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Stratégie optimale de revascularisation (chez le patient pluritronculaire diabétique)

Bernard Chevalier

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France

COI: CERC shareholder



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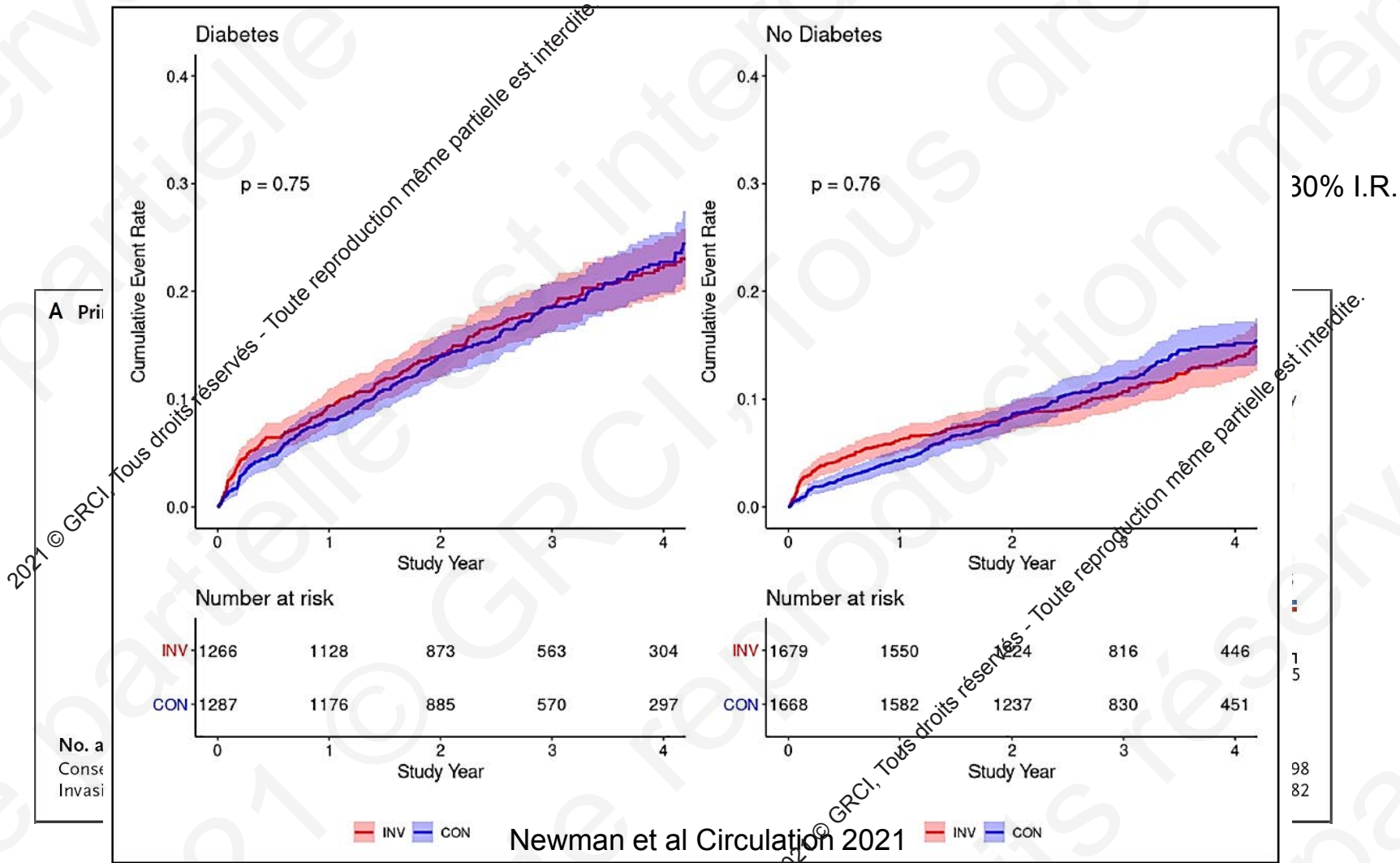
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Faut-il revasculariser ?

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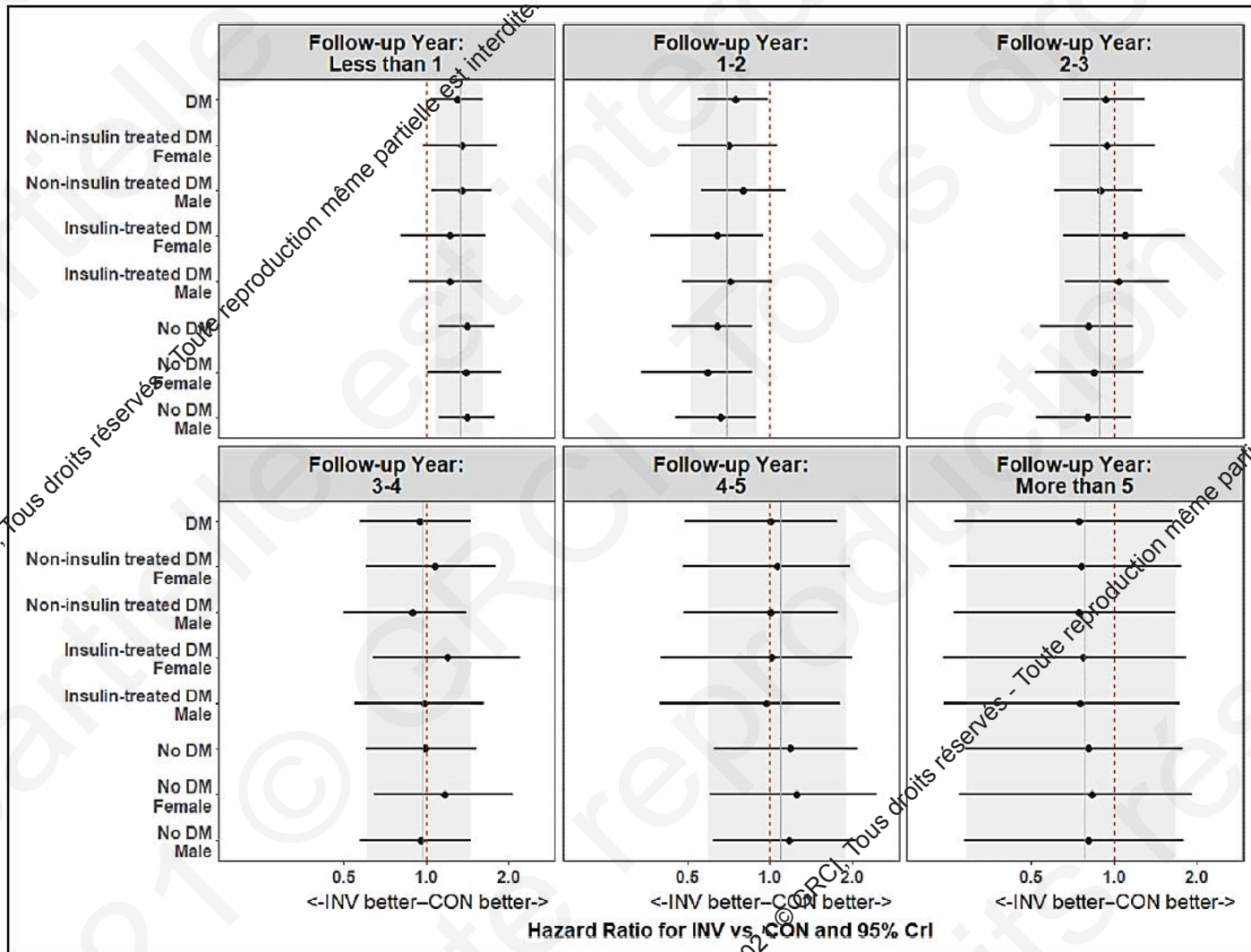
30% I.R.

