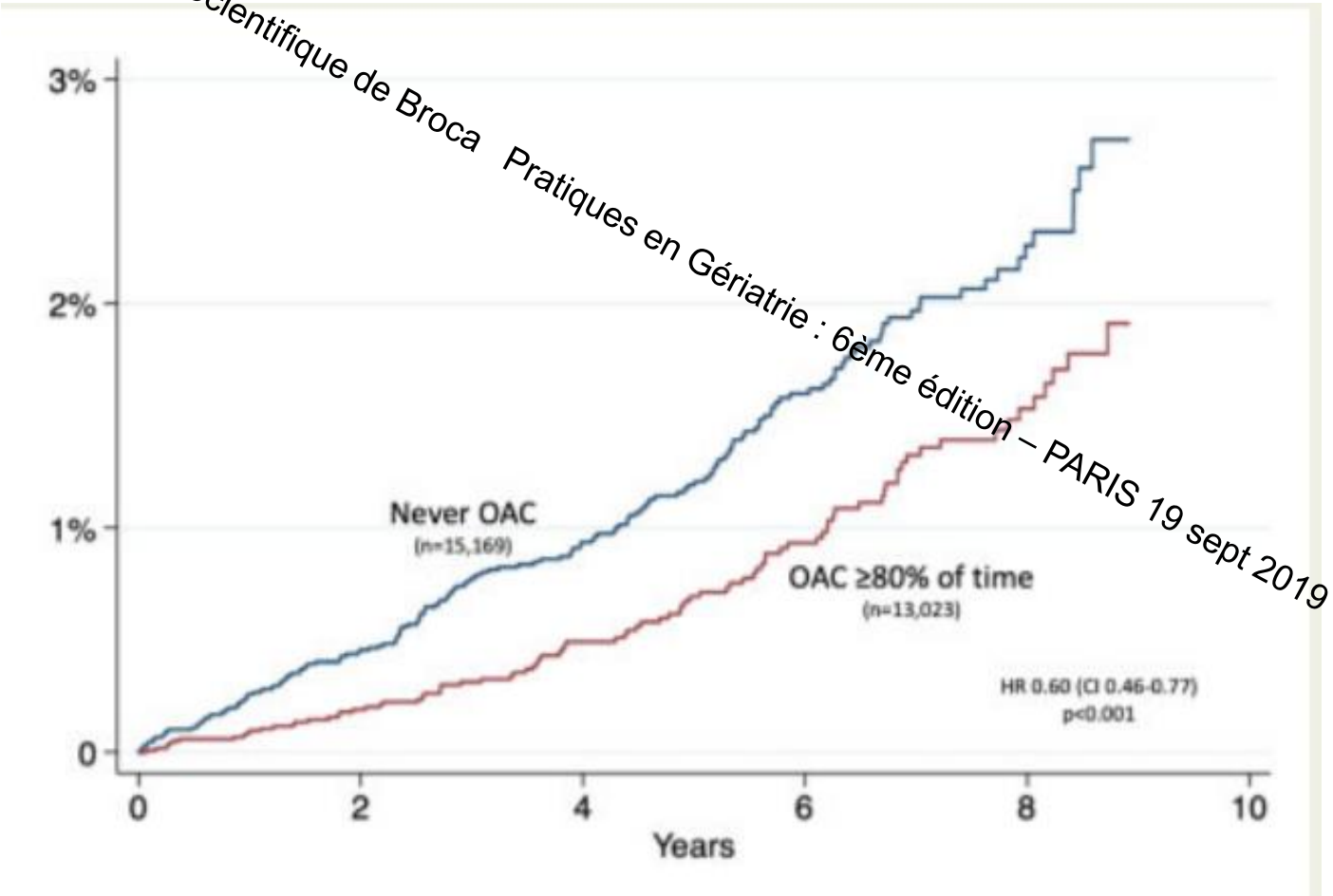
Apixaban in patients with atrial fibrillation in Real Life French Study

Conclusions

- In this large observational population-based comparison of OACs initiation in patients with NVAF, apixaban use was associated with superior safety, superior effectiveness and lower mortality than VKAs, consistent with the results from ARISTOTLE.
- Apixaban use was associated with lower bleeding and similar effectiveness as rivaroxaban or dabigatran.
- However, given the observational nature of these analyses, they should be viewed as hypothesis-generating.
- Given the lack of randomised comparisons between DOACs, these observations are of interest to patients, clinicians, regulators and payers.
- The magnitude of some differences between DOACs suggest that head-to-head RCTs appear warranted.

Less dementia and stroke in low-risk patients with atrial fibrillation taking oral anticoagulation

national registries of all individuals in Sweden with a hospital diagnosis of AF between 2006 and 2014 (**n = 91 254 patients)**



European Heart Journal (2019) 40, 2327–2335

Conclusions

- **Données de la vraie vie**
  - Medicare (US)
  - SNIIRAM (France)
  - **AOD > AVK**
  - Apixaban : très bon profil efficacité / sécurité

  (Comparaison entre AOD => étude randomisée nécessaire)

- **Intérêt des AC pour prévention démence en cas de FA**
  - **AOD > AVK**