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1
5

98
82





SPECT, PET, Stress Echo, Stress MRI, ECG

8518 Patients were enrolled

3339 Were excluded
1350 Did not have moderate or severe ischemia, according to stress core laboratory
1218 Did not have obstructive CAD
771 Had unprotected LMCA disease

5179 Underwent randomization
3783 (73.0%) Underwent trial CCTA
1396 (27.0%) Did not undergo trial CCTA
575 Had low eGFR
700 Had known coronary anatomy
121 Had other reason

16%

14%

20% FFR

2588 Were assigned to invasive strategy

2591 Were assigned to conservative strategy

Median follow-up, 3.2 yr (IQR, 2.1 to 4.3)
99.4% of projected follow-up was completed
28 (1.1%) Withdrew
36 (1.4%) Were lost to follow-up
2475 (95.6%) Underwent angiography
2054 (79.4%) Underwent revascularization

Median follow-up, 3.2 yr (IQR, 2.2 to 4.3)
99.7% of projected follow-up was completed
22 (0.8%) Withdrew
26 (1.0%) Were lost to follow-up
660 (25.7%) Underwent angiography
544 (21.0%) Underwent revascularization

74% PCI
26% CABG

9% pas de lésion coronaire



De la vie réelle à ISCHEMIA: 6 ans sur 320 centres

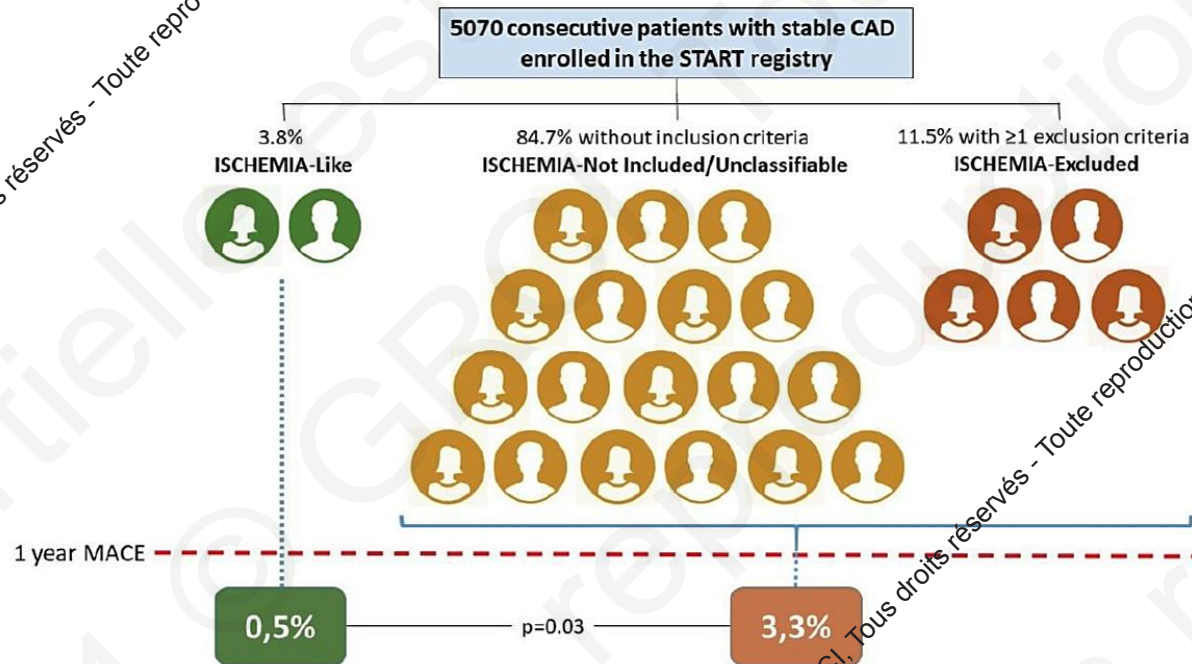
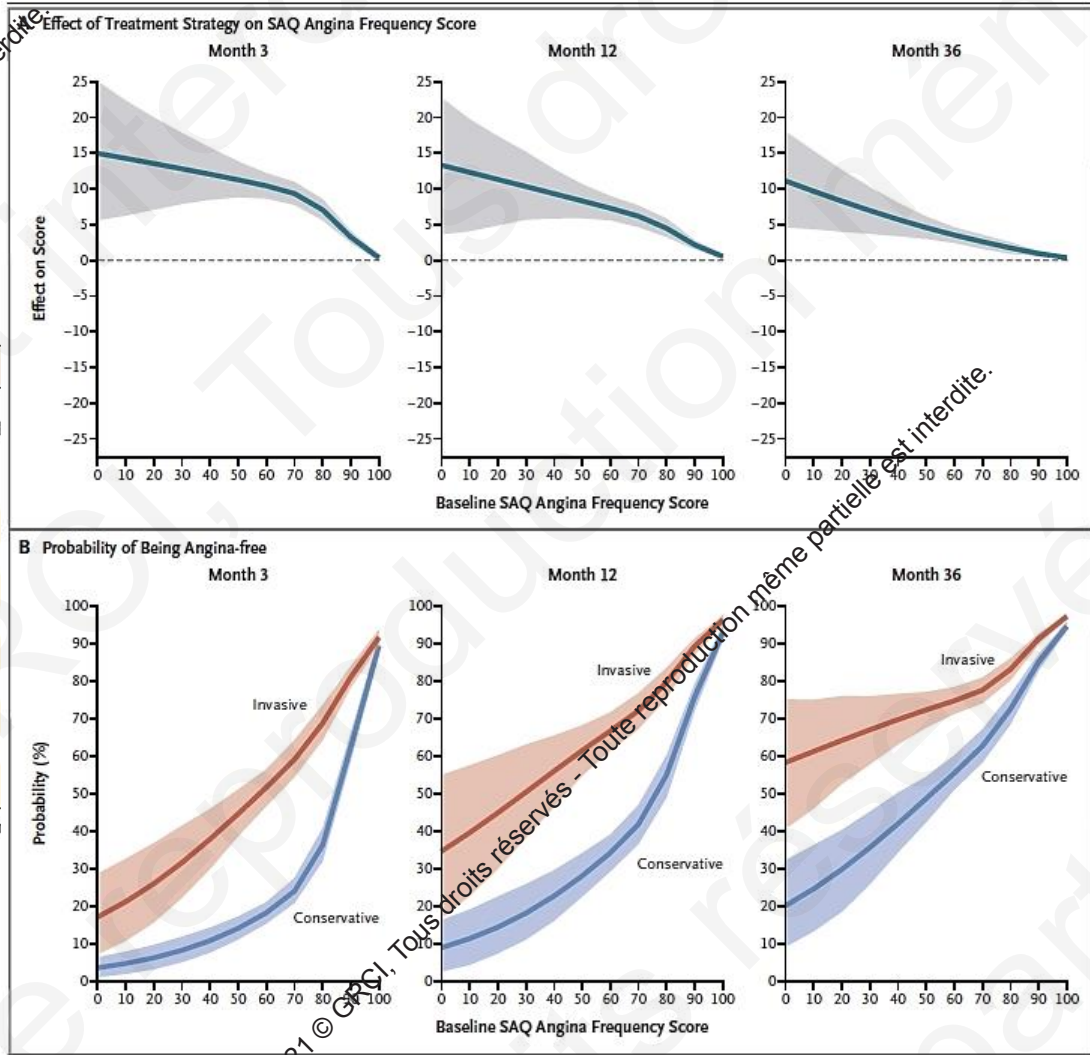


Table 2. Mean Estimated Effect of an Invasive Strategy on SAQ Summary Scores.*

Month	Overall (N= 4617)	Daily or Weekly Angina at Baseline (N=934)	Monthly Angina at Baseline (N= 2043)
		points (95% credible interval)	
3	4.1 (3.2 to 5.0)	8.5 (5.8 to 11.1)	5.5 (4.3 to 6.9)
6	4.4 (3.5 to 5.3)	10.5 (7.9 to 13.2)	5.1 (3.7 to 6.4)
12	4.2 (3.3 to 5.1)	7.3 (4.8 to 9.9)	4.8 (3.4 to 6.1)
18	3.3 (2.5 to 4.2)	6.3 (3.9 to 9.0)	3.6 (2.2 to 4.9)
24	2.8 (2.1 to 3.7)	5.0 (3.0 to 7.2)	3.5 (2.3 to 4.7)
30	2.9 (2.1 to 3.6)	5.2 (3.2 to 7.2)	3.3 (2.2 to 4.3)
36	2.9 (2.2 to 3.7)	5.3 (3.4 to 7.5)	3.1 (2.0 to 4.2)
42	3.0 (2.2 to 3.8)	5.5 (3.3 to 7.7)	2.9 (1.7 to 4.1)
48	3.1 (2.1 to 3.9)	5.6 (3.2 to 8.0)	2.7 (1.3 to 4.0)

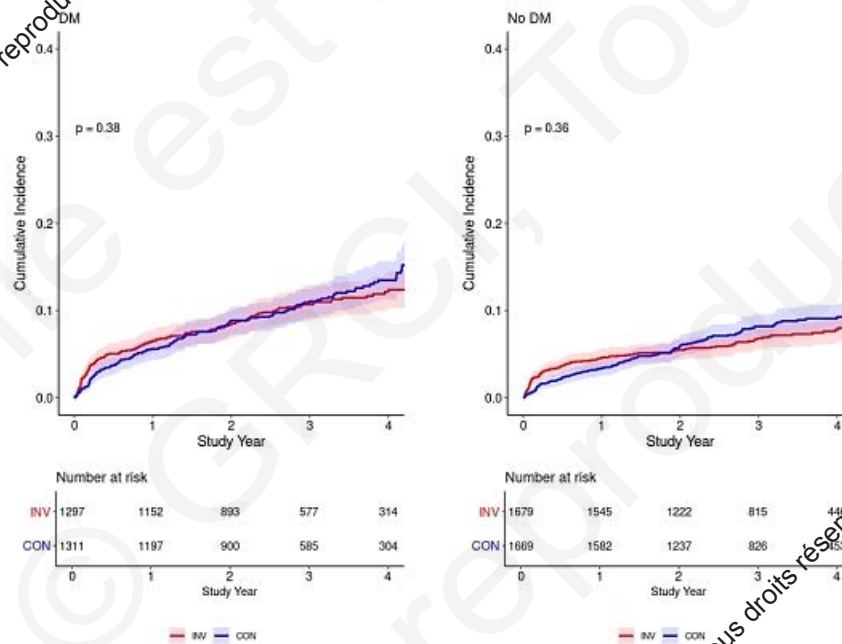
* Data are the posterior mean differences (invasive minus conservative) in SAQ Summary scores at each

From ISCHEMIA
Spertus JA et al NEJM 2020

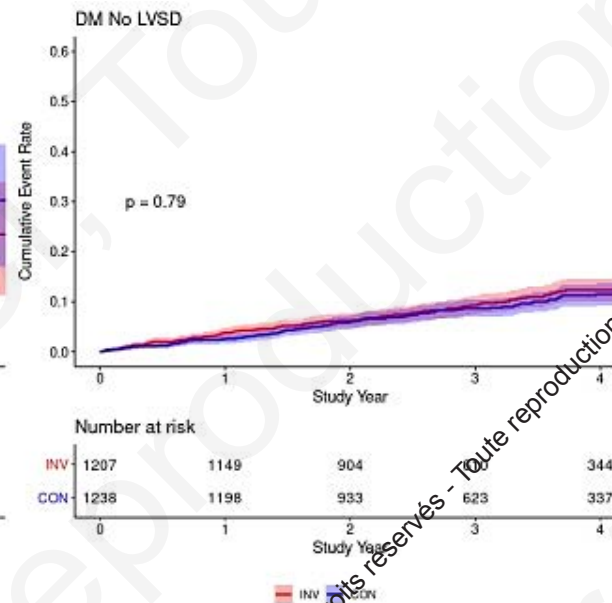
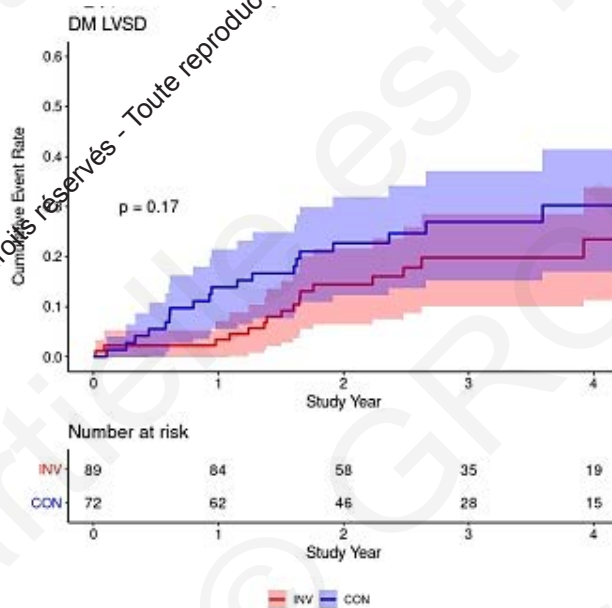


Spontaneous MI in ISCHEMIA

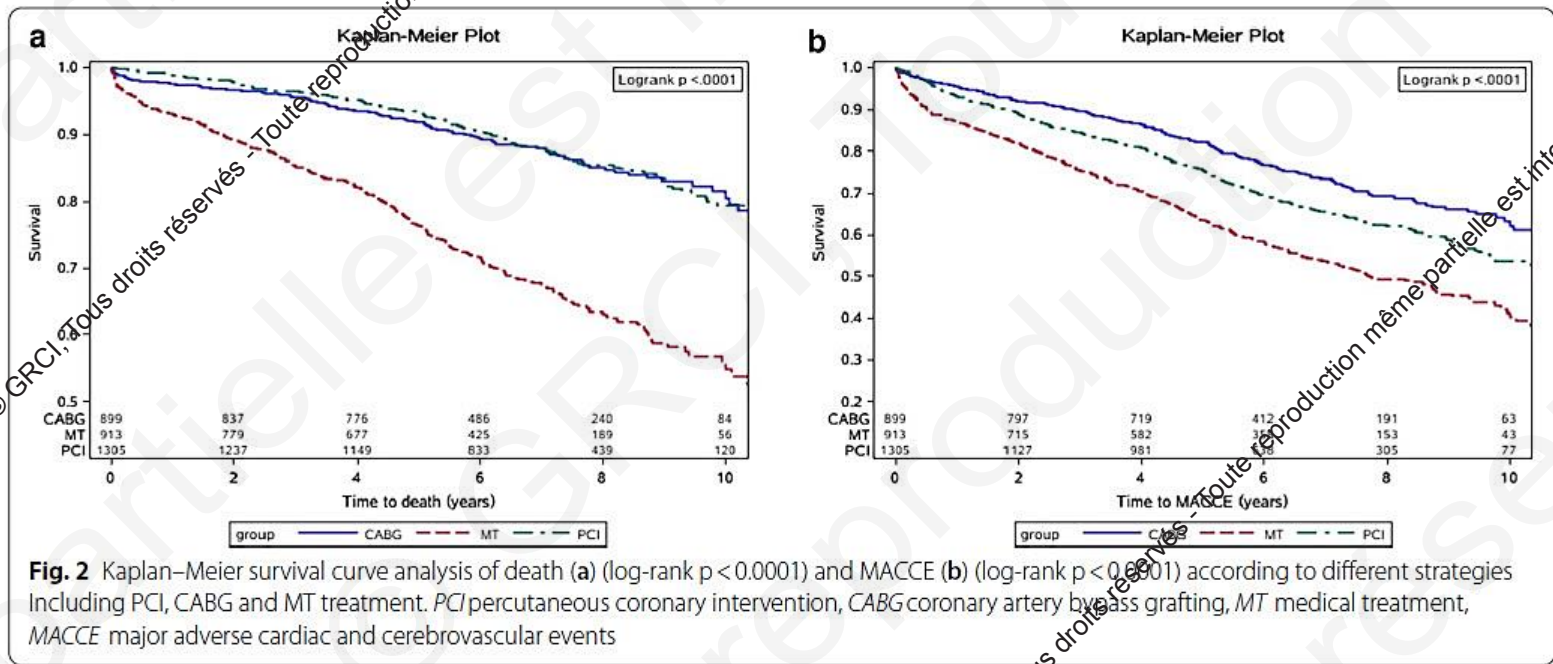
Figure VI.d. Cumulative incidence of fatal and non-fatal MI (accounting for competing risks) by treatment strategy, stratified by diabetes status



Death + MI in pts with LV systolic dysfunction



And I.R.L? MVD+Diabetes



Zhao et al Cardiovasc Diabetol 2021



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Que revasculariser ?

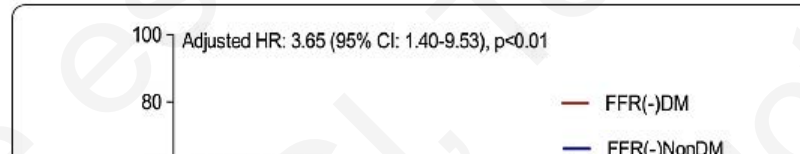
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Clinical outcomes of deferred revascularisation using fractional flow reserve in patients with and without diabetes mellitus

Mark W. Kennedy¹, Eliza Kaplan¹, Rik S. Hermanides¹, Enrico Fabris^{1,2}, Veemal Hemradj¹, Petra C. Koopmans², Jan-Hank E. de Brink^{1,2}, A. T. Marcel Gosselink¹, Arnoud W. J. van't Hof¹, Jan Paul Ottervanger¹, Vincent Poolevink¹, Wouter S. Remkes¹, Aize van der Sluis¹, Harry Suryapranata² and Elvin Kedhi^{1*}



Relation between fractional flow reserve value of coronary lesions with deferred revascularization and cardiovascular outcomes in non-diabetic and diabetic patients

Zhi Liu¹ • Yasushi Matsuzawa¹ • Joerg Hermann • Jing Li • Ryan J. Lennon • Daniel J. Crusan • Taek-Geun Kwon • Ming Zhang • Tao Sun • Shiwei Yang • Rajiv Gulati • Malcolm R. Bell • Lilach O. Lerman • Amir Lerman • Show less • Show footnotes

FFR(-)DM	122	109	82	58	32	14
FFR(-)NonDM	128	123	103	70	47	14

Fig. 2 Time-to-event estimates for target lesion failure according to FFR(-)DM and FFR(-)NonDM groups. *TLF* target lesion failure, *CI* confidence interval, *HR* hazard ratio (adjusted for age)



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Comment revasculariser ?

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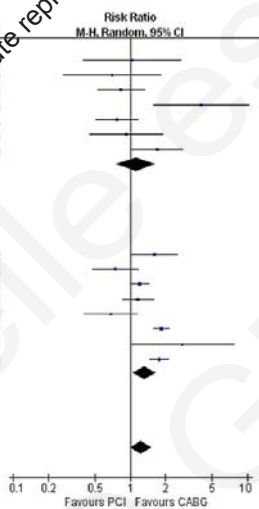
Recommendations according to the extent of CAD	CABG		PCI	
	Class ^a	Level ^b	Class ^a	Level ^b
One-vessel CAD				
With proximal LAD stenosis	I	A	I	A
Two-vessel CAD				
With proximal LAD stenosis	I	B		
LM CAD				
LM with low SYNTAX score 0 - 22	I	A	I	A
LM with intermediate SYNTAX score >22 and ≤32	I	A		
LM with high SYNTAX score >32. ^e	I	A	III	B
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score 0 - 22	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score >22 ^e	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0 - 22	I	A		
Three-vessel disease with intermediate or high SYNTAX score >22 ^e	I	A	III	A



Death / MACCE in MVD+Diabetes

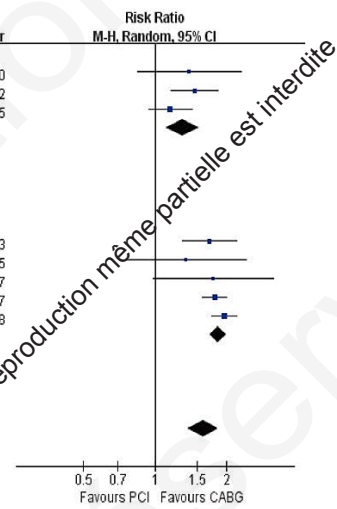
b

Study or Subgroup	PCI		CABG		Weight	Risk Ratio		Year
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	
1.1.1 mid-term								
Kapur 2010	0	172	0	178	3.3%	1.03	[0.40, 2.70]	2012
Iuo 2012	6	99	11	127	3.3%	0.70	[0.27, 1.93]	2012
Farkouh 2012	32	953	38	947	7.1%	0.84	[0.53, 1.33]	2012
Kamaleh 2013	21	101	5	97	3.4%	4.03	[1.58, 10.27]	2013
Ben-Gal 2015	74	1349	30	423	7.7%	0.77	[0.54, 1.17]	2015
Zheng 2016	10	348	25	808	4.7%	0.92	[0.45, 1.91]	2016
Milojkovic 2019	38	286	21	269	6.7%	1.02	[1.02, 2.81]	2019
Subtotal (95% CI)		3308		2846	36.2%		1.12 [0.76, 1.65]	
Total events: 199 (PCI), 138 (CABG)								
Heterogeneity: Tau ² = 0.15; Chi ² = 15.34, df = 6 (P = 0.02); I ² = 68%								
Test for overall effect: Z = 0.56 (P = 0.58)								
1.1.2 long-term								
Kappellein 2013	44	231	26	227	7.3%	1.62	[1.03, 2.54]	2013
Naito 2015	31	256	37	227	7.3%	0.74	[0.48, 1.18]	2015
Marui 2015	229	1065	93	933	10.2%	1.21	[1.01, 1.45]	2015
Bangalore 2015	80	773	77	773	8.9%	1.16	[0.95, 1.47]	2015
Yu 2015	20	147	27	131	6.4%	0.68	[0.40, 1.15]	2015
Ramanathan 2017	515	2311	192	1865	10.4%	1.95	[1.58, 2.41]	2017
Li Y 2017	14	286	5	408	3.0%	2.80	[1.02, 7.70]	2017
Nagendran 2018	67	669	149	669	10.2%	1.77	[1.40, 2.11]	2018
Subtotal (95% CI)		6453		5425	63.8%		1.32 [1.04, 1.67]	
Total events: 195 (PCI), 671 (CABG)								
Heterogeneity: Tau ² = 0.38; Chi ² = 39.36, df = 7 (P < 0.00001); I ² = 82%								
Test for overall effect: Z = 2.26 (P = 0.02)								
Total (95% CI)		9761		8271	100.0%		1.23 [1.00, 1.52]	
Total events: 1385 (PCI), 809 (CABG)								
Heterogeneity: Tau ² = 0.10; Chi ² = 62.02, df = 14 (P < 0.00001); I ² = 77%								
Test for overall effect: Z = 1.98 (P = 0.05)								
Test for subgroup differences: Chi ² = 0.51, df = 1 (P = 0.48), I ² = 0%								

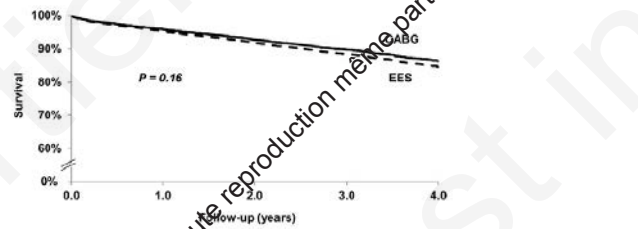


b

Study or Subgroup	PCI		CABG		Weight	Risk Ratio		Year
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	
2.1.1 mid-term								
Kapur 2010	31	172	23	178	6.4%	1.39	[0.85, 2.29]	2010
Farkouh 2012	157	953	106	947	14.7%	1.47	[1.17, 1.85]	2012
Ben-Gal 2015	326	1349	88	423	15.7%	1.16	[0.94, 1.43]	2015
Subtotal (95% CI)		2474		1548	36.8%		1.31 [1.11, 1.54]	
Total events: 514 (PCI), 217 (CABG)								
Heterogeneity: Tau ² = 0.00; Chi ² = 2.32, df = 2 (P = 0.31); I ² = 14%								
Test for overall effect: Z = 3.19 (P = 0.001)								
2.1.2 long-term								
Kappellein 2013	105	231	59	221	13.4%	1.70	[1.31, 2.21]	2013
Ahn 2015	23	102	15	90	5.0%	1.35	[0.75, 2.43]	2015
Li Y 2017	30	406	17	406	5.1%	1.76	[0.99, 3.15]	2017
Ramanathan 2017	808	2710	311	1865	20.0%	1.79	[1.59, 2.01]	2017
Nagendran 2018	484	869	246	869	19.8%	1.97	[1.74, 2.22]	2018
Subtotal (95% CI)		4318		3451	63.2%		1.84 [1.70, 1.99]	
Total events: 1450 (PCI), 648 (CABG)								
Heterogeneity: Tau ² = 0.00; Chi ² = 2.84, df = 4 (P = 0.58); I ² = 0%								
Test for overall effect: Z = 15.26 (P < 0.00001)								
Total (95% CI)		6792		4999	100.0%		1.59 [1.38, 1.85]	
Total events: 1964 (PCI), 865 (CABG)								
Heterogeneity: Tau ² = 0.03; Chi ² = 21.88, df = 7 (P = 0.003); I ² = 68%								
Test for overall effect: Z = 6.17 (P < 0.00001)								
Test for subgroup differences: Chi ² = 13.81, df = 1 (P = 0.0002), I ² = 93%								

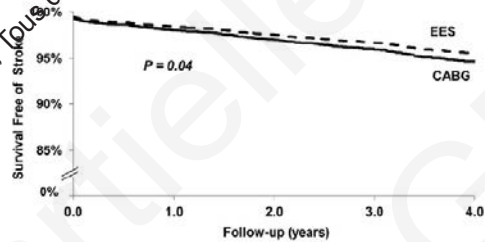


EES vs CABG in pts with MVD (NYS)



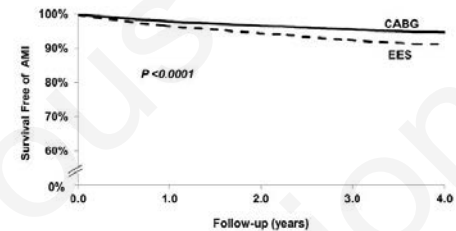
No. at Risk	0.0	1.0	2.0	3.0	4.0
CABG	4048	3872	2920	1922	937
EES	4048	3872	2592	1393	370

Figure 2. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) death.



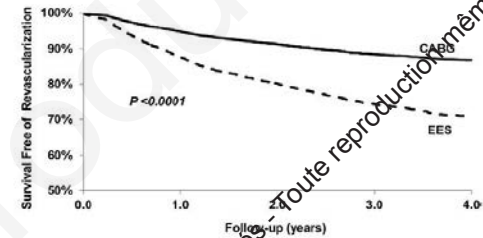
No. at Risk	0.0	1.0	2.0	3.0	4.0
CABG	4048	3803	2356	1867	902
EES	4048	3831	2546	1358	356

Figure 4. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) stroke.



No. at Risk	0.0	1.0	2.0	3.0	4.0
CABG	4043	3804	2833	1854	902
EES	4043	3742	2467	1319	351

Figure 3. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) myocardial infarction.

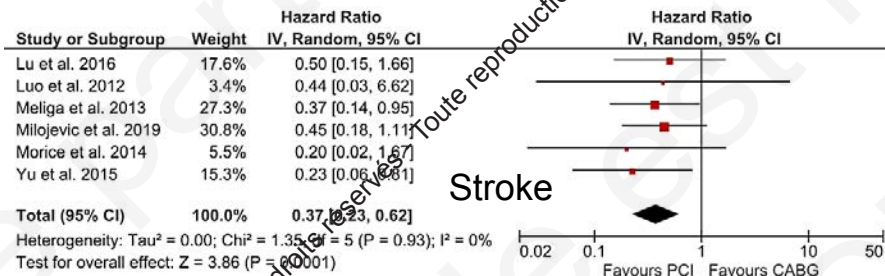


No. at Risk	0.0	1.0	2.0	3.0	4.0
CABG	4043	3673	2666	1690	806
EES	4043	3890	2048	1036	263

Figure 5. Everolimus eluting stent (EES) vs coronary artery bypass graft surgery (CABG): long-term (includes first 30 days) repeat revascularization.

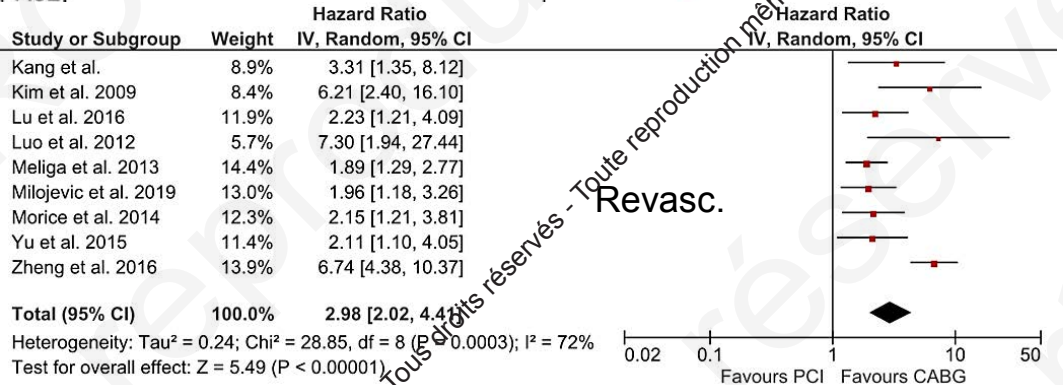
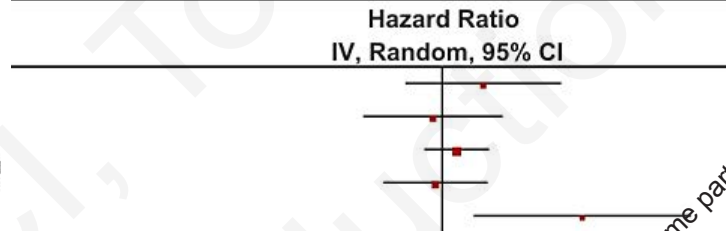


Death/MI/Stroke in LM+Diabetes



Study or Subgroup	Weight	Hazard Ratio IV, Random, 95% CI
Lu et al. 2016	4.17%	0.23 [1.01, 1.92]
Meliga et al. 2013	14.8%	1.22 [0.96]
Milojevic et al. 2019	11.6%	1.03 [0.71]
Morice et al. 2014	8.1%	0.74 [0.43]
Yu et al. 2015	8.2%	0.79 [0.46]
Zheng et al. 2016	14.4%	0.66 [0.51]
Total (95% CI)	100.0%	1.01 [0.82, 1.22]

Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 23.01$, $df = 9$ ($P < 0.0001$); $I^2 = 72\%$
 Test for overall effect: $Z = 0.06$ ($P = 0.96$)



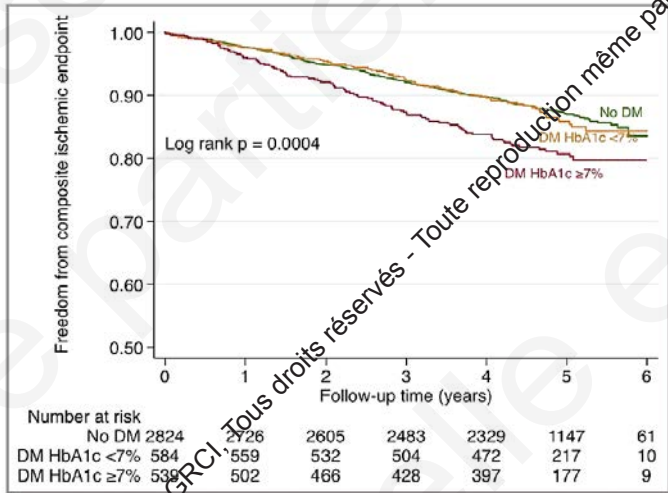
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Comment décider ?

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Qualité du contrôle glycémique?

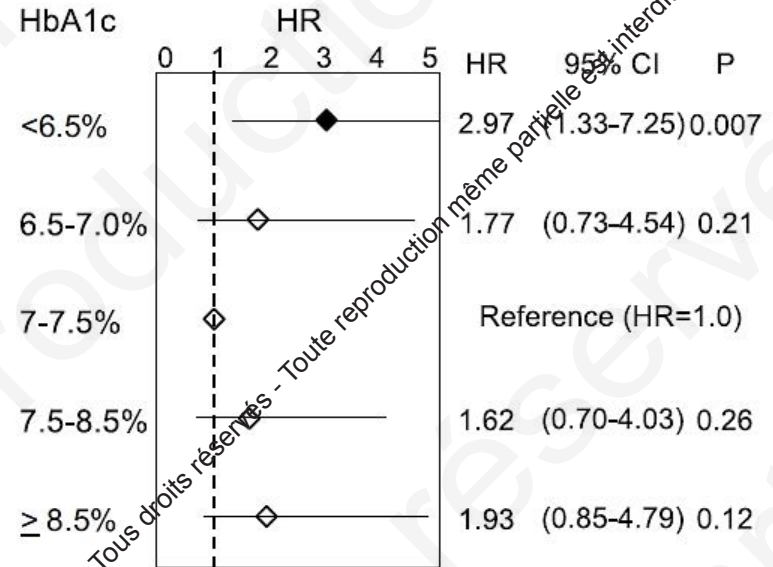


Lemesle et al JAHA 2018

Figure 1. Cardiovascular death, myocardial infarction, or ischemic stroke during 5-year follow-up, according to diabetic status and diabetes mellitus (DM) control. Unadjusted Kaplan-Meier curves are shown. HbA1c indicates glycosylated hemoglobin.

Increased risk of cardiovascular mortality by strict glycemic control (pre-procedural HbA1c < 6.5%) in Japanese medically-treated diabetic patients following percutaneous coronary intervention: a 10-year follow-up study

Takehiro Funamizu¹, Hiroshi Iwata¹, Yuya Nishida², Katsutoshi Miyosawa^{1,3}, Shinichiro Doi¹, Yuichi Chikata¹, Jun Shitara⁴, Hirohisa Endo¹, Hideki Wada⁴, Ryo Naito⁵, Manabu Ogita⁴, Tomotaka Dohi¹, Takatoshi Kasai¹, Shinya Okazaki¹, Kikuo Isoda¹, Katsumi Miyachi¹ and Hiroyuki Daida¹



Inégalité vis-à-vis de la progression (lésion versus vaisseau)

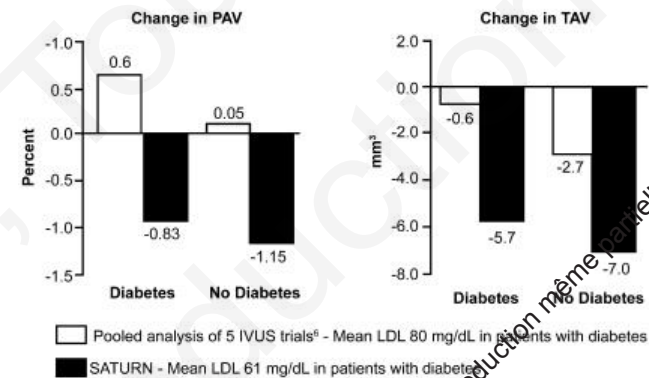
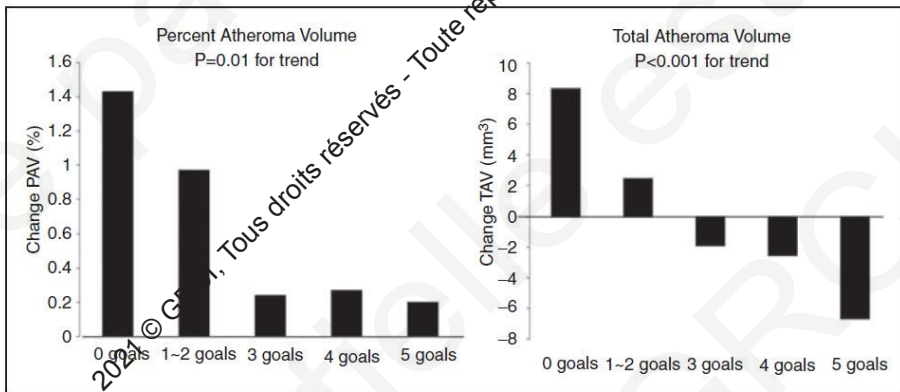


Figure 2—Comparison between current SATURN analysis and a previous pooled analysis of five serial IVUS trials. Comparison of change in PAV and TAV seen in the current analysis of SATURN (black bars) in which the mean LDL-C in patients with diabetes was 61 mg/dL and a previous pooled analysis of five IVUS trials (6) (white bars) in which mean LDL-C in patients with diabetes was 80 mg/dL. Of note, statistical methods for the current analysis and previous analysis represented on this figure were different; thus, no direct statistical comparisons between these analyses can be made.



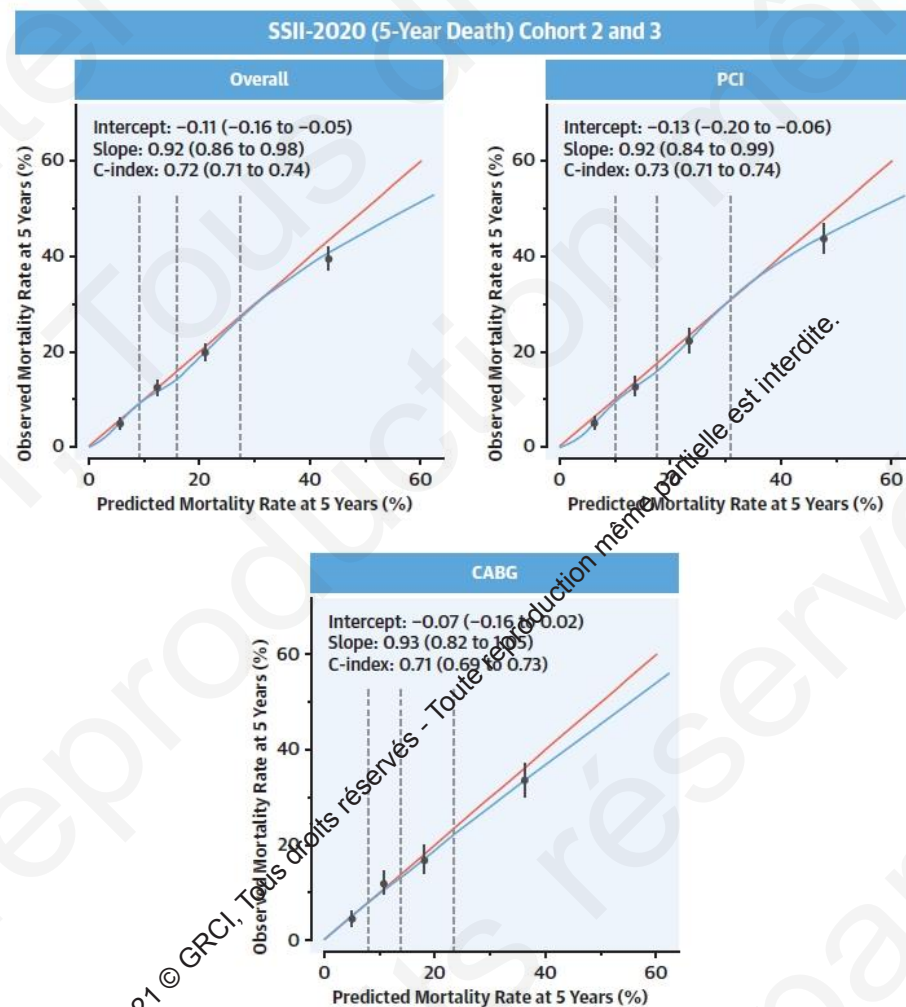
Syntax II-2020 Takahashi et al Lancet 2020

	Coefficient	HR (95% CI)	p value
Prognostic index			
Age, per 10 years	0.72	2.05 (1.51-2.33)	<0.0001
Creatinine clearance, per 10 mL/min per 1.73 m ² *	-0.07	0.97 (0.88-0.99)	0.0279
Left ventricular ejection fraction, per 10%†	-0.31	0.73 (0.63-0.84)	<0.0001
Chronic obstructive pulmonary disease	0.48	1.62 (1.24-2.12)	0.0004
Peripheral vascular disease	0.73	2.08 (1.63-2.62)	<0.0001
Medically treated diabetes	0.20	1.22 (0.95-1.57)	0.1251
Receiving insulin	0.46	1.58 (1.14-2.19)	0.0055
Current smoker	0.66	1.93 (1.52-2.45)	<0.0001
Predictive model			
Prognostic index	0.99	2.69 (2.42-3.01)	<0.0001
CABG × three-vessel disease	-0.40	0.67 (0.53-0.86)	0.0014
CABG × left main coronary artery disease	-0.08	0.92 (0.72-1.19)	0.5466
PCI × left main coronary artery disease	-0.10	0.90 (0.70-1.17)	0.4418
PCI × (SYNTAX score - 29)/10	0.16	1.17 (1.06-1.30)	0.0024

Table shows the estimated Cox regression coefficients for the prognostic index with seven variables, and for the predictive model with the predictive index and two predefined treatment interactions (three-vessel disease or left main coronary artery disease and anatomical SYNTAX score) entered into the SYNTAX II 2020 for predicting 10-year all-cause death. The formula used to predict this outcome is as follows: predicted probability of all-cause death at 10 years = $1 - \exp(-0.243 \times \exp[0.99 \times (\text{age} - 0.07 \times \text{creatinine clearance} - 0.31 \times \text{left ejection fraction} + 0.48 \times \text{chronic obstructive pulmonary disease} + 0.73 \times \text{peripheral vascular disease} + 0.20 \times \text{medically treated diabetes} + 0.46 \times \text{on insulin} + 0.66 \times \text{current smoker}) - 0.40 \times \text{CABG} \times \text{three-vessel disease} - 0.08 \times \text{CABG} \times \text{left main coronary artery disease} - 0.10 \times \text{PCI} \times \text{left main coronary artery disease} + 0.16 \times \text{PCI} \times (\text{SYNTAX score} - 29) / 10 - 2.80])$, where age is expressed in years per 10 years, the creatinine clearance is expressed per 10 mL/min per 1.73 m² (capped at 90 per 10 mL/min per 1.73 m²), and the left ventricular ejection fraction is expressed per 10% (capped at 50 per 10%). CABG=coronary artery bypass grafting. PCI=percutaneous coronary intervention. *Capped at 90 per 10 mL/min per 1.73 m². †Capped at 50 per 10%. HR=hazard ratio.

Table 2: Model for predicting risk of all-cause death at 10 years

FIGURE 1 Calibration Plots for 5-Year Mortality



Que retenir?

- Revasculariser comme un non-diabétique mais risque
- Attention à la stratégie « DEFER »
- PCI possible si
 - risque d'IDM précoce et de revascularisation tardive bas
 - Qualité de prévention secondaire élevée
- CABG le plus souvent si MVD (Syntax 20+)
- Utiliser le score SYNTAX 2020 pour gérer la Heart Team

